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Friday Report: Issue 44

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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

Fourth Vaccine Approved in the UK (link)

The MHRA has approved the Janssen (the vaccines arm of Johnson & Johnson) viral vector vaccine for use in over 18s, bringing a fourth option available to the JCVI for future deployment. Of particular note, the vaccine only needs a single dose, a great advantage in some situations.

The BBC reports that the vaccine has an efficacy rate of 85%, but notes that it has not been trialled in an environment where the B.1.617.2 is in circulation. It should also be noted that in Europe, where the vaccine is already in use, there have been reports of adverse reactions similar to those with the Astra Zeneca vaccine (which is now restricted in the UK to older lives – see also page 4 below).

The UK has ordered 20m doses, to be delivered "later this year". The vague timescale for delivery suggests that the vaccine is unlikely to be available to assist in completing the initial roll-out in the UK, but could be used in any booster programme.

Pfizer records 100% efficacy on 12-15 yr olds (link)

A paper published on 27 May confirms earlier reports from trials on older children that COVID-19 vaccines are highly successful in preventing infection. In a trial of 2,000 children, half given the vaccine and half the placebo, the placebo group counted 18 infections from 7 days after dose 2, compared with nil in the vaccine group.

If we include the relatively short period from 11 days after dose 1, the count in the placebo group increased to 26, with still none in the vaccine group. This suggests that pretty high protection is provided by one dose (although the duration of single dose protection cannot be assessed by the trial).

The trial also compared the immune response relative to those in a slightly older group (16-25 years), and found that the younger 12-15 group generated even higher immune responses, consistent with the excellent results seen.

With new variants appearing to be more transmissible, the need to vaccinate a higher proportion of the population overall may be important in dampening circulation. Whilst the MHRA and JCVI have yet to form a view on the appropriateness of vaccinating older school children, the European Medicines Agency has just announced approval of its use in 12 to 15 year olds (link), following equivalent approval in the U.S. earlier in May.

Table 3. Vaccine Efficacy against Covid-19 in Participants 12 to 15 Years of Age.*

Efficacy End Point†	BNT162b2		Placebo		% Vaccine Efficacy (95% CI)‡
	No. of Participants with Event/Total No.§	Surveillance Time (No. at Risk)¶	No. of Participants with Event/Total No.§	Surveillance Time (No. at Risk)¶	
Covid-19 occurrence at least 7 days after dose 2 in participants without evidence of previous infection	0/1005	0.154 (1001)	16/978	0.147 (972)	100 (75.3–100)
Covid-19 occurrence at least 7 days after dose 2 in participants with or without evidence of previous infection	0/1119	0.170 (1109)	18/1110	0.163 (1094)	100 (78.1–100)

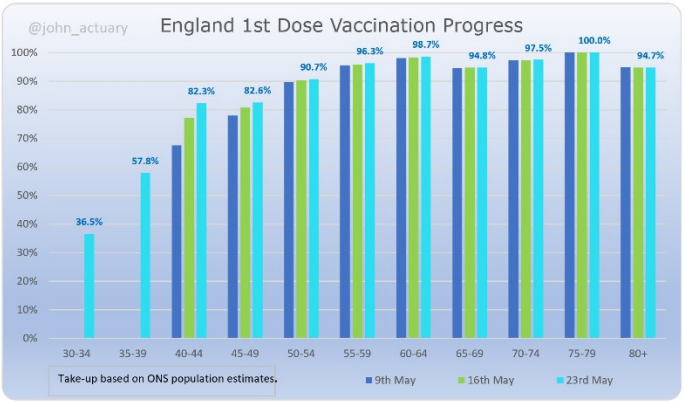
* Results are for the efficacy population that could be evaluated, which included all eligible 12-to-15-year-old participants who received two doses of BNT162b2 or placebo as randomly assigned, with dose 2 received within the prespecified window, and had no major protocol deviations.

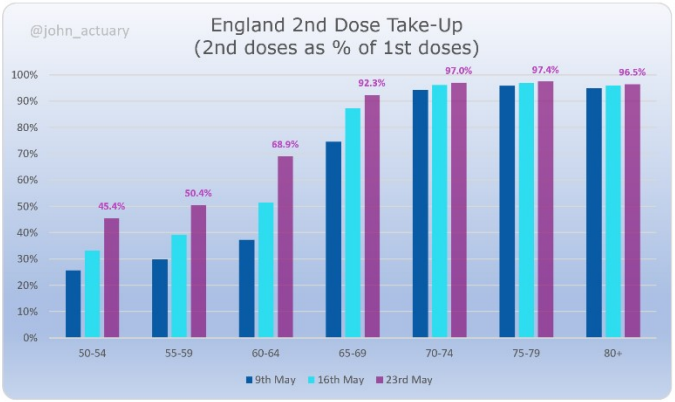
† Participants without evidence of previous infection were those who had no serologic or virologic evidence of past SARS-

Take-up Rates

Latest weekly figures from NHS England (link) show continued progress down through the lower age bands, albeit relatively slowly as focus has remained on second doses. Encouragingly, take-up in the 40-49 age group is above 80%, and may reach around 85%. It's too early yet to form a view on uptake for people in their 30s.

Turning to second dose uptake, we see a very good take-up for the older age groups, and with the recent acceleration of second doses, good progress in the remainder of Priority Groups 1 to 9, which accounted for around 99% of deaths in the unvaccinated population. The news that the Indian variant displays a significant degree of vaccine escape for those with just one dose, will hopefully encourage people to complete their course.





Clinical and medical news

New guidance from NHS England on seeing patients (link)

NHS England released new guidance on 20 May to GP practices on seeing patients. All GP practices must "ensure they are offering a blended approach of both face to face and remote appointments, so both are always available to patients according to what is clinically appropriate". Patients' input should be sought, and practices reflect preferences unless there are contrary clinical reasons.

Three leading patient organisations have welcomed the new guidance in a statement (link), and highlighted the significant number of patients that have struggled to get the care that they need, and difficulties in arranging face-to-face meetings when there was a specific need. At the same time, the numbers attending A&E departments have surged in recent weeks, with 1.9 million visits in April 2021 compared with 1.3 million visits in each of January and February 2021 (link). The explanation proposed is that the increase is due to people coming forward who had put off seeking care during the height of the 2nd wave, the "worried well", and those concerned that they may have COVID-19. In the absence of more detailed numbers, it is strange that no mention is made of those struggling to access care.

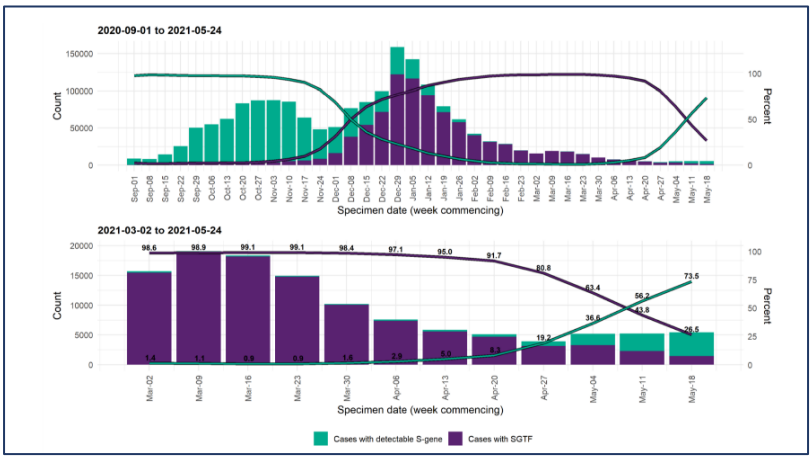
The guidance and the statement reflect on the sustainability of clinical workloads, with a survey by the Health Foundation of GP trainees highlighting that only 33% planned to be working full-time (10 4-hr sessions a week) one year after qualification. This contrasts with prior UK government commitments to increase the numbers of GPs by 6,000 by 2024.

Prevalence of B.1.617.2 (the "Indian" variant).

This continues to be the primary focus of concern in the UK, and PHE are now producing a large volume of data weekly on the situation, including this 69 page report (link).

We can see in the graph below the rise and fall of B.1.1.7 ("Kent") over the course of just a few months, now usurped by B.1.617.2 which accounts for around 75% of the virus circulating. Elsewhere in the report, the estimate of the increased transmissibility of the Indian variant over the Kent variant has increased from 50% to 67%, although it is not clear whether there are any underlying differences in the populations in which it has initially been seeded which distorts the comparison, and how much is due to vaccine escape.

On that note, the variant appears partly successful in escaping the vaccine, more particularly after one dose, where efficacy against infection reduces from 50% to 33%. After a second dose, efficacy is lowered from 88% to 80%. Note that the latter does mean that the chance of infection increases from 12% to 20%, a material increase of 67%.



It is expected that protection against serious illness, and thus hospitalisation or death, is still likely to be very high after a second dose, and this appears to be borne out by initial data around those recently admitted in Bolton with the Indian variant.

Explanation of rare blood clots with adenovirus vaccines (link)

Professor Marschalek at Goethe University has suggested a possible mechanism for the higher prevalence of rare cerebral venous sinus thrombosis in the presence of low levels of platelets that has been seen with AstraZeneca and Johnson & Johnson vaccines. Both vaccines deliver copies of the gene sequence for the spike protein into the cell nucleus, as opposed to the mRNA vaccines which target the cell cytoplasm where protein production normally takes place. Whilst in the cell nucleus, some of the produced spike proteins are altered through splicing and so are not able to bind to the cell membrane.

Presenting foreign proteins on the outside of the cell membrane is the process by which cells alert the immune system that they are infected and generate a rapid immune response. The research suggests that these modified spike proteins are ejected from the cell, and provide the kernel for the creation of the very rare blood clots (c. 1 in 100,000 individuals) as they bind to ACE2-receptors in endothelial cells lining blood vessels.

So far, according to the Yellow Card Adverse Reporting system maintained by the MHRA (link) there have been reports of 332 cases (and 58 ensuing deaths) of this rare blood clotting with the AstraZeneca vaccine out of 24.2m vaccinated in the UK. The research group is now investigating whether the implanted genetic sequences can be modified to reduce the likelihood of splicing. The research group notes that the risk of splicing was already recognised and investigated by Johnson & Johnson. This could provide a partial explanation for the lower prevalence rate of clots seen with the Johnson & Johnson vaccine which has reported 8 cases out of 7.4m vaccinated individuals.

After-effects of SARS-COV-2 infection where hospitalisation not required

As we have highlighted in previous Bulletins, various different studies have examined the long-term health effects of SARS-CoV-2 infection for those that have been admitted to hospital. However, there has been relatively little formal follow-up of those that were infected but not initially admitted.

A pre-print study (link) describes a Danish population cohort (10k) that was followed from February to May last year. The study found that the risk of severe post-acute complications was low, but that the number of general practitioner visits increased by 18% (95% CI 1.15-1.22) and outpatient appointments by 10% (95% CI 1.05-1.16).

Data

ONS Antibody data (link)

The latest antibody survey shows that levels in England have risen from 69% to 76% in the two weeks since the last update. Wales and Northern Ireland are similar, although Scotland is lagging behind slightly at 69%.

Looking at the age analysis, levels in those older cohorts which have now been fully vaccinated (and which also have exceptionally high take-up rates), are now in excess of 96%, with all age groups over 50 above 90%.

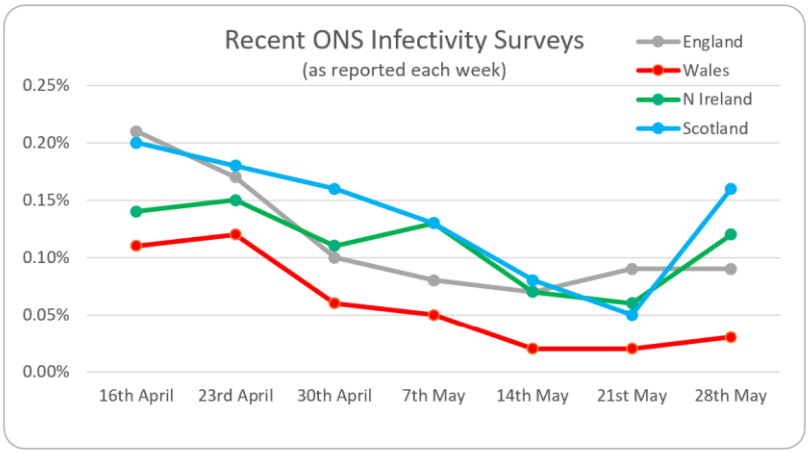
Note that this data is in respect of the week beginning 3rd May, and given the two to week period after vaccination before antibodies are generated, it reflects vaccination levels in mid-April.

ONS Infection Surveys (link)

In the two weeks since our last update, we've seen the steady fall in infections come to a halt, with all four countries showing increases of various levels. The most recent week shows what at first sight are alarming increases in Scotland and Northern Ireland, although these come with very wide confidence intervals (eg N Ireland is 0.04% to 0.27%), so we do need to treat the jumps with a degree of caution.

Nevertheless, it is clear that the steady fall that we enjoyed between January and April has now ended.

It is worth noting that the regular ONS survey is a random sample of the community population (with over 142,000 participants in the latest two week period). So, unlike the daily PHE figures on cases that we are familiar with, these will be unaffected by the high levels of surge testing in areas where there is concern over variants.



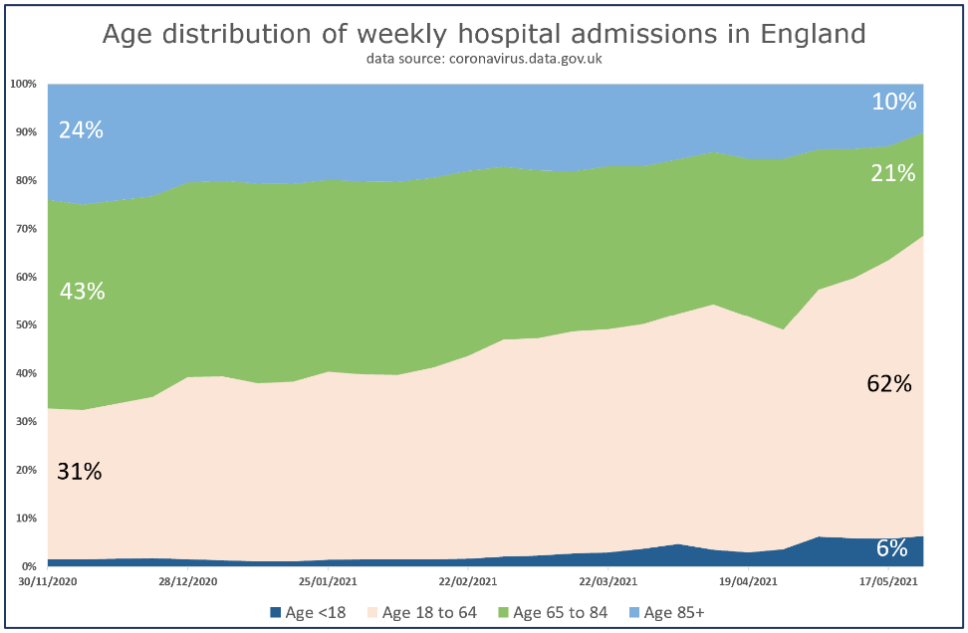
	Report Issued						
	16th April	23rd April	30th April	7th May	14th May	21st May	28th May
England	0.21%	0.17%	0.10%	0.08%	0.07%	0.09%	0.09%
Wales	0.11%	0.12%	0.06%	0.05%	0.02%	0.02%	0.03%
N Ireland	0.14%	0.15%	0.11%	0.13%	0.07%	0.06%	0.12%
Scotland	0.20%	0.18%	0.16%	0.13%	0.08%	0.05%	0.16%

Hospital Admissions Trend

As the vaccination programme has progressed there has been a very marked reduction in the proportion of older lives admitted. At the start of December those aged 65 represented two-thirds of those admitted, and that is now down to one-third.

Inevitably this means a much higher proportion is now those under 65, but it should be noted that in absolute numbers these have also fallen dramatically, with daily admissions down from 3,000+ a day to around 100.

This analysis of proportions is a simple and clear indicator of how the vaccine effect is working its way down the age groups in line with the JCVI recommendations, and how it has accelerated the decline in admissions over the last three months.



"R" Estimate (link)

For the first time since mid-January, the range of SAGE's estimate of R for England doesn't extend below 1, with this week's range being a relatively tight (1.0 to 1.1). The regional estimates are shown below; of note, London and the North West share the highest estimate of (1.0 to 1.2)

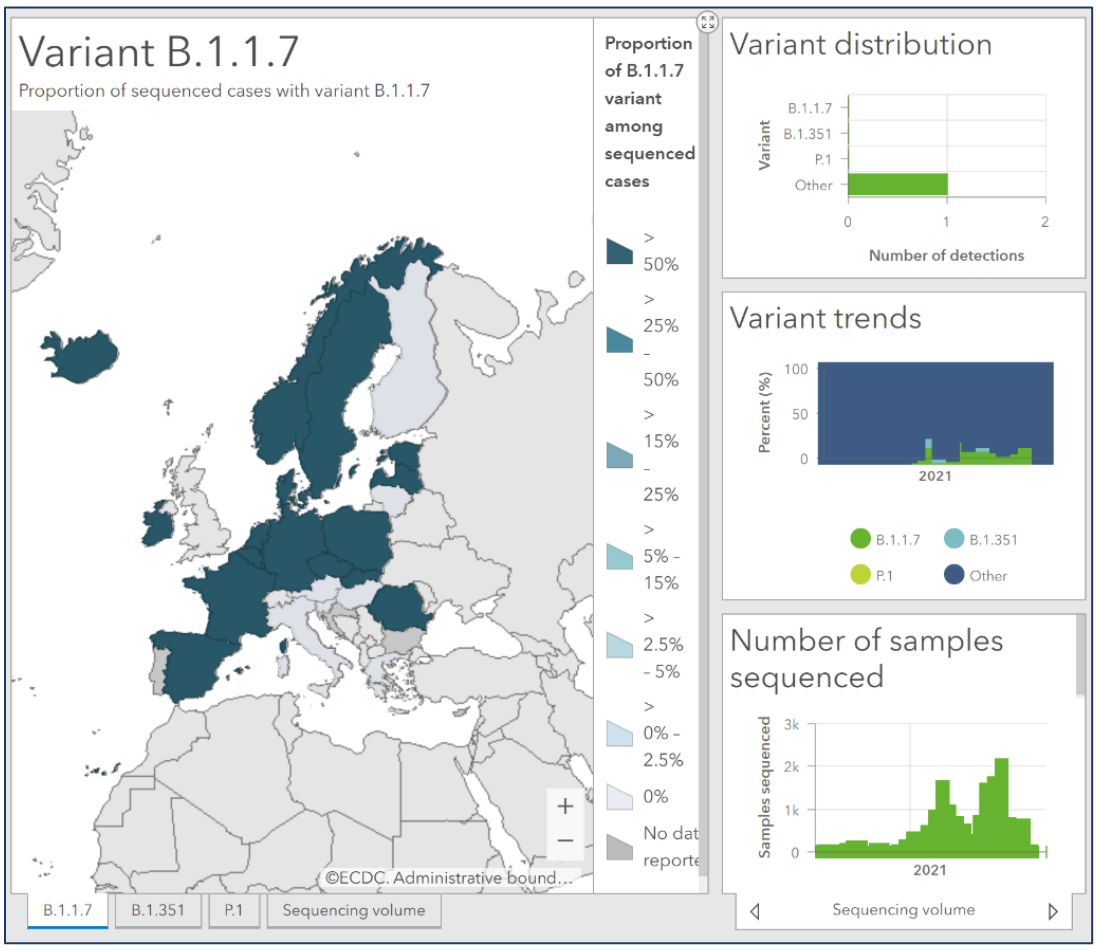
Latest by NHS England regions

These are the latest R and growth rate estimates by NHS England regions.

Region	R	Growth rate % per day
England	1.0 to 1.1	0 to 3
East of England	0.9 to 1.1	-1 to 3
London	1.0 to 1.2	0 to 3
Midlands	0.9 to 1.0	-2 to 1
North East and Yorkshire	0.8 to 1.0	-3 to 0
North West	1.0 to 1.2	0 to 4
South East	0.8 to 1.0	-3 to 0
South West	0.9 to 1.1	-1 to 3

ECDC – SARS-CoV-2 variants dashboard (link)

ECDC have released a new dashboard (first released 19 May) providing an overview of the key SARS-CoV-2 variants of interest and concern in EU and EEA member states.



The dashboard is intended to complement the weekly ECDC country overview report (link) – using the dashboard, the number and proportion of sequenced cases with particular variants (currently B.1.1.7, B.1.351 and P.1) can be tracked across countries and over time.

The data in the dashboard has been sourced from The European Surveillance System (TESSy link) and the Global Influena Surveillance and Response System (GISRS EpiCoV database link). Data can be downloaded for further analysis, and is updated every Thursday afternoon.

And Finally …

Upskilling with HDR and Cambridge Spark (link)

For those of you who have been inspired by the breadth of different datasets that have been assembled to tackle the greatest public health challenge of our generation, and want to upskill, HDR UK and Cambidge Spark have just launched an AI Apprenticeship Academy for Health that will enable an initial cohort of employers to support staff in gaining a masters-equivalent qualification in AI. Enrolment is open now for the course starting in September 2021.

28 May 2021