



Friday Report: Issue 58

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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.

Group News

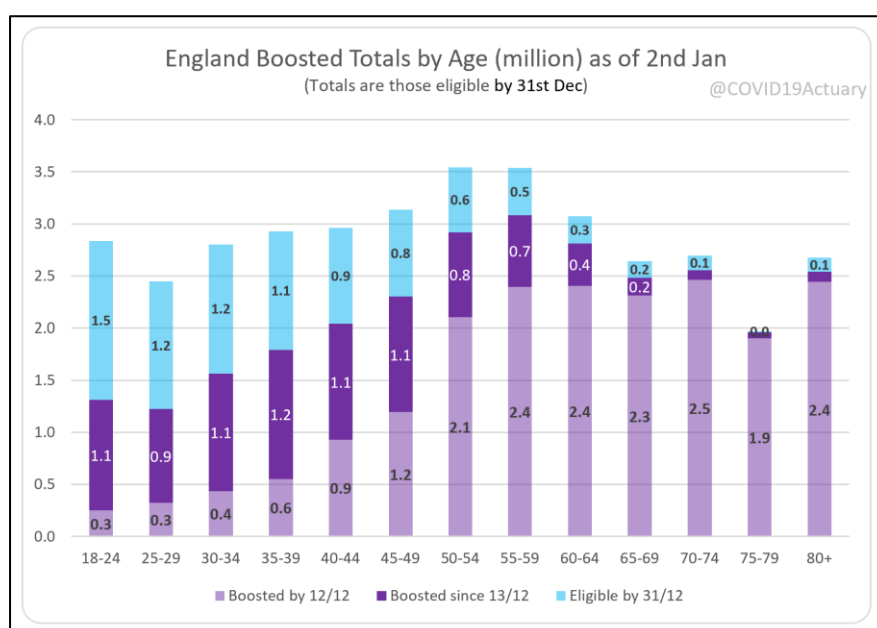
We're delighted to report that our co-chair, Stuart McDonald, was awarded an MBE for services to Public Health in the New Year Honours List. As well as the work that Stuart has done for the group, including an active presence on social and mainstream media, he has provided support to Government, notably modelling the potential mortality impact if hospitals become overwhelmed, and the morbidity impact of Long COVID. We congratulate Stuart on a well-deserved honour.

On a sadder note, Nicola Oliver, also a co-chair, has decided it is time to step back from her involvement. Nicola's contribution has been enormous, and the knowledge and skills she brought to the team have been of great value. Regular readers will also know that Nicola has been a regular part of the Friday Report compilation team, always providing excellent and timely copy for us. We all thank Nicola for her contribution and wish her well for the future.

Vaccines

Boosters Speed-up

With Government announcing just before the New Year that the target of offering everyone in England eligible a booster had been met, the position by 2nd January shows that whilst we have indeed boosted the vast majority of older people, the results are less positive at younger ages.



For over 50s, an impressive 91% of those eligible (and 89% of all those with second doses) have been boosted, but below 30 it is under 50%. Whilst some of those yet to come forward will be by choice, it is likely that many will have been unable to, having been infected with Omicron during December, which means that the vaccination needs to be postponed until 28 days after the positive test.

Nevertheless, the acceleration announced in mid-December undoubtedly increased the rate at which the population was able to be boosted, with the darker purple bars in the chart above totalling 8.9m, representing those boosted following the Prime Minister's announcement. It's therefore appropriate to acknowledge the considerable achievement by all those involved in the booster programme, whether paid or volunteer, in immediately rising to the challenge set by the PM and delivering the increase in capacity that we saw in the second half of the month.

Israel and Chile roll out fourth COVID-19 vaccinations

On 3 January Israel started administering fourth vaccine doses to people over 60, health workers and immunocompromised patients ([link](#)), following the release of preliminary results from a study conducted by the Sheba Medical Center. The study commenced on 27 December and included 150 healthcare workers whose antibody levels had dropped significantly since receiving their third vaccine doses four to five months earlier. The study demonstrated the safety of the Pfizer-BioNTech fourth dose with only mild side effects reported. It also showed a five-fold increase in antibody levels among participants a week after the jab was administered.

Chile has announced that from 10 January, immunocompromised citizens will start to receive fourth doses and starting on 7 February citizens aged 55 and older who received their third dose 6 or more months previously will become eligible for a fourth dose. ([link](#))

JCVI advise no need yet for a fourth dose in the UK. ([link](#))

As we go to press, UKHSA has published an update confirming that as of now the Joint Committee on Vaccines and Immunisation (JCVI) is not recommending a fourth dose programme, but will continue to review the situation. The update notes that, for Over 65s, protection against mild symptomatic infection from Omicron with a booster wanes to around 30% after 10 weeks, but that protection against serious illness remains high.

Clinical and medical news

Paxlovid Approved for Use in the UK ([link](#))

On New Year's Eve, the UK's medicines regulator, the MHRA, approved the use of Paxlovid for certain higher risk groups who have tested positive. Paxlovid is an antiviral medicine with a combination of active ingredients, PF-07321332 and ritonavir, taken as two separate tablets for a 5-day course. During trials an 89% drop in hospitalisations and deaths was recorded if taken early during the illness, preferably by the third day of symptoms, although effectiveness studies against Omicron are still ongoing.

The treatment will be available to anyone over 60, together with others who have at least one high risk condition, such as obesity, diabetes mellitus, or heart disease.

The government has purchased over 2.75m courses of the treatment, although the press release did not give details of timescales for delivery and roll-out of the treatment.

T Cell Responses Hold Up against Omicron [\(link\)](#)

With mutations in the spike protein for Omicron known to result in reduced effectiveness of antibodies (whether generated by vaccination or natural infection by previous variants), the question of protection from Omicron by T cells is inevitably of great interest.

A pre-print paper from South Africa has investigated this, concluding that T cells are relatively less impacted by the new variant than antibodies are, quoting that 70% to 80% of the response is maintained across various study groups. Well-preserved T cell immunity to Omicron is likely to be contributing to protection from severe COVID-19, which supports early clinical observations from South Africa (and more recently in the UK).

Uncovering the reasons for Omicron's success – new entry routes rather than just evading immune system [\(link\)](#)

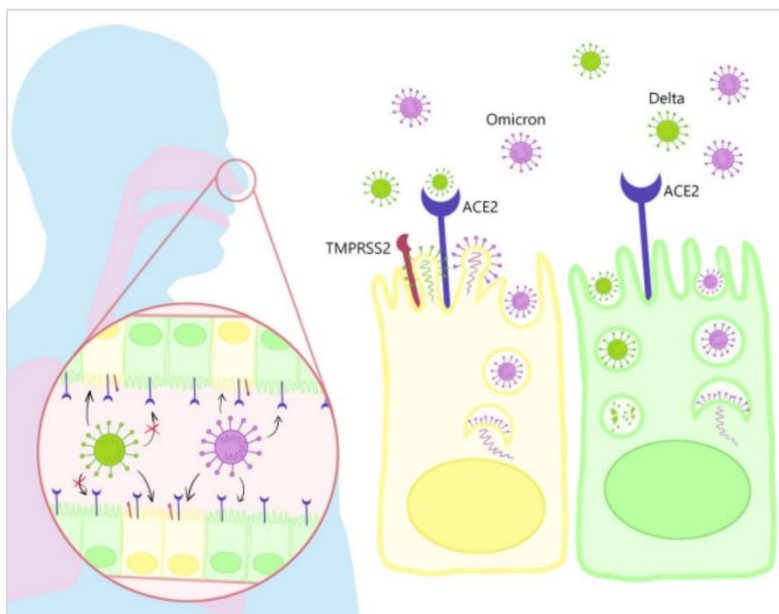
Omicron's ability to transmit more rapidly and to re-infect those with prior infections is self-evident, and has enabled it to become the dominant variant in little more than a month.

However, the important questions are

- what are the biological changes that lead to higher transmission, and
- do they also explain apparently lower rates of disease severity?

A previous study at Hong Kong University [\(link\)](#) had identified that Omicron was able to replicate much faster in cells lining the bronchus than Delta, but was slower in those cells lining the alveoli in the lung itself. A further study of viral transmission by Imperial College and the Pirbright Institute [\(link\)](#) has indicated that differences in the variants' transmissibility may be due to the way in which each variant is taken up into cells, rather than just an enhanced ability to escape the immune system.

While all versions of SARS-CoV-2 bind to the ACE2 receptor, previous variants required the simultaneous presence of the cell surface protein TMPRSS2. However, only a small proportion of those cells in the nasal airways expressing the ACE2 receptor also have the TMPRSS2 protein. The genetic modifications of Omicron appear to enable the virus to enter cells without the TMPRSS2 protein using an endosomal route where bubbles are internalised into the cell.



Omicron is therefore able to infect a much larger number of cells in the upper respiratory airways, but focuses replicatory activity there rather than in the deeper lung tissues. Further, viral entry mediated through the TMPRSS2 protein seems to have been associated with a greater likelihood of syncytia or infected cells fusing together. These syncytia underlie the pattern of diffuse damage and resulting immune reaction that we see with more severe COVID-19 infections, and so the change in the mechanism of viral entry may also underlie the lower likelihood of severe disease.

However, one further important finding was that Omicron appears to be able to bind more effectively to ACE2 receptors of other animals, such as mice and domestic birds, leading to the likelihood of SARS-CoV-2 spreading more widely into animal reservoirs and therefore proving impossible to eradicate through human vaccination. SARS-CoV-2 is here to stay.

Modelling

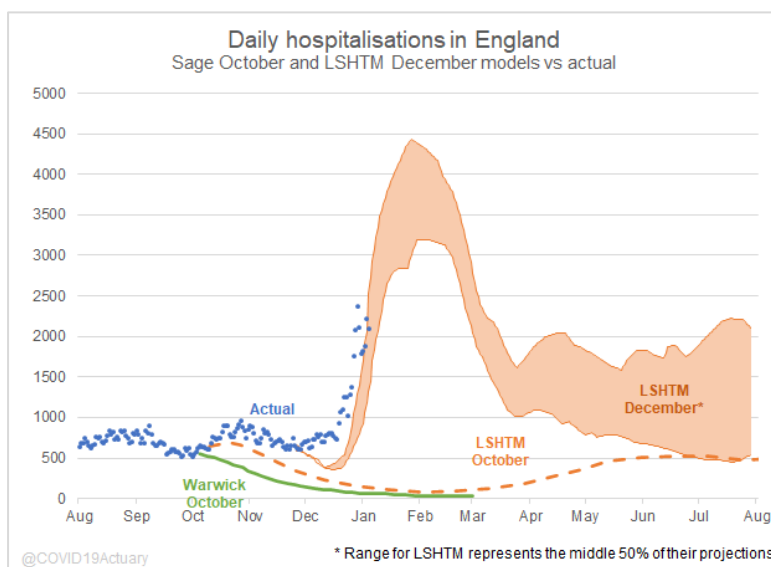
We first monitored actual hospitalisations in England against projections in Friday Report 48. This updated our bulletin ([link](#)) summarising papers from London School of Hygiene and Tropical Medicine (LSHTM), Warwick University and Imperial College London which modelled the move to Step 4.

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. 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, many projections are produced, depending on the 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 paper, 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 the numbers are currently broadly in line with projections. These figures represent the position for England in total, and we have seen considerable regional variations, particularly in regard to the timing of the surge.

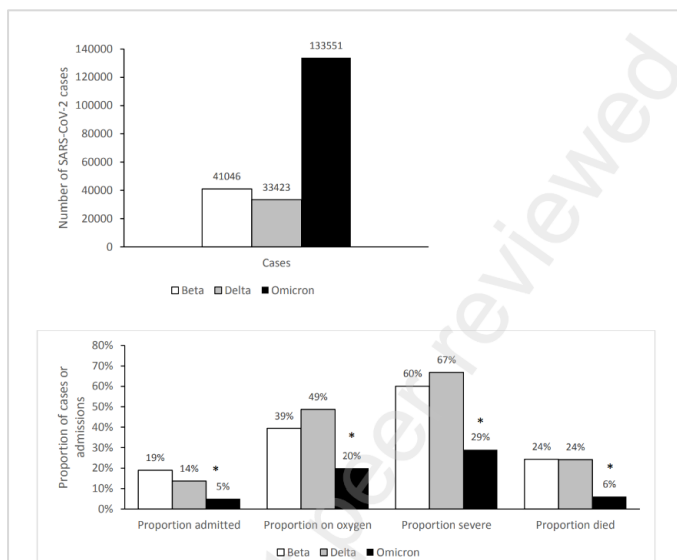
More positively, recent days' actual hospitalisation figures have fallen slightly from their peak so it's possible that the Omicron peak will be lower than the modelled scenarios – however it is worth noting that this is before any changes in mixing around Christmas have been factored in so it's possible that this is a temporary stall rather than a peak. We will continue to monitor how actual experience lines up with this projection.

Data

Comparison of Severity of Omicron in Gauteng [\(link\)](#)

A pre-print published in The Lancet investigates the severity of Omicron infection in Gauteng province in South Africa when compared with previous variants. The province was chosen because it was the first to experience the current wave. The comparison is restricted to the first four weeks of each wave, to ensure consistency.

As can be seen from the graphs below, it is clear that, for whatever reason (the paper does not seek to investigate), Omicron is relatively milder, although in terms of absolute numbers, the sheer volume of cases in comparison to earlier waves offsets this reduction in respect of hospitalisations.



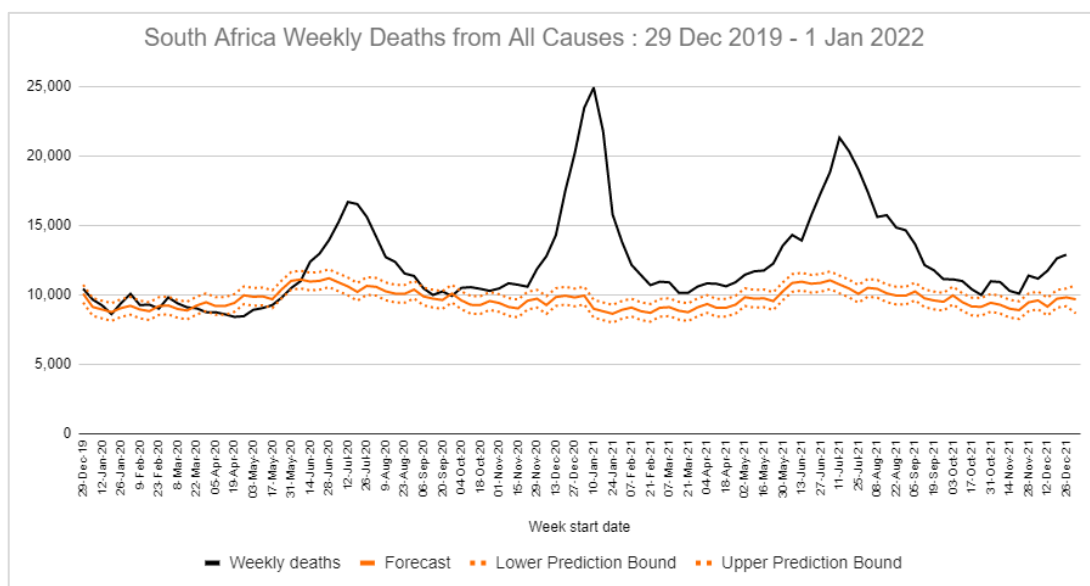
A further point of interest can be seen in the age split below, with younger, less vaccinated groups showing less of a reduction in comparison to previous variants than the older, more vaccinated, group. This effect is most noticeable in the Under 20 age group, where only 6% are jabbed, both in percentage terms and in absolute numbers.

Table 1: Summary of SARS-CoV-2 cases, COVID-19 admissions and in-hospital deaths in the Beta- (29 Nov-26 Dec 2020), Delta- (2 May-29 May 2021) and Omicron-dominated waves (14 Nov-11 Dec 2021), Gauteng Province, South Africa

Variant wave	Number of SARS-CoV-2 positive cases	Incidence of SARS-CoV-2 positive cases per 100,000 persons	Percent (Number) of cases admitted to hospital	Percent (Number) of admitted cases with an outcome who died in hospital (n)
All ages (population 15,488,137; fully vaccinated 30.9%*)				
Beta	41046	265.0	18.9 (7774)	24.3 (1892)
Delta	33423	215.8	13.7 (4574)	24.2 (1107)
Omicron	133551	862.3	4.9 (6510)	5.8 (258)
Age <20 years (population 4,710,102; fully vaccinated 5.8%*)				
Beta	4304	91.4	7.1 (306)	2.0 (6)
Delta	4217	89.5	3.8 (161)	1.9 (3)
Omicron	18817	399.5	6.1 (1151)	1.3 (11)
Age 20-39 years (population 6,140,703; fully vaccinated 31.7%*)				
Beta	18108	294.9	9.4 (1697)	8.4 (142)
Delta	10801	175.9	6.6 (714)	9.2 (66)
Omicron	67282	1095.7	3.9 (2624)	2.3 (43)
Age 40-59 years (population 3,327,121; fully vaccinated 54.3%*)				
Beta	14001	420.8	22.8 (3188)	20.4 (651)
Delta	13110	394.0	12.9 (1685)	16.6 (279)
Omicron	38266	1150.1	3.8 (1441)	7.9 (78)
Age >60 years (population 1,310,211; fully vaccinated 58.4%*)				
Beta	4633	353.6	55.8 (2583)	42.3 (1093)
Delta	5295	404.1	38.0 (2014)	37.7 (759)
Omicron	9186	701.1	14.1 (1294)	16.8 (126)

Excess deaths in South Africa

Staying in South Africa, the South African Medical Research Council (SAMRC) has released its estimates of excess deaths up until week 52 of 2021.



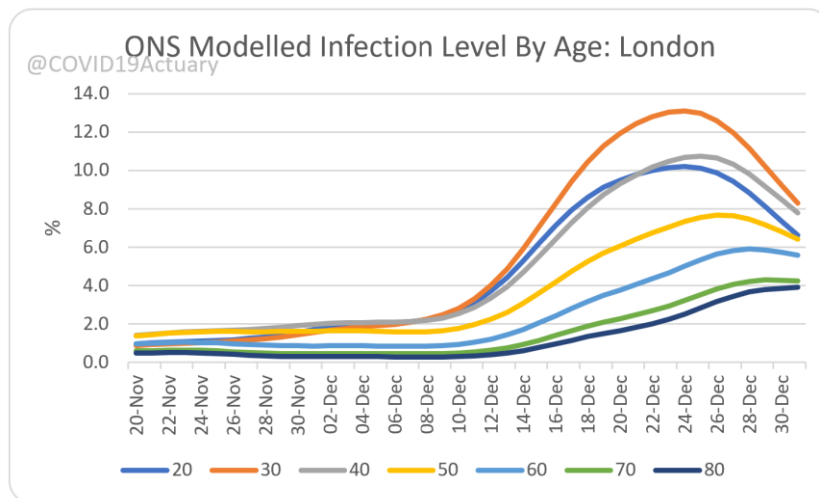
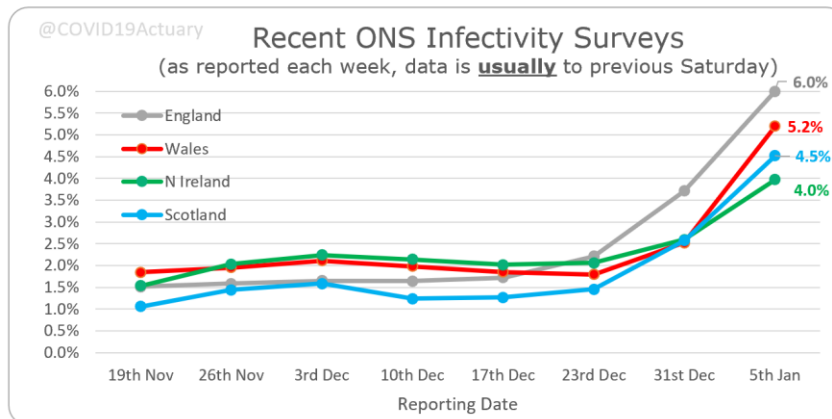
The SAMRC estimates that there have been 286,297 excess natural deaths in the period 3 May 2020 to 1 January 2021. Total natural deaths are estimated to be 137% of predicted natural deaths over the period. There were 10,229 excess deaths in the last four weeks of 2021 and natural deaths recorded were 131% of the deaths that would have been predicted.

While the Omicron wave has been associated with only a fraction of the excess deaths observed over the course of the pandemic, the recent excess is still high. The last time weekly deaths in England and Wales were more than 30% higher than the 2015-2019 average death count was in week ending 5 February 2021. This was during the Alpha wave when the population was still largely unvaccinated.

ONS Infection Study ([link](#))

An early release this week saw infection levels jump dramatically to record levels, with 6% prevalence estimated in England for the final week of 2021, and other nations not much lower. Notably, an age split time series is uniquely provided for London which shows that although levels there peaked around Christmas Day, older ages appear to have peaked up to a week later.

The subsequent normal release today ([link](#)) shows that in the last couple of days of the year, the North West appears to have overtaken London, with the underlying accompanying dataset suggesting prevalence in excess of 10% on 31 December.



ONS Self Reported Long COVID Study ([link](#))

The latest ONS report on Long COVID estimates that around 1.25m of the UK population were experiencing Long COVID symptoms with duration of at least 4 weeks. Of these, around 0.25m were first diagnosed with (or suspected to have had) COVID within the last 12 weeks. At the other end of the spectrum, around half a million were first diagnosed over a year ago.

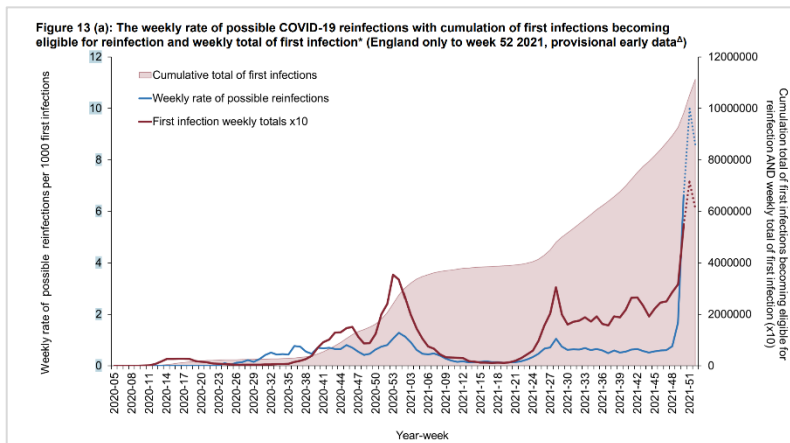
Of the 900k people who had COVID more than 12 weeks ago, 20% said it had a major impact on their ability to undergo day to day activities, and a further 45% said it had a minor impact.

The study has in the past been criticised for relying on self reporting of symptoms. Whilst a more clinical definition would be better, the ability of the ONS to undergo large sampling exercises (350k in this instance) enables a statistically more reliable picture to be obtained than would be possible with a more rigorous clinical approach.

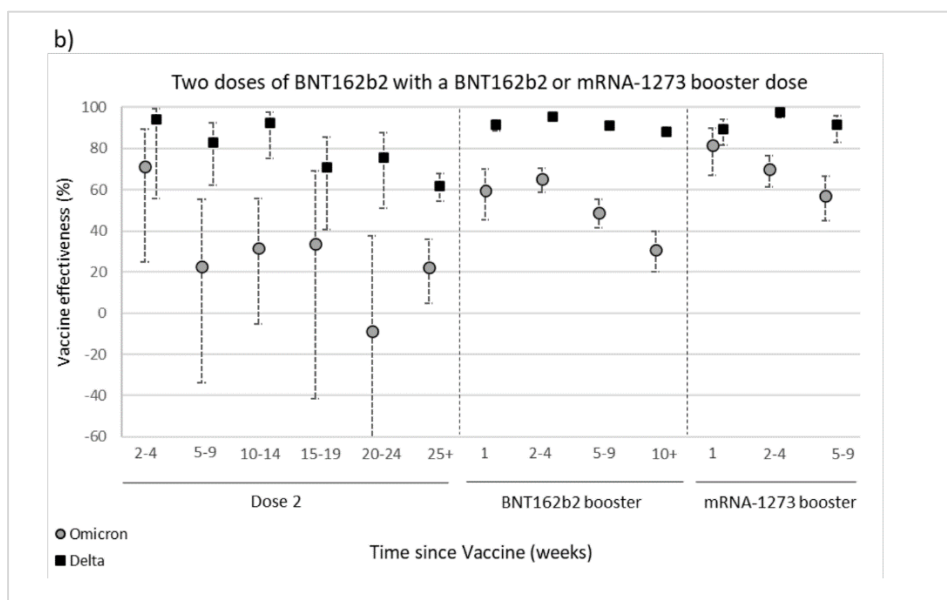
Regular UKHSA Reports

The regular reports issued by UKHSA are well worth reading, and produce a wealth of information that is far too extensive to even summarise here.

In the latest Flu & COVID Surveillance Report ([link](#)) we can see a big increase in the number of reinfections as a proportion of overall cases reported, up to 10% in recent days. This is consistent with evidence that Omicron is much better at reinfecting those infected with a previous variant. As reinfections are not currently included in daily case data, it suggests that there is now a material understatement in these data, which have already been at record levels.



We noted earlier the JCVI recommendation not to start a second booster campaign at the moment. Along with this some further data was published ([link](#)), showing how waning against symptomatic infection is fairly rapid following the booster for Over 65s. Shown below is the profile with Pfizer used for the primary course, a similar picture is seen where AZ has been used.



Also quoted is the degree of waning in protection against hospitalisation, with the central estimate falling from 94% to 89% efficacy after 10 weeks. This means that the likelihood of serious breakthrough infections has nearly doubled (from 6% to 11%), which is a better way of judging the potential impact of waning on health systems.

Table 1. Vaccine effectiveness against hospitalisation for Omicron (all vaccine brands combined). OR = odds ratio, HR = hazard ratio, VE = vaccine effectiveness, (CI=Confidence interval).

Interval after dose	OR against symptomatic disease (95% CI)	HR against hospitalisation (95% CI)	VE against hospitalisation (95% CI)
2 to 9 weeks	0.51 (0.43-0.6)	0.11 (0.06-0.21)	94% (89-97)
10+ weeks	0.72 (0.61-0.85)	0.15 (0.08-0.27)	89% (80-95)

And Finally [\(link\)](#)



Over the last couple of years we've seen lots of words and phrases enter the vocabulary as a result of the pandemic. Who had heard of "social distancing" before 2020? However, Time Out introduces us to some non-pandemic related words that have been added to the lexicon of English Dictionaries.

So do you know what a fluffernutter is? Maybe you thought that astroturf only refers to an artificial football pitch? And do you consider yourself cheugy?

But even in this list, there are a couple of entries that could easily be linked to the pandemic. We'll let you take a look and decide for yourself which they might be...

7 January 2022