Friday Report: Issue 69

By John Roberts, Adele Groyer and Matt Fletcher

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 produces an update on the last Friday of every month with a summary of key papers, articles and data.

Vaccines

Wider Roll-out for Autumn Boosters (link)

The final advice from JCVI in respect of the Autumn booster vaccination programme has widened the scope of the roll-out significantly from the previous (interim) expectation published in May. In particular, the age threshold has been lowered from 65 to 50. Ignoring any double-counting with other groups (see below), that adds around 13m to the total, which is now likely to be around 30m, not dissimilar to the number vaccinated in Priority Groups 1 to 9 in the initial programme.

Below age 50 the now familiar groups also offered the booster will include:-

- Frontline health and care workers
- Residents and staff of older age care homes
- Those over 5 in clinical risk groups*, also pregnant women
- Those over 5 who are household contacts of immunosuppressed people
- Adults who are carers

* the full list is given in the "Green Book" Chapter 14a, Tables 3 and 4.

Retrospective Study of Second Vaccine Durability (link)

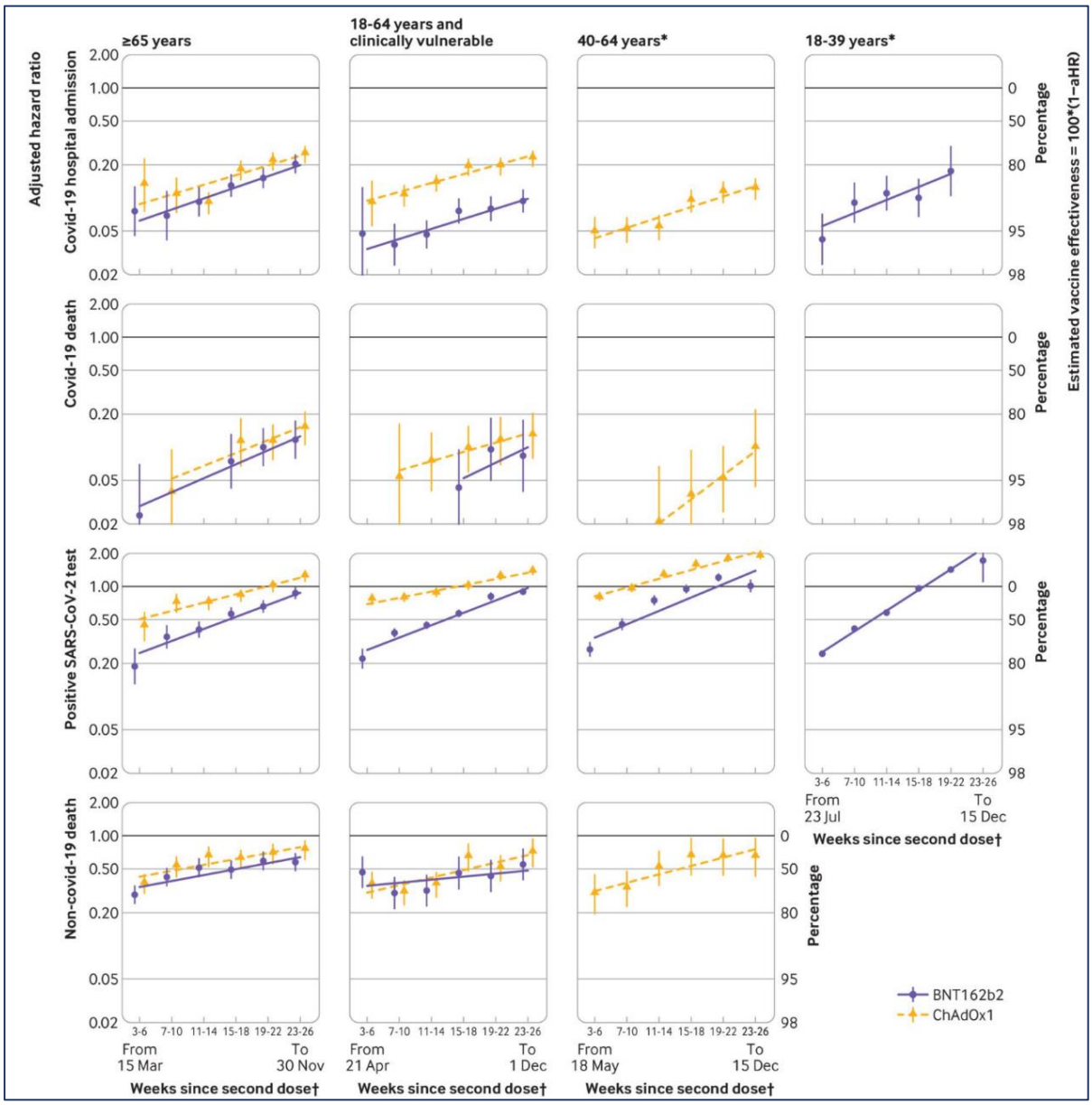
The summer of 2021 may seem like ancient history now in the context of the pandemic, but studies are still being published that are very helpful in understanding the impact the vaccination programme had in the UK, together with assessing the appropriate spacing between boosters.

Over the summer, the Alpha variant was replaced by Delta, and whilst the intial programme was still under way for younger adults, for those at the front of the queue for their two doses, waning was then beginning to become a concern in advance of the booster programme.

A study in the BMJ using OpenSAFELY data of electronically linked patient records confirms that high levels of protection continued until around 6 months after the second dose in respect of severe illness, but waning in terms of protection against infection was much more rapid. (Beyond the 6 month point the booster programme rapidly reduced the quantity of data available.)

Focusing on the left-hand set of results below, ie for age 65+, it can be seen that protection against severe illness and death had waned to around 80% by the six month point. As noted above though, by the same point the vaccine was offering very little protection against being infected (as evidenced by a positive test).

One of the difficulties in any such study is allowing for confounding factors, an obvious one being whether an individual had previously had a COVID infection that would subsequently provide a high degree of natural immunity. By using patient health records the study was able to exclude anyone with evidence of a prior infection, either through a positive test result, or a record of a probably COVID infection in primary care records.



Variants

Dominance of BA.5 and new variant BA.2.75

BA.5 is now the most frequently reported variant in the UK and accounts for almost 80% of available sequences (link). BA.5 is also the most frequently reported variant in most countries that provide up to date data to GISAID (link).

BA.2.75 is a sub-lineage of Omicron variant BA.2. It has been detected in many countries and, as at 18 July 2022, there were 24 cases with BA.2.75 in the UK (link). A snapshot of the most recent data point taken on 27 July from NextStrain shows that BA.2.75, denoted by clade 22D, accounted for the following proportions of sequences submitted to GISAID in the listed countries:

- India – 13%
- Nepal – 30%
- China – 44%
- South Korea – 61%

Note that sequenced samples may not be representative of total cases.

The World Health Organization is monitoring BA.2.75 but has not designated it as a variant of concern (VOC). The only currently circulating VOCs are the Omicron variants BA.1, BA.2, BA.3, BA.4 and BA.5. Alpha, Beta, Gamma and Delta are now listed as "previously circulating VOCs".

Immune escape and severity characteristics of BA.5

A pre-print study from Denmark covering the period April to June 2022 has found that prior Omicron infection was highly protective against BA.5 (93.6%, 95% CI 92.1-94.8). Infection with Delta or Alpha was also found to be protective but to a lesser extent against BA.5 than against BA.2. meaning that BA.5 has a greater degree of immune escape than BA.2

Prior infection variant	Protection against BA.2 infection (95% CI)	Protection against BA.5 infection (95% CI)
Omicron	96.3% (95.8%; 96.7%)	93.6% (92.1%; 94.8%)
Delta	77.2% (72.2%; 81.3%)	46.9% (27.0%; 61.3%)
Alpha	74.5% (68.7%; 79.2%)	65.4% (49.8%; 76.2%)

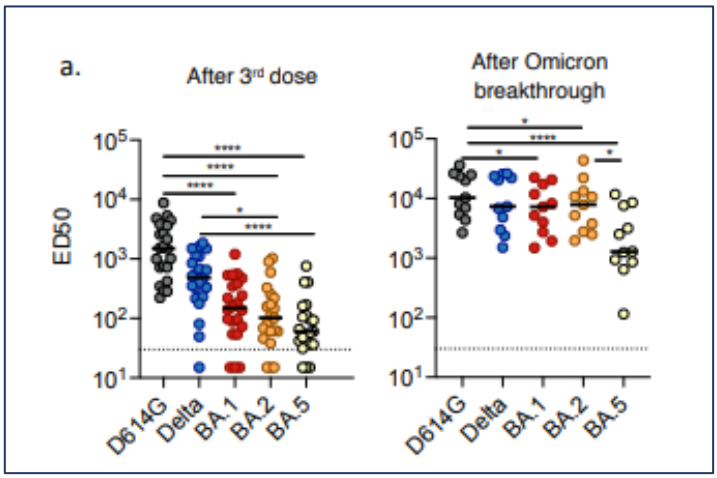
In triple-vaccinated individuals there was similar vaccine effectiveness for BA.5 as for BA.2 infection.

However, BA.5 infection was associated with an increased risk of hospitalisation compared with BA.2. After adjusting for age and calendar period, the odds ratio for hospitalisation with BA.5 vs BA.2 was 1.65 (1.16-2.34). This conclusion is based on 87 hospitalisations with BA.5.

A similar study conducted in Portugal also found no evidence of reduced vaccine effectiveness for BA.5 infection compared with BA.2. However, there was a greater risk of hospitalisation associated with BA.5 infection than with BA.2 infection, although this conclusion is based on only 34 hospitalisations among triple-vaccinated individuals.

These observations of greater immune escape in the Danish and Portuguese populations are consistent with a French laboratory study that measured neutralising antibody response among 27 individuals who had received Pfizer vaccination. Serum neutralising antibody titres were found to be reduced by 10-, 15-and 25-fold for BA.1, BA.2 and BA.5, respectively, compared with ancestral strain D614G.

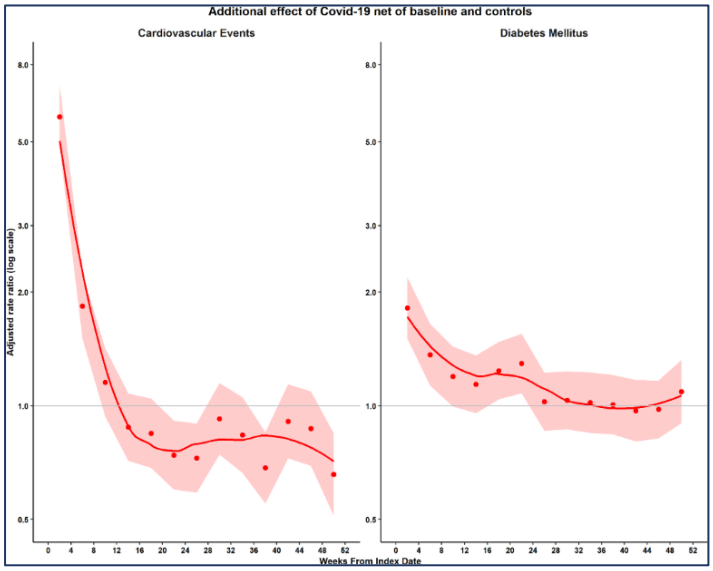
The same laboratory study found that an Omicron breakthrough infection restored antibody levels. This supports the observation in the Danish study that prior Omicron infection was associated with a high degree of protection against BA.5 infection.



Medical

Cardiometabolic outcomes after COVID-19 infection

A UK study evaluated new diagnoses of diabetes and cardiovascular diseases up to 12 months after COVID-19 infection. This was done by matching 428,650 COVID-19 patients with 428,650 control patients and comparing outcomes for COVID-19 patients with controls and adjusted for baseline differences in risk.



COVID-19 was associated with a 6-fold increase in cardiovascular diagnoses in the first 4 weeks after infection. Such diagnoses were 1.5x normal levels 5 to 12 weeks after infection.

Between 12 and 52 weeks post-infection, diagnoses fell back to usual background levels, and possibly below these levels.

This suggests some early diagnoses may have been accelerated by COVID-19.

Diabetes mellitus diagnoses were 1.8x normal levels in the first 4 weeks after COVID-19 infection. They were 1.3x normal levels 4 to 12 weeks after the infection and then returned to baseline levels.

Long Covid

Symptoms and risk factors for long COVID in non-hospitalised adults

The Therapies for Long Covid (TLC) study is a UK study with the aim of evaluating the symptom burden of Long COVID syndromes and evaluating potential therapies (link). As part of this study researchers investigated which of 115 symptoms were associated with confirmed SARS-CoV-2 infection beyond 12 weeks in non-hospitalised adults and the risk factors associated with developing persistent symptoms (link). They used a UK primary care database (CPRD) to match 486,149 adults with confirmed SARS-CoV-2 infection with 1,944,580 controls where there was no recorded evidence of SARS-CoV-2 infection.

The researchers found that 62 of the symptoms investigated were significantly associated with SARS-CoV-2 infection after 12 weeks, including a doubling of the risk of fatigue and shortness of breath at rest. The adjusted odds ratios for sexual dysfunction among those with SARS-CoV-2 infection were even higher.

Risk factors for Long COVID included female sex with an adjusted hazard ratio of 1.52 (1.48–1.56) and presence of symptoms before COVID-19 with adjusted hazard ratio of 2.07 (2.02–2.12). Other co-morbidities were also strongly associated with Long COVID symptoms. The risk of developing long COVID was found to be higher for those belonging to ethnic minority groups, with other risk factors including socioeconomic deprivation, smoking and obesity.

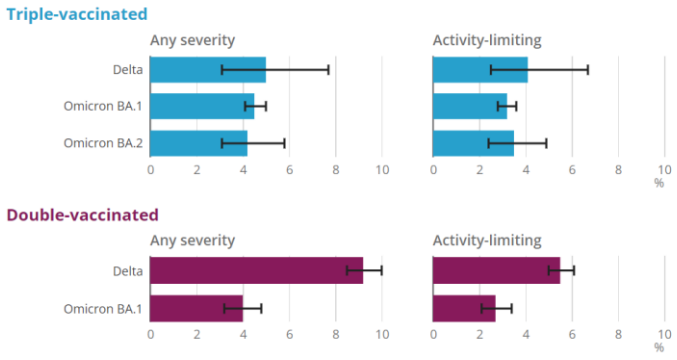
Risk of Long COVID appeared to reduce with increasing age which may reflect that older patients were more likely to have been hospitalised with COVID-19 and therefore excluded from the study.

The study has many strengths including its size and presence of a control group. A possible limitation is the reliance on routinely coded healthcare data and patients with COVID-19 possibly being more likely to consult their GP than those with no recorded infection.

Long COVID by Variant (link)

Figure 1: Approximately 4% of triple-vaccinated adults reported experiencing long COVID 12 weeks after being infected with the Omicron BA.1 or BA.2 variants

Percentage of study participants aged 18 years and over with self-reported long COVID 12 to 16 weeks after a first coronavirus (COVID-19) infection, stratified by compatible COVID-19 variant and vaccination status when infected, UK, 17 May 2021 to 27 May 2022



Source: Office for National Statistics - Coronavirus (COVID-19) Infection Survey

The ONS has published an analysis of self reported Long COVID levels split according to variant.

For those triple jabbed, across the three variants studied (Delta, BA.1 and BA.2 the rate varied between 4% and 5% for any severity of Long COVID reported between 12 and 16 weeks.

Of note, there was no statistically significant difference between the variants, possibly contrary to views that Omicron is milder than Delta.

A comparison was also made with those who had only received the initial two-dose course, and in contrast here there appeared a much higher level of 9% for those infected by Delta, with the level for those infected by BA.1 similar to those who are triple jabbed. A similar, but much less marked effect is seen for those reporting more severe levels of Long COVID.

Modelling

The role of regular asymptomatic rapid testing in reducing the impact of a COVID-19 wave (Silva et al (link))

This e-print (electronic pre-print) models the impact of various frequency levels of asymptomatic testing for SARS-CoV-2 infection, when combined with isolation and contact tracing of positive cases. The effectiveness was compared with lockdown interventions such as restrictions on gatherings and mandated working from home.

The paper finds that under a twice-weekly testing schedule, increasing the number of people participating in testing can have as much impact as reducing the number of contacts by 30%. The authors note that using rapid-response LFTs may help in epidemic control as PCR tests take longer to produce a test result – this delay offsets the lower sensitivity of LFTs.

The paper concludes that regular asymptomatic testing in the early stages of exponential growth of a future wave has the potential to reduce the impact without requiring additional lockdown measures.

Data

Characteristics of people testing positive for COVID-19, 20 July 2022 (link)

This analysis from the ONS COVID-19 Infection Survey sets out the latest information about the characteristics of those testing positive for COVID-19. In particular, it contains some interesting information about reinfection risk.

Based on the data, ONS conclude that reinfection risk was five times higher in the period when Omicron was dominant, compared with the period when the Delta variant was dominant. ONS also find that younger people were more likely to be infected than older people over the period 2 July 2020 to 1 July 2022.

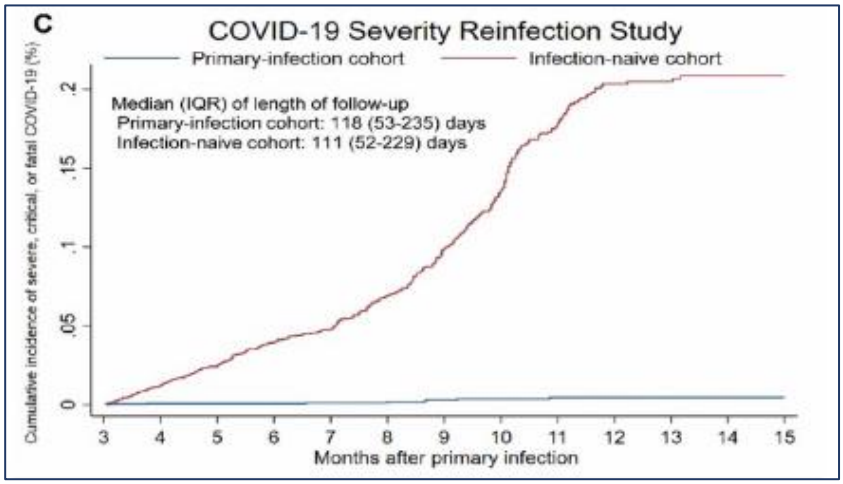
The ONS estimate that the reinfection rate is currently around 40 per 100,000 participant days at risk – a "day at risk" being the period where a participant's positive test could be considered a reinfection (rather than a continuation of a prior infection). It is possible that this figure underestimates the true reinfection risk – it has been noted that some reinfections may be missed as participants are sampled monthly whereas infection typically lasts around a week.

ONS also conclude that a large proportion of reinfections in the Omicron dominant period relate to people with first infections in the Alpha (37.9%) or Delta (37.1%) dominant periods. There have been people with first and second infections during the same variant dominant period (e.g. first infection Delta / second infection Delta) but the rate is far higher for the Omicron period.

Duration of immune protection of SARS-CoV-2 natural infection against reinfection in Qatar (Chemaitelly et al (link))

This preprint investigates the protection of natural infection against severe reinfection, based on three national matched retrospective cohort studies in Qatar – these studies have very large population sizes so conclusions should be robust.

The survey concludes that the protective effect of natural infection against reinfection wanes over time, with protection being low after some months (perhaps as low as 10% by the 15th month after infection) and with immune evasion of new variants accelerating this waning.



However, protection against severe infection remains high, with effectiveness at 97% irrespective of the variant of either primary or reinfection, with no evidence of waning.

It is worth noting that the population of Qatar is predominantly young, with low COVID-19 mortality. This is helpful for the conclusions of the study because it means there is less likelihood of bias towards healthier individuals in the cohorts, but it does mean that it's less possible to draw direct inferences for countries with older populations.

CMI Mortality Monitor Q2 2022 overview

The Continuous Mortality Investigation (CMI) continue to publish weekly updates on mortality in England & Wales, based on data published by ONS – the latest weekly report can be found here.

The CMI also publish more in-depth studies quarterly – the latest (covering up to 1 July 2022) can be found here.

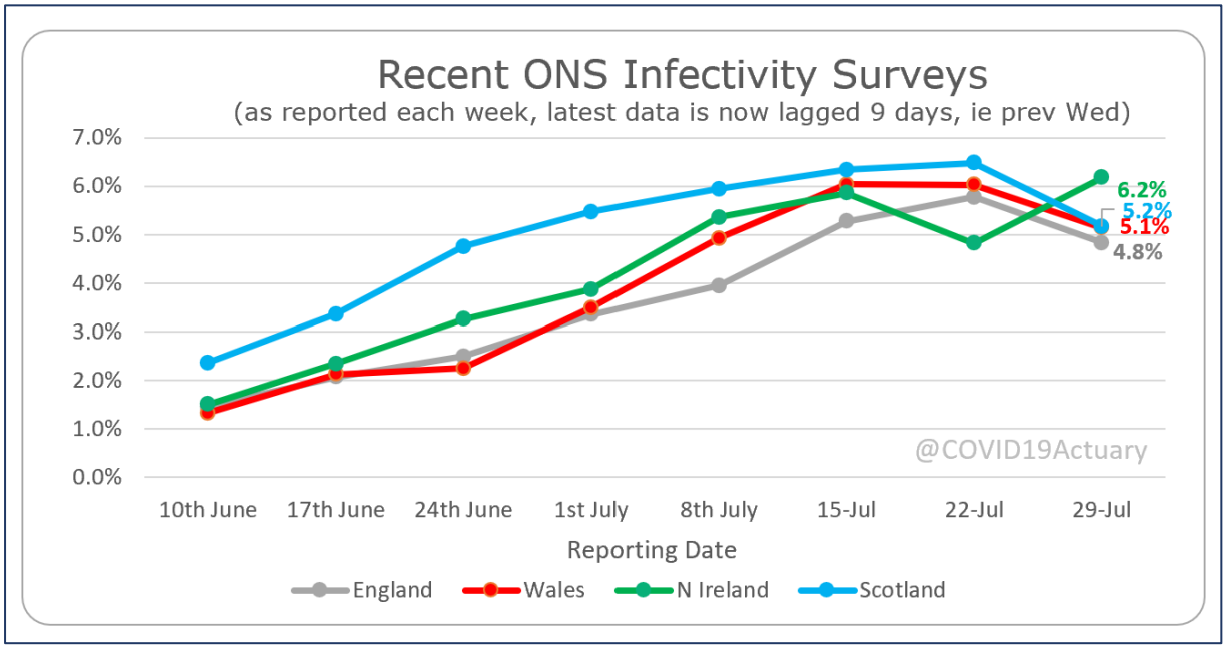
The analysis shows that, whilst mortality in the first quarter of 2022 was very low, it was higher in the second quarter. The cumulative mortality rate at the end of the first half of the year was significantly lower than the pandemic years (2020 and 2021) but 0.5% higher than 2019.

The CMI estimate that there were 112,000 excess deaths in England & Wales between the start of the pandemic and 1 July 2022, with 3,700 excess deaths since 1 January 2022. These figures differ from other published excess deaths figures (for example, from ONS) because the CMI calculate based on a population of standard size and age structure, and compare against a baseline of 2019 only (rather than an average over a number of years).

ONS Infection Survey (link)

After increasing for several weeks, Friday's update finally showed significant falls in three of the four nations, with only Northern Ireland being an outlier. We should note however that there can be significant volatility in the estimates for the smaller home nations, and so ONS describes the trend in the Province as "uncertain".

It should be noted that in recent weeks the survey has become slightly more out of date, and now finishes 9 days before publication (previously it was 6). In addition, the figure quoted is the mid point of the preceding 7 days, so now represents the position about 12 days ago.



The survey is currently undergoing a transition in the method of collecting data, with a change to a postal system, as opposed to doorstep engagement. This will undoubtedly make it more cost effective, although it remains to be seen what impact it has on the volume of data and reliability of the estimates.

And Finally …

Whisky Galore in Thailand

Over the course of the pandemic there have been some notable successes in finding treatments to improve the care of COVID patients. But there have also been some drugs put forward by some with uncertain motivation with no evidence to support their efficacy (and often the contrary). There have been some interesting candidates (link)…

A recent report in the New York Post tells the story of a drink-driving Buddhist monk in Thailand who claimed that he was inebriated because he was taking whisky as a protection against COVID.

Whilst there might be some (particularly from Ireland or Scotland) who may enjoy the idea of a daily tot to ward off COVID, and not mind how many "boosters" they need, we are reluctantly unable to endorse this potential treatment as an alternative to vaccination.

29 July 2022