



Friday Report: Issue 31

By Matt Fletcher, Nicola Oliver and John Roberts

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 will provide you with a regular Friday update with a curated list of the key papers and articles that we've looked at recently

Clinical and Medical News

Trajectories of anxiety and depression

The UCL [COVID-19 Social Study](#) is a large prospective panel study of the psychological and social experiences of over 70 000 adults (aged 18 years and older) in the UK during the COVID-19 pandemic. In this [analysis](#) there were two main aims: first, to explore trajectories of anxiety and depressive symptoms over the strict lockdown period and as lockdown was eased; and second, to identify who was most at risk of poorer trajectories of mental health across this period.

The study reports that the highest levels of depression and anxiety occurred in the early stages of lockdown but declined fairly rapidly.

Metformin and risk of mortality in patients hospitalised with COVID-19

Metformin is a drug commonly prescribed to treat type 2 diabetes and has an exceptionally long safety record (first used to treat diabetes in 1957). It is also being investigated for its potential anti-ageing properties. Its use in treating COVID-19 was investigated in this [study](#), a retrospective cohort analysis of claims data from UnitedHealth Group (UHG)'s Clinical Discovery Claims Database. Of interest was the effect of metformin use before diagnosis with SARS-CoV-2.

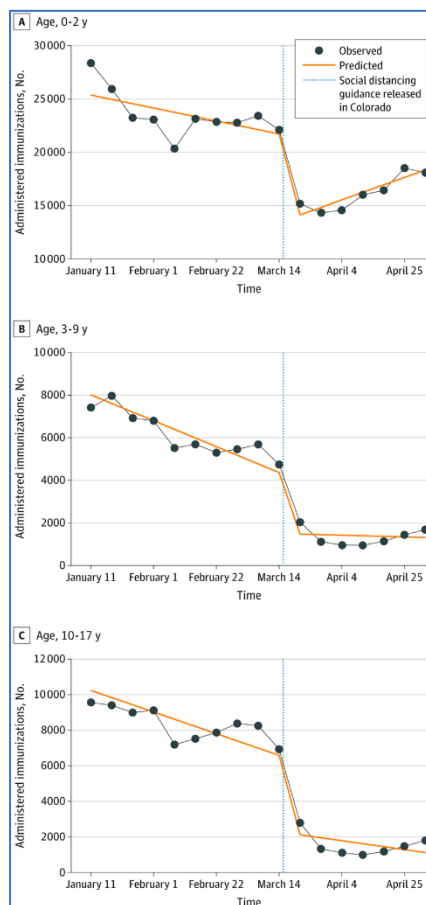
Results from this analysis suggest that outpatient metformin use may be associated with decreased mortality in women with either type 2 diabetes, or obesity. One of the mechanisms could be anti-inflammatory and anti-cytokine.

Assessment of Racial/Ethnic Disparities in Hospitalization and Mortality in Patients With COVID-19 in New York City

The association between ethnicity and COVID-19 has been analysed in this next [study](#), which looks at the differences in outcome by ethnicity. The cohort was drawn from patients who tested positive for COVID-19 in New York. The outcomes for comparison were: positive test, hospitalization, critical illness, death based on race/ethnicity.

Black and Hispanic patients were more likely, and Asian patients less likely, than White patients to test positive; once hospitalized, Black patients were less likely than White patients to have critical illness or die after adjustment for comorbidity and neighbourhood characteristics. The authors suggest that socioeconomic factors may play a role in these disparities.

Number of Childhood and Adolescent Vaccinations Administered Before and After the COVID-19 Outbreak in Colorado



Lockdown measure to counter the pandemic may have affected childhood vaccination rates. The number of childhood and adolescent vaccinations administered in the months before and after the start of the COVID-19 outbreak in Colorado were assessed in this [study](#). The central Colorado Immunization Information System contains immunisation records for all age ranges up to 18 years. Significant decreases in vaccination uptake were observed when comparing the pre- and post-social distancing period. The figure to the left displays the results for total vaccine doses administered by age groups.

This equates to a drop in mean immunisation rate between time periods of 31% for individuals aged 0 to 2 years, 78% for those aged 3 to 9 years, and 82% for those aged 10 to 17 years.

This is a significant public health concern, with a potential for some to miss the schedule entirely.

Efficacy of Tocilizumab in Patients Hospitalized with Covid-19

Tocilizumab is a biological therapy for rheumatoid arthritis and juvenile idiopathic arthritis (JIA). It has been investigated in a number of studies for its potential to be used as a treatment for COVID-19. In theory, it could counter the development of a cytokine storm through its ability to block a key receptor in this process.

In the latest [study](#) to release results, Tocilizumab was not found to be effective for preventing intubation or death in moderately ill hospitalised patients with Covid-19.

Increase in Hospital-Acquired Carbapenem-Resistant *Acinetobacter baumannii* Infection and Colonization in an Acute Care Hospital During a Surge in COVID-19 Admissions

Antimicrobial resistance is a global health threat – in particular, the impact of antibiotic resistance on human health and mortality. *Acinetobacter baumannii* is a relatively new pathogen, with cases of infection with the organism being found almost exclusively in hospital patients, particularly ICU patients. It is known to survive for long periods on dry inanimate surfaces and can infiltrate open wounds, catheters, and ventilation tubes. Unfortunately, it has a mortality rate of 20–60%, and a rapidly rising antibiotic resistance.

Carbapenem antibiotics are generally reserved for severe, multi-drug resistant bacterial infections, so carbapenem resistance is worrying. The CDC [report](#) a cluster of Carbapenem-resistant *Acinetobacter baumannii* (CRAB) cases during a surge in COVID-19 hospitalizations in a New Jersey hospital. This was thought to be as a result of infection prevention and control (IPC) breaches caused by shortages in personnel, personal protective equipment (PPE), and medical equipment.

Vaccines

It has been a big week for vaccine news. Two of the three phase trials that have reported positive results have now published these in peer-reviewed journals. The vaccination programme using the Pfizer vaccine is well under way in the UK.

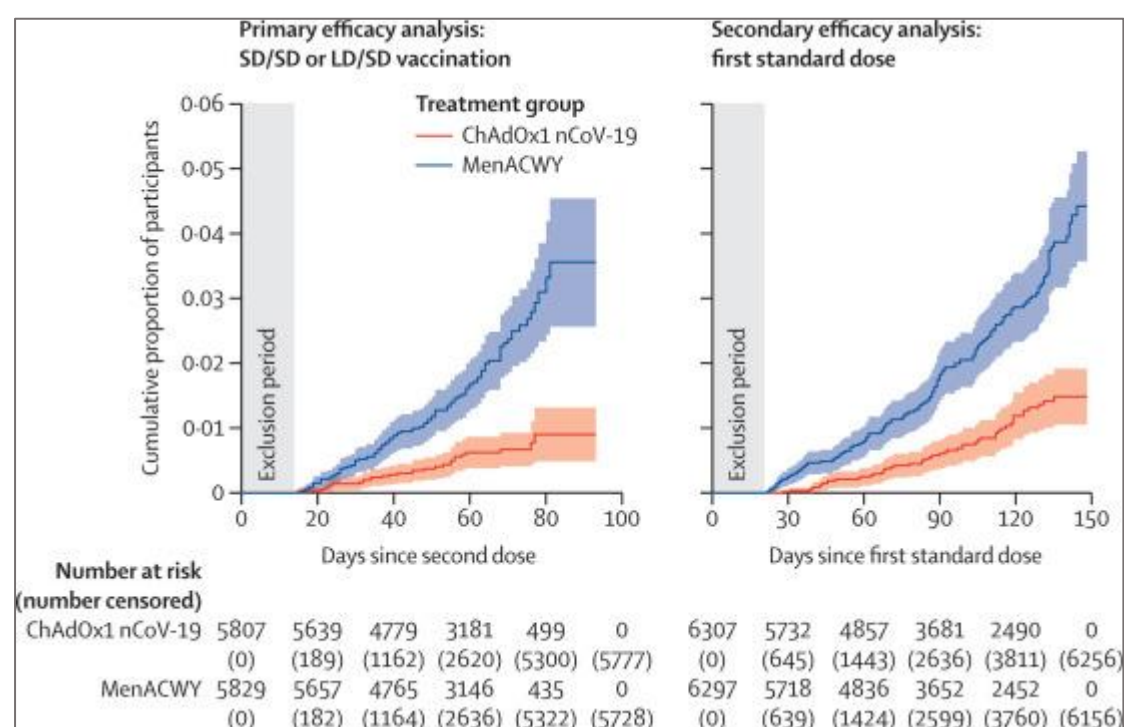
Oxford–AstraZeneca COVID-19 vaccine efficacy

This [analysis](#) includes data from four ongoing blinded, randomised, controlled trials done across the UK, Brazil, and South Africa. The plan for assessing efficacy and safety for the ChAdOx1 nCoV-19 vaccine, a viral vector vaccine, is based on global analyses using all available data from four studies with analysis pooled across the studies.

Between April 23 and Nov 4, 2020, 23,848 participants were recruited and vaccinated across the four studies: 1,077 in COV001 (UK), 10,673 in COV002 (UK), 10,002 in COV003 (Brazil), and 2,096 in COV005 (South Africa). The majority of participants were aged 18-55 years, and more females were recruited than males.

The figure shows the efficacy analysis. Cumulative incidence of symptomatic COVID-19 after two doses (left) or after first standard dose in participants receiving only standard-dose vaccines (right).

Grey shaded areas to the left of each chart show the exclusion period after each dose in which cases were excluded from the analysis. Blue and red shaded areas show 95% CIs. LD/SD=low-dose prime plus standard-dose boost. MenACWY=meningococcal group A, C, W, and Y conjugate vaccine. NAAT=nucleic acid amplification test. SD/SD=two standard-dose vaccines given.

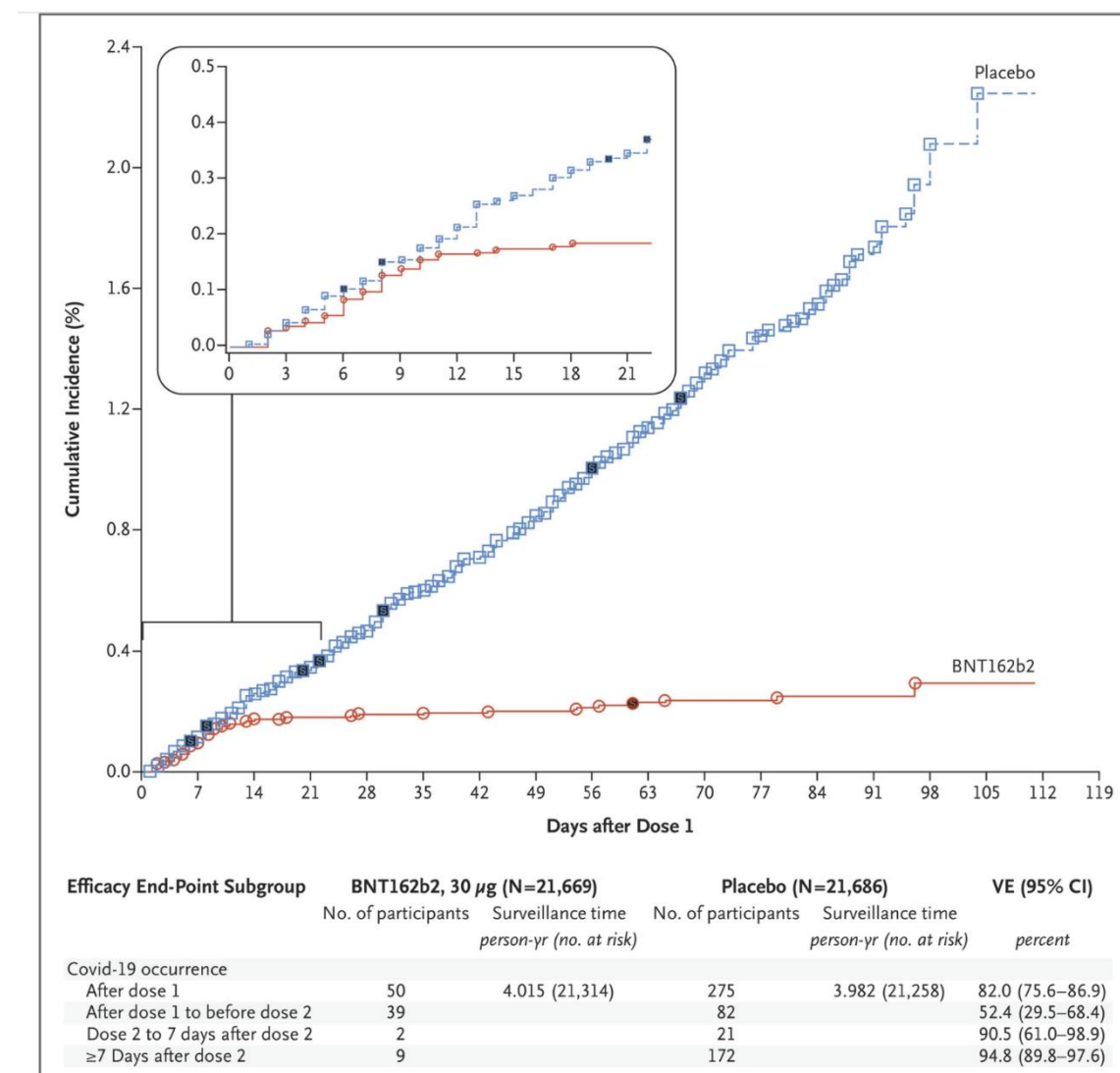


The study authors report that ChAdOx1 nCoV-19, evaluated in four trials across three continents, showing significant vaccine efficacy of 70.4% after two doses and protection of 64.1% after at least one standard dose, against symptomatic disease, with no safety concerns.

Pfizer COVID-19 vaccine efficacy [\(link\)](#)

As the roll-out of the Pfizer vaccine started this week, more details have been published in respect of the trial results.

Possibly the best way to visualise the stunning success of the vaccine is in this graph that shows the development of cases in both the vaccine and placebo groups, with immunity very clearly kicking in from around day 10 or 11 after the second dose.



As previously reported the overall 95% efficacy is matched at the key older age groups, with no apparent drop off. Similarly there seems to be comparable efficacy across all ethnic groups.

The report also gives detail as to side-effects experienced. Fatigue, muscle pain and headache were all raised in contrast to the placebo group, with a small percentage experiencing fever, with the most notable differences being after the second jab.

Sanofi/GSK vaccine setback [\(link\)](#)

It might be easy to become rather blasé as to the success of the 3 Western vaccines that have so far announced trial results. Elsewhere, there is proof that success of vaccine development is not at all guaranteed, with the news that the Sanofi/GSK trials have had a significant setback. The evidence

shows that the immune response generated in those over 50 years old was inadequate, probably due to an insufficient concentration of the antigen.

The plan is to reformulate the vaccine and conduct further Phase 2 trials beginning in February, but approval is likely to be pushed back until the fourth quarter of 2021. The UK has pre-ordered 60m doses of the vaccine – a demonstration that it was the right decision to avoid relying on any one or two vaccines before it was clear which would be successful.

CSL vaccine setback ([link](#))

Meanwhile, in Australia, a vaccine under development by the Australian firm CSL and the University of Queensland has been abandoned after trials showed that some recipients generated HIV antibodies and then tested positive for HIV. Thankfully further tests have shown that the positives were false.

The conclusion has been reached that the delay of up to a year in trying to address this, along with the likelihood of reduced public confidence in the vaccine, means that the programme is unviable, and thus the programme has been cancelled. The Australian government has entered into an alternative contract with Novovax and an increased order for the AstraZeneca vaccine.

Modelling

SARS-CoV-2 infection and transmission in educational settings: a prospective, cross-sectional analysis of infection clusters and outbreaks in England ([link](#))

This paper estimated the rate of SARS-CoV-2 infection amongst staff and students in educational settings during the summer half term in England. They found that infections and outbreaks were uncommon during that period, and that there was a strong correlation between regional COVID-19 incidence and educational incidence with the risk of an outbreak increasing by 72% each time the community incidence increased by 5 cases per 100,000.

The authors suggest that any interventions should focus on reducing transmission in and amongst staff, as staff to staff transmission was found to be the likely direction of transmission in 26 out of 55 outbreaks involving multiple infected individuals (lower likelihood of transmission was suspected in other directions i.e. staff to student, student to staff, and in particular student to student).

Detecting COVID-19 infection hotspots in England using large-scale self-reported data from a mobile application: a prospective, observational study ([link](#))

Tracking SARS-CoV-2 infection at the local level is becoming more important, as countries are looking to slow the spread without imposing national non-pharmaceutical interventions.

This study makes use of data from users of the COVID Symptom Study app (also known as the Zoe app) between 24 March and 29 September 2020. From April the DSHC allocated PCR tests for COVID-19 to app users who initially logged themselves as healthy and then reported any COVID-19 symptom.

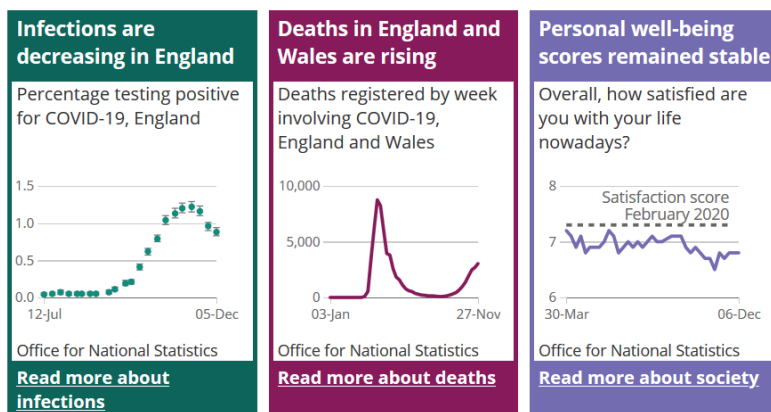
Using data on symptoms and swab test results, the authors estimated prevalence, incidence and the R rate across the country and on a more granular basis, providing a list of hot spots. The authors note that there are limitations to using the app data – users tend to live in less deprived areas than average, and there are few users in care homes and hospitals. In addition, a user's probability of using the app may be dependent on their likelihood of having COVID-19 which potentially biases their estimates of incidence and prevalence.

However, the authors do note that where there are high levels of official testing, the case estimates using app data match well with government data, suggesting that their estimates could be useful to forecast outbreaks in regions with lower levels of testing. They suggest that the estimates should be viewed as independent and complementary to the ONS and REACT studies.

Data

Coronavirus (COVID-19) latest insights

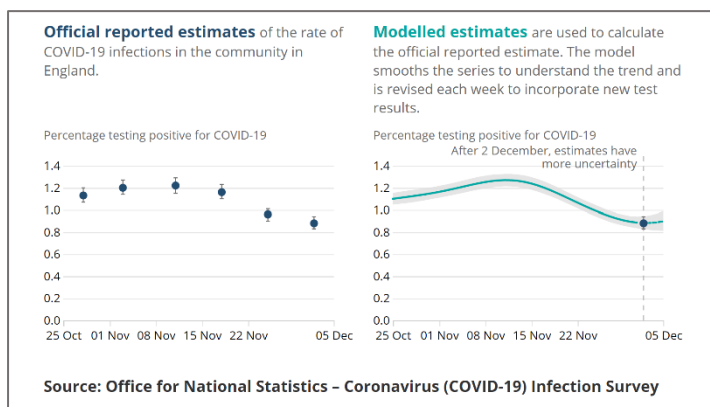
ONS have released a new interactive tool ([link](#)) allowing users to explore the latest trends and data about the pandemic. This includes the latest information about infections, deaths, societal impacts (for example, linking to findings from ONS's Opinions and Lifestyle survey), as well as infection and death data split by age and geographic area.



The ONS intend to develop this tool to include additional data, covering for example information about the impact of coronavirus on different ethnic groups, and the School Infection Survey, so it is likely to be worth bookmarking the page for future reference.

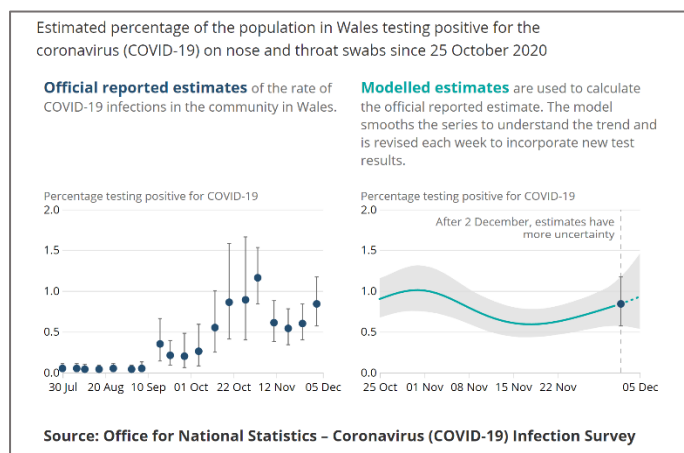
ONS Weekly Infectivity Report ([link](#))

The weekly surveillance report from ONS shows a very mixed picture across the UK. In order of increasing concern, Northern Ireland continues to fall, Scotland is level, England is showing signs of increasing again after falling during lockdown, and Wales is clearly on the increase.



Although the overall level of infections in England is estimated to have fallen by 3-4% to 481,000, the modelling suggests this has now levelled off. It should be noted that these models have come under some criticism from influential observers, as future iterations can markedly change the estimates for previous weeks. Nevertheless, the current trend appears very consistent with other data, notably hospital admissions.

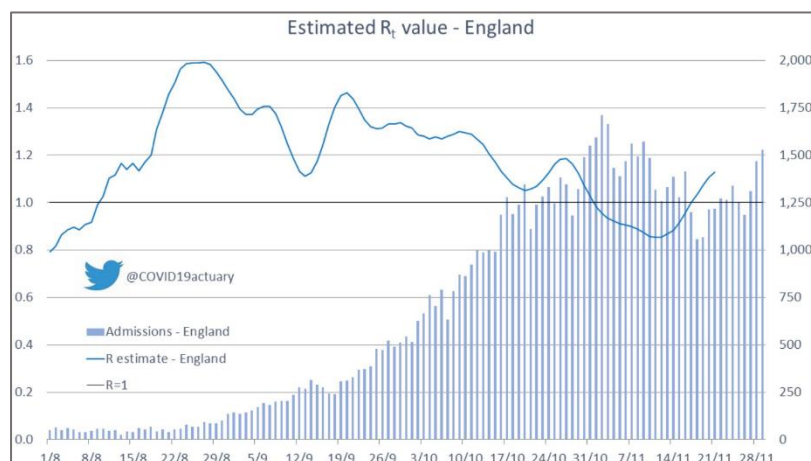
Wales is of much greater immediate concern, and with a month now elapsed since the end of the firebreak, the trend is very clearly upwards, with ONS quoting a 40% increase in the modelled estimate from 0.6% to 0.84%. With these figures only going to 5 December, it is likely that the rate has now surpassed prevalence prior to the firebreak.



The fall in infectivity in Northern Ireland continues, with the latest estimate falling from 0.52% to 0.43%. Finally, in Scotland, there has been a very modest increase from 0.78% to 0.82%, which given the size of the confidence intervals is effectively a no change position.

“R” Estimate

The latest SAGE estimate puts R for the UK at 0.9 to 1.1 and 0.8 to 1.0 for England. Most notably for England, the estimates for the South East, East and London are put at 0.9 to 1.1.



After several weeks of relative consistency, our own view of R for England is a little higher, now between 1.1 and 1.2, and still increasing. This reflects the recent increase in hospital admissions, which has been sustained for over a week now.

Vaccine Attitudes

With all the excitement surrounding the vaccine roll-out this week, it's worth revisiting a survey conducted back in the summer by Kings College London ([link](#)) as to people's propensity to have the vaccine when it becomes available.

The headline figures are that 53% were certain to have it, 20% fairly likely, and 16% unlikely or definitely won't have it. By age, there's a not unpredictable differential, with 22% of the under 35s in the “unlikely or won't” camp, but this falls to 11% between 55 and 75. Given the relative impact on age groups, the former figure is possibly understandable, but it may be a surprise that 1 in 9 people over 55 appear willing to take a risk of remaining unprotected.

An interesting set of questions try to understand attitudes that might influence people's decision not to have the vaccine. There appears a strong correlation between the extent of people's concern about the pandemic and also their attitude to too much direction from authorities. As an example, people who thought face masks were bad for your health, people who felt they were mandated purely so the government could get more control over society, and those who felt there was too much fuss about the pandemic, all had proportions choosing not to take the vaccine that were double the overall figure. It is likely however, that there is a significant overlap between these groups.

A final note is that those who use Whatsapp to get information about the pandemic were also significantly more likely to refuse the vaccine. Maybe they should be following @COVID19actuary on Twitter instead?

And finally ...

The following heartwarming story recently went viral – Millie Jacoby, a 21-year-old British student, tweeted about how much she'd enjoyed her first video meeting with her new 91-year-old "French Grandma".

<https://www.bbc.com/news/world-europe-55235378>

This was made possible via the "Share Ami" scheme which pairs language students with elderly French people who may have been left isolated by the pandemic. The scheme launched in May and has so far created 30 pairings – but since Millie's tweet, they've had almost 3,000 enquiries.

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