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Friday Report: Issue 43

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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

Pfizer-BioNTech vaccine authorised in the USA for children aged 12-15

As there is much discussion of the need to extend the vaccination program to younger ages in the UK, the FDA in the USA has extended (link) the authorisation of the Pfizer-BioNTech vaccine to children aged 12 to 15. Investigators such as Kawsar Talrat at John Hopkins Bloomberg School of Public Health have highlighted the difficulty of achieving herd immunity (expected to require 70-85% of the population) if children are excluded as they represent 25% of the US population.

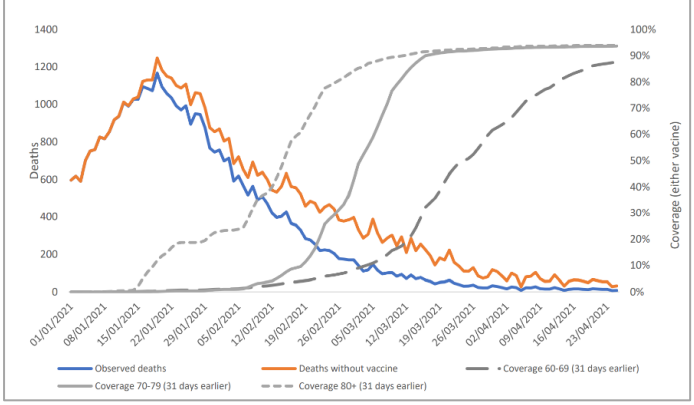
Authorisation was granted on the basis of a two-dose phase III RCT involving 2,260 children between 12 and 15. Impressively there were no reports of symptomatic COVID-19 in the vaccinated group. The question of course is whether families will allow their children to be vaccinated, given the low level of risk of severe COVID outcomes in children. Surveys by the Kaiser Family Foundation (link) are finding that 30% of parents are prepared to vaccinate their children as soon as vaccines are available, 25% will "wait and see" and 25% will definitely not allow their children to be vaccinated.

Over 11,000 lives saved to date

Public Health England's latest vaccine surveillance report (link) estimates that vaccination has saved 11,700 lives in England to 25th April. The estimate uses real world data on effectiveness, together with proportions of the different age groups vaccinated, to derive the counter-factual scenario without any vaccination.

This is actually a very conservative estimate, as it assumes that vaccination has played no part in bringing levels of virus prevalence down. There is now clear data to show that vaccination reduces transmission, and so it is highly likely that the programme has accelerated the reductions we've seen as a result of lockdown, though by how much is more difficult to quantify.

Figure 8: Daily Observed COVID-19 deaths aged 60 and over, and expected numbers in the absence of vaccination using the back calculation method

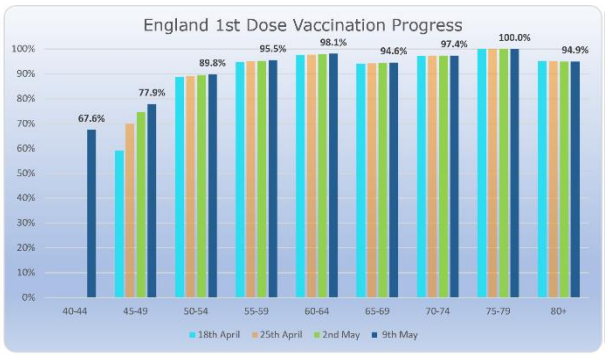


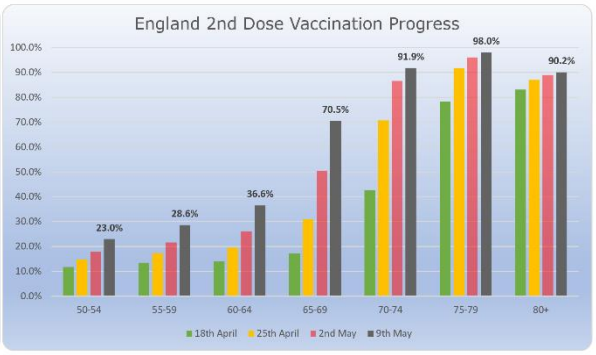
Take-up Rates

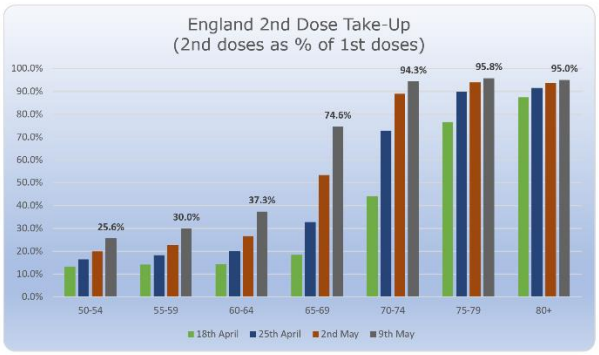
Latest weekly figures from NHS England (link) show an aggregate first dose take-up in excess of 95% for age 50+, an exceptionally high rate, and one that no doubt other public health officials in other countries will look at with some envy. There are however signs that hesitancy is increasing as we work our way down to younger ages, with 50-54 only achieving 90% and 45-49 looking as though it will level off at around 80%.

Second dosing is now concentrated on the 60-69 age group. Above that we can now derive "second dose take-up" rates, which appear to be around 95% for the Over 70s. Again, this is an exceptionally good result, although given the additional protection the second dose gives both in terms of strength and expected length, the programme should still try and reach those who have yet to return for their second dose.

With the announcement this evening of an acceleration of second doses in the Over 50s, we can expect an acceleration of between 5m and 6m doses in the period of transition.







Clinical and medical news

Delayed Pfizer Dosing Improves Antibody Response (link)

A study led by the University of Birmingham has found that delaying the second dose of the Pfizer vaccine to twelve weeks increased the peak SARS-CoV-2 spike specific antibody response 3.5-fold compared to those who had the second vaccine at three weeks. Although the peak cellular immune responses were lower after the delayed second vaccine, responses were comparable between the groups when measured at a similar time point following the first dose.

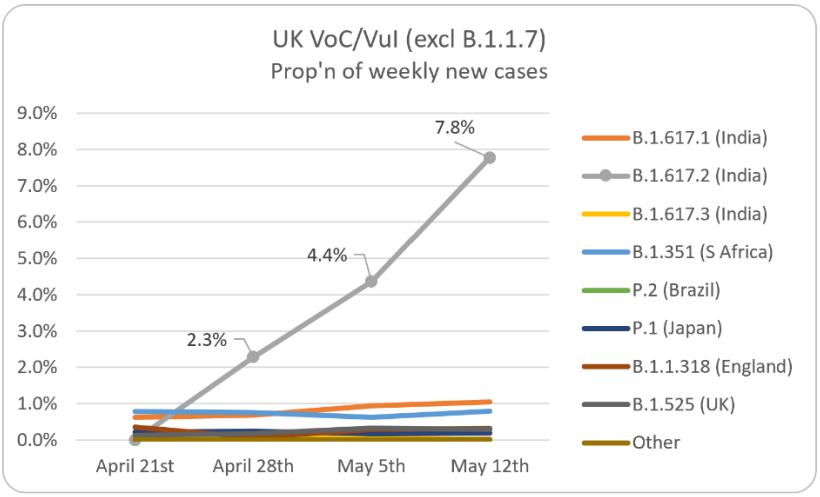
The JCVI's decision to delay the second dose was originally criticised by many, particularly for Pfizer where the trials only studied a three-week delay. However, it is typical with vaccines that a longer gap between two doses enhances protection, and this had also been confirmed by trials of the AZ vaccine. So these results should not be a surprise, but do help validate the decision to opt for the longer deferral period, which was taken to roll-out protection to as many people as quickly as possible.

Prevalence of Variants in the UK

Concern continues to mount with regard to the "Indian" variants, and in particular B.1.617.2, which continues to grow quickly, and now accounts for nearly 8% of all the cases sequenced, with 793 identified in the most recent data.

To date, there hasn't been a noticeable impact on overall case levels reported by PHE, which are currently broadly level, although hotspots are developing, most notably in the North West. As an example, Bolton's latest 7-day rate is 193per 100k, compared with 22 for England as a whole. It is suspected that B.1.617.2 is causing these hotspots, and evidence is growing to support this.

Although the vaccination programme has protected the majority of older lives, it is of concern that the hotspots to date are in areas where take-up has been relatively low, and thus may have a greater impact than might otherwise be expected.

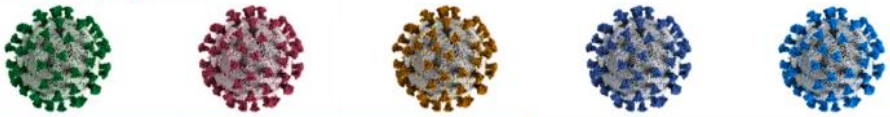


Mapping differences between the Variants of Concern and Variants of Interest

Since September 2020 we have heard an increasing amount about Variants of Interest (or Variants under Investigation) and Variants of Concern. Variants have mutations in the RNA genetic code of the virus that translate into different amino acids affecting the shape of viral proteins. Interest has intensified in the last week as the India variant B.1.617.2 is spreading rapidly in particular hotspots in the UK, as described above.

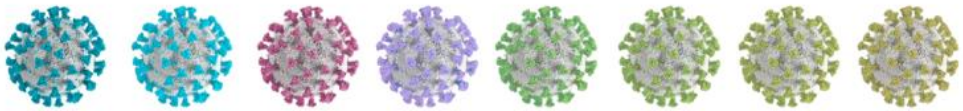
The Advisory Committee on Immunization Practices (ACIP) in the USA is a group of medical and public health experts that develop recommendations on vaccine usage, and have developed a number of very informative and useful presentations. Their most recent (link) illustrates similarities and differences between the main variants. Note that, while ACIP list B.1.617.2 as a Variant of Interest, it has been classified as a Variant of Concern by Public Health England and a Variant of Global Concern by the World Health Organisation. A Variant of Interest only can become a Variant of Concern once a risk assessment is carried out.

Variants of Concern



	B.1.1.7	B.1.351	P.1	B.1.427	B.1.429
First detected	United Kingdom	South Africa	Japan / Brazil	California	California
No. of spike mutations	10-13	10	11	4	4
Receptor binding domain mutations	N501Y	K417N E484K N501Y	K417T E484K N501Y	L452R	L452R
Attributes	• **50%** increased transmission • **Minimal** impact on neutralization by antibody therapies, convalescent or vaccine sera	• **50%** increased transmission • **Reduced** efficacy of some antibodies • **Reduced** neutralization by convalescent or vaccine sera	• **Reduced** efficacy of some antibodies • **Reduced** neutralization by convalescent or vaccine sera	• **20%** increased transmission • **Modest** decrease in efficacy of some antibodies • **Reduced** neutralization by convalescent or vaccine sera	• **20%** increased transmission • **Modest** decrease in efficacy of some antibodies • **Reduced** neutralization by convalescent or vaccine sera

Variants of Interest



	B.1.526	B.1.526.1	B.1.525	P.2	B.1.617	B.1.617.1	B.1.617.2	B.1.617.3
First detected	New York	New York	UK/Nigeria	Brazil	India	India	India	India
No. of spike mutations	3-7	6-8	8	3-4	3	7-8	9-10	7
Receptor binding domain mutations	(S477N*) (E484K*)	L452R	E484K	E484K	L452R E484Q	L452R E484Q	L452R T478K	L452R E484Q
Attributes	• **Reduced** antibody efficacy • **Reduced** neutralization convalescent or vaccine sera	• Potential reduced antibody efficacy • Potential reduced neutralization by vaccine sera		• Potential reduced antibody efficacy • **Reduced** neutralization by vaccine sera	• Potential reduced antibody efficacy • **Reduced** neutralization by vaccine sera	• Potential reduced antibody efficacy • Potential reduced neutralization by vaccine sera		

All of the Indian variants show the L452R alteration which has been associated with increased transmission in the Californian variant B.1.427. Further investigations are ongoing to assess whether the ability of the E484Q alteration which is found in some Indian variants is comparable to that of the E484K alteration.

Population studies from the Seychelles (link), whose population is 80% plus vaccinated and where the Indian variants are spreading widely, have indicated that 37% of new infections and 20% of hospitalisations are in those who have received two doses of either the Sinopharm or AstroZeneca vaccines. This illustrates why there is particular concern over the ability of the B.1.671.2 variant in particular to escape prior immune responses and to lead to more sustained outbreaks in the coming months.

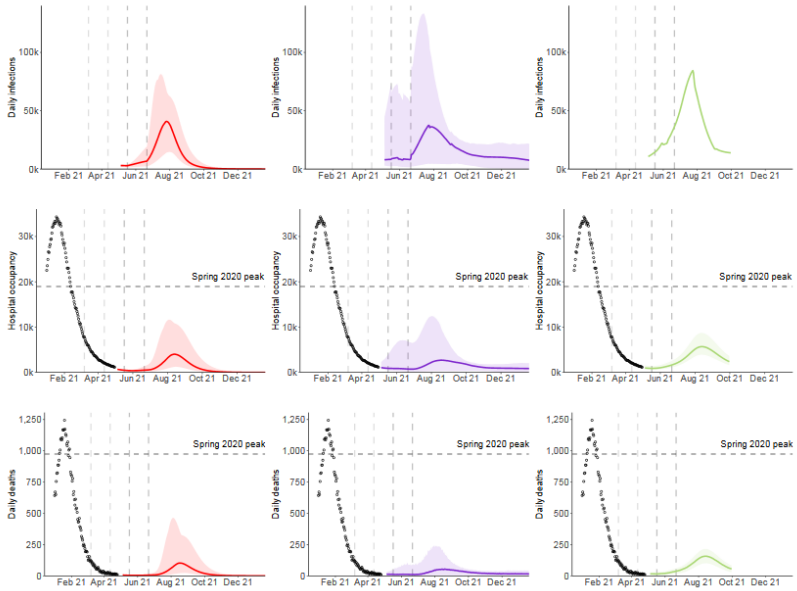
Modelling

SAGE SPI-M-O: Summary of further modelling of easing restrictions – roadmap step 3, 5 May 2021 (link)

This paper from the Scientific Pandemic Influenza Group on Modelling, Operational sub-group (SPI-M-O) was considered at SAGE meeting 88 on 5 May 2021. It summarises findings from three more detailed papers by Imperial College London (link), University of Warwick (link) and LSHTM (link) and updates the equivalent paper tabled at SAGE meeting 85 on 31 March 2021 (link).

Whilst all three models anticipate a wave of infections, hospitalisations and deaths as restrictions are eased, best estimate projections show a smaller wave than set out in the March paper. This is principally because two of the modelling groups now assume (based on new data) that onward transmission is reduced by up to a half in all those who are vaccinated but become infected.

Figure 5: England infections (top), hospital bed occupancy (middle), and deaths within 28 days of a positive test (bottom) in the Warwick (left – red), Imperial (middle – purple), and LSHTM (right – green) models, assuming central assumptions if Steps 3 and 4 are taken including 80%-90% coverage in the under 50-year olds and significant reduction in transmission from baseline measures continue after Step 4. Peaks in occupancy and daily deaths from January 2021 and levels seen in Spring 2020 are shown by dashed horizontal lines. Vertical dashed lines show the dates at which each Roadmap step is taken. Shaded regions show the 95% credible intervals and lines indicate the medians of the distributions.



The best estimates for moving to step 4 of the roadmap (full unlock with long-term mitigations and guidance) are for in the region of 10,000 additional deaths over roughly the next 12 months. The uncertainty around this figure is large, with a range of 1,500 to 24,000 quoted. This compares to central estimates closer to 20,000 in the March papers.

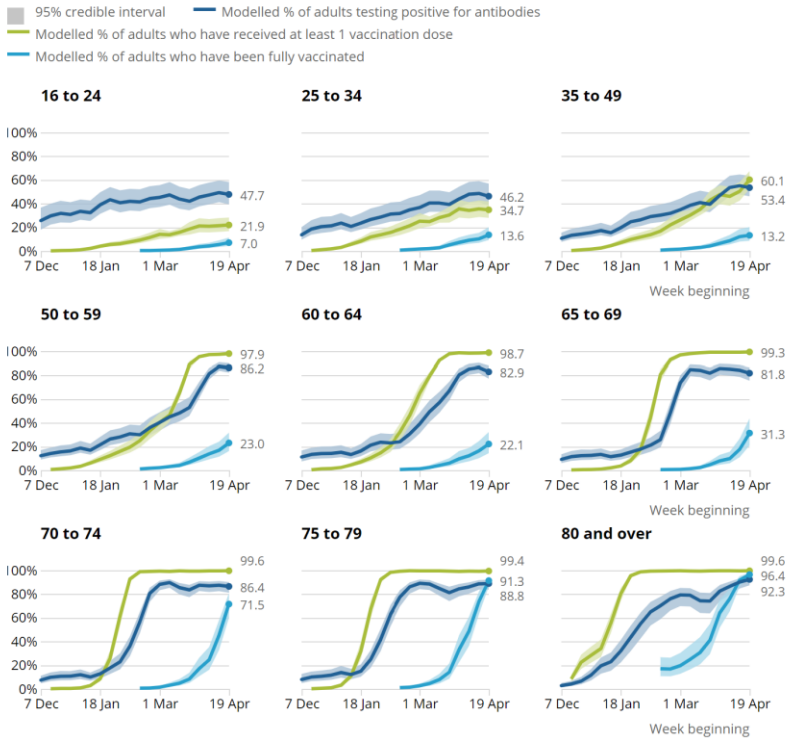
The groups' central scenarios do not consider waning immunity or the future emergence of variants of concern; these are modelled separately. For example, the Imperial group estimates that there could be 124,000 deaths in a scenario where a variant of concern which is as transmissible as B1.1.7 and has partial immune escape to vaccines becomes established in the UK population in the coming months.

Data

ONS Antibody data (link)

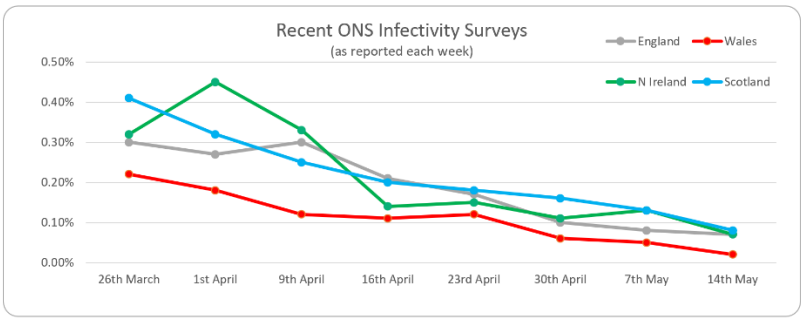
After a sharp jump in the previous antibody survey, this week's fortnightly update showed very modest increases of 1% or 2%, with England increasing from 68.3% to 69.3%.

There appears to be a pattern developing whereby the older age groups see dips in levels in the period preceding the second dose, and then a recovery to a higher eventual level. Currently it is the 60 to 64 group experiencing the dip, consistent with the fact that not many of this group would have had their second doses by the end date of the survey in late April.



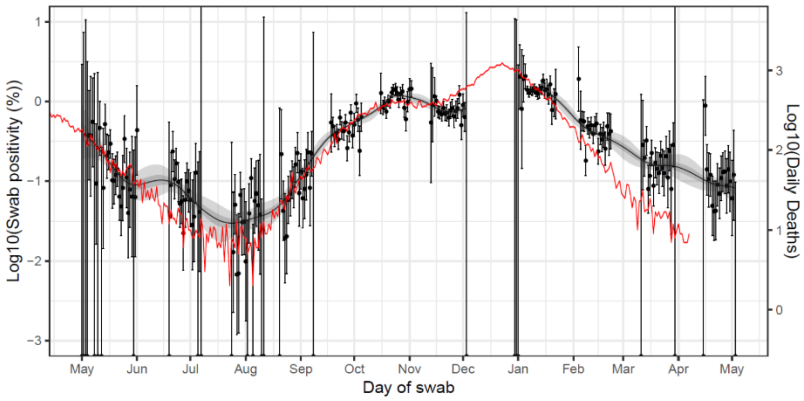
Infection Surveys

This week's ONS survey (link) continues to see big falls in prevalence, with Wales reaching a new low of 0.02%. Scotland and Northern Ireland have also fallen quickly, now bringing them more into line with England in terms of absolute levels of around 0.07%.



	Report Issued							
	26th March	1st April	9th April	16th April	23rd April	30th April	7th May	14th May
England	0.30%	0.27%	0.30%	0.21%	0.17%	0.10%	0.08%	0.07%
Wales	0.22%	0.18%	0.12%	0.11%	0.12%	0.06%	0.05%	0.02%
N Ireland	0.32%	0.45%	0.33%	0.14%	0.15%	0.11%	0.13%	0.07%
Scotland	0.41%	0.32%	0.25%	0.20%	0.18%	0.16%	0.13%	0.08%

This week we also had the latest REACT survey (link) which has shown a 50% fall since it's last update, with overall levels of 0.10%. REACT also notes the disconnect in the relationship between prevalence and deaths since January, which is a direct consequence of vaccination reducing the severity of illness in those who continue to become infected.



"R" Estimate (link)

There's no change to SAGE's estimate of R for England from our last report, which continues to be between 0.8 and 1.1 (although it dipped slightly last week to between 0.8 and 1.0). The regional estimates are shown below. It should be emphasised that these figures broadly reflect the position between two and three weeks ago, so any uncertainty due to increase in B.1.617.2 will not yet be included in the estimates.

Latest by NHS England regions

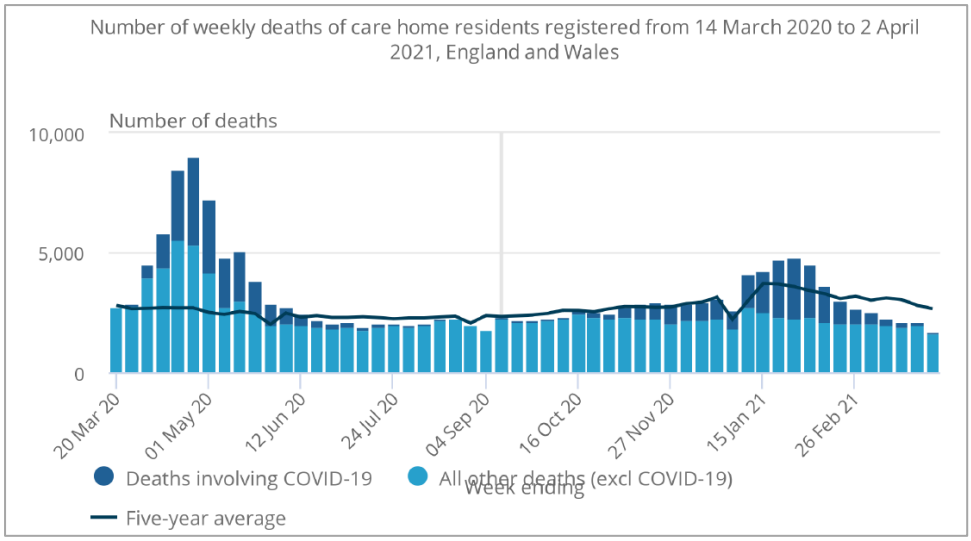
These are the latest R and growth rate estimates by NHS England regions.

Region	R	Growth rate % per day
England	0.8 to 1.1	-3 to 1
East of England	0.8 to 1.1	-5 to 1
London	0.8 to 1.0	-4 to 0
Midlands	0.8 to 1.0	-3 to 0
North East and Yorkshire	0.8 to 1.0	-4 to 0
North West	0.8 to 1.1	-3 to 2
South East	0.8 to 1.0	-5 to -1
South West	0.8 to 1.1	-4 to 1

ONS analysis of the impact of COVID-19 on care homes in England & Wales

The ONS has released provisional analysis (link) of the impact on care homes in England & Wales of the two waves of COVID-19. Amongst many valuable findings, the ONS re-iterates the importance of focusing on excess deaths because the number of COVID-19 registered deaths during the first wave is likely to be under-reported given limitations then on testing capacity.

The number of excess deaths between 14 March and 11 September 2020 was 27,079, as compared to 1,335 excess deaths between 12 September 2020 and 2 April 2021. Explanations include lack of access to care services and rapid testing in the first wave, the early discharge of 25,000 care home residents from hospital to free up capacity, and the availability of vaccines during the second wave.



Difficulties in accessing health services during the first wave are highlighted through analysis of recorded place of death. The excess number of deaths of care home residents who died in their care home during this wave was 25,615, whereas the excess number of deaths for those residents who died in hospital was 1,407. The split of excess deaths in the second wave by place of death was more comparable (2,537 vs 1,223).

To put this into further perspective, 173,974 residents were registered as dying from all causes over the period from 14 March 2020 to 2 April 2021, representing just over 40% of the care home population. The five-year average would have been 145,560 deaths.

OPENSAFELY – identifying how differences between ethnic groups have varied between the two COVID waves in the UK

In several previous Bulletins and Friday Reports, we have referred to the ground-breaking efforts of the OPENSAFELY platform to use electronic health records to better understand drivers of COVID infection, hospitalisation, mortality and most recently vaccination uptake.

A further study (link) published in the Lancet used multivariate Cox regression on a population of 17 million to explore differences in 16 ethnic groups, and in particular to contrast experience between the first and second waves. This new analysis identified that the relative risks for black ethnic groups had reduced in the second wave for hospitalisations (1.78 -> 1.23) and for COVID-19 deaths (1.51->0.92) after allowing for socio-demographic, clinical and household differences.

In contrast, the relative risks for South Asian ethnic groups had actually increased in the second wave for both hospitalisations (1.48->1.89) and for COVID-19 deaths (1.26->1.87).

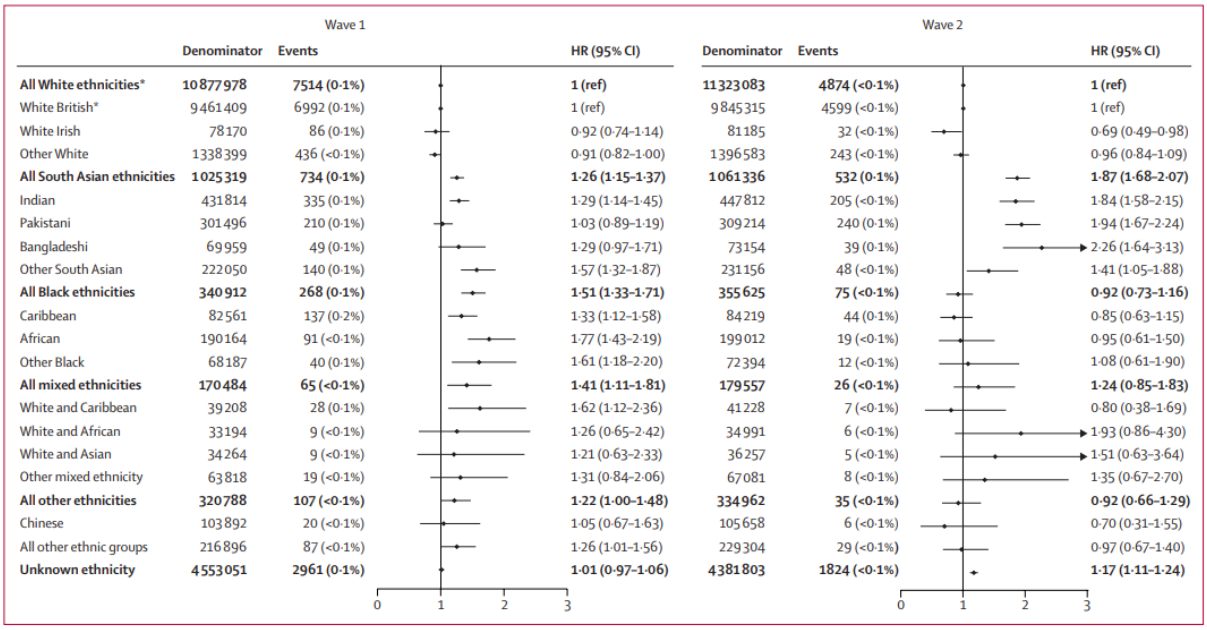


Figure 4: **Ethnic differences in the risk of COVID-19-related death**

And Finally…

With indoor hospitality poised to reopen on Monday, Company Debt (link) is reporting that every adult will have to drink 124 pints of beer to restore pubs to their pre-pandemic level of income. Alternatively 40 roast dinners or 976 packets of crisps would have the same effect. We note that the Pensions Minister has already endorsed this particular campaign.

Whilst increased consumer spending will be vital to assist the economy in recovering from the pandemic, we would suggest that any readers wishing to help their local hostelry spread any support over more than one weekend.

14 May 2021