



Friday Report: Issue 70

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Covid-19 Actuaries Response Group – Learn. Share. Educate. Influence.

Covid-19 is still among the most important health topics for scientific papers and articles. The Covid-19 Actuaries Response Group continues to focus on important Covid-related topics. The group produces an update on the last Friday of every month with a summary of key papers, articles and data.

Vaccines

UK Autumn Boosters ([link](#))

Between September and December the UK will offer a booster of the Covid-19 vaccine to people aged 50 and older, residents in older age care homes, people aged 5 and older who are in a clinical risk group and to front-line health and social care staff.

The booster vaccines will be either Pfizer or Moderna. While the Moderna bivalent Omicron/wild type vaccine will be offered to some, people are urged to accept whichever vaccine has been offered and not delay their appointment.

In exceptional circumstances, the Novavax adjuvanted wild-type vaccine may be used when no alternative UK approved vaccine is available ([link](#)).



Variants

Prevalence of Variants

In previous Friday Reports we noted the proportions of sequenced samples of the newer Omicron sub-lineages in selected countries. This data is now easily accessible via Our World in Data ([link](#)) and shows that BA.5 remains the dominant variant. The ONS infection survey statistics are not currently showing breakdowns by variant because of this BA.5 dominance, but they will resume reporting by variant if changes warrant this.

In the [GISAID](#) data reported by Our World in Data, a low proportion of cases involves newer variants, namely BA.2.12.1 which was first noted in the United States in April and BA.2.75 (nicknamed Centaurus) which appeared to be growing in a number of Asian countries last month. The most recent data for India as at 15 August suggests that 40% of sequenced cases there are BA.2.75.

Maria Van Kerkhove, the Covid-19 Technical Lead at the WHO, has noted that reduced surveillance and sequencing will make it harder to detect new variants ([link](#)).

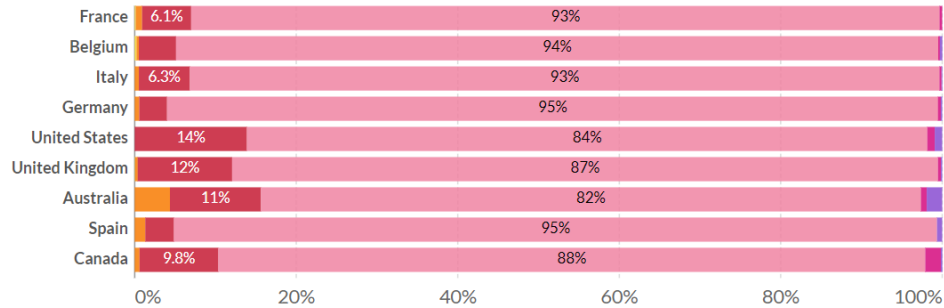
SARS-CoV-2 sequences by variant, Aug 22, 2022

The share of analyzed sequences in the preceding two weeks that correspond to each variant group. This share may not reflect the complete breakdown of cases since only a fraction of all cases are sequenced.

Our World in Data

+ Add country Relative

■ Delta
 ■ Alpha
 ■ Beta
 ■ Gamma
 ■ Omicron (BA.1)
 ■ Omicron (BA.2)
 ■ Omicron (BA.4)
 ■ Omicron (BA.5)
 ■ Omicron (BA.2.12.1)
 ■ Omicron (BA.2.75)
 ■ Other



Source: GISAID, via CoVariants.org - Last updated 22 August 2022

OurWorldInData.org/coronavirus • CC BY

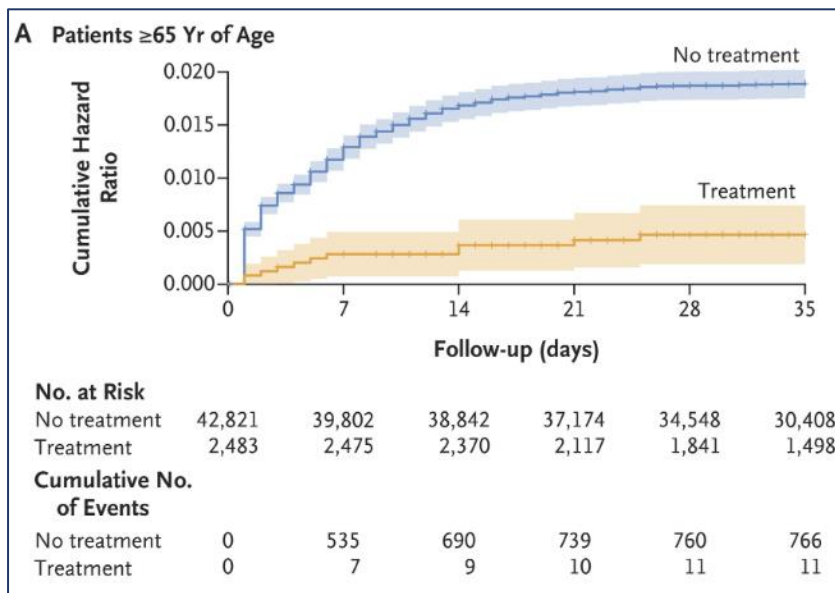
Note: Recently-discovered or actively-monitored variants may be overrepresented, as suspected cases of these variants are likely to be sequenced preferentially or faster than other cases.

Medical

Paxlovid effective at reducing Omicron-related hospitalisations and deaths ([link](#))

A study from Israel has evaluated the effectiveness of oral Nirmatrelvir (Paxlovid) against risk of death and hospitalisation in the presence of Omicron infection. The data came from Clalit Health Services where 3,902 patients received Paxlovid compared with 109,254 patients who met the eligibility criteria for receiving the drug. Eligibility is influenced by age, vaccination status and co-morbidities. The study adjusted for sociodemographic factors, comorbidities, and previous SARS-CoV-2 immunity status.

Cumulative Hazard Ratio for Hospitalisation Due to Covid-19

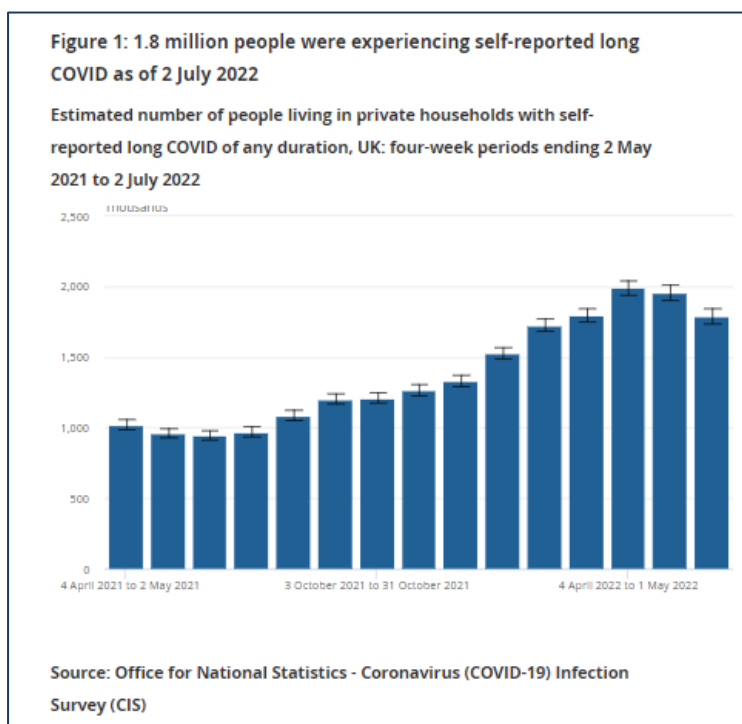


The drug was found to be effective for those aged 65 and older but there was no evidence of benefit for under 65s. For people aged 65 and above, the adjusted hazard ratio for risk of hospitalisation was 0.27 (95% CI 0.15 to 0.49). The adjusted hazard ratio for death due to Covid-19 was 0.21 (95% CI, 0.05 to 0.82).

Long Covid

Long Covid numbers decrease in the UK ([link](#))

The ONS's monthly study on those with Long Covid (LC) symptoms in the UK has started to show a fall in the number of cases. The study uses self-reported symptoms with a threshold of 4 weeks of post-infection symptoms for inclusion in the figures. The data is at 2 July 2022 so reflects recovery from the BA.1/BA.2 wave which peaked in late March / early April. The BA.5 wave peaked in early July so we might expect the LC numbers to rise again when these infections become eligible for inclusion.



Of the 1.8m people estimated to have had LC symptoms at 2 July, over 72% (1.3m) say that the symptoms adversely affect their ability to undertake day to day activities, with 21% saying that they have been “limited a lot”.

Over 761,000 people are estimated to have experienced symptoms for over a year, with over 380,000 now having experienced symptoms for over two years (and thus having been infected in the initial wave in March and April 2020).

Biomarkers for Long Covid

Researchers are hunting for biomarkers that can point to the reasons for Long Covid symptoms in order to develop suitable therapies.

A pre-print study from South Africa involving blood samples from 10 healthy controls and 20 Covid-infected patients has suggested that the extent of fibrin amyloid microclots is predictive of disease severity ([link](#)). Fibrinogen is produced in the liver and can clot into amyloid form which can eventually block blood vessels.

A study from Ireland involving blood samples from 50 patients with Long Covid, 36 acute Covid patients and 10 healthy controls found that patients with Long Covid had higher levels of a protein called Von Willebrand Factor (VWF) which enables blood clotting, and lower levels of a protein that normally breaks down VWF, called ADAMTS13. This suggests that excessive blood clotting may play a role in Long Covid ([link](#)).

A pre-print study from the US involving samples from 215 participants has shown that levels of cortisol are uniformly lower among those with Long Covid relative to matched control groups ([link](#)). Cortisol is a hormone that regulates a number of body functions and low levels of cortisol can cause fatigue.

Heart disease after Covid

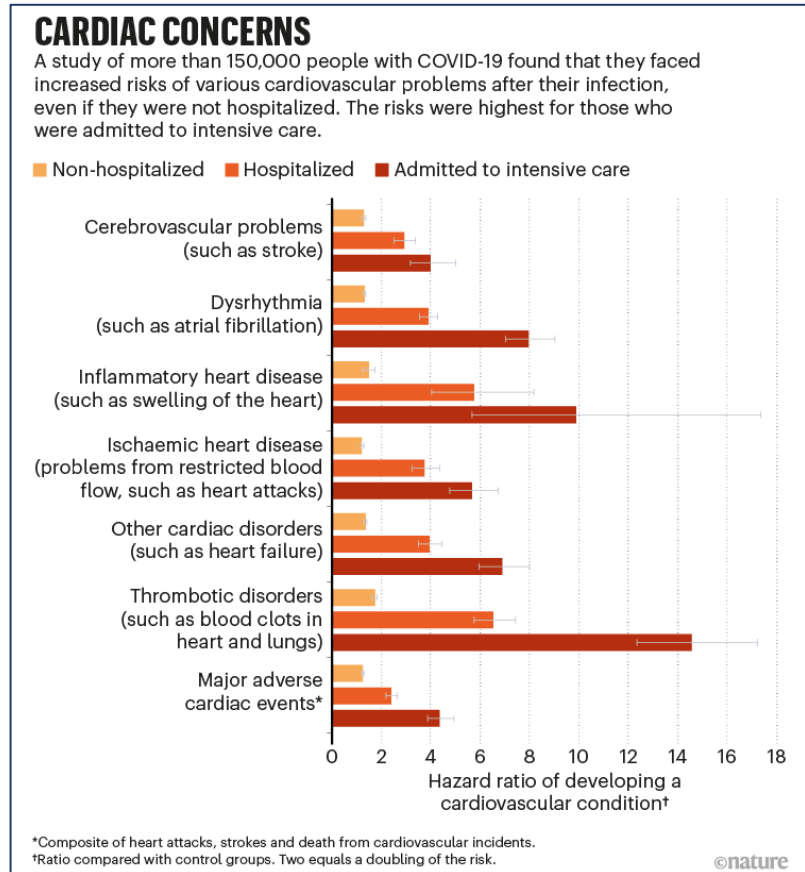
A recent article in Nature ([link](#)) sets out what is known about cardiovascular risk after Covid infection as well as ongoing studies into this topic. A study of 150,000 US veterans found elevated risks for 20 cardiovascular infections, including heart attacks and strokes, in the year after Covid infection.

The article suggests that post-Covid cardiovascular problems may be linked to blood clots.

A study based on more than 500,000 Covid-19 cases found that people who had been infected had a relative risk of 2.67 of developing a blood clot in the two weeks after infection compared with people who had had influenza.

Another possibility is that the immune system ramps up in response to Covid infection and inadvertently attacks the body's organs, including the heart.

UK studies have also shown higher risk of cardiovascular problems after Covid infection or hospitalisation.



In the US, the REsearching Covid to Enhance Recovery (RECOVER) project aims to follow 60,000 people for 4 years to catalogue Long Covid symptoms in subjects with Long Covid as well as among healthy controls.

In the UK, the Post-hospitalisation Covid-19 study (PHOSP-Covid) will focus on people who were hospitalised with Covid-19 to determine the prevalence of ongoing symptoms.

Neurological and psychiatric risk trajectories after Covid infection [\(link\)](#)

A study published in The Lancet reported on the incidence rates of neurological and psychiatric disorders among patients diagnosed with Covid relative to incidence of these disorders among a control group who were diagnosed with other respiratory infections during the study period. The study found a transient increase in mood and anxiety disorders, with risks returning to baseline after 1 to 2 months. The study found a persistent increase in risk of cognitive deficit (or “brain fog”), dementia, epilepsy or seizures, insomnia, myoneural junction or muscle disease and psychotic disorder.

	Hazard ratio (95% CI)	p value	Risk horizon (days)	Time to equal incidence (days)
Anxiety disorder	1.13 (1.11-1.15)	<0.0001	58	417
Cognitive deficit	1.36 (1.33-1.39)	<0.0001	NR	NR
Dementia	1.33 (1.26-1.41)	<0.0001	NR	NR
Encephalitis	0.96 (0.85-1.08)	0.50
Epilepsy or seizures	1.14 (1.09-1.19)	<0.0001	NR	NR
Guillain-Barré syndrome	1.12 (0.97-1.30)	0.12
Insomnia	1.13 (1.10-1.16)	<0.0001	90	NR
Intracranial haemorrhage	1.09 (1.01-1.18)	0.020	506	658
Ischaemic stroke	1.11 (1.06-1.17)	<0.0001	66	712
Mood disorder	1.08 (1.06-1.11)	<0.0001	43	457
Myoneural junction or muscle disease	1.89 (1.76-2.04)	<0.0001	497	NR
Nerve, nerve root, and plexus disorder	0.89 (0.87-0.91)	<0.0001
Parkinsonism	1.04 (0.92-1.17)	0.58
Psychotic disorder	1.27 (1.18-1.37)	<0.0001	NR	NR
Any first outcome	1.13 (1.11-1.15)	<0.0001	48	469

The risk horizon is the time at which the time-varying hazard ratio returns to 1 (ie, the baseline risk in the comparison cohort). The time to equal incidence is the time at which the cumulative incidences of the two cohorts become equal. The risk horizon and time to equal incidence are only included for outcomes with a significantly increased hazard ratio at 6 months; for outcomes that did not reach the risk horizon or time to equal incidence within the follow-up period (up to 730 days), they are shown as not reached (NR).

Table 2: Risk of neurological and psychiatric sequelae at 6 months, risk horizon, and time to equal incidence for each diagnosis after COVID-19 versus after other respiratory infections, in the propensity-score matched population

The data was extracted from the TriNetX electronic health records network, an international network of de-identified healthcare data mostly from the USA, but also from Australia, the UK, Spain, Bulgaria, India, Malaysia, and Taiwan. The subjects were 1.3m patients with COVID-19 diagnosed between 20 January 2020 and 13 April 2022 who were matched 1:1 to patients diagnosed with another respiratory infection.

Modelling

QCovid4 – Predicting risk of death or hospitalisation from COVID-19 in adults testing positive for SARS-CoV-2 infection during the Omicron wave in England (Hippisley-Cox et al ([link](#)))

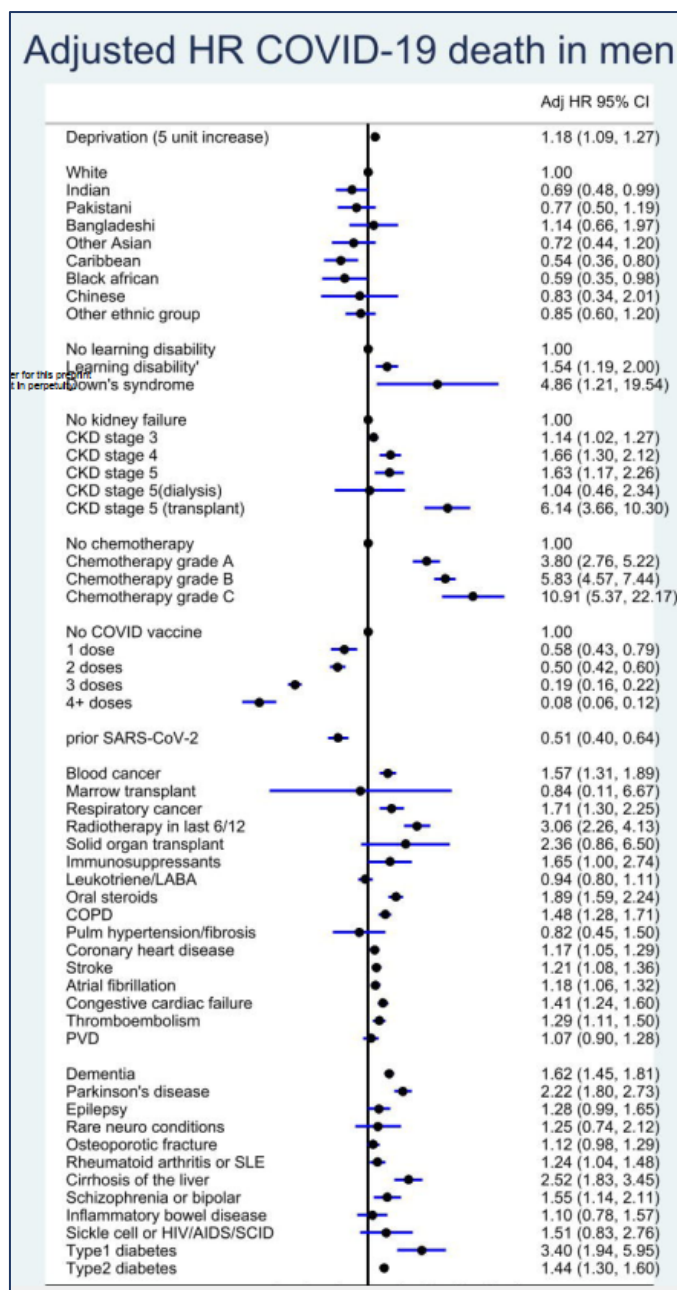
This pre-print aims to come up with algorithms to estimate the risk of hospitalisation and mortality in UK adults during the Omicron pandemic wave. It also evaluates the performance of previous versions of similar algorithms produced by the same group.

The dataset used is the QResearch database, including 1.3 million adults in the cohort used to derive the algorithms and 0.15 million adults in the cohort used to validate the algorithms. All individuals were aged 18-100, tested positive between 11 Dec 2021 and 31 March 2022, and were followed up to 30 June 2022.

The paper finds that the new QCOVID4 model more accurately identifies those at highest levels of absolute risk than the approach adopted by NHS Digital. It also finds that factors associated with increased risk in the original (QCOVID1) and second wave (QCOVID2) models were mostly still associated with increased risk in the QCOVID4 model, although previously elevated risks for South Asian and Black ethnicity were not apparent in the latest model.

The paper presents results for death by sex and hospital admission by sex; we show here the male death results.

Particularly interesting are the ethnic results (low BAME HRs), the strong effect of 3 or more vaccine doses, and the diabetes effects (Types 1 and 2).



Comparison of the 2021 Covid-19 roadmap projections against public health data in England (Keeling et al ([link](#)))

This is a retrospective of the modelling carried out by the Warwick team which fed into six Roadmap documents, co-ordinated through SPI-M-O (a subgroup of SAGE). This modelling helped to shape the relaxation of restrictions in England after January 2021.

The team stress that model projections are not forecasts (they represent illustrative scenarios), but note that the outcomes should be broadly consistent with actual outcomes if they are to be used in public health planning.

The paper analyses the actual dynamics of precautionary behaviour over time, and compares these with the scenarios set out in their models. The authors conclude that there was high agreement between the projections made and the trajectory of the epidemic, and that this agreement generally increased over time. They note the difficulties in communicating these projections to a lay audience, evidenced by some mistrust in the projections despite accurate assessments of the range of burdens on public health.

Modelling the medium-term dynamics of SARS-CoV-2 transmission in England in the Omicron era (Barnard et al ([link](#)))

This paper projects infections, hospital admissions and deaths in England to December 2022, noting and evaluating some of the key uncertainties (behavioural change, waning immunity, seasonality). It also assesses the effectiveness of the booster vaccinations in reducing the burden of disease over the period from October 2021 and December 2022. The emergence of new variants is explicitly not modelled.

The counterfactual where no booster programme was employed suggests that boosters will lead to 23,400 fewer deaths and 108,000 fewer hospitalisations between October 2021 and December 2022.

The base case scenario modelled results in 5.29 million infections, 65,200 hospital admissions, and 6,130 deaths between May and December 2022. A high waning scenario results in similar outcomes, whilst a very high waning scenario results in an earlier wave of infection, with 4,170 additional deaths compared with the base case scenario.

Data

Direct and indirect health impacts of COVID-19 in England ([link](#))

The Department of Health and Social Care and ONS have issued the fourth update in their research series that looks at direct and indirect impacts of Covid-19 in England. Previous editions were published on 18 September 2020, 29 January 2021 and 17 September 2021.

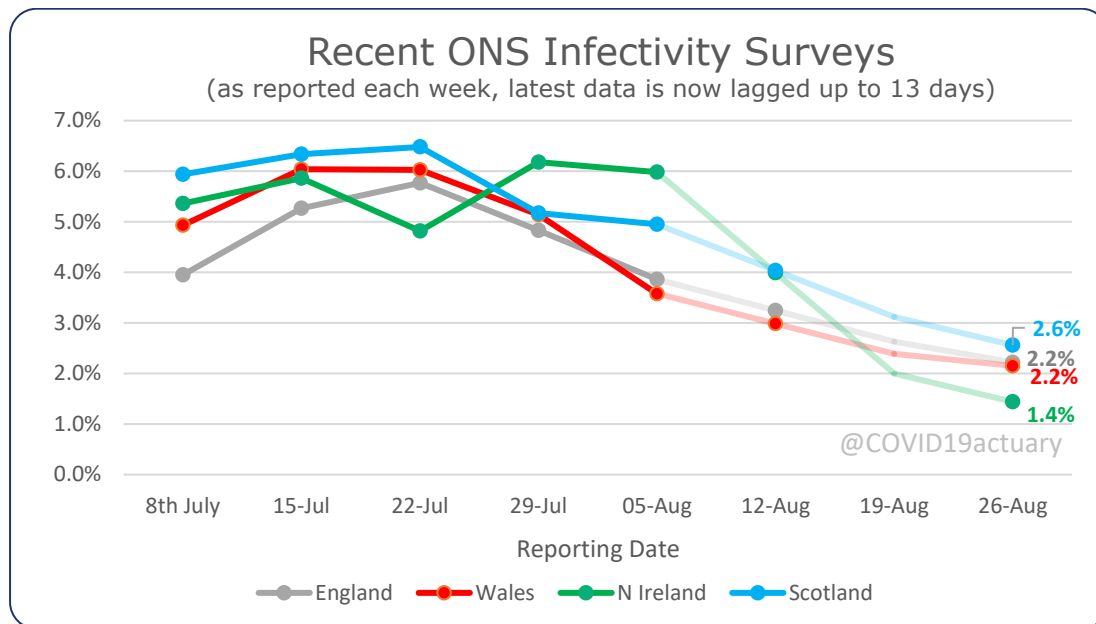
This paper gives a high-level overview of the short- and long-term health harms that have arisen as a consequence of Covid-19 infections and mitigating behaviours. The analysis covers the period from March 2020 (the start of the pandemic) to June 2022 where data permits.

The paper considers four areas, and we note the key findings from the latest version of the paper.

Area	Key findings
Direct mortality and morbidity impacts of Covid-19	<ul style="list-style-type: none"> • Deaths and hospitalisation due to Omicron have been much lower compared to previous infection waves. • An estimated 2 million people are experiencing self-reported Long Covid symptoms. High Covid infection rates since the emergence of the Omicron variant have led to increased Long Covid prevalence.
Impact of Covid-19 on NHS critical care capacity	<ul style="list-style-type: none"> • Omicron did not increase the number of Covid-19 positive patients in critical care beds. • Increases in staff absence may have led to increased pressure in critical care.
Indirect impacts of Covid-19 on population health due to living through a pandemic and restrictions	<ul style="list-style-type: none"> • Primary care appointments and referrals were resilient during the Omicron wave of infection. However, lower overall activity across the pandemic has led to 'missing' appointments and referrals. • The reported incidence of some conditions has returned to pre-pandemic trends, other conditions are still persistently below the pre-pandemic trend. • High levels of staff absence continue to put pressure on the NHS. • Supply constraints during the Omicron wave of infection have led to longer waits for elective and emergency patients in secondary care. • Elective activity remains below pre-pandemic levels. • Referrals to and people in touch with mental health services are higher than pre-pandemic levels.
Indirect impacts of Covid-19 on the wider population in the long-run	<ul style="list-style-type: none"> • Adult social care has suffered pressures since before the pandemic which have since been exacerbated, including workforce pressures. • Economic impacts from Omicron have been smaller compared to those seen during previous waves of infection. • Non-Covid-19 pressures mean that the wider economic climate remains fragile.

ONS Infection Study [\(link\)](#)

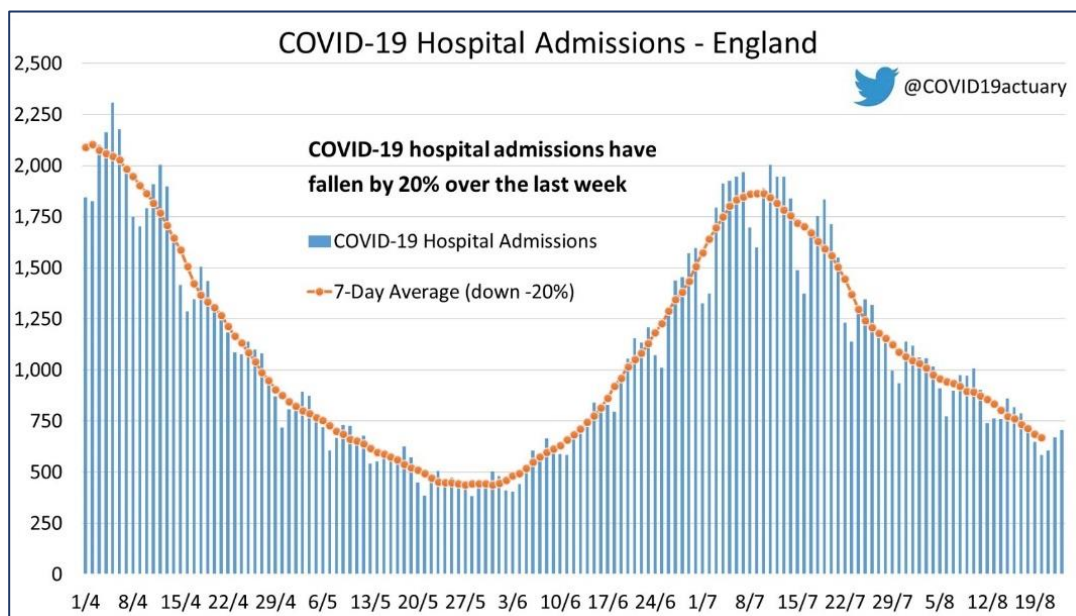
The percentage of people testing positive for Covid-19 has been falling over the most recently reported 5 weeks according to the ONS's random community survey.



The figures reported each week are now estimated to represent prevalence with a lag of 13 days following a change to postal rather than doorstep engagement. In July the lag was estimated to be 9 days. Figures were not reported in the week ending 12 August and after that the figures reflect the new survey characteristics.

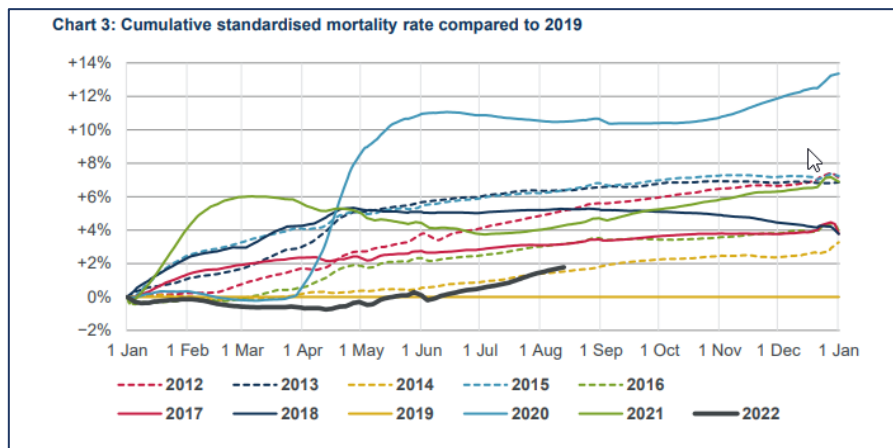
Hospitalisations

Covid-19 hospital admissions have fallen from over 1000 per day at the end of July to around 700 per day in late August. Routine asymptomatic Covid testing in hospitals is about to be paused which may result in a further drop in numbers of hospitalisations attributed to Covid.



Deaths

The weekly Mortality Monitor produced by the CMI shows that in England and Wales there has been excess mortality since April 2022, reversing the positive gains in the first quarter of the year ([link](#)). The excess is calculated on an age-standardised basis with 2019 serving as the reference year. The cumulative mortality rate including death registrations up to 12 August 2022 is now 1.8% above 2019's rate.



In a recent blog ([link](#)), Stuart McDonald sets out possible reasons for this out of season excess:

- Elevated cardiovascular risk following Covid-19 infection
- Current delays for urgent treatment in the NHS
- Missed and delayed diagnoses earlier in the pandemic

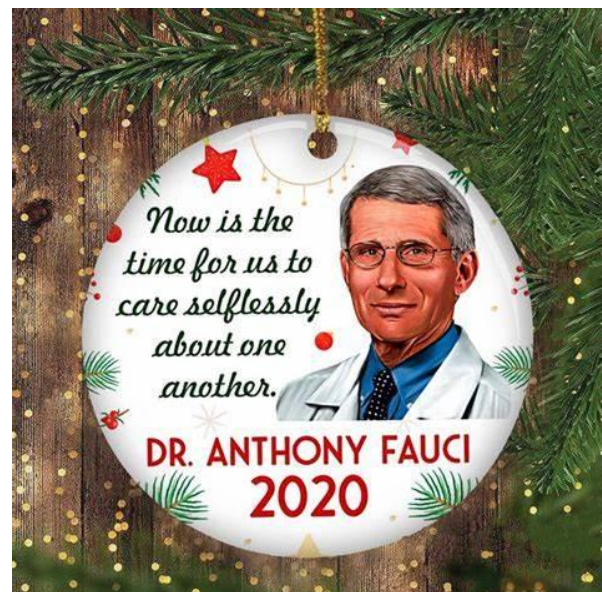
And Finally ...

Dr Fauci steps down but is not retiring ([link](#))

Dr Anthony Fauci is stepping down from his role as Chief Medical Adviser to the White House and director of the USA's National Institute of Allergy and Infectious Disease (NIAID).

Over the course of his 50 years of government service, Dr Fauci has advised seven US presidents on a host of issues including HIV/AIDS, West Nile virus, anthrax attacks, pandemic flu, bird flu, Ebola, Zika, Covid and monkeypox. He was awarded the Presidential Medal of Freedom in 2008.

At the height of the Covid pandemic, in his role as key US top infectious disease advisor, Dr Fauci became a celebrity, with his face adorning merchandise ranging from t-shirts to holiday ornaments.



At the age of 81 he says he has no plans to retire and is stepping down to pursue the next phase of his career.

26 August 2022