

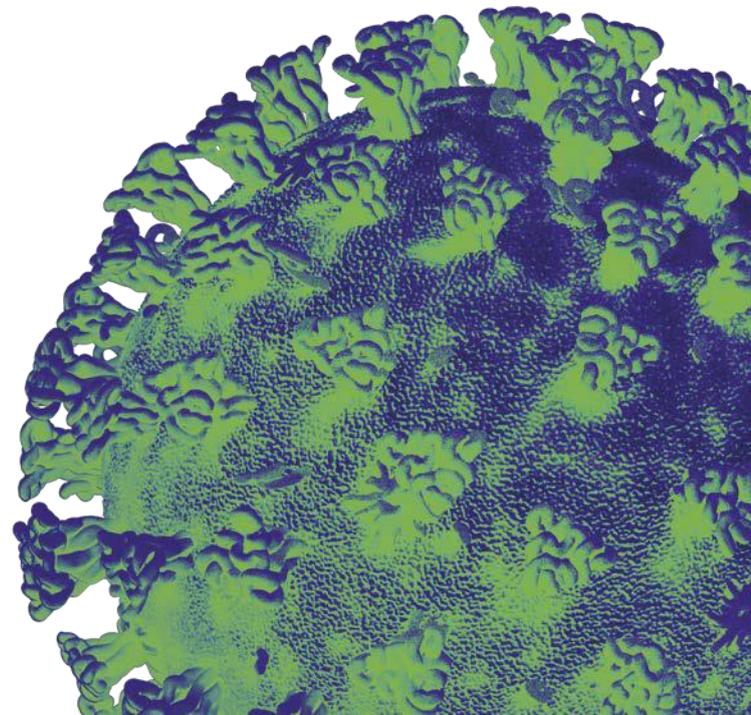
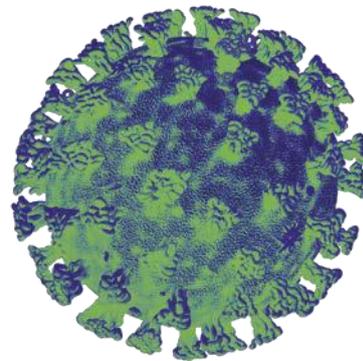
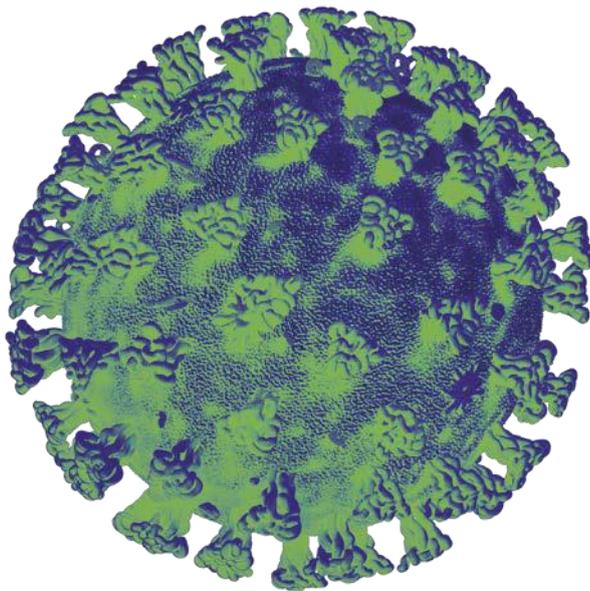


Llywodraeth Cymru
Welsh Government

Technical Advisory Cell

Summary of Advice

1 April 2022



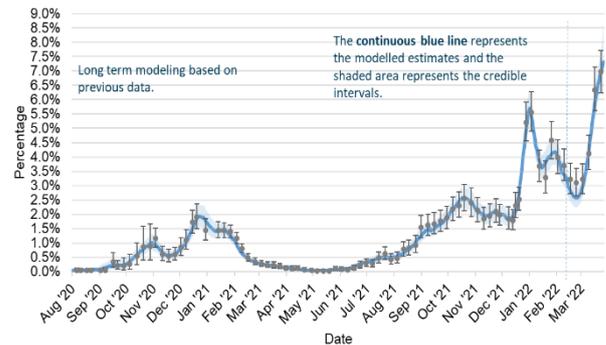
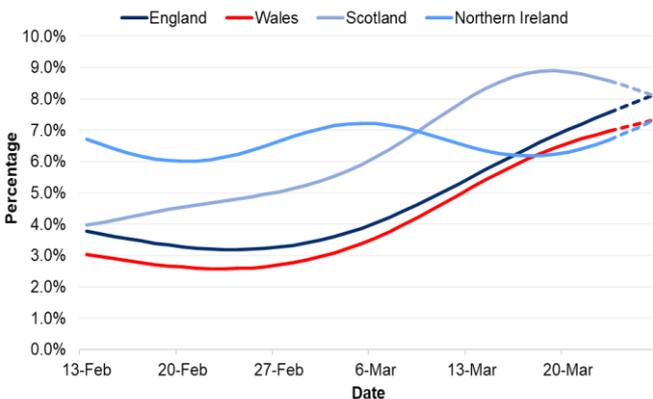
Technical Advisory Cell: COVID-19 evidence brief

01 April 2022

Wales Sitrep

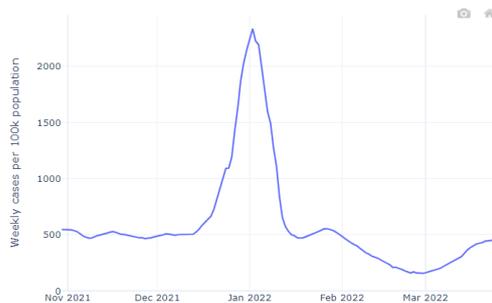
Recent estimates from the [ONS COVID Infection Survey](#), which provides a relatively unbiased but lagged estimate of levels of infection. The survey suggests in the period 20 to 26 March 2022 the percentage of people testing positive for COVID-19 increased in the most recent week. For the week 20 to 26 March 2022, it is estimated 6.97% of the community population had COVID-19 (95% credible interval: 5.62% to 7.13%). This equates to approximately 1 person in every 14 (95% credible interval: 1 in 18 to 1 in 14), or 192,900 people during this time (95% credible interval: 170,900 to 216,800) and are the highest recorded estimates for Wales from the COVID-19 Infection Survey.

- At a UK level, the ONS estimates that in the most recent week the percentage of people testing positive for COVID-19 has continued to increase in England, Scotland and Wales. In Northern Ireland, the percentage of people testing positive for COVID-19 has decreased in the most recent week. ONS estimates that around 1 in 14 people (6.97%) had COVID-19 during this period, compared to 1 in 13 in England (7.56%), 1 in 12 in Scotland (8.57%) and 1 in 15 (6.7%) in Northern Ireland.



- Note that the below PHW case data will be impacted by changes to testing behaviours and upcoming policy changes.** As at 25 March case numbers in Wales have increased by 9.5% compared to the previous week to 455 per 100,000, reflecting an apparent reduction in the rate of increase. Test positivity as reported by PHW has also increased in the most recent week but show signs of a reduced rate of growth, increasing from a weekly average of 38% in the previous week to 40% on 25 March.

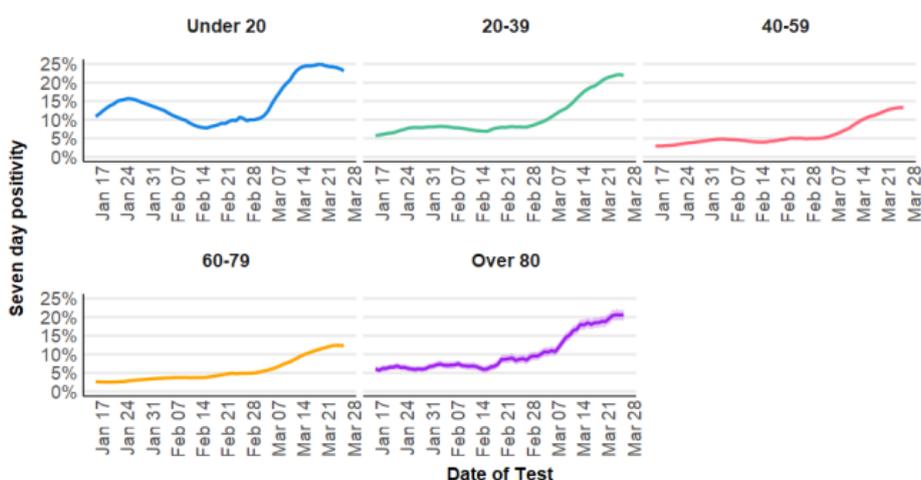
Cases per 100k (PHW Data) (7 day rolling sum)



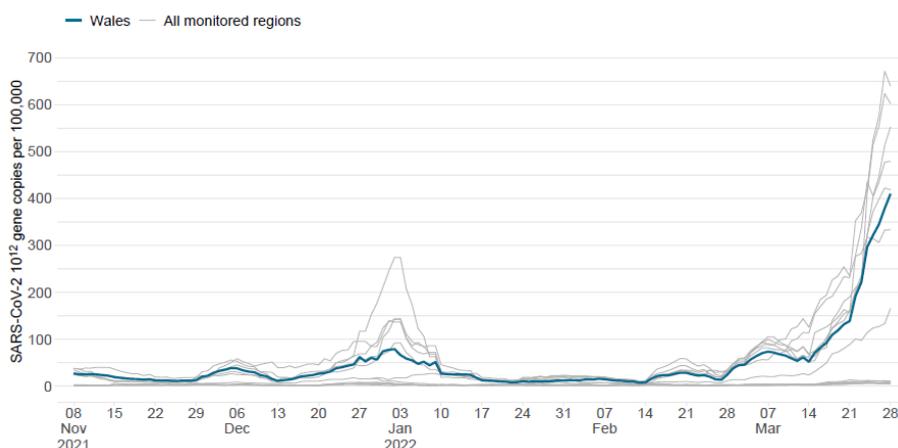
Positivity rate for COVID-19 (PHW Data) (7 day rolling average)



- Cases have increase in all age groups with the exception of under 10s in the most recent week, remaining highest in the 30-39 and 40-49 group at 700 and 592 cases per 100,000 respectively. As per the main case trends, there are signs that the growth observed since the beginning of March has begun to slow down. This is also the case with PHW reported hospital admissions by age, with decreases observed in all age groups over 60 in the most recent week.
- The most recent PHW [weekly Lateral Flow Testing Surveillance Report](#) suggests that for the week ending 30 March The number of LFTs reported increased from 239,485 in the previous week to 240,757. The number of positive testing episodes increased from 239,485 in the previous week to 240,757. The episode positivity rate increased from 22.83% in the previous week to 24.37%. The 20-39 age group recorded the highest incidence rate of 1307.0 positive testing episodes per 100,000 population. This also suggests that lateral flow test positivity may have peaked in most age groups (see below_, although this data is experimental and should be interpreted with caution.



- Waste water surveillance dated 31 March suggests since last week, SARS-CoV-2 viral load has increased across the country (excepting north-west Wales). Trends in the national mean wastewater signal are somewhat unstable, but the overall direction is upward across most of the country. There are indications in several regions in the north of Wales that the signal is beginning to level off or decline.

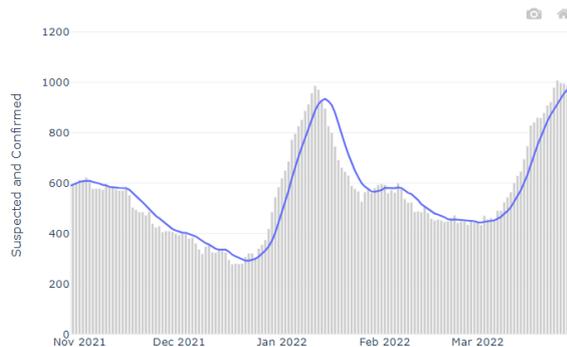


- As at 31 March, NHS Wales is under considerable pressure, with 14 out of the 20 sites at level 4 and two sites in business continuity. COVID continues to have an impact on primary, secondary and social care staff with increasing volumes of care home closed

to admission and sustained demanding impacting hospital flow. In the most recent data points there are signs of an improving picture, although it is uncertain if this trend will continue.

- The total number of COVID related patients in a hospital bed has increased to 1,466, 41 (3%) higher than the same day last week. The number of confirmed COVID cases in hospital has improved and is at 860 patients currently occupying a bed, 71 (7%) lower than last week.

StatsWales Hospital bed occupancy of suspected and confirmed COVID-19 positive patients (7 day rolling average)



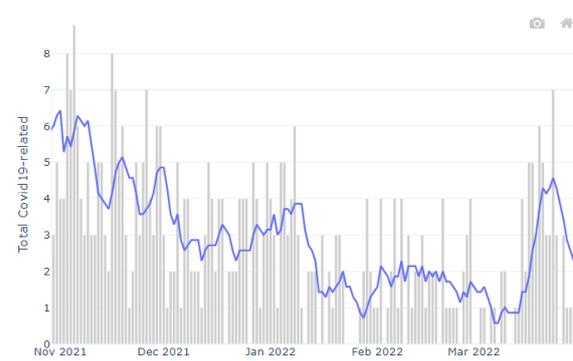
StatsWales Invasive ventilated bed occupancy of suspected and confirmed COVID-19 positive patients (7 day rolling average)



StatsWales Hospital admissions of suspected and confirmed COVID-19 positive patients (7 day rolling average)



ICU admissions of COVID-19 positive patients per day (7 day rolling average)



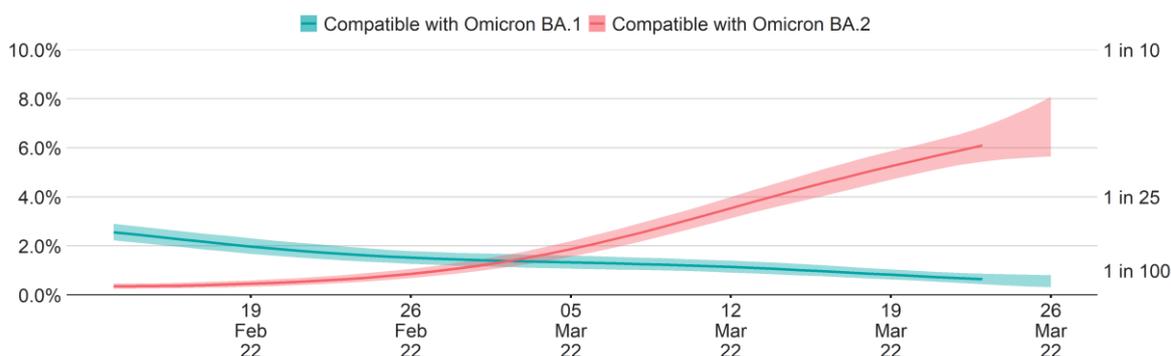
- The number of occupied surge and normal beds in a critical care environment is 173, 21 higher than the pre-COVID baseline and 3 lower than the previous week. The number of COVID related patients in critical care is at 17 occupying a bed, 3 higher than the previous week. The low volume continues to assure that COVID patients are less acutely unwell when compared to historic waves.
- Of the 691 confirmed COVID patients in an acute and major acute hospital bed (excluding Velindre), 91 patients (13%) are being treated primarily for COVID.
- As at 25 March the number of weekly COVID-19 deaths reported by PHW has increased by 28.6% 45 deaths compared to 35 the previous week. Lagged [ONS death reporting](#) up to 18 March shows a 17.5% increase in COVID deaths to 47 in the most recent week compared to 40 in the previous week. The total number of deaths registered in Wales was 669; 50 fewer than the previous week and 7.1% below the five-year average (51 fewer deaths).
- As at 23 March, 170 adult care homes in Wales have notified CIW of one or more confirmed cases of COVID-19, in staff or residents, in the last 7 days. 299 adult care homes in Wales have notified CIW of one or more confirmed cases of COVID-19, in staff or residents, in the last 20 days. In the last two weeks. There are 1,033 adult care

homes and 17 adult and child care homes in Wales. CIW have been notified of 250 reported death of care home residents, of which 12 were reported as COVID-19 related (Source: [StatsWales](#)).

- As at 30 March UKHSA estimate the Reproduction number (R) for Wales to be between 1.0 and 1.2 with a doubling time 20 to 36 days, while PHW's estimate of R for Wales, which is less lagged, is 1.05 with a doubling time of 26 days.
- As at 29 March 2022 in the most recent 7 day period Wales has genomically confirmed **+5,985** cases of the **Omicron** variant (112,188 total to date), of which **+1,003** (55,454 total) were **BA.1**, **+5,467** (15,769 total) were **BA.2** and **-485** (40,965 total) were 'Omicron not elsewhere classified'. No other variants of concern were confirmed by genomic sequencing in Wales in the most recent weekly period.
- Note on above: Due to the addition of the new VUI-22JAN-01 (BA.2), the genotype definition (as opposed to full sequencing) is no longer specific enough to whether an omicron case is BA.1 or BA.2. As a result Omicron cases identified by genotyping have been separated into their own category called "Omicron not elsewhere classified". This new category also includes sequenced cases defined as another lineage (e.g. BA.3), or private lab cases where we do not have enough information to further classify the case. **This category is likely to have negative changes as genotyped cases are confirmed as a specific lineage and moved into their respective categories.***
- The most recent ONS Coronavirus Infection Survey (see below) suggests that the percentage of people testing positive for strains compatible with Omicron BA.1 (blue) has decreased over the most recent two weeks, but the trend is uncertain in the most recent week. The percentage of people testing positive for strains compatible with the Omicron BA.2 (red) has continued to increase in the most recent week.

Percentage of people testing positive for COVID-19 in Wales

Modelled daily estimates



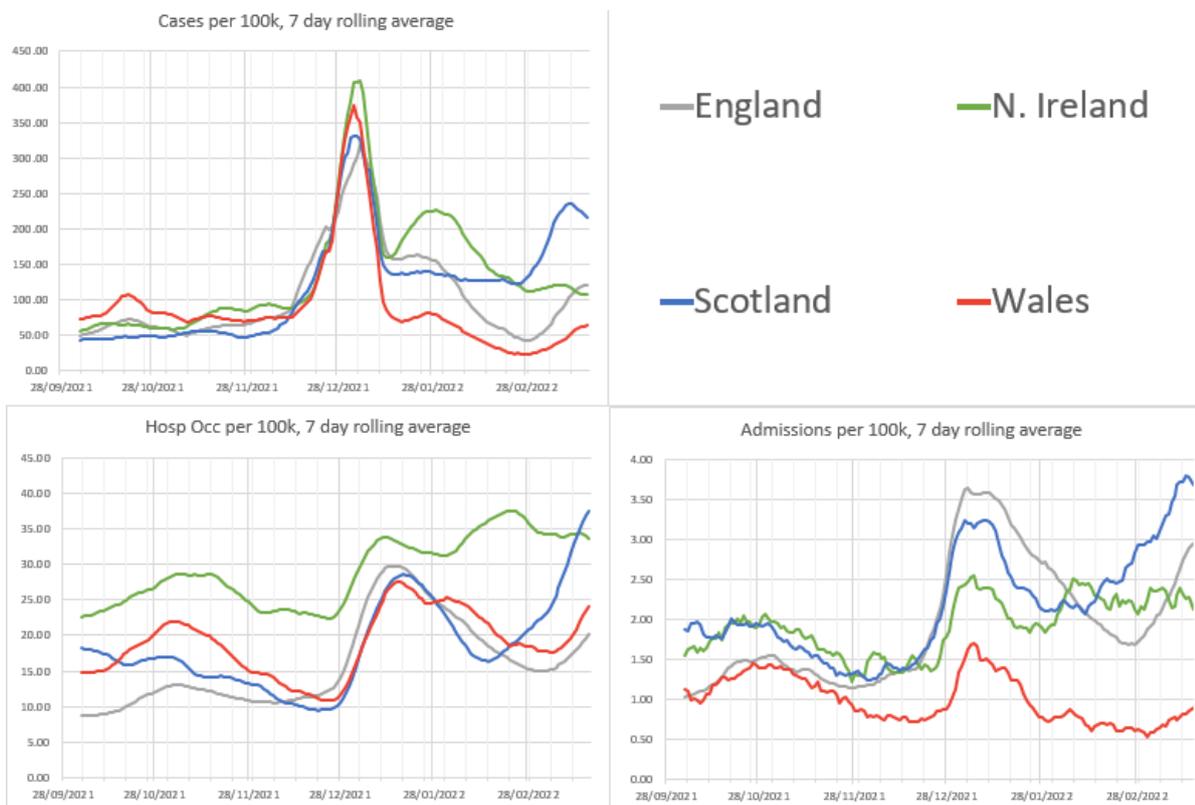
- PHW continue to [report](#) that **while influenza is not yet circulating widely, confirmed case numbers have increased in recent weeks**. During Week 12 (ending 27/03/2022) there were 46 cases of influenza confirmed. Confirmed cases of Respiratory Syncytial Virus (RSV) in children aged under 5 years increased to low levels this week. COVID-19 cases continue to be detected in symptomatic patients in hospital and in the community. Rhinovirus and adenovirus are the most commonly detected cause of non-COVID-19 Acute Respiratory Infection (ARI), with increasing confirmed cases in recent weeks.
- Welsh Government's [survey of public views](#) on COVID-19 dated 11 to 14 March 2022 found that perceptions of the threats posed by coronavirus remain at a low level this wave, after falling significantly in previous waves. The proportion of people only leaving

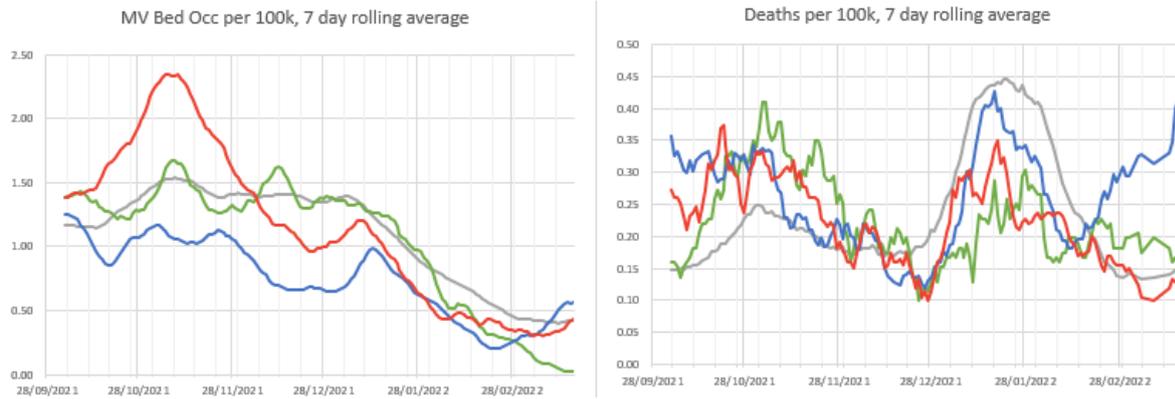
home for essential journeys and people trying to keep two metres away from others when out are at the lowest level recorded by this survey. About three quarters of people wear a face covering to protect themselves from COVID, and a third of people in work currently work from home.

- The Welsh Government and the NHS are generally seen to be doing a good job, with about two thirds of the Welsh public now saying the Welsh Government is doing a good job at containing the spread of the virus. Over a third of people are concerned they will not be able to pay their bills one month from now.
- Google mobility data dated 30 March suggests in the most recent week, using January to February 2020 as a baseline, public transport mobility increased by 3.6 percentage points -28.8 %. Residential (i.e. people spending time at home) decreased by 0.8 percentage points to +4.6%. Retail & recreation mobility increased by 6 percentage points to -1.6%. Supermarkets & pharmacy increased by 6.6 percentage points to +12.8%. Workplace mobility decreased by 0.6 percentage points to -20.1%.

UK Summary (UK Coronavirus Dashboard data)

- **Note that this data is classified as management information rather than official statistics and there may be differences in methodology between the nations.** As a result caution should be taken when interpreting this data. For example Wales admissions, unlike the other UK nations, does not include hospital acquired infections. Full documentation is available at [Metrics documentation | Coronavirus in the UK \(data.gov.uk\)](https://www.data.gov.uk)



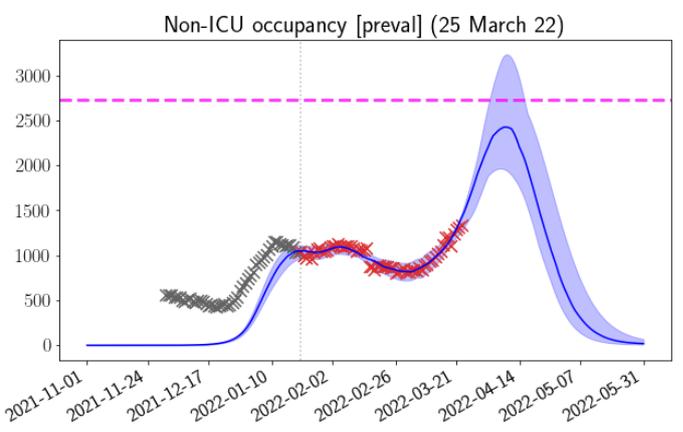
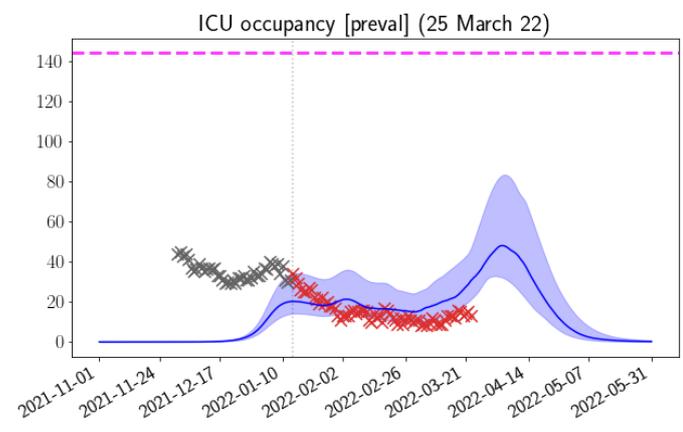
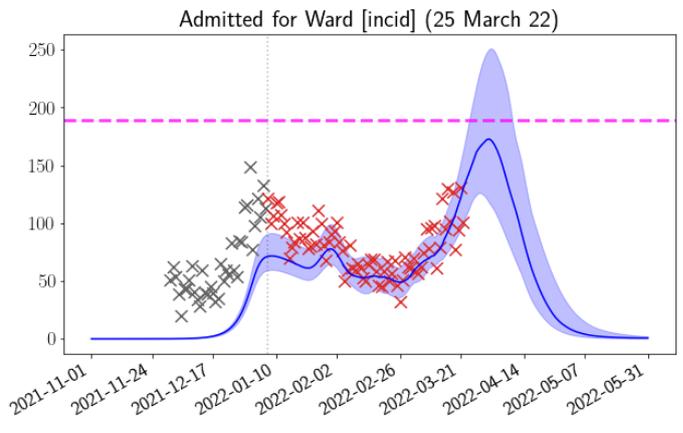
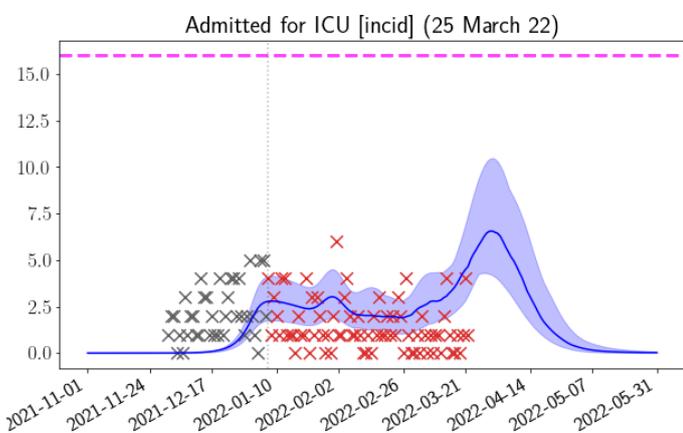


International – WHO update

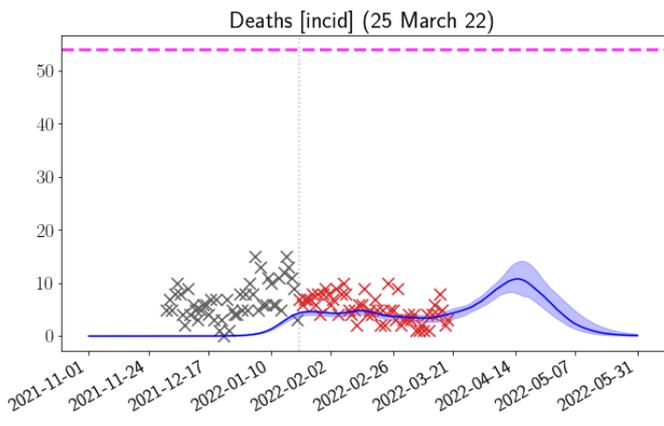
- The WHO Weekly Epidemiological Update [dated 22 March](#) reports that after a consistent decrease since the end of January 2022, the number of new weekly cases rose for a second consecutive week, with a 7% increase reported during the week of 14 through 20 March 2022, as compared to the previous week. The number of new deaths has continued a decreasing trend (-23% as compared to the previous week). Across the six WHO regions, over 12 million cases and just under 33 000 deaths were reported.
- As of 20 March 2022, over 468 million confirmed cases and over 6 million deaths have been reported globally.
- At the regional level, the number of new weekly cases increased in the Western Pacific region (+21%), remained stable in the European region, and decreased in the Eastern Mediterranean (-41%), Africa (-33%), South-East Asia (-23%) and Americas (-17%) regions.
- The current global epidemiology of SARS-CoV-2 is characterized by the global dominance of the Omicron variant. Among the 412 982 sequences uploaded to GISAID with specimens collected in the last 30 days, 412 119 (99.8%) were Omicron and 259 (0.1%) were Delta.
- Among the major Omicron descendent lineages, weekly trends (show that the relative proportion of BA.2 has increased steadily since the end of 2021, with BA.2 becoming the dominant lineage by week seven of 2022. However, the absolute numbers of submitted BA.1 and BA.1.1 sequences, as well as an apparent plateau in the absolute number of BA.2 sequences indicate a recent declining trend in the descendent lineages of Omicron since the beginning of 2022. This trend should be interpreted with some caution, as data for the most recent weeks may be incomplete due to the delay between specimen collection and submission of sequences to GISAID. This data should be interpreted with due consideration of surveillance limitations, including differences in sequencing capacities and sampling strategies between countries, as well as delays in reporting.

Swansea University Medium Term Projections

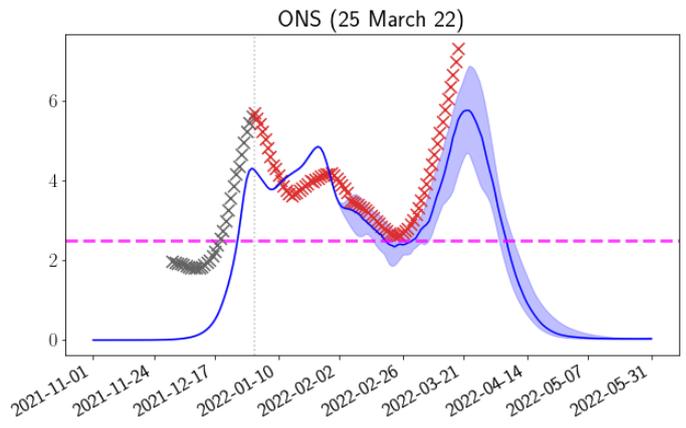
- As discussed in TAC's recent [21 day review advice](#), going forward Swansea University will be providing weekly Medium Term Projections. These scenarios are recalibrated each week depending on what has happened the week before.
- The most recent MTPs show a more challenging situation than last week, which is driven by hospital cases continuing to increase, and ONS prevalence reaching higher levels than any time since the survey began, which may be caused by changes in behaviour and the more transmissible BA2 subvariant.
- The modelled total hospital occupancy of up to around 2,500 beds occupied by covid patients will be very challenging if it is realised, as this is around 25% of the total bed base in Wales and is close to the peak seen in January 2021. However a high proportion of hospital cases are incidental and nosocomial, rather than community acquired cases who often require oxygen. Modelled occupancy includes recent long length of stay estimates, and if challenging levels are reached the peak could be reduced by shorter length of stay, as seen at previous stages of the epidemic.
- The burden of disease continues to be focused more around high prevalence rather than severe outcomes, with ICU occupancy and deaths projected to increase but both less than a third of the peaks seen in previous waves, which reflects high vaccine uptake and the lower intrinsic severity of the Omicron variant.
- These projections suggest a possible peak in the next two weeks, but in reality we may see a longer tail of continued high prevalence than these scenarios predict, as we saw with the Delta wave.



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COVID-19 evidence roundup- summary:

This section aims to summarise a selection of the recent COVID-19 papers, reports and articles that are relevant to a Welsh context or contain new data, insights or emerging evidence relating to COVID-19. It may contain pre-print papers, which should be interpreted with caution as they are often not yet peer-reviewed and may be subject to change when published. The exclusion of any publication in this section should not be viewed as a rejection by the Technical Advisory Cell.

Variants and vaccine effectiveness**UKHSA vaccine surveillance report, Week 12 ([Study link](#))**

- UKHSA continue to advise that, based on the results of several studies, vaccine effectiveness against symptomatic disease with the Omicron variant is substantially lower than against the Delta variant, with rapid waning. However, protection against hospitalisation remains high, particularly after 3 doses.
- After 2 doses of the AstraZeneca vaccine, vaccine effectiveness against the Omicron variant starts at 45 to 50% then drops to almost no effect from 20 weeks after the second dose. With 2 doses of Pfizer or Moderna effectiveness dropped from around 65 to 70% down to around 10% by 25 weeks after the second dose. Two to 4 weeks after a booster dose of either the Pfizer or Moderna vaccine, effectiveness ranges from around 60 to 75%, dropping to 25 to 40% from 15+ weeks after the booster. Vaccine effectiveness estimates for the booster dose are very similar, irrespective of the primary course received. Vaccine effectiveness is generally slightly higher in younger compared to older age groups
- The most recent report also includes a comprehensive analysis of the protection conferred by vaccines against hospitalisation over time. Since Omicron causes milder disease and all individuals who are hospitalised are tested for COVID-19, an increasing proportion of cases in hospital are likely to have COVID-19 as an incidental finding rather than as the primary reason for admission. As a result this analysis uses multiple definitions of hospitalisation to counter lower estimates attributable to broad definitions of hospitalisation that include these incidental cases and are therefore likely more reflective of VE against infection, rather than hospitalisation.
- Results (see table below) suggest that for 65+ year olds admitted for more than 2 days stay with a respiratory illness code as the primary diagnosis (second column), VE remained high at 85.3% (82.4 to 87.6%) at 15 weeks after a booster. For those who required oxygen/ventilation/ICU (third column), VE was 86.8% (77.1 to 92.3%) after 15 weeks. It is suggest the low effectiveness for under 65s for all COVID admissions (column 1 is due to the fact there will be a higher level of incidental admissions at younger ages.
- These findings are caveated by the fact that reason for admission was inferred using a proxy definition due to lags in hospital coding data around the actual reason reason for admission. The full methodology can be found at [Effectiveness of COVID-19 vaccines against Omicron and Delta hospitalisation: test negative case-control study \(khub.net\)](#)

Table 1. vaccine effectiveness against hospitalisation using different definitions of hospitalisations in a) 18 to 64 year olds and b) 65 year olds and over

		ECDS symptomatic with onset date	SUS at least 2 days with ARI code in primary field	SUS at least 2 days & either oxygen, ventilation or ICU with ARI code in primary field
18 to 64				
	Interval	VE	VE	VE
Dose 1	0 to 27	48.5 (12.3 to 69.7)	36.2 (-33.9 to 69.6)	
	28+	48.7 (32.8 to 60.8)	44.1 (25.6 to 58)	75 (42.4 to 89.1)
Dose 2	0 to 13	39.6 (-31.5 to 72.2)	88.9 (58.4 to 97)	
	14 to 174	54.7 (45.3 to 62.4)	69 (58.1 to 77)	86.7 (63.6 to 95.1)
	175+	34.6 (21.7 to 45.4)	56.1 (46.4 to 64)	82.3 (67.7 to 90.3)
Booster	0 to 6	63.9 (52.2 to 72.8)	74.3 (55.9 to 85)	90.7 (56 to 98.1)
	7 to 13	80.1 (73.5 to 85.1)	90.9 (83.2 to 95.1)	0 (100 to 100)
	14 to 34	82.4 (78.6 to 85.6)	88.6 (84.9 to 91.5)	97.1 (92.2 to 98.9)
	35 to 69	72.7 (67.2 to 77.2)	85.8 (82.4 to 88.5)	94.3 (88.9 to 97.1)
	70 to 104	66.9 (59.1 to 73.3)	80.2 (74.9 to 84.4)	89.9 (78.3 to 95.3)
	105+	53.6 (36.9 to 65.9)	67.4 (53.1 to 77.4)	75.9 (15.8 to 93.1)
65+				
	Interval	VE	VE	VE
Dose 1	0 to 27		43.9 (-41 to 77.7)	
	28+		53.4 (36.3 to 65.9)	78.3 (43.7 to 91.7)
Dose 2	0 to 13		0 (100 to 100)	
	14 to 174	77.8 (45 to 91)	82.3 (74.3 to 87.8)	90.9 (72.6 to 97)
	175+	66.7 (43.4 to 80.4)	57.7 (49.6 to 64.4)	73.4 (55.1 to 84.3)
Booster	0 to 6	85.8 (61.5 to 94.7)	77.9 (65.3 to 85.9)	89.2 (63.1 to 96.8)
	7 to 13	92.3 (76.3 to 97.5)	84.7 (76 to 90.2)	94.7 (71.6 to 99)
	14 to 34	92.4 (86 to 95.8)	91.3 (89.1 to 93.1)	95.8 (91.3 to 97.9)
	35 to 69	87 (79.2 to 91.8)	89.3 (87.3 to 90.9)	92.8 (88.4 to 95.6)
	70 to 104	84 (74.6 to 89.9)	88.1 (86.1 to 89.9)	92.5 (88.1 to 95.2)
	105+	76.9 (60.6 to 86.4)	85.3 (82.4 to 87.6)	86.8 (77.1 to 92.3)

ECDS = Emergency Care Dataset (this analysis includes all admissions with a positive COVID-19 test via emergency care except for those coded as injuries); SUS = Secondary Users Service (this analysis includes all admissions to secondary care for >=2 days with a respiratory code in the first diagnostic field) ([10](#)).

- High levels of protection (over 90%) are also seen against mortality with all 3 vaccines with relatively limited waning. Vaccine effectiveness against mortality with the Omicron variant has been estimated for those aged 50 years and older by combining the risk of becoming a symptomatic case with the risk of death among symptomatic cases in vaccinated (all vaccines combined) compared to unvaccinated individuals. At 25-plus weeks following the second dose, vaccine effectiveness was around 60% while at 2 or more weeks following a booster vaccine effectiveness was 95% against mortality.

[UKHSA SARS-CoV-2 variants of concern Technical briefing 39 25 March 2022 \(Study link\)](#)

- The most recent UKHSA technical briefing describes the three recombinant lineages have been designated by Pangolin. Two are a combination of Delta and BA.1 (XD and

XF). XD, which has an Omicron S gene incorporated into a Delta genome, requires biological characterisation. It is present in several European countries but has not been detected in the UK. XF caused a small cluster in the UK but has not been detected since 15 February.

- XE is a BA.1/BA.2 recombinant, with the majority of the genome including the S gene belonging to BA.2. XE shows evidence of community transmission within England, although it is currently <1% of total sequenced cases. Early growth rates for XE were not significantly different from BA.2, but using the most recent data up to 16 March 2022, XE has a growth rate 9.8% above that of BA.2. As this estimate has not remained consistent as new data have been added, it cannot yet be interpreted as an estimate of growth advantage for the recombinant. Numbers were too small for the XE recombinant to be analysed by region.
- An overview of the BA.2 variant summarises it has demonstrated an increased growth rate compared to BA.1 in all regions of England. Since mid-February, the growth rate has settled at approximately 75% greater relative growth for BA.2 compared to BA.1. Iterated analysis finds no evidence of a greater risk of hospitalisation following infection with BA.2 compared to BA.1.

PREPRINT: Second Booster Vaccine and COVID-19 Mortality in Adults 60 to 100 Years Old ([Study link](#))

- This study was performed in Israel, which began administering 4th shots for age 60+ in December, and subsequently across all adult age groups. Now Israel is confronting a BA.2 wave.
- This retrospective cohort study included all members of Clalit Health Services, aged 60 to 100, eligible for the second-booster. Mortality due to COVID-19 among participants who received the second-booster was compared with participants who received one booster dose, adjusting for demographic factors and coexisting illnesses. A total of 563,465 participants met the eligibility criteria. Of those, 328,597 (58%) received a second-booster dose during the 40-day study period.
- Death due to COVID-19 occurred in 92 second-booster recipients and in 232 participants who received one booster dose (adjusted hazard ratio 0.22; 95% confidence interval 0.17 to 0.28). This study therefore suggests a 78% reduction of death due to COVID in ~330,000 people who had 4th shot at least 4 months prior vs ~230,000 with 3 shots, adjusted for co-variables. The findings demonstrate the possibility of preventing the most severe COVID-19 outcomes with a fourth booster vaccine dose in elderly patients. However, studies with a longer follow-up period will be required to determine the longevity of the efficacy and safety of a second booster COVID-19 vaccine dose.

PREPRINT: Inconsistent directions of change in case severity across successive SARS-CoV-2 variant waves suggests an unpredictable future ([Study link](#))

- This preprint aims to determine how the severity of successively dominant SARS-CoV-2 variants has changed over the course of the COVID-19 pandemic through a prospective cohort analysis of community- and hospital-sequenced COVID-19 cases in the NHS Greater Glasgow and Clyde (NHS GG&C) Health Board for 1.2 million people.
- After adjusting for a number of covariates, it concludes the direction of change in disease severity between successively emerging SARS-CoV-2 variants of concern was inconsistent. This heterogeneity in virulence between variants, coupled with independent evolutionary emergence, supports previous advice from [NERVTAG](#) that severity associated with future SARS-CoV-2 variants is inherently unpredictable.

PREPRINT: Monitoring of the SARS-CoV-2 Omicron BA.1/BA.2 variant transition in the Swedish population reveals higher viral quantity in BA.2 cases ([Study link](#))

- This study tracked the rapid shift from Omicron BA.1 to BA.2 sub-variant dominance in the Swedish population during January-March 2022. By analysis of 174,933 clinical nasopharyngeal swab samples using a custom variant-typing RT-PCR assay, the authors uncover nearly two-fold higher levels of viral RNA in cases with Omicron BA.2. Importantly, increased viral load in the upper pharynx upon BA.2 infection may provide part of the explanation why Omicron BA.2 is more transmissible and currently outcompetes the BA.1 variant across populations.

Clinical

SARS-CoV-2 co-infection with influenza viruses, respiratory syncytial virus, or adenoviruses ([Study link](#))

- The latest paper from the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) analyses data from over 200,000 hospitalised COVID cases to add additional evidence that adults in hospital with COVID-19 and influenza at the same time are at much greater risk of severe disease and death: 4x greater odds of needing a ventilator; 2x greater odds of dying. It is likely flu will circulate more widely as restrictions are lifted, resulting in more coinfections with covid and flu. As a result the authors recommend that clinical settings should prepare by extending testing for hospitalised COVID patients to include flu. This study also highlights the protective benefits of getting the flu vaccine.

Immunity

Neutralization of the SARS-CoV-2 Omicron BA.1 and BA.2 Variants ([Study link](#))

- A letter to the Editor published in NEJM outlines findings of an analysis of antibody responses against the BA.1 and BA.2 variants. Overall, these data show that neutralizing antibody titres against BA.2 were similar to those against BA.1, (BA.2 lower by a factor of 1.3 to 1.4). A third dose of the BNT162b2 vaccine was needed for induction of consistent neutralising antibody titres against either BA.1 or BA.2.

Moreover, in vaccinated persons who had presumably been infected with BA.1, robust neutralizing antibody titres against BA.2 developed, which suggests a substantial degree of cross-reactive natural immunity.

- The authors argue these findings have important public health implications and suggest that the increasing frequency of BA.2 in the context of the BA.1 surge is probably related to increased transmissibility rather than to enhanced immunologic escape.

Modelling

PREPRINT: Comparison of the 2021 COVID-19 'Roadmap' Projections against Public Health Data ([Study link](#))

- This study by members of the original modelling team offers a retrospective analysis of the six Roadmap modelling documents produced in 2021 to assess the likely impacts of the step-by-step plan to ease restrictions in England (Warwick also produced some scenarios for Wales but these are not assessed in this paper) and considers whether projections were sufficiently close to what transpired to be informative for policy. For each model the authors directly compare results generated at the time with more recent public health data (primarily hospital admissions, but also hospital occupancy and death) to understand discrepancies and potential improvements.
- The authors suggest that, in general, their model projections generated a reliable estimation of medium-term hospital admission trends, with the data points up to September 2021 generally lying within projection intervals. The evolution of the models over time is characterised by an increasing understanding of vaccine efficacy, a greater appreciation for the uncertainty of population behaviours and a corresponding increase in model complexity. Estimates of vaccine efficacy were hampered by the lack of data in the early stages of the Alpha and Delta variant waves and tended to be pessimistic, possibly due to early biases in the initial vaccine prioritisation targeting those most likely to contact SARS-CoV-2 and require treatment.
- Estimates of social mixing and assumptions about human behaviour in the face of changing restrictions and risk suggest that the response to the introduction of measures was much quicker than the relaxation of measures, although population behaviour remains unpredictable over long timescales. The authors suggest that events such as UEFA football championship, the 'Pingdemic' or the timing of Omicron's emergence were unpredictable and difficult to incorporate into modelling. The authors suggest this uncertainty highlights why model results should be considered as projections of particular (epidemiological-plausible) scenarios, rather than predictions. Modelling the full uncertainty of public behaviour and the emergence of novel variants would likely lead to prediction intervals too large for the results to be useful.
- The paper concludes that these model projections have proved to be a useful policy tool, providing a mechanism for translating epidemiological knowledge and uncertainties into medium-term assessments of the likely range of public health burden. The paper is written by the modellers who produced the scenarios, does not have outside involvement and has not yet been peer-reviewed.

Modelling studies used to evaluate the effect of population-level non-pharmaceutical interventions on the reproduction number of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) ([Study Link](#))

- In order to inform any future 'COVID-19 urgent' situations, and to test possible combinations of non-pharmaceutical interventions (NPIs) that would be required to bring transmission under control again, TAC has developed a 'ready reckoner' NPI tool. The NPI tool enables the user to enter the current Rt value for their particular setting, chooses a modelling study, and then selects a number of NPIs from the chosen study. A new Rt number is outputted along with a waterfall chart showing the changes in Rt from each individually selected NPI.
- The implementation of the NPI tool is reliant on having a select number of relevant and well-conducted modelling studies upon which to draw. This Rapid Review documents the identification, selection, summary and critical appraisal of suitable modelling studies for use with the tool.
- Nine well-conducted reviews were selected. A summary of the study design and characteristics is provided and can be used to aid the selection of the most appropriate modelling study when using the NPI. Critical appraisal of these studies identified no major concerns with their design or conduct.
- Most of the studies reported data from the first wave (February to August 2020), with only three including second wave data (September 2020 to May 2021). No studies reported data for third wave or later (June 2021 onwards). Eight studies reported data from the UK; no data specific to Wales were reported.
- The NPIs were mostly reported in broad categories and included school closures, workplace closures, closure of public transport, restrictions on gatherings of different sizes and stay at home orders.

Indirect Health Harms from COVID-19

Wales COVID-19 Evidence Centre: Impact of the COVID-19 pandemic on the health and access to healthcare of disabled people ([study link](#))

- The COVID-19 pandemic has had a disproportionate impact on disabled people. In order to target and prioritise actions to prevent or address this, the Equality, Inclusion and Human Rights Branch of Welsh Government needed to develop a clear understanding of the systemic inequalities facing disabled people that have been created or exacerbated as a consequence of the COVID-19 pandemic, in order to inform the work of the Disability Rights Taskforce. This Rapid Review follows on from a Rapid Evidence Map based on scoping review methodology, which was used to identify a research area to prioritise.
- Several concerns or issues with accessing services were highlighted. One study reported that disabled people were over twice as likely to report waiting for a health intervention during the first wave of the COVID-19 pandemic compared to non-disabled people and were substantially more likely to report needing to access various services than non-disabled people. Experience and access to remote services varied. There were some positive reports for telehealth but this was not universal and individual needs have to be carefully considered. The use of facemasks and the lack

of face-to face appointments or replacement with other means had an impact on the abilities of people with hearing loss to hear and communicate.

- For health outcomes, disabled people were no more likely to report COVID-19 symptoms than non-disabled people but were more likely to be hospitalised due to COVID-19. In comparison to general population controls, patients with learning impairment were less likely to receive non-invasive respiratory support, intubation, and or to be admitted to the ICU while in hospital (no data were collected on the reasons why). Hospital stay was, on average 3.5 days longer for these study participants compared to controls.
- Considerable inequalities in mortality rates for disabled people were reported. Notably, the Office for National Statistics (2021) found the risk of death involving COVID-19 was 3.1 times greater for more-disabled men and 1.9 times greater for less-disabled men, compared with non-disabled men; among women, the risk of death was 3.5 times greater for more-disabled women and 2.0 times greater for less-disabled women, compared with non-disabled women. Statistical methods could not identify a single factor to explain the greater risks of death; the place of residence, socio-economic and geographical circumstances, and pre-existing health conditions all contributed.
- Studies reporting on mental health identified a range of negative impacts for both adults and children, although one study looking at the impacts on children with a learning impairment found no difference between pre- and post-lockdown periods; there were also some reports of improvements in mental health such as for children who felt safer at home or who had school related stress. Adults with a hearing loss reported enjoying quieter outdoor environments and relief at not having to attend social gatherings. One study noted that Third sector organisations had a positive impact upon mental health and wellbeing by filling gaps in social care. It was clear that individual experiences varied.
- More research is needed to evaluate the cross-cutting impact of other areas of potential inequalities. Consideration needs to be given to the recovery plans for patient services and how these will address the needs of disabled people.

Therapeutics

PREPRINT: Baricitinib in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial and updated meta-analysis ([Study link](#))

- A preprint from the RECOVERY trial suggests that in patients hospitalised for COVID-19, baricitinib significantly reduced the risk of death but the size of benefit was somewhat smaller than that suggested by previous trials. The total randomised evidence to date suggests that JAK inhibitors (chiefly baricitinib) reduce mortality in patients hospitalised for COVID-19 by about one-fifth.
- The benefit was in addition to those of dexamethasone and tocilizumab, two other anti-inflammatory treatments which have previously been shown to reduce the risk of death in these patients. The benefit of baricitinib was consistent regardless of which other COVID-19 treatments the patients were also receiving, including corticosteroids, tocilizumab, or remdesivir.

- Patients receiving baricitinib were also more likely to be discharged alive within 28 days (80% vs. 78%, age-adjusted rate ratio 1.10, 95% CI 1.04-1.15; $p < 0.001$). Among patients not on invasive mechanical ventilation when entered into the trial, baricitinib reduced the chance of progressing to invasive mechanical ventilation or death from 17% to 16% (risk ratio 0.90, [95% CI 0.81 to 0.99], $p = 0.026$). There was no evidence that the short course of baricitinib used in RECOVERY increased the risk of other infections or of thrombosis (complications of blood clotting).
- Work is currently underway on a UK wide clinical policy; however a recent letter from UK Government has outlined that responsibility for funding arrangements for COVID therapies will be returning from UKG to Devolved Governments as per pre-pandemic business as usual arrangements from April 2022. This means NHS Wales and NHS-E will likely decide not to introduce baricitinib until NICE confirm it meets the cost effectiveness thresholds set for medicines generally. It is anticipated NICE will do this in the next 6 months.