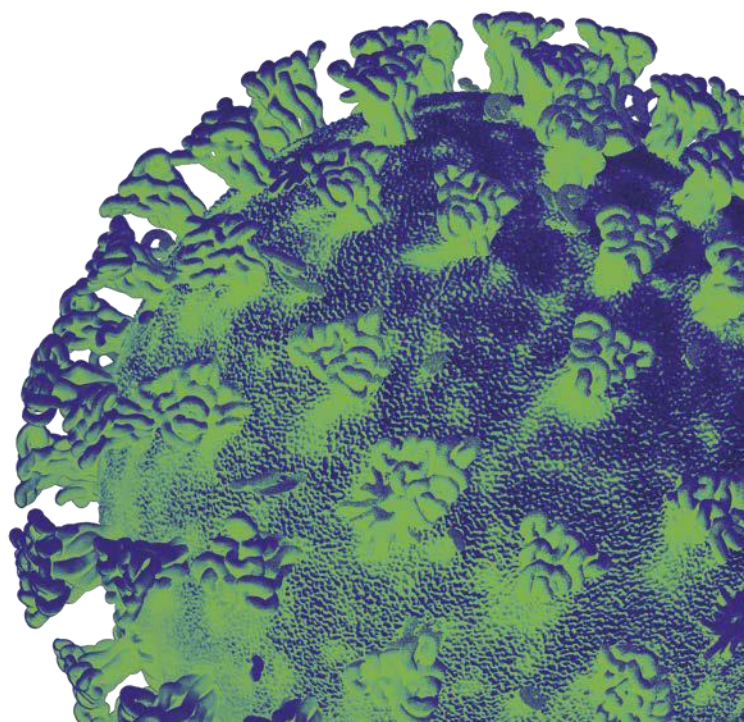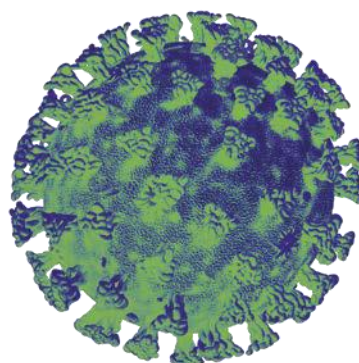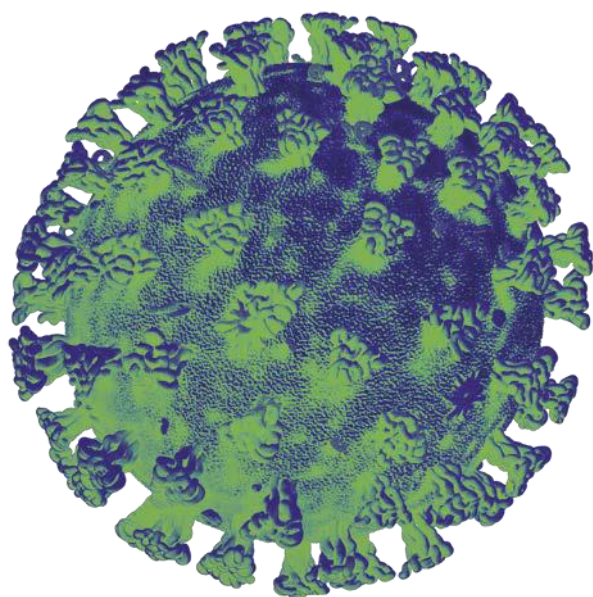Llywodraeth Cymru
Welsh Government

Technical Advisory Cell

Summary of Advice

6 May 2022

Technical Advisory Cell: COVID-19 evidence brief

6 May 2022

Wales Sitrep

Recent estimates from the ONS COVID Infection Survey, which provides a relatively unbiased but lagged estimate of levels of infection, suggests in the period 24 to 30 April 2022 the percentage of people testing positive for COVID-19 in Wales continued to decrease. It is estimated 4.33% of the community population had COVID-19 (95% credible interval: 3.69% to 5.03%). This equates to approximately 1 person in every 25 (95% credible interval: 1 in 25 to 1 in 20), or 131,600 people during this time (95% credible interval: 12,200 to 152,800).
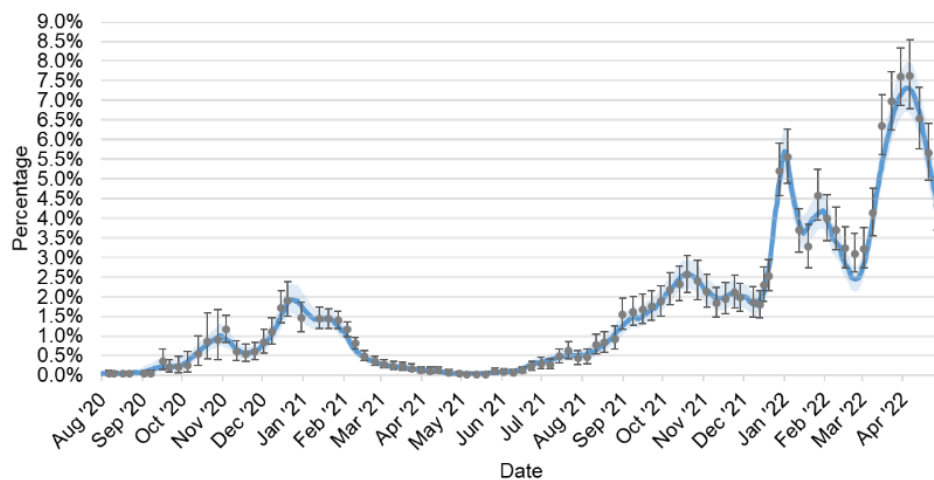
- Due to a technical issue that has now been resolved, a national comparison of wastewater surveillance data is not currently available this week. At a site and regional level, the levels of SARS-CoV-2 in wastewater appear to have declined in the last four weeks compared to a peak that was observed during March 2022. Reporting of this surveillance indicator is expected to resume next week.

- As at 5 May, NHS Wales remains under considerable pressure, although the situation is improving compared to the previous week. In emergency departments 12 out of the 20 hospital sites began the day at level 4, meaning a situation that requires national coordination. Hywel Dda, Cwm Taf Morgannwg and Cardiff & Vale reported all sites at Level 4. Poor discharge profiles are observed across a number of hospitals. Although Emergency Departments are busy, plans are in place to offload patients waiting in ambulances.

- In relation to COVID-19 figures the total number of COVID-19 related patients in hospital beds is 1,109. This is 108 (9%) lower than the same day last week and the lowest number of COVID related patients in hospital beds since 15 March 2022.

- The number confirmed COVID-19 patients in hospital improved with 440 patients currently occupying a bed. This is 100 lower than the same day last week and the lowest since 4 March 2022.

- The number of occupied surge and normal beds in a critical care environment today is 172, 20 higher than the pre-COVID-19 baseline of 152 for critical care beds. This is 4 lower than the same day last week.

- The number of COVID-19 related patients in critical care has decreased, with 16 patients occupying a bed. This is 9 lower than the same day last week.

- As at 29 April 2022, the number of weekly COVID-19 deaths reported by PHW has decreased by 16.3% 41 deaths compared to 49 the previous week. Lagged ONS death registration reporting up to 22 April shows a 37.3% increase in COVID deaths to 70 in the most recent week compared to 51 in the previous week. The total number of deaths registered in Wales was 668; 89 greater than the previous week and 2.3% the five-year average (15 more deaths).

- As at 27 April, 106 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. 265 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. There are 1,033 adult care homes and 17 adult and child care homes in Wales. In the last two weeks, there have been 19 reported deaths of care home residents relating to suspected or confirmed COVID-19. (Source: StatsWales).

- As at 3 May 2022, UKHSA's Epidemiology Modelling Review group estimate the Reproduction number (Rt) for Wales to be between 0.7 and 1, with a halving time of 11 days to flat (more than 40 days).

- PHW report that **Confirmed influenza case numbers have increased during April, and include a number of community cases confirmed in sentinel GPs. This is later than usual seasonal activity, at low levels**. During Week 17 (ending 01/05/2022) there were 54 cases of influenza confirmed with a further case reported late from a sample in a preceding week.

UK Summary

UK Infection positivity – ONS Coronavirus Infection Survey, 30 April

- According to the most recent ONS Coronavirus Infection Survey Results during the period 24 to 30 April 2022 positivity rates have decreased across the nations of the UK. ONS estimates that around 1 in 25 people (4.33%) in Wales had COVID-19 during this period, compared to 1 in 35 in England (2.91%), 1 in 30 in Scotland (3.55%) and 1 in 40 (2.45%) in Northern Ireland.
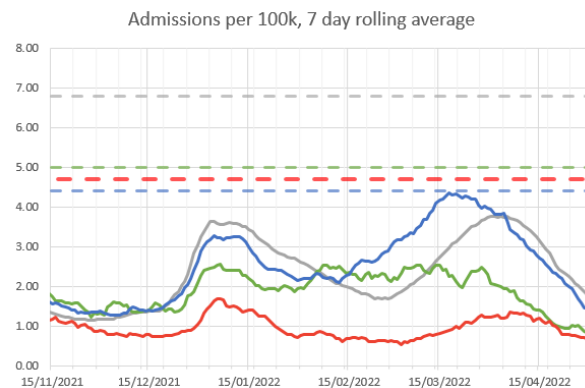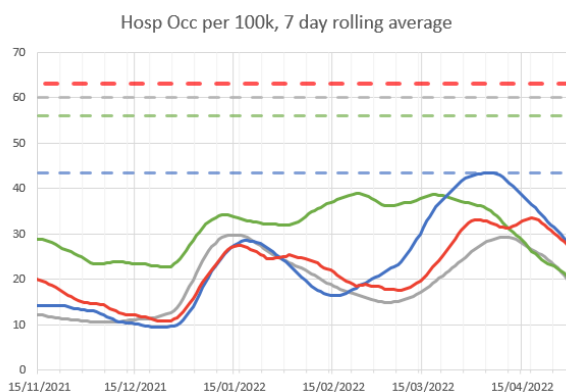
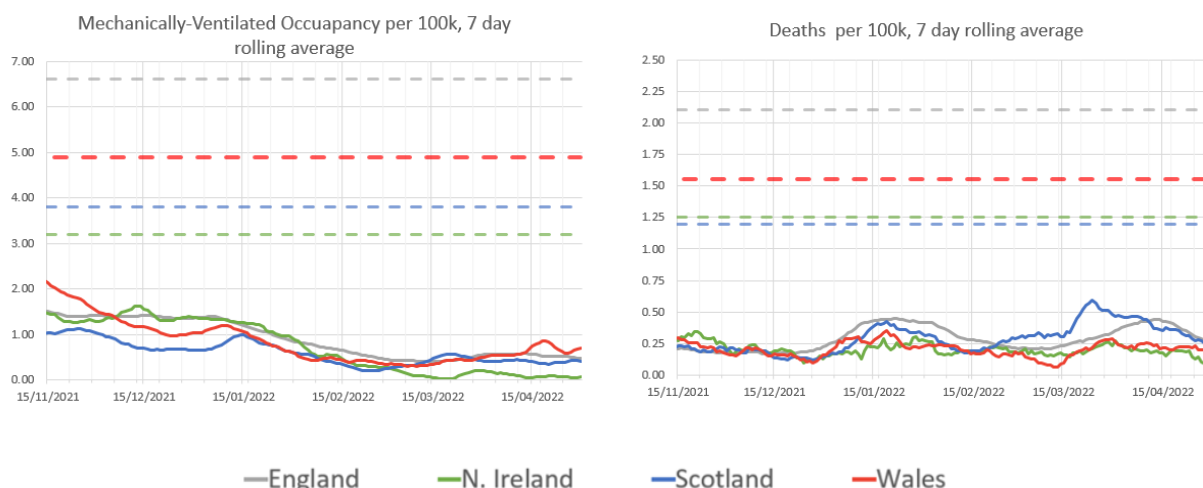**Positivity rates (%) across UK countries since 20 March 2022**
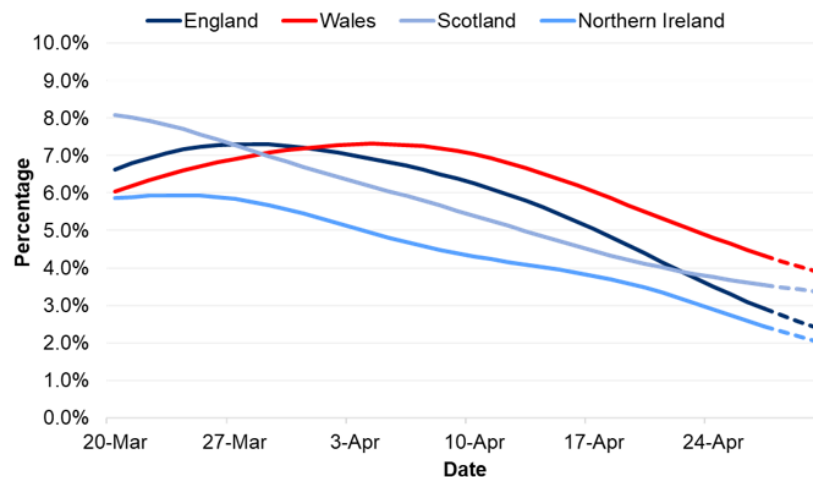
Source: Coronavirus (COVID-19) Infection Survey, ONS, 04/05/22

UK Hospitalisation and deaths- UK Coronavirus Dashboard data up to 30 April 2022

- **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, especially comparing between nations. Full documentation is available at Metrics documentation | Coronavirus in the UK (data.gov.uk). The dotted lines indicate peak levels.

- COVID-19 admissions and hospital occupancy is decreasing in all four UK nations, although unlike other nations Wales COVID-19 admissions include suspected cases and do not include patients who tested positive while in hospital, so comparisons of admissions with the other UK nations should be interpreted with caution.

- COVID-19 ICU/ Mechanically ventilated bed occupancy is stable at a low level relative to previous waves in all 4 nations, although Wales is less stable than the other nations and is increasing in the most recent data.

- Following an increase in February/March the number of COVID-19 deaths is decreasing or stable at a relatively low level across the four nations.

Mechanically-Ventilated Occuapancy per 100k, 7 day rolling average

Deaths per 100k, 7 day rolling average

—England   —N. Ireland   —Scotland   —Wales

Variant Update

Public Health Wales variant surveillance, 3 May (Source link)

- *Due to the inclusion of the new VOC-22JAN-01 (BA.2) variant, the genotype definition is not specific enough to confirm whether an Omicron case is VOC-21NOV-01 (BA.1) or VOC-22JAN-01 (BA.2). As a result, the genotyped cases have been separated out into their own category called 'Omicron (NEC)' prior to full genome sequencing to determine its lineage. This category also includes sequenced cases defined as another lineage (e.g. BA.3), or private lab cases where PHW do not have enough information to further classify the case.*

- The current dominant variant in Wales is VOC-22JAN-01 (Omicron, BA.2) which accounted for 92.67% of sequenced cases in the last 14 days.

- In the latest reporting week(2022 W17):

  o Omicron (NEC) accounted for 0% of all sequenced variant cases

  o VOC-22JAN-01 (Omicron, BA.2) accounted for 100% of all sequenced variant cases

  o VOC-21NOV-01 (Omicron, BA.1) accounted for 0% of all sequenced variant cases

- As of 03/05/2022 there have been 56,256 cases of VOC-21NOV-01 (Omicron, BA.1) and 27,113 cases of VOC-22JAN-01 (Omicron, BA.2)

Figure: Epicurve of all sequenced variant cases in Wales, data as at 03/05/2022, Public Health Wales Variant Surveillance Update
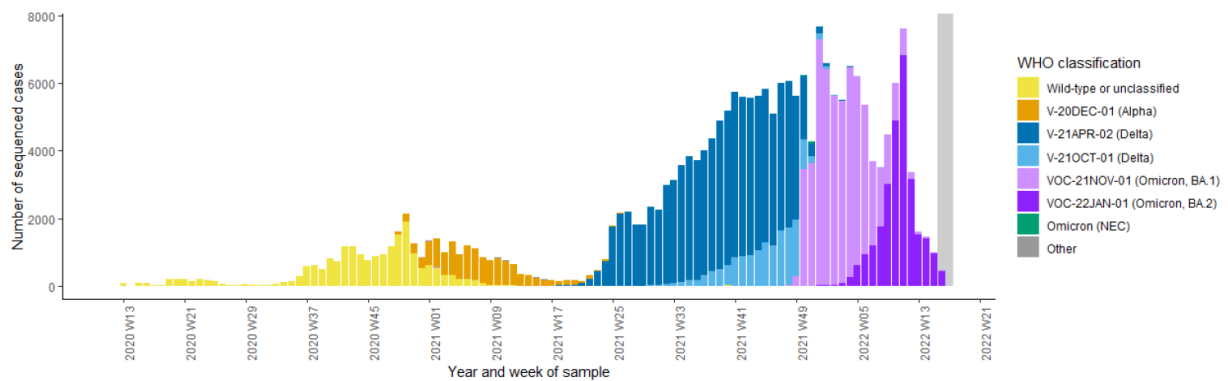
Please note data in the grey shaded region is indicative of a lag in sequencing data and should be interpreted with caution.

- Unofficial Public Health Wales data suggests as at 3 May there have been 0 cases of V-22APR-01 (XD) in Wales and 38 cases of V-22APR-02 (XE) and 1 case of V-22APR-03 (BA.4). **However, these cases are defined by Pango lineages rather than UKHSA case definitions and so should be treated as indicative rather than definitive**.

SARS-CoV-2 variants of concern and variants under investigation in England, Technical Briefing 41, 6 May 2022

- UKHSA has published an updated variant surveillance analysis, although they state that much of the data is preliminary and findings have a high level of uncertainty:

  - The reduction in tests processed through assays which can report S gene target failure (SGTF) has decreased substantially since the end of widespread community testing on 1 April, and this is no longer a reliable representation of variants in the population. As a result UKHSA have stated they will no longer be reporting on S-gene detection in future briefings.

  - Reduction in testing has also made growth rate analysis less reliable and confidence intervals around growth rates for individual variants are likely to be large, as demonstrated by XE, and this model may not be usable on the national dataset going forwards. Assessment of surveillance cohort datasets is being undertaken by UKHSA.

- A variant risk assessment has been published for V-22APR-03 (Omicron BA.4) and V-22APR-04 (Omicron BA.5) based on preliminary data (see below). These two variants are increasing in South Africa and may be associated with the current increase in incidence there. Small numbers of BA.4 sequences continue to be detected in the UK (total 40 genomes). As of 3 May 2022, there were 21 confirmed cases of BA.4 reported in England and 19 cases of BA.5.

28 April 2022   Risk assessment for SARS-CoV-2 variant: V-22APR-03/V-22APR-04   UK Health Security Agency

Indicator	Red, amber, or green status*	Confidence level	Assessment and rationale
			The risk assessment is presented in comparison to the current predominant variant (BA.2). Red indicates the assessed variant as worse than BA.2 in a characteristic, amber equivalent, green improved. The laboratory data are supplied by VTG members (Oxford University, Genotype to Phenotype Consortium) and have been reviewed by VTG but are unpublished.
Overall growth advantage	Red	Low	**Evidence of a growth advantage compared to BA.2, in the context of South Africa** Available data from South Africa suggest that BA.4 and BA.5 are increasing as a proportion of sequenced cases and based on SGTF may already be predominant. As of 26 April, the reported weekly incidence in South Africa has more than doubled compared to the previous week and test positivity has increased. The provinces with the greatest increases in BA.4 or BA.5 based on sequence data are also those showing the greatest rise in incidence. These data suggest BA.4/5 are showing a growth advantage over BA.2 in South Africa. However, it should be noted that South Africa has different background population immunity to the UK and has not experienced a large BA.2 wave. The conditions favouring BA.4/5 growth in South Africa may not be replicated elsewhere. There is evidence of international spread including small numbers of cases in the UK and Europe (note differences in testing and sequencing across countries). There is no other country where BA.4/5 is showing a clear growth advantage as yet.
Growth advantage 1: Transmissibility			**Insufficient data** There are no epidemiological data available.
Growth advantage 2: Immune evasion	Red	Moderate	**There is evidence of some antigenic change compared to BA.2 based on structural modelling and pseudovirus neutralisation data** BA.4 and BA.5 are most closely related to BA.2. Structural modelling indicates there is likely to be antigenic change related to L452R (found in Delta) and F486V (a more radical version of the F486L found in some mink adapted viruses), both of which may affect the binding of neutralising antibodies. In addition, the differences between BA.2 and BA.4/5 at position 493 may have some effect, as well as the two-residue deletion in the N-terminal domain in BA.4/5 compared to BA.2. In preliminary unpublished pseudovirus data from one laboratory there is a reduction in neutralising activity of vaccinee sera (including vaccinees who have also had BA.1) for BA.4 compared to BA.2. In a second laboratory, sera from BA.1 infected animals neutralised BA.4 poorly but sera from BA.2 infected animals did not show the same reduction in neutralisation. These findings support the modelled predictions of a degree of antigenic change. There are no data for vaccinees who have also had Delta or BA.2, both of which profiles are relevant in the UK context and require additional assessment.
Infection severity			**Insufficient data** There is no comparative data available. A slight increase in people admitted to hospital is noted in South Africa in the past week.

* Refer to scale and confidence grading slide.

- XE is a BA.1 and BA.2 recombinant (containing BA.1 mutations for NSP1-6 and BA.2 mutations for the rest of the genome). As of 3 May 2022, a total of 1,399 episodes of XE have been reported in England. XE remains at a low prevalence. Between 3 April 2022 and 3 May 2022, XE accounted for 0.7% of sequenced cases reported in England.

International – WHO update 4 May

- The WHO Weekly Epidemiological Update dated 4 May reports that globally, the number of new COVID-19 cases and deaths has continued to decline since the end of March 2022.

- During the week of 25 April through 1 May 2022, over 3.8 million cases and over 15,000 deaths were reported, decreases of 17% and 3% respectively, as compared to the previous week. However, an increase in the number of new weekly cases was reported from the African Region (+31%) and the Region of the Americas (+13%), and the number of new weekly deaths increased in the South-East Asia Region (+69%) largely due to a delay in the reporting of deaths from India. As of 1 May 2022, over 500 million confirmed cases and over six million deaths have been reported globally.

- Three Omicron sublineages BA.4, BA.5 and BA.2.12.1 have acquired a few additional mutations that may impact their characteristics. Based on GISAID data and reports from WHO regional offices and countries, the number of cases and the number of countries reporting the detection of these three variants are rising. Limited evidence to date, does not indicate a rise in hospital admissions or other signs of increased severity. Preliminary data from South Africa using S gene target failure data indicate

no difference in the risk of hospitalization for BA.4 and BA.5, as compared to BA.1; however, the short follow-up of BA.4 and BA.5 cases does not allow for conclusions on disease severity of these sublineages to be drawn at this stage.

Medium Term Projections, TAC modelling sub-cell

- These medium-term projections (MTPs) are produced regularly by Swansea University. The Swansea University (SU) projections are also combined with other models to go into a consensus MTP for admissions and deaths which is agreed every two weeks by the UKHSA Epidemiological Modelling Review Group (EMRG), which has recently taken over from SPI-M-O in agreeing these MTPs.

- The SU projections are typically more up-to-date and include more outcomes (e.g. ICU), but may be less robust because they are based on one model only. Both MTPs are based on projecting forward from current data and do not explicitly factor in policy changes, changes in testing, changes in behaviour, or rapid changes in vaccinations.

Swansea University MTPs, 4 May

In the below charts crosses represent actual data, while the blue line represents the central modelling estimate and blue highlight indicates confidence intervals. The pink dotted line represents previous peak levels.

- While showing a similar projection to last week's MTPs, this week's Swansea University MTPs project peaks at slightly lower values. They project a decline in NHS pressure and deaths over the next three weeks.

- Daily new hospital admissions are decreasing and are falling at a rate similar to that indicated by the MTP projection.

- Modelled hospital occupancy (excluding ICU) has started to decrease and is projected to continue decreasing throughout May 2022.

- ICU bed occupancy has increased slightly in recent days, but is projected to decrease throughout May 2022.

ICU occupancy [preval] (29 April 22)

Non-ICU occupancy [preval] (29 April 22)

Deaths [incid] (29 April 22)
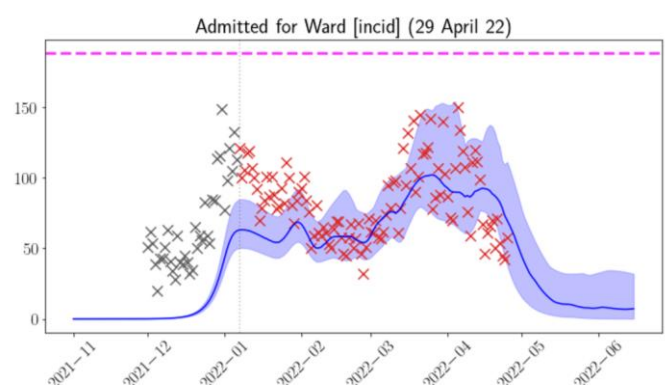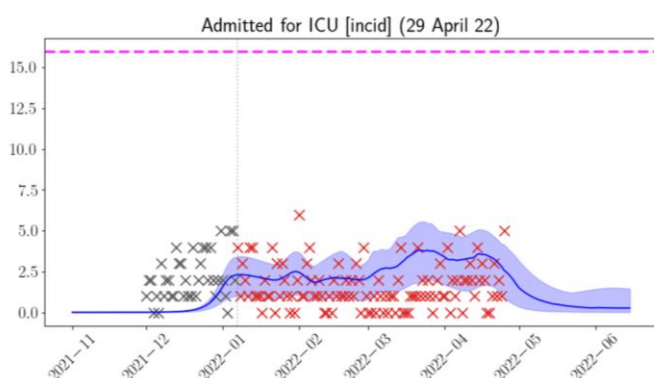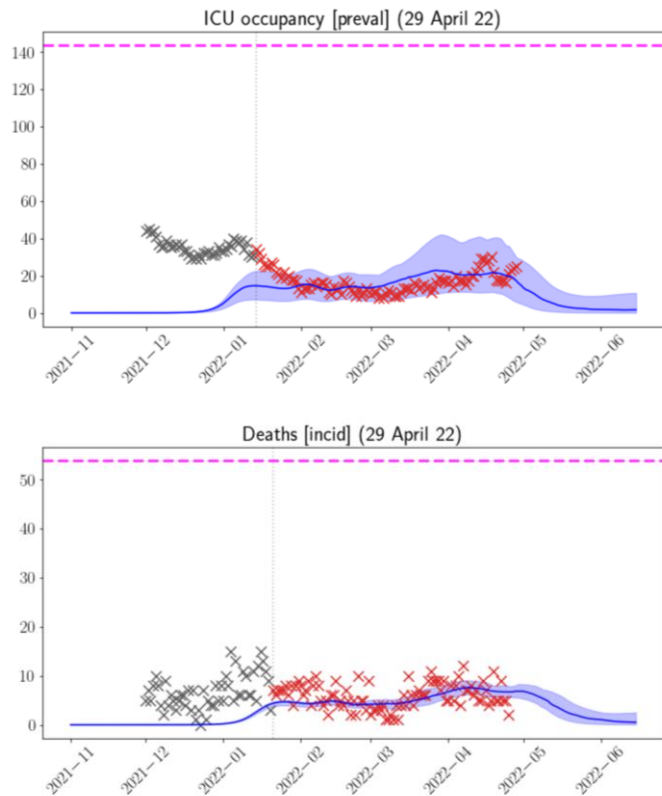
UKHSA EMRG Consensus MTPs, 28 April

- The UKHSA EMRG combined model projects both admissions and deaths as declining in Wales, although the latter is with much greater confidence intervals due to small numbers.

Wales

Wales

Key

- Combined England
- Combined Northern Ireland
- Combined Scotland
- Combined Wales

- Real data
- Expected to Increase
- Projection Midpoint
- High and low estimates 25th to 75th percentile
- High and low estimates 5th to 95th percentile
- Models
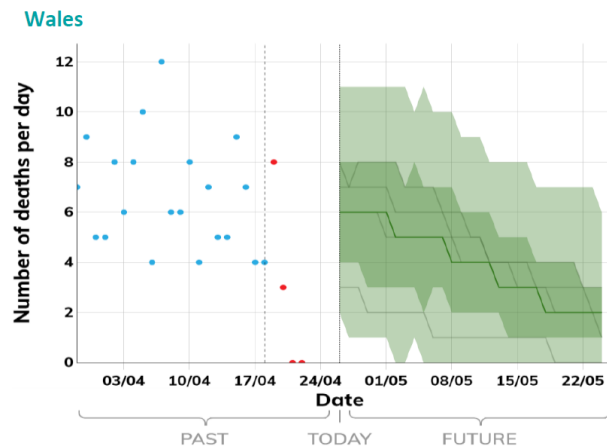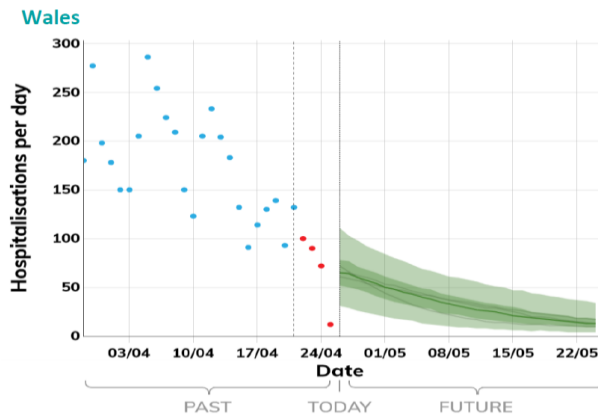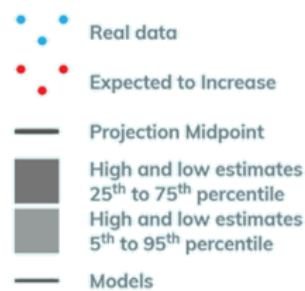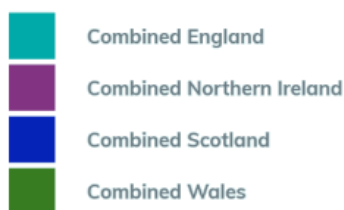
COVID-19 evidence roundup- summary:

> *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.*

Immunity and vaccine effectiveness

Comparative effectiveness over time of the mRNA-1273 (Moderna) vaccine and the BNT162b2 (Pfizer-BioNTech) vaccine | Nature Communications (**Study link**)

- This retrospective cohort study examines anonymised health data for over 3.5 million fully vaccinated individuals, of which 8,848 were recorded as having COVID-19 infections, to assess the rate of Covid-19 infection at least 14 days after the second dose of either the Pfizer or Moderna mRNA vaccines. Sub-analyses included the incidence of hospitalization, ICU admission, and death/hospice transfer. Separate analysis was conducted for individuals above and below age 65 and those without a prior diagnosis of Covid-19.

- Overall the study suggests 90 days after vaccination Moderna is slightly more effective than Pfizer at preventing infection; however there are no differences in vaccine effectiveness for protection against hospitalization, ICU admission, or death/hospice transfer (aOR 1.23, 95% CI (0.67, 2.25)). The authors suggest that for every 1 million individuals vaccinated with the Pfizer vaccine compared with the Moderna vaccine, this would represent 3,448 additional care-seeking cases (either a positive PCR test or Covid-19 related hospital claim) of Covid-19 at 90 days.

- The study is limited by the fact that asymptomatic or mild disease for which an individual did not seek care or a COVID-19 test are not captured in the available data. However more serious outcomes, which typically place the greatest strain on individuals and healthcare systems, are reliably captured. The analysis is also restricted to commercially insured and Medicare Advantage beneficiaries from a single U.S. insurer, a group that is unevenly distributed across the United States geographically and demographically.

PREPRINT **(not peer-reviewed)**: Protection against omicron severe disease 0-7 months after BNT162b2 booster in Israel | medRxiv (**Study link**)

- Recent studies have shown the 3rd dose provides a much lower protection against infection with the omicron variant compared to the delta variant and that this protection wanes quickly. This study used data from Israel to estimate the protection of the 3rd dose against severe disease up to 7 months from receiving the booster dose.

- The analysis shows that protection conferred by the 3rd dose against omicron did not wane over a 7-month period and that a 4th dose further increased protection, with a severe disease rate approximately 3-fold lower than in the 3-dose cohorts.

Variants

Comparative analysis of the risks of hospitalisation and death associated with SARS-CoV-2 omicron (B.1.1.529) and delta (B.1.617.2) variants in England: a cohort study - The Lancet (**Study link**)

- This study estimated the relative risk of hospitalisation and death for 4.1 million confirmed COVID-19 cases in England between Nov 29, 2021 and Jan 9, 2022, linked by vaccination status, hospital attendance and admission, and mortality. A secondary analysis estimated variant and vaccine-specific vaccine effectiveness and the intrinsic relative severity of omicron infection compared with delta (i.e. the relative risk in unvaccinated cases).

- The authors conclude the risk of severe outcomes following SARS-CoV-2 infection is substantially lower for omicron than for delta, with higher reductions for more severe endpoints and significant variation with age. The adjusted hazard ratio (HR) for hospital admission was estimated as 0·41 (0·39–0·43) and for death they were 0·31 (0·26–0·37). Underlying the observed risks is a larger reduction in intrinsic severity (in unvaccinated individuals) counterbalanced by a reduction in vaccine effectiveness. Documented previous SARS-CoV-2 infection offered some protection against hospitalisation and high protection against death in unvaccinated individuals, but only offered additional protection in vaccinated individuals for the death endpoint. Booster vaccination with mRNA vaccines maintains over 70% protection against hospitalisation and death in breakthrough confirmed omicron infections.

- Booster vaccination with an mRNA vaccine was highly protective against hospitalisation and death in omicron cases (HR for hospital admission 8–11 weeks post-booster vs unvaccinated: 0·22 [0·20–0·24]), with the protection afforded after a booster not being affected by the specific vaccine used for doses 1 and 2.

PREPRINT **(not peer-reviewed)**: BA.2.12.1, BA.4 and BA.5 escape antibodies elicited by Omicron infection | bioRxiv (**Study link**)

- The recently emerged SARS-CoV-2 Omicron sublineages BA.2.12.1, BA.2.13, BA.4 and BA.5 all show potential higher transmissibility over BA.21. This study shows that BA.2 sublineages, including BA.2.12.1 and BA.2.13, exhibit increased ACE2-binding affinities compared to BA.1; while BA.4/BA.5 displays the weakest receptor-binding activity. Importantly, compared to BA.2 BA.2.12.1 and BA.4/BA.5 exhibit stronger neutralization evasion against 3-dose vaccinees and, most strikingly, of vaccinated BA.1 patients.

- With regard to therapeutic neutralizing antibodies (Nabs), the authors report that Bebtelovimab and Cilgavimab can still effectively neutralize BA.2.12.1 and BA.4/BA.5, while the S371F, D405N and R408S mutations carried by BA.2/BA.4/BA.5 sublineages would undermine most broad sarbecovirus NAbs.

- Together, the results indicate that Omicron can evolve mutations with little cross-immunity with prior BA.1 infection. The continuous evolution of Omicron poses great challenges to SARS-CoV-2 herd immunity and suggests that BA.1-derived vaccine boosters may not be ideal for achieving broad-spectrum protection.

<u>PREPRINT **(not peer-reviewed)**</u>: Omicron sub-lineages BA.4/BA.5 escape BA.1 infection elicited neutralizing immunity (**Study link**)

- In another study, researchers in South Africa isolated live BA.4 and BA.5 viruses and tested them against neutralizing immunity following from infection in participants who were Omicron/BA.1 infected but unvaccinated (n=24) and vaccinated participants with breakthrough Omicron/BA.1 infection (n=15).

- In unvaccinated individuals, neutralization declined 7.6 and 7.5-fold for BA.4 and BA.5 respectively. In vaccinated BA.1 breakthrough infections, neutralisation declined 3.2-fold and 2.6-fold for BA.4 and BA.5 respectively. Absolute BA.4 and BA.5 neutralization levels were about 5-fold higher in this group versus unvaccinated BA.1 infected participants, although levels may decrease with waning.

- The observed escape of BA.4 and BA.5 from BA.1 derived immunity is more moderate than of BA.1 against previous immunity, where it was slight and non-significant. Given the higher escape and especially the low residual neutralization in the unvaccinated group, the authors speculate that a BA.4/BA.5 infection wave is a strong possibility. However, vaccination does increase neutralization capacity against these emerging variants and would likely offer good protection against severe disease.

<u>PREPRINT **(not peer-reviewed)**</u>: <u>Continued Emergence and Evolution of Omicron in South Africa: New BA.4 and BA.5 lineages</u> (**Study link**)

- South Africa's fourth COVID-19 wave was driven predominantly by three Omicron sublineages (BA.1, BA.2 and BA.3) of the SARS-CoV-2 Omicron variant of concern. Two new sublineages, BA.4 and BA.5, have now been identified and appear to be driving a fifth COVID-19 wave, with early signs of increasing hospital admissions in some provinces. This study estimates growth advantages for BA.4 and BA.5 of 0.08 (95% CI: 0.07 - 0.09) and 0.12 (95% CI: 0.09 - 0.15) per day respectively over BA.2 in South Africa. These estimates are similar to the estimated daily growth advantage of 0.07 of BA.2 over BA.1.

- It is possible that waning immunity is an important contributory factor, suggesting that BA.4 & BA.5 effects may differ by location, depending on the immune landscape. At present it remains unclear how large an effect this shift in the distribution of different Omicron lineages will have on the epidemic in South Africa and elsewhere in the world. Work is underway to characterise disease severity and immune escape. The authors argue this highlights the importance of continued global genomic surveillance and variant analysis in real-time to characterize the continuing evolution of SARS-CoV-2.

Clinical

<u>Global excess deaths associated with COVID-19, January 2020 - December 2021 (who.int)</u> (**Study link**)

- New estimates from the World Health Organization (WHO) show that the full death toll associated directly or indirectly with the COVID-19 pandemic (described as "excess mortality") between 1 January 2020 and 31 December 2021 was approximately 14.9 million (range 13.3 million to 16.6 million), representing 9.49 million more deaths than those globally reported as directly attributable to COVID-19.

- The impact of the pandemic has been over several waves with each characterized by unique regional distributions, mortality levels and drivers. Most of the excess deaths (84%) are concentrated in South-East Asia, Europe, and the Americas. Some 68% of excess deaths are concentrated in just 10 countries globally. Middle-income countries account for 81% of the 14.9 million excess deaths (53% in lower-middle-income countries and 28% in upper-middle-income countries) over the 24-month period, with high-income and low-income countries each accounting for 15% and 4%, respectively. The estimates for a 24-month period (2020 and 2021) include a breakdown of excess mortality by age and sex. They confirm that the global death toll was higher for men than for women (57% male, 43% female) and higher among older adults.

- A similar global excess deaths analysis published in the Lancet last month by the Institute for Health Metrics and Evaluation also suggests the full impact of the pandemic has been much greater than indicated by reported deaths due to COVID-19 alone, although their estimates were higher. Although officially reported COVID-19 deaths between Jan 1, 2020, and Dec 31, 2021, totalled 5.94 million worldwide, that study estimated that 18.2 million (95% uncertainty interval 17·1–19·6) people died worldwide because of the COVID-19 pandemic, as measured by excess mortality over that period.

Impact of the SARS-CoV-2 pandemic on female breast, colorectal and non-small cell lung cancer incidence, stage and healthcare pathway to diagnosis during 2020 in Wales (nature.com) (**Study link**)

- This study estimated the impact of pandemic responses on incidence, stage and healthcare pathway to diagnosis for female breast, colorectal and non-small cell lung cancers at population level in Wales by comparing 2019 and 2020 counts and estimated incidence rate ratios (IRR).

- Overall cases in Wales decreased 15.2%, representing over a thousand fewer cases of three common cancers diagnosed in 2020. Decreases were largest in 50–69 year olds for female breast and 80+ year olds for all cancers. This study therefore suggests large numbers of undiagnosed cancer patients more widely due to the ongoing pandemic, societal mitigations and health service reconfiguration in response. The authors argue ongoing surveillance to allow more accurate forecasting to inform effective cancer services' responses and health service optimisation such as screening programmes will be needed to mitigate these impacts.

Children and Education

Monitoring SARS-CoV-2 in air and on surfaces and estimating infection risk in buildings and buses on a university campus (nature.com) (**Study link**)

- The objective of this research was to collect data on SARS-CoV-2 viral load and to examine potential infection risks of people exposed to the virus in publicly accessible environments on a university campus. Viral shedding was demonstrated by the detection of viral RNA in multiple air and surface samples on a university campus.

- In total, 256 air samples and 517 surface samples were collected during the study period, among which positive rates were 1.6% and 1.4%, respectively. Analysis

suggests the total case number on campus was significantly higher in weeks with positive environmental samples than in non-positive weeks. The low overall positivity rate indicated that the risk of exposure to SARS-CoV-2 at monitored locations was low, although more likely in certain locations. Detection of SARS-CoV-2 was most common in gym rooms (75% of the positive air samples and 50% of the positive surface samples), although three out of four positive gym surface samples came from the drinking fountain buttons and none came from shared gym equipment. The authors suggest this may be due to users not being instructed to clean the water fountain after use, unlike gym equipment, highlighting the importance of effective mitigation strategies.

- Risk modelling results suggest inhalation was the predominant route of exposure compared to surface contact, emphasising the importance of protecting individuals from airborne transmission of SARS-CoV-2. The estimated probability of infection was about 1 per 100 exposures to SARS-CoV-2-laden aerosols through inhalation and as high as 1 per 100,000 exposures from contacting contaminated surfaces in simulated scenarios. Overall viral shedding on this university campus was less than viral shedding in healthcare settings and some public community settings that lack routinely scheduled cleaning and disinfection. The authors note that the study was carried out during a period of policies to mitigate the spread of COVID-19 and the negative results should be interpreted with caution as indoor activities return to pre-pandemic levels.

PREPRINT **(not peer-reviewed)**: No magic bullet: limiting in-school transmission in the face of variable SARS-CoV-2 viral loads | medRxiv (**Study link**)

- This study models in-school transmission from first principles to investigate the effectiveness of layered mitigation strategies on limiting in-school spread. The authors examine the effect of masks and air quality (ventilation, filtration and ionizers) on steady-state viral load in classrooms, as well as on the number of particles inhaled by an uninfected person. The effectiveness of these measures in limiting viral transmission is assessed for variants with different levels of mean viral load (Wuhan, Delta, Omicron).

- The results suggest that a layered mitigation strategy (using a "Swiss cheese" model) can be used effectively to limit in-school transmission, with certain limitations. First, poorly designed strategies (insufficient ventilation, no masks, staying open under high levels of community transmission) will permit in-school spread even if some level of mitigation is ostensibly present.

- Second, for viral variants that are sufficiently contagious, it may be difficult to construct any set of interventions capable of blocking transmission once an infected individual is present, underscoring the importance of other measures. The study offers several practical recommendations: the use of a layered mitigation strategy that is designed to limit transmission, with other measures such as frequent surveillance testing and smaller class sizes (such as by offering remote schooling options to those who prefer it) as needed.

- The model used has a number of key assumptions and limitations, such as assuming that children are equally susceptible and infectious as adults (discussed in detail in a supplementary paper). It also assumes perfect compliance with mask-wearing, which is not likely to be true in practice and does not consider the effect of vaccination on transmission or risk of infection.

Mental health

Healthcare contacts with self-harm during COVID-19: An e-cohort whole-population-based study using individual-level linked routine electronic health records in Wales, UK, 2016—March 2021 (plos.org) (**Study link**)

- This retrospective cohort study used routine electronic healthcare data for Wales in the SAIL Databank, from 2016 to March 14, 2021. Primary, emergency and secondary care contacts with self-harm at any time between 2016 and March 14, 2021 were identified. Weekly trends were modelled, with differences between 2020 (to March 2021) and comparison years 2016–2018 (to March 2017–2019) quantified using difference in differences, from which mean rate of odds ratios (µROR) across years was reported.

- The study included 3,220,784 individuals over the study period, using anonymous recorded data in the Welsh Demographic Service dataset which includes all individuals registered with a GP in Wales. Self-harm contacts reduced across services in March and December 2020 compared to previous years. Primary care contacts with self-harm reduced disproportionately compared to non-self-harm contacts (µROR = 0.7), while their proportion increased in emergency departments during April 2020 (µROR = 1.3) and hospital admissions during April-May 2020 (µROR = 1.2,). Despite this, those who self-harmed in April 2020 were more likely to be seen in primary care than other settings compared to previous years (µROR = 1.2,). A lower proportion of those with self-harm contacts in emergency departments were subsequently admitted to hospital in December 2020 compared to previous years (µROR = 0.5).

- These findings suggest that those who self-harmed during the COVID-19 pandemic in Wales may have been less likely to seek help, and those who did so faced more stringent criteria for admission. The authors suggest communications encouraging those who self-harm to seek help during pandemics may be beneficial. However, this needs to be supported by maintained provision of mental health services.

Testing

Analysis of Diagnostic Modalities in Hospital-admitted Patients Evaluated for COVID-19 | In Vivo (iiarjournals.org) (**Study link**)

- This study aimed to retrospectively assess the diagnostic performance of reverse transcriptase polymerase chain reaction (RT-PCR), low-dose chest computed tomography (CT), and serological testing, alone and in combinations, as well as routine inflammatory markers in patients evaluated for COVID-19 during the first wave in early 2020. The authors retrospectively analysed data of all patients who were admitted to the emergency department due to fever and/or respiratory symptoms. Sensitivities and specificities were calculated for RT-PCR, CT, and serology alone, as well as the combinations of RT-PCR+CT, RT-PCR+serology, CT+serology, and all three modalities.

- Of 221 patients with a median age of 72 years, 113 were classified as COVID-19 positive. Among 180 patients from which data on CT and RT-PCR were available, RT-PCR had the highest sensitivity to detect COVID-19 (0.87; 95%CI=0.78-0.93). Notably, the addition of CT in the analysis increased sensitivity to 0.89 (95%CI=0.8-0.94), but

lowered specificity from 1 (95%CI=0.96-1) to 0.9 (95%CI=0.83-0.95). The combination of RT-PCR, CT and serology (n=60 patients with complete dataset) yielded a sensitivity of 0.83 (95%CI=0.61-0.94) and specificity of 0.86 (95%CI=0.72-0.93).

- The authors conclude that overall, RT-PCR was the best single test in patients evaluated for COVID-19. Conversely, the routine performance of chest CT adds little sensitivity and decreases specificity, limiting the value of routine use. The authors therefore suggest that CT scans should be performed only in patients with negative RT-PCR but high clinical suspicion for COVID-19.

Non-pharmaceutical interventions

Face mask use in healthcare settings: effects on communication, cognition, listening effort and strategies for amelioration (springeropen.com) (**Study link**)

- This study investigated mask use and the difficulties it may pose in healthcare settings using a survey of mask use challenges in the domains of communication, listening effort, cognition, and rehabilitation among 243 participants.

- Overall, results show that in healthcare settings there is increased cognitive load and listening effort for both patients and providers, as well as changes in clinical efficiency for providers when utilizing masks. These effects are often greater with hearing loss. The authors suggest these results provide information about the clinical strain introduced from mask use in healthcare settings that may allow an improved experience with facemasks for both patients and providers in healthcare settings. Patients reported written and visual instructions would be most beneficial to include in appointments among the other rehabilitative strategies which are discussed.

Maintaining face mask use before and after achieving different COVID-19 vaccination coverage levels: a modelling study - The Lancet Public Health (**Study link**)

- In this computational simulation-model study, simulation experiments compared what would happen if face masks were used versus not used in a US population until given final vaccination coverages were achieved. Different scenarios varied the target vaccination coverage (70–90%), the date these coverages were achieved (Jan 1, 2022, to July 1, 2022), and the date the population discontinued wearing face masks.

- Results suggest that maintaining face mask use (at the coverage seen in the USA from March, 2020, to July, 2020) until target vaccination coverages were achieved was cost-effective and in many cases cost saving from both the societal and third-party payer perspectives across nearly all scenarios explored. Face mask use was estimated to be cost-effective and usually cost saving when the cost of face masks per person per day was ≤US$1·25. In all scenarios, it was estimated to be cost-effective to maintain face mask use for about 2–10 weeks beyond the date that target vaccination coverage (70–90%) was achieved, with this added duration being longer when the target coverage was achieved during winter versus summer. Factors that might increase the transmissibility of the virus (e.g., emergence of the delta [B.1.617.2] and omicron [B.1.1.529] variants), or decrease vaccine effectiveness (e.g., waning immunity or escape variants), or increase social interactions among certain segments of the population, only increased the cost savings or cost-effectiveness provided by maintaining face mask use.

- The authors argue their study provides strong support for maintaining face mask use until and a short time after achieving various final vaccination coverage levels, given that maintaining face mask use can be not just cost-effective, but even cost saving. The emergence of the omicron variant and the prospect of future variants that might be more transmissible and reduce vaccine effectiveness only increases the value of face masks.

Pandemic lessons learned and commentaries

Science Media Centre recommendations on science and the media based on experience during the COVID 19 pandemic (sciencemediacentre.org) (**Study link**)

- An article by the Senior Press Manager at the Science Media Centre outlines the organisation's recommendations regarding science and the media, based on their experiences during COVID-19. The post highlights which aspects they felt were most important and where changes or clarifications might be made ahead of the next emergency:

  o Recommendation 1: Scientists should be encouraged to engage with the media during a crisis when their area of expertise hits the headlines, no matter how controversial the topic. Universities, research institutes and funders should support their academics to speak to journalists, including offering media training to those who want it.

  o Recommendation 2: The scientific community and universities need to retain some capacity and expertise in their communications teams to be 'media-first' and to do research communication.

  o Recommendation 3: Newsrooms should retain and invest in their specialist science and health reporters.

  o Recommendation 4: Scientists should stay in their lane and be 'sciencey'.

  o Recommendation 5: Multiple voices and open scientific disagreement is part and parcel of good science.

  o Recommendation 6: The communication of new scientific data conducted in universities and research institutes should be separate from government communication, and announcements of new scientific data should not be on the government 'grid'.

  o Recommendation 7: Independent scientists appointed to a sage should be encouraged to speak to the media in their academic capacity about their science.

  o Recommendation 8: The nature of scientific advice should be better explained and understood before the next emergency.

  o Recommendation 9: The CSA and CMO should make themselves available to the media and public as well as advising and briefing ministers.

Long COVID

Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK - Office for National Statistics (ons.gov.uk) (**Study Link**)

- Based on data from the ONS Covid-19 Infection Survey, an estimated 1.8 million people living in private households in the UK (2.8% of the population) were experiencing self-reported long COVID (symptoms persisting for more than four weeks after the first suspected coronavirus (COVID-19) infection that were not explained by something else) as of 3 April 2022 (see Figure 1 below).

- Of people with self-reported long COVID, 21% first had (or suspected they had) COVID-19 less than 12 weeks previously, 73% at least 12 weeks previously, 44% at least one year previously and 13% at least two years previously.

- Of people with self-reported long COVID, 556,000 (31%) first had (or suspected they had) COVID-19 before Alpha became the main variant; this figure was 249,000 (14%) in the Alpha period, 446,000 (25%) in the Delta period, and 438,000 (24%) in the Omicron period.

- Long COVID symptoms adversely affected the day-to-day activities of 1.2 million people (67% of those with self-reported long COVID), with 346,000 (19%) reporting that their ability to undertake their day-to-day activities had been "limited a lot".

- Fatigue continued to be the most common symptom reported as part of individuals' experience of long COVID (51% of those with self-reported long COVID), followed by shortness of breath (33%), loss of sense of smell (26%), and difficulty concentrating (23%).

- As a proportion of the UK population, prevalence of self-reported long COVID was greatest in people aged 35 to 49 years, females, people living in more deprived areas, those working in social care, teaching and education or health care, and those with another activity-limiting health condition or disability.

- The estimates presented in this analysis relate to self-reported long COVID, as experienced by study participants who responded to a representative survey, rather than clinically diagnosed ongoing symptomatic COVID-19 or post-COVID-19 syndrome in the full population.
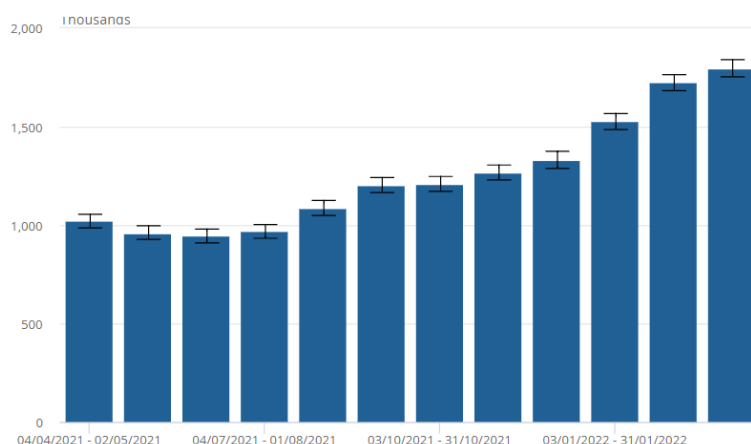

Figure: Estimated number of people living in private households with self-reported long COVID of any duration, UK: four-week periods ending 2 May 2021 to 3 April 2022

Clinical characteristics with inflammation profiling of long COVID and association with 1-year recovery following hospitalisation in the UK: a prospective observational study - ScienceDirect (**Study link**)

- The Post-hospitalisation COVID-19 study (PHOSP-COVID) is a prospective, longitudinal cohort study of adults (aged ≥18 years) discharged from hospital with COVID-19 across the UK.

- 2320 participants discharged from hospital between March 7, 2020, and April 18, 2021, were assessed at 5 months after discharge and 807 (32·7%) participants completed both the 5-month and 1-year visits. 279 (35·6%) of these 807 patients were women and 505 (64·4%) were men, with a mean age of 58·7 (SD 12·5) years, and 224 (27·8%) had received invasive mechanical ventilation. The proportion of patients reporting full recovery was unchanged between 5 months (501 [25·5%] of 1965) and 1 year (232 [28·9%] of 804). Cluster analysis (n=1636) corroborated the previously reported four clusters: very severe, severe, moderate with cognitive impairment, and mild, relating to the severity of physical health, mental health, and cognitive impairment at 5 months.

- Overall the sequelae of a hospital admission with COVID-19 were substantial 1 year after discharge across a range of health domains, with the minority in the PHOSP cohort feeling fully recovered. Patient-perceived health-related quality of life was reduced at 1 year compared with before hospital admission. The most common ongoing symptoms were fatigue, muscle pain, physically slowing down, poor sleep, and breathlessness. Health-related quality of life before COVID-19 was substantially greater than at 5 months after discharge across all four clusters, indicating that the persistent burden of impaired physical and mental health is not simply explained by pre-existing morbidity.

- Taken together, the authors argue this study highlights an urgent need for health-care services to support this large and rapidly increasing patient population in whom a substantial burden of symptoms exists, including reduced exercise capacity and large decrements in health-related quality of life 1 year after hospital discharge. Without effective treatments, long COVID could become a highly prevalent new long-term condition. The study also provides a rationale for investigating treatment strategies for long COVID with a precision-medicine approach to target treatments to the relevant phenotype to restore health-related quality of life.