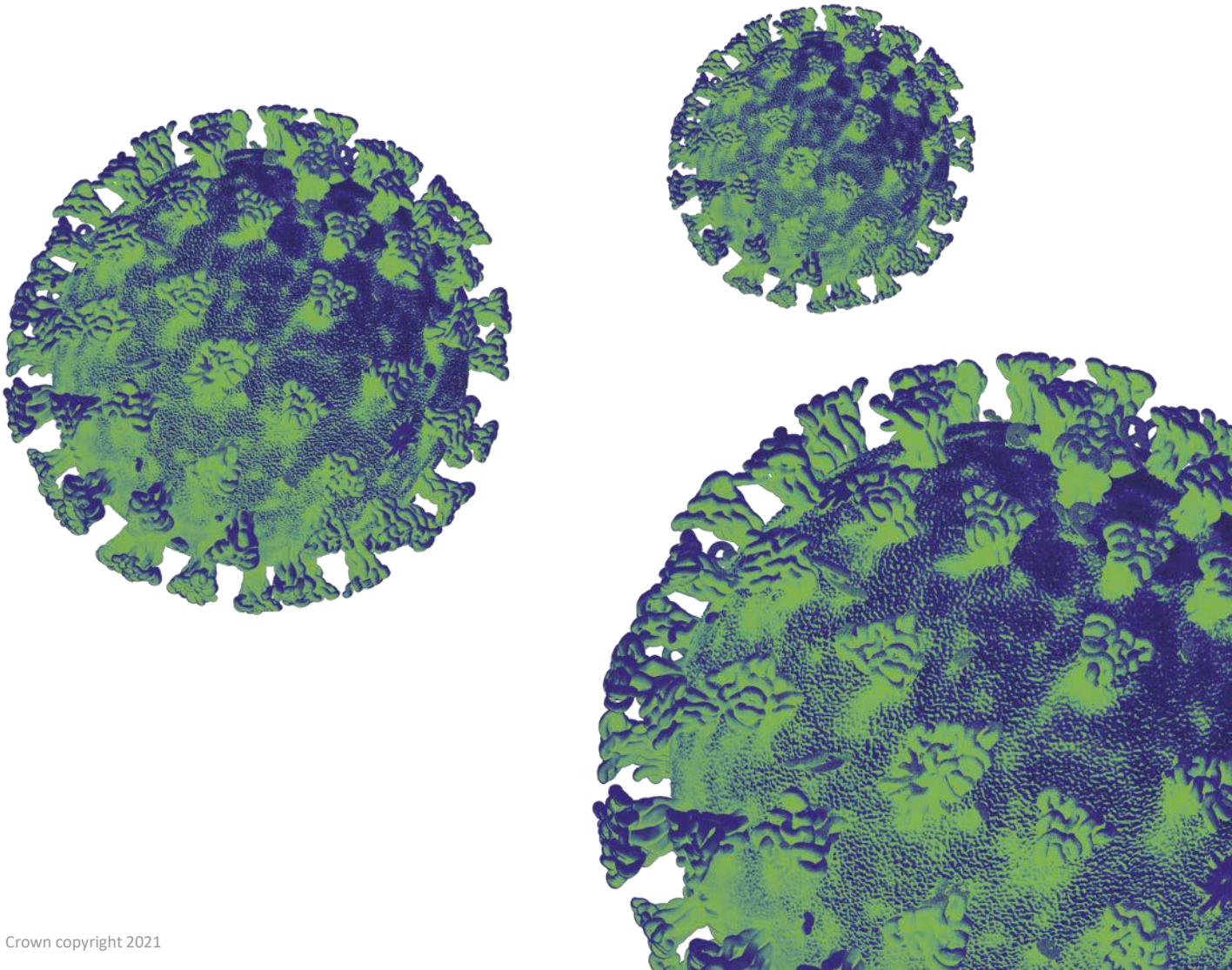
Llywodraeth Cymru
Welsh Government

Technical Advisory Cell

Summary of Advice

5 November 2021



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Top line summary

- Overall cases of COVID-19 have decreased across Wales and test positivity has remained stable, compared to last week. Cases have fallen by 22% in the 7-day period ending 29 October to 546 cases per 100,000. However test positivity during the same period has remained stable at a high level of 23%. It is uncertain to what extent this reduction in cases is driven by half term or other factors such as testing. We will need to continue monitoring case rates and other key indicators in each nation carefully to better understand the impact of easements of restrictions, return of schools and universities, and impact on the NHS.
- The number of beds occupied with COVID-19 patients (confirmed, suspected and recovering) is currently fluctuating, although in the most recent week COVID-19 pressure on the NHS has generally increased. This was due to an increase in recovering and suspected COVID-19 patients despite a decrease in confirmed COVID-19 patients. As at 3 November 2021, there were 857 COVID-19 related patients (suspected, confirmed and recovering) occupying a hospital bed. This compares to 829 (28 more occupied beds) on 27 October 2021. Confirmed patients accounted for 585 of the total occupied beds.
- There are 72 patients with suspected or confirmed COVID-19 in critical care beds in Wales. This is 92 lower than the maximum COVID-19 position of approximately 164. The total number of patients in critical care for both COVID-19 and non-COVID-19 is 187, 35 more than the 152 baseline number of critical care beds available before the COVID-19 pandemic.
- The number of deaths has decreased slightly during the 7-day period ending 30 October from 66 to 63 according to PHW, but remains relatively low in comparison to previous waves during periods of similar incidence.
- PHW's most recent Surveillance of vaccine status in confirmed COVID-19 episodes and hospital inpatients shows that, in the most recent 2-week reporting period ending 17 October, 27.9% of COVID-19 hospital inpatients are unvaccinated compared with 48.0% double-vaccinated. When split by age, 2.5% of hospitalised patients aged 60+ are unvaccinated compared with 96% double-vaccinated, and 14.0% of patients under 60 are unvaccinated compared with 79.8% of patients double-vaccinated. This data should not be interpreted as measures of vaccination effectiveness; for this see the most recent VEEP estimates.
- The UKHSA consensus estimate of the reproduction number for Wales is between 0.8 and 1.1 and a doubling time -31 days to flat (as at 3 November 2021), while PHW's estimate is 0.9 with a halving time of 15 days to flat (3 November 2021). Note that UKHSA's estimate is typically lagged by 2-3 weeks while PHW, which uses a different methodology, is lagged by around 1 week.

- As at 10pm 1 November 2021, a total of 5,159,580 doses of COVID-19 vaccine were given in Wales. 2,446,430 first doses and 2,244,866 second doses have been received by the Welsh population. 22,136 were third dose primary course for immunocompromised individuals, and 446,128 were booster doses. A breakdown of uptake by priority group and age is below (Source: PHW)
- The most recent issue of the ONS Coronavirus (COVID-19) Infection Survey results, 3 to 9 October, estimates the percentage of people testing positive increased over the most recent week in Northern Ireland and over the most recent two weeks in England. In Wales and Scotland the trend is uncertain in the most recent week. The survey also estimated that 2.39% of the community population in Wales had COVID-19 (95% credible interval: 1.92% to 2.92%). This equates to approximately 1 person in every 40 (95% credible interval: 1 in 50 to 1 in 35), or 72,700 people during this time (95% credible interval: 58,300 to 88,700).
- The most recent PHW weekly Influenza and Acute Respiratory Infection report suggests that RSV continues to circulate in Wales, while influenza does not, with 1 confirmed influenza-A case since the previous week. The current increase in RSV cases is earlier than the usual RSV season in Wales and it is unclear whether it will follow the usual epidemic pattern. RSV and rhinovirus are the most commonly detected cause of non-COVID-19 Acute Respiratory Infection (ARI).
- Observed levels of confirmed COVID-19 cases, COVID-19 admissions to hospital and ICU, and ICU occupancy are above the levels estimated by the June 2021 TAC reasonable worst case (RWC) modelling scenario. COVID-19 hospital bed occupancy and COVID-19-related deaths are between the most likely scenario (MLS) and the RWC scenario.

Research evidence summary

Vaccination and Immunity

- A preprint (non-peer reviewed) US study highlights the important immunological benefits of vaccination in the context of breakthrough infections of the Delta variant. Those included in the analysis who experienced breakthrough infections of SARS-CoV-2 following vaccination all experienced mild disease and had higher antibody and T-cell responses than unvaccinated participants.
- An Israel study of waning immunity indicates that immunity against Delta variant infection reduced in all age groups a few months after receipt of the second dose of vaccine. Vaccinated persons were found to be protected even after six months compared with unvaccinated persons; however vaccine effectiveness against infection was considerably lower than it had been closer to the vaccination date. A potential confounder for these findings relative to the UK is that Israel administered the majority of second doses three weeks after the initial injection, whereas the United Kingdom adopted a longer dosing interval which research suggests results in higher neutralising antibody levels.
- A Lancet evidence review of the impact of infection or vaccination on lasting immunity against SARS-CoV-2 concludes that current evidence from case studies and large observational studies suggests that, consistent with research

on other common respiratory viruses, a protective immunological response lasts for approximately 5–12 months from primary infection, notwithstanding a critical variant of concern. In the short-to-medium term current vaccines will require updating to maintain their effectiveness and ultimately it is likely the duration of protective immunity from natural infection and from vaccination will determine the frequency of outbreaks.

Variants and Transmission

- The most recent UKHSA variant technical briefing assesses the Delta sub-lineage AY.4.2, also referred to as 'Delta plus'. Estimated growth rates are slightly higher for AY.4.2 than for Delta (19% higher), and the household secondary attack rate is higher for AY.4.2 cases than for other Delta cases (6-12% higher). However there is no evidence that vaccine effectiveness against symptomatic or asymptomatic infection is lower for AY4.2 vs dominant Delta variant after 2 doses of vaccine or there is a significant difference in severity. Analysis will continue as more data becomes available.

- An analysis of Delta vs Alpha variant generation time (the time between infections in infector-infectee pairs) concludes the Delta variant transmits more quickly than previously circulating variants, likely due to a combination of both increased transmissibility and a shorter generation time (around 1 day shorter time between cases). This has implications for interventions such as contact tracing, testing and isolation, which are less effective if the virus is transmitted quickly, as well as transmission modelling.

- Analysis from the REACT-1 study shows that between 20 May and 12 July 2021 infections were increasing exponentially, primarily driven by the Delta variant with high infection prevalence among younger, unvaccinated people. Unvaccinated people were three times more likely than double-vaccinated people to test positive. However, after adjusting for age and other variables, vaccine effectiveness for double-vaccinated people was estimated at between ~50% and ~60% during this period in England. Increased social mixing in the presence of Delta had the potential to generate sustained growth in infections, even at high levels of vaccination. As the Delta variant became dominant in mid-April 2021, the associations between infections and hospitalisations and deaths began to re-converge, potentially reflecting the increased prevalence and severity of Delta, a changing age mix of hospitalised cases to younger ages, and possible waning of protection.

NPIs and Environmental Science

- A modelling paper looking to explain the observed phenomenon that most SARS-CoV-2 transmission occurs indoors whereas its outdoor transmission is rare suggests room ventilation rate significantly affects short-range airborne exposure. When the ventilation rate in a room is insufficient, the airborne infection risks due to both short- and long-range transmission are high. A ventilation rate of 10 L/s per person provides a similar concentration vs distance decay profile to that in outdoor settings and a low building ventilation rate worsens both long- and short-range airborne transmission.

- A study of focus group participants' perceptions of non-adherence to COVID-19 policy measures highlights the importance of clear policy decisions and

trustworthy policymakers in ensuring public adherence to COVID-19 protective measures.

- Another study examining the relationship of autonomy to follow NPIs with infection, how this varies and where support or public communication could be directed, using COVID-19 Infection Study data, finds that wearing a face covering or mask outside the home can reduce the unequal effects of exposure to COVID-19 exacerbated by individual or employment circumstances.

Modelling

- Modelling of the impact of testing and isolation on public health outcomes suggests strategic changes in the characteristics of the testing system, including test administration, test delays, and test sensitivity, can reduce reliance on preventative NPIs that cause severe socio-economic burdens without compromising public health outcomes in the future. Increasing testing capacity, including the number of tests available and the speed at which test results are provided, can reduce reliance on costly preventative interventions.

- Another modelling study looks at the impact of the delay to England's NPI-easing roadmap, showing the risk of a large wave of COVID-19 hospital admissions resulting from lifting NPIs can be mitigated if the timing of NPI relaxations is carefully balanced against vaccination coverage. However, Delta's high transmissibility means that population immunity, whether vaccine induced or infection induced, may be insufficient to keep Rt below one. Variants of Concern, their transmissibility, vaccine uptake, and vaccine effectiveness should therefore be carefully monitored as countries relax pandemic control measures.

Children and Education

- Round 14 of the REACT-1 study highlights that infections increased exponentially in the largely unvaccinated 5-to-17-year age group coinciding with the start of the autumn school term in England. In adults, the higher prevalence of swab-positivity following two doses of vaccine from three to six months compared to within three months of second dose supports the use of a booster vaccine.

- A Rapid Review conducted by the Wales COVID-19 Evidence Centre (WCEC) suggests that, subject to the limitations caused by a paucity of relevant research, overall there was no direct systematic review evidence that evaluated strategies to support learning for 16-19 year old learners following the COVID-19 pandemic. However there is consensus in pre-pandemic literature that targeting support activity at learners from the most deprived socio-economic backgrounds has a significant positive impact on their progress.

Epidemiology and Clinical

- A systematic review of in-patient mortality associated with nosocomial and community-acquired COVID-19 suggests adults who acquire SARS-CoV-2 whilst already hospitalised are at greater risk of mortality compared to patients admitted following community-acquired infection; this finding is largely driven by a substantially increased risk of death in individuals with malignancy or who had undergone transplantation. These findings inform public health and infection control policy and argue for individualised clinical interventions to combat the threat of nosocomial COVID-19, particularly for immunosuppressed groups.

- A longitudinal study measuring the long-term health-related quality of life of non-hospitalised COVID-19 cases with PCR-confirmed SARS-CoV-2 infection shows 1 in 6 cases report ongoing symptoms at six months, and 10% report prolonged loss of function compared to pre-COVID-19 baselines. A marked health burden was observed among older COVID-19 cases and those with persistent physical symptoms. Losses of health-related quality of life in non-hospitalised COVID-19 cases increase by age and for cases with symptoms after 6 months. At a population level, at least 21% of the total COVID-19-related disease burden in England is attributable to morbidity.
- Another WCEC evidence review reinforces that although pregnant women have the same risk of getting COVID-19 as other healthy adults, they are at slightly increased risk of becoming severely unwell, particularly in third trimester or if they have an identified risk factor and are more likely to have pregnancy complications like preterm birth or stillbirth. More than 200,000 women in the UK and USA have had a COVID-19 vaccine in pregnancy, with no concerning safety signals and excellent real-world evidence of efficacy. There has been no evidence to suggest foetal harm following vaccination against COVID-19. Vaccination against COVID-19 at any time during pregnancy and whilst breastfeeding is recommended, and preference is to offer the Pfizer-BioNTech or Moderna vaccines.

Wales Sit-Rep

- The latest fortnightly COVID-19 Situational Report, containing the most recent data on epidemiological surveillance, NHS status, wastewater monitoring, education and children, international travel, mobility, vaccination and population immunity and forward projections for Wales is available here.
- Overall cases of COVID-19 have decreased across Wales and test positivity has remained stable, compared to last week. Cases have fallen by 22% in the 7 day period ending 29 October to 546 cases per 100,000. However test positivity during the same period has remained stable at a high level of 23%. It is uncertain to what extent this reduction in cases is driven by half term or other factors such as testing. We will need to continue monitoring case rates and other key indicators in each nation carefully to better understand the impact of easements of restrictions, return of schools and universities, and impact on the NHS.
- In the week ending 29 October 2021 the mean wastewater signal for Wales is high but remains variable. The South Wales normalised SARS-CoV-2 wastewater signals trend data are currently difficult to interpret in terms of the COVID-19 cases for the associated wastewater catchment populations due to significant flow events. However, levels of both remain relatively high by comparison with the summer months.
- The number of beds occupied with COVID-19 patients (confirmed, suspected and recovering) is currently fluctuating, although in the most recent week COVID-19 pressure on the NHS has generally increased. This was due to an increase in recovering and suspected COVID-19 patients despite a decrease in confirmed COVID-19 patients. As at 3 November 2021, there were 857 COVID-19 related patients (Suspected, Confirmed and Recovering) occupying a hospital bed. This

`compares to 829 (28 more occupied beds) on 27 October 2021. Confirmed patients accounted for 585 of the total occupied beds.

- There are 72 patients with Suspected or Confirmed COVID-19 in critical care beds in Wales. This is 92 lower than the maximum COVID-19 position of approximately 164. The total number of patients in critical care for both COVID-19 and non-COVID-19 stands at 187, 35 more than the 152 baseline number of critical care beds available before the COVID-19 pandemic. Note: The charts presented do not include recovering patients.
- The number of deaths has decreased slightly during the 7 day period ending 30 October from 66 to 63 according to PHW, but remains relatively low in comparison to previous waves during periods of similar incidence.
- PHW's most recent Surveillance of vaccine status in confirmed COVID-19 episodes and hospital inpatients shows that in the most recent 2 week reporting period ending 17 October, 27.9% of COVID-19 hospital inpatients are unvaccinated compared with 48.0% double-vaccinated. When split by age, 2.5% of hospitalised patients aged 60+ are unvaccinated compared with 96% double-vaccinated, and 14.0% of patients under 60 are unvaccinated compared with 79.8% of patients double-vaccinated. This data should not be interpreted as measures of vaccination effectiveness- for this see the most recent VEEP estimates.
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- As at 10pm 1 November 2021, a total of 5,159,580 doses of COVID-19 vaccine were given in Wales. 2,446,430 first doses and 2,244,866 second doses have been received by the Welsh population. 22,136 were third dose primary course for immunocompromised individuals, and 446,128 were booster doses. A breakdown of uptake by priority group and age is below (Source: PHW)

Uptake by priority group and age, counting individuals in all groups in which they belong

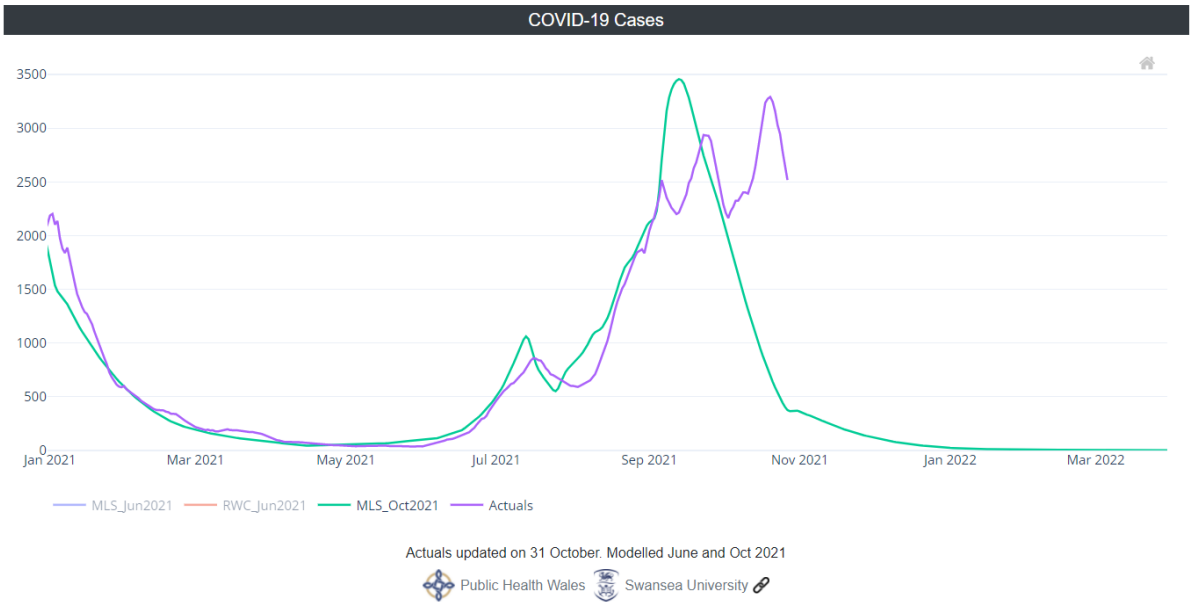
In this table groups are not mutually exclusive, so individuals appear in every group that describes them, and can be counted in more than one group. This is a 'public health' view, showing the total numbers in each priority group.

Group	Group size (n)	Received 1st dose (n)	Completed primary course* (n)	Received booster dose** (n)	First dose uptake (%)	Primary course uptake* (%)	Booster dose uptake** (%)
Severely Immunosuppressed	48,805	48,428	23,365		99.2%	47.9%	
Care home residents	13,900	13,647	13,459	9,867	98.2%	96.8%	71.0%
Care home worker	38,733	36,530	35,509	21,728	94.3%	91.7%	56.1%
80 years and older	165,660	159,320	157,973	103,796	96.2%	95.4%	62.7%
Health care worker	143,114	138,996	136,782	95,016	97.1%	95.6%	66.4%
Social care worker		45,524	44,994	28,796			
Aged 75-79 years	130,894	126,950	126,123	77,718	97.0%	96.4%	59.4%
Aged 70-74 years	181,997	175,377	174,320	87,005	96.4%	95.8%	47.8%
Clinically extremely vulnerable aged 16-69..	80,276	76,498	75,247	14,118	95.3%	93.7%	17.6%
Aged 65-69 years	179,677	171,002	169,520	39,506	95.2%	94.3%	22.0%
Clinical risk groups aged 12-64 years	357,429	321,631	308,304	10,610	90.0%	86.3%	3.0%
Aged 60-64 years	205,191	191,999	189,694	24,050	93.6%	92.4%	11.7%
Aged 55-59 years	233,434	214,437	211,214	27,342	91.9%	90.5%	11.7%
Aged 50-54 years	228,386	205,671	201,709	25,394	90.1%	88.3%	11.1%
Aged 40-49 years	395,171	336,756	325,490	36,552	85.2%	82.4%	9.2%
Aged 30-39 years	428,838	337,659	316,489	28,783	78.7%	73.8%	6.7%
Aged 18-29 years	488,708	382,064	346,110	21,446	78.2%	70.8%	4.4%
Aged 12-15 years***	164,568	76,054	872		46.2%	0.5%	
Aged 16-17 years	70,179	52,584	18,445	464	74.9%	26.3%	0.7%

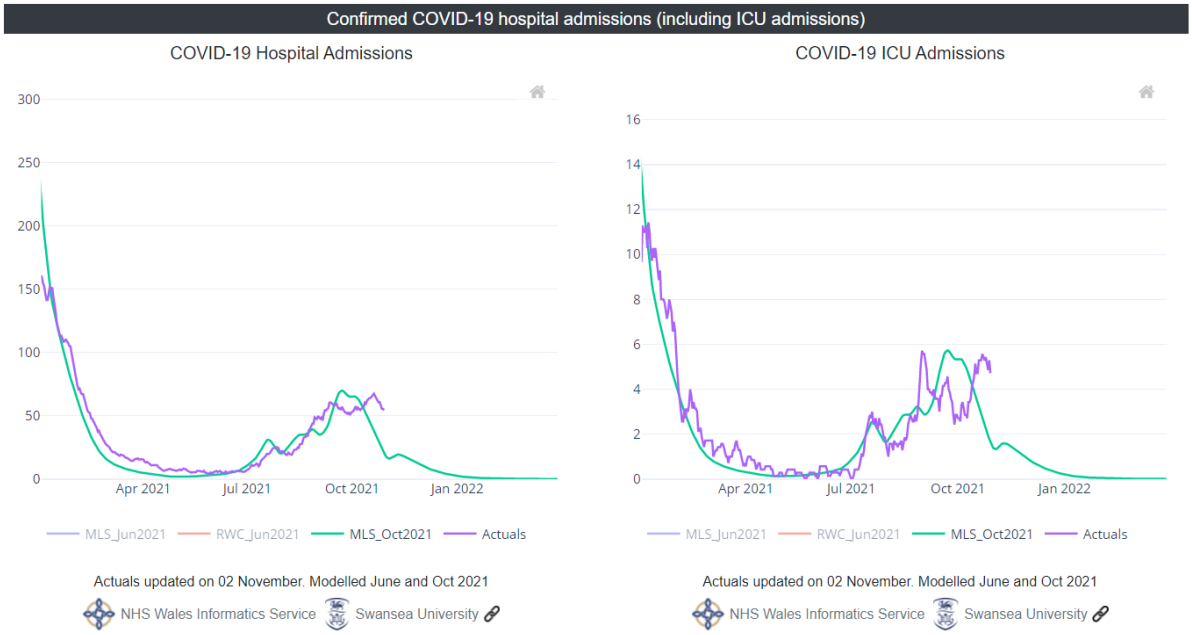
- The most recent issue of the ONS Coronavirus (COVID-19) Infection Survey results, 3 to 9 October, estimates the percentage of people testing positive increased over the most recent week in Northern Ireland and over the most recent two weeks in England. In Wales and Scotland the trend is uncertain in the most recent week.
- The survey also estimated that 2.39% of the community population in Wales had COVID-19 (95% credible interval: 1.92% to 2.92%). This equates to approximately 1 person in every 40 (95% credible interval: 1 in 50 to 1 in 35), or 72,700 people during this time (95% credible interval: 58,300 to 88,700).This compares to around 1 in 50 people in England, around 1 in 80 people in Scotland, and around 1 in 65 people in Northern Ireland.
- The most recent PHW weekly Influenza and Acute Respiratory Infection report suggests that RSV continues to circulate in Wales and influenza is not, 1 confirmed influenza-A cases since the previous week. The current increase in cases is earlier than the usual RSV season in Wales and it is unclear whether it will follow the usual epidemic pattern for RSV. RSV and rhinovirus are the most commonly detected cause of non-COVID-19 Acute Respiratory Infection (ARI).

TAC modelling: Most Likely Scenarios (MLS) Versus Actual Figures

- Observed levels of confirmed COVID-19 cases, COVID-19 admissions to hospital and ICU, and ICU occupancy are above the levels estimated by the June 2021 reasonable worst case (RWC) scenario. COVID-19 hospital bed occupancy and COVID-19-related deaths are between the most likely scenario (MLS) and the RWC scenario.
- In the charts below “MLS_Oct2021” is the current (October 2021) most likely scenario, and “Actuals” represents the actual observed values for each indicator.

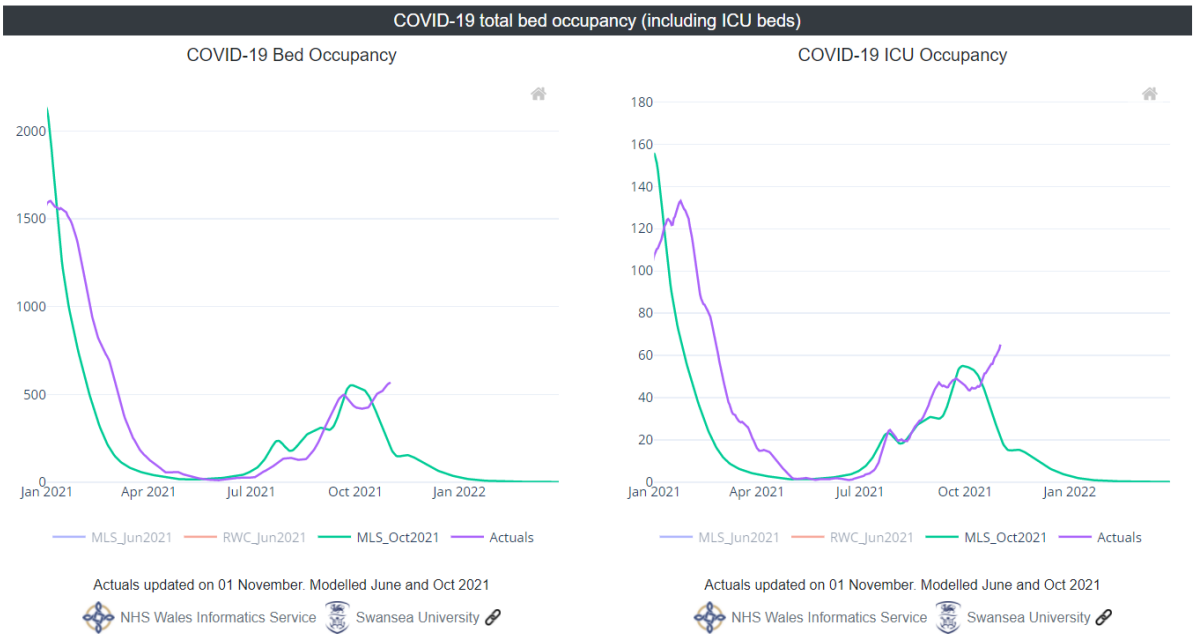


- Confirmed COVID-19 cases were low and stable throughout April and May but started to rise in June 2021. With the exception of a dip in July and early September, confirmed COVID-19 cases rose from June until late September. Since then, cases fell, before rising again until mid-October. Cases have been falling again since then but at present it is not possible to tell if this downward trend will continue or if it is another temporary decrease. On 27 October, confirmed COVID-19 cases were much higher than the MLS produced in October 2021. *Note that for the modelled scenarios, "Cases" refers to symptomatic cases only.*



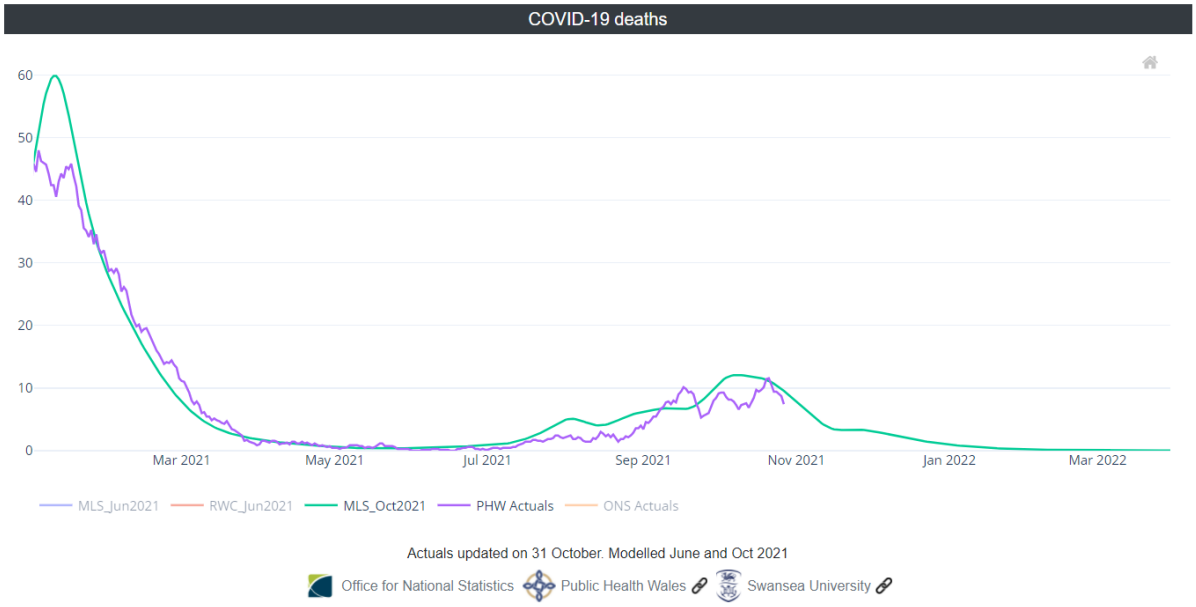
- COVID-19 hospital admissions decreased slowly in May and June 2021 before starting to increase in July. Other than a small dip in early August they continued increasing from July to mid-September, at which point they began to decrease, before rising again. Similar to cases, admissions have begun to fall again but it is unclear if this downward trend will continue.

- On 27 October 2021 the 7-day average for COVID-19 hospital admissions was 55 admissions per day and was higher than the MLS produced in October 2021.
- In May and June 2021 COVID-19 ICU hospital admissions were very low and stable. They rose in early July, reached a peak on 19 July 2021 and then fell. They have since risen again to a similar level to the peak in July, but numbers are still low overall. On 27 October 2021, the 7-day rolling average for COVID-19 ICU hospital admissions was 5 per day, which is higher than the MLS produced in October 2021.



- COVID-19 confirmed total bed occupancy (which includes ICU beds) was low and stable throughout May and June and started to rise in early July and has continued to rise, with the exception of a dip in mid-October, through to the end of October. As of 27 October 2021 the 7-day average for COVID-19 confirmed total bed occupancy was 539 beds occupied by COVID-19 confirmed COVID-19 patients – above the level estimated by the MLS produced in October 2021.

- Through most of May and June COVID-19 confirmed ICU occupancy was very low at between 1 and 2 per day. It began to rise in early July and rose at a rate similar to the MLS. ICU occupancy remained relatively constant in September but has been increasing again throughout October. As of 27 October 2021, COVID-19 confirmed ICU occupancy was 59, which is above the MLS.



- COVID-19 deaths were very low between April and mid-July 2021. They rose slowly from mid-July through to mid-September and have remained relatively constant since and mostly lower than the October 2021 MLS. As of 27 October, the 7-day average of COVID-19-related deaths reported by Public Health Wales was a little over 7 per day, lower than the MLS produced in October 2021.

COVID-19 evidence - round-up

This section aims to highlight 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.

Vaccination and Immunity

PREPRINT: Immune Responses in Fully Vaccinated Individuals Following Breakthrough Infection with the SARS-CoV-2 Delta Variant in Provincetown, Massachusetts

- This study highlights the important immunological benefits of vaccination in the context of breakthrough infections of the Delta variant. Those who experienced breakthrough infections of SARS-CoV-2 all experienced mild disease and had higher antibody and T cell responses than vaccinated uninfected individuals.
- A cluster of over 1,000 infections with the SARS-CoV-2 Delta variant was identified in a predominantly fully vaccinated population in Massachusetts in July 2021. Humoral and cellular immune responses were assessed in 35 vaccinated

individuals who were tested for SARS-CoV-2 in the Massachusetts Department of Public Health outbreak investigation, 14 of whom tested positive.

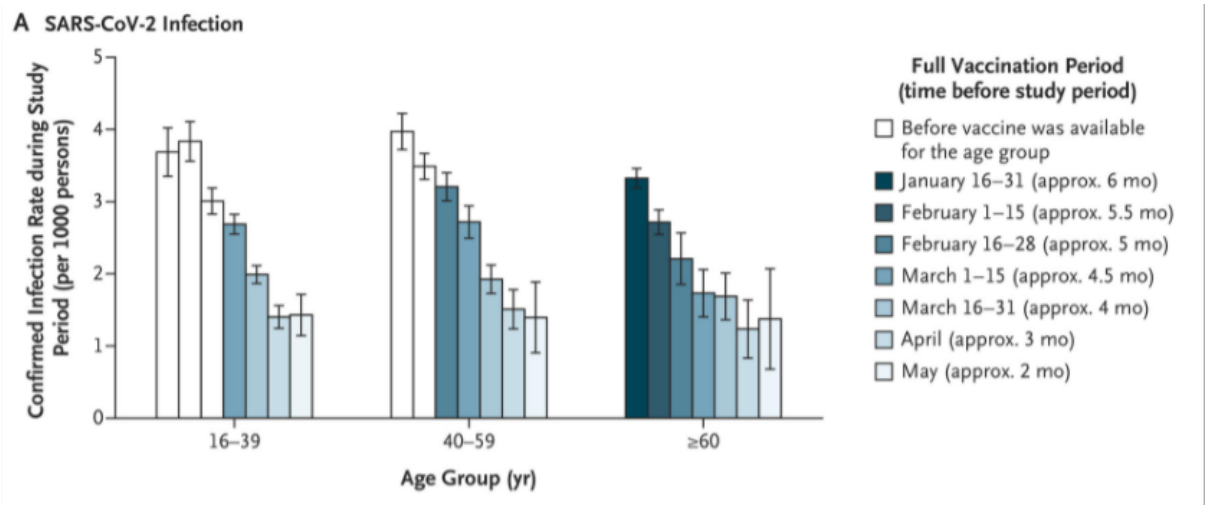
- Compared to vaccinated individuals who tested negative for SARS-CoV-2, vaccinated individuals who tested positive showed:
    - 28 times higher binding antibody titres against the Delta variant
    - 34 times higher neutralising antibody titres against the Delta variant
    - 4.4 times higher Spike-specific CD8+ T cell responses against the Delta variant
- Vaccinated infected individuals had markedly higher binding and neutralizing antibody responses as well as higher cellular immune responses compared with vaccinated uninfected individuals, suggesting that breakthrough infections triggered robust anamnestic immune responses. The authors speculate that the extraordinarily high antibody titres observed in vaccinated individuals who develop breakthrough infections may lead to subsequent long-term protection in those individuals.
- The study is limited by the relatively small number of individuals in this immunologic analysis compared with the large total number of individuals in the wider outbreak. Nevertheless, the magnitude and consistency of the immunologic differences observed between vaccinated infected and vaccinated uninfected individuals suggest the generalizability of the conclusions. The vaccinated infected group was generally younger than the vaccinated uninfected group, which may reflect different risk behaviours or exposures based on age. However, age did not appear to correlate with the magnitude of binding or neutralizing antibody titres in this cohort.
- Full paper: Immune Responses in Fully Vaccinated Individuals Following Breakthrough Infection with the SARS-CoV-2 Delta Variant in Provincetown, Massachusetts | medRxiv

Waning Immunity after the BNT162b2 Vaccine in Israel

- Following Israel's mass COVID-19 vaccination campaign in December, which led to a sharp curtailing of the outbreak, a resurgent Covid-19 outbreak began in mid-June 2021. Possible reasons for the resurgence in Israel were reduced vaccine effectiveness against the Delta (B.1.617.2) variant and waning immunity, although the extent of the latter is unclear.
- This modelling study used data on confirmed infection and severe disease collected from an Israeli national database for the period of July 11 to 31, 2021, for all Israeli residents who had been fully vaccinated before June 2021. Modelling was used to compare rates of confirmed SARS-CoV-2 infection and severe Covid-19 among persons vaccinated during different time periods, with stratification according to age group and adjustment for possible confounding factors.
- Among persons 60 years of age or older, the rate of infection in the July 11–31 period among persons who became fully vaccinated in January 2021 (when they

were first eligible) was higher than among those fully vaccinated 2 months later, in March at 1.6 (95% confidence interval [CI], 1.3 to 2.0).

- Among persons 40 to 59 years of age, the rate ratio for infection among those fully vaccinated in February (when they were first eligible), as compared with 2 months later, in April, was **1.7** (95% CI, 1.4 to 2.1).
- Among persons 16 to 39 years of age, the rate ratio for infection among those fully vaccinated in March (when they were first eligible), as compared with 2 months later, in May, was **1.6** (95% CI, 1.3 to 2.0).



- A similar pattern was observed in the analysis of severe Covid-19 in the group of persons 60 years of age or older, although confidence intervals were larger. The rate of severe Covid-19 among persons 60 years of age or older who were fully vaccinated in January was 0.34 cases per 1000 persons over the study period and decreased to 0.26 in February, 0.15 in March, and 0.12 in the April–May period.
- A potential confounder for these findings relative to the UK is that Israel has followed the original Pfizer–BioNTech protocol of administering the second dose 3 weeks (21 days) after the initial injection in most recipients, whereas the time between doses in the United Kingdom has typically been longer. Research suggests this longer dosing interval results in higher neutralising antibody levels.
- These findings emphasise the need to follow the effects of waning immunity closely and to inform policymakers who are facing decisions regarding the administration of booster vaccinations.
- Full paper: Waning Immunity after the BNT162b2 Vaccine in Israel | NEJM

Does infection with or vaccination against SARS-CoV-2 lead to lasting immunity?

- Many nations are pursuing the rollout of SARS-CoV-2 vaccines as an exit strategy from unprecedented COVID-19-related restrictions with significant social and economic harms. However, the success of this strategy relies critically on the duration of protective immunity resulting from both natural infection and vaccination. A review published in the Lancet looks to thoroughly evaluate the

existing evidence on SARs-Cov-2 and other respiratory viruses, with a focus on immunity from infection and vaccination.

- Current evidence from case studies and large observational studies suggests that, consistent with research on other common respiratory viruses, a protective immunological response lasts for approximately 5–12 months from primary infection, with reinfection being more likely given an insufficiently robust primary humoral response. Emerging data, including evidence of breakthrough infections, suggest that vaccine effectiveness might be reduced significantly against future variants of concern, and hence secondary vaccines will need to be developed to maintain population-level protective immunity. Nonetheless, other interventions will also be required, with further outbreaks likely to occur due to antigenic drift, selective pressures for novel variants, and global population mobility.
- The duration and breadth of the antibody response to SARS-CoV-2 infection varies markedly by age and disease severity with more severe disease tending to have higher initial neutralising antibodies titres than milder disease, but these differences appear to wane within a few months. These antibody dynamics are consistent with those of other acute infections, including seasonal and pandemic coronaviruses.
- The duration of the humoral immune response is less clear for patients with milder symptoms, and although there is substantial variation within and between studies, the data might be consistent with a prolonged response over 5–6 months. In asymptomatic patients, the decline in circulating antibody levels seems to be more pronounced than that in symptomatic patients. This is consistent with what is known about humoral dynamics following infection with other respiratory viruses, such as SARS-CoV and MERS-CoV
- In addition to neutralising antibodies, Memory B cells (MBCs) can generate potent neutralising antibodies against the receptor binding domain (RBD) upon rechallenge and may counteract a relatively short-lived circulating antibody response. Some emerging evidence suggests MBCs might evolve towards non-neutralising profiles over time, particularly in older patients, highlighting the ongoing benefit of vaccination. Various studies of SARS-CoV and MERS-CoV also suggest an effective T-cell response protects against severe outcomes in SARS-CoV-2 infection.
- Although observational studies are limited by the short time period since SARS-CoV-2 emergence, current evidence suggests reinfection can occur within 5–12 months of primary infection, a timeframe that is similar to that for other acute respiratory viral infections. Nonetheless, it is unclear whether the time to reinfection suggested by the available data could become shorter with escape from neutralisation by variants of concern (VOCs).
- Aside from natural infections, with regards to the long-lasting immune response from SARS-CoV-2 vaccines, it remains to be seen whether breakthrough infections will become substantially more frequent in the coming months due to the relatively short time since vaccine rollout began. Early data suggests the durability of vaccine-induced immunity is affected by VOCs, although breakthrough infections appear to infrequently result in onwards transmission, and to occur less often in previously exposed individuals who have been vaccinated.

- Although the mutation rate of coronaviruses is notably lower than, for example, that for influenza A virus—and hence, in the majority of vaccinated individuals, protection is unlikely to be lost completely beyond 12 months—in the short-to-medium term current vaccines will require updating to maintain their effectiveness; indeed, this development is already underway for the gamma and beta variants.
- Particular attention should be paid to higher-risk populations, including immune-compromised patients and those on immunosuppressant drugs, who might not mount durable immune responses, particularly when vaccination is improperly coordinated with immunosuppressant therapy.
- Ultimately, it is likely the duration of protective immunity from natural infection and from vaccination will determine the frequency of outbreaks (e.g., annual, biennial, or more sporadic) and the burden on healthcare systems of symptomatic disease, and in turn shape the public health policies of nations around the world in the years to come.
- Full paper: Does infection with or vaccination against SARS-CoV-2 lead to lasting immunity? - The Lancet Respiratory Medicine

Variants and transmission

UKHSA SARS-CoV-2 variants of concern and variants under investigation in England: Variant technical briefing 27 (ay.4.2)

- The most recent UKHSA variant technical briefing has now been published, with a focus on the Delta sublineage AY.4.2 (VUI-21OCT-01), which accounts for a slowly increasing proportion of cases in the UK. It accounts for 8.5% of Delta cases in the most recent complete week of sequencing (4 October 2021 to 10 October 2021). In more recent weeks, sequencing data are incomplete, however AY.4.2 accounts for 10.3% of Delta cases in the week 11 October 2021 to 17 October 2021 and 11.3% in the week 18 October 2021 to 24 October 2021.
- The growth rate and secondary attack rates have been refreshed with new data-estimated growth rates are slightly higher for AY.4.2 than for Delta (19%), and the household secondary attack rate is higher for AY.4.2 cases than for other Delta cases (6-12%). There is no evidence that vaccine effectiveness against symptomatic or asymptomatic infection is lower for AY4.2 vs dominant Delta variant after 2 doses of vaccine.
- Early analysis of severity suggests no increased risk from AY.4.2 and analysis of neutralising antibody response is in progress.
- Full paper: SARS-CoV-2 variants of concern and variants under investigation in England: Technical briefing 27, 29 October 2021 (publishing.service.gov.uk)

PREPRINT: Comparison of generation time of the Alpha and Delta SARS-CoV-2 variants

- This preprint modelling study analysed transmission data from the HOCO2 UKHSA household study to understand whether the more transmissible Delta variant generation time (the time between infections in infector- infectee pairs) is typically shorter–i.e., transmissions are happening more quickly–or whether infected individuals simply generate more infections.
- The mean intrinsic generation time (the generation time if there had been a constant supply of susceptibles throughout infection) was shorter for the Delta variant (4·6 days, 95% CrI 4·0-5·4 days) than the Alpha variant (5·5 days, 95% CrI 4·6-6·4 days), although within uncertainty ranges. However, there was a larger difference in the realised mean household generation time between the Delta (3·2 days, 95% CrI 2·4-4·2 days) and Alpha (4·5 days, 95% CrI 3·7-5·4 days) variants. This is because higher transmissibility led to faster susceptible depletion in households, in addition to the reduced intrinsic generation time.
- Overall the Delta variant transmits more quickly than previously circulating variants, likely due to a combination of both increased transmissibility and a shorter generation time. This has implications for interventions such as contact tracing, testing and isolation, which are less effective if the virus is transmitted quickly. It is strongly recommended that epidemiological models are updated to reflect the generation time of the variants driving transmission, and the generation time is assessed in future as the characteristics of SARS-CoV-2 transmission continue to change.
- Full paper: Generation time of the Alpha and Delta SARS-CoV-2 variants | medRxiv

REACT-1: Exponential growth, high prevalence of SARS-CoV-2, and vaccine effectiveness associated with the Delta variant

- This study looked at REACT-1 data from 200,000 people across England gathered from rounds 12 and 13, carried out between 20 May and 12 July 2021. It found that despite the highly successful vaccination campaign, infections were increasing exponentially, primarily driven by the Delta variant with high infection prevalence among younger, unvaccinated people.
- The rapid roll-out of the vaccination program in England has so far limited the number of infections and serious cases relative to the unvaccinated population. However, without additional interventions, increased mixing (including indoors) during the autumn and winter in the presence of the Delta variant may lead to renewed growth, even at high levels of vaccination. Continued surveillance to monitor the spread of the epidemic is therefore required.
- Unvaccinated people were three times more likely than double-vaccinated people to test positive. However, after adjusting for age and other variables, vaccine effectiveness for double-vaccinated people was estimated at between ~50% and ~60% during this period in England. Increased social mixing in the presence of Delta had the potential to generate sustained growth in infections, even at high levels of vaccination. The authors suggest expansion of the vaccination program

to those at highest risk of infection has the potential to reduce transmission in the autumn and winter 2021 as levels of social mixing, including indoors, increase.

- Estimates of vaccine effectiveness (VE) are not absolute but will vary depending on a variety of factors. Unlike routine testing, these data are based on a random sample of the population and include asymptomatic people, as well as symptomatic individuals who may not present for testing; the results may therefore give a less biased representation of infection risk. More generally, estimates of VE may depend on vaccine type, interval between doses, possible waning over time and the extent of past natural infection among the comparator (unvaccinated) group.
- Investigating how swab-positivity measured in REACT-1 related to daily hospital admissions and deaths in publicly available data, a best fitting lag was found between swab-positivity and hospitalisations of 20 days and between swab-positivity and deaths of 26 days. At these lags, from early February 2021, there was a clear divergence between swab-positivity and deaths, coinciding with the roll-out of England's mass vaccination campaign, with a smaller divergence between swab-positivity and hospitalisations. This reflects estimates of VE against serious outcomes elsewhere of greater than 90% when Alpha was dominant. However, as the Delta variant became dominant in mid-April 2021, the associations between infections and hospitalisations and deaths began to re-converge, potentially reflecting the increased prevalence and severity of Delta, a changing age mix of hospitalised cases to younger ages, and possible waning of protection.
- The authors highlight that compared to earlier study rounds there has been a reduction in response rates the sample may be becoming less representative, particularly in some groups such as young people (18 to 24 years) and those living in the most deprived areas where response rates by round 13 had fallen to 4.2% and 5.1% respectively.
- Full paper: Exponential growth, high prevalence of SARS-CoV-2, and vaccine effectiveness associated with the Delta variant (science.org)

NPIs and Environmental Science

Poor ventilation worsens short-range airborne transmission of respiratory infection

- To explain the observed phenomenon that most SARS-CoV-2 transmission occurs indoors , a simple macroscopic aerosol balance model is developed to link short- and long-range airborne transmission. The model considers the involvement of exhaled droplets with initial diameter ≤50 µm in the short-range airborne route, whereas only a fraction of these droplets with an initial diameter within 15 µm or equivalently a final diameter within 5 µm were considered in the long-range airborne route.
- Room ventilation rate is shown to significantly affect short-range airborne exposure. When the ventilation rate in a room is insufficient, the airborne infection risks due to both short- and long-range transmission are high. A ventilation rate of 10 L/s per person provides a similar concentration vs distance decay profile to

that in outdoor settings, which provides additional justification for the widely adopted ventilation standard of 10 L/s per person.

- For some respiratory infections such as COVID-19, a low building ventilation rate worsens both long- and short-range airborne transmission. Policy makers in public health should target indoor environments with insufficient ventilation by either mandating improved ventilation or setting a maximum occupancy when the total ventilation supply is fixed.
- Full paper: Poor ventilation worsens short-range airborne transmission of respiratory infection - Li - - Indoor Air - Wiley Online Library

Public perceptions of non-adherence to pandemic protection measures by self and others: A study of COVID-19 in the United Kingdom

- A qualitative study of 12 focus groups in late 2020 explores participants' perceptions of non-adherence to COVID-19 policy measures by self and others in the UK, focusing on perceived reasons for non-adherence. Participants were 51 UK residents aged 18 and above, reflecting a range of ages, genders and race/ethnicities. Participants reported observing a decrease in adherence to COVID-19 protective measures *in others* throughout the course of the pandemic. Reports of non-adherence in self were lower than reports of non-adherence in others.
- This study highlights the importance of public trust in Government. Clear policy decisions and trustworthy policymakers play a significant role in ensuring that the public adheres to COVID-19 protective measures.
- A number of systemic failures were perceived by participants, e.g. unclear policy, untrustworthy policymakers, which strongly contributed to two forms of non-adherence – violations and errors.
- Latent and systemic failures—in the form of policy decisions that are commonly experienced as too changeable, inconsistent and confusing, and policy makers that are commonly perceived as untrustworthy– may play a significant role in creating the conditions that enable or encourage non-adherence.
- Full paper: Public perceptions of non-adherence to pandemic protection measures by self and others: A study of COVID-19 in the United Kingdom (plos.org)

Factors affecting adherence to non-pharmaceutical interventions for COVID-19 infections in the first year of the pandemic in the UK

- Non-pharmaceutical interventions (NPIs), including wearing face covering/masks, social distancing and working from home, have been introduced to control SARS-CoV-2 infections. This study examines individual-level empirical evidence of the relationship of autonomy to follow NPIs with infection, how this varies and where support or public communication could be directed, using data from the COVID-19 Infection Study (CIS) from 10 May 2020 to 2 February 2021. It finds that wearing a face covering or mask outside the home can reduce the unequal

effects of exposure to COVID-19 due to individual and employment circumstances.

- Inability to comply with NPIs predicted higher infections when individuals reported not wearing a face covering outside. The main effect for inability to comply was an odds ratio of 0.79 (95% CI 0.67 to 0.92), for wearing face covering/masks was OR 0.29 (95% CI 0.15 to 0.56) and the interaction term being OR 1.25 (95% CI 1.07 to 1.46).
- The youngest age groups had a significantly higher risk of infection (OR 1.52, 95% CI 1.28 to 1.82) as did women in larger households (OR 1.04, 95% CI 1.02 to 1.06). Effects varied over time with autonomy to follow NPIs only significant in the pre-second lockdown May–November 2020 period. Wearing a face covering outside was a significant predictor of a lower chance of infection before mid-December 2020 when a stricter second lockdown was implemented (OR 0.44, 95% CI 0.27 to 0.73).
- Overall the protective effect of wearing a face covering/mask was the strongest for those who were most unable to comply with other NPIs. Higher infection rates were found in younger groups and women in large households. Wearing a face covering or mask outside the home consistently and significantly predicted lower infection before the 2020 Christmas period and among women.
- Full paper: Factors affecting adherence to non-pharmaceutical interventions for COVID-19 infections in the first year of the pandemic in the UK | BMJ Open

Modelling: Synergistic interventions to control COVID-19: Mass testing and isolation mitigates reliance on distancing

- Stay-at-home orders and shutdowns of non-essential businesses are powerful, but socially costly, tools to control the pandemic spread of SARS-CoV-2. Mass testing strategies, which rely on widely administered frequent and rapid diagnostics to identify and isolate infected individuals, could be a potentially less disruptive management strategy, particularly where vaccine access is limited. This paper assesses the extent to which mass testing and isolation strategies can reduce reliance on socially costly non-pharmaceutical interventions, such as distancing and shutdowns. It provides insight into relaxation of distancing measures, and lays the groundwork for future public health economic analyses on the cost-effectiveness of combined management strategies.
- A multi-compartmental model of SARS-CoV-2 transmission incorporating both preventative non-pharmaceutical interventions (NPIs) and testing and isolation is used to evaluate their combined effect on public health outcomes. The model is designed to be a policy-guiding tool that captures important realities of the testing system, including constraints on test administration and non-random testing allocation.
- This study shows how strategic changes in the characteristics of the testing system, including test administration, test delays, and test sensitivity, can reduce reliance on preventative NPIs that cause severe socio-economic burdens without compromising public health outcomes in the future. Increasing testing capacity, including the number of tests available and the speed at which test results are

provided, can reduce reliance on costly preventative interventions. Such reduction is possible with more isolation of active infections, including those without reported symptoms. The lowest NPI levels are possible only when many tests are administered and test delays are short, given limited immunity in the population. Reducing reliance on NPIs is highly dependent on the ability of a testing program to identify and isolate unreported, asymptomatic infections. However, failing to maintain preventative interventions without sufficient testing capacity can lead to large increases in infection burdens.

- Changes in NPIs, including the intensity of lockdowns and stay at home orders, should be coordinated with increases in testing to ensure epidemic control; otherwise small additional lifting of these NPIs can lead to dramatic increases in infections, hospitalizations and deaths. Importantly, our results can be used to guide ramp-up of testing capacity in outbreak settings, allow for the flexible design of combined interventions based on social context, and inform future cost-benefit analyses to identify efficient pandemic management strategies.
- Full paper: Synergistic interventions to control COVID-19: Mass testing and isolation mitigates reliance on distancing (plos.org)

Modelling

Non-pharmaceutical interventions, vaccination, and the SARS-CoV-2 Delta variant in England: a mathematical modelling study

- This mathematical modelling study assesses the England NPI-easing roadmap, the impact of the Delta variant of SARS-CoV-2, and potential future epidemic trajectories to estimate the resulting number of daily infections and hospital admissions, and daily and cumulative deaths. Three scenarios spanning a range of optimistic to pessimistic vaccine effectiveness, waning natural immunity, and cross-protection from previous infections were investigated, along with three levels of mixing after the lifting of restrictions.
- According to this study, the roadmap policy was successful in offsetting the increased transmission resulting from lifting NPIs starting on March 8, 2021, with increasing population immunity through vaccination. However, because of the emergence of the Delta variant fully lifting NPIs on June 21, 2021, as originally planned might have led to 3900 (95% Credible Interval 1500–5700) peak daily hospital admissions under our central parameter scenario. Delaying until July 19, 2021, reduced peak hospital admissions by three fold to 1,400 (95% CrI 700–1700) per day.
- The study's modelling projects that a substantial autumn wave of transmission is possible, at least in the absence of substantial additional vaccination (e.g., booster doses and vaccination of teenagers), but with large uncertainty around the resulting peak number of hospital admissions and total deaths. This uncertainty is driven by uncertainty around levels of mixing after NPIs are lifted and the overall level of population immunity accounting for waning and imperfect cross-protection. At high vaccine coverage, even a difference of 98% versus 95% in vaccine effectiveness against mortality translates to a doubling of projected deaths. The duration of infection-induced and vaccine-induced immunity for all

SARS-CoV-2 lineages remains another key unknown that will determine long-term transmission dynamics.

- Full paper: Non-pharmaceutical interventions, vaccination, and the SARS-CoV-2 Delta variant in England: a mathematical modelling study - The Lancet

Children and Education

REACT-1 study round 14: High and increasing prevalence of SARS-CoV-2 infection among school-aged children during September 2021 and vaccine effectiveness against infection in England

- This research from the REACT-1 programme looked at data from swab samples taken at home by around 100,000 people aged 5 years and over in England, between 9 and 27 September. The research found that 1 in 120 people had the virus during this period with R around 1. However, infections were high and increasing in school-age children. The study also looked at vaccination effectiveness against infection and prevalence of swab-positivity among double-vaccinated individuals, and how this changed over time.

- This study observed stable or rising prevalence (with an R of 1.03 (0.94, 1.14) overall) during round 14 with a weighted prevalence of 0.83% (0.76%, 0.89%). The highest weighted prevalence was found in children aged 5 to 12 years at 2.32% (1.96%, 2.73%) and 13 to 17 years at 2.55% (2.11%, 3.08%). All positive virus samples analysed correspond to the Delta variant or sub-lineages of Delta with one instance of the E484K escape mutation detected.

- The epidemic was growing in those aged 17 years and under with an R of 1.18 (1.03, 1.34), but decreasing in those aged 18 to 54 years with an R of 0.81 (0.68, 0.97). For all participants and all vaccines combined, at ages 18 to 64 years, vaccine effectiveness against infection (rounds 13 and 14 combined) was estimated to be 62.8% (49.3%, 72.7%) after two doses compared to unvaccinated people when adjusted for round, age, sex, index of multiple deprivation, region and ethnicity; the adjusted estimate was 44.8% (22.5%, 60.7%) for AstraZeneca and 71.3% (56.6%, 81.0%) for Pfizer-BioNTech, and for all vaccines combined it was 66.4% (49.6%, 77.6%) against symptomatic infection (one or more of 26 surveyed symptoms in month prior).

- Across rounds 13 and 14, at ages 18 years and over, weighted prevalence of swab-positivity was 0.55% (0.50%, 0.61%) for those who received their second dose 3-6 months before their swab compared to 0.35% (0.31%, 0.40%) for those whose second dose was within 3 months of their swab, while weighted prevalence among unvaccinated individuals was1.76% (1.60%, 1.95%). In round 14, age group, region, key worker status, and household size jointly contributed to the risk of higher prevalence of swab-positivity.

- In September 2021 infections were increasing exponentially in the 5-to-17-year age group coinciding with the start of the autumn school term in England. Relatively few schoolchildren aged 5 to 17 years have been vaccinated in the UK though single doses are now being offered to those aged 12 years and over. In adults, the higher prevalence of swab-positivity following two doses of vaccine from 3 to 6 months compared to within 3 months of second dose supports the

use of a booster vaccine. It is important that the vaccination programme maintains high coverage and reaches children and unvaccinated or partially vaccinated adults to reduce transmission and associated disruptions to work and education.

- Full paper: REACT-1 study round 14: High and increasing prevalence of SARS-CoV-2 infection among school-aged children during September 2021 and vaccine effectiveness against infection in England | medRxiv

WCEC Rapid Review: Strategies to support learning and wellbeing among 16-19 year old learners who have experienced significant disruption in their education as a result of the COVID-19 pandemic

- This Rapid Review was conducted as part of the Wales COVID-19 Evidence Centre Work Programme. The above question was suggested by the post-16 and transitions team working as part of the Welsh Government's Renew and Reform programme.
- Subject to the limitations caused by a paucity of relevant research, overall there was no direct systematic review evidence that evaluated strategies to support learning for 16-19 year old learners following the COVID-19 pandemic. Most included studies were appraised as 'critically low-quality' (review) evidence.
- Pre-COVID evidence for several methods demonstrated a positive impact for 3-18 year old learners to enable them to progress with their learning. These included additional tutor support; additional hours of tuition (extension of the teaching day, or school holiday interventions); metacognition and self-regulation; and additional maths and English tuition. Although supported by a limited volume of evidence, targeting support activity at learners from the most deprived socio-economic backgrounds has a significant positive impact on their progress.
- The evidence showed no benefit in withdrawing students from core lessons for additional English tuition and there was no evidence that evaluated whole group additional tutor support and online additional tutor support. There was no direct systematic review evidence found for evaluating 16-19 years old learners' wellbeing related to the COVID-19 pandemic.
- Pre-COVID evidence showed that screening and effective referral pathways to clinical treatment are beneficial in improving student wellbeing for older teenagers (16-19) and sixth form college students. Additionally, mindfulness interventions are successful in improving wellbeing for a wide range of learners especially in post-secondary education. Mixed evidence was found for therapy-based prevention programmes and social and emotional learning and no evidence found for evaluating support from family and friends.
- Despite the limited evidence available, there was reasonable agreement among all the included literature, which may be considered to imply some degree of reliability. There were no contradictory findings, and the recommendations of the organisational reports were concordant with the findings of the reviews. Further research is required to evaluate whether interventions that were successful in relatively "normal" circumstances will be as successful during / post-pandemic.

- Full paper: RR_00016_Wales COVID-19 Evidence Centre. Rapid review Post-16 education_September 2021[74].pdf (primecentre.wales)

Epidemiology and Clinical

A Systematic Review and Meta-Analysis of Inpatient Mortality Associated With Nosocomial and Community COVID-19 Exposes the Vulnerability of Immunosuppressed Adults

- This systematic review examines the peer-reviewed and pre-print literature from 1/1/2020 to 9/2/2021 for studies reporting severe outcomes of nosocomial and community-acquired COVID-19 to estimate the 1) relative risk of death and 2) critical care admission, stratifying studies by patient cohort characteristics and nosocomial case definition.
- 21 studies were included in the primary MA, describing 8,251 admissions across 8 countries during the first wave, comprising 1513 probable or definite nosocomial COVID-19, and 6738 community-acquired cases. Across all studies, the risk of mortality was 1.3 times greater in patients with nosocomial infection, compared to community-acquired (95% CI: 1.005 to 1.683). Rates of critical care admission were similar between groups (Relative Risk, RR=0.74, 95% CI: 0.50 to 1.08). Immunosuppressed patients diagnosed with nosocomial COVID-19 were twice as likely to die in hospital as those admitted with community-acquired infection (RR=2.14, 95% CI: 1.76 to 2.61).
- Adults who acquire SARS-CoV-2 whilst already hospitalised are at greater risk of mortality compared to patients admitted following community-acquired infection; this finding is largely driven by a substantially increased risk of death in individuals with malignancy or who had undergone transplantation. These findings inform public health and infection control policy and argue for individualised clinical interventions to combat the threat of nosocomial COVID-19, particularly for immunosuppressed groups.
- Full paper: Frontiers | A Systematic Review and Meta-Analysis of Inpatient Mortality Associated With Nosocomial and Community COVID-19 Exposes the Vulnerability of Immunosuppressed Adults | Immunology (frontiersin.org)

PREPRINT: Long-term health-related quality of life in non-hospitalised COVID-19 cases with confirmed SARS-CoV-2 infection in England: Longitudinal analysis and cross-sectional comparison with controls

- This longitudinal study measured the long-term health-related quality of life of non-hospitalised COVID-19 cases with PCR-confirmed SARS-CoV-2 infection using a recommended instrument for estimating QALYs in the UK (the EQ-5D-5L). The cohort included cases aged 12-85 years and followed up for six months from 01 December 2020, with cross-sectional comparison to SARS-CoV-2 negative controls. The main outcomes assessed were loss of quality-adjusted life days (QALDs); physical symptoms; and COVID-19-related private expenditures.

- Of 548 cases (mean age 41.1 years; 61.5% female), 16.8% reported physical symptoms at month 6 (most frequently extreme tiredness, headache, loss of taste and/or smell, and shortness of breath). Cases reported more limitations with doing usual activities than controls. Almost half of cases spent a mean of £18.1 on non-prescription drugs (median: £10.0), and 52.7% missed work or school for a mean of 12 days (median: 10). On average, all cases lost 15.9 (95%-CI: 12.1, 19.7) QALDs, while those reporting symptoms at month 6 lost 34.1 (29.0, 39.2) QALDs. Losses also increased with older age. Cumulatively, the health loss from morbidity contributes at least 21% of the total COVID-19-related disease burden in England.
- 1 in 6 cases report ongoing symptoms at 6 months, and 10% report prolonged loss of function compared to pre-COVID-19 baselines. A marked health burden was observed among older COVID-19 cases and those with persistent physical symptoms. Losses of health-related quality of life in non-hospitalised COVID-19 cases increase by age and for cases with symptoms after 6 months. At a population level, at least 21% of the total COVID-19-related disease burden in England is attributable to morbidity.
- Full paper: Long-term health-related quality of life in non-hospitalised COVID-19 cases with confirmed SARS-CoV-2 infection in England: Longitudinal analysis and cross-sectional comparison with controls | medRxiv

WCEC Rapid Evidence Summary: What is the evidence of direct harm from COVID-19 infection and COVID-19 vaccine in pregnant/post-partum women and the unborn child?

- In July 2021, guidance from the Royal College of Obstetricians and Gynaecologists changed to recommend that all pregnant women are vaccinated against COVID-19. However, there is concern in Wales that COVID-19 vaccine uptake in pregnant women is low, contributing to increased hospital admissions in this population group.
- The rapid evidence summary is based on a limited search of key resources and the assessment of abstracts. Priority is given to studies representing robust evidence synthesis. No quality appraisal or evidence synthesis are conducted, and findings should be interpreted with caution. Owing to the relatively recent emergence of COVID-19 and the rapidly evolving nature of the pandemic, highest quality evidence is lacking.
- There is growing evidence that pregnant women may be at increased risk of severe illness from COVID-19 but high quality evidence is lacking. However, data and evidence are constantly emerging and evolving which may strengthen current understanding. There is currently unclear evidence on the long-term effects of COVID-19 in pregnancy for either women or their children.
- Robust evidence based guidance are available that highlight excellent real-world evidence of vaccine efficacy in pregnancy, with no concerning safety signals. Health professionals should recommend pregnant women receive the COVID-19 vaccination. This is particularly relevant for pregnant women in an at risk group

for becoming severely unwell, including women working in healthcare or other public facing occupations.

- Pregnant women have the same risk of getting COVID-19 as other healthy adults. If they do catch COVID-19, they are at slightly increased risk of becoming severely unwell, particularly in third trimester or if they have an identified risk factor and are more likely to have pregnancy complications like preterm birth or stillbirth. Risk factors for becoming severely unwell include: ethnic minority backgrounds, having a BMI above 25 kg/m^2 , having a pre-pregnancy co-morbidity, (e.g. diabetes or hypertension), a maternal age of 35 years or older, living in increased socioeconomic deprivation and working in healthcare or other public-facing occupations.
- More than 200,000 women in the UK and USA have had a COVID-19 vaccine in pregnancy, with no concerning safety signals and excellent real-world evidence of efficacy. There has been no evidence to suggest foetal harm following vaccination against COVID-19. Vaccination against COVID-19 at any time during pregnancy and whilst breastfeeding is recommended, and preference is to offer the Pfizer-BioNTech or Moderna vaccines.
- There is no evidence to suggest that COVID-19 vaccines affect fertility and women planning a pregnancy or fertility treatment can also receive a COVID-19 vaccine and do not need to delay conception.
- Full paper: RES00024_Wales_COVID-19_Evidence_Centre-Pregnant_Post_Partum_Women_unborn_child.pdf (primecentre.wales)