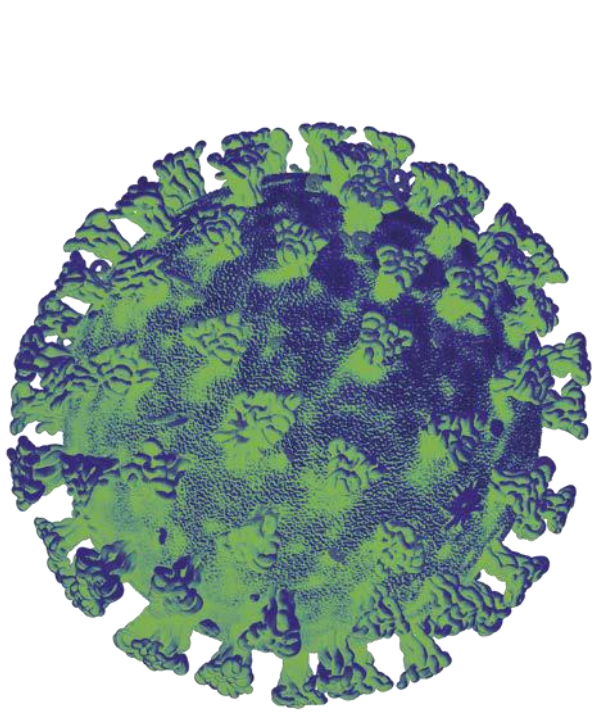
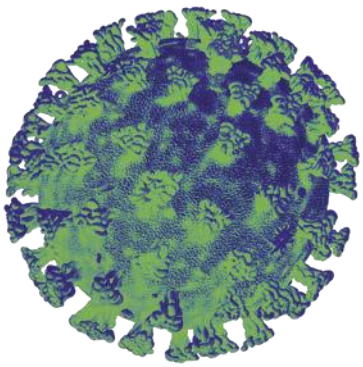
Llywodraeth Cymru
Welsh Government

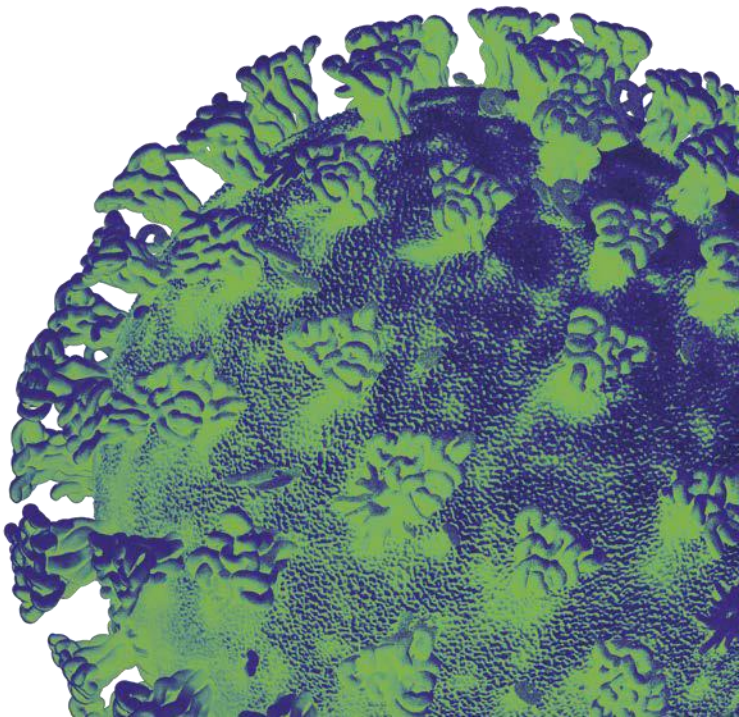
Technical Advisory Cell

Summary of Advice

19 November 2021







Technical Advisory Cell: Summary of Advice

19 November 2021

Contents

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 3% in the 7 day period ending 11 November to 498 cases per 100,000. However test positivity during the same period has remained stable at a high level of 19%. It is uncertain to what extent this reduction in cases is driven by half term or other factors such as testing.
- In the week ending 12 November 2021 the mean wastewater signal for Wales is indicating a reduced level in signal compared to the previous 4 weeks. This is believed to be a genuine reduction in observed signal.
- The number of beds occupied with COVID-19 related patients (confirmed, suspected and recovering) fluctuates. Taking this into account, from early July 2021 to early November 2021, COVID-19 pressure on the NHS generally increased. Over the latest week, the number of beds occupied with COVID-19 related patients has decreased.
- The total number of weekly COVID-19 deaths has increased slightly during the most recent 7-day period ending 30 October from 65 to 70 according to PHW, but remains relatively low in comparison to previous waves during periods of similar incidence.
- The UKHSA consensus estimate of the reproduction number for Wales is between 0.8 and 1.0 and a halving time of 34 days to flat (as at 18 November 2021), while PHW's estimate is 1.05 with a doubling time of 702 days (as at 17 November 2021). Note that the UKHSA estimate is typically lagged by 2-3 weeks while PHW, which uses a different methodology, is lagged by around 1 week. *Source: PHW*
- As at 16 November 2021, a total of 5,386,809 (+95,661) doses of COVID-19 vaccine were given in Wales and recorded in the COVID-19 Welsh Immunisation System. 2,459,583 were first doses. 2,253,495 were second doses. 637,169 were booster doses. 36,562 were third dose primary course recommended for severely immunosuppressed individuals. *Source: PHW*. A breakdown of uptake by priority group and age is below (Source: PHW)
- As at 17 November, 705,553 people have received a booster or a third dose primary course in Wales, although a further 221,662 people are eligible (having received their second dose six+ months ago) but yet to receive their booster vaccination.
- The most recent issue of the ONS Coronavirus (COVID-19) Infection Survey results, 7 to 13 November, estimates during this period that 55,800 people in Wales had COVID-19 (95% credible interval: 44,800 to 68,100), equating to around 1 in

55 people. This compares to around 1 in 65 people in England, around 1 in 65 in Northern Ireland and around 1 in 95 people in Scotland.

- The most recent PHW weekly Influenza and Acute Respiratory Infection report dated 17 November suggests there has been a decrease in the number of confirmed cases of RSV in children aged under 5 years across Wales, compared to the previous week, but remains at medium intensity levels. Influenza is not currently circulating in Wales, with three influenza cases confirmed during week 45.

Research evidence summary

Serology/Immunity

- A preprint study shows that individuals who received the AstraZeneca vaccine are likely to experience waning immunity more quickly than those who received the Pfizer vaccine, in addition to being at a higher risk of breakthrough infections. Booster doses are important in maintaining protection of the elderly and clinically vulnerable- particularly those who received the AstraZeneca vaccine as their primary course

- A nature article illustrates those who received an earlier dose (January/ February 2021) of the Pfizer-BNT162b2 vaccine during Israel's vaccination programme were at an increased risk of infection when compared to a person vaccinated later in the programme (March/April 2021). Risk of hospitalisation followed the same pattern. These results were similar across all age groups.

- A cohort preprint study from OpenSAFELY suggests that rates of COVID-19 breakthrough were higher in those undergoing renal replacement therapy, those undergoing organ transplant, those with haematological malignancy, and those who are immunocompromised. Other risk factors included being female or belonging to a minority ethnic group. Finally, residents in care homes were seen to suffer higher rates of hospitalisation and death. As numbers of fully vaccinated individuals increase and follow-up time lengthens, so too will the number of COVID-19 breakthrough cases.

Vaccines

- A clinical trial funded by BioNTech and Pfizer has shown that a Covid-19 vaccination regimen consisting of two 10-µg doses of BNT162b2 administered 21 days apart was found to be safe, immunogenic, and efficacious in children 5 to 11 years of age.

- A study of vaccine coverage by occupation suggests that the vaccination rates of adults aged 40 to 64 years in England differed markedly by occupation. Vaccination rates were high in administrative and secretarial occupations, professional occupations and managers, directors and senior officials (90.7%) and lowest in people working in elementary occupations (83.1%). Vaccination rates were also associated with the ability to work from home, with the vaccination rate being higher in occupations which can be done performed from home.

- Results from a test-negative case-control study provide real world evidence of significant increased protection from the booster vaccine dose against symptomatic disease in those aged over 50 year of age, irrespective of which primary course was received

Infection control/ non-pharmaceutical interventions

- A follow-up evidence review to UKHSA's recent publication on the effectiveness of face coverings increase the certainty of the results and strengthens the evidence for the effectiveness of face coverings in reducing transmission in the community.
- The findings of a BMJ systematic review suggests that several personal protective and social measures, including handwashing, mask wearing, and physical distancing are associated with reductions in the incidence COVID-19. Public health efforts to implement public health measures should consider community health and sociocultural needs, and future research is needed to better understand the effectiveness of public health measures in the context of COVID-19 vaccination.

Education

- A modelling study highlights the particular significance of mask wearing and social distancing in universities with vaccinated populations. Also, quarantining infected students has a higher importance than quarantining staff. In contrast, other measures such as environmental disinfection seem to be less important. The implementation of non-pharmaceutical interventions is still fundamental to reduce the number of infections to one tenth of the number of infections appearing in a completely uncontrolled scenario.

Modelling

- A modelling study considering the impact of the increased transmissabiltiy of the Delta variant suggests this results in greater geographic spread and lower outbreak extinction probability, indicating that lockdowns may not be as immediately successful as with previous variants at eliminating community transmission. . Social distancing and masking remain effective mitigation strategies for the Delta variant where vaccination rates are low, as we estimate maintaining at least 1.5 m of separation during conversation drives R at close proximity below 1 even in a fully susceptible population.
- An article highlights that a standardised methodology for Disability-Adjusted Life Years (DALYs) attributable to COVID-19 may allow more accurate and comparable estimates of the burden of this disease. Uncertainties persist around COVID-19 data quality and availability of information concerning sequelae from COVID-19. Transparent reporting of uncertainties and limitations is warranted to favour a correct interpretation of the results.

Variants

- UKHSA's updated risk assessment of the emerging AY.4.2 variant suggests AY.4.2 is slightly more infectious than the original Delta variant but comparable in other areas. UKHSA identified the Delta + E484K variant as being better evolved to evade the immune system. Neutralisation studies have put it on par with the Beta variant at immune system evasion. However the immune advantage of this variant comes at a cost to viral fitness, meaning it doesn't often survive long enough to be widely transferred. *[As at 16 November there have been 5 cases of Delta +E484K detected in Wales to date, with the last case on 3 November, according to PHW data.]*

Behavioural

- A systematic review of how behavioural science principles can be embedded into public health messaging highlights the importance of engaging communities in the development of messaging, addressing uncertainty quickly and transparently, focusing on unifying messages and framing messages aimed at increasing understanding, social responsibility and personal control.

Wales COVID-19 Evidence Centre

- The WCEC has published reviews on healthcare education and innovations to improve backlog in endoscopy.
- Evidence reviews on the following are due to be published:
    - Impact of educational and other COVID-19 restrictions on children aged 3-13 years
    - Infection control and prevention measures in care homes
    - Active and Prospective Long-COVID Research in Wales
    - Effectiveness of service delivery interventions for adult orthopaedic patients on a surgical waiting list

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 3% in the 7 day period ending 16 November to 498 cases per 100,000. However test positivity during the same period has remained stable at a high level of 19%. 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 12 November 2021 the mean wastewater signal for Wales is indicating a reduced level in signal compared to the previous 4 weeks. This is believed to be a genuine reduction in observed signal.
- In South Wales, the 'bounce back' in wastewater signal compared to the week before is primarily led by marginal increases at the five largest sites under surveillance: Cardiff, Barry, Swansea, Newport, and Bridgend. Despite the slight variance, the signal is comparable to that observed in the second half of August 2021. In North Wales, the trend in the normalised wastewater signal continues to be stable. Furthermore, North Wales' signal remains aligned with the trends in reported COVID-19 cases in the region.
- The number of beds occupied with COVID-19 related patients (confirmed, suspected and recovering) fluctuates. Taking this into account, from early July 2021 to early November 2021, COVID-19 pressure on the NHS generally increased. Over the latest week, the number of beds occupied with COVID-19 related patients has decreased. This was due to a decrease in confirmed patients despite an increase in suspected and recovering patients. As at 17 November 2021, there were 744 COVID-19 related patients (confirmed, suspected and recovering) occupying a hospital bed. This compares to 805 (61 fewer occupied beds) on 10 November 2021. Confirmed patients accounted for 468 of the total occupied beds.
- There are 60 patients with suspected or confirmed COVID-19 in critical care beds in Wales. This is 104 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 180, 28 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 total number of weekly COVID-19 deaths has increased slightly during the most recent 7-day period ending 30 October from 65 to 70 according to PHW, but remains relatively low in comparison to previous waves during periods of similar incidence.
- The UKHSA consensus estimate of the reproduction number for Wales is between 0.8 and 1.0 and a halving time of 34 days to flat (as at 18 November 2021), while PHW's estimate is 1.05 with a doubling time of 702 days (as at 17 November 2021). Note that the UKHSA estimate is typically lagged by 2-3 weeks while PHW, which uses a different methodology, is lagged by around 1 week. *Slide 3, Source: PHW*
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- The most recent issue of the ONS Coronavirus (COVID-19) Infection Survey results, 7 to 13 November, estimates the percentage of people testing positive continued to decrease over the most recent week in England and Wales. The

percentage of people testing positive remained level in Scotland, whilst the trend was uncertain in Northern Ireland.

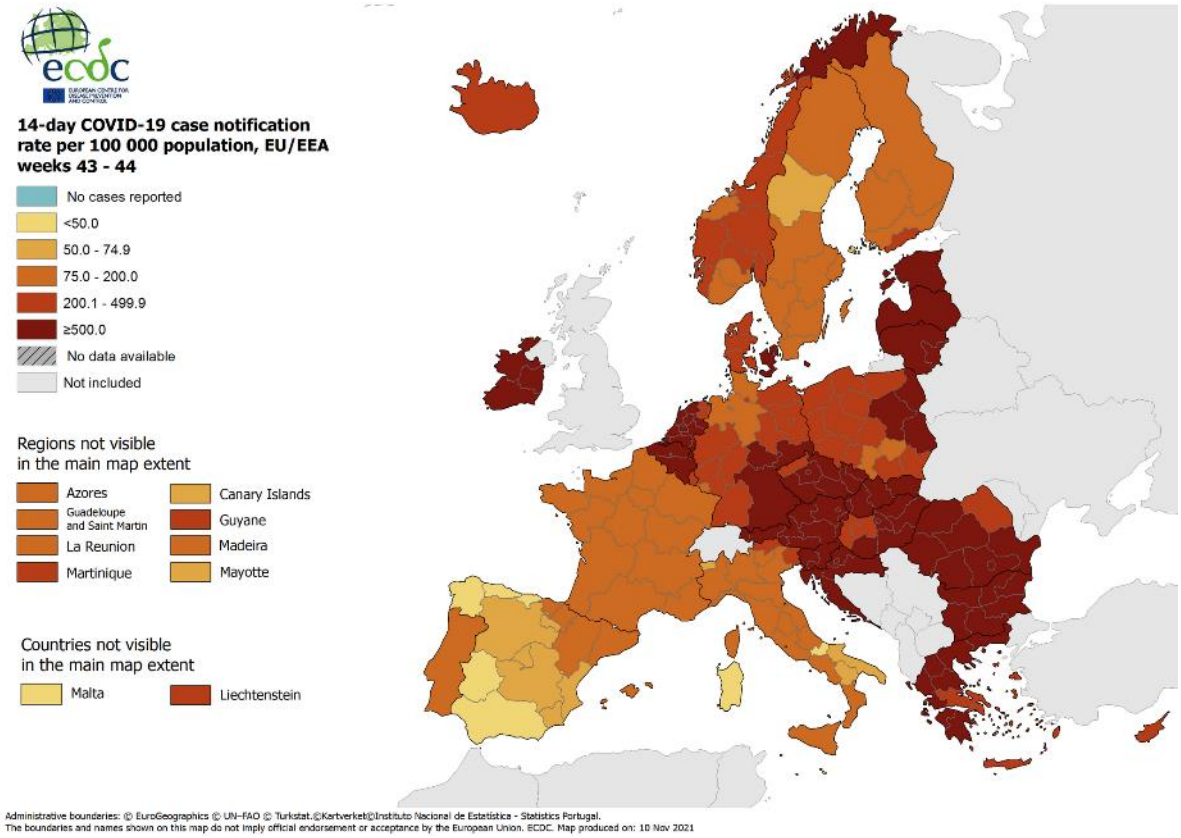
- The survey also estimated that 55,800 people in Wales had COVID-19 (95% credible interval: 44,800 to 68,100), equating to around 1 in 55 people. This compares to around 1 in 65 people in England, around 1 in 65 in Northern Ireland and around 1 in 95 people in Scotland.
- The most recent PHW weekly Influenza and Acute Respiratory Infection report dated 17 November suggests there has been a decrease in the number of confirmed cases of RSV in children aged under 5 years across Wales, compared to the previous week, but remains at medium intensity levels. Influenza is not currently circulating in Wales, with three influenza cases confirmed during week 45. 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. Rhinovirus, human metapneumovirus and enterovirus are the most commonly detected cause of non-COVID-19 Acute Respiratory Infection (ARI).
- In the most recent analysis from the ONS, an estimated 48,000 people living in private households in Wales self-reported long COVID of any duration (for the four week period ending 2 October 2021).

International comparators

Europe

The European Region has continued to show an increasing trend in both cases and deaths, with over 2.1 million new cases and over 28 000 new deaths reported, increases of 8% and 5%, respectively as compared to the previous week. Nearly half (46%) of the countries which were widely distributed across the Region reported increases of over 10% in new cases in the past week, including Germany which reported the second-highest number of new cases in the past week and a 50% increase in cases as compared to the week before (254 436 new cases; 305.9 new cases per 100 000; a 50% increase). The other countries reporting the highest numbers of new cases were the Russian Federation (275 579 new cases; 188.8 new cases per 100 000; similar to the previous week's figures), and the United Kingdom (252 905 new cases; 372.5 new cases per 100 000; similar to the previous week's figures).

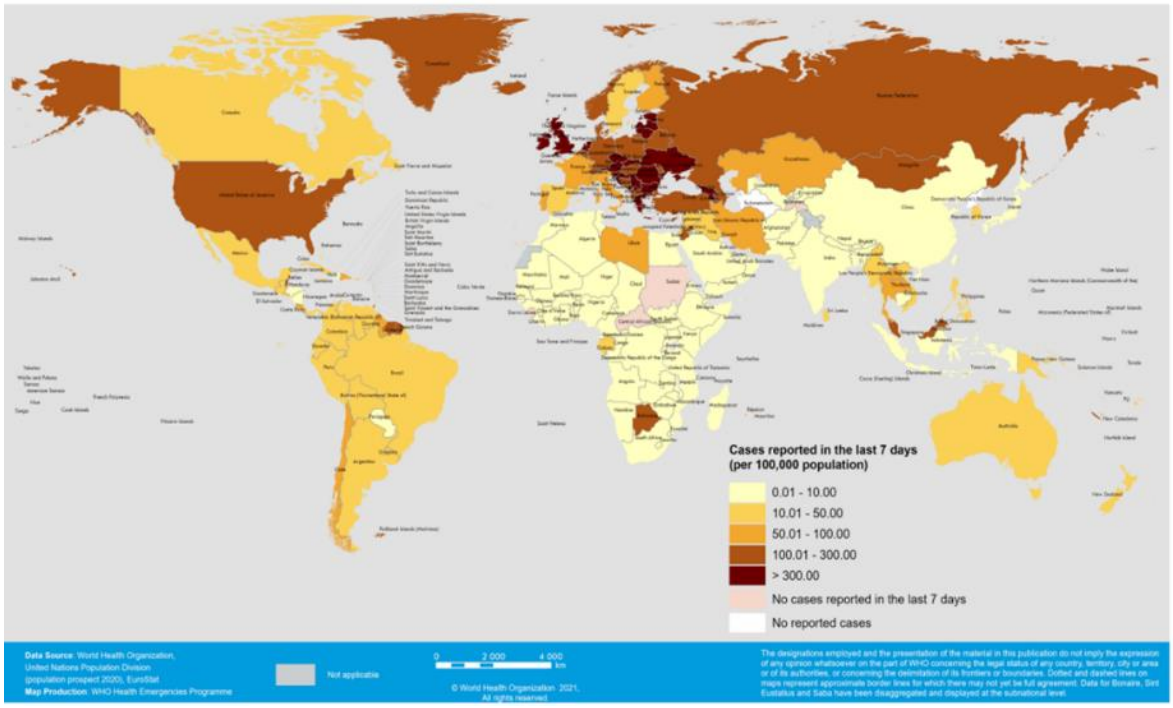
An increase of over 10% in deaths in the past week was seen in 38% of the countries with the greatest change seen in Norway (a 67% increase), Slovakia (a 58% increase), and Croatia (a 55% increase). *(Source: WHO weekly Epi update)*

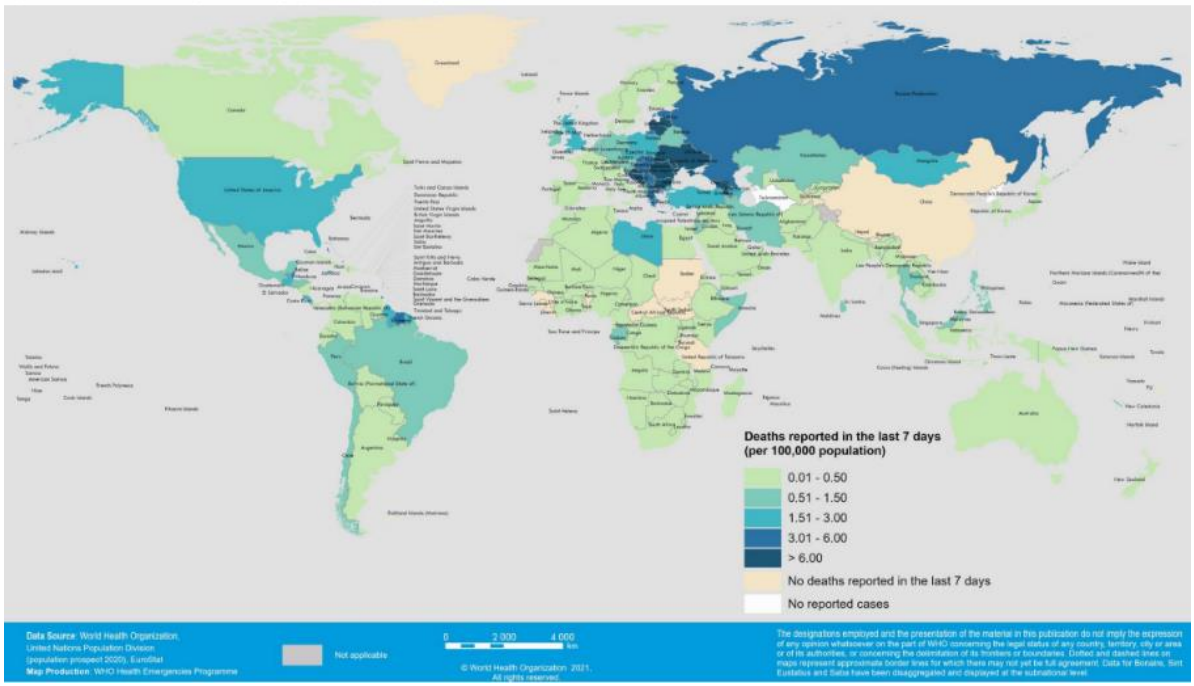


Source: ECDC

World overview

During the week 8 to 14 November 2021, the increasing trend in new global weekly cases continued, with over 3.3 million new cases reported – a 6% increase as compared to the previous week (Figure 1). The Region of the Americas, the European and the Western Pacific Regions all reported increases in new weekly cases as compared to the previous week, while the other regions reported stable or declining trends . Similarly, the European Region reported a 5% increase in new deaths, while the other regions reported stable or declining trends. Globally, just under 50 000 new deaths were reported, similar to the previous week's figures. As of 14 November, over 252 million confirmed cases and over 5 million deaths have been reported *(Source: WHO weekly Epi update)*



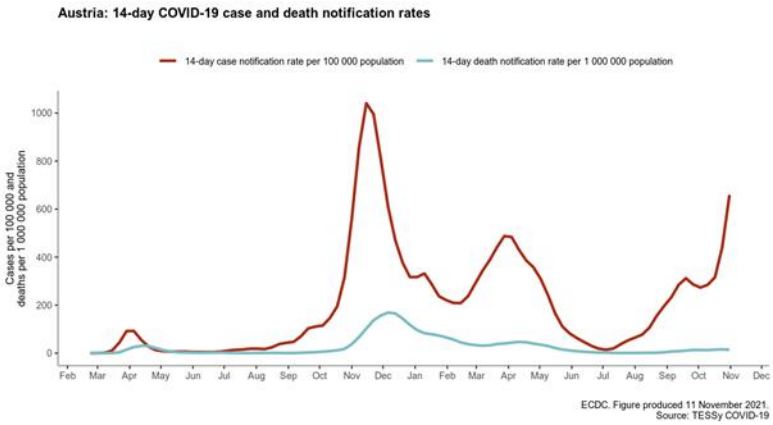


Below are a selection of analyses of several western European countries from the TAG International subgroup:

AUSTRIA

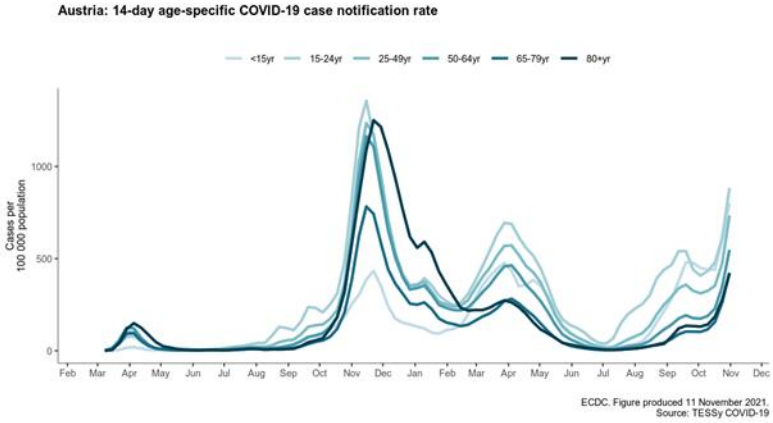
Daily confirmed new cases per 100,000 (red line) and deaths per million (blue line).

Cases are high and increasing but deaths remain low. Death rate 22.2/1M 6th lowest in EU with a case rate of 1027/100,000 the 7th highest in EU



The WHO have stated that Covid cases in Europe are at or surpassing record levels because of uneven vaccine coverage and a relaxation of preventive measures

Recent increase in older cohort is a cause for concern. Case rate in the 65yr+ is 625/100K. Hospital occupancy is increasing rapidly to levels seen in earlier waves.



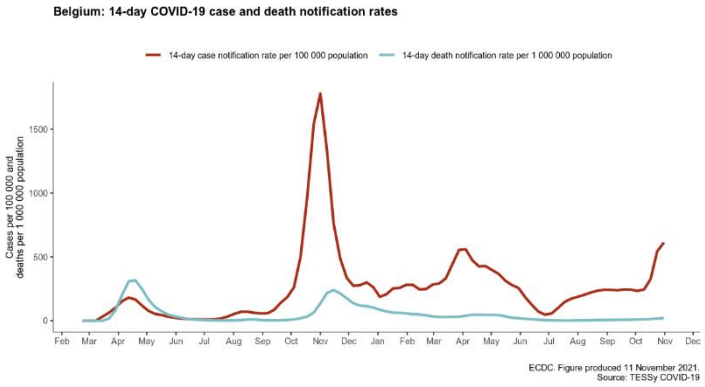
Days after announcing people who are not fully vaccinated will face a lockdown in the provinces of Upper Austria and Salzburg, as of 19 November the government has announced a full national lockdown will be starting the following week, lasting for a maximum of 20 days. There will also be a legal requirement to get vaccinated from 1 February 2022.

Infections in both Germany and Austria soar to record highs and intensive care units face an increasing strain, but are not at 2nd/3rd wave levels yet. Upper Austria records just under 60% of the total population as being vaccinated. Austria overall has 64% fully vaccinated

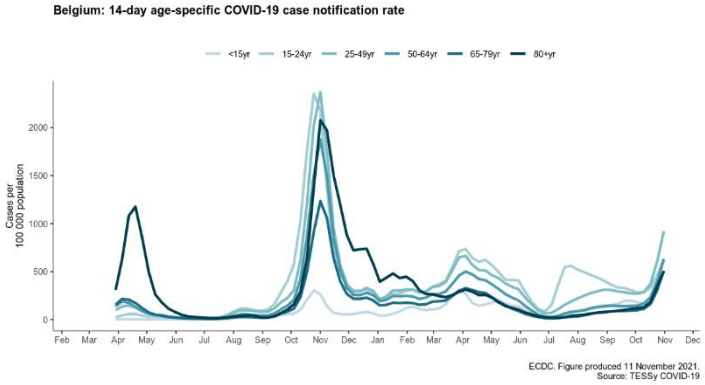
Germany vaccination level is 67% but it is lower in the former GDR in eastern Germany where hesitancy is higher linked with support for the right-wing party, AfD.

BELGIUM

Daily confirmed new cases per 100,000 (red line) and deaths per million (blue line).Their current case rate is 943/100K and death rate of 25/1M. In comparison Bulgaria with a similar case rate 912/100K has a death rate of 283/1M a tenfold difference. Belgium vaccination rate



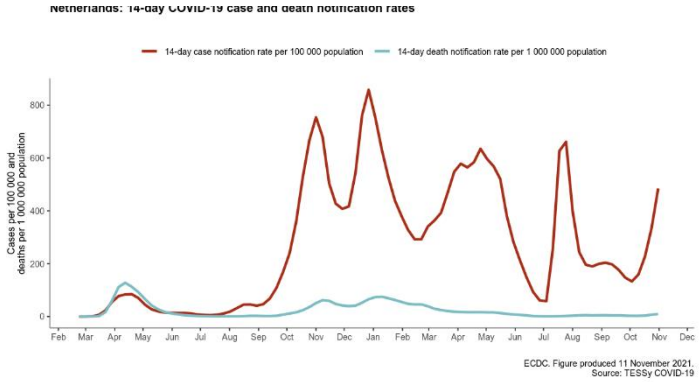
Belgium like Austria has a high case rate amongst the 65+yr cohort of 623/1M but with 74% fully vaccinated is in a better position heading into this wave.



Hospital admissions rapidly increasing by 30% on a weekly basis, and the number of patients in intensive care have risen to more than 500, putting strain on hospitals (popn. 11 million). Authorities re-imposed some pandemic restrictions such as face coverings in public places and a COVID-pass to enter hospitality and leisure centres three weeks ago after relaxing them just a few weeks earlier.

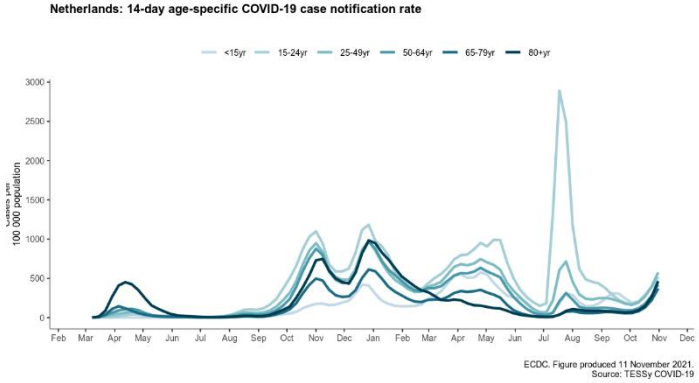
NETHERLANDS

Daily confirmed new cases per 100,000 (red line) and deaths per million (blue line).



Similar to Belgium the Netherlands has 73% fully vaccinated. The case rate is 683/100K and the death rate is 14/1M

The case rate amongst the 65s and over is 571/100K so like Belgium and Austria a cause for concern. Hospital occupancy is still well below previous waves



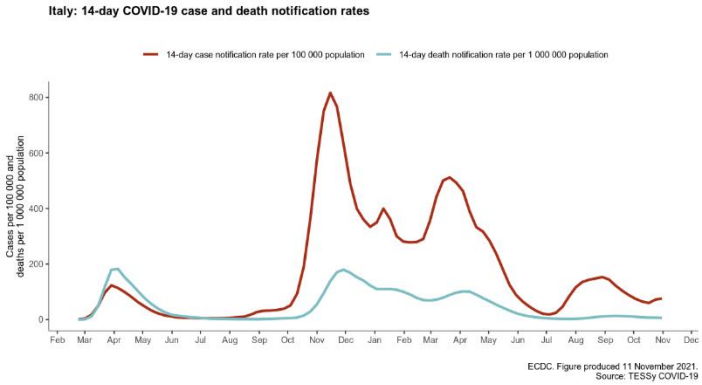
The Dutch have a proposed 2G policy in which only people who have been fully vaccinated or recently recovered from coronavirus would be able to get a coronavirus pass, but are facing political opposition.

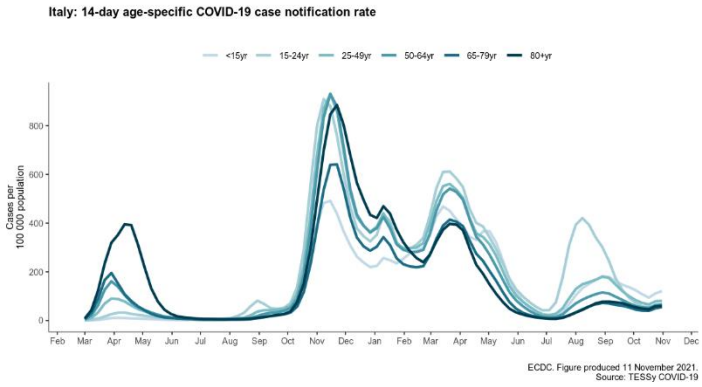
ITALY

Daily confirmed new cases per 100,000 (red line) and deaths per million (blue line).

Italy is not seeing the case rate increase that its northern neighbours are. It has a similar vaccination level to the Netherlands at 73% fully vaccinated

Case rate 94/100K death rate 7/1M





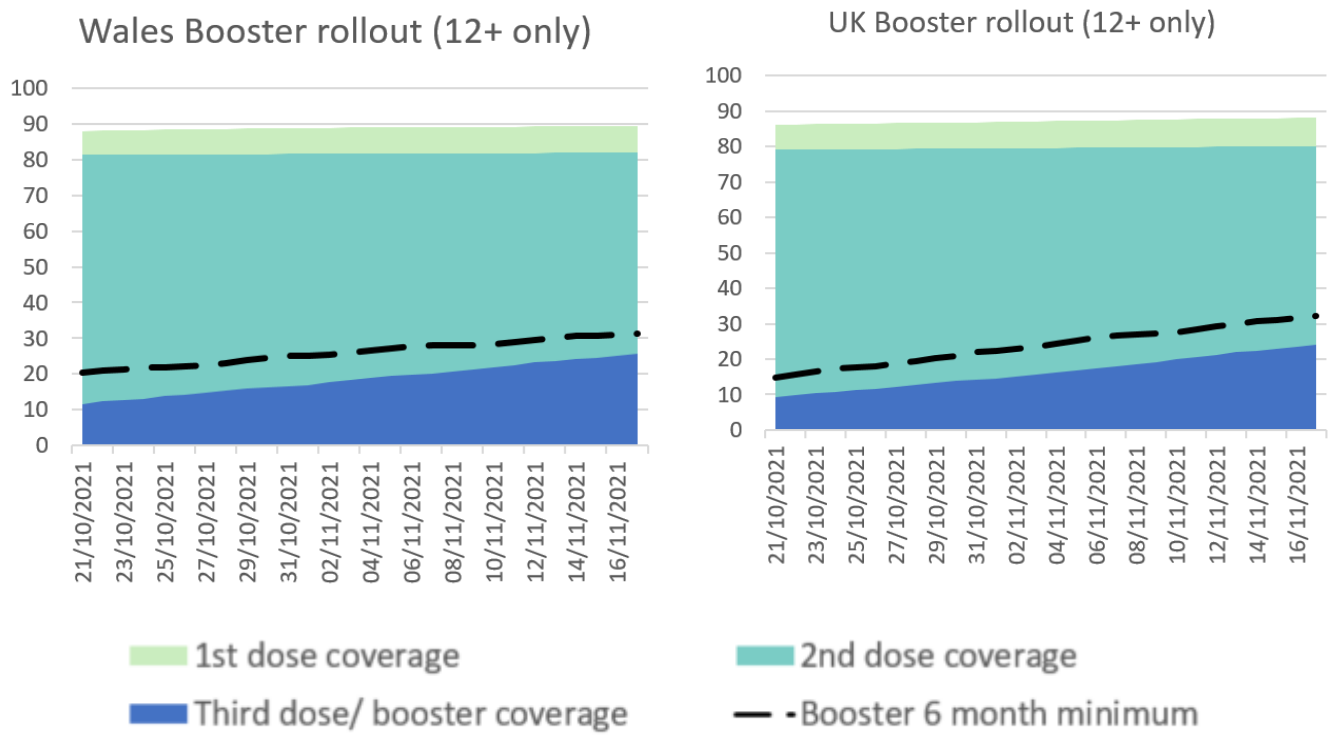
Italy has had stricter COVID restrictions and perhaps human behaviour is playing its role. Italy was the first European nation to be impacted by COVID.

This week two potential new sets of restrictions are being debated to avoid a winter wave of COVID-19 deaths. Mandatory boosters for all health workers after soaring infection rates were reported among doctors and nurses in particular over the past two months. Boosters will be available to all over-40s from December. The other proposal will cut the validity of Italy's COVID-19 health certificate "green pass" from 12 to nine months for people who are vaccinated, including with a third dose. The issue of the validity of green passes based on testing is debated after the pass became a requirement at all workplaces in October.

Italy want to avoid business closures or new lockdowns and is relying heavily on the green pass system and vaccinations.

Booster progress- Wales

- As at 17 November, 705,553 people have received a booster or a third dose primary course in Wales, although a further 221,662 people are eligible (having received their second dose six+ months ago) but yet to receive their booster vaccination.
- As a whole 13,879,311 the UK population has received a booster or a third dose, while an additional 6,667,141 people are eligible but yet to receive their booster dose. (Data: UK Summary | Coronavirus (COVID-19) in the UK (data.gov.uk))



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.

Serology/Immunity

PREPRINT: Waning of SARS-CoV-2 antibodies targeting the Spike protein in individuals post second dose of ChAdOx1 and BNT162b2 COVID-19 vaccines and risk of breakthrough infections: analysis of the Virus Watch community cohort

- This study shows that individuals who received the AstraZeneca vaccine are likely to experience waning immunity more quickly than those who received the Pfizer vaccine, in addition to being at a higher risk of breakthrough infections. Booster doses are important in maintaining protection of the elderly and clinically vulnerable- particularly those who received the AstraZeneca vaccine as their primary course.
- Antibody levels and trajectory of waning following vaccination may differ between vaccines. This will influence the level of protection, the speed at which protection is reduced, and thus inform the optimum timing of booster doses. For context, SARS-CoV-2 vaccines stimulate production of antibodies targeting the spike

protein (anti-S). Anti-S levels were compared after Pfizer or AstraZeneca vaccination using time since second dose of vaccination, age, sex and clinical vulnerability to investigate antibody waning.

- Results showed that three weeks after the second dose of Pfizer, mean anti-S levels were 9039 U/ml. Comparatively, AstraZeneca were 1025. For both Pfizer and AstraZeneca, waning anti-S levels declined from three weeks after administration of the second dose of vaccine. Anti-S levels declined at similar rates, but due to the Anti-S levels being substantially lower in individuals vaccinated with the AstraZeneca, this indicates that waning immunity will occur earlier in those vaccinated with AstraZeneca rather than Pfizer. There was a reduced risk of infection post-second dose for individuals with anti-S levels greater than or equal to 500 U/ml. It took approximately 96 days for AstraZeneca to reach an anti-S threshold of 500 U/ml and 257 days for Pfizer. Individuals who had been vaccinated with AstraZeneca were at a higher risk of a breakthrough infection than those who received the Pfizer vaccine.
- The study concludes booster doses are important in maintaining protection of the elderly and clinically vulnerable- particularly those who received the AstraZeneca vaccine as their primary course. Ascertainment of breakthrough infections relied on self-reported tests and linked data, therefore there will have been under ascertainment of breakthrough infections.
- It should be noted circulating anti-S levels are unlikely to be the only immunological correlate of protection against COVID-19 infection and severe disease. However data from this study is consistent with findings from other longitudinal studies
- Full paper: Waning of SARS-CoV-2 antibodies targeting the Spike protein in individuals post second dose of ChAdOx1 and BNT162b2 COVID-19 vaccines and risk of breakthrough infections: analysis of the Virus Watch community cohort | medRxiv

Nature article: Correlation of SARS-CoV-2-breakthrough infections to time-from-vaccine

- This study showed those who received an earlier dose (January/ February 2021) of the Pfizer-BNT162b2 vaccine during Israel's vaccination programme were at an increased risk of infection when compared to a person vaccinated later in the programme (March/April 2021). Risk of hospitalisation followed the same pattern. These results were similar across all age groups.
- The study controlled for potential confounders such as age and comorbidities. After controlling, a significant 1.51 fold (95% CI, 1.38–1.66) increased risk for infection for early vaccine recipients was found compared to those vaccinated 2-3 months later. The increased risk reached 2.26-fold (95% CI, 1.80–3.01) when comparing those who were vaccinated in January to those vaccinated in April (largest difference in administration time in this study).
- The study concluded by suggesting a possible relative decrease in the long-term protection of the Pfizer vaccine against the Delta variant, although further evaluation is recommended.

- Full paper: Correlation of SARS-CoV-2-breakthrough infections to time-from-vaccine | Nature Communications

PREPRINT: Describing the population experiencing COVID-19 vaccine breakthrough following second vaccination in England: A cohort study from OpenSAFELY

- COVID-19 vaccine breakthrough is occurring, however events are currently rare and mostly mild in nature. Considering the characteristics of those who have experienced a COVID-19 vaccine breakthrough could be key in determining who may be at greatest risk and therefore benefit most from booster doses of vaccine.
- A retrospective cohort study was conducted which used routine clinical data from the OpenSAFELY TPP database of fully vaccinated individuals, linked to secondary care and death registry data. It was found that rates of COVID-19 breakthrough were higher in those undergoing renal replacement therapy, those undergoing organ transplant, those with haematological malignancy, and those who are immunocompromised. Other risk factors included being female or belonging to a minority ethnic group. Finally, residents in care homes were seen to suffer higher rates of hospitalisation and death.
- This study concludes that the continued increase in numbers of positive SARS-CoV-2 tests are concerning, and as numbers of fully vaccinated individuals increases and follow-up time lengthens, so too will the number of COVID-19 breakthrough cases.
- Limitations of these findings are that the number of COVID-19 vaccine breakthrough cases is relatively small, especially those resulting in hospitalisations and deaths. Additionally, the cohort represents a mostly elderly and vulnerable population due to the nature of the COVID-19 vaccine rollout. Thirdly, follow-up time is systematically different amongst individuals and no adjustment for this has been made. Fourthly, symptomatic testing patterns vary between individuals, as asymptomatic individuals without underlying health issues are less likely to get tested. Finally, characteristics linked to COVID-19 vaccine breakthrough in fully vaccinated individuals may be reflective of higher infection rates regardless of vaccination in some groups, not because of vaccination (i.e. due to higher exposure due to behavioural differences)
- Full paper: Describing the population experiencing COVID-19 vaccine breakthrough following second vaccination in England: A cohort study from OpenSAFELY | medRxiv

Vaccines

NEJM: Evaluation of the BNT162b2 Covid-19 Vaccine in Children 5 to 11 Years of Age

- The UK Chief Medical Officers have recently recommended that 12-15 year olds be offered the COVID-19 vaccine, after reviewing evidence on the public health

benefits of extending vaccination to younger people. Israel has recently extended their vaccination program to children aged 5-11.

- A study funded by BioNTech and Pfizer has shown that a Covid-19 vaccination regimen consisting of two 10-µg doses of BNT162b2 administered 21 days apart was found to be safe, immunogenic, and efficacious in children 5 to 11 years of age.
- In the phase 2–3 trial, a total of 2268 children were randomly assigned to receive the BNT162b2 vaccine (1517 children) or placebo (751 children). At data cut-off, the median follow-up was 2.3 months. In the 5-to-11-year-olds, as in other age groups, the BNT162b2 vaccine had a favourable safety profile. No vaccine-related serious adverse events were noted.
- One month after the second dose, the geometric mean ratio of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) neutralising titres in 5-to-11-year-olds to those in 16-to-25-year-olds was 1.04 (95% confidence interval [CI], 0.93 to 1.18), a ratio meeting the pre-specified immunogenicity success criterion (lower bound of two-sided 95% CI, >0.67; geometric mean ratio point estimate, ≥0.8). Covid-19 with onset 7 days or more after the second dose was reported in three recipients of the BNT162b2 vaccine and in 16 placebo recipients (vaccine efficacy, 90.7%; 95% CI, 67.7 to 98.3).
- Full paper: Evaluation of the BNT162b2 Covid-19 Vaccine in Children 5 to 11 Years of Age

PREPRINT: Differences in COVID-19 vaccination coverage by occupation in England: a national linked data study

- This study considers occupational differences in vaccine hesitancy using nationwide population-level data by calculating the proportion of people who had received two doses of a COVID-19 vaccine by detailed occupational categories in adults aged 40-64 and estimated adjusted odds ratios to examine whether these differences were driven by occupation or other factors, such as education. The study also examined whether vaccination rates differed by ability to work from home.
- The findings suggest that the vaccination rates of adults aged 40 to 64 years in England differed markedly by occupation. Vaccination rates were high in administrative and secretarial occupations, professional occupations and managers, directors and senior officials (90.7%) and lowest in people working in elementary occupations (83.1%). Adjusting for other factors likely to be linked to occupation and vaccination, such as education, did not substantially alter the results. Vaccination rates were also associated with the ability to work from home, with the vaccination rate being higher in occupations which can be done performed from home. Policies aiming to increase vaccination rates in occupations that cannot be done from home and involve contacts with the public should be a priority.
- The study found substantial differences in vaccination rates looking at finer occupational groups even after adjusting for confounding factors, such as education. Vaccination rates were higher in occupations which can be done from

home and lower in those which cannot. Many occupations with low vaccination rates also involved contact with the public or with vulnerable people

- Increasing vaccination coverage in occupations with low vaccination rates is crucial to help protecting the public and control infection, especially in occupations that cannot be done from home and involve contacts with the public. Policies such as 'work from home if you can' may only have limited future impact on hospitalisations and deaths
- Full paper: Differences in COVID-19 vaccination coverage by occupation in England: a national linked data study

PREPRINT: Effectiveness of BNT162b2 (Comirnaty, Pfizer-BioNTech) COVID-19 booster vaccine against covid-19 related symptoms in England: test negative case-control study

- As part of the UK Government's booster vaccine rollout, over 50s and those in a clinical risk group were offered either a full dose of the Pfizer vaccine or a half dose of the Moderna vaccine, irrespective of the vaccine received as the primary course. A recent preprint study from UKHSA provides real world evidence of significant increased protection from the booster vaccine dose against symptomatic disease in those aged over 50 year of age, irrespective of which primary course was received.
- This study used a test-negative case-control design to estimate the Vaccine Effectiveness (VE) of the booster dose BNT162b2 (Comirnaty, Pfizer-BioNTech) in those aged over 50 against symptomatic disease in post booster time intervals compared to individuals at least 140 days post a second dose with no booster dose recorded. In a secondary analysis, we also compared to unvaccinated individuals and to the 2 to 6 day period after a booster dose was received. Analyses were stratified by which primary doses had been received and any mixed primary courses were excluded.
- Results showed that the vaccine effectiveness estimate in the 14 days after the Pfizer booster dose, compared to individuals that received a two-dose primary course, was 87.4 in those individuals who received two doses of AztraZeneca as a primary course and 84.4 in individuals who received two doses of Pfizer as a primary course. The absolute vaccine effectiveness from 14 days after the booster was 93.1 with the AstraZeneca vaccine as their primary course. It was 94.0 for Pfizer as their primary course.
- Limitations of this study are that it is observational with a number of possible biases which should be interpreted with caution. Also, the unreliability of PCR testing could cause misclassification of both cases and controls. Many individuals will also have been previously infected so the VE measured is in the context of a population where many have already had natural exposure. There is currently insufficient follow-up to estimate the effects on severe disease which leads to hospitalisation and death, and it's not yet clear how long protection against COVID-19 following booster vaccination will last.

- Full paper: Effectiveness of BNT162b2 (Comirnaty, Pfizer-BioNTech) COVID-19 booster vaccine against covid-19 related symptoms in England: test negative case-control study | medRxiv

Infection control/ non-pharmaceutical interventions

The effectiveness of face coverings to reduce transmission of COVID-19 in community settings. A rapid review [Update 2]

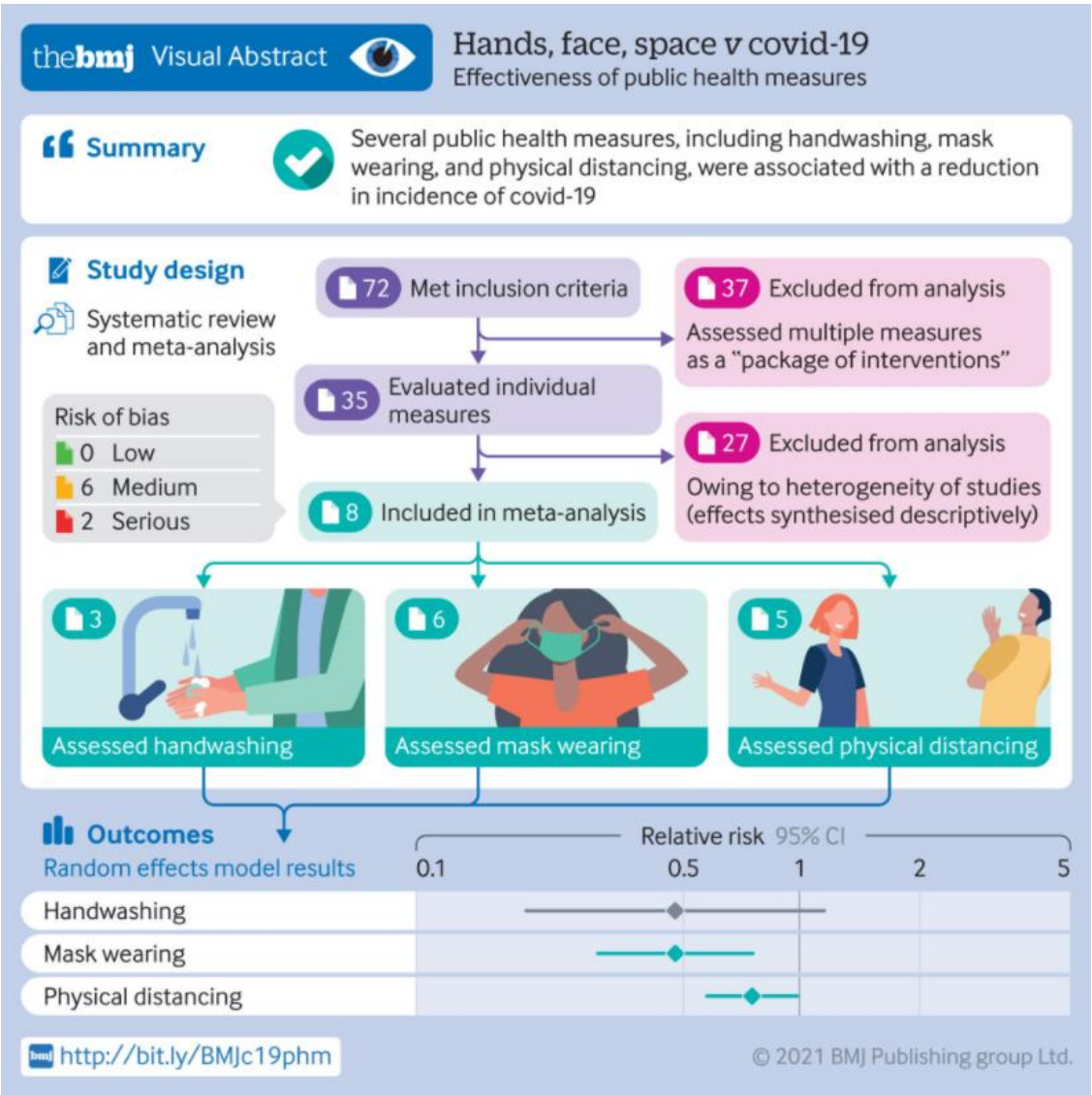
- This review identified evidence from 2 randomised control trials and 23 observational studies that predominantly suggested that face coverings reduce the spread of COVID-19 in the community, through source control, wearer protection, and universal masking. However, the studies identified did not support an assessment of whether face coverings were more effective as source control or wearer protection.
- One RCT provided direct evidence that face coverings (surgical and cloth face coverings) are effective when used as universal masking, particularly for surgical masks and for older people. Interventions that encourage an increase in face covering use also increased social distancing. Another RCT was inconclusive, reporting a non-significant reduction in COVID-19 infections from wearer protection.
- Eight contact tracing studies suggested that contacts of primary cases were less likely to develop COVID-19 if either the primary case or the close contact, or both, wore a face covering.
- These results are broadly in line with the results of the previous PHE review; however, the addition of RCTs and other studies increases the certainty of the previous results and strengthens the evidence for the effectiveness of face coverings in reducing transmission in the community.
- As with all reviews, the evidence identified may be subject to publication bias, whereby null or negative results are less likely to have been published by the authors. Also, the type of face covering and if it was worn correctly was not recorded.
- Full paper: The effectiveness of face coverings to reduce transmission of COVID-19 in community settings. A rapid review [Update 2]

Effectiveness of public health measures in reducing the incidence of covid-19, SARS-CoV-2 transmission, and COVID-19 mortality: systematic review and meta-analysis

- This evidence review of the effectiveness of public health measures in reducing the incidence of COVID-19, SARS-CoV-2 transmission, and covid-19 mortality has been published in the BMJ.
- The findings suggest that several personal protective and social measures, including handwashing, mask wearing, and physical distancing are associated

with reductions in the incidence COVID-19. Public health efforts to implement public health measures should consider community health and sociocultural needs, and future research is needed to better understand the effectiveness of public health measures in the context of COVID-19 vaccination.

- Current evidence from quantitative analyses indicates a benefit associated with handwashing, mask wearing, and physical distancing in reducing the incidence of COVID-19. The narrative results of this review indicate an effectiveness of both individual or packages of public health measures on the transmission of SARS-CoV-2 and incidence of COVID-19. Some of the public health measures seem to be more stringent than others and have a greater impact on economies and the health of populations. When implementing public health measures, it is important to consider specific health and sociocultural needs of the communities and to weigh the potential negative effects of the public health measures against the positive effects for general populations. Further research is needed to assess the effectiveness of public health measures after adequate vaccination coverage has been achieved. It is likely that further control of the COVID-19 pandemic depends not only on high vaccination coverage and its effectiveness but also on ongoing adherence to effective and sustainable public health measures.



- Full paper: Effectiveness of public health measures in reducing the incidence of covid-19, SARS-CoV-2 transmission, and covid-19 mortality: systematic review and meta-analysis | The BMJ

Education

PREPRINT: Ranking the Effectiveness of Non-Pharmaceutical Interventions to Counter COVID-19 in UK Universities with Vaccinated Population

- Many universities have resumed in-person teaching following a period of virtual learning due to the COVID-19 pandemic. This study investigated the best non-pharmaceutical interventions to maximise on-campus activities while controlling spread, and found that mask wearing and social distancing are key.
- The model enables staff-to-staff infections student-to-staff cross infections, student-to-student infections, and environment-to-individual infections. Input variables are then modelled which represent the implementation of different NPIs and formulate and solve optimal control problems for the four desired scenarios: minimum number of cases, minimum intervention, minimum non-quarantine intervention, and minimum quarantine intervention.
- Results revealed the particular significance of mask wearing and social distancing in universities with vaccinated populations. Also, quarantining infected students has a higher importance than quarantining staff. In contrast, other measures such as environmental disinfection seem to be less important. The implementation of non-pharmaceutical interventions is still fundamental to reduce the number of infections to one tenth of the number of infections appearing in a completely uncontrolled scenario.
- A limitation of this study is that the model doesn't consider infections brought from outside the campus. Secondly, the input variables (the interventions) in the optimal control problem are modelled as not changing over time. It may be difficult to give practical significance to the numerical values representing the interventions.
- Full paper: Ranking the Effectiveness of Non-Pharmaceutical Interventions to Counter COVID-19 in UK Universities with Vaccinated Population | medRxiv

Modelling

ScienceDirect: Increased close proximity airborne transmission of the SARS-CoV-2 Delta variant

- This study estimates the increased transmissivity of the Delta variant through the close proximity airborne route in order to re-evaluate the proportion of COVID-19 cases expected to reproduce infection.
- The study suggests transmission of the Delta variant is more homogeneous, with a higher rate of transmissibility and lower outbreak extinction probability, indicating that lockdowns may not be as immediately successful as with previous

variants at eliminating community transmission. Social distancing and masking remain effective mitigation strategies for the Delta variant where vaccination rates are low, as we estimate maintaining at least 1.5 m of separation during conversation drives R at close proximity below 1 even in a fully susceptible population. However, given the difficulty of maintaining at least 1.5 m of separation at all times, there is continuing need for masking in the absence of a high degree of population immunity.

- The Delta variant of SARS-CoV-2 causes higher viral loads in infected hosts, increasing the risk of close proximity airborne transmission through breathing, speaking and coughing. Modelling using a social contact network and exponential dose-response model to quantify the close proximity reproduction number of both wild-type SARS-CoV-2 and the Delta variant estimates more than twice as many Delta variant cases will reproduce infection in their close proximity contacts (64%) versus the wild-type SARS-CoV-2 (29%).
- The modelling also suggests room-scale airborne transmission contributes significantly to R0 for wild-type SARS-CoV-2, meaning improved ventilation, air filtration, and/or air disinfection are needed to mitigate community spread of past, present, and future variants of concern. Higher attack rates are predicted for the close proximity contacts of Delta cases, with our mean estimates being 50% for Delta versus 23% for wild-type. As such, additional emphasis should be placed on reducing household transmission.
- The authors recommend public health authorities should immediately revise guidelines to address the close proximity airborne pathway and recommend improved personal respiratory protection (e.g., N95 masks) for high-risk workers even in the absence of aerosol-generating procedures.
- Limitations of the analysis include viral load data for the Delta variant that is only preliminary, with similar uncertainty surrounding the dose-response model for SARS-CoV-2. Further, we limit the model to one day of normal contacts by an infected person without any mitigation measures. With respect to masking, we note that the respiratory jet is completely altered when an infected host wears a mask, and an entirely different thermo-fluid dynamic model would be required for more detailed analysis on the resulting reduction of inhaled dose. However, the consistency with other models supports the conclusion that most transmission of SARS-CoV-2 occurs during a narrow 1–2 day window of peak infectivity.
- Full paper: Increased close proximity airborne transmission of the SARS-CoV-2 Delta variant

Burden of Disease Methods: A Guide to Calculate COVID-19 Disability-Adjusted Life Years (ssph-journal.org)

- To date, most efforts to understand the comparative population health impact of COVID-19 have been made using mortality-based metrics. This article assessed the use of Disability-Adjusted Life Years (DALY's) for estimating the burden of COVID-19 to allow more accurate and comparable estimate of the burden of COVID-19. DALY's can serve as burden of disease estimates and can inform policy makers about the actual magnitude of the overall burden of the COVID-19

pandemic that could help trigger policy decisions, particularly around the extent of direct and indirect consequences of actions taken.

- So far, the direct impact of COVID-19 on population health has varied across countries, with wide variation in incidence and infection fatality rates. An understanding of this can be achieved by estimating summary measures of population health like disability-adjusted life years (DALYs). The estimation of DALYs is useful to provide comprehensive and comparative public health intelligence to inform decision-making for the management of the COVID-19 pandemic, particularly around the extent of direct and indirect consequences.
- A standard methodology for DALYs attributable to COVID-19 may allow more accurate and comparable estimates of the burden of this disease. Uncertainties persist around COVID-19 data quality and availability of information concerning sequelae from COVID-19. Transparent reporting of uncertainties and limitations is warranted to favour a correct interpretation of the results.
- Full paper: Burden of Disease Methods: A Guide to Calculate COVID-19 Disability-Adjusted Life Years

Variants

SARS-CoV-2 variants of concern and variants under investigation in England Technical briefing 28 and AY.4.2 Risk Assessment

- UKHSA provided an updated briefing of SARS-CoV-2 VOC's and VUI's. As of 8 November, Delta accounted for 79.3% of cases and 5,066 deaths. UKHSA reported 152 sequences of Delta + E484K in the UK, with only three being from Wales.
- UKHSA conducted a risk assessment of the emerging AY.4.2 variant. Overall AY.4.2 is slightly more infectious than the original Delta variant but comparable in other areas. As a result it has been categorised Red for transmissibility as it has an advantage over Delta, but Green for severity and immunity.
- Vaccine efficacy against AY.4.2 symptomatic infection is the same as the first Delta variant (for AZ, Pfizer and Modern vaccines). Vaccine efficacy against AY.4.2 hospitalisation is the same as the first Delta variant (for AZ and Pfizer vaccines only).
- AY.4.2 is gaining approximately 1-2% prevalence each week in sequenced cases. Growing from 11.2% of cases (17 Oct-23 Oct) to 14.7% of cases (31 Oct-6 Nov). UKHSA identified the Delta + E484K variant as being better evolved to evade the immune system. Neutralisation studies have put it on par with the Beta variant at immune system evasion.
- There are only 170 cases of Delta + E484K in UK currently. With the majority of these being found in 3 self-limiting outbreaks. The immune advantage of this variant comes at a cost to viral fitness, meaning it doesn't often survive long enough to be widely transferred.
- Full papers: SARS-CoV-2 variants of concern and variants under investigation in England - Technical briefing 28 (publishing.service.gov.uk)

- 10 November 2021 Risk assessment for SARS-CoV-2 variant: VUI-21OCT-01 AY.4.2 (publishing.service.gov.uk)

Behavioural

What influences people's responses to public health messages for managing risks and preventing infectious diseases? A rapid systematic review of the evidence and recommendations.

- This systematic review examines individual behaviour changes, such as hand hygiene and physical distancing, required on a population scale to reduce transmission of infectious diseases such as COVID-19. Little is known about effective methods of communicating risk reducing information, and how populations might respond.
- The research synthesises evidence relating to characteristics of effective public health messages for managing risk and preventing infectious disease, as well as what influences people's responses to messages. Note the cut off for article inclusion was May 2020. Study designs evaluating public health messaging interventions targeted at adults and concerning a communicable disease spread via primary route of transmission of respiratory and/or touch were included. Outcomes included preventative behaviours, perceptions/awareness and intentions. Only English language papers were included.
- Due to high heterogeneity studies were synthesised narratively focusing on determinants of intentions in the absence of measured adherence/preventative behaviours. Themes were developed independently by two researchers and discussed within the team to reach a consensus. Recommendations were translated from narrative synthesis to provide evidence-based methods in providing effective messaging.
- Sixty-eight eligible papers were identified, with characteristics of effective messaging including delivery by credible sources, community engagement, increasing awareness/knowledge and mapping to stage of epidemic/pandemic. To influence intent effectively, public health messages need to be acceptable, increase understanding/perceptions of the health threat and perceived susceptibility.
- The paper includes four recommendations:
    - engage communities in development of messaging;
    - address uncertainty immediately and with transparency;
    - focus on unifying messages from sources; and
    - frame messages aimed at increasing understanding, social responsibility and personal control.
- Embedding principles of behavioural science into public health messaging is an important step towards more effective health-risk communication during epidemics/pandemics.

- Full paper: What influences people's responses to public health messages for managing risks and preventing infectious diseases? A rapid systematic review of the evidence and recommendations | BMJ Open

Clinical

Wales COVID-19 Evidence Centre (WCEC) Review: Healthcare education

- This rapid review investigated the effectiveness of alternative education delivery strategies during the COVID-19 pandemic for medical, dental, nursing and pharmacy students.
- No relevant existing reviews were identified, so the review focused on 23 primary studies, all in undergraduate education and none was UK-based. Studies were recent, but of low or very low quality with small sample sizes.

Findings suggested:

- Remote learning is appreciated by students and enables continued teaching and learning in the short-term within the emergency circumstance.
- Supplementary alternative or in-person practical sessions may be required post-emergency to address learning needs for some disadvantaged student groups.
- The transition from the traditional into remote teaching methods seems to affect students' performance at exams, particularly for practical-based subjects in dentistry and medicine.
- The available evidence is insufficient to demonstrate equivalence for other healthcare student speciality groups.
- It is unclear whether planned remote teaching, rather than relying on emergency adaptation, would be more effective.
- Further research with robust methods to evaluate alternative education delivery strategies is needed to inform policy decision-making in this area.

WCEC Review: Innovations to improve backlog in endoscopy

- This rapid review investigated which innovations can be used to accelerate the patients' journey through the endoscopic cancer diagnosis pathway.
- Nine papers were included in total (2 reviews and 7 primary studies). The evidence presented in this review is recent, however small samples, short-term follow up periods and assumptions required for modelling studies, reduces the generalisability and confidence of conclusions.

Findings suggested:

- Increased use of faecal immunochemical testing (FIT) could reduce the endoscopy backlog and save NHS resources if those with low FIT scores can be excluded from further testing.
- Innovations to reduce backlog and speed up time to diagnosis should be explored including:

- Triage in primary care settings such as GP surgeries using innovations such as the cytosponge for oesophageal symptoms (e.g. reflux).
- Direct referral from primary care settings to specialist investigation, without the need for prior additional referrals in secondary care.

Full paper: Wales COVID-19 Evidence Centre reports