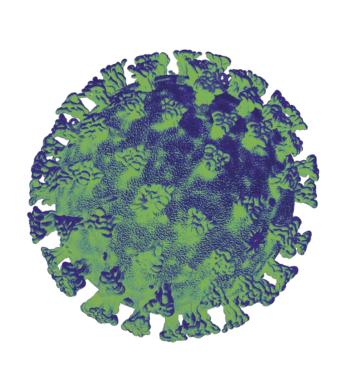
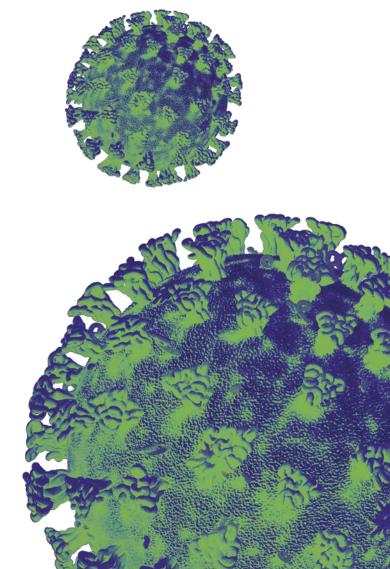


Technical Advisory Cell Summary of Advice

15 October 2021





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Top line summary

- Overall the decrease in both cases and test positivity that began around two
 weeks ago now appears to have stabilised at a high level of around 500 cases
 per 100,000 population. This is likely driven by a reproduction number close to 1
 combined with high prevalence, resulting in fluctuations in growth rates between
 weeks as R_t goes above or below 1.0. However wastewater surveillance in
 Wales, which is more unbiased than traditional testing, indicates a strong
 increase in levels of infection throughout South Wales.
- From early July 2021 to mid-September 2021, COVID-19 pressure on the NHS generally increased, however, this has remained relatively stable over recent weeks. As at 14 October 2021, there were 669 COVID-19 related patients (Suspected, Confirmed and Recovering) occupying a hospital bed.

- There are 51 patients with Suspected or Confirmed COVID-19 in critical care beds in Wales. This is 113 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 178, 26 more than the 152 baseline number of critical care beds available before the COVID-19 pandemic.
- The number of deaths has increased in the most recent week to 54 according to PHW, but appears to be decreasing and remains relatively low in comparison to previous waves.
- PHW's most recent <u>Surveillance of vaccine status in confirmed COVID-19 episodes and hospital inpatients</u> shows that 14.9% of COVID-19 hospital inpatients are unvaccinated, compared with 78.6% double vaccinated. When split by age, 6.4% of hospitalised patients aged 60+ are unvaccinated compared with 90.8% double vaccinated, and 38% of patients under 60 are unvaccinated compared with 45% of patients double vaccinated. Note this data should not be interpreted as measures of vaccination effectiveness and even with a highly effective vaccine, it is expected that a large proportion of cases would occur in vaccinated individuals.
- The JBC consensus estimate of the reproduction number for Wales is between 0.8 and 1.1 (as at 14 October 2021), while PHW's estimate is around 1.0 with a flat doubling time (13 October 2021). Note that JBC's estimate is typically lagged by 2-3 weeks while PHW, which uses a different methodology, is lagged by around 1 week.
- As at 22:00 14 October 2021 2,404,237 (+19,103) first doses and 2,232,967 (+6,827) second doses have been received by the Welsh population. A breakdown of uptake by priority group and age is provided in the relevant later section of this report. (Source: PHW)
- The ONS Coronavirus Infection Survey estimates that 2.18% of the community population had COVID-19 for the period 3 to 9 October. This is an increase from the previous week and is the highest recorded positivity rate for Wales from the Coronavirus Infection Survey.
- The most recent PHW weekly Influenza and Accurate Respiratory Infection report shows that flu activity remains stable, with only 6 confirmed influenza cases since the previous week. There was a small increase in the number of confirmed cases of Respiratory Synctial Virus (RSV) in children aged under 5 years across Wales, compared to the previous week. Incidence of confirmed RSV cases remains above the threshold that would normally indicate very high intensity seasonal activity, although testing levels are also currently higher than in previous seasons.

Research evidence summary:

 The first report from the ATACCC study on community household infections suggests the secondary attack rate among fully vaccinated household contacts is around 20%, compared with around 35% in the unvaccinated. Around one third of contact exposures arose from fully-vaccinated index cases and half of infected contacts were fully-vaccinated. Although current evidence suggests that vaccines remain highly effective at preventing severe disease and deaths from COVID-19, this study provides evidence that vaccination is not sufficient to fully prevent efficient transmission of the Delta variant in closed settings with prolonged exposures.

- Another pre-print paper has similar findings, suggesting vaccination reduces transmission of Delta, but by less than the Alpha variant. Two doses of the Pfizer vaccine reduced Delta transmission more than AstraZeneca. Transmission reductions declined over time since second vaccination, reaching similar levels to unvaccinated individuals by 12 weeks for AstraZeneca and attenuating substantially for Pfizer.
- A pre-print paper from Israel suggests that the Israeli booster vaccination campaign, which has been expanded to younger age groups, is having a significant effect on infection rates, with an approximately 10-fold reduction in the booster vs non-booster group, ranging from 8.8 to 17.6-fold across five different age groups. Severe illness rates were also reduced by almost 19-fold, and for ages over 60, COVID-19 mortality was reduced by almost 15-fold, suggesting that rollout of booster vaccinations to those at risk will make a significant difference to harm from COVID-19.
- A peer-reviewed paper using a novel method to examine accuracy of lateral flow tests (LFTs) emphasises important differences between antigen lateral flow tests (LFTs) and RT-PCR tests for SARS-CoV-2. The authors find this calibrated sensitivity to be markedly higher than the equivalent relative sensitivity, approaching or even exceeding 80% in certain circumstances.. The authors suggest it most likely that if someone's LFT is negative but their PCR is positive, then this is because they are not at peak transmissible stage. The authors state that according to the findings LFTs also continue to have a high specificity. However the reliability of LFTs is also dependent on sampling errors and experience of the person performing the sampling and the test.
- A published cohort study of electronic health records in the US, investigating nine features of long COVID, suggests that although incidence of these features was higher in older individuals and those with more severe illness, they also occurred in children and young adults with relatively mild illness, and in more than half of nonhospitalised patients. Almost 40% of patients with long-COVID symptoms recorded between 3 and 6 months had no such diagnosis in the first 3 months, suggesting some patients may have a delayed onset of long-COVID.
- The first report of the post-hospitalisation COVID-19 study highlights a large burden of symptoms persisting at 5 months in the majority of those who survive hospital admission with COVID-19, as well as a substantial proportion reporting a new disability and disruption to employment. Only 29% of survivors were fully recovered and 19% experienced a health-related change in occupation. Predictors of not recovering included female sex, comorbidities, middle age, and requiring invasive mechanical ventilation during admission.
- The most recent TAG policy modelling from Swansea University up to the end of March 2022 has been published, suggesting it is likely cases, hospitalisations and deaths will continue to increase until up to the end of September/October 2021, though the exact turning point is not clear. COVID-19 cases may reach a peak

similar to that observed in previous waves with some higher scenarios. COVID-19 hospitalisations and deaths are likely to peak a few weeks after COVID-19 cases but at a lower daily level than previous waves.

- TAG modelling of waning immunity has is also being prepared for publication, suggesting waning immunity starts to have a bigger effect in Spring 2022 but it does not lead to a significant fourth wave in the time horizon that the scenarios cover. Where immunity is assumed to wane more quickly (less than or equal to 240 days), introducing boosters for the over 50s can dramatically reduce the lengthy tail of infection. In a slower waning scenario, boosters in the autumn will have limited impact over the winter period studied and a later booster campaign in 2022 may be more effective.
- An evidence review from the TAG Environmental Science subgroup, incorporating
 the findings of the Wales COVID-19 Evidence Centre's rapid evidence review,
 concludes that ozone machines are not suitable for use in education settings due
 to potential secondary harms and a lack of robust evidence for effective use.
- A paper investigating the characteristics of 27,000 vaccine hesitant students aged 9-18 in England suggests around half would opt-in to vaccination, 37.0% were undecided, and 13% would opt-out. 'Opt-in' was lower in younger students (35.7% of 9-year-olds, 51.3% of 13-year-olds, 77.8% of 17-year-olds) and students who were vaccine hesitant were more likely to come from deprived socioeconomic contexts, supporting the need for targeted efforts to increase awareness and vaccination uptake.
- A detailed and comprehensive review of the available evidence underlying the role
 of face coverings in mitigating COVID-19 transmission has been published by
 UKHSA. The current evidence on face coverings suggests that when worn
 correctly all types of face coverings are, to some extent, effective in reducing
 transmission of SARS-CoV-2 in both healthcare and community settings.
- ONS modelling of vaccine effectiveness using COVID Infection Survey data suggests vaccination significantly reduced the risk of people testing positive with the Delta variant of COVID-19 (67% reduction), although to a lesser extent compared with the Alpha variant, particularly in preventing infections with symptoms. The Pfizer vaccine also showed a greater reduction in risk of testing positive than the AstraZeneca vaccine.

Wales Sit-Rep

- The latest 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. Note that as described in the recent Updated Coronavirus Control Plan publication has now changed to a fortnightly, rather than weekly, release so no update is available this week.
- Overall the decrease in both cases and test positivity that began around two
 weeks ago now appears to have stabilised at a high level. This is likely driven by
 a reproduction number close to 1 combined with high prevalence, resulting in

rapid fluctuations in growth rates. Cases have fallen from a peak of 643 cases per 100,000 on 1 October, or around 1 in every 155, to 499 as at 6 October, or 1 in 200. Test positivity has fallen from a peak of 20% on 30 August to 15.2% as at 4 October.

- However, wastewater surveillance in Wales indicates a strong increase in levels
 of infection throughout South Wales. Wastewater surveillance is very unbiased
 compared to traditional testing as it is not impacted by behaviour, policy or
 whether an individual is asymptomatic/symptomatic.
- From early July 2021 to mid-September 2021, COVID-19 pressure on the NHS generally increased, however, this has remained relatively stable over recent weeks. As at 14 October 2021, there were 669 COVID-19 related patients (Suspected, Confirmed and Recovering) occupying a hospital bed. This compares to 615 (54 more occupied beds) on 7 October 2021. Confirmed patients accounted for 484 of the total occupied beds.
- There are 51 patients with Suspected or Confirmed COVID-19 in critical care beds in Wales. This is 113 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 178, 26 more than the 152 baseline number of critical care beds available before the COVID-19 pandemic.
- The number of deaths has increased in the most recent week to 54 according to PHW, but appears to be decreasing and remains relatively low in comparison to previous waves.
- PHW's most recent <u>Surveillance of vaccine status in confirmed COVID-19</u> episodes and hospital inpatients shows that 14.9% of COVID-19 hospital inpatients are unvaccinated compared with 78.6% double vaccinated. When split by age, 6.4% of hospitalised patients aged 60+ are unvaccinated compared with 90.8% double vaccinated, and 38% of patients under 60 are unvaccinated compared with 45% of patients double vaccinated. Note this data should not be interpreted as measures of vaccination effectiveness- see <u>VEEP table</u>. Even with a highly effective vaccine, it is expected that a large proportion of cases would occur in vaccinated individuals, simply because a larger proportion of the population are vaccinated than unvaccinated (as at 3 October, 95% of those currently aged 60 and over had been vaccinated with 2 doses, and 78% of those currently aged 18- 60 had been).
- The JBC consensus estimate of the reproduction number for Wales is between 0.8 and 1.1 (as at 14 October 2021), while PHW's estimate is around 1.0 with a flat doubling time. (13 October 2021). Note that JBC's estimate is typically lagged by 2-3 weeks while PHW, which uses a different methodology, is lagged by around 1 week.
- As at 22:00 14 October 2021 2,404,237 (+19,103) first doses and 2,232,967 (+6,827) second doses have been received by the Welsh population. 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)	Received 2nd dose (n)	1st dose uptake (%)	2nd dose uptake (%)
Severely Immunosuppressed	8,827	8,628	8,486	97.7%	96.1%
Care home residents	14,216	13,953	13,688	98.1%	96.3%
Care home worker	39,116	36,850	35,748	94.2%	91.4%
80 years and older	166,702	160,315	158,768	96.2%	95.2%
Health care worker	144,044	139,820	137,338	97.196	95.3%
Social care worker		45,741	45,162		
Aged 75-79 years	131,162	127,185	126,269	97.0%	96.3%
Aged 70-74 years	182,092	175,437	174,301	96.3%	95.7%
Clinically extremely vulnerable aged 16-69 years	80,468	76,632	75,297	95.2%	93.6%
Aged 65-69 years	179,723	170,996	169,415	95.1%	94.3%
Clinical risk groups aged 12-64 years	359,178	322,434	308,440	89.8%	85.9%
Aged 60-64 years	205,142	191,892	189,460	93.5%	92.4%
Aged 55-59 years	233,392	214,300	210,886	91.8%	90.4%
Aged 50-54 years	228,352	205,527	201,278	90.0%	88.1%
Aged 40-49 years	395,037	336,170	324,205	85.196	82.196
Aged 30-39 years	428,401	336,040	313,522	78.496	73.296
Aged 18-29 years	487,678	379,278	341,075	77.896	69.9%
Aged 16-17 years*	70,042	51,506	14,762	73.596	21.196
Aged 12-15 years*	164,446	37,667	337	22.9%	0.296

All age groups are based on age as at 31 March 2021, with the exception of the 12-15 year olds age group which is age as at 31 March 2021 plus those who turned 12 between 1st April 2021 and 4th October 2021. This age cut-off date is an interim method and is subject to change in the future as more individuals become eligible for vaccination.

number entered in the 'Group size' column refers to all those with the specific risk that places them in their priority group, as recorded in the Welsh Immunisation System (WIS).
Individuals who belong to more than one priority group will appear in more than one line in the table. For example, a person age 52 with a condition that places them at
moderate risk will be counted in the group for 'moderate risk adults 15 years to under 65 years' and also in the '60-64 years' group. In national and health board totals (in weekly

- The most recent issue of the ONS Coronavirus (COVID-19) Infection Survey
 results, 3 to 9 October, suggests the percentage of people testing positive has
 increased in the most recent weeks in Wales and England but decreased in
 Northern Ireland and Scotland.
- The survey also estimated that 2.18% of the community population had COVID-19 (95% credible interval: 1.79% to 2.61%). This is the highest recorded positivity rate for Wales from the Covid Infection Survey. This equates to approximately 1 person in every 45 (95% credible interval: 1 in 55 to 1 in 40), or 66,200 people during this time (95% credible interval: 54,400 to 79,300). This compares to around 1 in 60 people in England, around 1 in 80 people in Scotland, and around 1 in 120 people in Northern Ireland.
- The most recent PHW weekly Influenza and Accurate Respiratory Infection report shows that flu activity remains stable with 6 confirmed influenza cases since the previous week. There was a small increase in the number of confirmed cases of Respiratory Synctial Virus (RSV) in children aged under 5 years across Wales, compared to the previous week. Incidence of confirmed RSV cases remains above the threshold that would normally indicate very high intensity seasonal activity, although testing levels are also currently higher than in previous seasons. 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).

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. This section only includes available in the public domain and does not include papers not yet published.

PREPRINT: Community Transmission and Viral Load Kinetics of SARS-CoV-2 Delta (B.1.617.2)Variant in Vaccinated and Unvaccinated Individuals (ATACCC Study)

- The majority of SARS-CoV-2 transmission occurs in households but transmission between fully vaccinated persons in this setting has not been demonstrated. Moreover, Delta viral load (VL) kinetics between vaccinated and unvaccinated persons with mild or asymptomatic infection, typical of community cases, has not hitherto been compared. The first report from the Assessment of Transmission And Contagiousness of COVID-19 in Contacts (ATACCC) study has now been published in the Lancet as a pre-print, prior to peer-review.
- The study found that the secondary attack rate among fully vaccinated household contacts is surprisingly high, at around 20%. It demonstrated efficient transmission of the Delta variant between fully vaccinated index cases and their fully vaccinated contacts in several households and confirmed that index:contact pairs were infected with the same Delta variant strain by whole genome sequencing.
- Peak VL was similar in vaccinated and unvaccinated individuals with Delta variant infection, but vaccinated Delta cases saw significantly faster VL decline than unvaccinated Alpha or Delta cases. Within infected individuals, faster VL growth was correlated with higher peak VL and slower decline. Since the findings are derived from community household contacts in a real-life setting, they are likely generalizable.
- The household secondary attack rate for fully-vaccinated contacts exposed to Delta was 19.7% (95%CI:11.6-31.3%), compared with 35.7% (95%CI:16.4-61.2%) in the unvaccinated. One third of infections in Delta-exposed contacts arose from fully-vaccinated index cases and one half of infected contacts were also fully-vaccinated. Seven transmission events between fully vaccinated indexcontact pairs occurred.
- Genomic analysis confirmed transmission pathways between fully-vaccinated individuals within three households. Peak VL was similar in vaccinated and unvaccinated individuals with Delta variant infection but vaccinated Delta cases saw significantly faster VL decline than unvaccinated Alpha or Delta cases. Within infected individuals, faster VL growth was correlated with higher peak VL and slower decline

- Although vaccination reduces the risk of Delta infection and causes some changes to viral kinetics, fully-vaccinated individuals with breakthrough infections have peak URT VL similar to unvaccinated cases and can efficiently transmit infection in household settings, including to fully vaccinated contacts.
- Overall although current evidence suggests that vaccines remain highly effective
 at preventing severe disease and deaths from COVID-19, this study provides
 evidence that vaccination is not sufficient to prevent efficient transmission of the
 Delta variant in closed settings with prolonged exposures. It highlights the
 importance of community studies in characterising the epidemiological phenotype
 of new virus variants in increasingly highly vaccinated populations and the use of
 non-pharmaceutical interventions to limit household transmission (See SAGE 76
 paper).
- Full paper: Community Transmission and Viral Load Kinetics of SARS-CoV-2
 Delta (B.1.617.2) Variant in Vaccinated and Unvaccinated Individuals

PREPRINT: The impact of SARS-CoV-2 vaccination on Alpha & Delta variant transmission

- Pre-Delta, vaccination reduced transmission of SARS-CoV-2 from individuals infected despite vaccination, potentially via reducing viral loads. Vaccination still lowers risk of infection, however similar viral loads in vaccinated and unvaccinated individuals infected with Delta question the degree to which onward transmission is prevented by vaccination
- A retrospective observational cohort study of contacts of SARS-CoV-2-infected index cases using contact testing data from England has been published in preprint, using multivariable logistic regression to investigate the impact of index case and contact vaccination on transmission, and how this varies with Alpha and Delta variants and time since second vaccination.
- 51,798/139,164(37.2%) contacts tested were PCR-positive. Two doses of Pfizer or AstraZeneca vaccines in Alpha variant index cases independently reduced PCR-positivity in contacts (aOR, adjusted odds ratio vs. unvaccinated=0.18[95%CI 0.12-0.29] and 0.37[0.22-0.63] respectively).
- The Delta variant attenuated vaccine-associated reductions in transmission: two Pfizer doses reduced Delta transmission (aOR=0.35[0.26-0.48]), more than AstraZeneca (aOR=0.64[0.57-0.72]; heterogeneity p<0.001). Variation in viral load (Ct values) explained only a modest proportion of vaccine-associated transmission reductions. Transmission reductions declined over time since second vaccination, for Delta reaching similar levels to unvaccinated individuals by 12 weeks for AstraZeneca and attenuating substantially for Pfizer. Protection from vaccination in contacts also declined in the 3 months after second vaccination.</p>
- Overall vaccination reduces transmission of Delta, but by less than the Alpha variant. The impact of vaccination decreased over time. Factors other than PCRmeasured viral load are important in vaccine-associated transmission reductions. Booster vaccinations may help control transmission together with preventing infections.

 Full paper: The impact of SARS-CoV-2 vaccination on Alpha & Delta variant transmission | medRxiv

PREPRINT: Protection Across Age Groups of BNT162b2 Vaccine Booster against Covid-19

- Following administration to persons 60+ years of age, the booster vaccination campaign in Israel was gradually expanded to younger age groups who received a second dose >5 months earlier. A preprint from Israel looking at the booster effect on COVID-19 outcomes has been published comparing confirmed Covid-19 infections, severe illness, and death of those who received a booster ≥12 days earlier (booster group) with a nonbooster group. In a secondary analysis, the authors compare the rates of confirmed infection and severe COVID-19 at 3-7 days post booster administration with that at 12 days or more post booster administration, when the booster effect is expected to be small and behavioural changes after vaccination are less marked.
- Confirmed infection rates were approximately 10-fold lower in the booster versus non-booster group (ranging 8.8-17.6 across five age groups) and 4.8-11.2 fold lower in the secondary analysis. Severe illness rates in the primary and secondary analysis were 18.7-fold (95% CI, 15.7-22.4) and 6.5-fold (95% CI, 5.1-8.3) lower for ages 60+, and 22.0-fold (95% CI, 10.3-47.0) and 3.2-fold (95% CI, 1.1-9.6) lower for ages 40-60. For ages 60+, COVID-19 associated death rates were 14.7-fold (95% CI, 9.4-23.1) lower in the primary analysis and 4.8-fold (95% CI, 2.8-8.2) lower in the secondary analysis.
- The authors highlight potential confounders around differences in protective behaviours between those who receive the booster and those who do not. Nevertheless overall across all age groups, rates of confirmed infection and severe illness were substantially lower among those who received a booster dose of the Pfizer vaccine, suggesting that rollout of booster vaccinations to those at risk will make a significant difference to harm from COVID-19. The findings provide evidence for the effectiveness of the booster dose against the currently dominant Delta variant in people 16+ years of age, as well as evidence for the maintenance of the effectiveness over an extended follow-up time for people 60+ years of age.
- Full paper: Protection Across Age Groups of BNT162b2 Vaccine Booster against Covid-19 | medRxiv

SARS-CoV-2 antigen rapid lateral flow test (LFT) sensitivity

- A paper published in Clinical Epidemiology emphasises important differences between antigen lateral flow tests (LFTs) and RT-PCR tests for SARS-CoV-2.
- The authors describe a method for calculating a calibrated sensitivity for antigen lateral flow tests (LFTs) as an alternative to the usual calculation of sensitivity relative to the RT-PCR test. The authors find this calibrated sensitivity to be markedly higher than the equivalent relative sensitivity, approaching or even exceeding 80% in certain circumstances.. The authors suggest it most likely that if someone's LFT is negative but their PCR is positive, then this is because they

- are not at peak transmissible stage. The authors state that according to the findings LFTs also continue to have a high specificity.
- This level of accuracy is considerably higher than previously suggested by other studies, which evaluated the sensitivity of LFTs by their ability to identify the same cases that the PCRs picked up. In contrast this study proposes a novel method to calculate accuracy of LFDs that accounts for their intended use more accurately. The paper presents a formula for calibrating the sensitivity of LFTs suggesting that, in reality, the sensitivity of the typical LFT in being able to identity someone who is likely to be infectious, may exceed 80%.
- The authors of the study acknowledge that the sensitivity of the LFTs is dependent on sampling errors and experience of the person performing the sampling and the test and that these uncertainties are not taken into account in their formula calibrations.
- Further longitudinal studies where individuals, and ideally contacts of cases, are tested daily by LFTs and PCR tests would help to further understand false negatives (and false positives) and, importantly, the time differences of between turning PCR positive, LFT positive, and symptom onset.
- Full paper: Recalibrating SARS-CoV-2 antigen rapid lateral flow test relative-sens peer-reviewed

Incidence, co-occurrence, and evolution of long-COVID features: A 6-month retrospective cohort study of 273,618 survivors of COVID-19

- A study of electronic health records in the US published in *PLOS Medicine* looks at incidence, co-occurrence, and evolution of long-COVID features following COVID-19 infection and influenza infection.
- The authors investigated the impact on age, sex and other factors on the development of nine features of long COVID, the distribution and overlap between features of long COVID and finally they compared onset of these features following COVID-19 and following influenza.
- 273,618 patients with COVID-19 were identified, and 114,449 patients with influenza were available for matching. Headaches, abdominal symptoms and anxiety/depression were significantly more likely to occur in women and younger patients. Breathing difficulties and cognitive symptoms were significantly more likely to occur in men. Breathing difficulties, cognitive symptoms, pain and fatigue were more likely to occur in older patients. Only minor differences were observed between white and non-white patients.
- 6 months after diagnosis, 57% had at least one feature of long-COVID recorded. In the 90 to 180-day "long" phase post-diagnosis, 36.6% had a long-COVID feature recorded.
- Overall, of patients with long-COVID features recorded between 90 and 180 days, 39.9% had not had any feature recorded in the first 90 days; the remaining 60.1% had at least one long-COVID feature in the first 90 days and developed additional or recurrent features in the next 90 days. This suggests the risk of long

COVID features occurring, or co-occurring, continues to increase 6 months after initial illness.

- Differences in severity of the COVID-19 illness were also associated with differences in incidence of long-COVID features. Patients with more severe illnesses had significantly more features overall, and significantly more cognitive difficulties, but were less likely to have myalgia or headaches. There were no significant differences in the clinical feature networks in any of these subgroup comparisons.
- Among people who had a given long-COVID feature reported at least once, the
 total number of recorded occurrences of that feature was significantly larger
 among patients with COVID-19 than patients with influenza for all clinical features
 except chest/throat pain, pain, and myalgia, highlighting differences between the
 two viruses.
- The authors do acknowledge most of the limitations in their report. There are some limitations inherent in electronic health record studies, such as quality of coding, and the completeness and the representativeness of the data. Although the 9 selected post-COVID symptoms are probably the most common in previous reports, it is well known that there are several other common symptoms and up to 200 symptoms reported by long COVID sufferers. As a result the reported incidence of symptoms after COVID infection is likely to be an underestimate.
- Full paper: Incidence, co-occurrence, and evolution of long-COVID features: A 6-month retrospective cohort study of 273,618 survivors of COVID-19 (plos.org)

<u>Long-COVID: Physical, cognitive, and mental health impacts of COVID-19 after hospitalisation (PHOSP-COVID)</u>

- The first report of the Post-hospitalisation COVID-19 (PHOSP-COVID) study, looking at the effects of COVID-19-related hospitalisation on health and employment to identify factors associated with recovery and outline recovery characteristics, has been published in Lancet Respiratory Medicine.
- This a multicentre, long-term follow-up study of adults (aged ≥18 years) discharged from hospital in the UK with a clinical diagnosis of COVID-19, involving an assessment between 2 and 7 months after discharge, including detailed recording of symptoms, and physiological and biochemical testing. It reports findings for 1077 patients discharged from hospital between March 5 and Nov 30, 2020, who underwent assessment at a median of 5·9 months (IQR 4·9–6·5) after discharge.
- Participants had a mean age of 58 years (SD 13); 384 (36%) were female, 710 (69%) were of white ethnicity, 288 (27%) had received mechanical ventilation, and 540 (50%) had at least two comorbidities. At follow-up, only 239 (29%) of 830 participants felt fully recovered, 158 (20%) of 806 had a new disability (assessed by the Washington Group Short Set on Functioning), and 124 (19%) of 641 experienced a health-related change in occupation.

- The findings confirm a large burden of symptoms persisting at 5 months after discharge, but also highlight a substantial proportion of survivors reporting a new disability and disruption to employment. Predictors of not recovering included female sex, comorbidities, middle age, and requiring invasive mechanical ventilation during admission. The mental and physical health impairments were only weakly associated with the severity of acute illness. There were significant differences in perceived recovery, impact on health-related quality of life, occupation change due to health, and disability across the four clusters, and higher C-reactive protein levels among patients experiencing the most severe ongoing impairments.
- The severity of physical and mental health impairments were closely related, whereas cognitive health impairments were independent. In clinical care, a proactive approach is needed across the acute severity spectrum, with interdisciplinary working, wide access to COVID-19 holistic clinical services, and the potential to stratify care.
- The findings suggest that there are underlying mechanisms causing severe mental and physical impairments, independent of the degree of acute lung injury and potentially related to persisting systemic inflammation. This data suggest that a proactive approach and holistic clinical care are needed owing to the large burden of health impairments. The four clusters highlight the potential to stratify and personalise care, and emphasise the need for wide access to interventions to improve mental, physical, and cognitive health.
- The paper has some limitations- the study's definition for recovery is based on patient perception and is likely to reflect post-COVID care demand, as well as subject to recall bias. The study also only considers infections leading to hospitalisation and additional investigation is needed on those infected with COVID-19 but not hospitalised, in order to understand this study's findings compared with other critical illnesses and those with long-term symptoms in the community.
- Full paper: Physical, cognitive, and mental health impacts of COVID-19 after hospitalisation (PHOSP-COVID): a UK multicentre, prospective cohort study -The Lancet Respiratory Medicine

TAG: Welsh Government COVID-19 Policy Modelling Update – 24 September 2021

- The most recent policy modelling from Swansea University up to the end of March 2022 has been published. Overall the modelling suggests it is likely cases, hospitalisations and deaths will continue to increase until up to the end of September/October 2021, though the exact turning point is not clear.
- COVID-19 cases may reach a peak similar to that observed in previous waves, with some higher scenarios. COVID-19 hospitalisations and deaths are likely to peak a few weeks after COVID-19 cases but at a lower daily level than previous waves.
- The current models suggest a potential peak in hospital occupancy but this is very sensitive to length of stay assumptions since length of stay has typically

been shorter in the third wave than previous waves, it is likely that the peaks will be lower than the current models predict, by a large margin. The current models predict that bed occupancy for COVID-19 positive patients might reach around 1,900 which would surpass the January peak, but with shorter observed length of stay this could be much lower at up to 750 beds occupied.

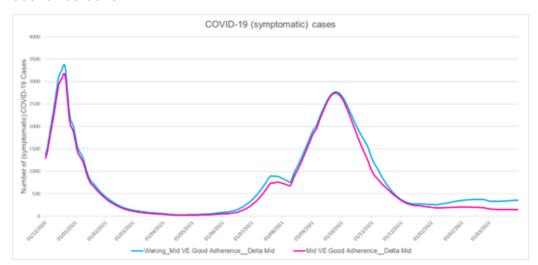
- The figures illustrate the uncertainty around the size and timing of the third COVID-19 wave, with the peak in daily cases ranging from well below the second wave peak in December 2020 to more than twice the height of the second wave's peak under different scenarios. The uncertainty in model estimates are driven by the uncertainty in effectiveness of vaccines on the Delta variant, increased transmissibility of the Delta variant and adherence levels.
- In this third wave, and with emerging evidence of waning immunity, we are still in a race between vaccines and the Delta variant. School closures may have reduced mixing over the summer, but increased mixing from easing restrictions acted as an additional opposing force. The recent return to school means there will likely be continued high transmission in children and young people so any policy response needs to consider the balance of harms to children.
- Changes to TTP self-isolation rules may have increased transmission; previous modelling suggested this could increase Rt by approximately 0.2, under recently observed R values.
- Modelling from SPI-M the Academy of Medical Sciences are also included for comparison to the Swansea University models.
- The current modelled scenarios do not include the impact of further antigenic drift; so are likely to be robust for the next few months, but further modelling may be required over the coming months. The model is updated regularly to capture any signals in increased/decreased transmission patterns.
- Further work is underway around a new MLS and RWC that takes into account rapidly changing transmission dynamics, waning vaccine effectiveness scenarios, the impact of third / booster vaccinations and vaccines for children aged 12-15 and scenarios for other respiratory viruses like influenza and RSV for Winter 2021/22.
- Full paper: <u>Technical Advisory Group</u>: policy modelling update 24 September 2021 | GOV.WALES

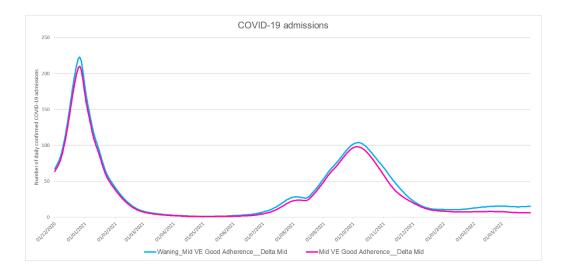
TAG: Covid-19 Waning Immunity (Publication pending)

- There is compelling evidence from numerous sources indicating that waning of
 immunity, particularly immunity gained from vaccination, is a very real possibility.
 Results from studies may not be comparable due to differing age/priority order of
 vaccinations, differing length of time between doses, different vaccines offered,
 etc. Confounding factors and limitations of studies need to be taken into account
 when assessing the duration and impact of waning immunity, of which there is
 still great uncertainty.
- A recent study from Public Health England (PHE) indicated that vaccine effectiveness (VE) against Delta is generally lower with the AstraZeneca (AZ)

vaccine than the Pfizer vaccine, but with both vaccines, waning of VE against symptomatic disease is seen from around 10 weeks.

- A recent rapid review on hospital admissions by Public Health Wales (PHW) summarised the characteristics of patients admitted to hospital who had a COVID -19 positive test result (in a 4 week period ending 05/09/2021). Overall, 61% of admissions were recorded as having received 2 doses of vaccine; the median interval from full vaccination to admission was 201 days (between 6 and 7 months).
- Vaccine efficacy against death remains high for both vaccines over time with minimal waning prior to 20 weeks following vaccination. However, even a small decrease in vaccine efficacy from 98% to 96% may double the number of deaths observed in a long term, high prevalence scenario.
- Modelling has been carried out to determine the effect different levels of immunity may have on COVID-19 cases, hospitalisations and deaths.
- The latest Swansea University modelling includes scenarios with waning immunity taken into account. It assumes that natural immunity from infection wanes after 3 years and that vaccine effectiveness wanes after 8 months post vaccine (one dose). In the short term, there is minimal impact of waning immunity. However, over longer time periods, it will have more of an effect. In the central scenarios below, waning immunity starts to have a bigger effect in Spring 2022 but it does not lead to a significant fourth wave in the time horizon that the scenarios cover.





Where immunity is assumed to wane more quickly (less than or equal to 240 days), introducing boosters for the over 50s (can dramatically reduce the lengthy tail of infection. The increased benefit from re-vaccinating younger individuals is likely to be minimal. For the slower waning rates (360 to 480 days) there is far less impact (between Sept 2021 to April 2022) with the greatest drop in protection for the over 50's not occurring until later in 2022. In this scenario, boosters in the autumn will have limited impact over the winter period studied and a later booster campaign in 2022 may be more effective.

• Full paper: Technical Advisory Cell | GOV.WALES (publication pending)

TAG: evidence review of ozone generators, including appropriateness as mitigation in classrooms

- An evidence review from the TAG Environmental Science subgroup, incorporating
 the findings of the Wales <u>COVID-19 Evidence Centre</u>'s <u>rapid evidence review</u> has
 been published. This review also considers the potential for ozone disinfection
 within educational settings. Overall the review concludes that ozone machines are
 not suitable for use in education settings.
- The paper makes the following high confidence conclusions:
 - Surface disinfection only mitigates infections acquired from contaminated surfaces. These account for a minor proportion of SARS-CoV-2 infections compared with other routes of infection
 - SAGE-EMG and NERVTAG (2020) support the view that SARS-CoV-2 is transmitted by three main mechanisms: exposure to close range aerosols or droplets, longer range respiratory aerosol exposure, and direct contact with contaminated surfaces or items
 - Hand hygiene addresses transmission from hands contaminated by contact with contaminated surfaces or direct contact
 - Techniques generating airborne disinfection chemicals present potential harms from introducing harmful agents into the indoor atmosphere

- Ozone is a highly harmful indoor pollutant which is associated with harm to human health at low concentrations and damages diverse and integral components of indoor environments
- Children and those with underlying respiratory conditions are particularly sensitive to ozone exposure
- Ozone reacts with a range of compounds present indoors to generate persistent harmful secondary aerosols
- o Evidence for effective ozone disinfection is limited in scope and quality
- Deployment of ozone to educational settings will require substantial resources to ensure safety and the protection of sensitive surfaces
- Deployment of ozone to educational settings will be reactive to contamination from transmission events effectively mitigated by other means (e.g. ventilation, routine cleaning, the spontaneous passage of time).
- Full paper: <u>Technical Advisory Group</u>: <u>evidence review of ozone generators</u> including appropriateness as mitigation in classrooms | GOV.WALES

EClinicalMedicine: Willingness of children and adolescents to have a COVID-19 vaccination: Results of a large whole schools survey in England

- Vaccine hesitancy has affected COVID-19 adult vaccination programs in many countries, however data on hesitancy amongst child and adolescent populations is largely confined to proxy surveys through parent opinion. This paper investigates the characteristics of vaccine hesitant children and adolescents using results from a large, school-based self-report survey of the willingness to have a COVID-19 vaccination in students aged 9 –18 years in England.
- The findings highlight how attitudes towards the COVID-19 vaccination in adolescent populations as well as parents follow many similar patterns to those in studies of adult populations. A UK household survey of 920 16-24 year-olds reported a vaccine hesitancy rate of 27% which was higher than for their adult counterparts. For the six studies reporting on over 7500 parents questioned on intentions to vaccinate their children, 45%–62% reported that they would vaccinate their children.
- 27,910 students aged 9-18 from 180 schools across four English counties answered the vaccine hesitancy question between 14th May and 21st July 2021, of whom 13984 (50.1%) would opt-in to take a vaccination, 10322 (37.0%) were undecided, and 3604 (12.9%) would opt-out. A lower percentage of younger students reported that they would opt-in to vaccination, for example, 35.7% of 9-year-olds and 51.3% of 13-year-olds compared to 77.8% of 17-year-olds would opt-in to take a vaccination.
- Students who were 'opt-out' or 'undecided' (a combined 'vaccine hesitant' group)
 were more likely to come from deprived socioeconomic contexts with higher rates
 of home rental versus home ownership and their school locations were more
 likely to be in areas of greater deprivation. They were more likely to smoke or

vape, spend longer on social media, feel that they did not belong in their school community but had lower levels of anxiety and depression. The vaccine hesitant students- the undecided and opt-out groups- were similar in profile, although the opt-out students had higher reported confirmed or probable previous COVID-19 infection than the opt-in group, whereas those undecided, did not.

- If government vaccination strategies move towards vaccinating younger schoolaged students, efforts to increase vaccination uptake may be necessary. Compared with students who would opt-in, those who were vaccine hesitant had greater indicators of social deprivation and felt a lack of community cohesion by not feeling a sense of belonging at their school. If programmes are rolled out, focus on hesitant younger students will be important, targeting more marginalised and deprived young people with information from trusted sources utilising social media; improving access to vaccination centres with provision both in and outside school; and addressing fears and worries about the effects of the vaccine. The main limitation of this study is that the participant group may not be wholly representative of England or the UK, which may bias population-level estimates of willingness to be vaccinated.
- The authors highlight a number of limitations of the study. It is unknown how representative the study sample is of either the UK as a whole or individual regions. Furthermore, response rates differed by school and class year. In addition, participation was impacted by classes and 'student bubbles' needing to isolate throughout this period. In terms of demographic representativeness, no information on ethnicity or free school meals were collected in the survey and current school-level data on gender by year group were not available. A further key limitation is that all the responses were self-reported and so limited by the inherent information and social desirability biases of self-report surveys including recall bias. Finally, it would be essential to triangulate these findings with more qualitative data from current students about reasons behind their choices and how to address any factors or concerns that might be drivers in their decision-making, especially, for example, in those who have previously had confirmed or probable COVID-19 infection.
- Full paper: Willingness of children and adolescents to have a COVID-19
 vaccination: Results of a large whole schools survey in England (nih.gov)

Published lessons learned exercises

- A number of organisations and groups have begun to publish their perspective on the UK's performance and lessons learned during the course of the COVID-19 pandemic. Each of these sets of lessons learned are a product of the organisation which produced it and do not necessarily present an unbiased or fully peer-reviewed perspective.
- Nevertheless these reports provide a wealth of insight and lessons learned that should be given careful and methodical consideration by advisors, policy makers and decision makers. A summary of some of them is below:
- The House of Commons and Science and Technology Committee and Health and Social Care Committee: Coronavirus: lessons learned to date.

 This report examines the initial UK response to the covid pandemic, concluding some initiatives were examples of global best practice but others represented mistakes. Both must be reflected on to ensure that lessons are applied to better inform future responses to emergencies.

The Longevity Science Panel: COVID-19 report

This is a comprehensive review of COVID-19 effects and responses up to October 2021, bearing in mind that the pandemic is still evolving. It is intended as a resource for professional users of longevity data including actuaries, risk managers, public health professionals, epidemiologists and researchers. It asks 'what do we know?', 'what have we learned?' and 'what are the uncertainties' over a range of issues that could potentially drive the pandemic and longevity going forward.

• The Royal Society- What the COVID-19 pandemic reveals about science, policy and society

The global COVID-19 pandemic of 2020–2021 required politicians to work alongside and depend on scientists more closely than any other event in recent times. It also saw science unfold in real time under intense public scrutiny. As a result, it highlighted as never before the ways in which science interacts with policy-making and with society, showing with sometimes painful clarity that science does not operate in a social or political vacuum. This article considers these issues with particular reference to the situation in the UK—which, as with any nation, illustrated some considerations of more general applicability but also had aspects unique to this country. This article argues there are many lessons to be learnt, and that, as this is surely not the last infectious-disease crisis of such magnitude that the world will face, we must hope they will be heeded.

• OSR: Improving health and social care statistics: lessons learned from the COVID-19 pandemic

- The Office for Statistics Regulation (OSR) has published its report: Improving health and social care statistics: lessons learned from the COVID-19 pandemic. The COVID-19 pandemic highlighted the need for health and social care statistics to command public confidence and enhance public understanding. This supports individuals to make informed decisions and hold their governments to account.
- The report states that the efforts of those producing health and social care statistics in the pandemic have been remarkable, with producers reacting impressively to an unprecedented rise in demand for statistics. The report recommends that strong leadership, transparency, and investment in data sharing and linking, data infrastructures, and analytical resource are required in order to build on the achievements of the pandemic and overcome existing challenges.

- WHO: Lessons learned from the COVID-19 pandemic achieving resilience for the next health emergency.
 - A new strategic document has been published following the WHO "Lessons learned from COVID-19: getting ready for the next pandemic" event. Within it are outlined 10 major lessons that have so far been identified by Member States in the Region and their partners. This document is intended to enhance national and community resilience against health emergencies and safeguard regional and global health security now and in the future.

Public Health England Respiratory Evidence Panel: The role of face coverings in mitigating the transmission of SARS-CoV-2 virus

- The UK Health Security Agency has published An expert panel statement, informed by evidence and expertise, on the role of face coverings in mitigating COVID-19 transmission.
- This paper draws on review-level evidence (searches up to 28 April 2021) to consider the potential effectiveness of face coverings in mitigating transmission of SARS-CoV-2. It includes evidence examining:
 - the role of airborne transmission in relation to SARS-CoV-2
 - the transmissibility of new SARS-CoV-2 variants
 - the effectiveness of face coverings, including efficacy of different types of face coverings and factors that may impact on this
- Current evidence on the potential for airborne transmission of SARS-CoV-2 is heterogeneous and mainly based on environmental sampling studies, modelling studies and outbreak investigations. While sampling studies suggest that SARS-CoV-2 can be detected in the environment, they usually do not provide evidence on infectiousness of the aerosols. Evidence from outbreak investigations suggests that long distance airborne transmission can occur and when it happens, it is usually in poorly ventilated indoor settings where the potential primary and secondary cases have stayed for extended durations of time. Other factors such as air flow or singing might also be contributing factors for long distance airborne transmission. Airborne transmission can also occur in healthcare settings, although it might predominantly happen during aerosol generating procedures.
- Evidence on the transmissibility of new variants of concern is still in its early stages and based on a small number of low-quality reviews. The available evidence suggests an increased transmissibility for Alpha variant (B.1.1.7), although the magnitude of reported increase varies by geographic region, modelling approach, relative transmissibility of concurrent circulating strains and current control measures in place. The evidence available for Beta (B.1.351) and Gamma (P.1) variants is more limited but does also suggest an increased transmissibility (Delta/B.1617.2 variant was not considered). The biological mechanism of the increase in transmissibility is not yet clear though for Alpha variant (B.1.1.7) the most likely explanations are increased viral load and lower average infectious dose required to start infection.

- The current evidence on face coverings suggests that all types of face coverings are, to some extent, effective in reducing transmission of SARS-CoV-2 in both healthcare and community settings. N95 respirators are likely to be the most effective, followed by surgical masks, and then non-medical masks, although optimised non-medical masks made of 2 or 3 layers might have similar filtration efficiency to surgical masks. The evidence specific to coronavirus (COVID19) is still limited and does not allow for firm conclusions to be drawn for specific settings and type of face coverings. Wider evidence from other respiratory viruses suggests that, in healthcare settings, N95 respirators might be more effective than surgical masks in reducing infection risk.
- Evidence mainly based on laboratory studies suggests that face coverings should be well-fitted to increase effectiveness.
- No evidence on the effectiveness of face coverings against specific variants of SARS-CoV-2 was identified.
- More research is needed to fully understand the contribution of airborne transmission to the COVID-19 pandemic and factors that may influence this. More robust research from well-designed intervention studies is also needed to better understand the effectiveness of different types of face coverings in mitigating the risk of different modes of transmission across settings. Finally, more research is needed to improve knowledge on how face coverings are used by subgroups of the population across settings and how this might impact on their effectiveness.
- Full paper: Face coverings and COVID-19: statement from an expert panel -GOV.UK (www.gov.uk)

Covid-19 Infection Survey: Analysis of vaccine effectiveness against infection

- This technical analysis published by ONS suggests vaccination significantly reduced the risk of people testing positive with the Delta variant of coronavirus (COVID-19), although to a lesser extent compared with the Alpha variant, particularly in preventing infections with symptoms.
- Two vaccines doses (≥ 14 days ago) reduced the risk of testing positive from Delta by 67% (95% CI: 64 to 70%) relative to the unvaccinated group. Two vaccines doses (≥ 14 days ago) reduced the risk of testing positive with symptomatic infection by 75% (95% CI: 71% to 78%) relative to the unvaccinated group with Delta; a smaller risk reduction than the 95% (95% CI: 91% to 98%) seen with Alpha.
- Both Pfizer-BioNTech and Oxford-AstraZeneca vaccines provided a similar level of protection as prior natural infection against the Delta variant. Two doses (≥ 14 days ago) of Pfizer-BioNTech reduced the risk of testing positive by 73% (95% CI: 70% to 76%), a greater reduction than Oxford-AstraZeneca which reduced the risk by 62% (95% CI: 58% to 66%) relative to the unvaccinated group. However, care must be taken when comparing the vaccine effectiveness of Oxford-AstraZeneca and Pfizer-BioNTech vaccines.
- Two doses of either vaccine provided significantly greater protection than one dose across all analyses (59%, 95 CI: 52% to 64%).

- Two doses (≥ 14 days ago) of Pfizer-BioNTech or Oxford-AstraZeneca remained as effective at preventing infection as previous natural infection, which reduced the risk of testing positive with Delta by 71% (95% CI: 65% to 77%).
- Full paper: Coronavirus (COVID-19) Infection Survey Technical Article: Impact of vaccination on testing positive in the UK Office for National Statistics