Top line summary

- Overall, case numbers have increased across Wales, with a 21% increase in the 7 day period and a 50% increase in the 14 day period ending 4 September. Test positivity remains high at 19% for the 7 day period ending 4 September.

- Hospital bed and ICU occupancy is also increasing in all health boards across Wales. Breakdown of admissions by age suggest that admissions have increased in all age groups, particularly over 60s. Deaths remain low.
• Observed levels of confirmed COVID-19 cases, COVID-19 admissions to hospital and ICU, and ICU occupancy are above the levels estimated by the June 2021 reasonable worst case (RWC) scenario. COVID-19 hospital bed occupancy and COVID-19-related deaths are below the most likely scenario (MLS).

• Following a statement around vaccination of children aged 12 to 15 years from the JCVI, four nations CMOs are now considering expanding the vaccination programme to these age groups. The JCVI has also recommended third dose vaccination for those who are severely immunosuppressed as part of their routine COVID-19 vaccination schedule.

• The largest study of long COVID in children to date has suggested that as many as 1 in 7 may still have symptoms 15 weeks later.

• A pre-print (not peer reviewed) analysis from the ONS COVID Infection Survey of duration of effectiveness comparing duration trends of the UK vaccines against the Delta variant suggests that while both vaccines were found to be highly effective, efficacy against infection is higher initially for Pfizer but wanes faster compared to AstraZeneca. While age effects may be a confounding factor, waning appears to be greatest in the 35-64 age group. The study did not include individuals aged 65+ due to data limitations.

• This contrasts with recent findings by PHE at SAGE, which suggests that AstraZeneca has a greater drop-off in effectiveness against symptomatic disease, hospitalisation and death. Despite these differences in findings, overall waning for both vaccines is strongest in older and clinical risk groups.

• Those individuals vaccinated in late 2020 and early 2021 will have less protection in the coming months, an issue exacerbated by recent estimates of lower effectiveness in older age groups and the vulnerable, many of whom were vaccinated in this period. Third doses and booster vaccinations, which are able to reverse waning of protection, will limit the impact of waning immunity.

• Early evidence from Israel suggests expanding the vaccine programme to a third dose results in an increased vaccine efficacy against infection of 70-84% 20 days after the booster shot. Additional data to follow around longer-term impacts and efficacy against severe disease as data becomes available.

• Results of a global trial of the anti-inflammatory drug Baricitinib suggest that while there was no reduction in the frequency of disease progression overall, the drug was associated with a 38% reduction in all-cause mortality, with one patient in every 20 treated by Baricitinib surviving that would not otherwise have done.

• TAG Winter modelling of the impact of other respiratory viruses suggests that the 2021-22 flu season could be 50%-100% higher than a typical season and could peak at a different time. Isolation and staying at home with symptoms, and other changes in terms of infection prevention and control in health and social care, will have longer term effects in preventing transmission of several viruses, but this remains to be seen, and we need to prepare for the possibility of very challenging conditions with lots of viruses in circulation. These models will be iterated and refined over time.
Consideration in TAG of the social value of a COVID-19 case and how this has changed estimates that while it is likely that in December 2020, it was good value for money to spend £12,000 to prevent one COVID case, whereas now it is unlikely to be good value for money to spend more than £4,000 to prevent one COVID case, on average. This is because the social costs of one COVID-19 case are estimated to be lower than in December 2020 because of the vaccination programme reducing severe outcomes and therefore it may be favourable to allocate spending to other areas of improving health.

SPI-M states that we are currently in a time of significant uncertainty given the competing factors of return to school, evidence of waning immunity, population behaviour changes and upcoming decision point in a number of policy areas such as vaccine guidance and certification.

There is consensus that the earlier that interventions are brought in, the lower prevalence is kept, reducing the direct COVID-19 burden and reducing the risk of needing more stringent measures to quickly reduce transmission (and hence prevalence). A basket of measures, light enough to keep the epidemic flat, would be sufficient if enacted when hospitalisations were at a manageable level. It is considered highly likely that a significant decrease in homeworking in the next few months would result in a rapid increase in hospital admissions.

The age distribution of cases is very likely to change over the short-term with the return of children to schools and so the number of cases in older people is of particular importance. It is critical that the vaccine status of hospital patients is monitored and reported in real time to detect clusters of admissions.

As mentioned above, there is some indication of waning against hospitalisation from 15 weeks after the second dose, in particular among recipients of the AstraZeneca vaccine, though this waning appears to be predominantly in clinical risk groups. This conflicts with the earlier ONS analysis and more investigation is required to understand this.

CO-CIN analysis of NIMS vaccination data suggests that vaccination has had little impact on the risk of in-hospital mortality in immunocompromised patients even after two doses. Admissions remained proportionately highest for elderly “Tier 2” patients across the different vaccine status categories, however absolute numbers were significantly lower in the first and second dose failures. Notably although the majority of elderly patients in hospital are vaccine failure there are also admissions of a large cohort of young fit patients who have not been vaccinated.

Factors associated with admission to critical care in children and young people were similar to those observed in the first wave of this disease in the UK. Around 1 in 5 children were admitted for other reasons with incidental asymptomatic COVID-19 and this should be considered in other analyses of hospital admissions.

SAGE analysis of the direct and indirect health impacts of COVID-19 in England suggests 722,000 Quality Adjusted Life Years (QALYs) lost as a result of deaths in the first 13 months of the pandemic. The paper also estimates around 150,000 QALY
lost due to morbidity in the first 12 months. QUALYs are a measure of a person’s ability to carry out the activities of daily life, and freedom from pain and mental disturbance, with 1 QUALY equal to 1 year of life in perfect health.

- The paper also estimates age standardised mortality rates in the most deprived fifth of the population was almost double that of the least deprived fifth and the greatest mortality impact was in older age groups, while the highest QALY lose was through morbidity in middle age groups. There is a risk of further long term health effects and the adverse economic shock and impacts on education are likely to lead to poorer health in the population and future health care need that could take 2-3 years to fully realise.

- Case-control studies around hotels and managed quarantine facilities suggest strong evidence that staying in overnight holiday accommodations generally, and hotels/bed and breakfast accommodations (B&Bs) specifically, was associated with increased likelihood of being a COVID-19 case. This is not the same as evidence of increased risk of transmission, but does highlight the reason for a particular focus on these settings as part of risk management.

### 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 immunity and forward projections is available [here](#).

- Overall, case numbers have increased across Wales, with a 21% increase in the 7 day period and a 50% increase in the 14 day period ending 4 September. Test positivity remains high at 19% for the 7 day period ending 4 September.

- Hospital bed and ICU occupancy is also increasing in all health boards across Wales. As at 8 September 2021, there were 553 COVID-19 related patients (Suspected, Confirmed and Recovering) occupying a hospital bed (+170 since previous week), of which 443 were confirmed. There are 49 patients with Suspected or Confirmed COVID-19 in critical care beds in Wales; 115 lower than the maximum COVID-19 position of approximately 164. Breakdown of admissions by age suggest that admissions have increased in all age groups, particularly over 60s. Deaths remain low.

- The JBC consensus estimate of Reproduction number (Rt) for Wales is between 1.1 and 1.3 (as at 8 September 2021), with a daily growth rate of between +1% and +4% and a halving time of 18 days to flat (longer than 40 days). Note this is typically lagged by 2-3 weeks. Prevalence of COVID-19 is estimated to be 1.3 to 2.0% of the Wales population currently positive with COVID_19.

- PHW’s national estimate of Rt, which is lagged by around 1 week, is an Rt of 1.15 to 1.2 for Wales and a doubling time of 19 days (95% confidence interval 10 to 158).
As at 22:00 9 September, 2,364,393 first doses and 2,195,417 second doses have been received by the Welsh population. A breakdown of uptake by priority group and age is below (Source: PHW)

The most recent issue of the ONS Coronavirus (COVID-19) Infection Survey results, 28 August to 3 September, suggests the percentage of people in the community population testing positive has levelled off in England, but has increased in Scotland and Wales. The trend is uncertain in Northern Ireland. Positivity is highest in Scotland (2.23%) and lowest in England (1.38%).

It is estimated that an average of 46,800 people in Wales had COVID-19 (95% credible interval: 35,700 to 59,500), equating to around 1 in 65 people or 1.54% of the community population (up from 0.92% last week). This compares to around 1 in 70 people in England, around 1 in 45 people in Scotland, and around 1 in 60 people in Northern Ireland.

Reasonable Worst Case and Most Likely Scenarios versus actual figures

Key message: Following a dip at the end of July, confirmed COVID-19 cases have been increasing. Observed levels of confirmed COVID-19 cases, COVID-19 admissions to hospital and ICU, and ICU occupancy are above the levels estimated by the June 2021 reasonable worst case (RWC) scenario. COVID-19 hospital bed occupancy and COVID-19-related deaths are below the most likely scenario (MLS).

This report compares observed levels of COVID-19 indicators with the June 2021 reasonable worst case (RWC) scenario and most likely scenario (MLS) for the first time. These scenarios take account of the impact of the Delta variant. These model scenarios are due to be updated soon to take into account updated assumptions and the move to alert level zero on 7 August 2021.
• In the charts below “RWC_Jun2021” is the June 2021 RWC scenario, “MLS_Jun2021” is the current (June 2021) most likely scenario, and “Actuals” represents the actual observed values for each indicator.

• Confirmed COVID-19 cases were low and stable throughout April and May but started to rise in June 2021. They peaked on 16 July 2021, then fell until 3 August 2021, and have been increasing since that date. Through June and much of July, confirmed COVID-19 cases followed the MLS very closely. On 3 September 2021, this indicator was above the RWC scenario and MLS. Note that for the model scenarios, “Cases” refers to symptomatic cases only so may be an underestimate.

• Confirmed COVID-19 hospital admissions decreased slowly in May and June 2021 before starting to increase in July. Other than a small dip in early August they have
continued increasing since July. On 3 September 2021 the 7-day average for COVID-19 hospital admissions was just above the MLS at 37 admissions per day.

- In May and June 2021 COVID-19 ICU hospital admissions were very low and stable. They rose in early July, reached a peak on 19 July 2021 and then fell almost to the level of the MLS. Since early August, COVID-19 ICU hospital admissions have been increasing. On 3 September 2021 the 7-day average for COVID-19 ICU hospital admissions was 5 per day, which is higher than the MLS and RWC scenario.

- COVID-19 confirmed total bed occupancy (which includes ICU beds) was low and stable throughout May and June and started to rise in early July. As of 3 September 2021 the 7-day average for COVID-19 confirmed total bed occupancy was a little under 300 beds occupied by COVID-19 confirmed patients – a little under the level forecast by the MLS.

- Through most of May and June COVID-19 confirmed ICU occupancy was very low at between 1 and 2 per day. It began to rise in early July, about 10 days later than forecast by the RWC, and rose at a rate similar to the RWC. Following a peak on 27 July 2021, COVID-19 confirmed ICU occupancy decreased, but it started to increase again after 11 August 2021. As of 3 September 2021 COVID-19 confirmed ICU occupancy was a little under 43, which is above the MLS and RWC scenario.
COVID-19 deaths were very low between April and mid-July 2021. They have been rising slowly since mid-July. As of 3 September, the 7-day average of COVID-19-related deaths reported by Public Health Wales was a little over 3 per day.

COVID-19 evidence - round-up

JCVI statements on COVID-19 vaccination of children aged 12 to 15 years and third dose vaccination for severely immunosuppressed

- The JCVI has now published its statement regarding vaccination of 12 to 15 year olds. Whilst it notes that “the health benefits from vaccination marginally outweigh the potential known harms”, it believes it is too finely balanced to recommend supporting universal vaccination of this younger group. The Committee does however recommend that those at heightened risk be vaccinated, and that the list of underlying health conditions that would qualify for vaccination be expanded to include haematological malignancy, sickle cell disease, type 1 diabetes, congenital heart disease and other health conditions as described under ‘COVID-19 clinical risk groups for children aged 12 to 15 years’.

- JCVI notes that it is not within its remit to incorporate in-depth considerations on wider societal aspects of vaccinating this group, including education benefits, although it does allude to the potential disruption to education caused by vaccination or on the influenza vaccine programme. The statement suggests the government may wish to seek further views on the wider societal and educational impacts from the 4 nation Chief Medical Officers and this is now in train.

- A summary of the risk benefit assessment of COVID-19 vaccination in those aged 12 to 15 years who do not have underlying health conditions that increase the risk of serious COVID-19 disease is below:
Paediatric intensive care unit (PICU) | Hospitalisations | Paediatric inflammatory multisystem syndrome (PIMS-TS) | PICU | Hospitalisations | PIMS-TS
---|---|---|---|---|---
2.39 | 87.01 | 15.31 | 0.16 | 5.74 | 12.67

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<th>Table 3: prevented per course</th>
<th>Table 4: myocarditis risk per million</th>
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<td>PICU</td>
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- Link to full statement: [JCVI statement on COVID-19 vaccination of children aged 12 to 15 years: 3 September 2021 - GOV.UK (www.gov.uk)]

- The JCVI has also advised that people with severely weakened immune systems should have a third vaccine dose as part of their primary COVID-19 vaccination schedule. Preliminary data from the OCTAVE trial showed that while almost immunosuppressed recipients mounted an immune response after 2 doses, in around 40% of people, the levels of antibodies were low.

- This third dose should be offered to people over 12 who were severely immunosuppressed at the time of their first or second dose, including those with leukaemia, advanced HIV and recent organ transplants. These people may not mount a full response to vaccination and therefore may be less protected than the wider population.

- The JCVI advises that for adults aged 18 and older, either the Moderna or Pfizer-BioNTech COVID-19 vaccines be administered for the third dose, as a number of studies have reported an increased immune response in some immunosuppressed people after a third dose of an mRNA vaccine. For those aged 12 to 17, the Pfizer-BioNTech vaccine is preferred.

- A third primary dose is an extra ‘top-up’ dose for those who may not have generated a full immune response to the first 2 doses. In contrast, a booster dose is a later dose to extend the duration of protection from the primary course of vaccinations. The Joint Committee on Vaccination and Immunisation (JCVI) is still deliberating the potential benefits of booster vaccines for the rest of the population and is awaiting further evidence to inform this decision.

- In the event of a booster programme, it is expected that severely immunosuppressed people will also be offered a booster dose, at a suitable interval after their third dose.

- Full statement: [JCVI issues advice on third dose vaccination for severely immunosuppressed - GOV.UK (www.gov.uk)]
Long COVID - the physical and mental health of children and non-hospitalised young people 3 months after SARS-CoV-2 infection; a national matched cohort study (The CLoCk) Study.

- A pre-print report on non-hospitalised SARS-CoV-2 positive children and young people and prolonged symptoms after COVID infection has reported that as many as 1 in 7 may still have symptoms 15 weeks later.

- This is the largest study on symptoms post-COVID in children to date and, uniquely, uses child-reported symptoms, is confined to PCR-proven SARS-CoV-2 status, has a PCR-negative control group, and uses standardised measures to assess mental health, well-being, and fatigue. It provides valuable insight to inform discussions of risk of COVID-19 infections in children. It was conducted during January to March 2021 when the alpha variant was dominant.

- The study found that, when surveyed at an average of 15 weeks after their test, 14% more young people in the test positive group had three or more symptoms of ill health, including unusual tiredness and headaches, than those in the test negative group, while 7% (1 in 14) had more had five or more symptoms.

- At time of PCR-testing, 35.4% of test-positives and 8.3% of test-negatives had any symptoms whilst 30.6% and 6.2%, respectively, had 3+ symptoms. At 3 months post-testing, 66.5% of test-positives and 53.3% of test-negatives had any symptoms, whilst 30.3% and 16.2%, respectively, had 3+ symptoms.

- The research demonstrates prevalence estimates and definitions of Long COVID should consider the presence of multiple symptoms, proven SARS-COV-2 status and include control groups.

- The study needs to be carefully interpreted in the context of other paediatric and long COVID literature- as a self-selected online study it is prone to possible response or recall bias, potentially resulting in an over-representation of symptom prevalence.

- Full paper: Long COVID - the physical and mental health of children and non-hospitalised young people 3 months after SARS-CoV-2 infection; a national matched cohort study (The CLoCk) Study. | Research Square

Comparison Between Two Doses and Three doses of the BNT162b2 Vaccine – Israel (pre-print)

- With evidence of waning immunity of the Pfizer vaccine, Israel began a third dose vaccination campaign during August 2021; the first data regarding the effectiveness of booster shots has now begun to emerge. By August 27, over 1.9 million individuals had received a booster shot. Current guidelines state that a minimum interval of 5 months since receipt of the second dose is required to be eligible for the booster dose

- A preliminary study considering the effectiveness of boosters suggests a significant reduction in the likelihood of testing positive following a third dose. Results are stated
at a 48-68% efficacy 7-13 days after the booster shot compared to two doses, increasing to a 70-84% efficacy in days 14 to 20. These estimates are in relation to previously having two doses, as opposed to an unvaccinated scenario.

- The paper acknowledges the study is limited by the early stage of the booster programme only having started in early and that these are very early results and do not cover longer time periods or efficacy against serious illness.

- Full paper: Short Term Reduction in the Odds of Testing Positive for SARS-CoV-2: a Comparison Between Two Doses and Three doses of the BNT162b2 Vaccine | medRxiv

Impact of Delta on viral burden and vaccine effectiveness against new SARS-CoV-2 infections in the UK - ONS

- Large UK study examines impact of Delta variant on viral burden and vaccine effectiveness (news-medical.net)

- A comprehensive analysis of data from the ONS COVID Infection Survey compares duration of efficacy of the AstraZeneca and Pfizer vaccines used in the UK in relation to the Delta variant.

- Results indicate that while both vaccines were found to be highly effective, efficacy against infection is higher initially for Pfizer but wanes faster compared to AstraZeneca. While age effects may be a confounding factor, waning appears to be greatest in the 35-64 age group.

- The study supports that vaccination of those who have previously had COVID-19 results in a higher efficacy for both vaccines, at around 90% or higher. The paper also estimates that immunity for those with natural immunity only is estimated to be around 70%.

- Figure: Protection against all new PCR-positive episodes with Ct<30 over time from second dose, overall and by potential subgroups in those 18-64 years in the Delta-dominant period (BNT162b2 = Pfizer, ChAdOx1 = AstraZeneca; lthc=self-reporting a long term health condition)
Preprint on new potential variant of concern c.12 (first identified in South Africa)

- A new variant first identified in South Africa in May 2021 with multiple mutations also seen in variants Alpha, Beta and Gamma and that are associated with increased transmissibility and reduced neutralisation sensitivity, has been characterised in a pre-print study.

- This variant has been detected throughout the third wave of infections in South Africa from May 2021 onwards and has been detected in seven other countries within Europe, Asia, Africa and Oceania. The study points out that this lineage has the potential to become a variant of concern. The UK is monitoring this variant but has not yet designated it as a Variant Under Investigation. No data on the number of sequences of this variant found in the UK have therefore been published as yet, but the number is likely to be low.

- Future work aims to determine the functional impact of these mutations, which likely include neutralizing antibody escape, and to investigate whether their combination confers a replicative fitness advantage over the Delta variant, although early real-world evidence suggests this is not the case and the variant accounts for a low percentage of infections.

Full paper: The continuous evolution of SARS-CoV-2 in South Africa: a new lineage with rapid accumulation of mutations of concern and global detection | medRxiv
Published SAGE papers

SAGE: SPI-M Consensus Statement

- The UK is currently experiencing high prevalence and likely entering a period of growth as a result of changes in behaviour. It is also a time of significant uncertainty given the scope for increased transmission after the end of the school holidays, the possibility for further evidence to emerge on the duration of immunity against COVID-19, and several policy areas such as JCVI advice on booster vaccinations, CMO advice on vaccinations for 12-15 year olds and UK government policy on certification likely to become clearer. It will take a further three to four weeks for the full impacts of likely forthcoming changes in behaviour to be reflected in the data, such as the return of schools in England and any reduction in working from home.

- Although previous roadmap modelling did not foresee such rapid transient change in dynamics, these scenarios can still be used to consider the future autumn and winter trajectory. For England?, It is likely that the future trajectory of the epidemic may be some combination of the Step 4 Roadmap scenarios but with a delay of any peak, for example with peaks occurring in October to December instead of August to October.

- Given the large number of infections that have occurred in recent months and the additional vaccine doses delivered, it is unlikely that the highest levels seen in Step 4 Roadmap scenarios from July will be reached without waning immunity or a novel variant emerging. It is also possible that the epidemic peak could be flatter and/or broader than those seen in Step 4 Roadmap modelling scenarios.

- There is a clear consensus in SPI-M that continued high levels of homeworking has played a very important role in preventing sustained epidemic growth in recent months. It is highly likely that a significant decrease in homeworking in the next few months would result in a rapid increase in hospital admissions.

- Prevalence has remained high for some weeks, and hospital admissions in the older population have increased, albeit relatively slowly from a low base. It is unclear how high prevalence and admissions may go without intervention. While it is too early to observe in the data, it is possible that transmission will increase as the majority of schools have now returned and many adults are returning to the office after an extended period of working from home.

- There is now evidence of waning vaccine effectiveness, particularly 140 days after the second dose. Those individuals vaccinated in late 2020 and early 2021 will have less protection in the coming months, an issue exacerbated by recent estimates of lower effectiveness in older age groups and the vulnerable, many of whom were vaccinated in this period. Third doses and booster vaccinations, which are able to reverse waning of protection, will limit the impact of waning immunity.

- The actual epidemic trajectory over autumn and how difficult winter will be for the health and care service will depend on whether contact patterns continue to increase at the same rate; it is quite possible that any future scenarios may be ruled in or out quite rapidly. While the longer-term trajectory cannot be modelled with certainty, it is
possible to look at a plausible selection of projection scenarios over the next eight weeks.

- Modelling by SPI-M considers the impact of changes in behaviour in England on resulting in R values of 1.1, 1.5 and 2.0 on 6 September and the following eight weeks (R=1.1 – Green; 1.5 –Blue; 2.0 – Red). These reflect possible scenarios and are neither forecasts nor predictions as recent changes have not yet filtered through into surveillance data.

- SPI-M-O deems the scenario where R = 2.0 (red) to be an extreme and unlikely trajectory for the epidemic over the next few weeks, albeit more likely if waning immunity to play a greater role or if a new variant of concern were to emerge. The two scenarios of R = 1.1 and R = 1.5 attempt to provide an envelope which contains the likely epidemic trajectory over the next couple of months. Even in the R = 1.1 scenario, a large number of COVID-19 hospital admissions (up to around 2,000 a day) in England for a potentially protracted period of time is projected.

- While the relationship between cases and hospitalisations has changed due to vaccination, increasing cases remain the earliest warning sign that hospital admissions are likely to rise. The age distribution of cases is very likely to change over the short-term with the return of children to schools and so the number of cases in older people is of particular importance. Increasing positivity (from ONS) indicates that rising prevalence is likely to be the reason for increasing cases, rather than changes in test-seeking behaviour.

- It is critical that the vaccine status of hospital patients is monitored and reported in real time to detect clusters of admissions that may be the result of a novel variant.
It remains the case that the earlier that interventions are brought in, the lower prevalence is kept, reducing the direct COVID-19 burden and reducing the risk of needing more stringent measures to quickly reduce transmission (and hence prevalence). A basket of measures, light enough to keep the epidemic flat, would be sufficient if enacted when hospitalisations were at a manageable level. If the epidemic were allowed to continue to grow until hospitalisations were at a level that needed to be rapidly reduced, much more stringent (and therefore more disruptive) measures would be needed to bring prevalence down quickly. There was no consensus at SPI-M on the strength of measures that could be needed if the growth rate were high and the number of hospitalisations needed to be reduced rapidly.

Full paper: [SPI-M-O: Consensus statement on COVID-19, 8 September 2021 - GOV.UK (www.gov.uk)]

**SAGE: Duration of Protection of COVID-19 vaccines against clinical disease – Waning Immunity**

- The latest PHE data on vaccine effectiveness (VE) against clinical disease by period after a two-dose course of vaccine has been presented to SAGE. Overall, the results indicate that there is waning of VE against symptomatic disease with both the Pfizer and AstraZeneca vaccines from approximately 10 weeks after the second dose. This is most evident in older adults.

- There is some indication of waning vaccine efficacy against hospitalisation from 15 weeks after the second dose, in particular among recipients of the AstraZeneca vaccine, though this waning appears to be **predominantly in clinical risk groups**. This is a broad group of clinical conditions including those who are immunosuppressed, where faster waning may be predicted. Nevertheless, protection against hospitalisation remains high throughout the follow-up period and even within clinical risk groups, VE against hospitalisation at 15-20 weeks is 75-90% with the AstraZeneca vaccine and over 90% with the Pfizer vaccine.

- Finally, those aged 80 years and older who received the Pfizer vaccine within a 3-week interval between doses showed a greater degree of waning compared to the broader 65+ age group who had a 20+ week interval between doses though further analysis is needed to understand this difference.

- This analysis provides a different message to the ONS study (pre-print) discussed earlier in this report which suggested efficacy against infection is higher initially for Pfizer but wanes faster compared to AstraZeneca. This has been attributed to PHE having a larger data set and longer follow-up, along with other confounding factors that need more understanding. **As a result of these uncertainties, it is recommended these analyses should be read and communicated with caution.** Overall however, across both studies waning protection against infection is identified, with a lower waning in deaths and hospitalisations but a larger effect in the most clinically vulnerable (high confidence).
• Full paper: **PHE: Duration of protection of COVID-19 vaccines against clinical disease, 9 September 2021 - GOV.UK (www.gov.uk)**

**SAGE: Hospital Admission for COVID-19 and impact of vaccination: analysis of linked data from the National Immunisation Management Service (NIMS) and the Coronavirus Clinical Information Network (CO-CIN)**

• Vaccination data from the National Immunisation Management Service (NIMS), which gives information on patient’s vaccinations, has recently been shared with the ISARIC Coronavirus Clinical Characterisation Consortium (ISARIC4C.net). The study population was restricted to admissions that occurred between the December 8th, 2020, when vaccination started and July 28th, 2021, to allow for at least 28 days of follow-up from most recent data pull.

• In order to identify patients admitted “because of COVID-19” i.e. with severe disease, rather than merely “with SARS-CoV-2 infection” (admitted for another reason, and found positive on screening), asymptomatic patients were excluded along with a number of other categories (see paper for details). Of the remaining 40,000 patients included in this analysis, 33,496 (83.7%) were unvaccinated, 5,198 (13.0%) had received their first vaccination and 1,274 (3.3%) had received their second vaccination.

• Vaccine failure is defined by patients admitted to hospital with COVID-19 who have received one or two vaccine doses, plus adequate time to mount an immune response. The term ‘failure’ does not imply no vaccine protection, only failure to protect from admission to hospital with COVID-19.

• The study shows that age remains significantly associated with mortality, with vaccination having little impact on the risk of in-hospital mortality in *immunocompromised patients* after both first and second dose vaccines.

• Admissions remained proportionately highest for elderly “Tier 2” patients across the different vaccine status categories, however absolute numbers were significantly lower in the first and second dose failures. The greater presence of elderly “Tier 2” vs younger “Tier 10” vaccine failures may in part represent the vaccination programme in the UK, where vulnerable patients have had more opportunity to receive two vaccines by the time of this analysis.
Vaccine failure immunocompetent vs immune compromised – snapshot June 17 – 25 August.

- The majority of elderly patients in hospital are vaccine failure but there is also a large cohort of young fit patients who have not been vaccinated.
- Full paper: CO-CIN: Hospital admission for COVID-19 and impact of vaccination, 9 September 2021 - GOV.UK (www.gov.uk)

SAGE: Comparison of children and young people admitted with SARS-CoV-2 across the UK in the first and second pandemic waves: prospective multicentre observational cohort study

- Children and young people (CYP) were less affected than adults in the first wave of SARS-CoV-2 in the UK. This study tests the hypothesis that clinical characteristics of hospitalised CYP with SARS-CoV-2 in the UK second wave would differ from the first due to the combined impact of the alpha variant, school reopening and relaxation of shielding.
- Severe disease in CYP admitted with symptomatic SARS-CoV-2 in the UK remains rare, and death extremely rare. The study found no evidence of increased disease severity in W2 compared with W1. Length of stay remained short with little difference in hospital admissions of CYP and subsequently limited increase of burden on the health care system.
- Factors associated with admission to critical care in CYP were similar to those observed in the first wave of this disease in the UK. Around 1 in 5 children were admitted for other reasons with incidental asymptomatic disease; a factor that may not have been picked up in a ‘big data’ approach to dataset analysis. As a result it is critical for future studies to differentiate between symptomatic and asymptomatic/incidental SARS-CoV-2 infection in the paediatric population when considering hospitalisation. Plans are in train to continue this analysis for Wave 3.
It was also highlighted in SAGE that around half of admitted CYP with no comorbidities do not meet the current JCVI high risk criteria for vaccination, highlighting a limitation of this approach.

Full paper: ISARIC: Comparison of children and young people admitted with SARS-CoV-2 across the UK in the first and second pandemic waves – prospective multicentre observational cohort study, 9 September 2021 - GOV.UK (www.gov.uk)

SAGE: Direct and Indirect health impacts of COVID-19 in England

This short paper by the Department of Health and Social Care (DHSC) and the Office of National Statistics (ONS) summarises four routes through which COVID-19 has had an impact on health:

3. Indirect impacts of COVID-19 on health-related behaviours and healthcare.

The total Quality Adjusted Life Years (QALYs) lost due to mortality between March 2020 and April 2021 are estimated to be 722,000. The paper also estimates around 150,000 QALY lost due to morbidity during this period. The age standardised mortality rates in the most deprived quintile was almost double that of the least deprived quintile (264.6 deaths per 100,000 people and 140.4, respectively). The greatest mortality impact was in older age groups, while the highest QALY loss was through morbidity in middle age groups. The 25-44-year-old age groups suffered the greatest QALY losses of the age bands with an estimate of 28,000 lost QALYs, partly as this age cohort is the largest age cohort used in the analysis, and this age bands is a high risk of suffering COVID-19 symptoms for a greater duration of time. During the first wave of the pandemic people from all ethnic minority groups (except for women in the Chinese or "White Other" ethnic groups) had higher rates of death involving COVID-19 compared with the White British population. In the second wave of the pandemic the differences in COVID-19 mortality compared with the White British population increased for people of Bangladeshi and Pakistani ethnic backgrounds.

Recent estimates for “Long COVID” (August 2021) also show that self-reported symptoms are 50% higher in people in the most deprived quintile, compared to the least deprived (1.89% of people experiencing Long COVID compared to 1.24%).

There were an estimated 23 million fewer GP consultations (including both in-person and telephone consultations) in 2020 compared with 2019. The drop in consultations was particularly sharp in the first wave of infections and has recovered somewhat, though once flu vaccinations are excluded consultation rates in autumn 2020 remain below pre-pandemic levels. The fall in consultations reflects the combined impact of
patient health-seeking behaviour and health system adaptations put in place to respond to the pandemic.

- Reduced GP activity may impact the management of existing long term conditions, limit the diagnosis and treatment of new chronic conditions, reduce referrals for secondary care treatment and result in those with urgent care needs either not being treated or attending A&E. Diagnosis of a range of chronic conditions fell significantly, though management of existing long term conditions appears less negatively affected. Routine referrals to January 2021 generally remained below the four-year average. Young people, particularly under 11 years, saw the largest fall in consultation rates and were most likely to have reduced GP appointments relative to older age groups.

<table>
<thead>
<tr>
<th>Long term condition</th>
<th>Reduction in newly diagnosed cases (2020 compared to 2019)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Obstructive Pulmonary Disease</td>
<td>51%</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>26%</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>20%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>19%</td>
</tr>
<tr>
<td>Coronary Heart Disease</td>
<td>17%</td>
</tr>
<tr>
<td>Stroke &amp; Transient Ischemic Attack</td>
<td>16%</td>
</tr>
</tbody>
</table>

- Hospital activity declined sharply in the first wave, recovering steadily in most specialties but patient wait times have continued to increase as non-COVID-19 hospital activity fell. Case studies on cancer and mental health diagnosis and treatment explore in detail the effects being observed for these conditions.

- There is a risk of further long term health effects and the adverse economic shock and impacts on education are likely to lead to poorer health in the population and future health care need. Depending on similarities to previous recessions, there could be prevalence increases in long term conditions - these effects would take two to three years to realise: 2.1% for mental health conditions, 1.3% for musculoskeletal disorders, 1.2% for cardiovascular conditions, 1% for respiratory conditions and 1.2% for other chronic conditions.


SAGE: COVID-19 Transmission in Hotels and Managed Quarantine Facilities (MQFs)

- Transmission is a continuous risk in settings where people interact, and can occur in any of the environments encountered during an individual’s day.

- There are three main routes through which the SARS-CoV-2 virus is thought to be transmitted: air, through inhalation of aerosols; person-to-person, through inhalation of aerosols and direct exposure to larger droplets; surfaces, through contamination by droplet deposition or hands which are transferred to mucous membranes by touch. The relative importance of each of these pathways remains unclear, and will
depend on the behaviour and activities undertaken by individuals as well as their physical environment.

- In the context of hotels, there are a breadth of activities where there is evidence for risk. The risk of activity varies depending on how likely it is that individuals, whether guests or staff, interact closely with one another, if they are largely independent, if communal spaces are used, or if individuals pass in the corridor or dining room for example. The range of activities include (inter alia):
  - Transport to the hotel for guests and staff;
  - Common areas for guests and staff;
  - Kitchens, staff changing rooms, staff toilets and facilities;
  - Hotel bedrooms, staff accommodation;
  - Spa/swimming, gym, bar/restaurant, retail, toilets
  - Use as a venue for parties or weddings;
  - Business guest use, conference or function rooms.

- In the context of MQFs, there is a smaller proportion of risk associated with guest-related social activities or with building/room use as a venue for events, as these activities are limited due to isolation of guests. But where transmission in MQFs does happen, it can be between different community groups who have connection to different countries, with associated risk of transmission of variants of concern.

- In case-control studies conducted in late June/early July 2021, there was strong evidence that staying in overnight holiday accommodations generally, and hotels/bed and breakfast accommodations (B&Bs) specifically, was associated with increased likelihood of being a COVID-19 case. This is not the same as evidence of increased risk of transmission, but does highlight the reason for a particular focus on these settings as part of risk management.

- Suitable and sufficient risk assessments should be completed for these specific settings, within the context of an overall risk management strategy. It is critical that the risk assessment covers all activities undertaken by all staff (including night workers, security staff etc.) and guests, and that mitigations are considered for each activity and each of the three routes of exposure outlined above. The selection of appropriate control measures should follow the hierarchy of risk control, and the objective should be to reduce the risk of transmission to as low as reasonably practicable, taking into account both the expected behaviours of staff and guests.

- The first level of control is where possible to minimise the chance of the virus entering an environment, in this context, the community. Mitigations in MQFs need to be particularly strict owing to the potential risk of importation of Variants of Concern. This is also a risk with guests from overseas arriving and staying in mainstream hotels. The evidence so far is that most outbreaks within MQFs have been small and generally amongst staff, however, the consequences of a new variant reaching the community from a MQF are potentially severe.
- The second level (which is less effective) is minimising transmission risk within an environment, in this context, within MQFs and hotels. Mitigations in mainstream hotels need to be proportionate to the risk.

- Other communal accommodation settings, which are beyond the scope of this paper, such as cruise ships, backpacker and similar hostels, student halls of residence, prisons and homeless shelters can pose specific risks especially within facilities which are shared and where vaccine uptake is low (e.g. in homeless shelters). Communal accommodation often involves an increased number of close contacts, sharing bedrooms, and sharing communal areas, all of which are associated with increased risk of transmission.

- Regular checking of compliance with risk mitigations can help ensure adherence to the agreed hierarchy of controls in all settings.


Papers from TAG

TAG: Winter modelling update- Modelling other viruses
- This paper outlines some scenarios of flu and RSV models to compliment the regular updated of COVID-19 models that we publish.

- We are at a point where the COVID modelling that Welsh Government commission from Swansea University has been quite robust in predicting what happens over the next two months or so, with the last few most likely scenarios (MLS) from Swansea University being close to the actual data. This has been useful for policy makers in Government and for the NHS.

- This has led to questions about modelling other respiratory viruses like influenza (flu) and RSV (respiratory syncytial virus) which were largely absent in Winter 2020/21 but are likely to recur, and may rebound at a higher rate than a typical Winter, partly due to an ‘immunity debt’ where lack of exposure means low immunity, for instance in 1-2 year olds who have not been exposed to RSV. In general, nearly 90% of children may be infected with RSV in the first two years of life, but a small proportion may develop bronchiolitis and need hospital treatment including for some, Paediatric ICU.

- The incidence of RSV in children is increasing quickly as of July 2021, with the RSV season starting 15 weeks earlier than normal in Wales.

- Both flu and RSV may show asynchronous growth in different parts of Wales, and the impact of flu will depend on type, clade and vaccine composition.

- Influenza vaccines are less effective than the COVID vaccines and are not effective enough to reach herd immunity type effects. However there is evidence that repeated annual vaccination boosts effectiveness. Awareness of COVID might increase flu vaccine uptake.
• There is no current RSV vaccine in use although very high risk infants are given monthly injections of the monoclonal antibody, Palivizumab to prevent severe disease caused by RSV – this is around 50% effective.

• Current modelling carried out by PHW is based on detecting the onset of annual influenza and RSV epidemics and providing a series of thresholds to compare severity against historical seasons. This is the WHO/ECDC agreed approach for seasonal respiratory infection surveillance, which allows for country to country comparison of thresholds reached. In terms of planning, this allows PHW to compare seasons to historical seasons hit very high/high/medium/low levels of severity for scenario planning, and highlighting any relevant antigenic differences in emerging influenza viruses. There may be an increased chance of vaccine mismatch this winter as there has been very little flu activity in the Southern hemisphere in their winter/our summer.

• There may be a view that the way things have happened pre-COVID has worked well, but there may also be a view that there is an opportunity to model several viruses at once and estimate potential combined scenarios of respiratory pressures on the NHS system. This may be more important because of the backlog of elective care which is in turn putting pressure on emergency care in the NHS.

• It may be that individual behaviours around wearing face coverings, self-isolation and staying at home with symptoms, and other changes in terms of infection prevention and control in health and social care, will have longer term effects in preventing transmission of several viruses, but this remains to be seen, and we need to prepare for the possibility of very challenging conditions with lots of viruses in circulation. The R0 for influenza is likely to be lower than COVID-19 at around 1.8 whereas R0 for Delta variant of SARS-COV2 is much higher at around 6. R0 for RSV may be around 3.5 so it is quite infectious and most children are infected in the first two years of life.

• There are other viruses like the common cold (especially rhinovirus), parainfluenza, adenovirus and metapneumovirus, that can cause acute respiratory illness and lead to hospital admissions which are not explicitly considered here.

• It may be that we move beyond modelling respiratory viruses to including scenarios for impacts of other viruses like norovirus which often lead to problems in the health system during the busy winter period if hospital bed bays or wards need to be closed due to outbreaks.

• It may also be useful to model excess winter deaths from other causes like CVD, COPD and fractures related to falls.

• With any models, we can start with simple models and refine them over time. Modelling is always an iterative process but even simple models can produce useful results if they give a possible outcome space that the system can expect, for instance if a model says that respiratory viruses will occupy between 500 and 2,000 beds on 1\textsuperscript{st} December, this is a huge range but is still useful for preparations. Once we know the dominant strains of influenza that are in circulation, models can be updated.
- Modelling shared with JCVI has suggested that the 2021-22 flu season could be 50%-100% higher than a typical season and could peak at a different time.¹

- The scenarios in this report suggest that we say a greater than normal sized flu and RSV season, which may be shifted in time from their normal peak. When combined with other pressures on the NHS this may pose particular challenges.

- Continued surveillance of infections in schools, supply, uptake and effectiveness of vaccines, and impact and spread of COVID variants and other virus types is crucial in helping to understand what trajectory Wales is following.

- Full paper: *Publication under way for TAC webpage.*

**TAG: What is the social value of a COVID case and how has it changed?**

- This paper outlines the estimated direct social cost of one COVID-19 case in December 2020, and in July 2021, to understand how this has changed over time. This is based on the ratio of cases to other outcomes – hospital admissions, ICU admissions, deaths and estimated long COVID cases.

- In December 2020, it is estimated that one COVID-19 case had a social cost of around £13,000 whereas in July 2021, because of the vaccination programme and other interventions put in place to reduce cases and severe outcomes, the social cost of one COVID-19 case is around £2,500. These estimates were robust to changes in assumptions around the costs and Quality Adjusted Life Year losses (an estimate of quality and quantity of life; QALY) associated with cases, admissions, and long COVID. This has implications for the value for money for future policies to prevent COVID-19 cases, while continuing to consider that preventing one infection prevents onward infections.

- Although there is some uncertainty around the social costs in this paper, and they may not include all relevant costs, it is likely that in December 2020, it was good value for money to spend £12,000 to prevent one COVID case, whereas now it is unlikely to be good value for money to spend more than £4,000 to prevent one COVID-19 case, on average. This is because the direct social costs of one COVID-19 case are estimated to be lower than in December 2020 and therefore it may be favourable to allocate spending to other areas of improving health. However because COVID-19 is an infectious disease, one case leads to another, so any interventions need to ideally be modelled to see their effect on the whole epidemic curve.

- Full paper: *Publication under way for TAC webpage.*

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¹ JCVI interim advice: potential COVID-19 booster vaccine programme winter 2021 to 2022 - GOV.UK (www.gov.uk)