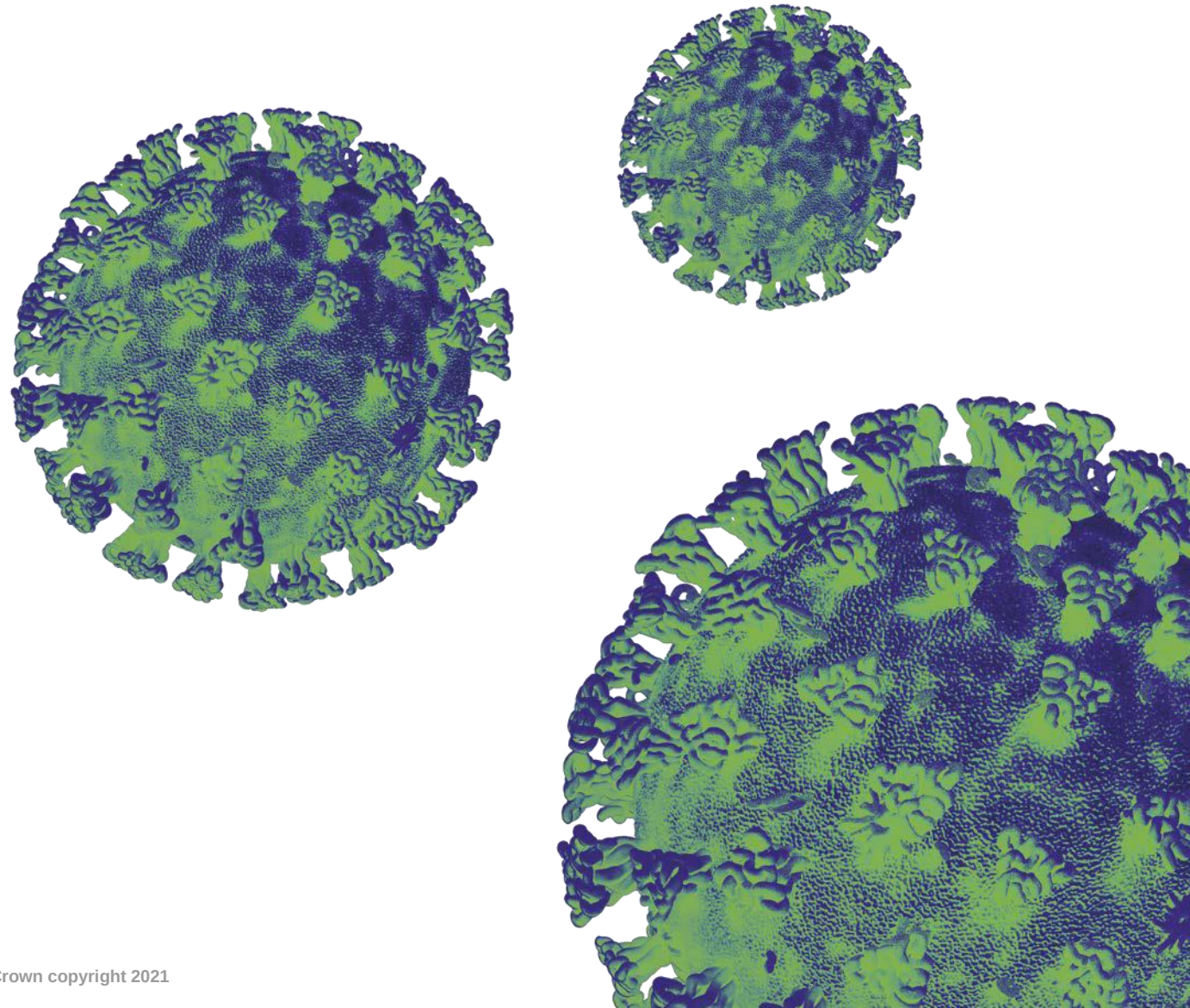
Llywodraeth Cymru
Welsh Government

Technical Advisory Group

Summary of Advice

15 July 2021



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Summary

- The scale of the resurgence in hospital admissions after relaxations is highly uncertain and depends on unknowable factors including how behaviours change in the coming weeks and months. Many modelled scenarios show a peak in hospital admissions well below that of January 2021, but a wave of a similar or even larger scale cannot be ruled out. This will need to be monitored carefully.
- Further work to better understand the public's willingness and ability to sustain protective behaviours longer term (e.g. working from home, isolating on symptoms) is likely to be important for COVID-19 and other seasonal respiratory viruses (e.g. flu).
- Refining baseline control measures that have minimal pain and maximum gain will to be important. Considering measures differently in places where people have to go (e.g. healthcare, workplace) versus settings where people choose to go (e.g. leisure) might help people who are more at risk (e.g. immunosuppressed, older people) to live their lives more freely.
- Measures like TTP alongside some personal protective behaviours is likely to have a meaningful impact on the trajectory of the epidemic in Wales.
- Rationalising policy decisions using the five harms as a policy or decision making matrix is likely to be helpful. It is important to realise that there are no zero harm options and that harms should be considered and balanced using the best quantitative and qualitative evidence available.
- A summary is provided for TAG's recent policy modelling update, indicators and thresholds paper, statement on baseline measures and harms and advice on considerations for nightclubs and adults entertainment venues.

Wales situation update

- The TAG Advice dated 5 July is still extant and this paper seeks to build on that advice. The most recent situational assessment for Wales is documented in the COVID-19 Situational Report here. A significant amount of material included below was provided to SAGE 93 to support England's Roadmap policy decisions but is relevant to relaxations in Wales.
- Cases and positivity in Wales are increasing which is likely driven by increased contacts and the Delta variant. At a national level Wales has risen from 12 per 100,000 cases a month ago to at 123 cases per 100k, and test positivity is around 6.5%. There is a slight increase in hospital cases and no clear increase in deaths.
- Although there are differences in the prevalence of infection across the UK, all four nations are seeing a substantial increase in case numbers. As at 7 July R is estimated by SAGE to be between 1.2 and 1.5 in England, in Scotland and in Wales, and between 1.3 and 1.6 in Northern Ireland. Note that this is a lagged

indicator, typically representing transmission around 2-3 weeks ago. Estimates from Public Health Wales (PHW) as at 7 July, which are less lagged than SAGE, suggest an R of between 1.5 and 1.6 and a doubling time of 10 days (95% confidence interval 7 to 23 days)

- ONS analysis[1] continues to show that people from some ethnic minorities have experienced a substantially higher risk of COVID-19 related mortality, even after adjusting for sociodemographic characteristics and health status. The Health Foundation have also recently published an impact inquiry into the inequalities that have added to the harm caused by Covid-19[2].

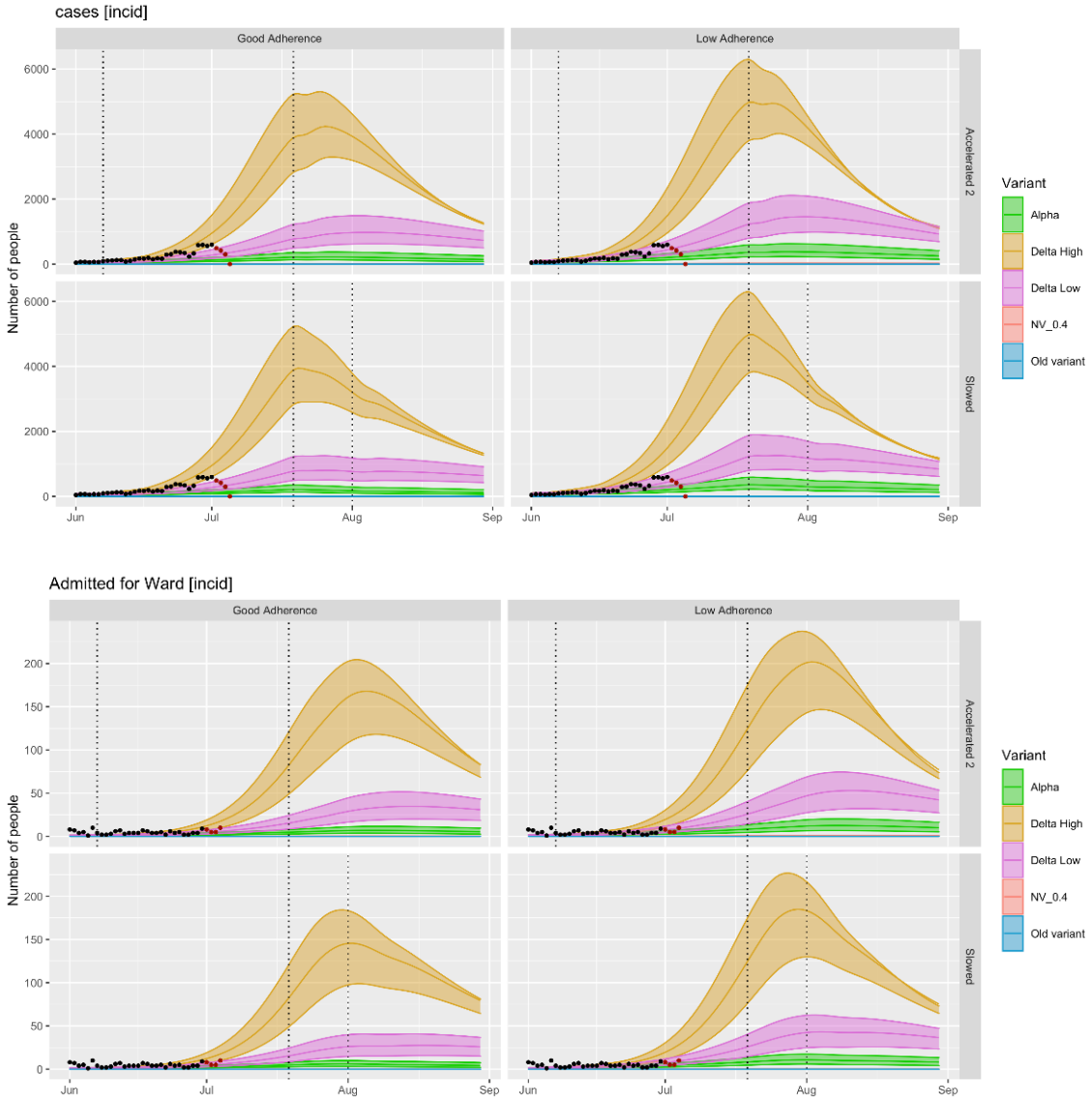
  CO-CIN analysis shows reductions in morbidity and mortality in hospital patients, due to the lower average age of patients and the impact of vaccination.

Policy modelling update

- *The full paper is available here. A summary is below:*

- A policy modelling update dated 25 June outlines new modelling scenarios for the coming months. The modelling included the impact of vaccination and Delta variant, with outputs leading to increased growth of infections, corresponding with the relaxing of many restrictions.
- Since this report, evidence has continued to emerge around the effectiveness of vaccines in preventing severe disease; observed trends in England and Scotland have seen a significant resurgence in cases, but a much smaller increase in hospital admissions and deaths.
- This means that the most pessimistic scenarios for hospital admissions and deaths that were included in the previous modelling are looking increasingly unlikely. A new report includes Swansea University modelling with updated vaccine effectiveness and how the actuals track to those scenarios, and modelling we have received from Warwick University.
- The most recent tracking to the Swansea University modelling suggests we are tracking closer to the ‘delta low’ scenarios than ‘delta high’ scenarios – however this does not mean that the transmission advantage of delta is at the low end, it may be that the impact of vaccinations or reduced contacts is continuing to have an effect.

[1] SpringerLink | Ethnic differences in COVID-19 mortality during the first two waves of the Coronavirus Pandemic: a nationwide cohort study of 29 million adults in England, 16 June 2021
[2] The Health Foundation | Unequal pandemic, fairer recovery, July 2021



Exponential growth (and uncertainties)

- Exponential growth means that very small changes in assumptions on vaccine effectiveness (or uptake) and behaviours after level zero is taken could lead to very large differences in the trajectories observed. Uncertainty means it will not be possible to project which scenario will likely occur nor can the peak's timing be predicted until it has passed (SAGE 93).
- For example with regard to vaccine effectiveness (VE) the number of infected vaccinated people who go on to be admitted to hospital with a 94% effective vaccine would be triple that with a 98% effective one (SAGE 93).
- While the number of vaccinated people is precisely known, the number of unvaccinated people is not, so estimates of vaccine uptake are uncertain. Models are also very sensitive to this; for example, there would be twice as many

unvaccinated people in an age group if its uptake is 92% compared to if uptake is 96% (SAGE 93).

- The proportion of the population who have previously been infected cannot be precisely determined and yet influences the extent to which the epidemic can grow before herd immunity is reached. Plotting actual observed data against modelled scenarios will remain important in help us assess and adapt plans.
- Bristol roadmap modelling[3] estimates that a 10% drop in vaccine uptake (with all adults having been offered at least 1 dose) increases the number of cases in England by 3 million cases and results in a three-fold increase in COVID deaths due to older individuals not being protected. Retaining some more limited social distancing restrictions has the potential to make a meaningful contribution, resulting in non-linear reductions in cases and deaths by bringing R closer to 1.
- LSHTM and Warwick roadmap models use an assumed 80% vaccination of 18-39 year olds. Producing a reasonable worst case for vaccine uptake, lower than this threshold, will likely help inform future plans for the vaccination programme.
- Recent events, like Euro 2020, may have stimulated surges in some areas (e.g. Scotland, 20 June) that may have changed the trajectory of the epidemic in that area4.
- Interim findings covering 24 June to 5 July from Imperial College London and Ipsos MORI show infections have quadrupled since the last REACT-1 study, which took place from 20 May to 7 June, with 1 in 170 people infected and a recent doubling time of 6 days. Infection rates for double vaccinated under-65s are 3 times lower than in unvaccinated under-65s, demonstrating the impact of the vaccination roll out5.
- If the current trend of high, uncontrolled transmission continues, the final percentage of people infected may overshoot the herd immunity threshold if it is reached.
- Given this uncertainty, it would be prudent for contingency plans to be put in place for how to respond if hospital admissions approached levels that could disrupt the smooth functioning of health services.
- Given the delay between infection and hospitalisation, increases in admissions for the coming two to three weeks are already determined by infections to date. Consequently, whilst cases continue to increase exponentially, admissions are expected to double (regardless of any measures put in place). While SPI-M-O does not know what threshold of daily hospital admissions would lead to

[3] SAGE 93 | JUNIPER: Transitioning from non-pharmaceutical interventions to vaccination to control COVID-19 transmission, 7 July 2021
[4] Third wave in Scotland driven by SARS-CoV-2 Delta VOC: Forecast of cases, hospitalizations and deaths (manuscript submitted for publication)
[5] GOV.UK (www.gov.uk) | Latest REACT-1 study findings show COVID-19 infection rates 3 times lower for double vaccinated people, 8 July 2021

unsustainable pressure for the NHS, the moment when half that level is reached would be the time at which contingency plans would need to be implemented (SAGE 93).

- However, the next peak in deaths will almost certainly be considerably smaller than that of January 2021. The prevalence of infection will almost certainly remain extremely high for at least the rest of the summer.

Changes to the Alert Level Control Plan Indicators

- The full content of this paper is available here. A summary is provided below:

- Overall the percentage of cases resulting in hospitalisation has decreased by around 80% from December 2020 and the percentage of cases resulting in death has reduced by 94%. The average length of stay has also reduced significantly, with more than 75% of patients currently discharged by day 10, compared with less than 50% during the second wave.
- In spite of this, there main other factors to consider with regards to a rise in Covid-19 cases. This includes the risk of antigenic drift and virus evolution, particularly in those with a weakened immune system and the possibility of international travel providing a route for new variants of concern to enter the UK and vice versa. The risk of long covid, discussed further below, is also a cause for consideration.
- The Technical Advisory Cell has identified a number of leading indicators that should be used, alongside local intelligence and public health expertise, to determine the point at which a worrying situation with regards to COVID-19 may be developing and further action is required:
    - COVID-19 case rate (7 day rolling sum) – there are reasons why a rise in COVID-19 cases may or may not be a cause for concern. This indicator would need to be considered in the context of other indicators.
    - The relationship between COVID-19 cases to admissions and deaths - The COVID-19 case to admissions ratio and COVID-19 case to deaths ratio could be used for this.
    - Vaccine efficacy and uptake of current COVID-19 vaccines offered at a regional level
    - Population Immunity levels (including vaccine uptake and percentage of the population of Wales vaccinated). Focus on immunity levels by age bands and/or vaccine priority groups, particularly as children have not been offered vaccinations.

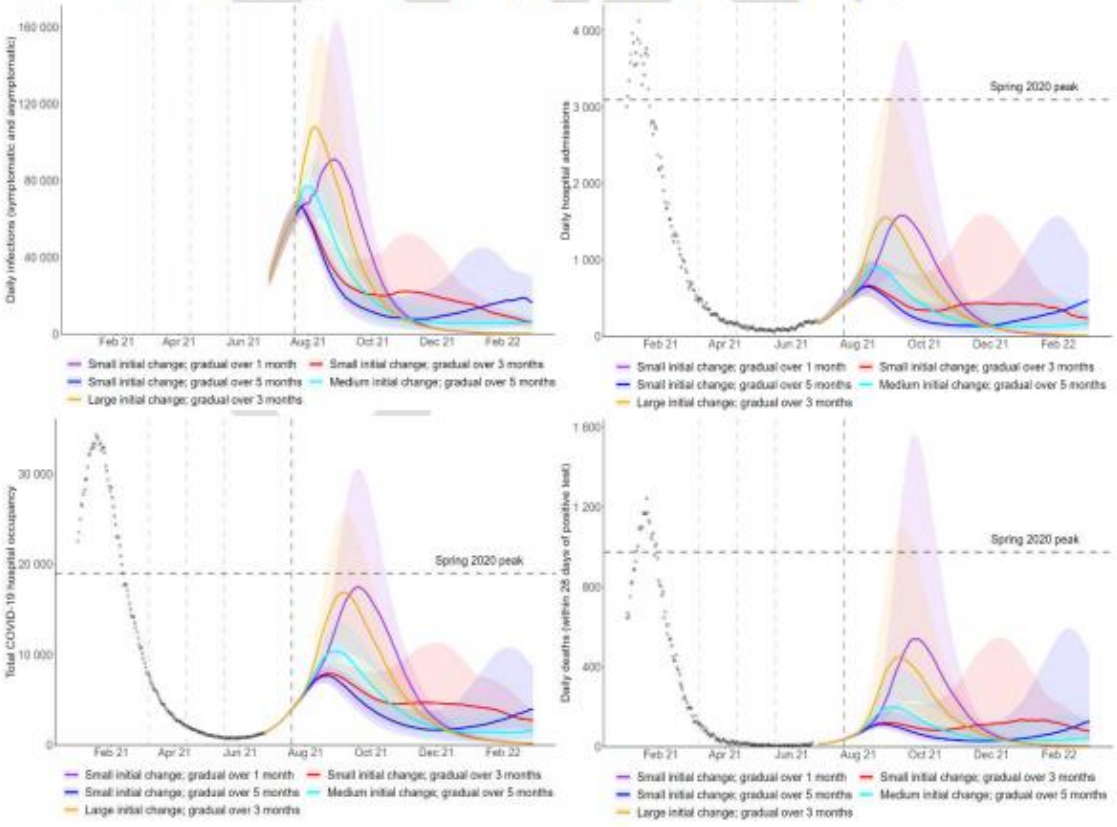
- Outbreaks in care homes or other closed settings containing vulnerable individuals.
- NHS hospital pressure – Length of stay in hospitals and hospital bed occupancy (including ICU) as well as the number of hospital and ICU admissions and NHS staff self-isolating.
- COVID-19 case rates in the UK (Especially areas close to Welsh border. This has often been a driver, e.g. in north east Wales).
- TTP performance metrics.

Sustainable protective behaviours

- If behaviours take longer to return to pre-pandemic levels (and/or if the seasonal effect of transmission is higher), then the peak of the summer resurgence is likely to be lower. This could result in a wave that is broader, or partially shifted to autumn and winter.
- However, gradual relaxations coupled with sustained protective measures (e.g. working from home, isolation on symptoms) does not necessarily mean significant winter resurgence. There are uncertainties in these assumptions that need to be monitored carefully as relaxations proceed.
- Some of Warwick's scenarios for the English Roadmap modelling see a further resurgence in autumn or winter (Figure 2, red and blue). The fewer people that are infected during the wave that is currently happening, the more are infected in the next one. Neither Imperial nor LSHTM's scenarios show a significant autumn or winter wave. Any contingency planning will need to be able to flex to a wide range of scenarios.

Figure 2: Infections, hospital admissions and occupancy, and deaths as estimated under five different behavioural scenarios as modelled by Warwick.

(Purple – small drop in precautionary behaviour from 19th July then gradual reduction to pre-pandemic levels over one month; Red – as purple, but gradual reduction to pre-pandemic levels over three months; Blue – as red, but gradual reduction to pre-pandemic levels over five months; Orange - large drop in precautionary behaviour from 19th July then gradual reduction to pre-pandemic levels over three months; Cyan - medium drop in precautionary behaviour from 19th July then gradual reduction to pre-pandemic levels over five months)



- COMIX[6] reports that adult contacts have been steady since mid-May, contacts are at levels higher than those seen after the lifting of the second lockdown but lower than those seen in August last year.
- Leisure contacts appear to still be increasing for those aged 70+, and is now highest in that age group with a mean of 1.5 people per day. Mean contact rates reported for school-aged (5-17 years) children remain consistent with those seen when schools are open. Leisure contacts for children have continued to increase for 5-11 year olds but have reduced slightly for 12-17 though these are proxy reports from parents.

[6] London School of Hygiene and Tropical Medicine, Social contacts in the UK from the CoMix social contact survey Report for survey week 65, 23 June

Long COVID

- At the moment we are slowly moving towards a situation where most children and young people have been, or will be infected. Although serious illness and deaths are very rare[7], there is a reduced but still present risk of long COVID in young people (Table 1 below).

Domain	Group	Estimate	Lower 95% confidence limit	Upper 95% confidence limit
All people	All people	1.49	1.44	1.54
Age group	2 to 11 years	0.16	0.10	0.23
	12 to 16 years	0.51	0.39	0.63
	17 to 24 years	1.21	1.03	1.39
	25 to 34 years	1.55	1.38	1.72
	35 to 49 years	2.12	1.98	2.25
	50 to 69 years	2.19	2.09	2.29
	≥70 years	1.06	0.97	1.15

Table 1. Estimated percentage of people living in private households with self-reported long COVID of any duration, UK: four-week period ending 6 June 2021

- The most recent ONS data[8] shows lower percentage of long COVID reported for younger children compared to other age groups, with the proportion affected by increasing with age

[7] Research Square | Deaths in Children and Young People in England following SARS-CoV-2 infection during the first pandemic year: a national study using linked mandatory child death reporting data, 7 July 2021

[8] Office for National Statistics (ons.gov.uk) | Prevalence of ongoing symptoms following coronavirus (COVID-19) infection in the UK, 1 July 2021

High prevalence

- There are four major risks associated with high numbers of infections. These are an increase in hospitalisations and deaths, more 'Long-COVID'; workforce absences (including in the NHS); and the increased risk of new variants emerging[9].
- The combination of high prevalence and high levels of vaccination creates the conditions in which an immune escape variant is most likely to emerge. The likelihood of this happening is unknown, but such a variant would present a significant risk both in the UK and internationally. Current Roadmap modelling for relaxations is based upon delta remaining dominant.
- New data from Public Health England on the prevalence of mutations of predicted antigenic significance in the global dataset shows that there is an increase in mutations of predicted antigenic significance over time, even outside the designated variants of concern and variants under investigation. Additional spike mutations are occurring on Delta but are present at relatively low frequencies both in the UK and global datasets. They also report an increase in PCR positivity in the SIREN (national healthcare worker) cohort and a small but increasing number of possible reinfections[10].
- High prevalence also presents a challenge to testing, contact tracing and sequencing. If PCR testing and genomic sequencing capacity are overwhelmed, it may not be possible to rapidly identify a new variant.
- Effective surveillance systems both nationally and internationally to understand the impact of significant policy decisions on isolation, vaccination and travel will be very important so that the importation of new deleterious variants can be detected and contained.
- Previous experience has shown that the introduction of more transmissible (and pathogenic) variants into Wales leads to more cases, hospitalisations and deaths and should therefore be avoided.

Baseline measures and TTP

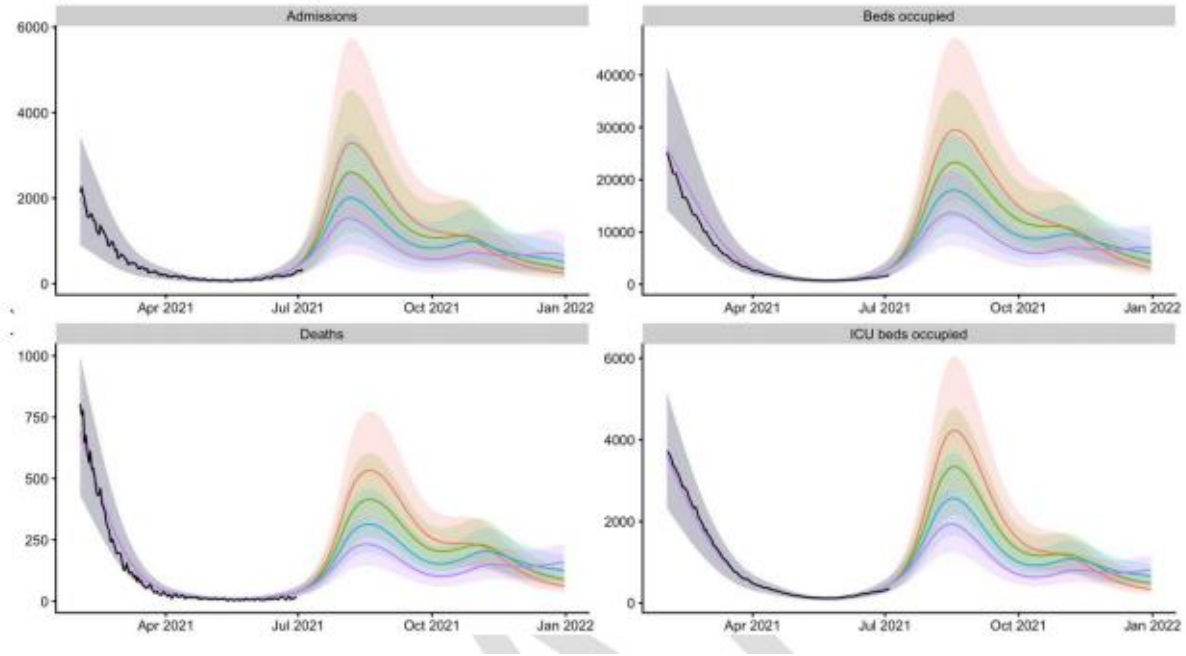
- Previous work by TAG on the effectiveness of the TTP system in Wales has shown the system to reduce Rt by 0.3-0.4 (based on alpha variant)[11]. There is significant uncertainty on the reduction in transmission from vaccination, compared to disease severity. However, full vaccination will reduce the chances of someone shedding virus, and reduces the amount of virus they shed. As a priority a range of assumptions of transmission reduction (e.g. 40-80%) should be

[9] SAGE 93 minutes: Coronavirus (COVID-19) response, 7 July 2021
[10] PHE, SARS-CoV-2 variants of concern and variants under investigation in England Technical Briefing 18, 9 July 2021
[11] Technical Advisory Group | Modelling the current Welsh Test, Trace, Protect system, 24 March 2021

used to remodel TTP effectiveness particularly given changes in policy about isolation and quarantine of double vaccinated people.

- Isolation of people likely to be infectious remains particularly important for reducing transmission (high confidence). Further evidence on the effectiveness of daily testing as an alternative to isolation for contacts of known cases is expected within the next month and will be important for informing future approaches. Effective test and trace remains an important part of preventing spread[9].
- LSHTM have modelled underlying mitigation parameters against direct harms for the England Roadmap. The graphs below show that hospital activity and deaths [are significantly lower with assumptions on 20% (purple) mitigation measures (TTP and protective behaviours) compared to 5% (red) .

Figure 7: Hospital admissions (top left), occupancy (top right), ICU occupancy (bottom right) and deaths (bottom left) in the LSHTM model assuming a 20% (purple), 15% (blue), 10% (green), or 5% (red) reduction in transmission post July 19th as a result of Test, Trace, and Isolate, and baseline behaviour change. Two doses of either vaccine is assumed to be 90% effective against hospital admission with delta, and medium mobility is assumed.



- Bristol modelling[12] shows that COVID-security and contact tracing and retaining some more limited social distancing restrictions (e.g. home working), as implemented in the model, has the potential to make a meaningful contribution to reducing cases and deaths. With all adults eligible for two doses, retaining some social distancing could bring the reproduction number close to 1 and result in non-linear decreases in cases and deaths (Figures below, Delta is estimated to have an R0 of 7).

[12] SAGE 93 | JUNIPER: Transitioning from non-pharmaceutical interventions to vaccination to control COVID-19 transmission, 7 July 2021

- Covid security is simulated by reducing the transmission probability of contacts by X%. For future scenarios, two scenarios were considered; future scenario 1 where all adults over 18 years old have been offered a first dose with uptake and future scenario 2 where all adults over 18 years of age have been offered 2 doses. Both scenarios make assumptions around uptake in different age groups.

Impact on Rt

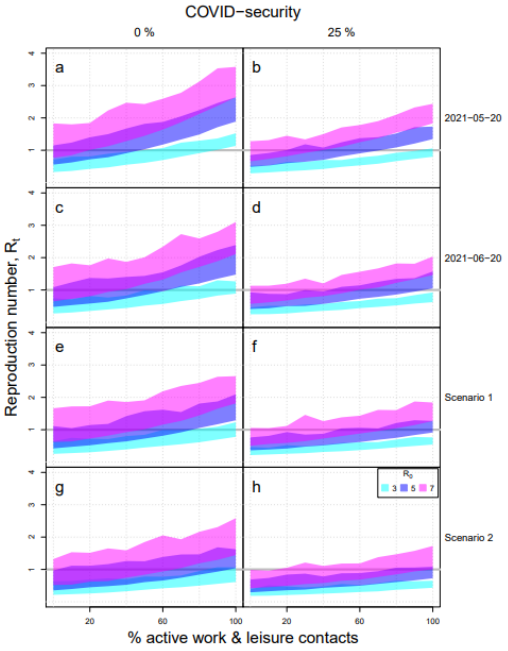


Figure 1: The projected reproduction number as a function of active contacts for different initial reproduction numbers.

Impact on total future deaths

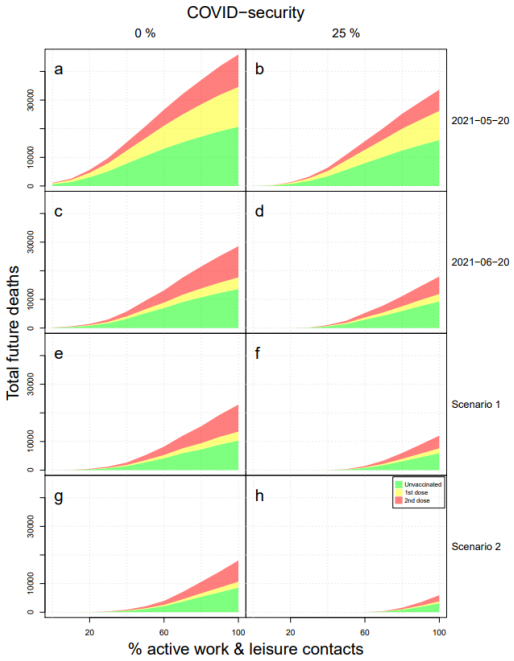


Figure 4: The number of deaths broken down by vaccine status as a function of active social contacts, for a delta-like variant with $R_0 = 7$.

Impact on Rt (lower vaccine uptake)

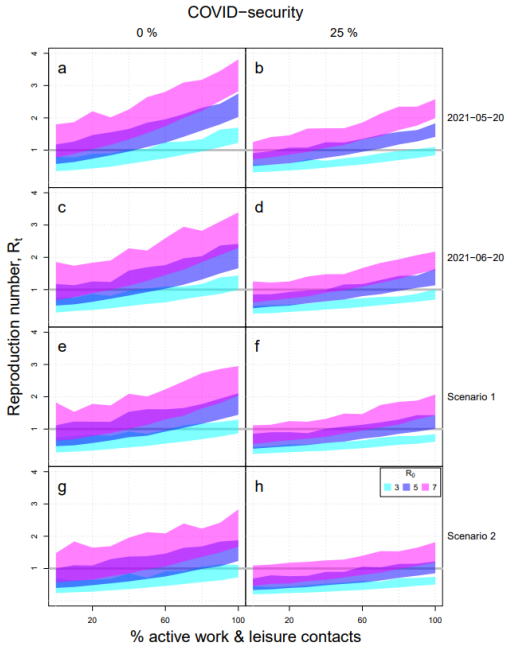


Figure 6: The projected reproduction number as a function of active contacts for different initial reproduction numbers with lower vaccine uptake.

Social contacts in workplace

- A COMIX social contact survey[13] in the UK suggests that individuals who attended work on the day of the survey tend to report more than twice the mean number of contacts as individuals who were in employment but did not attend work on the day of the survey (Figure 1).
- Current mean levels of reported contact are roughly 7 contacts per person per day for those attending work and 3 per person per day for those in employment but not attending work. This difference is large with overall mean rates of contact for all adults (including those not in employment) being less than 3.5 (3.2 to 3.8) contacts per person per day.
- This pattern has persisted over time, but during the lockdown period (from January to March 2021) the difference in contact rates between those who attended and did not attend work was somewhat smaller (Figure 1), suggesting that those who went to work made slightly fewer contacts during the lockdown.

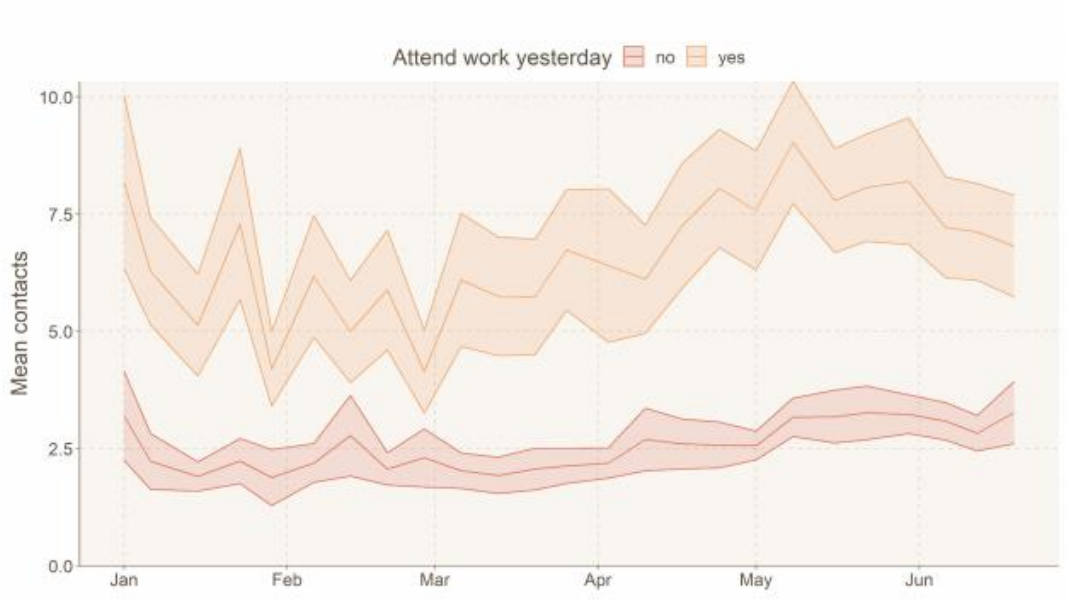


Figure 1: Mean contacts in the UK since Jan 2021 for individuals attending or not attending work on the day of the survey for people that are employed and their work is open. 95% Uncertainty interval calculated assuming a standard normal mean of two times the standard error of the meanusing bootstrapping. Contacts truncated to 50 contacts per participant. Observations are smoothed over two weeks to account for panel effects. Date on x axis refers to the midpoint of the survey period.

[13] London School of Hygiene and Tropical Medicine, Social contacts in the UK from the CoMix social contact survey Report for survey week 65, 23 June

Advice on nightclubs and sexual entertainment venues

- The full content of this paper is available here. A summary is below:

- It is likely that nightclubs would represent a high risk of transmission based on the evidence available. In many respects Sexual Entertainment Venues (SEVs) have some similar risks to those of nightclubs but also have different norms and practices which may reduce the levels of transmission risk. In addition, the evidence base surrounding transmission risk in SEV's is incomplete.
- There aren't any single feasible mitigations that would reduce the largest risks of these venues. However, should there be a decision to re-open, mitigations which would go some way in reducing risk could include (but not limited too):
    - Limiting the amount of people into these venues at any one time
    - Ensuring effective ventilation is enhanced in line with guidance
    - Limiting queue sizes both on entry and at bars
    - Ensuring staff members have appropriate protective equipment and physical separation barriers
    - Limiting amount of alcohol on sale and especially to those showing signs of intoxication
    - Reducing the volume of music
    - Availability of hand sanitisers
    - Identify ways to limit singing and dancing
    - Ensure effective wearing of face coverings
    - Undertake risk assessments in line with guidance
    - Encourage vaccinations of staff members
    - Frequent cleansing of high contact surfaces and services in line with guidance
- As with all other advice, if a person is symptomatic, has tested positive for COVID-19, or been told to self-isolate then they should isolate in line with current guidance.

Five Harms Arising from COVID-19: Consideration of Potential Baseline Measures

- The full content of this paper is available here. A summary is below:

- Harm related to COVID-19 can be broadly grouped into 5 key areas:
    1. Harm directly arising from SARS-CoV2 infections;

2. Indirect COVID-19 harms due to surge pressures on the health and social care system and changes to healthcare activity, such as cancellation or postponement of elective surgeries and other non-urgent treatments (e.g. harm from cessation of screening services) and delayed management of long-term conditions.

3. Harms arising from population based health protection measures (e.g. lockdown) such as, educational harm, psychological harm and isolation from shielding and other measures.

4. Economic harms such as unemployment and reduced business income arising both from COVID-19 directly and population control measures, like lockdown.

5. Harms arising from the way COVID-19 has exacerbated existing, or introduced new, inequalities in our society.

- Direct and indirect harms should continue to be central to government policy development in order to minimise, reduce or balance harm as we consider both the releasing and retaining of Covid-19 control measures.

- It makes sense for Wales to have a continued level of baseline measures as part of adaptive management of the virus but there is no ‘zero harm’ option - we need to consider how to balance harms, where they cannot be minimised completely.

- Provision of support to encourage adherence to remaining measures (e.g. self-isolation) and to enable risk-based decision making (e.g. where guidance replaces legal duties, such as 2m distancing) is important to minimise harms associated with baseline measures.

- Covid-19 is a syndemic, building on existing inequalities – there are ‘shadow pandemics’ happening, such as food insecurity, violence against women and children, etc. Covid-19 has illuminated issues around health and financial resilience in the population. We need to ensure we have a portfolio of interventions that improve health and reduce inequalities.

- The report gives an initial qualitative assessment of harms associated with potential baseline measures. It is not exhaustive, and is to some extent subjective, based on contributor knowledge and experience of the emerging field. More work may be required to look at the relative magnitude of harms. However, the paper does offer a more systematic approach to considering harms (and benefits) of COVID-19 related policies together. This approach may prove useful for other issues, like climate change, where impacts, mitigations and benefits affect different areas of society.

Policy modelling update 12th July 2021

- The full content of this paper is available here. A summary is below:

- A policy modelling update, dated 25th June, outlined some new scenarios for the coming months, which included the impact of vaccination, and the impact of the Delta variant which has led to increased growth in infections in Wales, at the same time as restrictions being released.
- Since that report, evidence has continued to emerge around the effectiveness of vaccines in preventing severe disease, and we have been monitoring trends in places like England and Scotland which have seen a significant resurgence in cases, but a much smaller resurgence in hospital admissions and deaths, even when considering spread across age groups and time lags between case onset and severe health outcomes.
- This means that the most pessimistic scenarios for hospital admissions and deaths that were included in the previous modelling are looking increasing unlikely.
- The present report includes Swansea University modelling with updated vaccine effectiveness and how the actuals track to those scenarios, and modelling we have received from Warwick University.
- Overall there is still a risk of a wave in hospital admissions and deaths, especially as Wales is seeing very rapid growth in cases, but it looks like the vaccination programme is currently holding up in the race with the Delta variant.
- This increase in cases is mainly in young people, where the risk of long covid seems to be lower than in older people. It is likely that cases will continue to be high in children and young people unless we reach a point where population immunity effects start to have an impact on transmission.
- With continued high force of infection, any point where we may expect to see population immunity effects may be overshot by some distance.
- These models are only accurate for the current situation with the Delta variant; if other variants with greater vaccine escape properties become widely distributed, then the models will change.
- Any models are likely to be more accurate for the shorter term than the longer term picture.
- The most recent tracking to the Swansea University modelling suggests we are tracking closer to the ‘delta low’ scenarios than ‘delta high’ scenarios – however it does not mean that the transmission advantage of delta is at the low end, it may be that the impact of vaccinations or reduced contacts is continuing to have an effect.

- The ratio of confirmed cases to hospital admissions is falling, and the ratio of cases to deaths has fallen more dramatically over time. There are some potential biases with these data, as vaccines may increase the proportion of cases with minimal symptoms, and testing behaviour may change over time.
- The Warwick / JUNIPER modelling in this paper suggests more optimistic worst case scenarios than the Swansea University scenarios, with later peaks in early 2022 rather than late summer 2021 as estimated by Swansea models.
- By triangulating actual data and comparing the modelled scenarios, we may surmise that it is likely that Wales is not headed for a bigger wave in hospital admissions and deaths than previous waves, despite the very rapid increase in cases.
- It may be that cumulative deaths by the end of 2021 are less sensitive to levels of restrictions, because eventually most deaths are in people who have been vaccinated twice where the vaccine has not worked. Understanding more about these cases and whether booster vaccines would help is important.

Swansea results and tracking

- So far the actuals data for confirmed cases is tracking closest to the 'Delta high, good adherence, high vaccine effectiveness' or the 'Delta low, low adherence, low vaccine effectiveness'. Hospital and deaths are still very low and have not really taken off so far in the third wave which makes tracking them to any specific scenario very difficult, but they are closest to the most optimistic of scenarios.

Figure 1. Results from Swansea University model, with actual trend in cases.

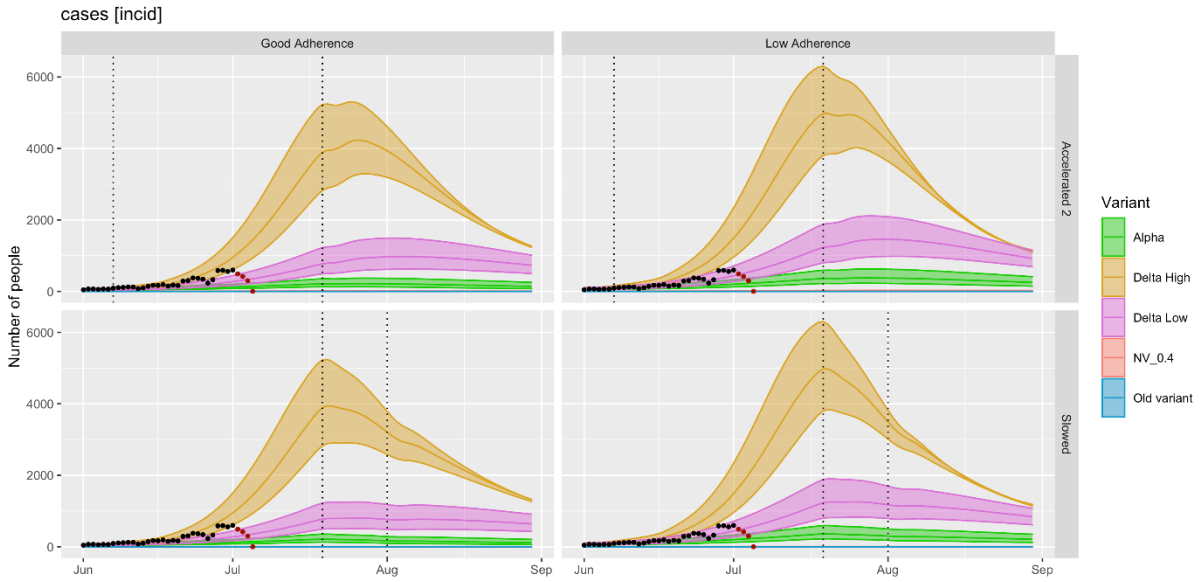


Figure 2. Results from Swansea University model, with actual trend in hospital cases.

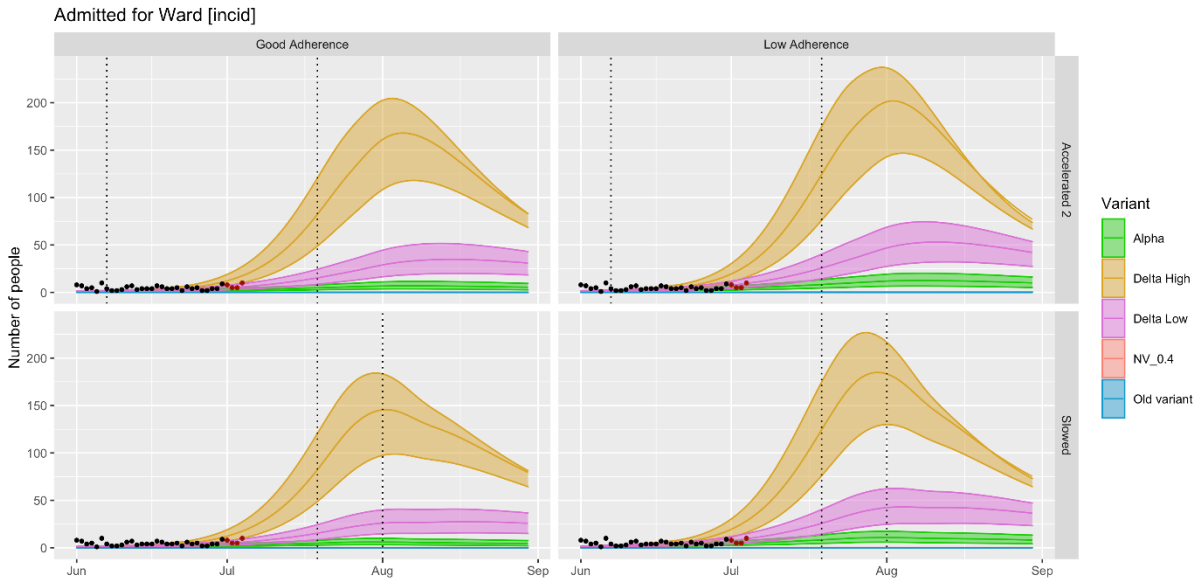


Figure 3. Results from Swansea University model, with actual trend in ICU admissions.

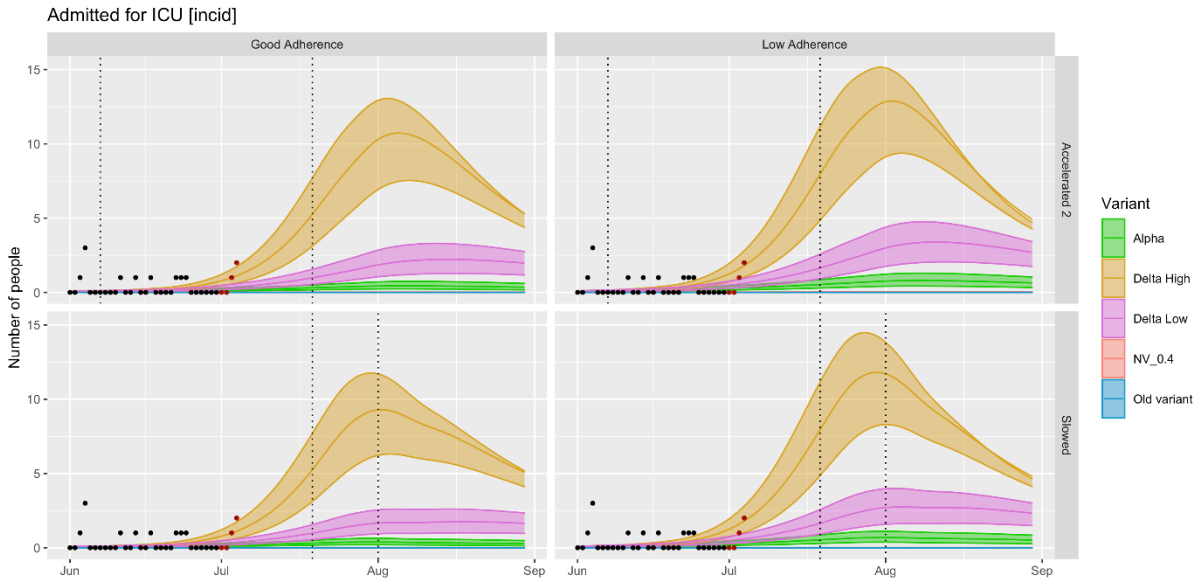
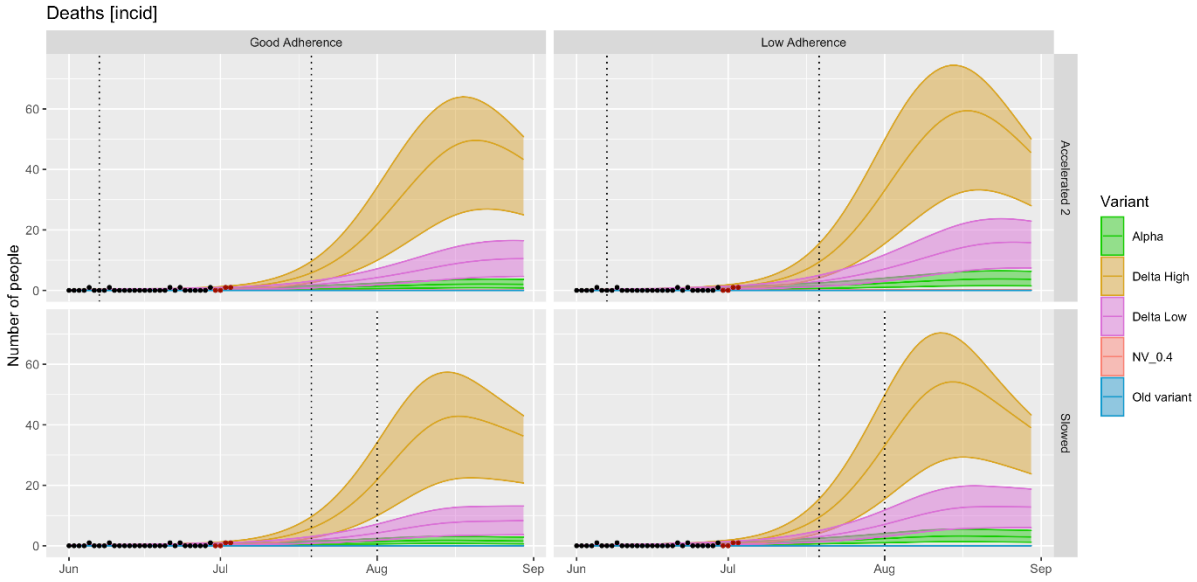


Figure 4. Results from Swansea University model, with actual trend in deaths.


Deaths [incid]
Good Adherence
Low Adherence
Accelerated 2
Slowed
Number of people
0
20
40
60
Jun
Jul
Aug
Sep
Variant
Alpha
Delta High
Delta Low
NV_0.4
Old variant

Warwick / JUNIPER consortium modelling results for Wales

This section is taken from a paper supplied to Welsh Government by Sam Moore, Matt J. Keeling, Louise Dyson, Edward Hill, Mike Tildesley from JUNIPER (Joint Universities Pandemic and Epidemiological Research, *https://maths.org/juniper/*). We are very grateful to JUNIPER for carrying out this analysis for Wales.

Methodology and key uncertainties

- This work uses the model that has been developed in Warwick over the past year and matched to a variety of epidemiological data. The model operates and is fitted to data from the seven NHS regions in England and the three devolved nations (Wales, Scotland and Northern Ireland) between the start of the pandemic in 2020 up until the 25 June 2021. The results of this model have been presented to SPI-M and SAGE on a number of occasions, and the model has been used to examine short-term and medium-term projections as well as reasonable worst case scenarios. More recently, the model has been extended to include vaccination, initially to investigate priority ordering and subsequently increased in complexity to include two-dose schedules and multiple actions of vaccine protection.

- Vaccine uptake within the model to date mirrors the recorded data in terms of dose and age of those vaccinated in each region separately. Projecting forwards, we follow the JCVI priority ordering for both Phase 1 and Phase 2, though include a small amount of noise in this to reflect adherence to the ordering to date. The uptake of vaccines so far has been far higher than initially anticipated, exceeding 95% in many areas and age-groups. Here we assume that uptake in those 40 and over is determined by historical uptake, while for those 18-39 the uptake level is set at 80%.

- Numbers of doses delivered are projected forward in line with recent delivery rates (at the daily rate average of the past 2 weeks for each region), this gives completion dates for vaccinating all adults with two doses between late August and early September for each region.

- The effect of seasonality is assumed to reduce transmission in summer months, with a trough of -15% (default) or -5% (lower) in mid-August followed by a peak with no reduction in February.

Variants

- Modelling includes estimated prevalence of variants to date, with the Alpha variant becoming dominant in January 2021, succeeded by Delta variant dominance in May/June. The Delta variant is estimated to have a transmission advantage over the Alpha strain of approximately 56%, though sensitivity to this

estimate is included in the analysis.

- The modelling has not accounted for the possibility of other future variants emerging that may evade the vaccine protection provided by the presently available vaccines or have further increased transmissibility which could undermine the huge gains that have been achieved by the vaccination programme to date and should be monitored accordingly.

Vaccine action

- Having been vaccinated, the protection generated can affect multiple components of the infection, illness and transmission process. This has been updated from the original calculations and now considers five elements separately: efficacy against infection; efficacy against disease (which also affects transmission, as our default assumption is that asymptomatic infections transmit less than symptomatic infections); efficacy against onward transmission; efficacy against hospital admission and death. We are also basing our central estimates of vaccine efficacy on the data that are slowly being generated on protection observed in the UK population and elsewhere (see Table 1). These estimates are getting tighter all the time and as such the bounds are likely to change.

- Three vaccines are now in use in the UK (Pfizer, AstraZeneca and Moderna). The efficacy for Moderna is not currently well defined and we therefore make the assumption that Moderna and Pfizer are equivalent given their single mode of action. The three vaccine efficacies are combined by taking the weighted average for each age group within the model based on the amount of the three vaccines used to date in the UK; and in the ratio 60% (AstraZeneca), 30% (Pfizer), 10% (Moderna) in the future for those above 40 and 0% (AstraZeneca),75% (Pfizer), 25% (Moderna) in remaining adults below 40.

Table 1. Vaccine efficacies against the Alpha variant (blue) and Delta variant (red) as given by current PHE estimates (https://www.gov.uk/government/publications/covid-19-vaccine-surveillance-report). Here we give central estimates as well as a (bracketed) lower and higher estimate.

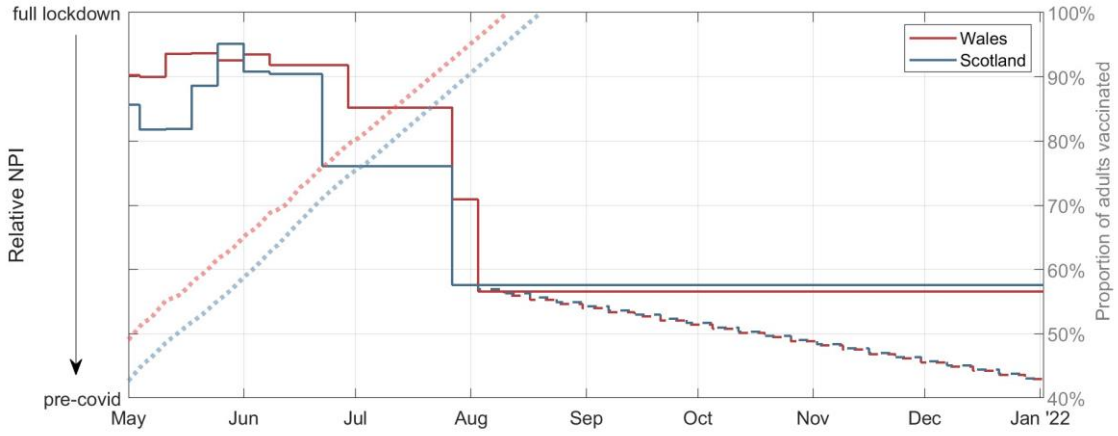
	Pfizer/Moderna		AZ	
	1st Dose	**2nd Dose**	**1st Dose**	**2nd Dose**
Efficacy against	63% (55-70%)	80% (70-90%)	65% (60-70%)	73% (60-85%)
Infection	45% (38-50%)	71% (62-80%)	46% (43-50%)	65% (53-75%)
Efficacy against	63% (55-70%)	88% (75-90%)	65% (60-70%)	78% (65-90%)
Symptoms	45% (38-50%)	78% (75-80%)	46% (43-50%)	69% (58-80%)

Efficacy against **hospitalisation/death**	80% (75-85%) 80% (75-85%)	95% (90-99%) 95% (90-99%)	80% (75-85%) 80% (75-85%)	91% (85-97%) 91% (85-97%)
Efficacy against **Transmission**	45% (35-55%) 45% (35-55%)	45% (35-55%) 45% (35-55%)	45% (35-55%) 45% (35-55%)	45% (35-55%) 45% (35-55%)

Controls

- For each nation, we model the relaxations to date by fitting to available data and considering the impact of the remaining relaxation steps as outlined in current policy for each nation. Following official removal of restrictions we assume mixing behaviour will not immediately revert to pre-COVID levels, but instead levels of caution will remain and systems such as track and trace will continue to have an impact for some time. We additionally consider a scenario where mixing is allowed to gradually return to pre-COVID levels over a 12 month period, though significant uncertainty makes such long term predictions unreliable. An illustration of each scenario is shown in Figure 1.

Figure 5. NPI assumptions for different nations together vaccination levels. Darker lines show estimated NPI effects by date for each nation with solid lines representing a scenario with maintained NPI levels and dashed lines waning NPIs. Paler dotted lines show progress of the vaccination program for each nation with 100% completion corresponding to 2 doses of vaccine having been offered to everyone above the age of 18.



Wales

- We consider three scenarios: firstly, with a low level of NPI maintained steadily into the future (Fig 2); secondly, with NPIs reducing gradually to near pre-COVID levels over a 12 month period (Fig 3); and a final scenario as the first but with reduced seasonal advantage (Fig 4). We expect the second scenario to most closely resemble realistic behaviour, though with a large amount of uncertainty surrounding long term forecasts, accurate predictions of future waves of infection incurred by behaviour going into 2022, is likely to be unreliable.

- For each scenario we show sensitivity to vaccine efficacy assumptions (with high and low estimates given by PHE in (Table 1), mixing behaviour following release of NPI measures and transmissibility of the Delta variant.
- Due to the advanced progress Wales' vaccination program and previous infection levels, we predict only minimal future waves to be likely in all scenarios, though a notable further wave of infection may occur once pre-COVID behaviour is resumed (Fig 3) . We have not considered waning immunity or further future variants of concern which may act to disrupt this however.

Figure 6. (Anticlockwise from the top) predicted daily hospital admissions, infections, hospital occupancy and deaths for Wales in scenarios with a steady low level of NPIs maintained into the future following final relaxations. Moderate seasonal effects are assumed. Each line represents the mean of 100 separate simulations drawn from a parameter set (including uncertainties in age dependent transmissibility, infectivity and mixing behaviour for each region) fitted to reported data to date. The solid black line shows default assumptions for this scenario. Sensitivity to: vaccine assumptions is shown by the blue lines with cross and circle markers showing mean values for more higher and lower efficacy estimates as detailed in table 1; mixing assumptions is shown by the green lines with cross and circle markers showing mean values for 25% higher and lower NPI effects immediately following released restrictions; transmission advantage of the Delta variant is shown by the red lines with cross and circle markers showing mean values for a 20% more or less transmissible variant.

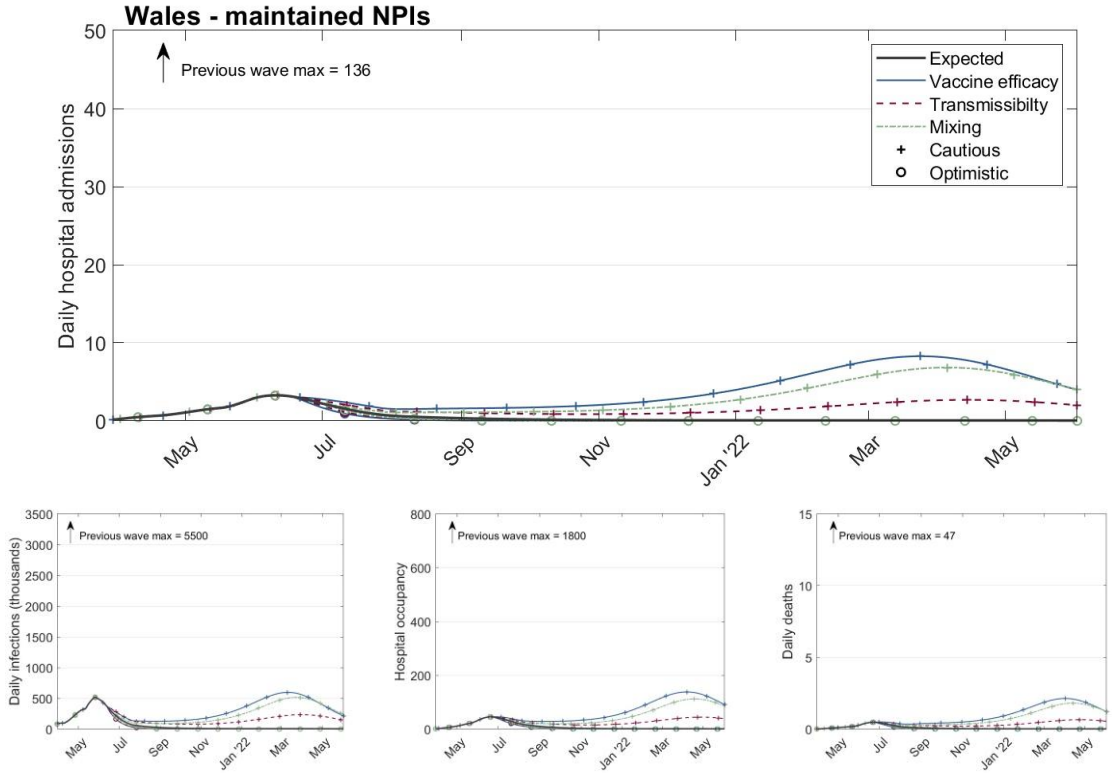


Figure 7. (Anticlockwise from the top) predicted daily hospital admissions, infections, hospital occupancy and deaths for Wales in scenarios with waning NPIs gradually reducing to near pre-Covid levels 12 months after the lifting of final relaxations. Moderate seasonal effects are assumed. Each line represents the mean of 100 separate simulations drawn from a parameter set (including uncertainties in age dependent transmissibility, infectivity and mixing behaviour for each region) fitted to reported data to date. The solid black line shows default assumptions for this scenario. Sensitivity to: vaccine assumptions is shown by the blue lines with cross and circle markers showing mean values for the higher and lower efficacy estimates as detailed in table 1; mixing assumptions is shown by the green lines with cross and circle markers showing mean values for 25% higher and lower NPI effects immediately following released restrictions; transmission advantage of the Delta variant is shown by the red lines with cross and circle markers showing mean values for a 20% more or less transmissible variant.

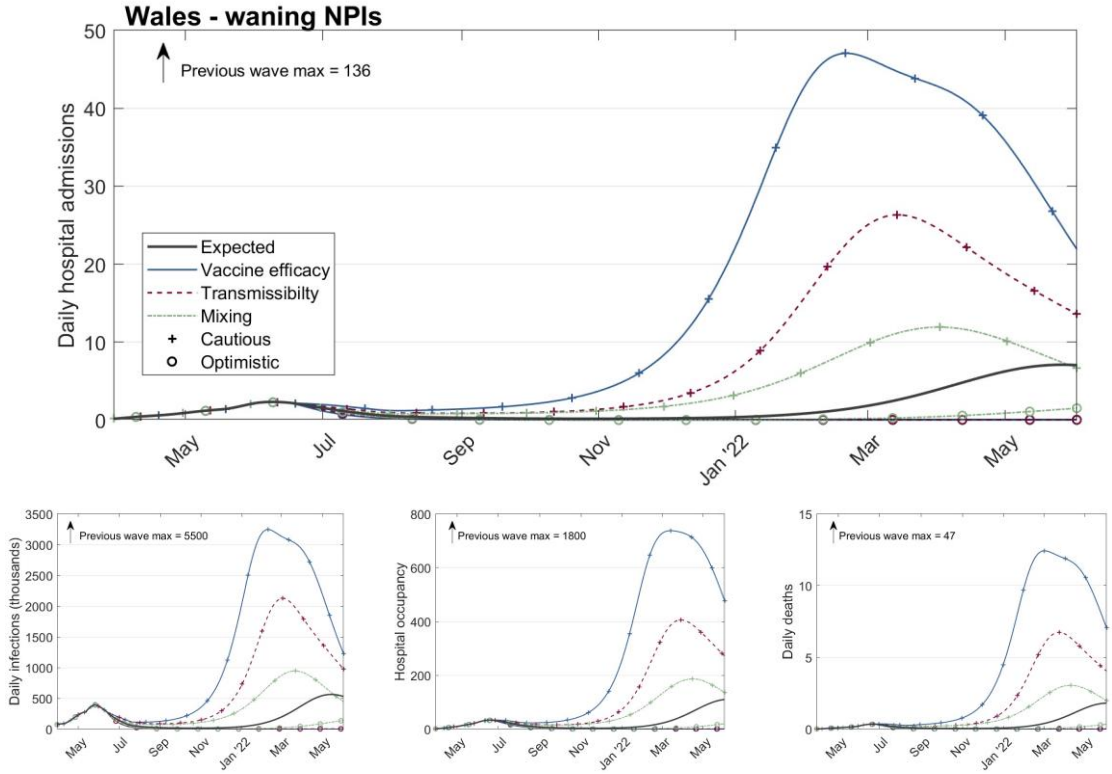
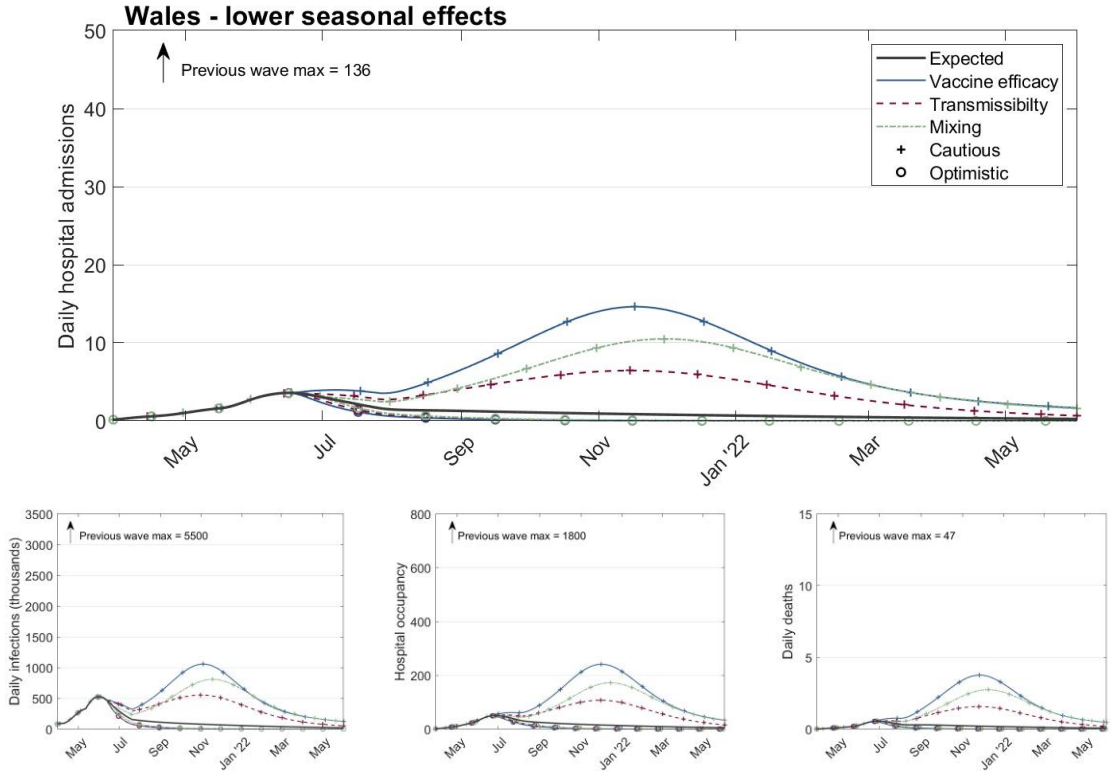


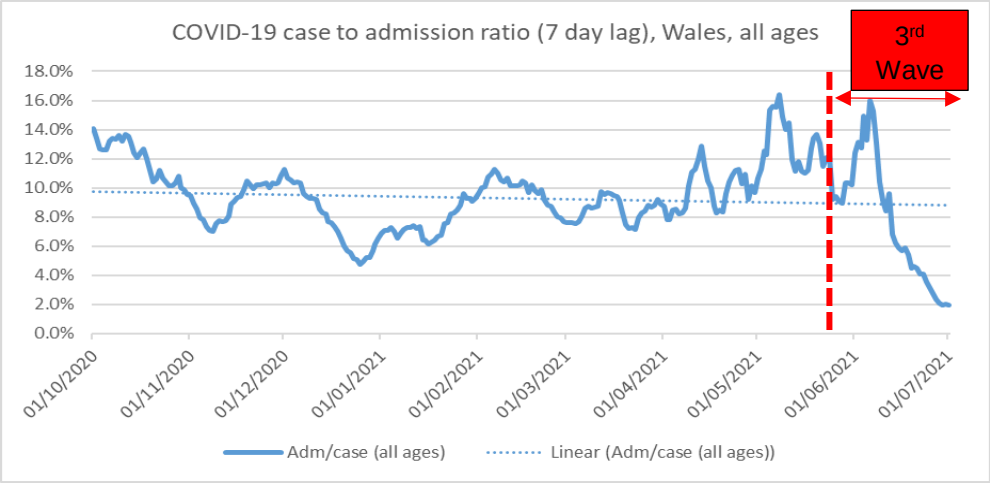
Figure 8. (Anticlockwise from the top) predicted daily hospital admissions, infections, hospital occupancy and deaths for Wales in scenarios with a steady low level of NPIs maintained into the future following final relaxations though with lower seasonal effects at a 5% summer transmission reduction. Each line represents the mean of 100 separate simulations drawn from a parameter set (including uncertainties in age dependent transmissibility, infectivity and mixing behaviour for each region) fitted to reported data to date. The solid black line shows default assumptions for this scenario. Sensitivity to: vaccine assumptions is shown by the blue lines with cross and circle markers showing mean values for the higher and lower efficacy estimates as detailed in table 1; mixing assumptions is shown by the green lines with cross and circle markers showing mean values for 25% higher and lower NPI effects immediately following released restrictions; transmission advantage of the Delta variant is shown by the red lines with cross and circle markers showing mean values for a 20% more or less transmissible variant.



Ratios of COVID-19 cases to admissions and deaths, Wales

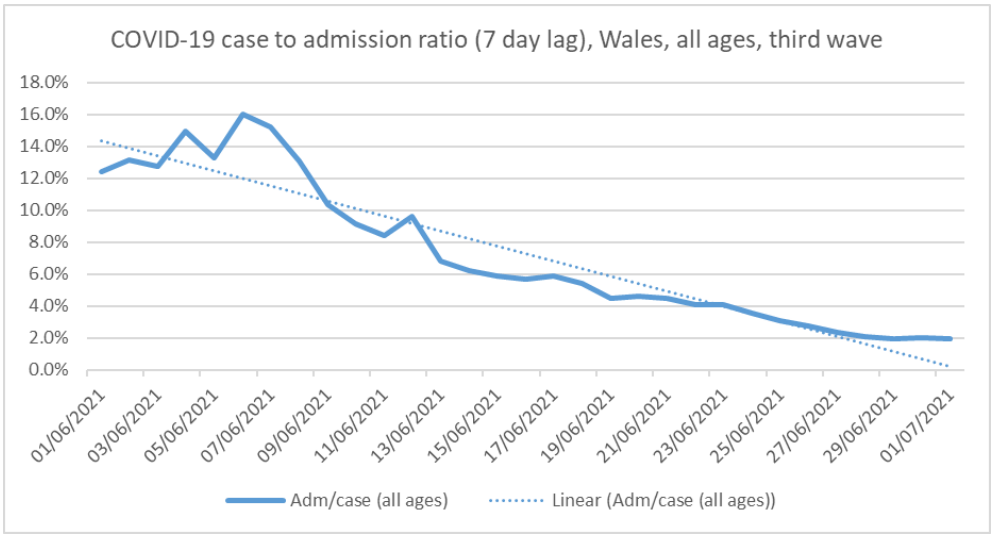
- The percentage of confirmed COVID-19 cases resulting in hospitalisation has decreased from around 10% in December 2020, before the introduction of COVID-19 vaccines, to 2% on 1st July 2021. When considering the third wave alone, which began at the start of June 2021, when cases started to increase, the decrease in the case to admissions ratio is much more pronounced. This could be due the effects of the highly transmissible delta variant taking hold, particularly in the younger, unvaccinated individuals who are likely mixing more following easing of restrictions. This would lead to an increase in cases that are unlikely to lead to many hospitalisations. It could also be due to vaccinated adults being protected against COVID-19 hospitalisations.

Figure 9. COVID confirmed case to hospital case ratio (using 7 day time lag)



Source: PHW ICNet. Ratios are calculated using 7 day rolling averages of cases and admissions and applying lags.

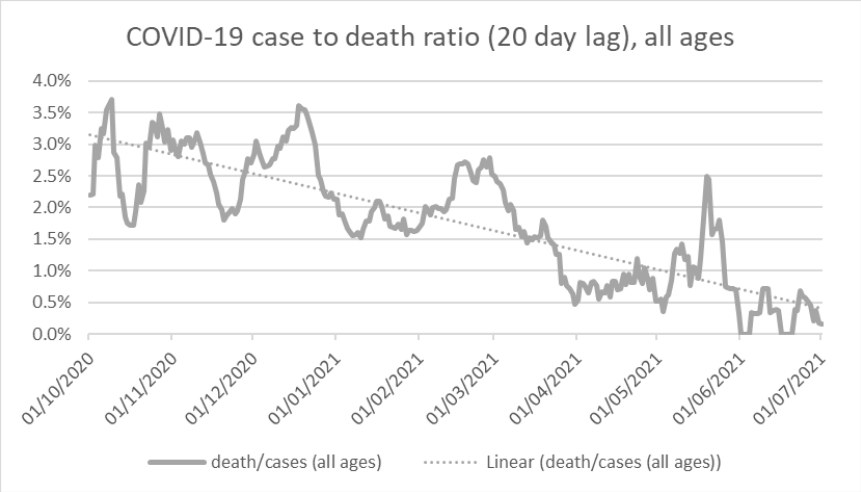
Figure 10. COVID-19 confirmed case to hospital case ratio in June 2021.



Source: PHW ICNet. Ratios are calculated using 7 day rolling averages of cases and admissions, and applying lags.

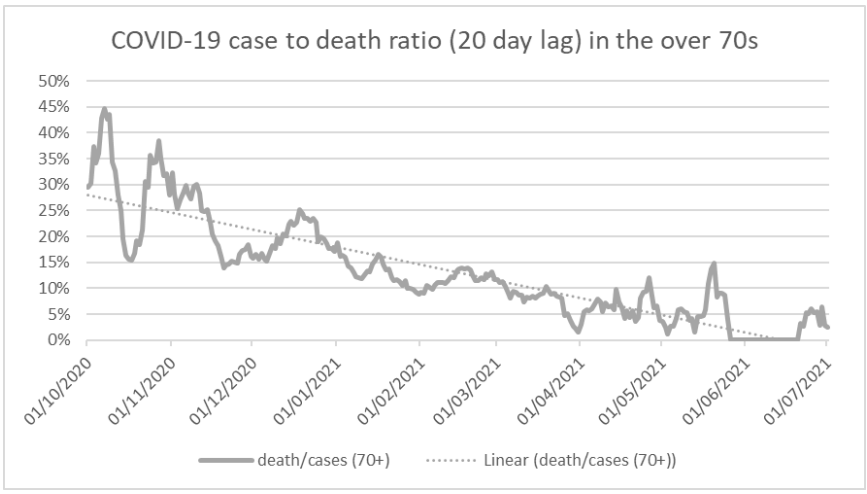
- The over 70s show a large reduction in the percentage of COVID-19 deaths produced on average from COVID-19 cases. Overall, the ratio of deaths in all ages has decreased following the introduction of COVID-19 vaccines from 3.5% in December 2020 to 0.2% on 1st July 2021. This is mostly driven by the over 70s where the ratio of cases to deaths has reduced from 24% in December 2020 to 2% on 1st July 2021. This is likely due to the effects of the COVID-19 vaccines.

Figure 11. COVID-19 confirmed case to death ratio (using 20 day time lag)



Source: PHW ICNet. Cases by specimen date and deaths by date of death are used. Ratios are calculated using 7 day rolling averages of cases, admissions and deaths and applying lags

Figure 12. COVID-19 confirmed case to death ratio in people aged over 70



Source: PHW ICNet. Cases by specimen date and deaths by date of death are used. Ratios are calculated using 7 day rolling averages of cases, admissions and deaths and applying lags

- Using linked data with cases, hospital and deaths may allow us to improve these estimates. There are potential biases with comparing cases to admissions and cases to deaths over time; if vaccines move individuals down a ladder of severity, then some symptomatic cases may move a step down the ladder and become asymptomatic or not detected; so the ratios may not be comparing the same type of cases over time. Using measures like ONS infection survey may negate some of these issues as it picks up all infections, although the numbers of infections in the survey are currently quite low and subject to uncertainties, especially when splitting by age group.

Triangulating the current data and the modelling – implications for MLS and RWC

- By triangulating the current data, and the modelling from Swansea and Warwick, it looks like there are, and will continue to be, fewer seriously ill patients from COVID than in previous waves. The most pessimistic scenarios from the Warwick modelling are similar to the more optimistic 'Delta low' scenarios from Swansea, which may indicate that, despite the evidence accumulating for the increased transmissibility of the Delta variant, the 'Delta low' type scenarios might be the best fit for the current trajectory. It might be that a new most likely scenario should be something like Delta low plus high vaccine effectiveness, while a new Reasonable Worst Case (RWC) should be something like Delta high plus high vaccine effectiveness. However since none of the Warwick scenarios are as pessimistic as the best of the 'Delta high' scenarios, it might be most appropriate to use a more optimistic, 'Delta low' scenario for the new RWC.

Figure 13. Comparison of Warwick/JUNIPER model scenarios, Swansea University scenarios, and actuals for cases in Wales.

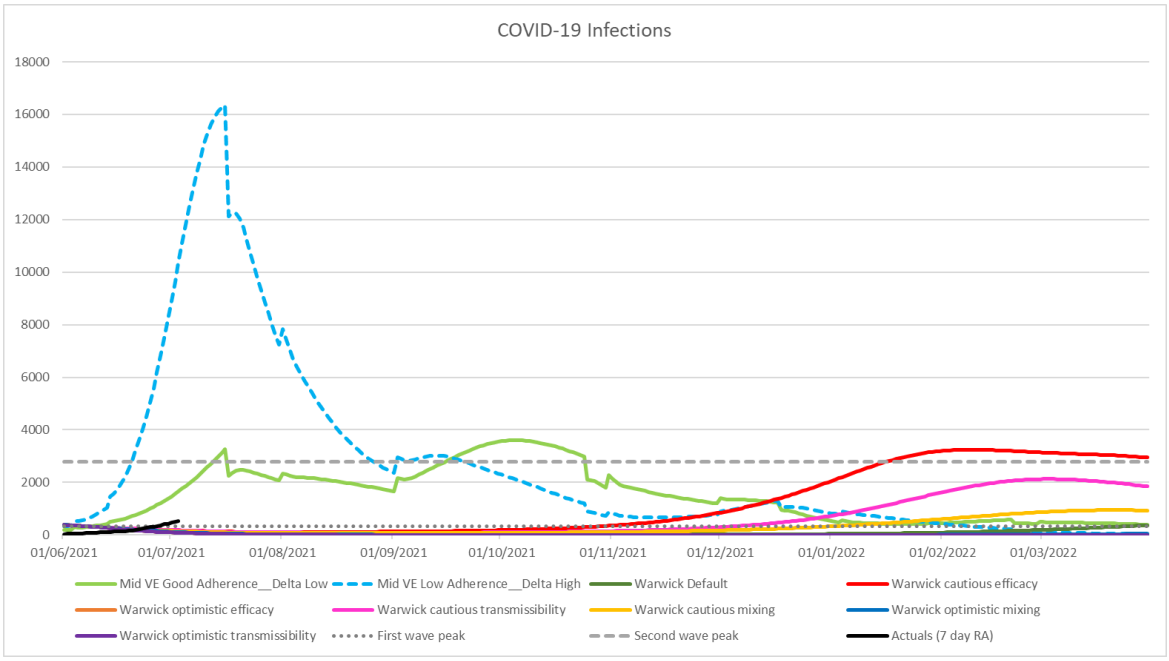


Figure 14. Comparison of Warwick/JUNIPER model scenarios, Swansea University scenarios, and actuals for hospital cases in Wales.

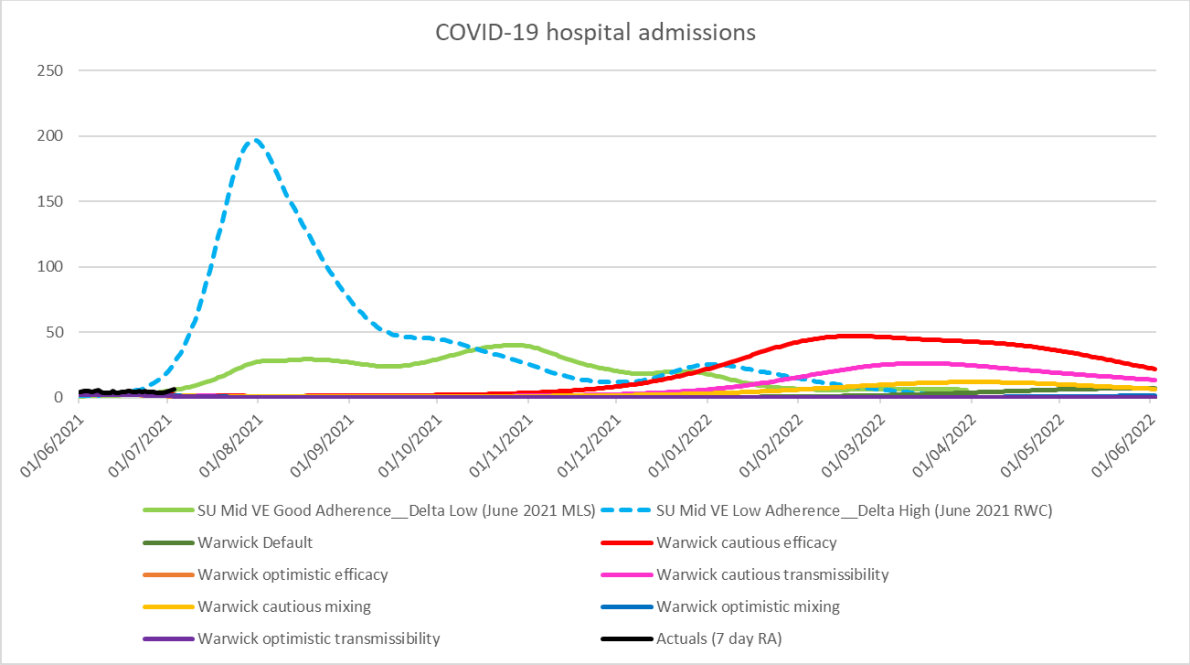


Figure 15. Comparison of Warwick/JUNIPER model scenarios, Swansea University scenarios, and actuals for deaths in Wales.