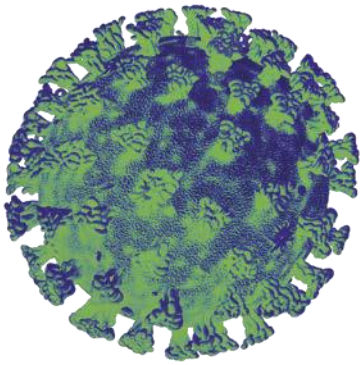
Llywodraeth Cymru
Welsh Government

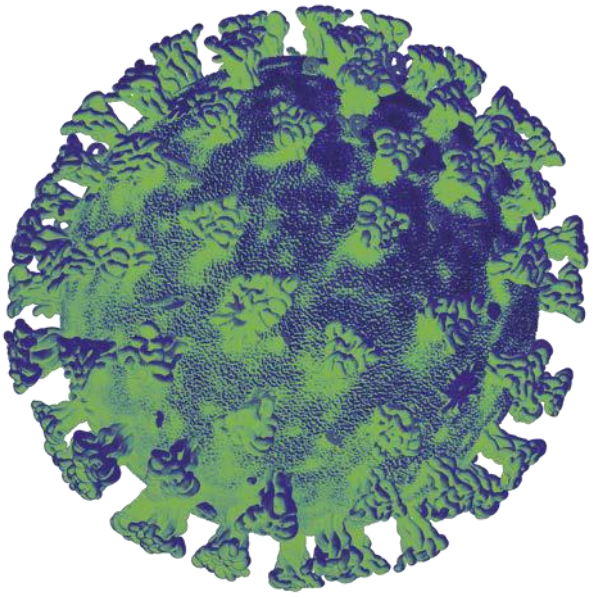
Technical Advisory Group

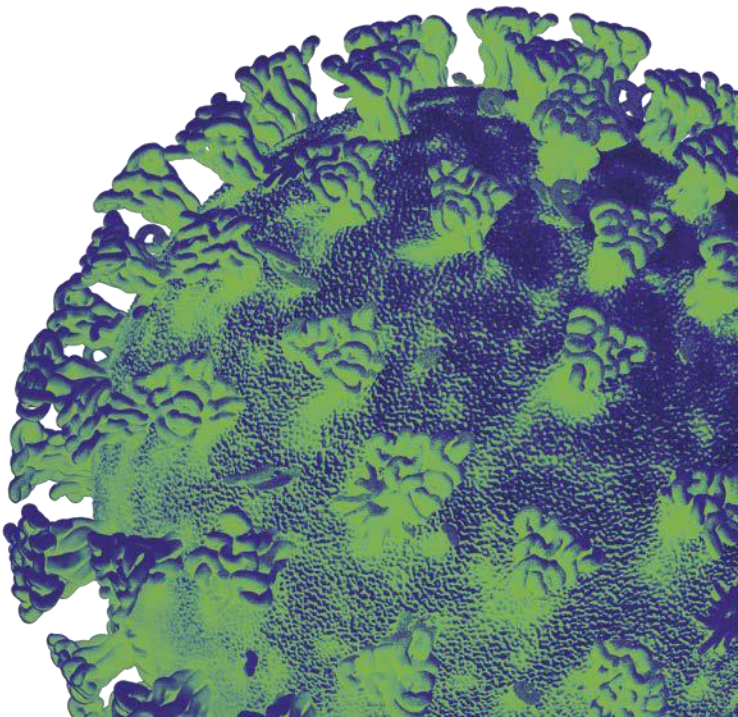
Winter modelling update

Modelling other viruses

10th September 2021







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Modelling other winter viruses

Welsh Government COVID-19 TAG Policy Modelling Subgroup

1. Summary

1. This paper outlines some scenarios of flu and RSV models to compliment the regular update of covid-19 models that we publish.
2. 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.
3. 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.
4. RSV cases and admissions have increased in Wales and the RSV season began 15 weeks earlier than normal (in July) but may be plateauing now, as may also be the case in parts of England. There was an initial peak followed by a fall in RSV cases in the North West of England although this fall is partly due to less testing for RSV in Manchester hospitals.
5. 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.
6. 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. Flu vaccines are being rolled out to more children and young people than in previous years, up to secondary school year 11.
7. 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.
8. Current modelling carried out by Public Health Wales (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 World Health Organisation / European Centre for Disease Prevention and Control (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.

9. 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 simultaneously 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.
10. 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. The 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.
11. 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.
12. 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.
13. It may also be useful to model excess winter deaths from other causes like CVD, COPD and fractures related to falls.
14. 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 suggests that respiratory viruses will occupy between 500 and 2,000 beds on 1st December, this is a wide range but is still useful for preparations. Once we know the dominant strains of influenza that are in circulation, models can be updated.
15. 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]
16. The scenarios in this report suggest that we may see greater than normal sized flu and RSV seasons, which may be shifted in time from their normal peaks. When combined with other pressures on the NHS this may pose particular challenges.

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

17. 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.

2. Respiratory Syncytial Virus modelling

RSV is a virus that affects people of all ages but typically infects up to 90% of children in the first two years of life, and some children get acutely ill and require hospital treatment. RSV causes bronchiolitis – inflammation of the lungs, dry cough, and breathing problems. There is some protection against severe illness in infants in the early weeks of life, due to transplacental antibody transfer in third trimester of pregnancy. The monoclonal antibody treatment Palivizumab is given to some high risk infants (mainly those born premature) to prevent severe RSV illness. This is given as a monthly injection in the RSV season.

RSV immunity through previous infection usually wanes quite quickly. Evidence suggests that young children are often infected by older siblings but children without older siblings are still infected, presumably from other children or adults. RSV season usually starts in September and peaks in November-December. There were very few cases of RSV detected in the 2020/21 season due to covid-19 social distancing so there is concern over a large rebound in cases in 2021/22 as has been observed in Australia and New Zealand; this may be in children aged 1-2 years who have not yet been exposed to RSV, and with infants where maternal immunity is not passed on due to lack of exposure to RSV in the mother.

Current data suggests RSV season has already started in Wales, 15 weeks early. But this may be asynchronous across different parts of Wales. We looked at data for bronchitis and bronchiolitis hospital admissions by age, LHB, hospital and date, ICD10 and HRG for 2016-2020 and found that the shape of the epi curve for admissions was remarkably similar by year and LHB – with hospital activity peaking between 22nd November and 2nd December. The median length of stay is one day. 91% of admissions are age 0, 8% age 1, and very few admissions over age 5. The data included zero day admissions which may be where children are observed for a few hours then sent home.

Welsh Government RSV Modelling Scenarios

In Wales we have modelled 4 scenarios for pressures around paediatric bronchiolitis which is mainly caused by RSV. These are:

1. An earlier outbreak with a 50% increase in total number of RSV cases / admissions.
2. An early, but normal or quieter than normal, RSV season (particularly if non-pharmaceutical Interventions are maintained).
3. An earlier, larger outbreak with 100% increase in total number of RSV cases /

admissions.

4. As scenario 3, but with the 2022 peak returned to normal timing

Since the RSV season has started early, these scenarios have been transposed 15 weeks earlier than they have been in previous seasons. For scenarios 1-3, both the 2021 and 2022 seasons start 15 weeks early, but in scenario 4, the 2022 season returns to normal timing. While it is unlikely that the 2022 season will start as early as the 2021 season, it is also not known when winter viruses will return to normal seasonality.

The results are shown below. These produce a possible peak of 336-672 hospital admissions per week that would have occurred around mid-August 2021. These admissions include zero day admissions. The PICU scenarios are based on a proportion of admissions so might be higher if the admissions.

Figure 1. Comparison of RSV hospital admissions scenarios for Wales, based on previous hospital admissions data.

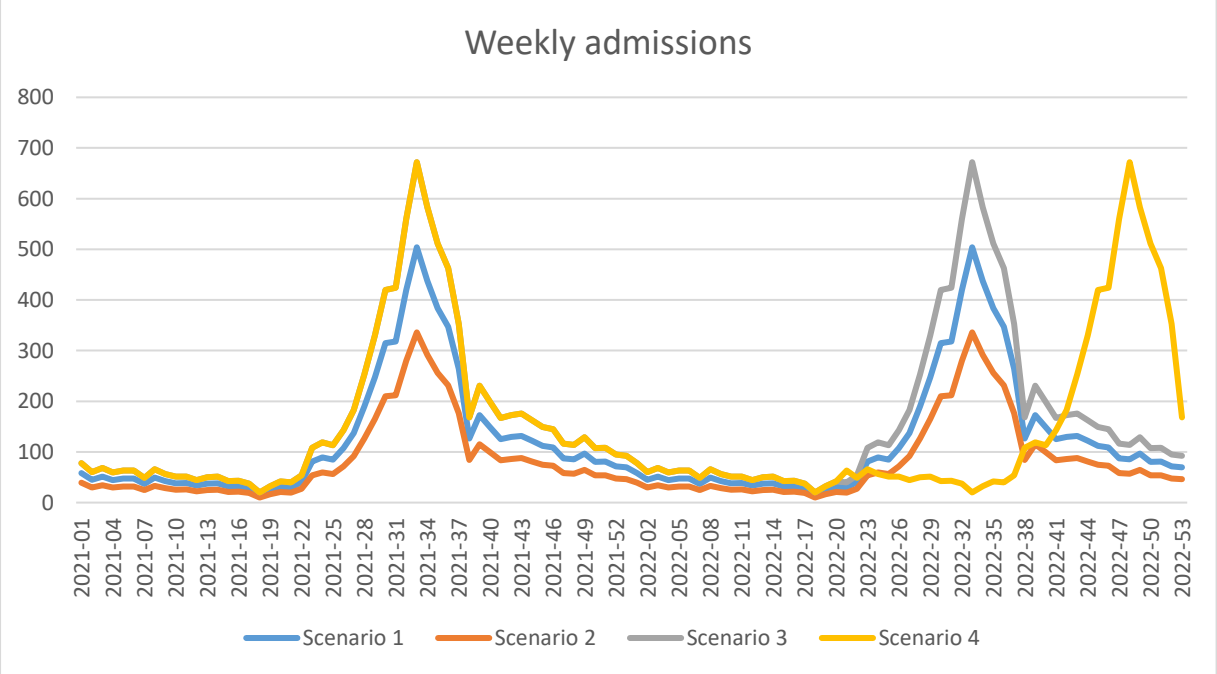
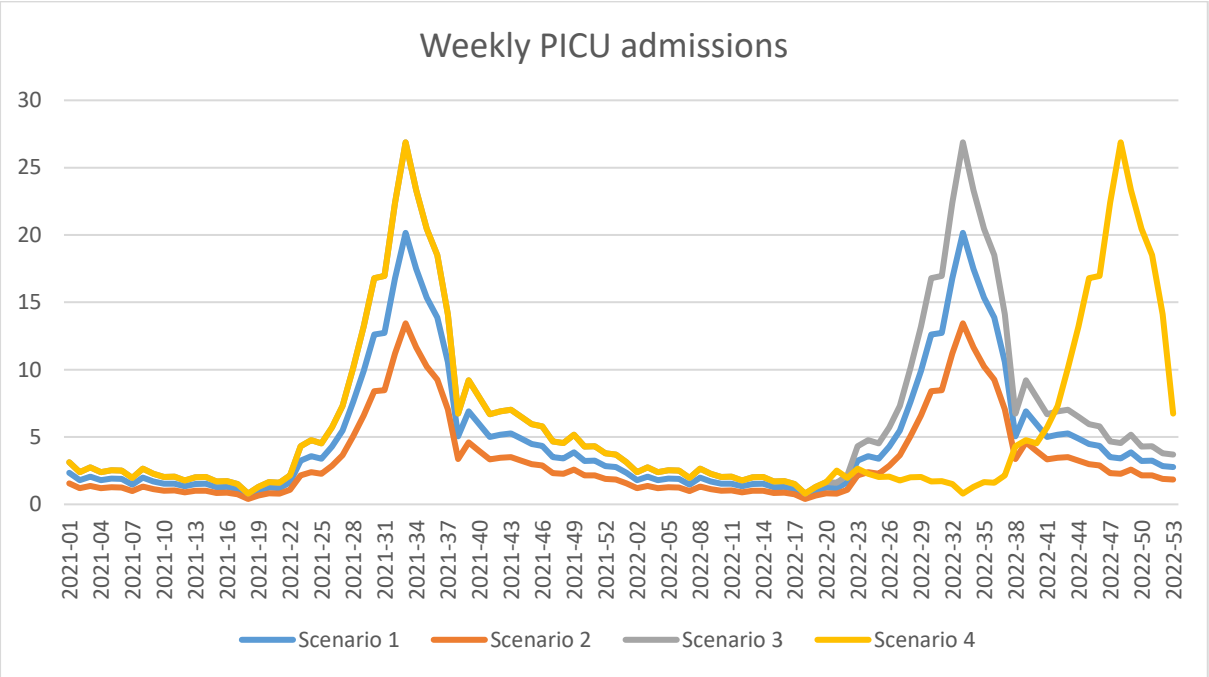


Figure 2. Comparison of RSV paediatric intensive care (PICU) scenarios for Wales, based on previous hospital admissions data.



Academy of Medical Sciences (AMS) RSV Modelling Scenarios

The Academy of Medical Sciences (AMS) have recently published a winter planning report, “COVID-19: Preparing for the future”. The paper explores the health and social care challenges we may be facing over the coming winter and beyond. It includes a range of modelled scenarios for winter 2021/22 for COVID-19, influenza and respiratory syncytial virus (RSV). We are grateful to Dr Alexandra Hogan from Imperial College London for sharing the model and discussing the results with us.[2]

The AMS paper considers two RSV scenarios:

1. In Scenario 1, they assume that maternal protection decays over the period that behavioural and environmental interventions are in place due to a lack of exposure. In this scenario, a peak outbreak would be roughly 2 times the magnitude of a normal year, with an increase of
    - 65% in cases in children <5 years,
    - 100% in cases in youngest infants, and
    - 40% in infection across the population.

This leads to an overall increase of 86% in RSV notifications in children under 5 in the model.

[2] The ONS 2020 mid-year estimates are used to obtain the population estimates for Wales and the UK.

2. In Scenario 2, they assume no change in pre-existing levels of maternal protection. In this scenario, a peak outbreak would be roughly 1.5 times the magnitude of a normal year, with an increase of
    - 25% in cases in children <5 years,
    - 30% increase in cases in youngest infants, and
    - 40% increase in infection across the population.

For both scenarios, they assume that the level of behavioural and environmental interventions in place between March 2020 and June 2021 reduced transmission of RSV by 30%, a level that is sufficient to interrupt transmission for most of this period. The model is fitted to data from England (PHE reports from DataMart). Similar patterns would be expected in Wales, Scotland and Northern Ireland.

When we looked at the data, the two scenarios included in the AMS report equate to a normally timed season but 86% or 40% higher than normal. In order to line up with what the current position of the RSV season in Wales is showing, we have applied these scenarios to our hospital admissions data, whilst still bringing the season forward by 15 weeks. The 3 scenarios are:

1. An earlier outbreak with 40% increase in total number of RSV cases / admissions.
2. An early, but normal RSV season (for comparison).
3. An earlier, larger outbreak with 86% increase in total number of RSV cases / admissions.

These produce a similar scenario to those above but slightly lower than the 100% scenario. The North West of England saw a peak in late July-early August 2021 which seems to have then fallen, but this may be partly related to changes in testing practice. Overall, there is still considerable uncertainty about what will be observed in terms of RSV-related pressures on the system and whether we will see a shifted peak, a double peak, or a peak followed by a plateau. There are implications in terms of pressure on the NHS, particularly around capacity in terms of PICU beds and patient transport, as young children who require PICU in North Wales often travel to Alder Hey Hospital in Liverpool.

Figure 3. Comparison of RSV hospital admissions scenarios for Wales, based on previous hospital admissions data (AMS scenarios)

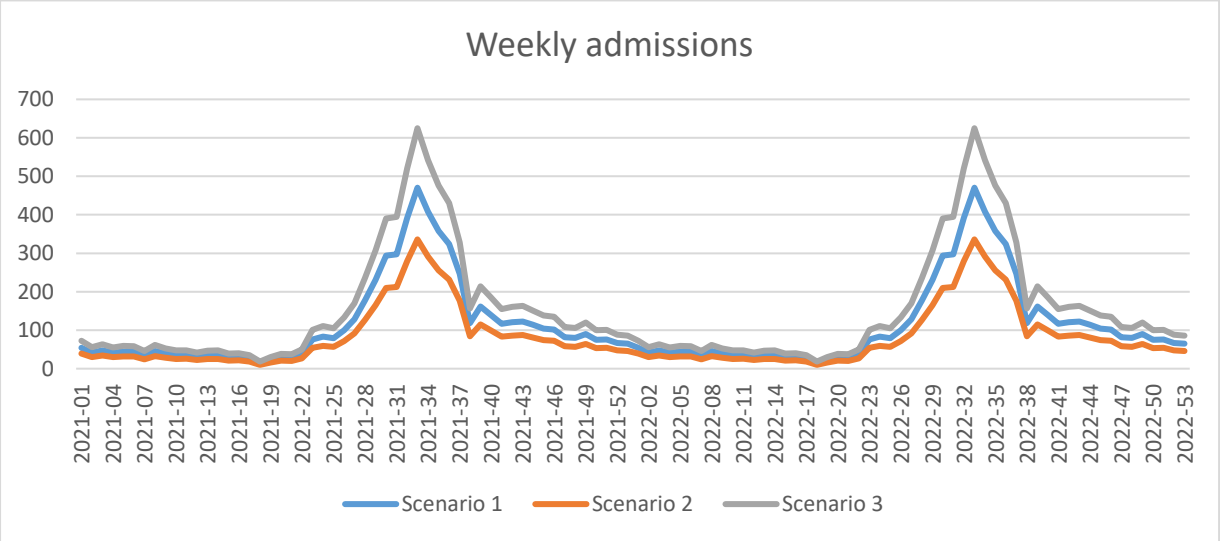
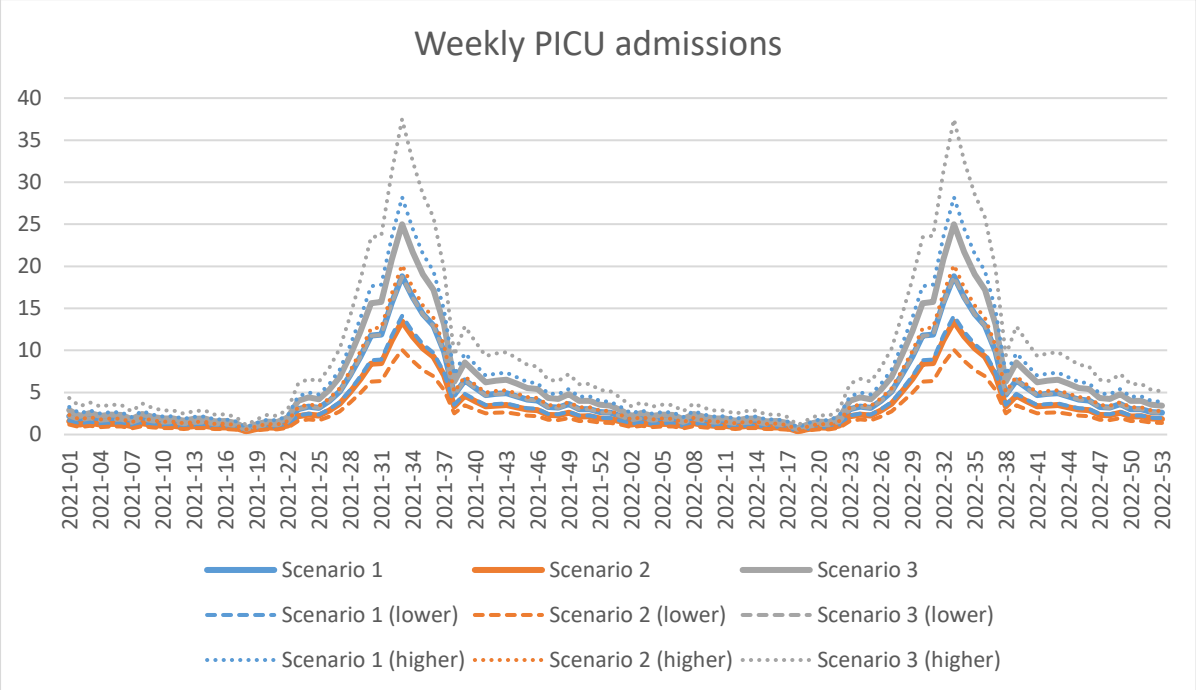


Figure 4. Comparison of RSV paediatric intensive care (PICU) scenarios for Wales, based on previous hospital admissions data (AMS scenarios)



3. Influenza modelling

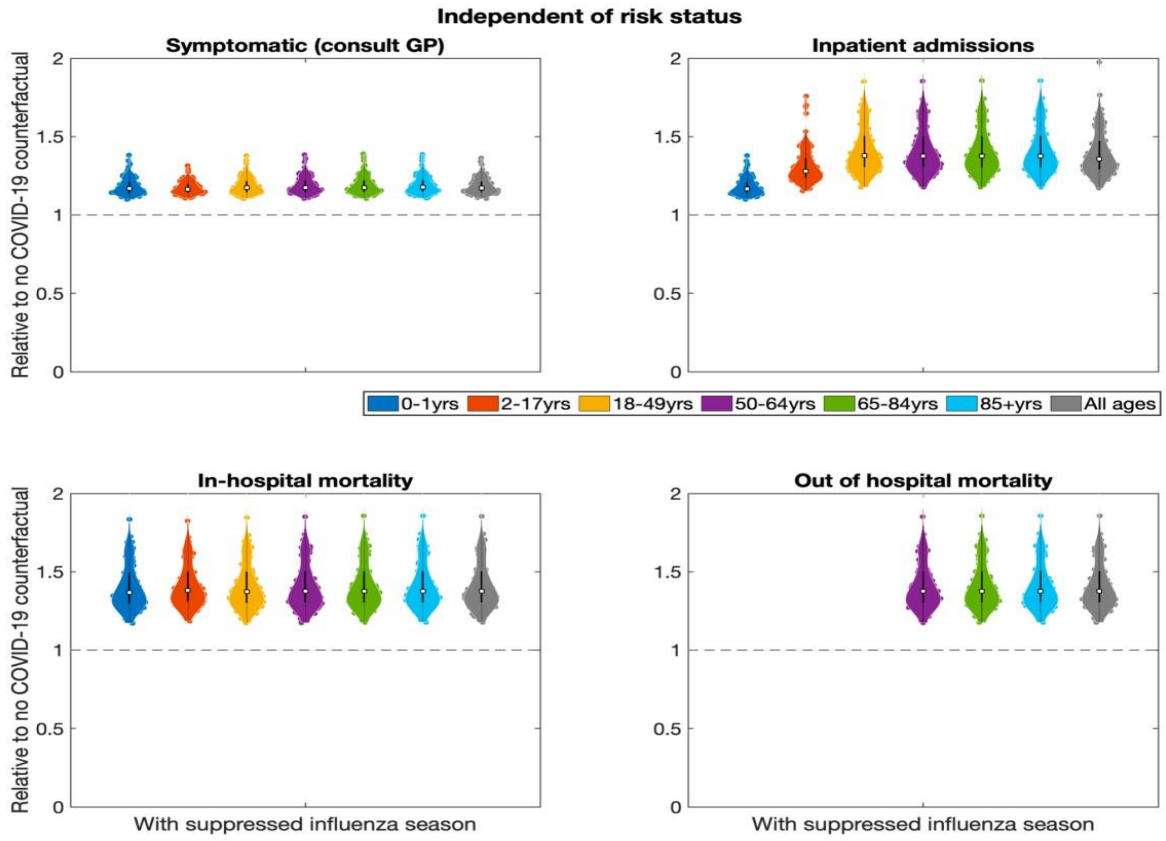
Trying to predict the volume of healthcare activity related to seasonal influenza is very difficult. It may be best to have scenarios for what a high, mid and low flu season looks like and then track which scenario we are closest to. For instance 2017/18 is a recent example of a flu season that produced a lot of hospital pressures and deaths.

Flu seasons vary with some flu types, subtypes and clades producing different effects in terms of the balance between primary and secondary care pressure, which is partly related to severity by age, as well as vaccine match and uptake. The 2010/11 flu season (the third wave of the A(H1N1)pdm09 pandemic) was the most intense in terms of primary care consultations and perhaps younger adults being admitted to hospital, but the 2014/15 and 2017/18 flu seasons (both due to newer A(H3N2) clades) were much worse in terms of respiratory-related mortality and care home outbreaks. Cold weather can make a difference as well. The GP signal in 2014/15 brushed ‘medium’ levels of intensity, but the winter mortality was the worst seen in more than 20 years.

We have received influenza modelling from the University of Warwick that was used by JCVI around influenza decision making. We also have influenza scenarios from the AMS report.

Figure 3 shows the relative number of influenza health episode occurrences in a flu season following a suppressed flu season, compared to a no COVID-19 counterfactual scenario (with no alterations to population mixing patterns in the previous flu season). The University of Warwick modelling suggests that outcomes such as cases, hospital and deaths are almost certain to be higher in a flu season following a suppressed flu season (e.g. winter 2020/21), with counts up to two times a normal flu season plausible.

Figure 3. Age-stratified health episode occurrences (influenza) relative to the no COVID-19 counterfactual scenario. Each age grouping is measured relative to the outcomes attained for that age grouping under the counterfactual scenario. White squares represent the medians. Solid black lines the interquartile range. Results are produced accounting for both low- and at-risk groups.



Source: Hill and Keeling, 2021 University of Warwick (unpublished report to JCVI). Based on Hill et al, 2020 [3]

Academy of Medical Sciences influenza modelling

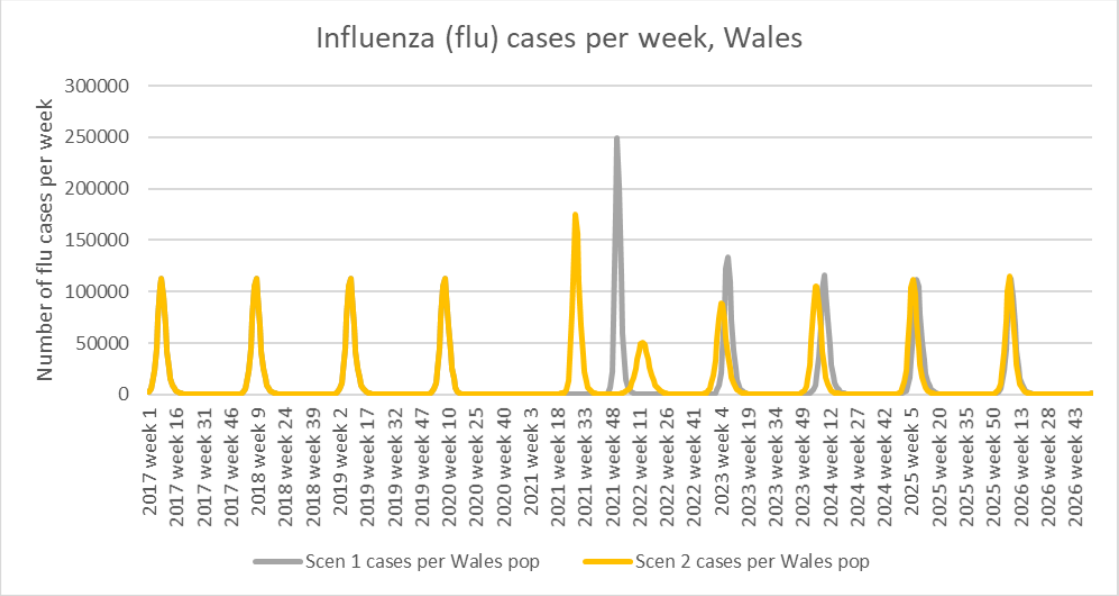
Welsh Government received data from Professor Azra Ghani, Imperial College, of the AMS influenza modelling which was based on Princeton's influenza modelling.[4] Applying the Princeton modelling to the UK, this gives a reasonable worst-case scenario with an influenza epidemic could be between 1.5 and 2.2 times the magnitude of a 'normal' year. These outbreaks may reach peak numbers in the winter, increasing the burden to healthcare systems at a time when admissions

[3] Hill et al (2020) Optimising age coverage of seasonal influenza vaccination in England: A mathematical and health economic evaluation. PLoS Comput Biol **16**(10): e1008278. https://doi.org/10.1371/journal.pcbi.1008278

The impact of COVID-19 nonpharmaceutical interventions on the future dynamics of endemic infections | PNAS[4]

related to cold weather may have increased, at the same time as the NHS is trying to tackle a backlog in elective activity. It may also be that a winter wave in covid pressure occurs at the same time. High rates of influenza will also increase the pressure on TTP as flu symptoms are very similar to covid symptoms.

Figure 4. Wales apportioned model of AMS flu scenarios, total cases per week.



4. Summary

This paper has outlined some potential scenarios of influenza and RSV. Because of 'immunity debt' due to a lack of infection during the pandemic, we may see a bigger than normal RSV and flu season which may also be shifted outside of the regular winter peak times. This may also co-occur with covid related pressure on the NHS, and cause diagnostic uncertainty and increased pressure on TTP. Having more scenarios and tracking these scenarios against surveillance data will be important this winter. In the future the ambition is to have combined scenarios of pressure from all respiratory viruses, which varies in which part of the system it is felt (primary vs secondary care) and the age groups that are most affected by these viruses – so RSV is mainly very young children, influenza mainly young children and older adults,

and covid-19 may be different again with high rates of vaccination uptake across the population.

The data for these scenarios can be shared with LHBs so that they can take a proportion of them to see what they mean for their own localities. In future, it would be useful to also model flu mortality and critical care demand.

Thank you

Thank you to the Academy of Medical Sciences for sharing their data, and in particular to Professor Azra Ghani and Dr Alexandra Hogan (Imperial College London) for their help with this work. Thank you to Dr Ed Hill from University of Warwick for his help with this work.