

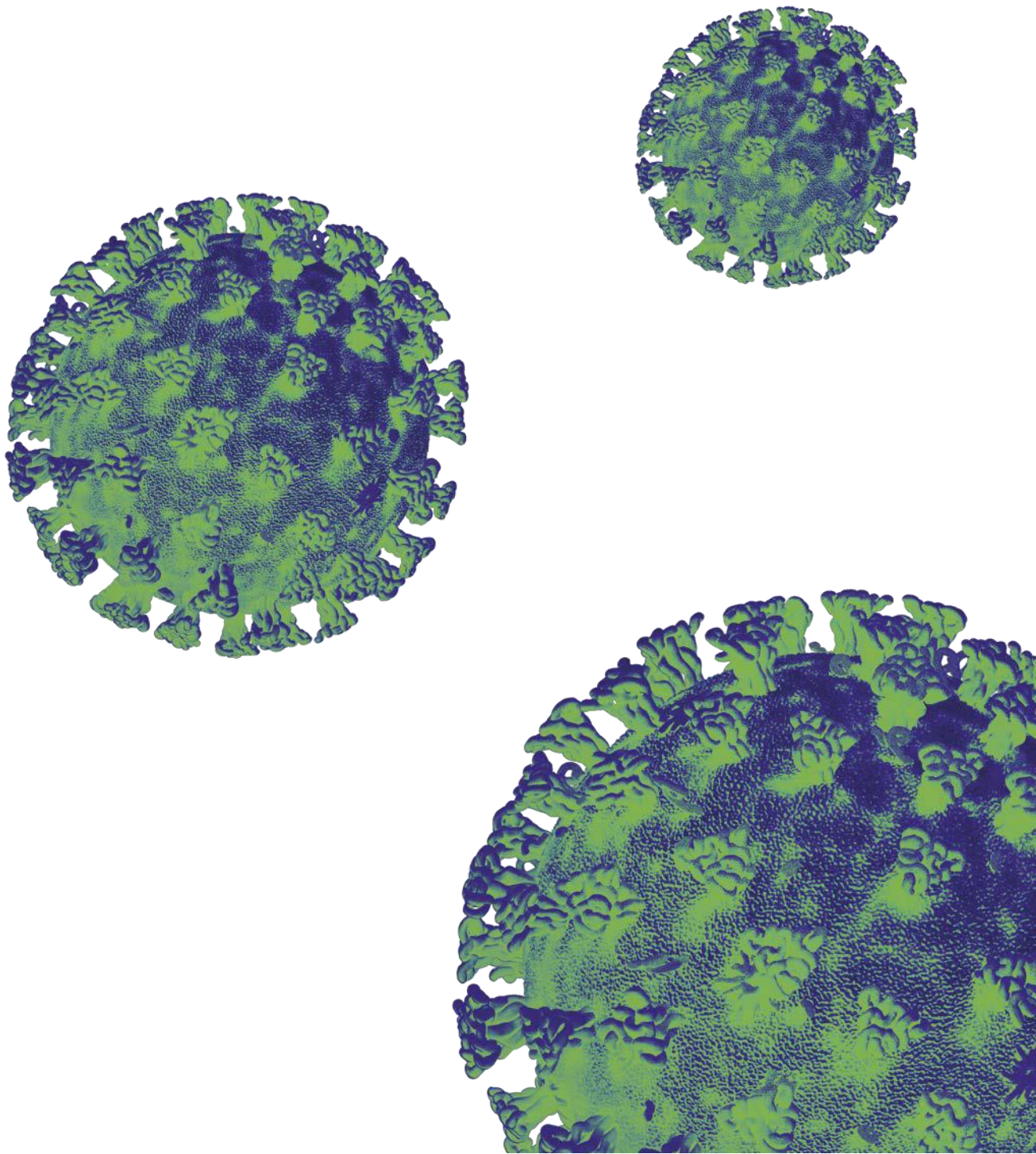
# Technical Advisory Group

## Covid-19 Waning Immunity

September 2021



Llywodraeth Cymru  
Welsh Government



# COVID-19 Waning Immunity

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### Summary

- There is compelling evidence from numerous sources indicating that waning of immunity, particularly immunity gained from vaccination, is a very real possibility. Results from studies may not be comparable due to differing age/priority order of vaccinations, differing length of time between doses, different vaccines offered, etc. Confounding factors and limitations of studies need to be taken into account when assessing the duration and impact of waning immunity, of which there is still great uncertainty.
- A recent study from Public Health England (PHE) indicated that vaccine effectiveness (VE) against Delta is generally lower with the AstraZeneca (AZ) vaccine than the Pfizer vaccine, but with both vaccines, waning of VE against symptomatic disease is seen from around 10 weeks.
- A recent rapid review on hospital admissions by Public Health Wales (PHW) summarised the characteristics of patients admitted to hospital who had a COVID-19 positive test result (in a 4 week period ending 05/09/2021). Overall, 61% of admissions were recorded as having received 2 doses of vaccine; the median interval from full vaccination to admission was 201 days (between 6 and 7 months).

## Introduction

Since the start of the COVID-19 pandemic over 18 months ago, immunity has been building in individuals across Wales (and the world) either from a COVID-19 infection and/or from vaccination. Once a certain proportion of the population, spread evenly across the population, are considered to be immune against COVID-19 infection, we can expect the virus to stop spreading at an exponential rate. This proportion of the population is called the herd immunity threshold and there is uncertainty about what it is for COVID-19. It is currently estimated that over 80% (may be closer to 90%) of the population, spread evenly across Wales, must be immune to COVID-19 before population immunity effects would be observed.<sup>1</sup> This is based on the R0 for the current dominant Delta variant being around 6, but R0 may be different in different populations.

However, if immunity of individuals in the population were to wane over time, it would make reaching and particularly maintaining the 'herd immunity' threshold difficult. The potential impact of waning immunity is a key uncertainty in the COVID-19 pandemic currently.<sup>2</sup> However, there is early evidence of waning of vaccine effectiveness against severe disease. Several studies from England and internationally report differing estimates and impacts of waning.

## Waning Immunity studies to date

The ONS COVID-19 Infection Survey (CIS) measures the presence of antibodies in the community population to understand who has had COVID-19 in the past, and the impact of vaccination. Testing positive for antibodies does not equate to having immunity. An immune response does not rely on the presence of antibodies alone. An individual's "T cell" response also provides longer term protection. However, the presence of COVID-19 antibodies is a good proxy for the level of immunity in an individual.<sup>3</sup> Antibody levels may drop naturally over time.

The CIS has also been used to provide data about COVID-19 reinfections. The findings indicate that reinfections are possible, but rare (occurring in an estimated 15.2 per 100,000). Where they occur, the infection is milder with fewer reported symptoms, and the viral load is lower than in primary COVID-19 infections.<sup>4</sup>

Earlier studies have reported that antibodies are detectable for at least 6 months and probably 8 months or more.<sup>5</sup> The SIREN study of healthcare workers reported that a previous history of SARS-CoV-2 infection was associated with an 84% lower risk of infection, with median protective effect observed 7 months following primary infection.<sup>6</sup> The Vivaldi study of care home residents and staff indicated that natural

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<sup>1</sup> [Advice from TAG and the Chief Scientific Advisor for Health on the Delta Variant \(B.1.617.2\), 15 June 2021 GOV.WALES](#)

<sup>2</sup> [S1360\\_SAGE\\_95\\_minutes.pdf \(publishing.service.gov.uk\)](#)

<sup>3</sup> [Coronavirus \(COVID-19\) Infection Survey, antibody and vaccination data, UK - Office for National Statistics](#)

<sup>4</sup> [Coronavirus \(COVID-19\) Infection Survey technical article: analysis of reinfections of COVID-19 - Office for National Statistics](#)

<sup>5</sup> [NERVTAG: Immunity certification update, 4 February 2021 - GOV.UK \(www.gov.uk\)](#)

<sup>6</sup> [SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study \(SIREN\) - The Lancet](#)

immunity to COVID-19 substantially reduced the risk of reinfection for approximately 10 months following primary infection.<sup>7</sup>

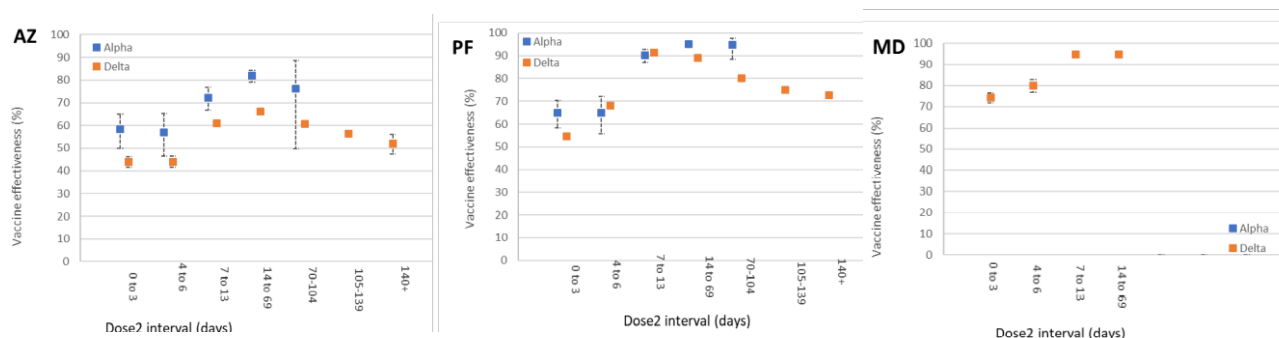
However, more recent studies from Public Health England (PHE), Public Health Wales (PHW) and Israel have investigated waning vaccine effectiveness.

### PHE SAGE paper

A paper on duration of protection from COVID-19 vaccines by Public Health England was presented at the 9 September SAGE meeting.<sup>8</sup> This study compared vaccination status in persons with symptomatic Covid-19 with vaccination status in persons who reported symptoms but had a negative test (test-negative design) to help control for biases. Adjustments for characteristics such as age and sex were also made to account for differences between populations.

The results showed that vaccine effectiveness (VE) against Delta is generally lower with the AstraZeneca (AZ) vaccine than the Pfizer vaccine, but with both vaccines, waning of VE against symptomatic disease is seen from around 10 weeks, reaching just over 50% with AZ and just over 70% with Pfizer by 20+ weeks. (With the Moderna vaccine, data is not yet available beyond 10 weeks).

Figure 1: VE against symptomatic disease – all ages



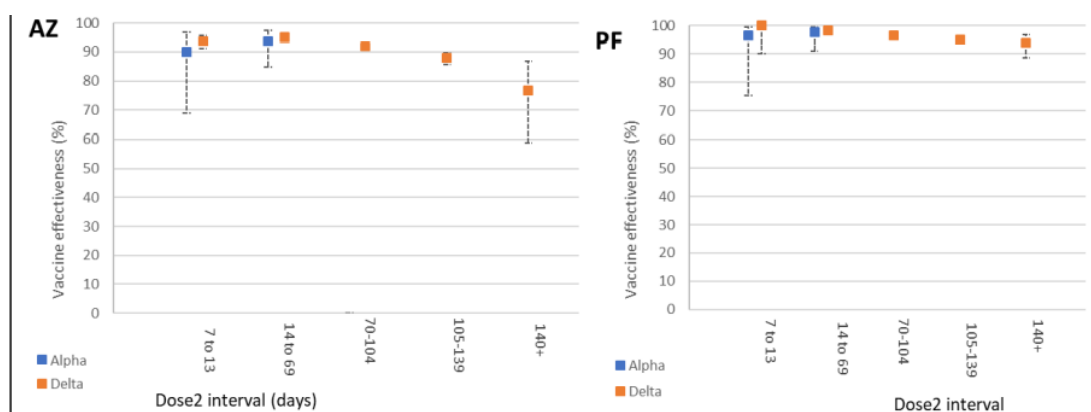
VE against hospitalisation and deaths remains higher for longer than VE against symptomatic disease.

With the Pfizer vaccine, around 95% VE against hospitalisation continues to be seen beyond 20 weeks after vaccination. With the AZ vaccine, there appears to be some waning to just under 80% VE against hospitalisation from 20+ weeks however there are wide confidence intervals.

<sup>7</sup> [Vivaldi 2: COVID-19 reinfection in care homes study report - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/research-data-and-analysis/publications/vivaldi-2-covid-19-reinfection-in-care-homes-study-report)

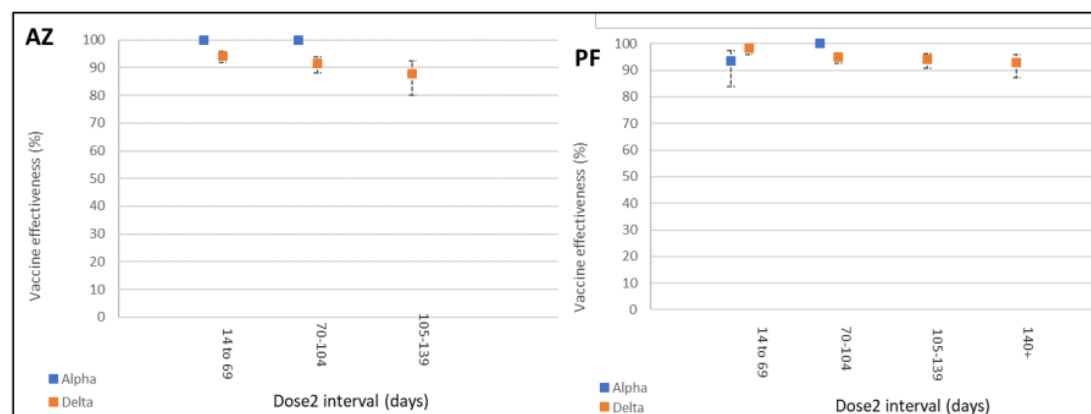
<sup>8</sup> [PHE: Duration of protection of COVID-19 vaccines against clinical disease, 9 September 2021 - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/research-data-and-analysis/publications/phe-duration-of-protection-of-covid-19-vaccines-against-clinical-disease-9-september-2021)

Figure 2: VE against hospitalisation - all ages



Vaccine efficacy against death remains high for both vaccines over time with minimal waning prior to 20 weeks following vaccination. However, even a small decrease in vaccine efficacy from 98% to 96% may double the number of deaths observed in a long term, high prevalence scenario.

Figure 3: VE against death - all ages



The PHE study also looks at VE in individuals in different age bands with similar results to those above. However, when further stratifying by clinically at risk group, waning of immunity appears to be greater with both AZ and Pfizer among those in the clinically extremely vulnerable groups.

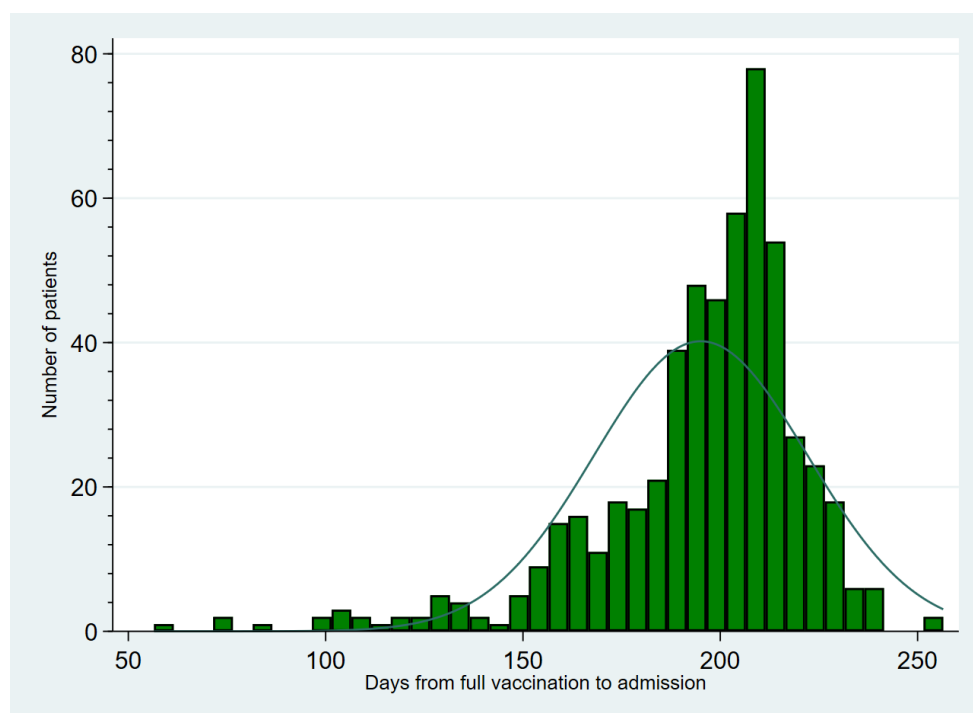
### PHW admissions in vaccinated

A rapid review on hospital admissions by Public Health Wales (PHW) summarised the characteristics of patients admitted to hospital who had a COVID-19 positive test result (in a 4 week period ending 05/09/2021). Data on the reasons for admission were not available and likely reflect admissions due to COVID-19 and also admissions for other reasons, with an incidental COVID-19 positive test result. During this period, just under 900 individuals were admitted to a hospital in Wales with a positive COVID test within 28 days before or 48 hours after admission; overall the highest numbers of admissions were in the 60-79 age group (280).

Overall 61% of admissions were recorded as having received 2 doses of vaccine.

Amongst the 545 patients who had both doses prior to admission, the median interval from full vaccination to admission was 201 days (between 6 and 7 months). The median time interval from 2nd dose to the current COVID-19 admission was approximately one month shorter for those aged under 60 (168 days), compared to those aged 60 years and older (205 days). This finding may partly reflect the timing of the third wave as this began in June 2021, around 3-4 months after many older and vulnerable groups have had their second dose.

Figure 4: Interval from vaccination to admission for all fully vaccinated COVID 19 patients admitted to hospital from 09 August 2021 to 5 September 2021

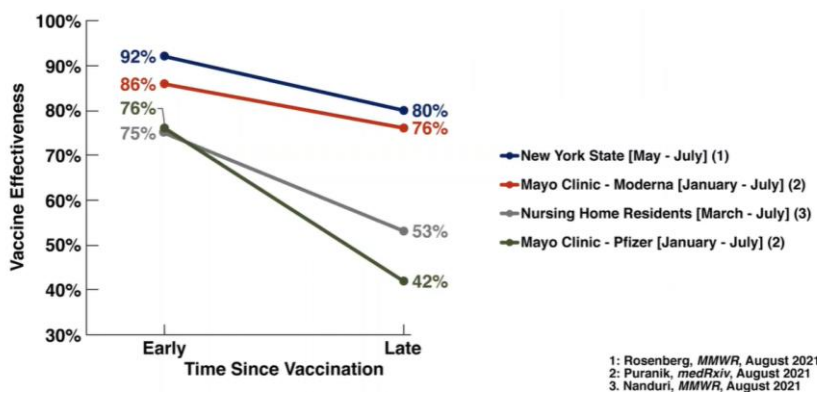


### USA Studies

Published studies from the USA covered the remaining challenges of the COVID-19 epidemic.<sup>9</sup> This included the waning of vaccine effectiveness over time. Figure 5 shows the waning of vaccine effectiveness from four different sources/studies. Decreases are shown in vaccine effectiveness over time though the length of time it takes to wane is not specified.

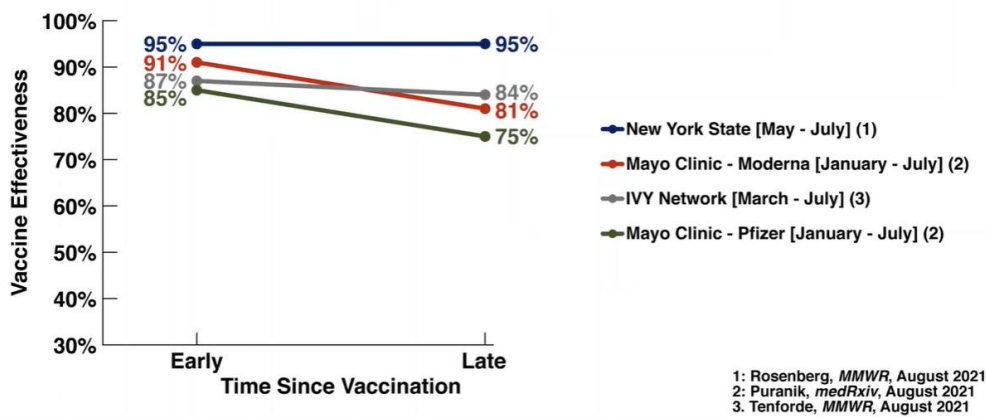
<sup>9</sup> [Pumphandle Lecture 2021: Dr Anthony Fauci | LSHTM](#)

Figure 5: VE against COVID-19 infection over time



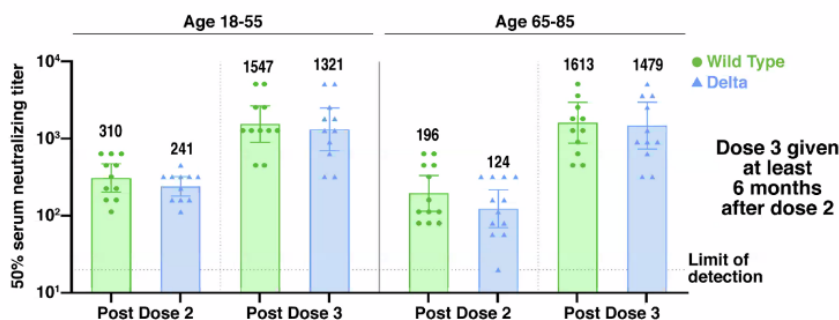
The following figure indicates that COVID-19 vaccine effectiveness against hospitalisation remains high though there is suggestion of some waning.

Figure 6: VE against hospitalisation



Evidence of waning immunity and waning vaccine effectiveness increases the argument for booster COVID-19 vaccines. The following figure indicates the exponential increases in 50% serum neutralising titre (antibodies) observed in individuals who have received their third Pfizer vaccine doses compared with those who had received two doses.

Figure 7: Amount of COVID-19 antibodies in individuals post 2 doses and 3 doses of Pfizer vaccine, by age band (18 to 55, 65 to 85)



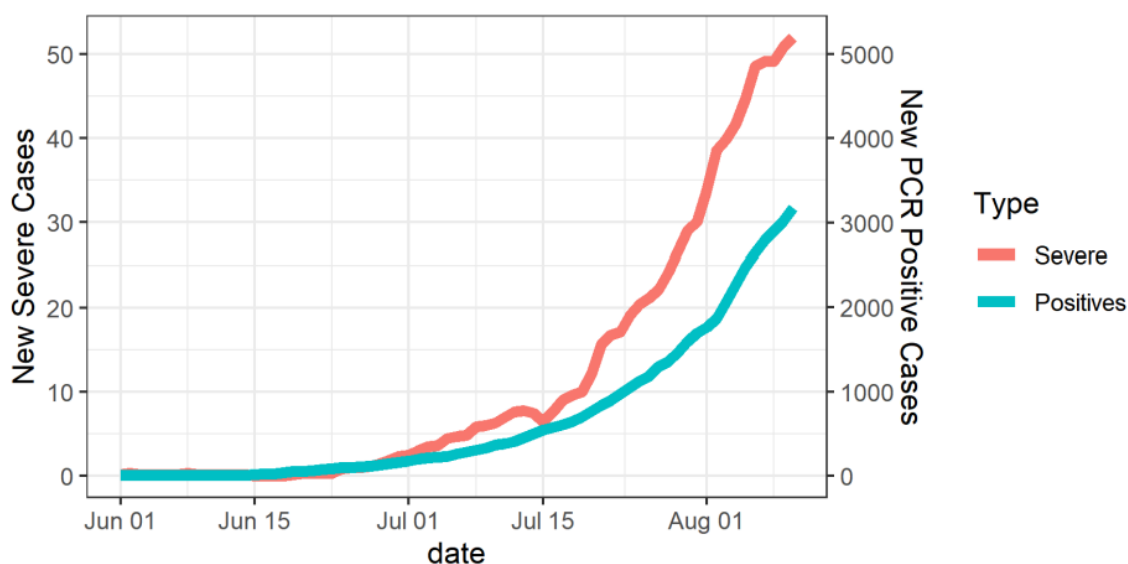
■ Post dose 3 titers vs. the Delta variant are >5-fold post dose 2 titers in 18-55 y/o & >11-fold post dose 2 titers in 65-85 y/o

Source: Pfizer July 28, 2021 Public Teleconference

## Israel studies

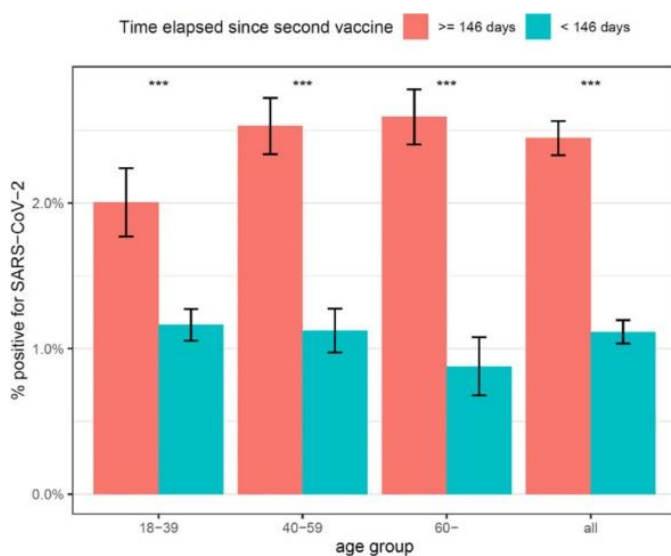
The mass vaccination programme in Israel began in December 2020 using the Pfizer vaccine which led to a sharp decline of COVID-19 cases. After a period with almost no infections, a resurgent COVID-19 outbreak began mid-June 2021. This may have been due to reduced effectiveness of the vaccines against Delta and/or waning immunity.<sup>10</sup>

Figure 8: COVID-19 documented infections (blue) and severe COVID-19 cases (red) in fully vaccinated individuals in Israel, from 1 June 2021



Recent studies from Israel have reported higher infection rates in individuals vaccinated earliest compared with those vaccinated later.<sup>11</sup> In this large population study of patients tested for COVID-19 following two vaccine doses, we observe a significant increase of the risk of infection in individuals who received their last vaccine dose since at least 146 days ago, particularly among patients older than 60.

Figure 9:



<sup>10</sup> [Waning immunity of the BNT162b2 vaccine: A nationwide study from Israel \(medrxiv.org\)](#)

<sup>11</sup> [Elapsed time since BNT162b2 vaccine and risk of SARS-CoV-2 infection in a large cohort \(nih.gov\)](#)



The number of positive polymerase chain reaction (PCR) tests started to rise exponentially (doubling roughly every 10 days) in Israel during June 2021, with a significant number of infections reported in vaccinated individuals. The second dose was administered three weeks after the first dose in the vast majority of recipients, in contrast to the UK where there was a 12 week gap between doses. The longer gap between doses is thought to have offered an advantage to the UK compared to Israel. Direct comparison with the UK is difficult because the vaccination programmes in the UK and Israel are different, principally in the length of time between first and second dose (3 months in the UK, 3 weeks in Israel) and the majority of vaccine used (predominantly AZ in the UK, Pfizer in Israel).

### **Further Studies**

Analysis of other coronaviruses has led to an estimation that natural antibody-mediated protection for SARS-CoV-2 is likely to last for 1–2 years and therefore, if vaccine-induced antibodies follow a similar course, booster doses may be required. However, other factors such as memory B- and T-cells and new viral strains will also affect the duration of both natural and vaccine-mediated immunity.<sup>12</sup>

The latest analysis from the ZOE COVID-19 study (which investigates real world vaccine effectiveness) estimates protection provided by two doses of the Pfizer and the AstraZeneca covid-19 vaccines wanes within six months.<sup>13</sup>

### **Limitations**

All studies point towards there being a possibility of COVID-19 waning immunity, particularly from vaccination. However, when interpreting the results, the limitations of the studies must be taken into account.

Firstly, in the UK, certain groups were targeted for certain vaccines (i.e. health care workers were mainly given Pfizer, whereas care home residents were more likely to have had AZ). Adjustments and stratified analyses were used to account for these factors in the PHE study, however, this is unlikely to account for all confounding.

Secondly, as the pandemic has progressed, there will be an increasing number of individuals who have been previously infected, both in the vaccinated and the unvaccinated group. Protection due to previous infection in the comparator group will attenuate VE over time.<sup>14</sup>

Additionally, care should be taken when comparing studies from the UK with international studies since vaccination programmes may differ. For example, Israel had a 3 week gap between first and second doses of the Pfizer vaccine whereas the UK had longer periods between doses, and administered AZ also.

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<sup>12</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8319587/> , published 29 July 2021

<sup>13</sup> [Covid-19: Protection from two doses of vaccine wanes within six months, data suggest \(bmj.com\)](#)

<sup>14</sup> [PHE: Duration of protection of COVID-19 vaccines against clinical disease, 9 September 2021 - GOV.UK \(www.gov.uk\)](#)

## Modelling

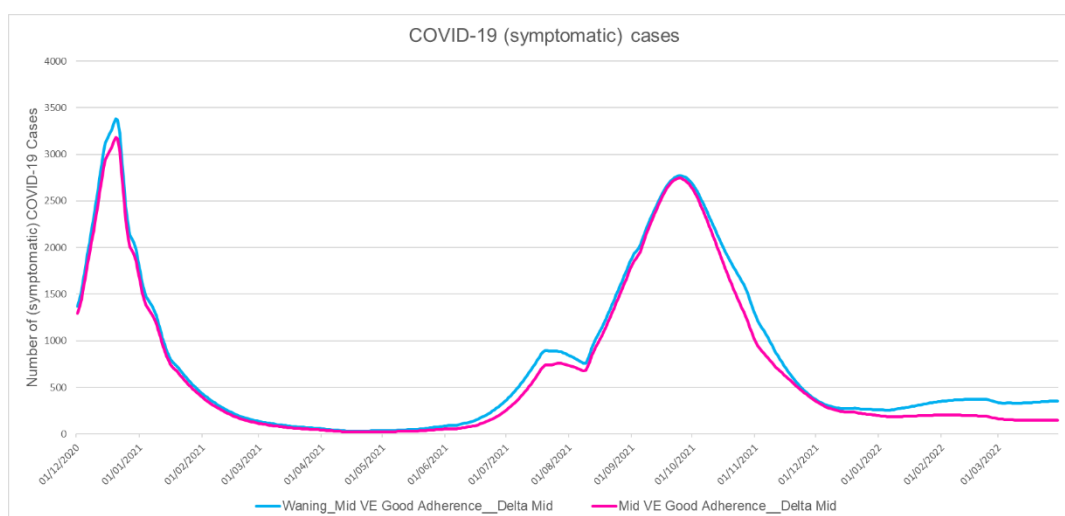
There is compelling evidence that waning of immunity occurs over time though there is considerable uncertainty around the timing and impact. Modelling has been carried out to determine the effect different levels of immunity may have on COVID-19 cases, hospitalisation and deaths.

### Swansea University Epidemiological modelling

The latest Swansea University modelling includes scenarios with waning immunity taken into account. It assumes that natural immunity from infection wanes after 3 years and that vaccine effectiveness wanes after 8 months post vaccine (one dose). In the short term, there is minimal impact of waning immunity. However, over longer time periods, it will have more of an effect.

For ease, we have included the central Swansea University scenarios only (mid-delta variant assumptions, mid vaccine efficacy, good adherence to restrictions). The 'standard' scenario where waning immunity is not included and the 'waning' scenario where it is, are included in the following charts for comparison. Tables showing the totals and peaks for each of these scenarios between 1 October 2021 and 31 December 2021 are also included.<sup>15</sup> In these scenarios, waning immunity starts to have a bigger effect in Spring 2022 but it does not lead to a significant fourth wave in the time horizon that the scenarios cover.

Figure 10: The number of COVID-19 (symptomatic) cases estimated by the Swansea University model central scenarios to 31 March 2022.



<sup>15</sup> More detail on Swansea University modelling can be found [here](#)

Figure 11: The number of confirmed COVID-19 admissions estimated by the Swansea University model central scenarios to 31 March 2022.

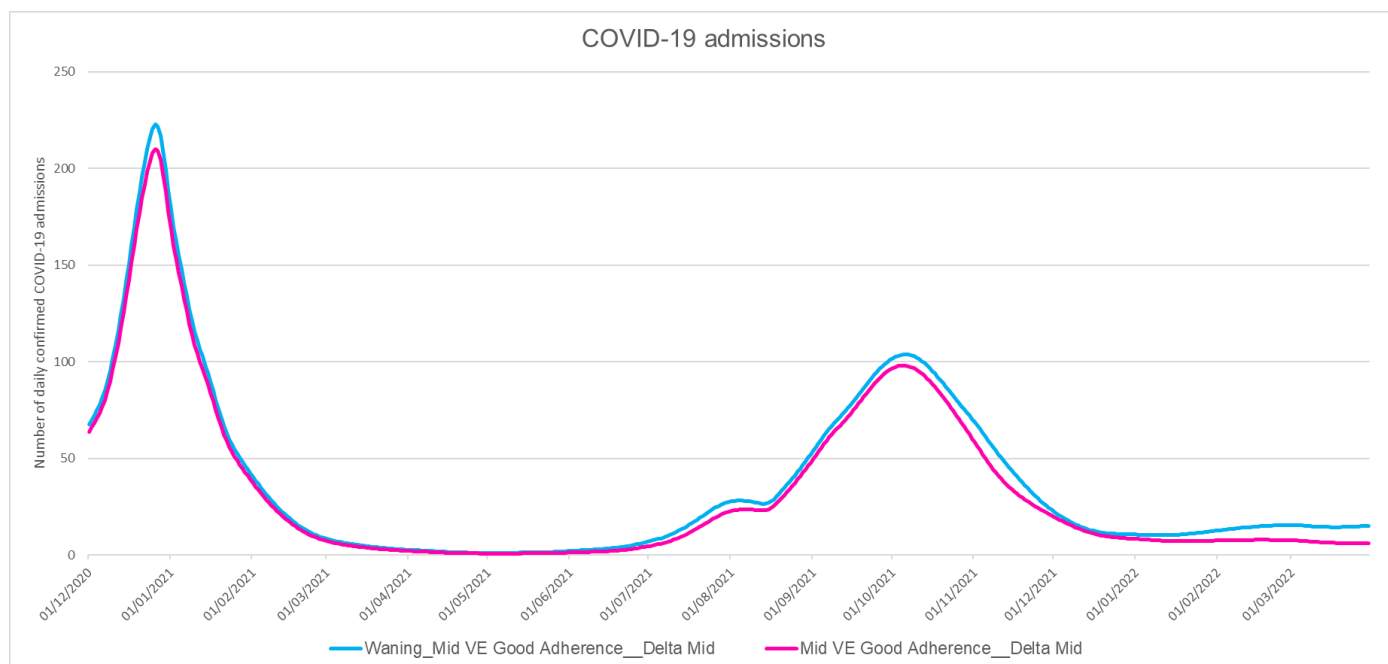


Table 1: Total number of cases, deaths, admissions and ICU admissions between 1 October and 31 December 2021

	Cases	Deaths	Admissions	ICU Admissions
Central scenario - no waning immunity	83,900	1,180	4,100	330
Central scenario - waning immunity included	94,100	1,300	4,600	380

Table 2: Peak number of cases, deaths, admissions and ICU admissions between 1 October and 31 December 2021

	Cases	Deaths	Admissions	Bed occupancy	ICU bed occupancy
Central scenario - no waning immunity	2,600	20	100	1,000	90
Central scenario - waning immunity included	2,700	20	100	800	80

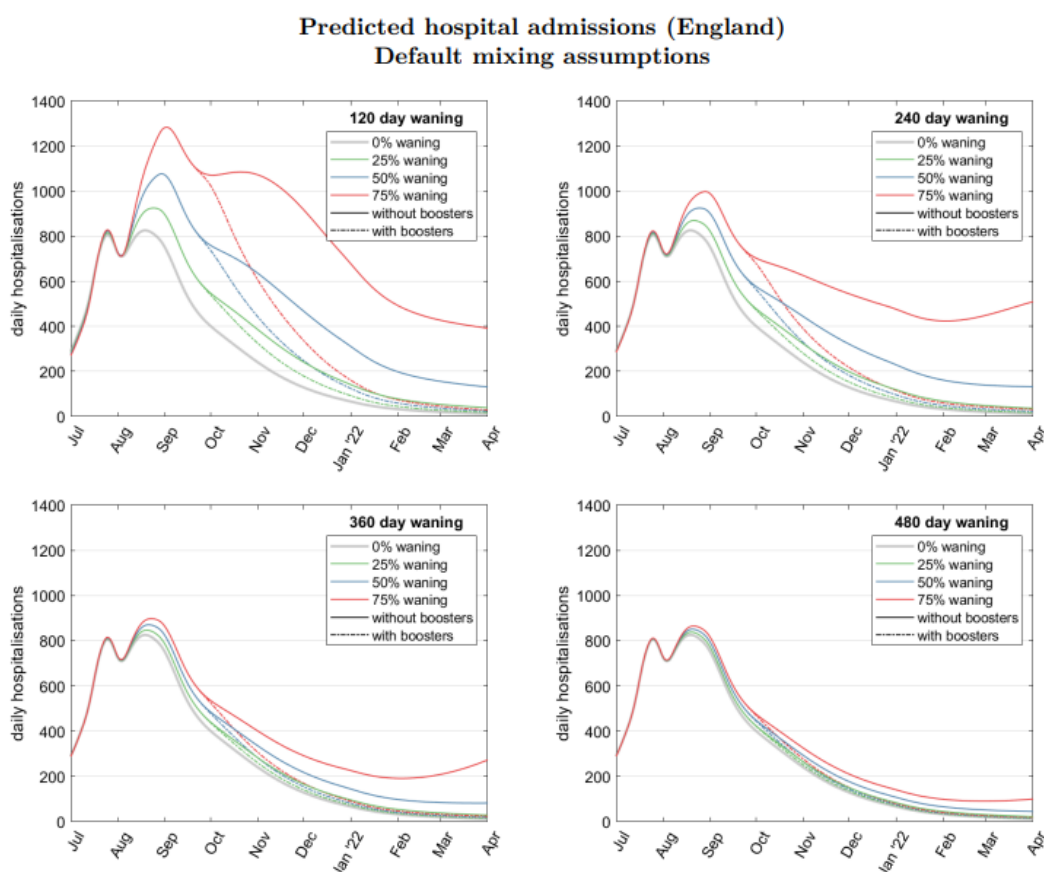
### Warwick University modelling

Warwick University modelled the impact of booster vaccines by considering the total number of hospital admissions over the period September 2021 to April 2022. The no-waning scenario is predicted to generate around 31-55 thousand total hospital admissions over the period of study. Rapid waning has the potential to generate over 102-313 thousand hospital admissions. Therefore, waning immunity can increase the

number of admissions by up to ten times the number of admissions if immunity did not wane.

The scenarios produced by Warwick University have 3 vaccine efficacy waning immunity assumptions where vaccine efficacy wanes by 25%, 50% and 75%, and 4 assumptions on the time taken for vaccine efficacy to wane: 120, 240, 360, and 480 days.

Figure 12: Projected daily hospitalisation admissions for each waning scenario. Solid lines show scenarios without boosters, and dashed lines include boosters given to all individuals over the age of 50 in age order. Thicker grey lines show projections with no waning.



Where immunity is assumed to wane more quickly (less than or equal to 240 days), introducing boosters for the over 50s (dashed lines in Figure 11) can dramatically reduce the lengthy tail of infection. The increased benefit from re-vaccinating younger individuals is likely to be minimal. The Swansea University scenarios above assume that immunity to vaccines wanes after 8 months, this is closest to the '240 day waning' Warwick University' scenario. With 75% waning scenario in the top right chart of Figure 12, the peak of around 1,000 admissions occurs in September 2021. This is for England only, and would equate to around 56 admissions for Wales if apportioned by population size (ONS 2020 mid-year estimates). However, the Swansea University models estimates a peak of around 100 in October.

For the slower waning rates (360 to 480 days) there is far less impact (between Sept 2021 to April 2022) with the greatest drop in protection for the over 50's not occurring until later in 2022. In this scenario, boosters in the autumn will have limited impact over the winter period studied and a later booster campaign in 2022 may be more effective.

In all the scenarios simulated, the greatest impact (over the period Sept 2021 to April 2022) comes from the vaccination of those over 70 (priority groups 1-4) while vaccinating everyone over 50 (priority groups 1-9) does not generate much additional benefit.

Careful estimation of the waning period from available data will be key to determine the likely impact of boosters; but the degree of waning (here models consider 25%, 50% and 75%) remains uncertain.

Limitations of this model is that after a vaccine booster dose returns individuals to original efficacy levels, further waning of immunity is no longer considered. Also, there is no differentiation between vulnerable and non-vulnerable individuals although there is growing evidence to suggest that the vulnerable may experience lower levels of efficacy.

### Population immunity modelling

COVID-19 population immunity estimates provided by the Technical Advisory Cell (TAC) modelling team were published in August 2021.<sup>16</sup> The paper details the analysis carried out and shows the effect of waning immunity on the percentage of the population of Wales estimated to have immunity against COVID-19 infection. Additionally, an update of this population immunity level (without waning immunity) are published each week in the COVID-19 situation report (CSR).<sup>17</sup>

Scenarios have modelled assuming immunity wanes after 7 months and 10 months.

- Assuming immunity wanes after 210 days (roughly 7 months), 65% [58%, 72%] of people **aged 16 and over** in Wales were estimated to have had some immunity against COVID-19 infection at 4 September 2021.
- Assuming immunity wanes after 210 days (roughly 7 months), 54% [48%, 60%] of the **total population of Wales** were estimated to have had some immunity against COVID-19 infection at 4 September 2021.

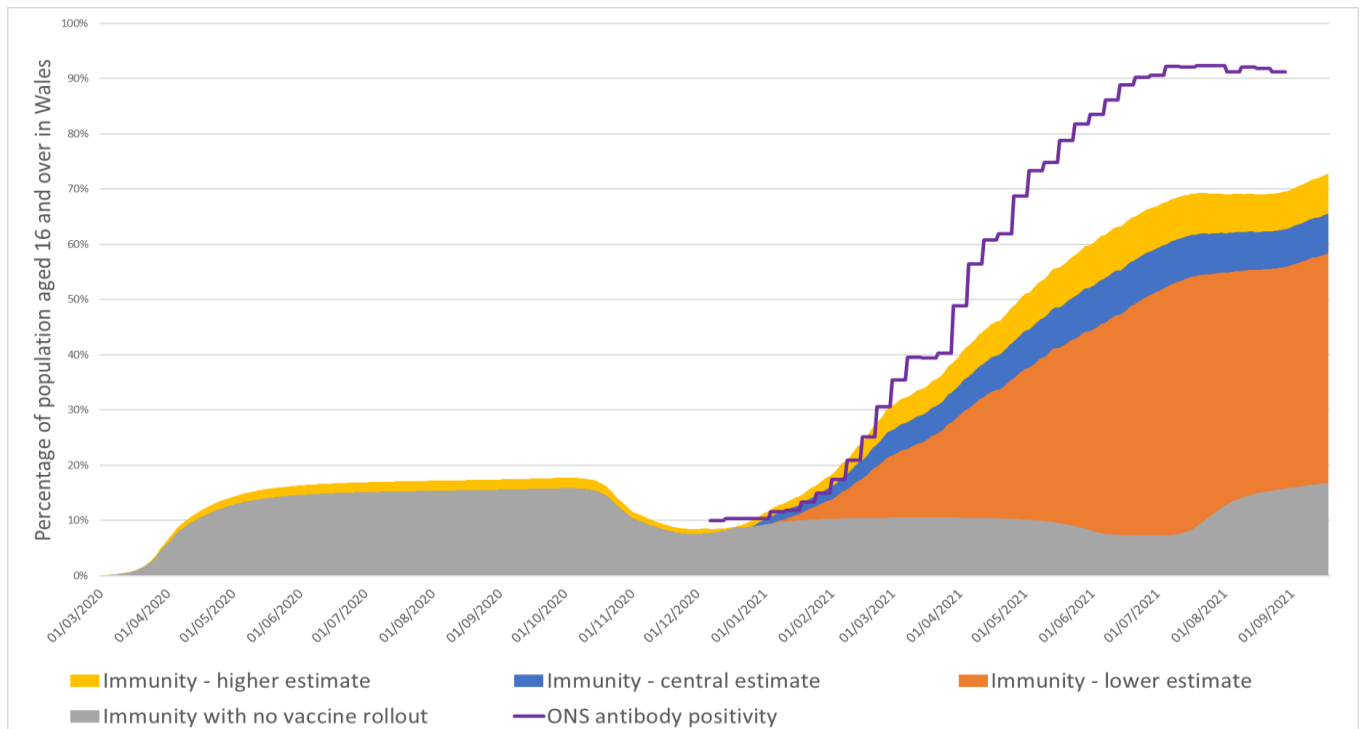
*Figure 13: Immunity estimates and antibody status of individuals aged 16 and over in Wales (assumption: immunity against infections wanes after 210 days)*

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<sup>16</sup> [Technical Advisory Group: COVID-19 population immunity estimates in Wales | GOV.WALES](#)

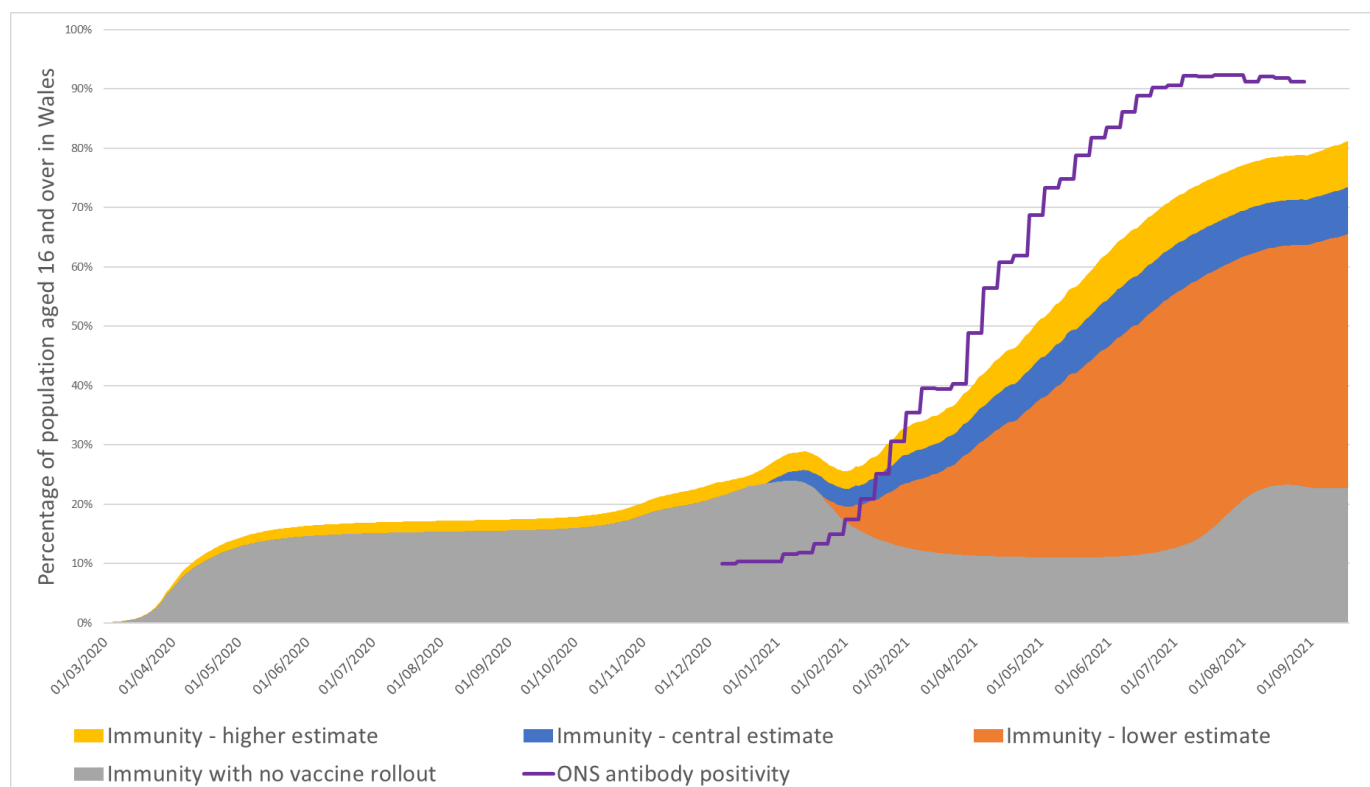
<sup>17</sup> [COVID-19 situational reports | GOV.WALES](#)

Sources: [ONS COVID-19 Infection Survey](#), [PHW](#), [SAGE vaccine effectiveness estimates](#), Swansea University modelling



- Assuming immunity wanes after 300 days (roughly 10 months), 73% [66%, 81%] of people **aged 16 and over** in Wales were estimated to have had some immunity against COVID-19 infection at 4 September 2021.
- Assuming immunity wanes after 300 days (roughly 10 months), 61% [55%, 68%] of the **total population of Wales** were estimated to have had some immunity against COVID-19 infection at 4 September 2021.

Figure 14: Immunity estimates and antibody status of individuals aged 16 and over in Wales (assumption: immunity against infections wanes after 300 days)



Sources: [ONS COVID-19 Infection Survey](#), [PHW](#), [SAGE vaccine effectiveness estimates](#), Swansea University modelling

## Interpretation/Conclusion

There is still great uncertainty around the duration and impact of waning immunity. Multiple sources indicate that waning of immunity particularly immunity gained from vaccination is a very real possibility. It is especially pronounced in older and more vulnerable individuals. Immunity gained from vaccines against hospitalisations and deaths is much stronger than immunity against infections, and immunity from vaccines wanes more quickly and dramatically in the AZ vaccine compared with Pfizer.

Modelling shows the potential impact that waning of immunity can have on cases, hospitalisations and deaths. However, the models included in this report assumes an individual is either immune to COVID-19 or they are susceptible to it. In reality, the immune system is far more complex and even without the presence of detectable antibodies, an individual may still have some immunity against infection and particularly against more severe illness if immunity from infection or vaccination was previously acquired. An immune response does not rely on the presence of antibodies alone. An individuals' "T cell" response also provides longer term protection. The long term memory of the immune system can often fight off a reinfection for years. However, reinfections of COVID-19, though rare, are being observed. The studies summarised here are trying to infer the likely time until waning immunity for a whole population from a sample of the tail end of the distribution who

have been reinfected – they are stratified by age and vaccine, and studies have attempted to control for other characteristics, but there may be other unobserved factors that mean that the people who have been reinfected so far are not representative of the whole vaccinated or previously infected population.

Numerous studies conclude immunity against COVID-19 wanes anywhere from 10 weeks to 10 months. However, caution should be taken when interpreting results due to the limitations of the studies and the significant uncertainties around understanding of immunity.