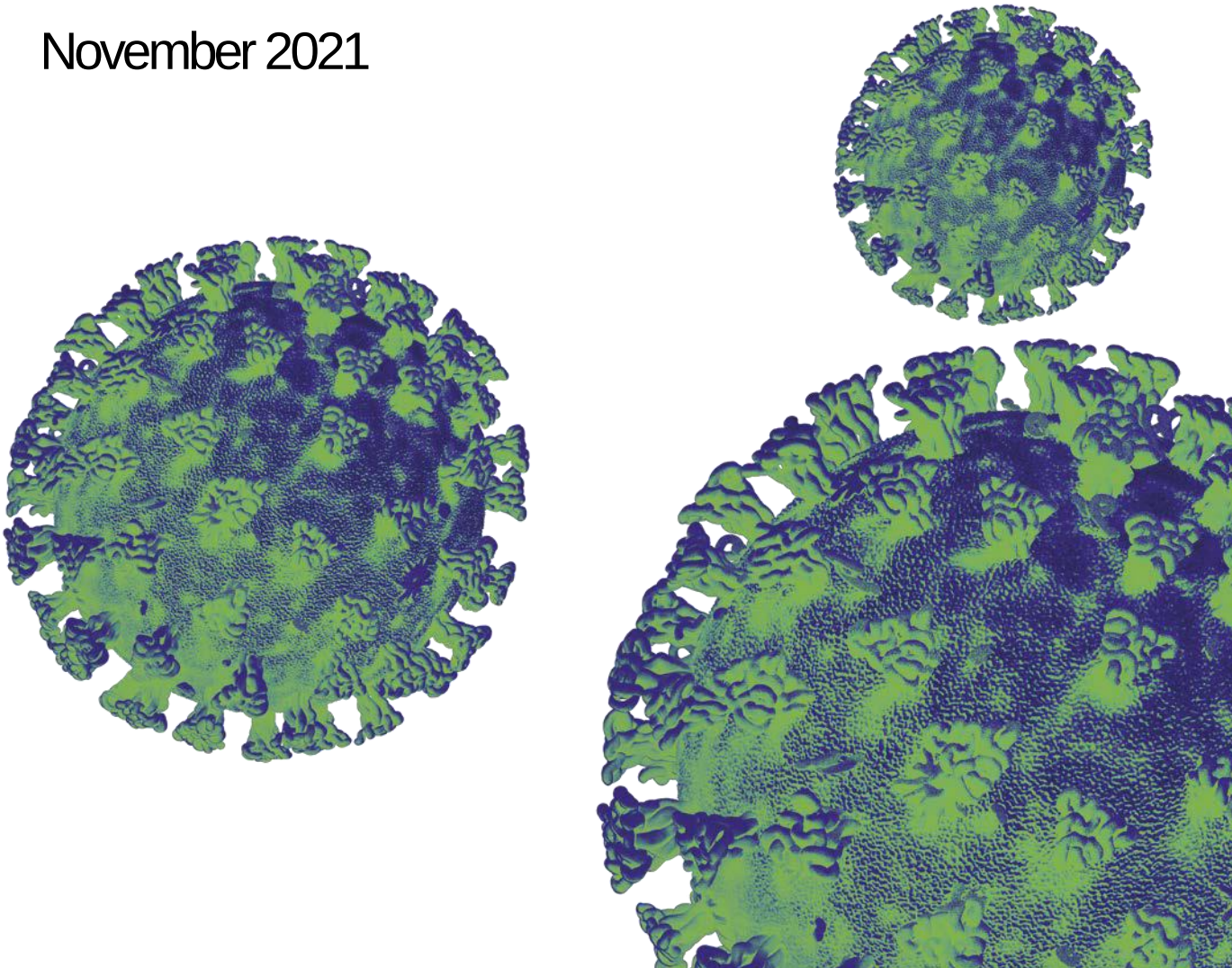
Llywodraeth Cymru
Welsh Government

Technical Advisory Group

The impact in Wales of the COVID-19 ‘false negative’ PCR tests reported during September/October 2021

November 2021



The Impact of the COVID-19 'False Negatives' PCR tests, in Wales

November 2021

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Summary

- There were an estimated 43,000[1] falsely assigned negative COVID-19 tests for England and Wales from one lab (Immensa) during September and October 2021.
- Public Health Wales (PHW) have carried out analysis estimating that this led to around 6,600 incorrectly assigned negative cases in Wales during the affected period (2 September to 12 October 2021).
- During the weeks commencing 27 September 2021 and 4 October 2021, there was a mismatch between a large proportion of linked LFT-PCR tests (83% and 93% respectively). This mostly occurred where a previous LFT was positive, yet the follow up PCR result was negative.
- The knock on effects on numbers of secondary cases generated and the subsequent admissions and deaths are unknown and difficult to estimate. Our

[1] Testing at private lab suspended following NHS Test and Trace investigation - GOV.UK (www.gov.uk)

current understanding is that there was a modest impact in some areas of Wales.

Objective

The objective of this paper is to estimate of how many false negative cases of COVID-19 there were in Wales as a result of the Immensa PCR laboratory issue that occurred in September to October 2021, and try to characterise the impacts.

Background

During September/October 2021, one COVID-19 testing lab, Immensa health Clinic Limited ('Immensa') sent incorrect negative PCR test results to some recipients who would have tested positive for COVID-19. The exact number is unknown, but out of 400,000 negative results between 2 September 2021 and 12 October 2021, around 43,000 in England and Wales are estimated to have been incorrectly assigned as a negative results ('false negative').[2] The number of these false negatives assigned to Wales has been estimated by PHW to be around 6,600.

The Immensa lab was a 'surge' lab, meaning samples were sent to the lab from areas of high prevalence where there was difficulty meeting the testing demand. The areas affected seems to largely have been South West England and South Wales. The impact in Wales in missed positive test numbers (and therefore lower test positivity) was estimated to be greatest in Blaenau Gwent, Newport, Neath Port Talbot, Caerphilly and Rhondda Cynon Taf.

Although the Immensa Lab operated from 2 September 2021 to 12 October 2021, most tests sent from Wales occurred in a 3 week window within this period (from 26 September to 12 October) when between 4% and 11% per week of Welsh residents' COVID-19 tests were directed to the Immensa lab.

[2] Testing at private lab suspended following NHS Test and Trace investigation - GOV.UK (www.gov.uk)

Surveillance information on COVID-19 cases

COVID-19 confirmed cases were under-reported in Wales for up to 7 weeks between 2 September and 12 October 2021.

From visual examination of surveillance indicators by Local Authority (LA), those areas most affected observed a small, likely false, decline in COVID-19 activity during the period affected, followed by a sharp rise. This rise may have been contributed to from people not self-isolating because of false negatives but also a small number of people being retested within the ten day period.

This trend is observed in LAs within the Aneurin Bevan Health Board area. It is plausible that the sharp rise observed in affected LAs (such as Blaenau Gwent), but not observed in LAs not affected by the incident, may have resulted from secondary transmission in people who would otherwise have been isolating. However, it is not possible to confirm this hypothesis without further more detailed analysis and it may also be the case that areas that were increasing more quickly before and during the Immensa issue sent more samples to the Immensa lab, which makes discerning cause and effect more difficult.

Analysis

Several pieces of analysis to estimate the impact of the Immensa issue have been carried out by different organisations. The results differ due to different methodologies being used to estimate the number of ‘false negatives’ attributed to Welsh residents. An overview of the methods used by PHW and Swansea University and the results obtained are detailed in this section.

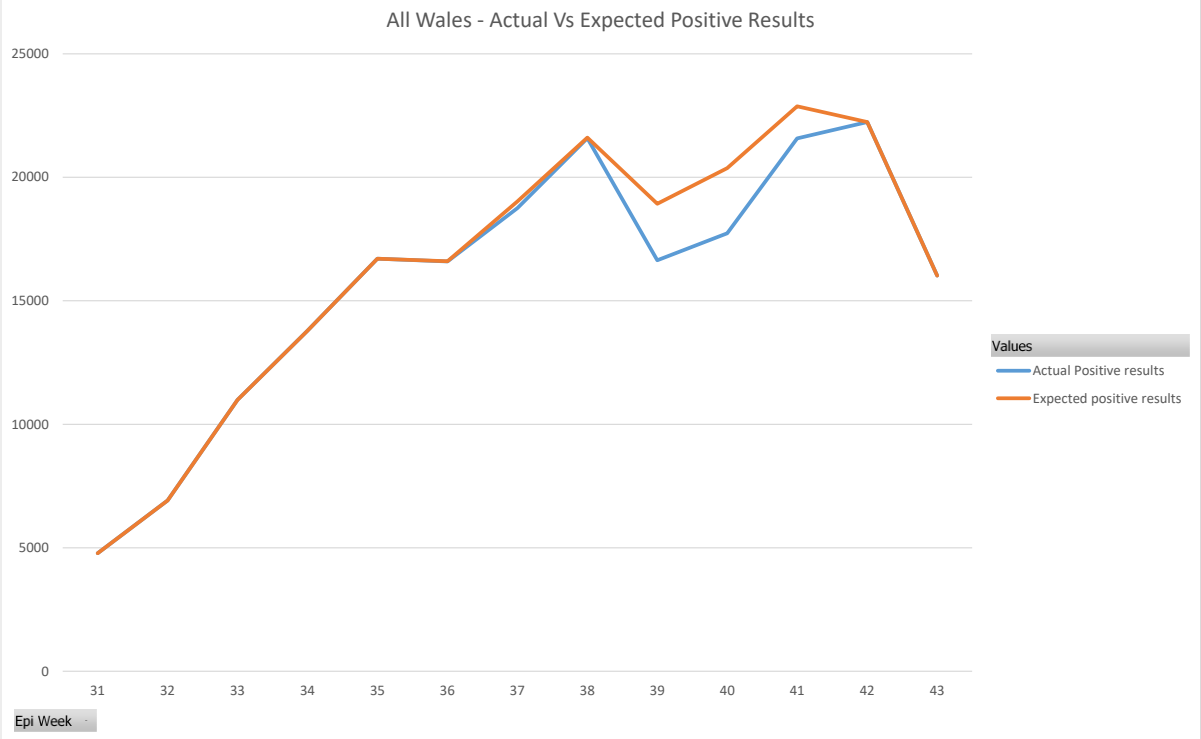
Public Health Wales (PHW) – Estimation of missing cases analysis

PHW used the positivity rates of other testing labs to estimate the number of positive COVID-19 cases missed in Wales. The unit of analysis (for the numerator and denominator) was a test, rather than deduplicating where individuals had taken more than one test over this time period.

One percent of the tests undertaken by the Immensa lab were reported as positive compared to 11.4% from other laboratories. By applying the positivity in all non-

Immensa labs to tests carried out in the same period by the Immensa lab, the expected number of positives based on all routine test data for that period was 215,683, giving 5,273 missed positive tests (expected minus actual). By applying predicted positive proportions to each local authority/age group/week number stratum, expected positives increased to **6,606**.

Figure1: All Wales actual positives tests Vs expected positive tests displayed by Epi Week



PHW also carried out a deduplication analysis, showing that around 90% of tests represented unique individuals. Since this does not greatly alter the overall results, and also because individuals may respond to individual testing episodes in terms of their precautionary behaviour, the estimates including duplicate testing episodes are reported with this limitation recognised.

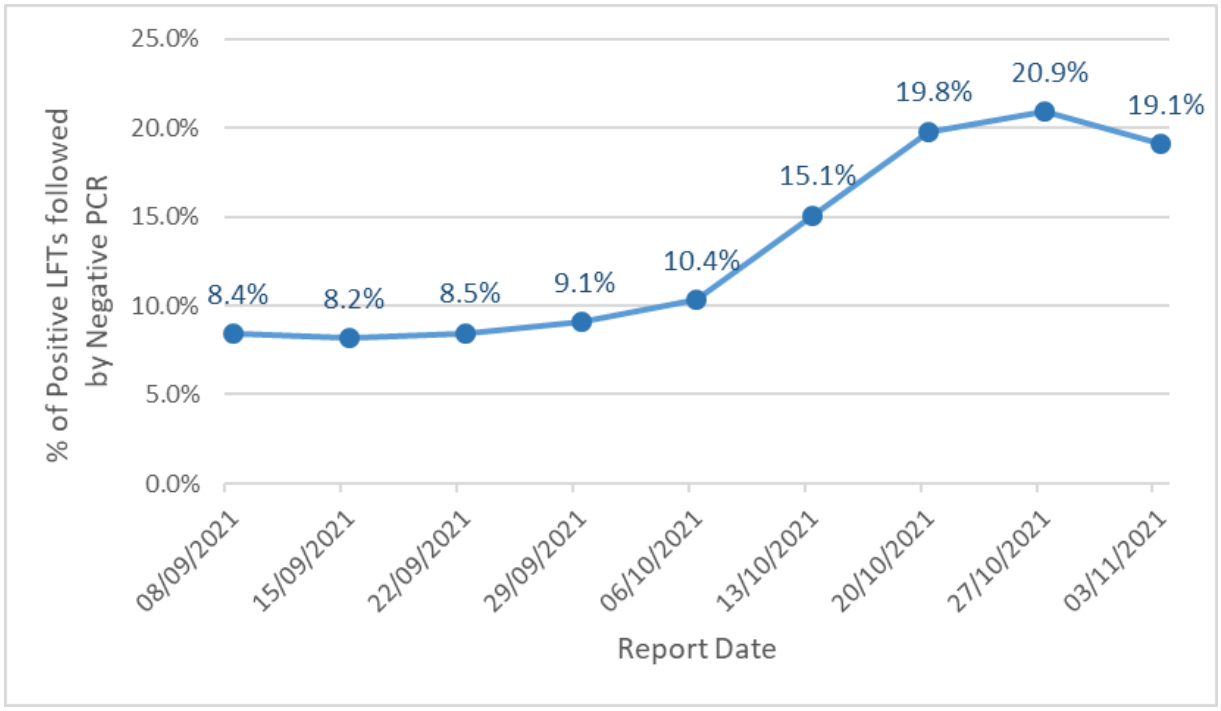
PHW LFT-PCR linkage analysis

PHW carried out retrospective lateral flow testing (LFT) -PCR linkage analysis, which in Wales is analysed as a separate surveillance system as the reasons and methods for accessing testing are different to those for PCR tests. This analysis could be useful in the future to determine at what point the surveillance data may indicate a

problem with testing, although this is not a substitute for quality monitoring at the laboratory level.

The percentage of Positive LFTs followed by Negative PCR began to increase in the report dated 29 September. However, this only became noticeable on 13 October 2021 as can be seen by figure 2 below.

Figure 2: Reported LFT Positive-PCR Negative results as a percentage of total LFT positive tests followed by a PCR (+/- 1 day), since 08/09/2021 (date of change of linkage methodology).



Out of all the follow up PCR tests processed in Immensa which were linked to LFTs in the reporting weeks commencing 27 September and 4 October 2021, there was a mismatch between a large proportion of tests (83% and 93% respectively). This mostly occurred where a previous LFT was positive, yet the follow up PCR result was negative.[3] This occurred over 1,700 times during this reporting fortnight.

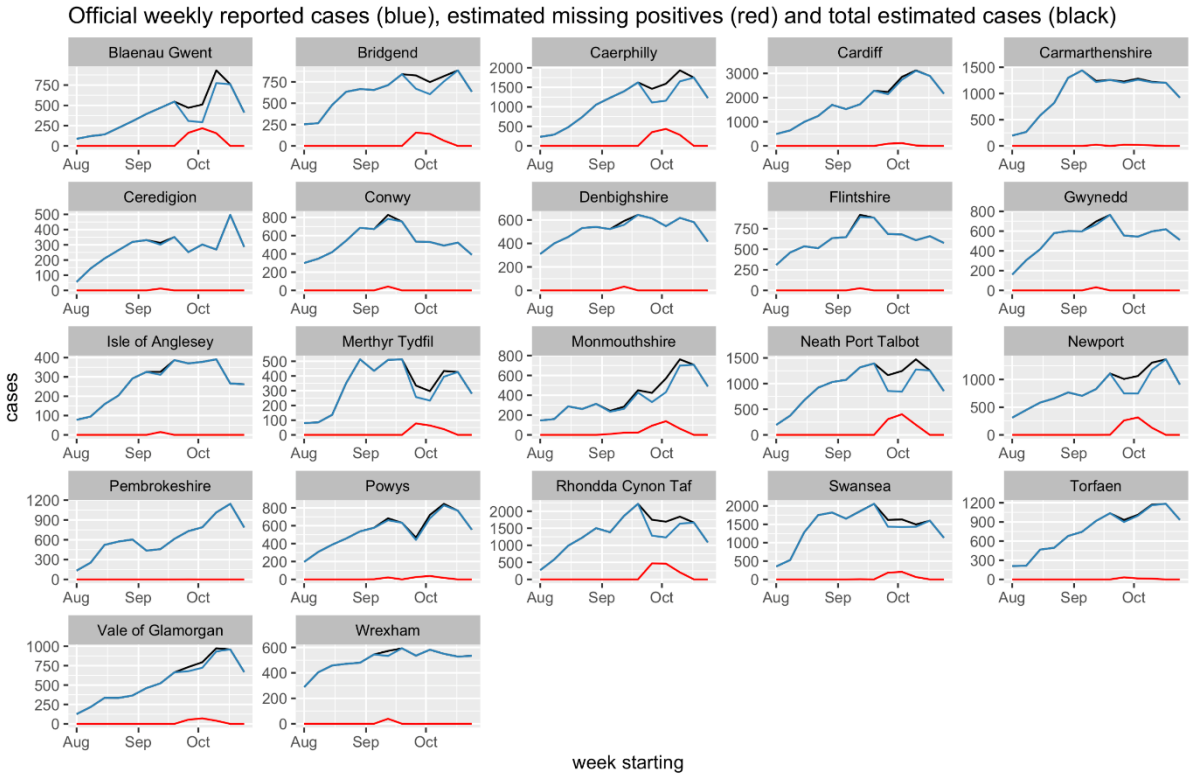
[3] Only 1% of tests were mismatched where the LFT result was negative and the PCR was positive in the reporting week commencing 27 September 2021, and 0% in the week commencing 4 October 2021.

Swansea University analysis and modelling

Impact on transmission

The estimated number of weekly missing positive COVID-19 results was plotted against the number of official reported cases, by local authority (LA). The results are shown in Figure 3. The localised distribution of the missing cases can clearly be seen. In addition, the cases were almost exclusively missed during a period of 3 weeks.

Figure 3: Reported (blue), estimated missing (red), and estimated total cases (black) by local authority



Given the wide distribution of impact, further analysis was carried out to consider whether there was evidence of an increase in transmission in the period following the reporting of false negatives, in comparison to the period immediately prior. The growth rate in total cases (using the estimate of total cases shown in Figure 3) was

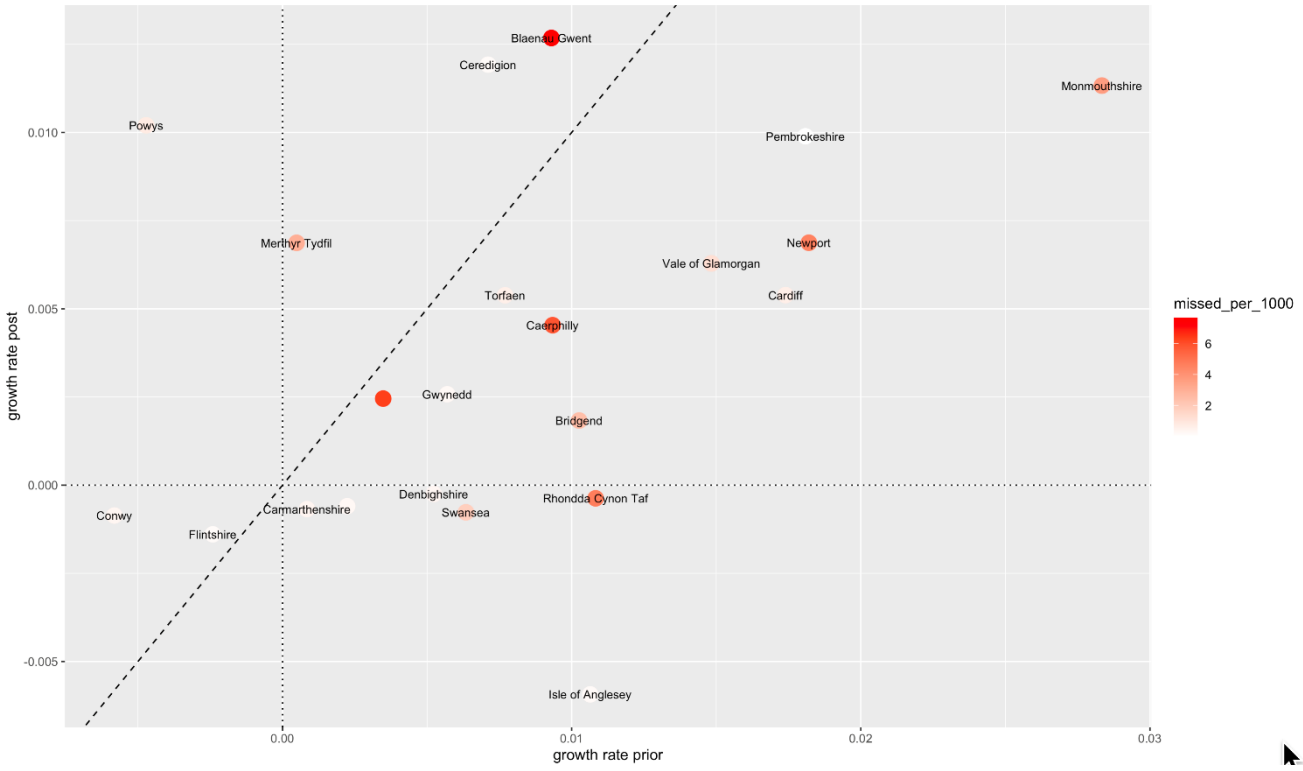
estimated by fitting a linear regression to the log transformed case count in each LA in two time periods:

- Growth rate prior to event estimated between 06/09/21 and 25/10/21
- Growth rate post event estimated between 26/09/21 and 24/10/21

There was no strong signal that would represent an increase in case growth rate dependent on number of missed cases. Figure 4 shows the estimated growth rates prior and post the laboratory event. In general, there was a weak positive correlation of growth rates at the LA level ($p = 0.08$), however over this period there was considerable variation, with case rates increasing, decreasing, or staying the same, over the period. The case growth rate post event was not significantly associated with the number of missing cases.

During this period there was considerable variability between LAs. It is possible that in some areas that experienced large numbers of missed cases, there was an increase in case rates following the laboratory event. However this pattern is not consistent across all affected LAs. For example a change in case rates was noted in the heavily affected Blaenau Gwent and Merthyr Tydfil LAs, but not in the similarly affected Neath Port Talbot or Caerphilly. Furthermore, LAs that were unaffected also showed variability, and could be seen to show increased (e.g. Powys), decreased (e.g. Isle of Anglesey), or unchanged (Carmarthenshire) case rates over the period. This high variability may reflect the stage of the epidemic in different areas having different levels of population immunity, making it difficult to tease out effects of laboratory false positives.

Figure 4: Change in case growth rates by LA before (x axis) and after (y axis) the laboratory event. The region above the dashed line indicates an increase in growth rate. LAs are colour coded by the number of missed cases per 100,000 population. Note that growth rates were fitted to adjusted case numbers (observed + estimated missed).



Conclusion

The true number of missed cases due to the Immensa Lab event may never be known. PHW estimate the figure to be around 6,600 missed test positives. Swansea University analysis suggests the case growth rate following the Immensa lab event was not significantly associated with the number of missing cases. Additionally, there was considerable variability between Local Authorities (LAs). It is possible that in some areas that experienced large numbers of missed cases, there was an increase in case rates following the laboratory event. However this pattern is not consistent across all affected LAs.

Overall it is likely that there was a modest impact, albeit with variation between areas in Wales, which is unlikely to have changed the underlying patterns of transmission.