Institute and Faculty of Actuaries

Mortality Impact of COVID-19 Vaccination in England:

publication of models and an update

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Disclaimer

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Introduction

This report presents updated data and findings, as a follow-up to the earlier results in the paper "Mortality Impact of COVID-19 Vaccination in England: Counterfactual Insights from Gompertz to Machine Learning", published on 1st March 2021. Additionally we provide estimation of the number of deaths prevented by vaccination and compare against the Public Health England and Warwick University studies.

Publication of models

We have now published the associated actuarial and machine learning mortality models for open access at https://github.com/wuihuajohnng/Mortality_Impact_Vaccination.

Methodology and data sources

1. **Vaccination rate** is the cumulative percentage uptake of first doses in National Immunisation Management Service (NIMS) data, published by the National Health Service (NHS).

2. **Community antibody positivity** is based on Office of National Statistics (ONS) data on presence of antibody to the coronavirus within the community population, excluding those in care homes or other institutional settings. Blood test results testing positive for antibodies could be resulting from past infection or vaccination.

3. **Mortality improvement** measures the reduction in weekly mortality rates of the 80+ age group since the start of vaccination program. It is calculated as *1 - 'Actual'/'Expected'* and reflects the cumulative effect of the vaccination roll out as discussed in *Results*.

   'Actual' is the observed weekly mortality rate of ages 80+, according to reported ONS registered deaths and NHS hospital deaths. *'Expected'* is the expected level of weekly mortality of ages 80+ under the counterfactual scenario with no vaccination, which could be predicted from the observed weekly mortality of the largely unvaccinated younger age groups (see original paper for detailed methodology).

Results

Updated results of experience in ages 80+ are shown in Figure 1:

- Vaccination rates exceeded 90% by 7th February 2021
- 75.7% of community antibody positivity during the period 4th February to 3rd March 2021
- 67% reduction in hospital mortality, as of week-ending 13th March 2021
- 60% reduction in ONS registered deaths, as of week-ending 12th March 2021

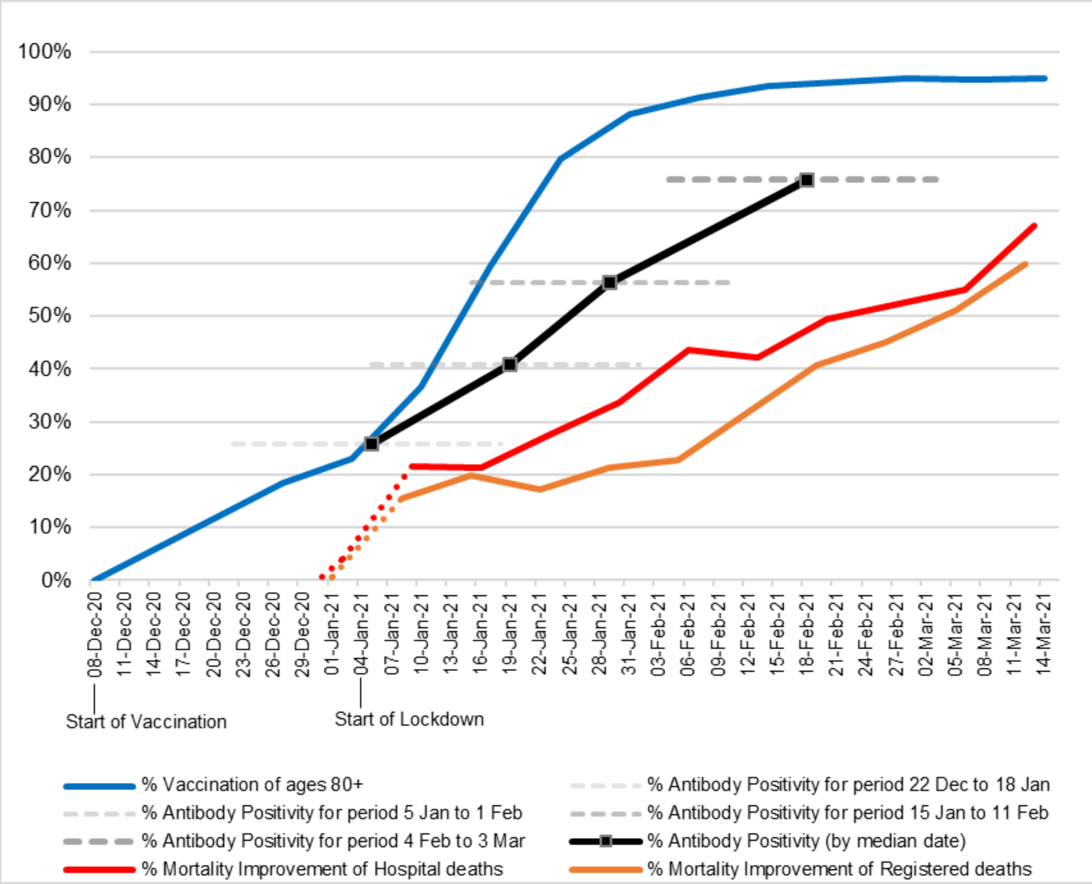
The percentage of community antibody positivity and mortality improvement are expected to continue to increase.

In terms of cumulative numbers of deaths prevented, we estimate that:

- During the period from mid-January 2021 until end of February 2021, vaccination is estimated to have prevented 8,000 deaths in those aged 80 and over

- During the period from mid-January 2021 until 12th March 2021, vaccination is estimated to have prevented 10,300 deaths in those aged 80 and over

Figure 1: Timeline of percentage of vaccination uptake, percentage of community population testing positive for antibodies to SARS-CoV-2, as well as estimated mortality improvement of hospital deaths and registered deaths of ages 80+ in England



The mortality improvement of registered deaths and hospital deaths, represented by red and orange lines in Figure 1, are calculated as *1 - 'Actual'/'Expected'*. They are the reflections of *'Actual'/'Expected'* shown in Figure 4 and Figure 8, where their confidence intervals are also shown. The solid red and orange lines imply the difference between actual and expected deaths is statistically significant at 95% level, in contrast to dashed lines above which demonstrate statistically insignificant difference.

It is worth noting the mortality improvement calculation does not rely upon the vaccination rate or the level of antibody positivity data. Therefore, the time-series data associated with the vaccination rates, antibody positivity and mortality improvement in Figure 1 does provide greater insight into the drivers of mortality improvements.

Figure 1 shows a high degree of association between the slope of lines for vaccination rates, antibody positivity and hospital mortality reduction. This likely depicts the real-world impact of the logical sequence of the three interlinked events:

1. Starting with a rise in vaccination rates since early December 2020, this most likely caused an increase in percentage of ages 80+ testing positive for antibodies, which is the same causal conclusion made by an [ONS Infection Survey antibody data report (see Section 5).]

2. The rise in community antibody positivity (excludes those of care home residents) is followed by mortality reduction in hospital deaths. While the data shows strong association, the original paper considered the timing, other confounding factors (such as the January lockdown) and the pattern of trends, hence suggesting the positive mortality outcome is likely causative.

The mortality trend of ONS registered deaths was disrupted by care home outbreaks in January 2021, which affected hospital mortality to a lesser extent. However, the trend of ONS registered deaths returned to track closely to hospital mortality in February 2021, with a time lag that is within expectation.

Figure 2: Timeline of percentage of vaccination uptake, as well as percentage of community population of ages 70, 75, 80 and 85 testing positive for antibodies to SARS-CoV-2 in England

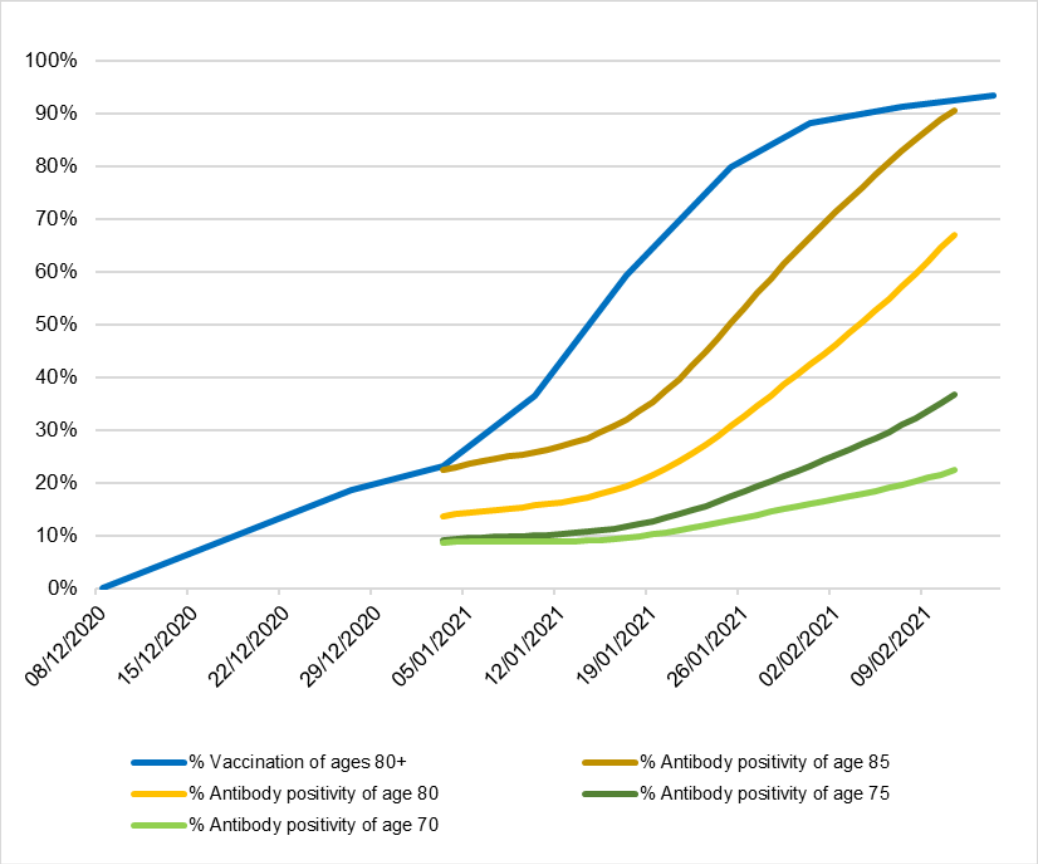


Figure 2 demonstrates that the likelihood of testing positive for COVID-19 antibodies in ages 80+ was already diverged from those of ages 70s in early January 2021, suggesting the vaccination might have started to increase antibody levels in December 2020. Thereafter, antibody positivity of 85-year-olds went over 90% by 11th February 2021, implying the success of vaccination coverage in this vulnerable subgroup.

Discussion

The mortality models are consistent with subsequent publication of antibody data. The results demonstrate that the high uptake of COVID-19 vaccination in ages 80+ is translating into substantial mortality improvement at the population level, an encouraging trend that has sustained for over two months.

Vaccine efficacy is defined as the performance of a vaccine in a vaccinated group compared to an unvaccinated group under optimal conditions (e.g. Randomised Controlled Trial). In contrast, *vaccine effectiveness* refers to the performance of vaccine in the real world. Our analysis of population-level data suggests a high vaccine effectiveness against death, which is independent of clinical trials. More accurate estimates of vaccine effectiveness could be derived from cohort studies, case-control studies and more granular data.

If the vaccines continue to have very high effectiveness against death in all age groups, (re)insurers could apply sensitivity testing on simpler assumption of vaccination supply and uptake to overlay mortality projections under an unvaccinated scenario, as one possible approach to estimate the COVID-19 related mortality outlook.

As one of the limitations, data shows the antibody level for ages 60 and below started to increase since the end of February 2021, so unsurprisingly from that point it began to violate the assumptions that the input age groups should be unvaccinated. The shelf life of the models is coming to an end, because the increasing vaccination rates in the younger ages would underestimate the expected mortality of ages 80+, and hence would underestimate the respective mortality improvement. Nevertheless, the models still have some value going forward if one adjusts the input mortality rates in younger age groups to account for prevalence of vaccination, or alternatively treat the output mortality improvement of ages 80+ as a minimum value (lower bound) due to the aforementioned risk of underestimation.

Comparison with the Public Health England model and Warwick model

Since the publication of our original paper, we have become aware of the research published by Public Health England (PHE) and Warwick University on 26th March 2021, titled "Impact of COVID-19 vaccines on mortality in England: December 2020 to February 2021".

There are similarities between their approach and our approach. Their analysis also adopted a counterfactual approach, where the observed number of deaths is compared with the number of deaths that would have been expected, if the vaccine had not been given during this time period.

Table 1 compares the approaches, assumptions and results of the PHE model, Warwick model and our model. The key differences are reliance on vaccine-related assumptions. Both the PHE model and Warwick model rely on assumptions of vaccine effectiveness against death, vaccine doses administered to date and time lags from vaccination to protection. Our model does not rely on any of these assumptions.

Rather than taking these assumptions as input into the model ("a priori"), it is possible to estimate them as output from the model ("a posteriori") where insights are extracted from observed actual mortality experience. Our model was then validated against the vaccination data and real-world antibody data.

Table 1: Comparison of Public Health England model, Warwick model and our model, in modelling mortality impact of COVID-19 vaccination in England

	PHE model	Warwick model	Our Model
Death definition	Deaths within 28 days of positive test	Deaths within 28 days of positive test	ONS registered deaths
Approach	Daily mortality impact = Vaccine effectiveness against mortality multiplied by vaccine coverage Then observed deaths were divided by the impact to estimate expected deaths	Use a dynamic age-structured model, matched to national and regional data, to compare simulations with and without vaccination. Include action of vaccination and capture prevention of infection and reduction in severe illness. Run multiple simulations to explore range of estimated parameters, to obtain mean of deaths by age.	Weekly expected deaths of ages 80+ is predicted from the observed mortality of younger age groups. Observed deaths were divided by expected deaths to estimate mortality impact
Vaccine effectiveness against death	81%	82%	Independent
Vaccine doses administered to date	Dependant	Dependant	Independent
Time lag from vaccination to deaths	31 days. This is used to estimate vaccine coverage	14 from vaccination to developing protection. See cited paper for more information	Independent
Deaths prevented in 80+ age group	5900 by the end of Feb 21	-	8000 from mid-Jan to end of Feb 21 10,300 from mid-Jan to mid-March 21
Total deaths prevented	Total deaths prevented in ages 70+ is 6100 by the end of Feb 21, based on 81% vaccine effectiveness If assuming 85% vaccine effectiveness, total deaths prevented is 6700	6592 deaths	-

Additional analysis and visualisation of mortality impact of the above three models are shown in the *Appendix*.

PHE reported an estimated reduction of 6100 deaths (5900 in ages 80+, 200 in ages 70-79), as a result of the COVID-19 vaccination programme up to the end of February 2021. The estimate of the

Warwick model is slightly higher, possibly because it accounts for deaths averted across all age groups and it also incorporates the secondary effects of the vaccine reducing transmission.

PHE's estimation of 6100 deaths averted is based on the assumption of 81% of vaccine effectiveness against death. If 85% of vaccine effectiveness was used instead, it would increase the number of deaths averted from 6100 to 6700. PHE acknowledged that their estimate is likely an underestimation due to conservative assumption of vaccine effectiveness against death and it does not account for reduction in transmission.

The above estimates, allowing for the conservative factors, are broadly similar to our estimate of 8000 deaths prevented from mid-January to end of February 2021, which increases to 10,300 deaths prevented by mid-March 2021.

All three models adopted counterfactual approaches and yielded broadly consistent results.

Conclusion

The vaccines are already preventing deaths at scale in England. The results show strong positive signs that the vaccines are increasing antibody levels significantly and achieving the most important outcome of preventing deaths in the vaccinated population, despite primarily rolled out in first doses and from two brands, namely Pfizer and AstraZeneca. The vaccination was estimated to have already saved over 10,000 lives in the 80+ age group by mid-March 2020, and this number is likely even higher at a population level as the vaccination is rolled to younger age groups.

Appendix

Comparison of mortality impact by PHE model, Warwick model and our model

Figure 3: Our Model Structure

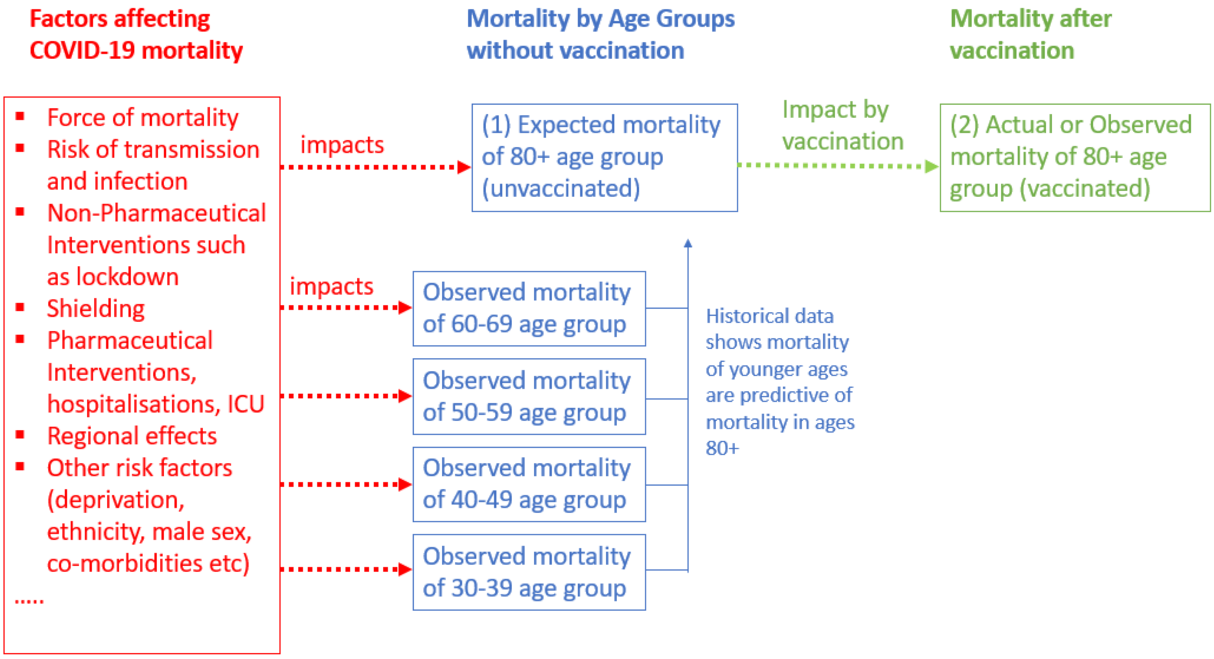


Figure 3 shows how our approach models the general relationship between the mortality between different age groups, various drivers of mortality risks and the impact of vaccination.

Figure 4b, Figure 5 and Figure 6 shows similar patterns of mortality impact of vaccination on the population. Note Figure 4 is based on weekly deaths while Figure 5 and Figure 6 are based on daily deaths. The number of deaths prevented is the gap between the actual and expected deaths.

Figure 4 and Figure 8 shows updated results of ONS registered deaths and hospital deaths in our original paper (presented as Figure 13 and Figure 14 respectively).

Figure 4: Registered deaths analysis using the Gompertz Network approach. ONS registered deaths of ages 80+ by (a) Actual vs Expected % (b) Actual number of deaths and the expected number of deaths in the counterfactual unvaccinated scenario

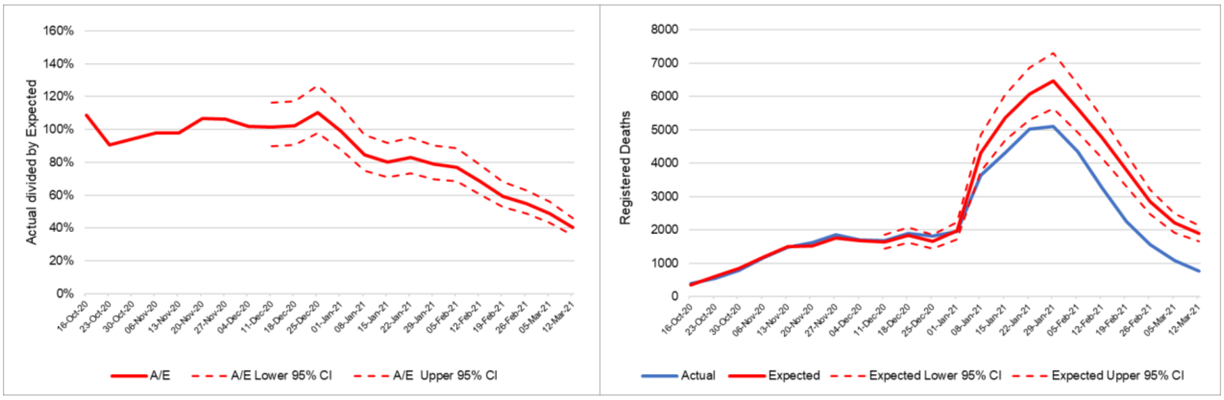
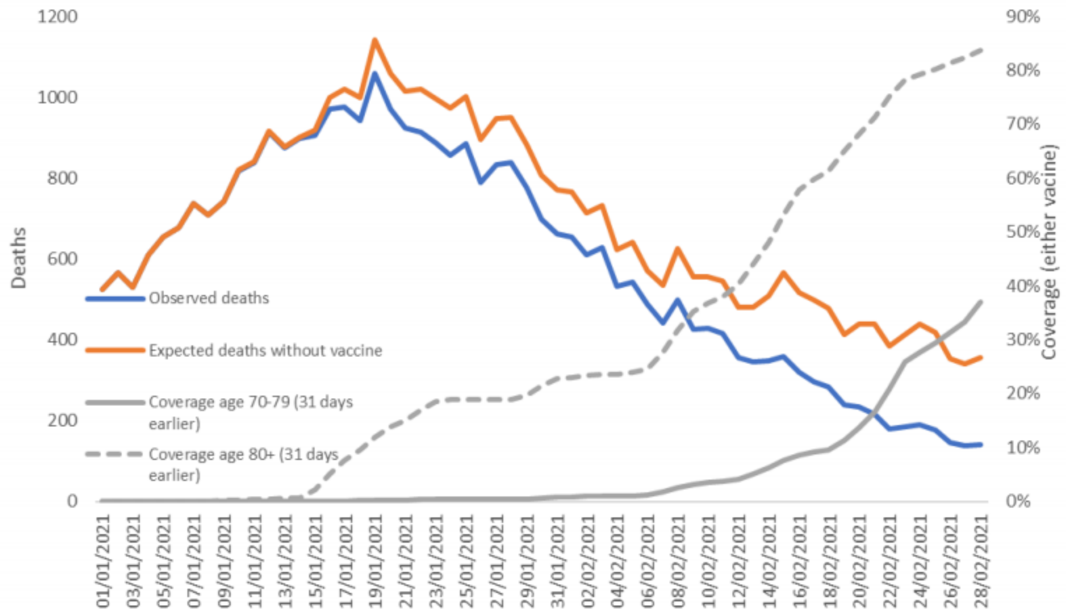


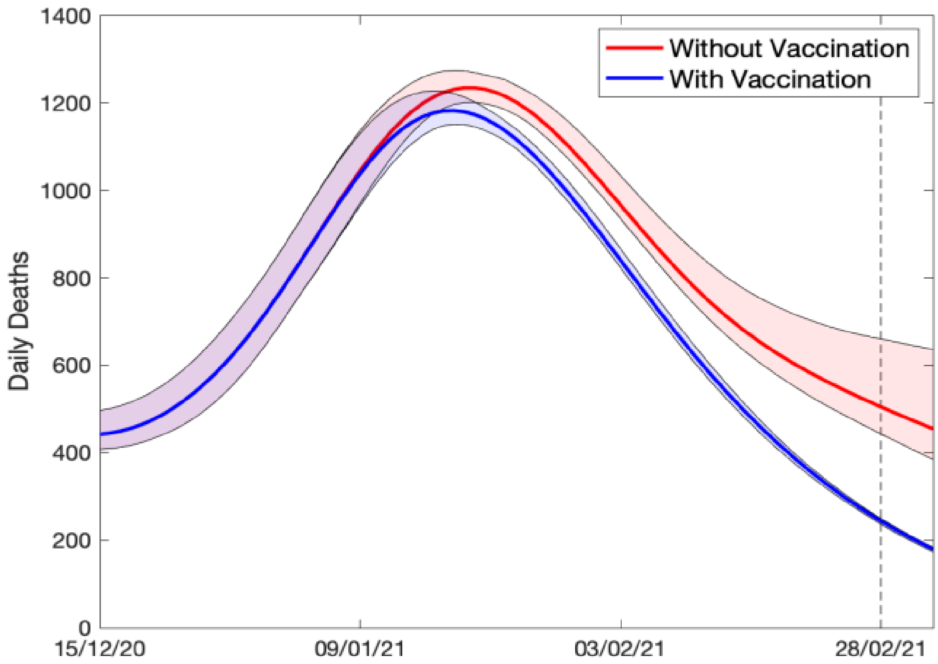
Figure 5: Analysis of PHE model. Daily Observed COVID-19 deaths aged 70+ and expected numbers in the absence of vaccination using the back-calculation method.



Source: Figure 1 in [PHE/Warwick paper]

In Figure 5, the blue line represents the daily observed deaths and has a zig-zag pattern. The orange line represents the expected deaths without vaccine, which closely follows the pattern of observed deaths because the approach is based on back-calculation incorporating vaccine-related assumptions.

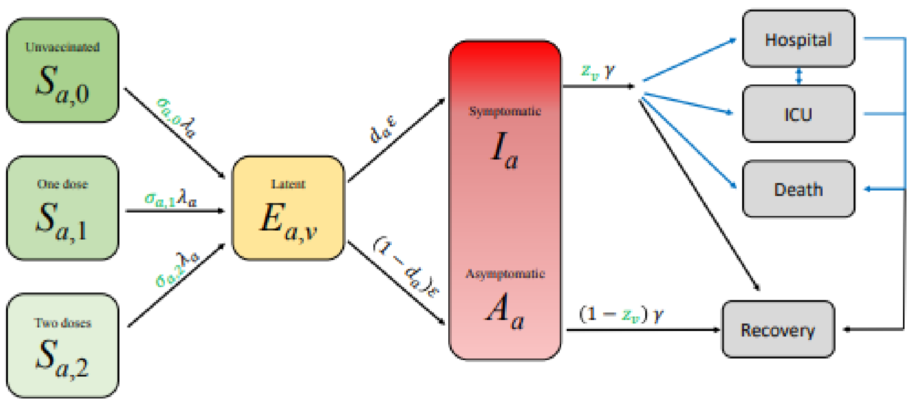
Figure 6: Analysis of Warwick model. Predicted dynamics of the number of daily deaths (within 28 days of a positive test) for the default model that captures historic patterns of vaccination (blue) and the counterfactual in which vaccination has been removed (red).



Source: Figure 2 in [PHE/Warwick paper]

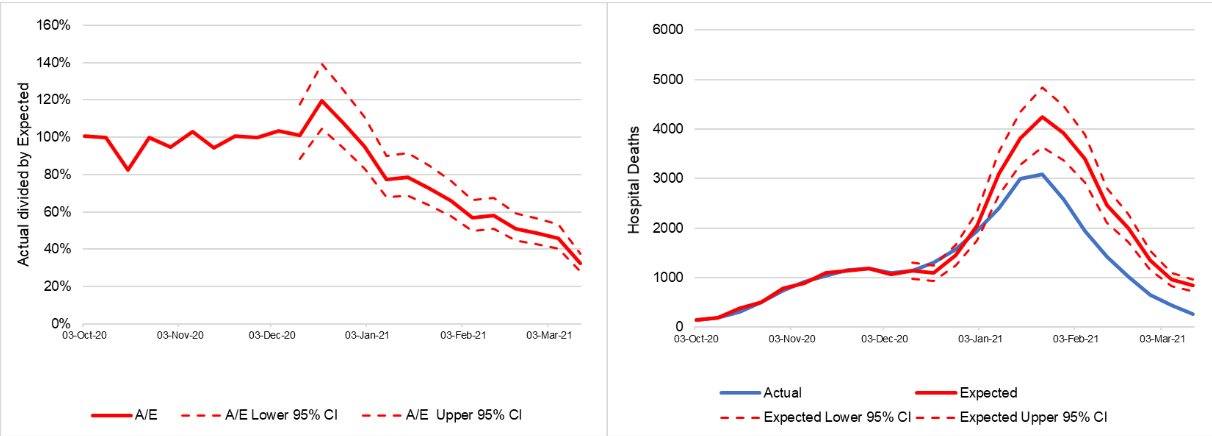
In Figure 6, the lines are smooth because both predictions with and without vaccination are based on simulations exploring the range of estimated parameters in the age-structured model.

Figure 7: Representation of the basic model states and transition in the age-structured model. Black arrows show key epidemiological transitions while blue arrow show movements to observable states. Parameters in green show the action of vaccine on infection and probability of disease.



Source: Figure S12 in supplementary appendix of "[Vaccination and non-pharmaceutical interventions for COVID-19: a mathematical modelling study]"

Figure 8: Hospital deaths analysis using the Linear Regression approach. Hospital deaths of ages 80+ by (a) Actual vs Expected % (b) Actual number of deaths and the expected number of deaths in the counterfactual unvaccinated scenario



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