# Modelling the Return of Freedoms

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**Summary**

On 14 June, a large batch of papers was published by SAGE. These set out further modelling of the impact of easing restrictions in England – in particular, moving to Step 4 of the roadmap. These were part of the decision-making process by the UK Government which resulted in delaying Step 4 from 21 June to 19 July.

Each of the modelling papers sets out many scenarios, using different assumptions for things like:

- Vaccine uptake
- Transmission advantage of Delta (B.1.617.2) against Alpha (B.1.1.7)
- Vaccine efficacy
- Behavioural impact in response to Step 4

In this bulletin, we summarise the number of deaths that are projected under some of the key scenarios set out in the papers. We identify similarities and differences between the modelling approaches and consider what new evidence might be gathered in the coming weeks to determine which path the UK might follow once Step 4 is reached.

We consider the more extreme adverse scenarios unlikely given the latest evidence on the effectiveness of two doses of the vaccine against hospitalisation and death, even for the Delta variant.

**The data**

The publications include detailed modelling papers by three separate teams[1] and an overall summary.

**General comments**

These papers are emblematic of the uncertainty around the current position. Each modelling team has used different assumptions about key aspects of the development of the pandemic in the context of the Delta variant. Depending on the assumptions made, the models produce radically different projections of cases, hospitalisations, and deaths.

Under any scenario that can reasonably be produced based on the available evidence, it is clear that:

- We are already at the start of a third wave of infections
- Vaccination and prior infection will mitigate the impact of this on hospitalisations and deaths
- The emergence of the Delta variant means that there are still many unknowns about the likely absolute size of the exit wave
- Pushing back the date by which restrictions are lifted reduces the overall numbers of cases, hospitalisations and deaths in the Warwick and Imperial models, but not in the LSHTM model, although the peak volumes are lower.

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[1] University of Warwick, London School of Hygiene and Tropical Medicine, and Imperial College London.

The numbers of deaths and hospitalisations projected are especially sensitive to assumptions about vaccine efficacy against severe outcomes, and immune escape. Data is still emerging to support these assumptions for the Delta variant, which means that the range of outcomes produced by the different modelling teams is wide, even where the assumptions are intended to be best estimates. Early data on efficacy was concentrated among the oldest age groups that were vaccinated first; it is unclear whether the findings will be better or worse for younger age groups.

**Warwick model**

Central estimates from the Warwick model generally result in lower estimates of deaths between June 2021 and June 2022 compared to the Imperial and LSHTM central models.

Some sample results from this model on different assumptions are shown below:

| Delta transmission advantage | Vaccine efficacy | Step 4 Date | Roll out speed | Deaths June 2021 – June 2022 |
|---|---|---|---|---|
| 56% | Central | 21 June | Central | **17,100** (8,490 – 36,800) |
| **46%** | Central | 21 June | Central | **10,600** (4,920-23,600) |
| **66%** | Central | 21 June | Central | **24,900** (13,100 – 51,500) |
| 56% | Central | **26 July** | Central | **8,500** (4,140 – 18,200) |
| 56% | **Optimistic** | 21 June | Central | **6,320** (3,280 – 13,500) |
| 56% | **Pessimistic** | 21 June | Central | **72,400** (44,100 – 128,000) |
| 56% | Central | 21 June | **25% slower** | **19,900** (10,100 – 42,100) |

Warwick modelled many more scenarios, but it is clear the results are particularly sensitive to vaccine efficacy, with a pessimistic assumption producing 10 times more deaths than an optimistic one.

**London School of Hygiene and Tropical Medicine (LSHTM) model**

The LSHTM model results are shown below for sample scenarios. Note that this model only projects to the end of 2021, unlike the others which are based on a full year.

| Delta transmission advantage | Vaccine efficacy | Step 4 Date | Roll out speed | Deaths June 2021 – Dec 2021 |
|---|---|---|---|---|
| 50% | Central | 21 June | Central | **57,400** (46,800 - 70,900) |
| **70%** | Central | 21 June | Central | **65,000** (53,700 - 80,400) |
| 50% | Central | **26 July** | Central | **62,300** (48,600 - 78,300) |
| 50% | **Optimistic** | 21 June | Central | **45,400** (36,900 - 55,800) |

The LSHTM model produces the most pessimistic results of the three models. It appears very cautious regarding time taken for the vaccine to become effective (28 days) which may produce a larger build-up of cases over the coming months. LSHTM also allow for a decline in vaccine acquired immunity in their central projections, which is not mirrored in the other models.

An important difference in the results is that the delay in moving to Step 4 actually results in an increase in hospitalisations and deaths, although peak levels are reduced.

Given the sensitivity of the models to the vaccine efficacy assumption, we contrast the Warwick and LSHTM figures against death – a higher percentage implies a more optimistic assumption.

|  | Warwick | **Warwick** | Warwick | LSHTM | **LSHTM** | LSHTM |
|---|---|---|---|---|---|---|
|  | Optimistic | **Central** | Pessimistic | Optimistic | **Central** | Pessimistic |
| AstraZeneca 1 Dose | 80% | **60%** | 60% | 85% | **69%** | 54% |
| AstraZeneca 2 Doses | 99% | **96%** | 93% | 95% | **90%** | 86% |
| Pfizer/Moderna 1 Dose | 80% | **60%** | 58% | 85% | **71%** | 57% |
| Pfizer/Moderna 2 Doses | 99% | **96%** | 93% | 95% | **92%** | 89% |

For first doses LSHTM is more optimistic than the Warwick central assumption but for second doses (more relevant for older ages where most deaths occur), the reverse is true. For second doses, the LSHTM optimistic model is closest to the Warwick central model.

**Imperial model**

| Delta transmission advantage | Vaccine efficacy | Step 4 Date | Roll out speed | Deaths June 2021 – June 2022 |
|---|---|---|---|---|
| 50% | Central | 21 June | Central | **47,941** (21,723 – 86,506) |
| **65%** | Central | 21 June | Central | **59,180** (33,140 – 101,218) |
| 50% | Central | **26 July** | Central | **34,743** (21,767 – 58,718) |
| 50% | **Optimistic** | 26 July | Central | **19,187** (12,238 – 32,568) |
| **40%** | **Pessimistic** | 26 July | Central | **80,515** (52,968 – 114,076) |

Again, given the sensitivity of the models to the vaccine efficacy assumption for the Delta variant, we contrast the Imperial and Warwick figures against death (which in the case of the Imperial model are the same as for severe disease). A higher percentage implies a more optimistic assumption.

|  | Warwick | **Warwick** | Warwick | Imperial | **Imperial** | Imperial |
|---|---|---|---|---|---|---|
|  | Optimistic | **Central** | Pessimistic | Optimistic | **Central** | Pessimistic |
| AstraZeneca 1 Dose | 80% | **60%** | 60% | 78% | **73%** | 68% |
| AstraZeneca 2 Doses | 99% | **96%** | 93% | 87% | **85%** | 77% |
| Pfizer/Moderna 1 Dose | 80% | **60%** | 58% | 76% | **73%** | 68% |
| Pfizer/Moderna 2 Doses | 99% | **96%** | 93% | 90% | **89%** | 84% |

As for LSHTM, for first doses Imperial is more optimistic than the Warwick central assumption but for second doses (more relevant for older ages where most deaths occur), the reverse is true.

For second doses, the Imperial optimistic assumptions are more pessimistic than that the Warwick pessimistic assumptions!

**Vaccine efficacy**

Given that the modelling teams have significantly differing assumptions on vaccine efficacy, it is sensible to ask which set of assumptions appears most appropriate.

The modelling teams relied on the best data available at the time, which inevitably was predominately in respect of protection against Alpha. In particular, Public Health England (PHE) data from March suggested 80% efficacy against hospitalisations, 14 days after a first dose for 80-year-olds, but confidence intervals were very wide.

A study by Hyams et al is referenced, again looking at data from people aged 80 or older. In this study, efficacy against hospitalisation after a first dose of AstraZeneca was 80.4% (36.4-94.5) and for Pfizer 71.4% (43.1-86.2) – these figures are broadly in line with Imperial's assumption set.

However, in the past week PHE released a pre-print study that used hospital emergency department data from England to suggest the following level of efficacy of vaccines against hospitalisations. The vaccine efficacy is reported relative to unvaccinated individuals within the same variant, so the figures do not allow for direct comparison between vaccine efficacy for Alpha and Delta.

|  | **Alpha** | **Delta** |
| --- | --- | --- |
| AstraZeneca:  1 Dose | 76% (61-85) | 71% (51-83) |
| AstraZeneca:  2 Doses | 86% (53-96) | 92% (75-97) |
| Pfizer/Moderna:  1 Dose | 83% (62-93) | 94% (46-99) |
| Pfizer/Moderna:  2 Doses | 95% (78-99) | 96% (86-99) |

This data was only available after the models were produced, but the point estimates appear to support figures between the Warwick central and optimistic assumptions for efficacy against hospitalisation. Efficacy against death is generally assumed to be at least as high as efficacy against hospitalisations. It will be very important to firm up on these estimates to get a clear view on the likely outcome of this wave of infections.

A final related point is that PHE, in its regular weekly surveillance of variants, is now suggesting that the risk of hospitalisation is around twice as high for Delta as for Alpha. Again, this evidence has come too late for the modellers to include (and is still uncertain), but must result in some additional, possibly significant risk. It highlights the problems faced by the modellers when evidence continues to emerge as to the changing risk environment.

**How will we know which path we're on?**

There are many scenarios set out in the papers (we have only summarised a small subset), but we can't yet have a firm idea which outcome is most likely.

At this stage, given uncertainty in key parameters, we can't give a best estimate figure for deaths following Step 4 with any certainty. However, we can consider the ways in which the estimates will become more concrete, and the statistics to keep an eye on.

The first indicator (which we are already seeing) is an increase in the number of cases. The rate of growth in this will give us an idea of the transmissibility advantage of Delta over Alpha.

Despite the presence of Delta, the impact of this wave on more serious outcomes (hospitalisation and death) will differ from previous waves because of high levels of vaccination in the UK. The key things we'll watch out for are in the hospitalisation statistics:

- Absolute numbers
- Average age
- Vaccination status

Given recent increases in hospitalisations, we expect to see increased numbers of deaths. To date this has not been the case, but given the usual delay period between admission and death, any rises should become apparent very soon. We are already seeing fewer admissions per case, and it is likely that we'll also see less deaths per admission.

Thus, these indicators should give an idea of how effective the vaccines are in practice against hospitalisation and death (that is, the extent to which the link between cases and more serious outcomes has weakened. Further studies are also likely to be published relating to effectiveness and transmissibility).

We publish regular information on transmission rates, hospitalisations and deaths both on Twitter and in our Friday Reports; we will continue to monitor these indicators closely, including updates of how thinking on the key areas of uncertainty develop, as data is published and parameters become clearer.

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