Vaccine-mediated exit strategies from England's Covid-19 lockdown

Philip Thomas*

Safety Systems Research Centre, South West Nuclear Hub, Faculty of Engineering, University of Bristol, Queen's Building, University Walk, Bristol BS8 1TR, UK

An assessment is made of vaccine-mediated exit strategies from England's Covid-19 lockdown. Two linked methods are considered. The first, termed the gradualist approach, assumes that the R-rate is controlled to a value close to 1.0 and that the social distancing index (SDI), which measures the nation's level of interpersonal contact, is allowed to increase continuously to the point where it can grow no further and society and the economy are fully open. The second method, termed the two-step strategy, adopts the gradualist approach initially, but then, after a certain time, the SDI is stepped to its maximum value, which implies the immediate removal of all restrictions. It is found that, while vaccination-generated immunity makes a very valuable contribution to overall immunity, the other components—prior T-cell immunity and immunity generated by infection—are just as important. Infection-generated immunity needs to be the largest component if all restrictions are to be removed, under both strategies. Leaving lockdown to the point where all restrictions can be fully eased requires a narrow path to be followed during the spring and early summer of 2021, keeping the R-rate in a central band around 1.0. Close control of the R-rate is needed and this will require it to be measured accurately, continuously and rapidly. The gradualist approach might allow all restrictions to be lifted by the end of the summer 2021, while the two-step strategy might offer the prospect of full derestriction by the end of May 2021.

Keywords: coronavirus, Covid-19, lockdown, lockdown exit strategies, predictor–corrector coronavirus filter, PCCF

1. Introduction

The UK government's Vaccine Task Force was successful in securing vaccines from the first companies to gain licences for their new products. 40 million doses were ordered from the early leader, Pfizer–BioNtech, which is supplying an RNA-based vaccine, while 100 million are on order from the Oxford–AstraZeneca consortium, whose licensed product employs a genetically

* E-mail: philip.thomas@bristol.ac.uk; research website: www.jvalue.co.uk

Nanotechnology Perceptions **17** (2021) 30–73
Received 16 February 2021; *accepted* 21 March 2021

doi: 10.4024/N02TH21A.ntp.17.01

modified virus and is known as a viral vector. Orders have also been placed for17 million doses of a newly licensed vaccine from Moderna, which is again based on RNA technology. Supplies have also been purchased of two further vaccines that are well advanced towards licensing in the UK: 60 million doses from Novavax (protein-based) and 30 million of the viral vector type from Janssen. The first four require an initial and then a booster dose, whereas the Janssen vaccine is administered in one injection.

Conditioned by the requirement to ensure the vaccines progressed through all stages of development in record time (less than a year, as it turned out), the interval between doses explored in the field for some of the vaccines was set at three weeks. A longer period has been found now to be desirable between injections, and the British government has decided on a gap of 12 weeks to allow the fastest possible roll-out of the first protective dose.

Subsequent research has suggested that the AstraZeneca vaccine has an average effectiveness of 76% in eliminating symptomatic infection for the period from three weeks to 15 weeks from the first dose and of 67% in eliminating all SARS-CoV-2 infections, whether symptomatic and asymptomatic,[1] in the same interval. The latter figure is of key importance because it means that no transmission will occur following two thirds of potentially infectious encounters. This figure will be used in the analysis that follows, which applies to England.[2] It was also reported that the only adverse cases found in the Stage 3 field trial were mild, with no serious illness and no deaths. It will be assumed, therefore, that vaccines will prevent death with an effectiveness of 95%. This figure will be assumed to apply to all vaccines used in England.

No data were supplied on the performance of the AstraZeneca vaccine in the first three weeks after administering the first injection. A conservative characterization would assume that there was no benefit until three weeks after vaccination. This could be modelled by employing a step function with the value zero up to and including 21 days and then rising asymptotically to 0.67 over the interval from 22 days to 90 days. In fact it is almost certain that there will already be some benefit from the vaccination earlier, hence the process was modelled as a first-order exponential lag, initially so that it would give the same average value over the 13-week interval. Subsequent data on antibodies published by ONS[3] suggested that the effect of vaccination came through more quickly, hence a shorter time constant was chosen. Both approaches are shown in Appendix D, where the shorter time constant is chosen as more representative (see Figure 1).

It was then assumed that the second dose of vaccine would lock in the 67% chance of preventing infection for the duration of the pandemic. (For information, a more complete characterization of the second dose is provided in Appendix E; this allows for the effectiveness to rise eventually to 80% after the second of two doses.)

---

[1] Voisey, M., et al., Single dose administration, and the influence of the timing of the booster dose on immunogenicity and effectiveness of ChAdOx1 nCoV-19 (AZD1222) vaccine. Submitted to *The Lancet* (2 February 2021) https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3777268

[2] England constitutes a separate health jurisdiction from those of Wales, Scotland and Northern Ireland, although vaccines are distributed to each of the constituent countries of the UK on an egalitarian basis, in proportion to their populations. England's population makes up 84% of that of the United Kingdom.

[3] ONS, Coronavirus (COVID-19) Infection Survey, antibody data for the UK: 16 February 2021 https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19infectionsurveyantibodydatafortheuk/16february2021#likelihood-of-testing-positive-for-covid-19-antibodies-in-england-wales-northern-ireland-and-scotland

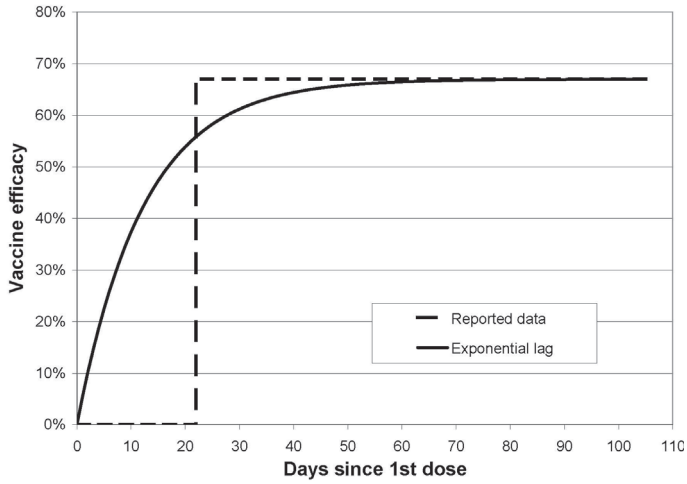

Figure 1. Matching an exponential lag to reported vaccine effectiveness.

The government's timetable for the Covid-19 vaccinations was based on vulnerability, interpreted principally in terms of age,[4] although morbidities were also taken into account. The programme of first doses in England used in this analysis is summarized in Figure 2. The timetable follows (apart from health workers) a sequence ordered in terms of decreasing age, with those of age 80 and over being invited first, then those between 70 and 79 and so on. Recorded daily vaccinations are used up to 6 February 2021 and then a constant 400,000 first doses a day is assumed, a rate that was exceeded on several occasions prior to 6 February 2021.

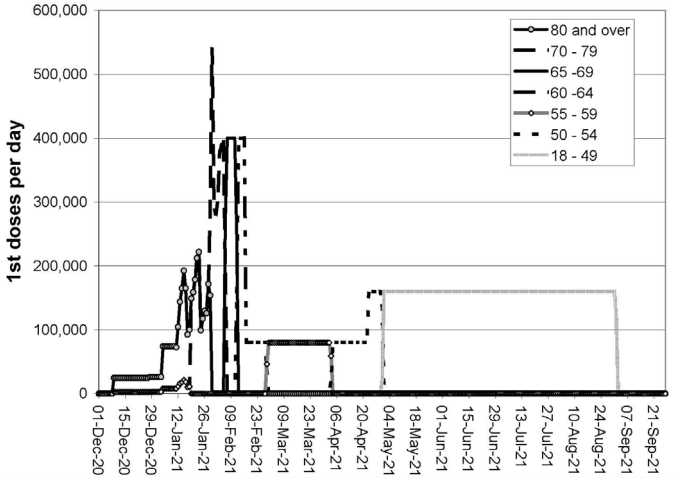

Figure 2. Programme of doses administered to the seven age groups for adults in England.

[4] An explanation of the age effect is given in §2.1 of Thomas, P., Measuring and controlling the Covid-19 pandemic. *Nanotechnology Perceptions* **16** (2020) 267–330.

Second doses will need to be given after a maximum of 12 weeks, and this is assumed to decrease the vaccination capability available for further first doses. In this analysis it is assumed that administering second doses begins in earnest in the second half of February 2021, and that only 80,000 first doses per day are given between the middle of February and the middle of April, with 160,000 first doses given daily from 23 April onwards.

The Office of National Statistics (ONS) has found that 92% of the adult population of Great Britain have received or would be likely to accept the COVID-19 vaccine if offered,[5] and this figure has been adopted for vaccine coverage in the present study.

The vaccination exercise will be complete by the beginning of September 2021.

As of late January 2021, England was living under strictly observed lockdown, with the R-rate (the average number of people a person with Covid-19 will infect between contracting the virus and recovering) having a value of roughly 0.6, based on measurements made by the predictor–corrector coronavirus filter (PCCF),[6,7] This paper will consider two sets of scenarios for leaving lockdown and moving towards getting back fully to normal. The first set will involve a gradualist approach, where lockdown restrictions will be eased continuously until society and the economy are fully open. The second set of scenarios uses a two-step method, whereby a gradualist approach is used first, until the danger has been significantly mitigated by vaccination, but then all restrictions are lifted on a specified date.

The paper is laid out as follows. §2 of the paper derives a value for the maximum of the social distancing index (SDI), which will be associated with a fully open society and economy. §3 explains the two basic strategies examined in the paper and the scenarios to be considered within them. A sensitivity study to be carried out on the maximum value Σ_0 of the SDI, corresponding to full derestriction, is outlined. §4 contains the results found for the three scenarios analysed under the gradualist approach. §5 provides the results for two scenarios enacted under the potentially quicker two-step strategy. §6 contains sensitivity studies for the two-step strategy. The discussion is given in §7, while a note on the accuracy of the modelling is provided in §8. §9 gives conclusions.

There are six appendices. Appendix A explains the adaptation of the PCCF model to allow it to cater for eight age groups. Appendix B details the modelling of the age prioritization used in the vaccination campaign. Appendix C derives a set of base death probabilities for the different age bands, valid in the absence of vaccination. Appendix D gives two possible derivations for a value for the vaccination maturity time constant. Appendix E explains how the beneficial effect of the second, booster dose of vaccine may be modelled. Appendix F offers an additional method for allowing for differences in the number of swab tests administered each day, relevant to the corrected data points provided for cases by date recorded.

---

[5] Office of National Statistics (ONS), Coronavirus and the social impacts on Great Britain: 12 February 2021 https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthandwellbeing/bulletins/coronavirusandthesocialimpactsongreatbritain/12february2021#attitudes-to-covid-19-vaccination

[6] Thomas, P., The options for the UK leaving the coronavirus lockdown of 2020. *Nanotechnology Perceptions* **16** (2020) 130–150.

[7] *The Spectator* Covid-19 data tracker, where PCCF measurements of the number of active cases in England and England's R-rate are updated daily: https://data.spectator.co.uk/city/national

2. The SDI when there are no social distancing restrictions

The SDI originates from the observation that any virus stands a better chance of being passed on within a country if its inhabitants are habitually coming into close contact with each other. Rather in the way that a flow pattern in water becomes visible once a tracer dye has been introduced, the degree of social mixing can be measured once a virus has been introduced, from how quickly people are becoming infected. The SDI is the average number of people in a wholly vulnerable population to whom a person infected with the virus will pass on his or her infection, and, as such, it is a fully scientific measure of the nation's social mixing behaviour at any time.

The SDI will start out high when people are acting normally just before the virus strikes, but it will then decrease as people cut down on their close interactions to restrict the spread of the disease, either through voluntary action or as a result of government directives. Society will eventually begin the process of getting back to normal and allow its SDI to increase when it judges the disease is on its way out. The rise in the SDI may come about either through individual choices or as a result of government guidance or, more likely, from a mixture of the two.

Σ_0 is estimated to be about 3.0 for the original form of Covid-19, but the B.1.1.7 variant may be 50% more infectious.[8] This implies that Σ_0 will be 4.5 for B.1.1.7. Weekly ONS infection surveys[9] covering the period between 13 January 2021 and 3 February found the prevalence of B.1.1.7 in England was stable at about 60% (although a sizeable fraction of positive samples were carrying too low a viral load for the variant to be identified, so the prevalence might be higher). Taking a weighted mean of Σ_0 for the original SARS-CoV-2 and for B.1.1.7 assuming 60% prevalence produces $\Sigma_0 = 3.9$.

The threshold for population ("herd") immunity is defined to occur when any new infections introduced will fade away because they cannot be sustained.[10] The rate of change in the number of people carrying the infection will be negative, and this will occur when the fraction of people with immunity to the infection is above the limiting value $1-\Sigma^{-1}$, where Σ is the SDI. The highest value of herd immunity will occur in the fully unrestricted state, when it takes the value $1-\Sigma_0^{-1}$. This denotes the immunity level at which a new infection cannot take hold when no social distancing restrictions at all are observed. Thus, when Σ_0 = 3.9, the threshold for unrestricted herd immunity is 74%.

To study sensitivity the case was examined where the new variant, B.1.1.7, became fully dominant in England (i.e., responsible for all infections), and moreover was twice as infectious as the original virus (rather than 50% more so). This has the effect of raising the derestricted SDI from 3.9 to $\Sigma_0 = 6$, and the threshold for unrestricted herd immunity is then 83%.

---

[8] Public Health England, What do we know about the new COVID-19 variants? (5 February 2021) https://publichealthmatters.blog.gov.uk/2021/02/05/what-do-we-know-about-the-new-covid-19-variants/

[9] Office of National Statistics (ONS), Coronavirus (COVID-19) Infection Survey, UK: 12 February 2021, and previous three issues. See: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/coronaviruscovid19infectionsurveypilot/12february2021

[10] Thomas, P., J-value assessment of how best to combat COVID-19. *Nanotechnology Perceptions* **16** (2020) 16–40.

3. The options considered

The reproduction number ("R-rate") differs from the SDI by being applicable to the current level of immunity and thus differs from the SDI, which applies when everyone is vulnerable. The R-rate is thus the average number of people in the population at the current level of immunity to whom an infected person will pass on his or her infection. Unlike the SDI, the R-rate depends not only on the time-varying degree of social mixing in the country but also on the fraction of people who are immune to the disease as it develops over time. It is, of course, possible to calculate the SDI from the R-rate and vice versa as soon as the immune fraction is known.

3.1 Mortality rate

A model[11] was matched to the official data for England's "cases by date reported" from the beginning of December 2020 to the end of January 2021. An estimate was then made of the infection fatality rate over all ages that would be produced in the absence of vaccination by matching its prediction for the peak death rate in January 2021 to the highest recorded number based on specimen date (see Figure 3). The resultant figure, 1.32%, is retained for all the scenarios under the assumption that the B.1.1.7:original virus prevalence ratio remains at 60:40 throughout the rest of the epidemic.

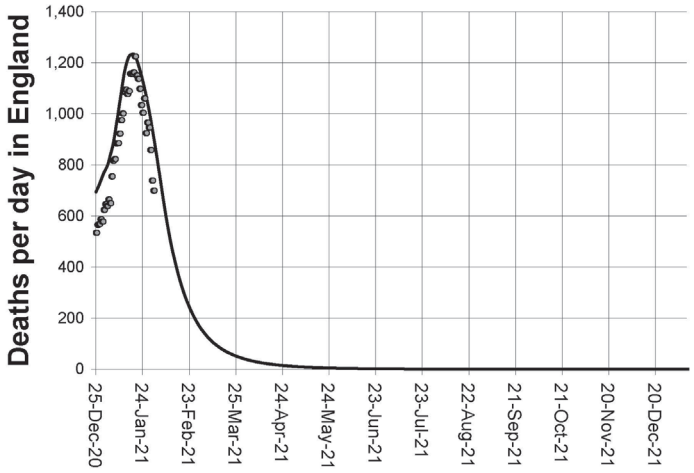

Figure 3. Adjusting the model's infection fatality rate to match the prediction to the peak daily deaths recorded in England in January 2021 (the R-rate is held at 0.6 in the model from the end of January onwards, leading to the continuing decline in deaths per day).

It is no longer clear whether the new B.1.1.7 variant is more lethal than the original virus, with some studies suggesting it is 60% more deadly, while others finding no difference in the

[11] Thomas, P., The length and severity of the coronavirus recession estimated from the dynamics of relaxing lockdown. *Nanotechnology Perceptions* **16** (2020) 100–129.

fatality rate.[12] It is assumed here that its fatality rate is 30% higher,[8] which would make the infection fatality rate for the original virus 1.12% and for B.1.1.7 1.45%. For the sensitivity studies, where the new variant is assumed to be completely dominant, the infection fatality rate is therefore taken to be 1.45%.

3.2 Gradualist approach

In the gradualist approach, the R-rate is assigned a set point at the end of January 2021, at which is maintained thereafter by judicious control of the amount of social distancing that is allowed. Three scenarios are explored, with the R-rate kept at set points of 0.6, 0.95 and 1.1 from the end of January 2021 onwards. Active infections will decrease in the first two scenarios, when $R < 1$, and will start to increase when $R > 1$ in the third.

Formally, the SDI ($\Sigma(t)$, which is also known as the basic reproduction number, $R_0(t)$, or even as "R excluding the effect of immunity"[13]) is defined as the number of contacts the average person infected with Covid-19 makes with other people in the interval between becoming infected and recovering, provided that the encounter is close enough to infect the other person and would, in fact, do so in a fully "naïve" population, in which no one had any immunity.

People's social distancing behaviour will change both with the season and in response to government orders and guidance, which may also change over time. This is what makes the SDI a function of time: $\Sigma = \Sigma(t)$. A high degree of social distancing, which will happen when personal contact is minimized, will be associated with a low value of the SDI. On the other hand, a low degree of social distancing (lots of direct interaction) will lead to a high value of the SDI.

The SDI may be calculated from the R-rate, $R(t)$, by dividing by the fraction of the population that is still susceptible: $\Sigma(t) = R(t) \div \left(n_s(t)/N\right)$, where $n_s(t)$ is the number of susceptible people in the population of size, N. The fraction, $n_s(t)/N$, must fall in all epidemics through the combined effects of recovery from infection and also vaccination, where it is offered (and taken up). As a corollary, holding the R-rate constant will inevitably cause the SDI to rise. It will attain its maximum value, $\Sigma = \Sigma_0$, first at the beginning of the epidemic and then at the end. In both cases, no restrictions on social distancing are imposed by the Government or adopted voluntarily by the public, and people mix entirely freely. Σ_0 can be seen to be independent of time. Once the SDI reaches its highest possible value, corresponding to full opening up, according to the relationship just cited the R-rate can no longer remain constant, but must fall instead: $R(t) = \left(n_s(t)/N\right)\Sigma_0$.

[12] Retter, R., UK coronavirus variant not more deadly, just spreads more easily, studies find. *LiveScience* (13 April 2021) https://www.livescience.com/uk-coronavirus-variant-severity.html

[13] This is the terminology used for the SDI by the SPI-M-O Committee of the UK Government's Scientific Advisory Group for Emergencies (SAGE). See SPI-M-O: Summary of further modelling of easing restrictions—Roadmap Step 2 https://www.gov.uk/government/publications/spi-m-o-summary-of-further-modelling-of-easing-restrictions-roadmap-step-2-31-march-2021

3.3 Two-step strategy

3.3.1 Main cases

The two-step strategy will be applied using two initial set points for the R-rate, namely 0.6 and 0.95. These set points are both below 1.0, which implies that cases will start off by falling. Then full derestriction will happen at the end of May 2021, modelled by stepping the set point for the R-rate up to 1.6.

3.3.2 Sensitivity studies

The maximum value of the SDI corresponding to full derestriction is now set at $\Sigma_0 = 6$. The two initial set points, 0.6 and 0.95, were retained for the R-rate in the gradualist first phase, but full derestriction was delayed two months to the beginning of August 2021 in view of the approximately 50% increase in the Σ_0-value. The overall infection fatality rate is assumed to be 1.45%, as explained in §3.1.

4. Results for the gradualist approach

4.1 The R-rate is held at 0.6 from the end of January 2021 onwards

Holding the R-rate at 0.6 from the end of January 2021 onwards produced the uniform fall in England's cases by date reported shown in Figure 4. Meanwhile the active infections in England are also predicted to fall away rapidly, dropping below 10,000 in the second half of May, as shown in Figure 5. As shown in Figure 3, daily deaths fall rapidly, dropping to less than 100 a day by the middle of March 2021.

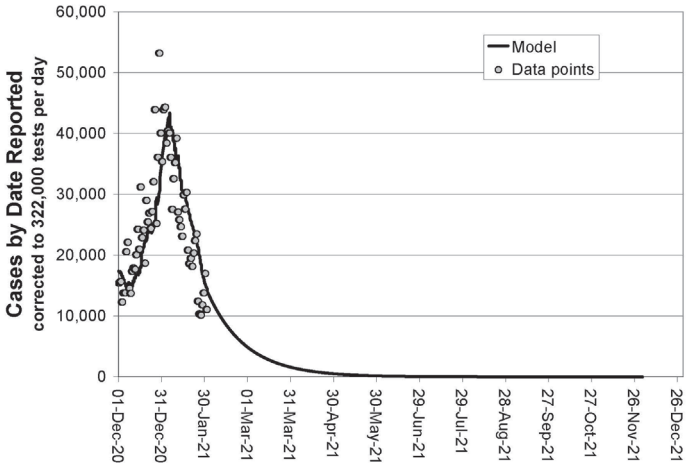

Figure 4. The effect on cases by date reported of keeping the R-rate at 0.6 from the end of January 2021 onwards.

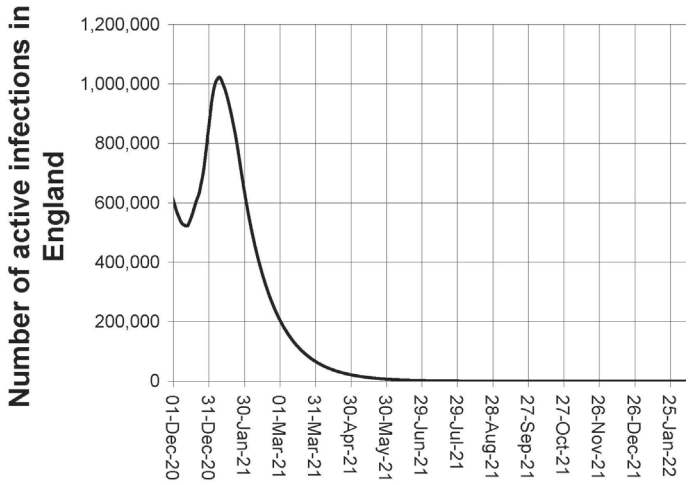

Figure 5. Active infections in England ($R = 0.6$).

However, while the SDI rises to just below 1.9 by early autumn, its progress then stalls, with its value still less than half the SDI of 3.9 that is necessary for the full lifting of restrictions—the country will remain in a highly restricted state of social distancing (see Figure 6). Nor is there any possibility of escaping the restrictions at any time in the future while the R-rate is kept at 0.6, despite the fact that all the adult population has now been vaccinated.

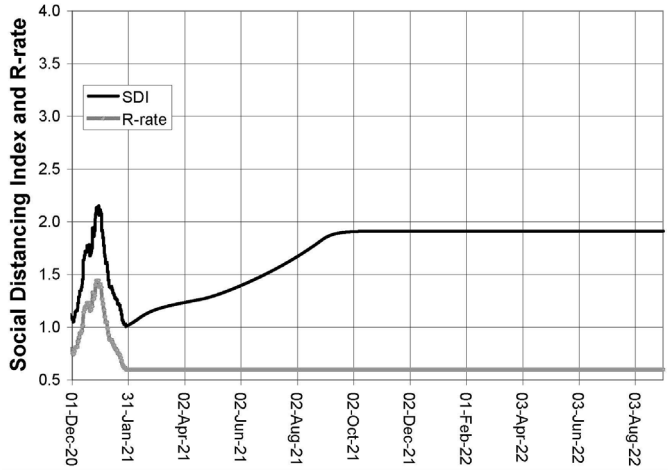

Figure 6. Social distancing index (SDI) and R-rate; $R = 0.6$.

Figure 7 shows that vaccination immunity ends by rising to 30%, which is above the immunity generated by infection, 26%. But even when the T-cell immunity of 13% is added, the total population immunity is only 69% and, although sizeable, this is insufficient to allow all restrictions to be ended.

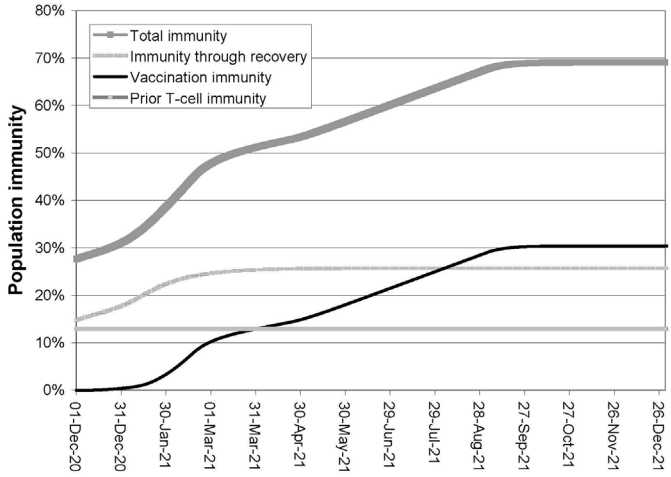

Figure 7. Components of population immunity ($R = 0.6$).

Coronavirus restrictions would need to remain in place permanently in England if the R-rate were to be kept constant at 0.6, even after all the adult population has been offered a vaccination.

4.2. The R-rate is held at 0.95 from the end of January 2021 onwards

Increasing the R-rate to 0.95 still allows both cases by date reported and active infections in England to decrease continuously, although more slowly than when $R = 0.6$ (see Figures 8 and 9). Deaths per day fall away continuously, dropping to 200 a day by mid-April 2021. The decrease becomes slower over the summer, but deaths drop away faster from late August 2021 and deaths per day are numbered in the tens by the end of December 2021 (Figure 10). Full derestriction is now possible, with the SDI reaching the necessary value of 3.9 that implies full opening-up of society and the economy by mid-August 2021 (see Figure 11). Crucially, the infection-generated immunity has risen to 40%, as shown in Figure 12. The vaccine immunity is now 25%, and the total immunity, in excess of 80%, is high enough to permit all restrictions to be lifted.

4.3 The R-rate is held at 1.1 from the end of January 2021 onwards

Increasing the R-rate to 1.1 will cause both cases by date reported and active infections in England to increase until the SDI reaches $\Sigma_0 = 3.9$ at the start of May 2021, at which point all restrictions are lifted (see Figure 13). Figure 14 shows new daily cases rising to 70,000 at the beginning of May 2021, while Figure 15 shows the number of active infections surging to 2 million, almost double the previous peak of 1.1 million seen at the beginning of January 2021, although active infections drop rapidly thereafter, falling to below 100 by the end of November 2021. But the vaccination campaign will have contained the daily deaths to a peak of about 600 per day in late May 2021, after which they fall away rapidly, dropping to below 10 by the start of September 2021 and zero by mid-October. Infection-generated immunity rises to

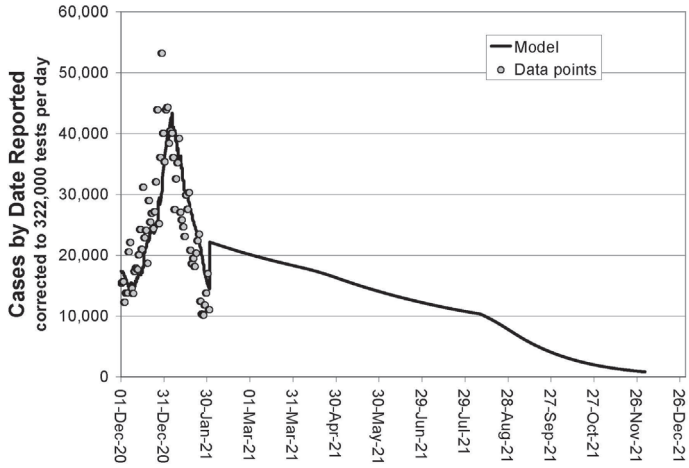

Figure 8. The effect on cases by date reported of keeping the R-rate at 0.95 from the end of January 2021 onwards.

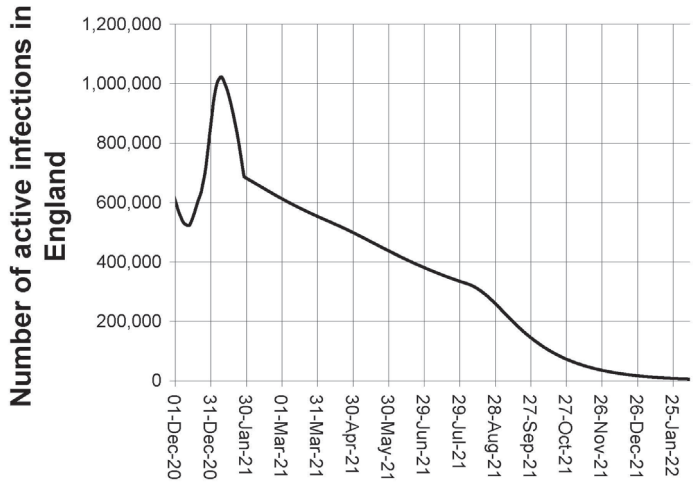

Figure 9. Active infections in England ($R = 0.95$).

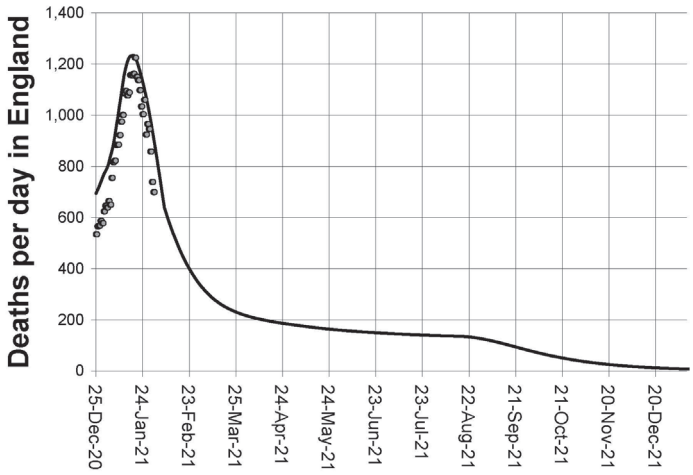

Figure 10. Deaths per day ($R = 0.95$).

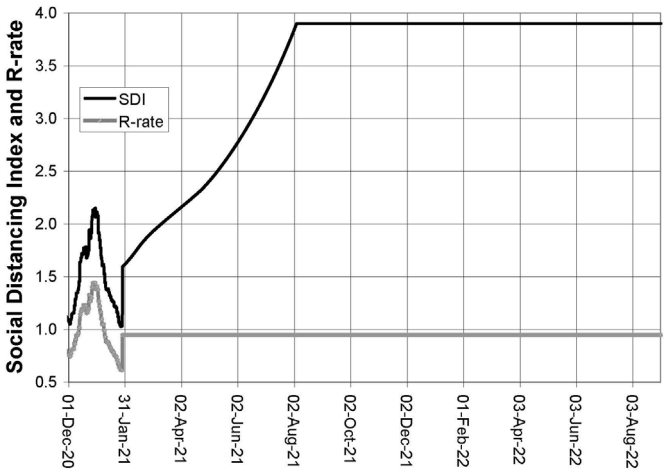

Figure 11. Social distancing index (SDI) and R-rate; $R = 0.95$.

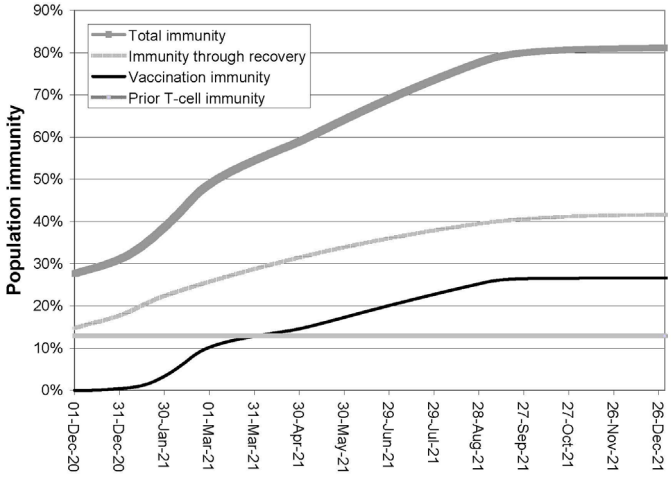

Figure 12. Components of population immunity ($R = 0.95$).

57% eventually. But it should be noted that the number of new infections that lead to death has been very significantly reduced. The vaccine immunity levels out at 21%, and the total immunity is 90%, which is significantly higher than is needed for all restrictions to be lifted.

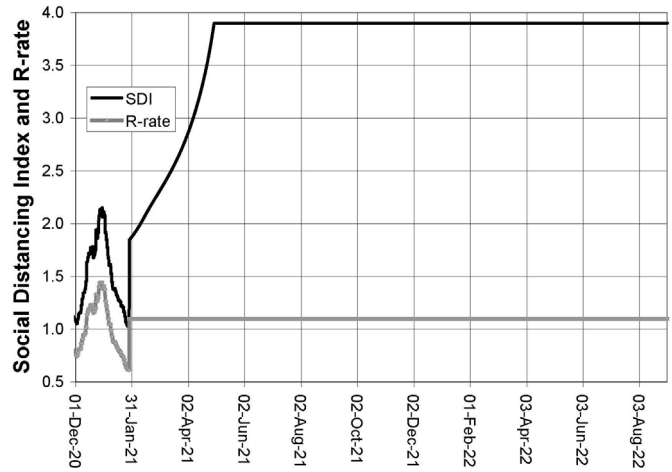

Figure 13. Social distancing index (SDI) and R-rate ($R = 1.1$).

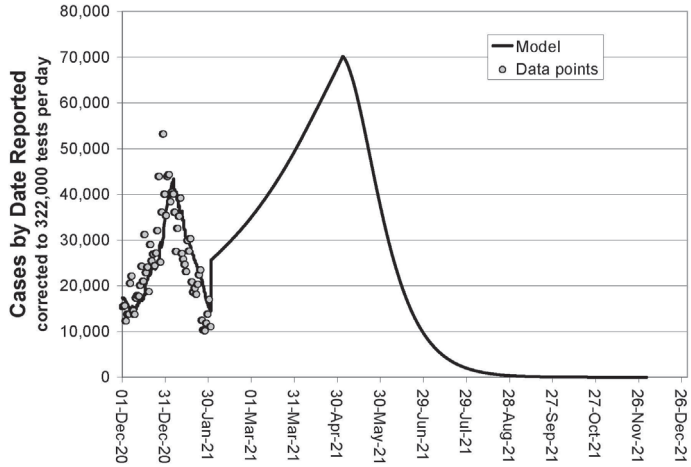

Figure 14. The effect on cases by date reported of keeping the R-rate at 1.1 from the end of January 2021 onwards.

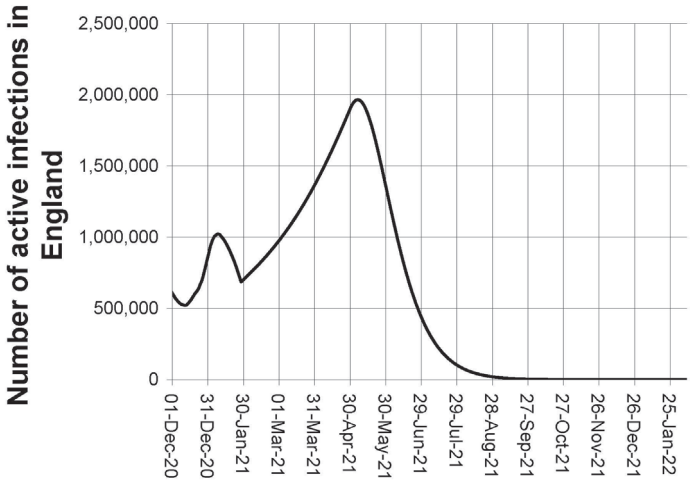

Figure 15. Active infections in England ($R = 1.1$).

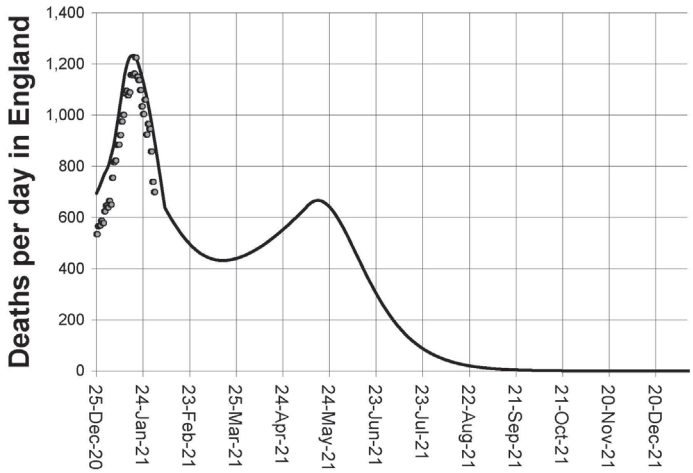

Figure 16. Daily deaths ($R = 1.1$).

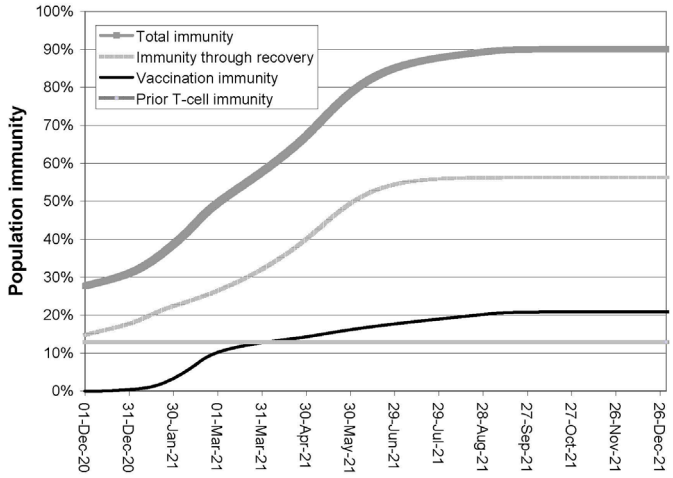

Figure 17. Components of population immunity ($R = 1.1$).

5. Results for the two-step approach

5.1 $R = 0.6$ initially and then all restrictions are lifted at the end of May 2021

Figure 18 shows the step-lifting of the SDI from 1.35 to 3.9 at the end of May 2021. This results in the cases by day reported starting gradually to increase, rising to just under 20,000 a day in September 2021 before falling away at the end of November (Figure 19). Figure 20 shows the total number of active infections in England rising above 500,000 in September and then receding over the next 6 months. But Figure 21 shows that the associated increase in daily deaths is modest, with the number peaking at about 250 at the beginning of October 2021 before declining. The principal component of the final population immunity of 79% is that generated by infection—36%, with immunity deriving from vaccination making up 30% (Figure 22).

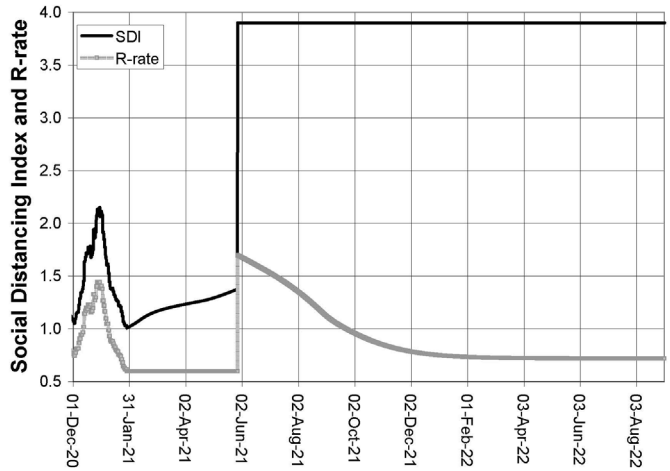

Figure 18. Social distancing index (SDI) and R-rate. Two-step strategy, $R = 0.6$ initially.

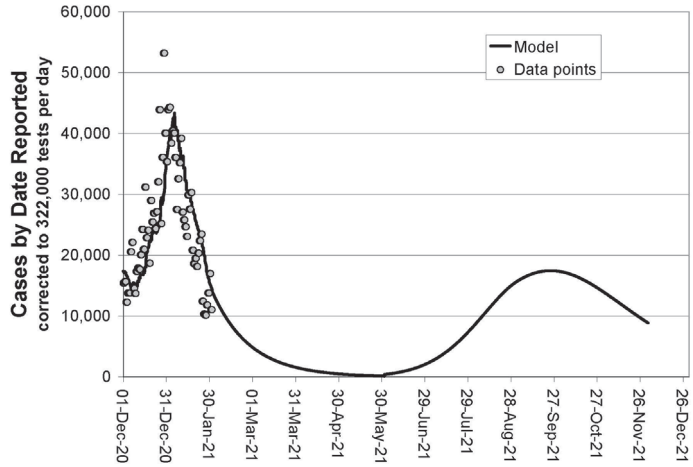

Figure 19. Cases by date reported. Two-step strategy, $R = 0.6$ initially.

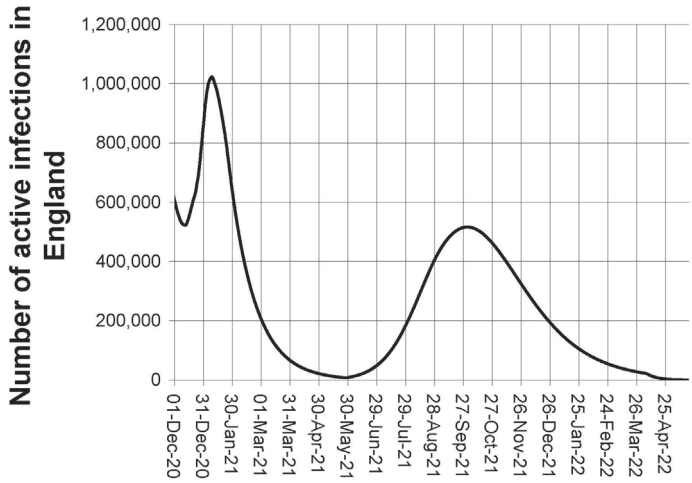

Figure 20. Active infections in England. Two-step strategy, $R = 0.6$ initially.

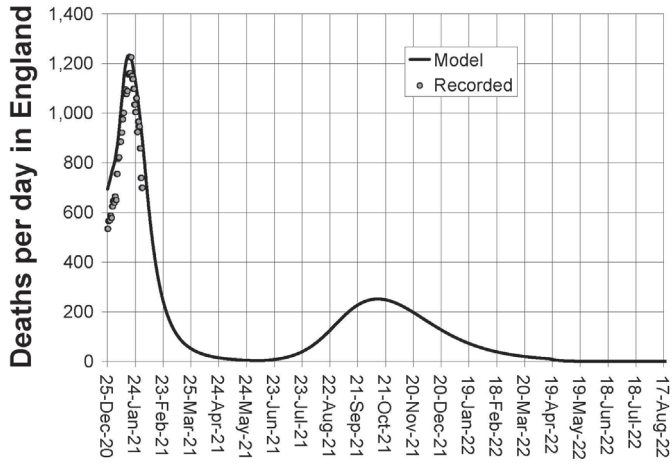

Figure 21. Daily deaths. Two-step strategy, $R = 0.6$ initially.

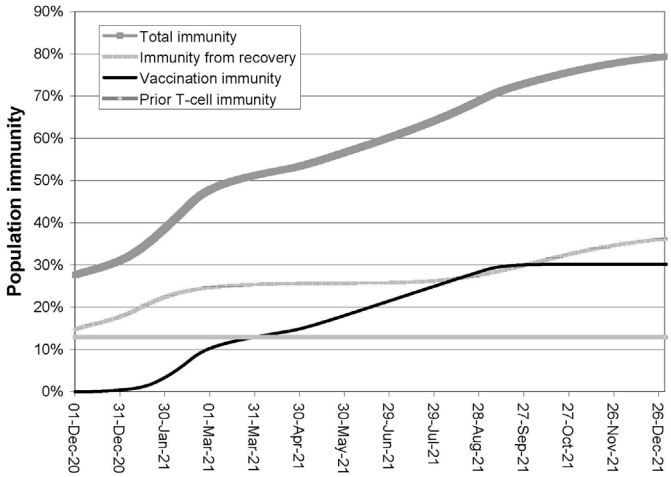

Figure 22. Components of population immunity. Two-step strategy, $R = 0.6$ initially.

5.2 $R = 0.95$ initially and then all restrictions are lifted at the end of May 2021

In this case the SDI has already reached 2.65 by the time the final step-up occurs (Figure 23). The cases by date reported rise to about 32,000 a day in early July and then retreat (Figure 24), and the number of active infections rises back up to 900,000 cases, comparable with early January 2021 (Figure 25). But the number of deaths per day is much lower now, peaking at about 350 in late July, as shown in Figure 26—similar in magnitude to the number of additional daily cases when $R = 0.6$. Population immunity levels out at 85%, the largest part of which (47%) is infection-generated immunity. Vaccination produces 25% immunity (see Figure 27).

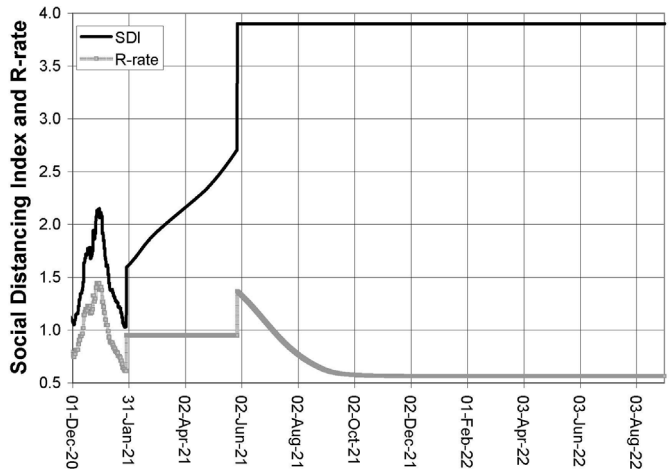

Figure 23. Social distancing index (SDI) and R-rate. Two-step strategy, $R = 0.95$ initially.

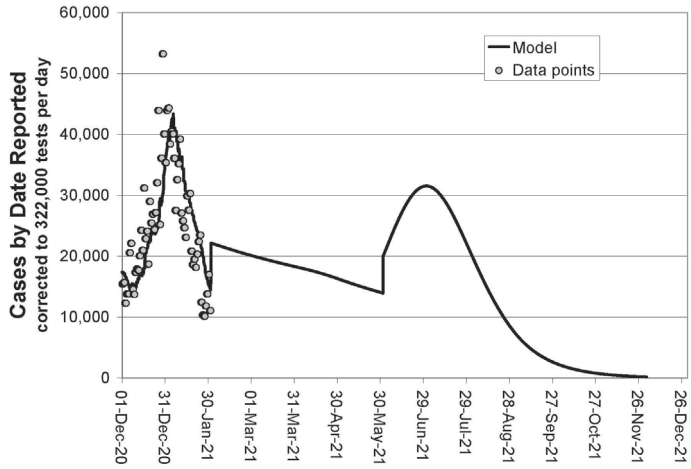

Figure 24. Cases by date reported. Two-step strategy, $R = 0.95$ initially.

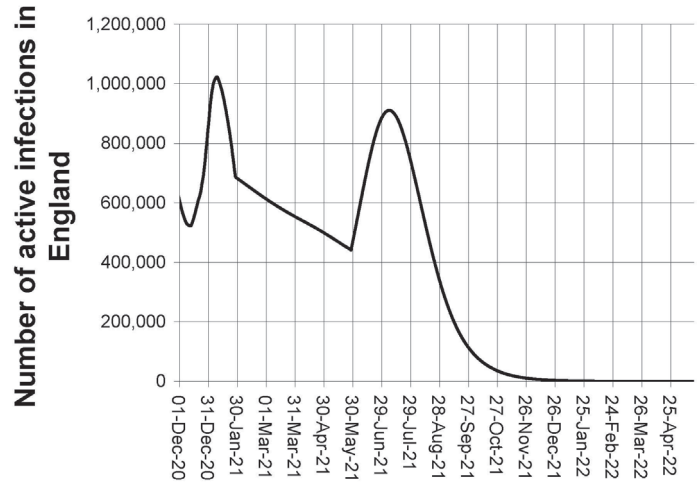

Figure 25. Active infections in England. Two-step strategy, $R = 0.95$ initially.

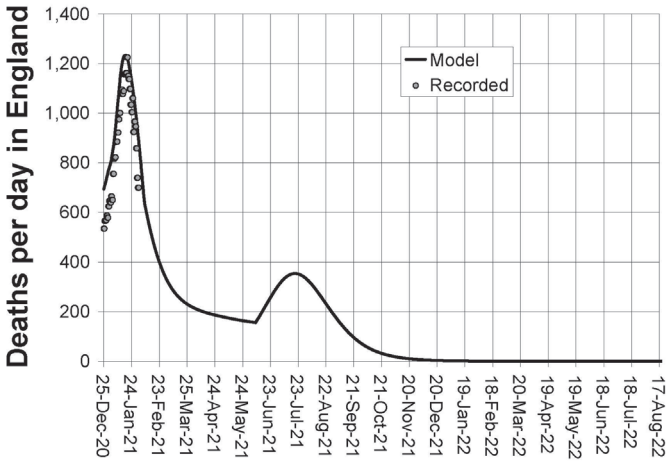

Figure 26. Daily deaths. Two-step strategy, $R = 0.95$ initially.

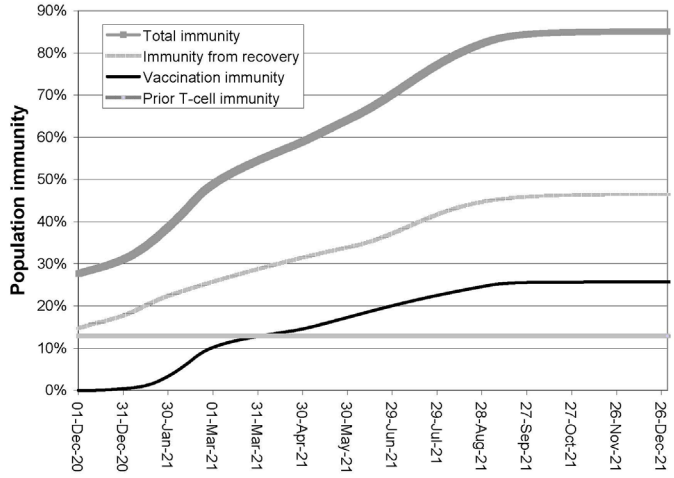

Figure 27. Components of population immunity. Two-step strategy, $R = 0.95$ initially.

6. Two-step strategy: sensitivity studies, where the SDI associated with full unlocking is $\Sigma_0 = 6$ and the second step occurs at the end of July 2021

6.1 $R = 0.95$ initially and then all restrictions are lifted at the end of July 2021

The SDI now rises from 3.6 to 6 in a step at the end of July 2021 (Figure 28). This causes the cases by date reported to rise to 35,000 in mid-September, a little higher than in the scenario of Section 5.2, as shown in Figure 29. The active infections in England also rise to 970,000, see Figure 30. The deaths per day now peak at 500 at the end of September before fading away in the autumn of 2021, as illustrated in Figure 31. Population immunity rises to 90%, with infection-generated, 51%, followed by vaccine-induced, 27%, being the principal components. It is striking how delaying the second step by two months has rendered the sensitivity scenario

of this section so similar to that of the scenario of Section 5.2, despite the much greater infectivity assumed and the higher infection fatality rate. The same does not apply when the initial value of the R-rate is kept constant at 0.6.

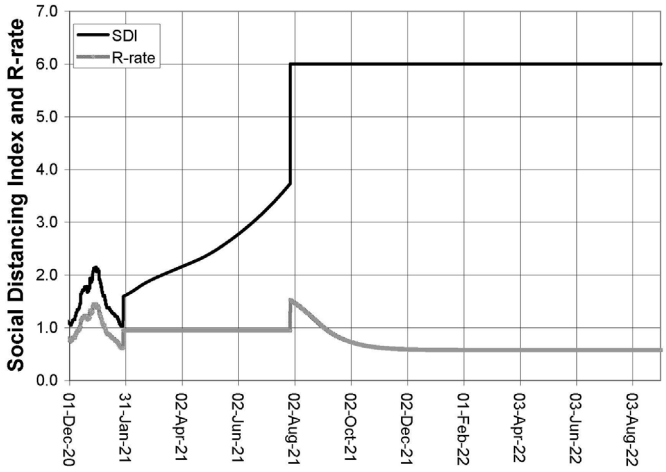

Figure 28. Social distancing index (SDI) and R-rate. Two-step strategy, $R = 0.95$ initially. Sensitivity study with $\Sigma_0 = 6$.

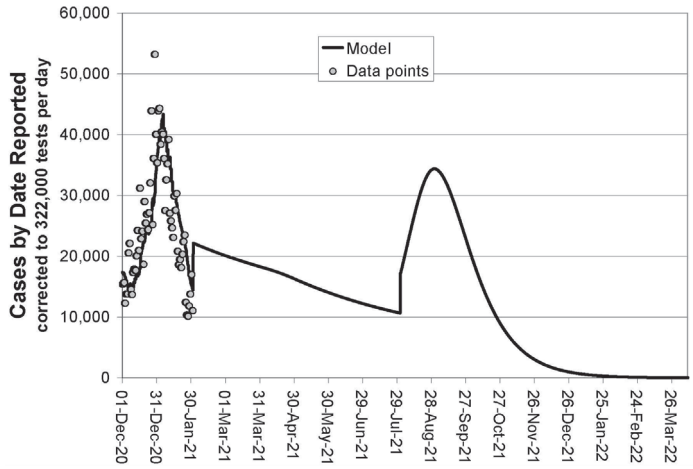

Figure 29. Cases by date reported. Two-step strategy, $R = 0.95$ initially. Sensitivity study with $\Sigma_0 = 6$.

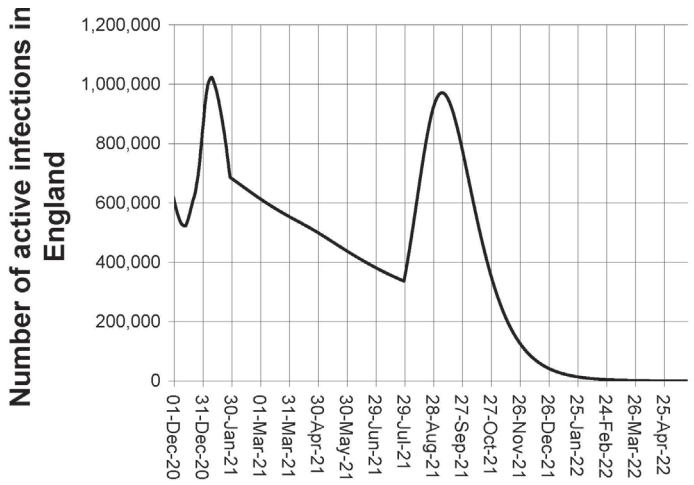

Figure 30. Active infections in England. Two-step strategy, $R = 0.95$ initially. Sensitivity study with $\Sigma_0 = 6$.

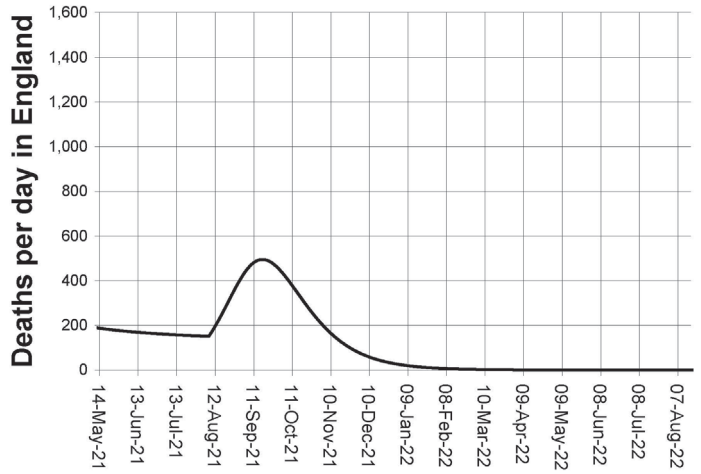

Figure 31. Daily deaths. Two-step strategy, $R = 0.95$ initially. Sensitivity study with $\Sigma_0 = 6$.

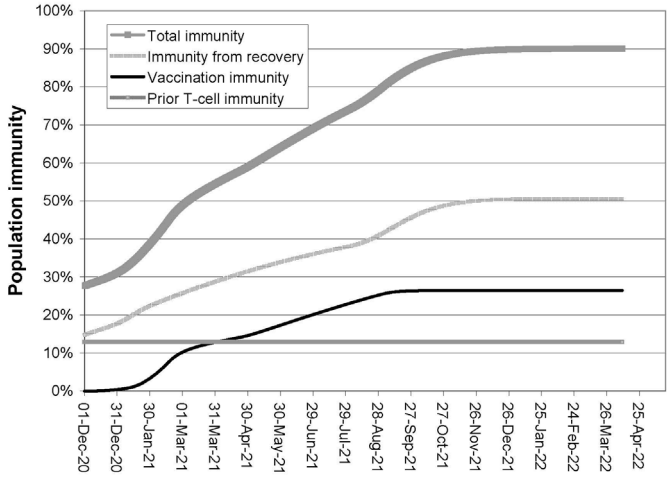

Figure 32. Components of population immunity. Two-step strategy, $R = 0.95$ initially. Sensitivity study with $\Sigma_0 = 6$.

6.2 $R = 0.6$ initially and then all restrictions are lifted at the end of July 2021

Figure 33 shows that the SDI now rises in a step from 1.6 to 6 at the end of July 2021. There is a delayed but very large rise in the number of cases by date reported, which reaches a peak of 85,000 at the beginning of November 2021, higher than England has seen hitherto (Figure 34). Meanwhile the active cases in England rise to 2.3 million in the middle of November 2021, double the highest seen previously, as shown in Figure 35. Deaths peak at 1200 a day at the end of November before falling back to a low level in February 2022, see Figure 36. 93% immunity is finally achieved, with 49% coming from recovery from infection and 30% vaccine-generated.

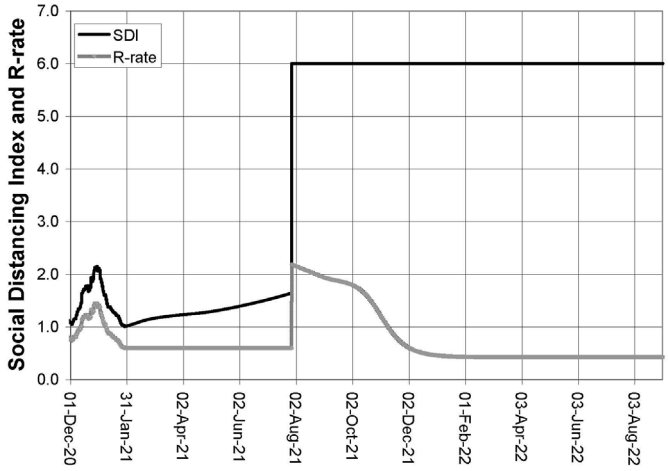

Figure 33. Social distancing index (SDI) and R-rate. Two-step strategy, $R = 0.6$ initially. Sensitivity study with $\Sigma_0 = 6$.

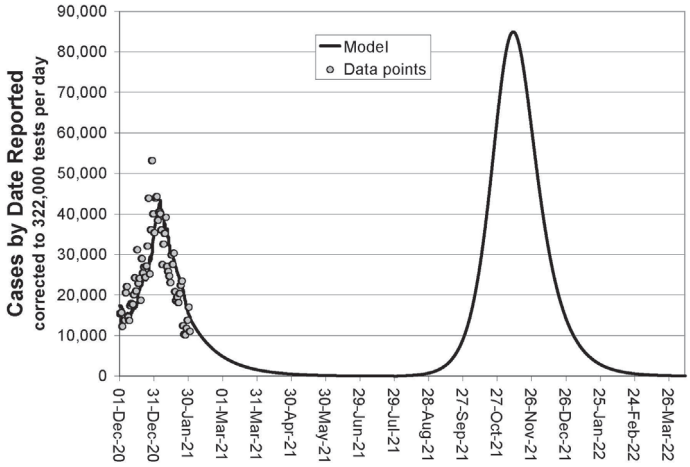

Figure 34. Cases by date reported. Two-step strategy, $R = 0.6$ initially. Sensitivity study with $\Sigma_0 = 6$.

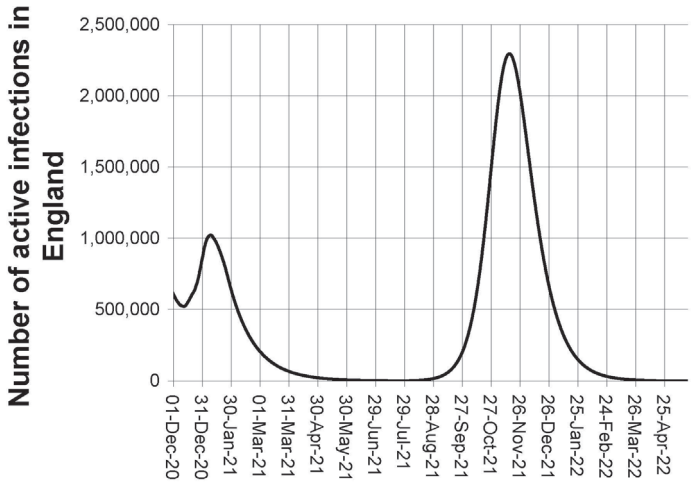

Figure 35. Active infections in England. Two-step strategy, $R = 0.6$ initially. Sensitivity study with $\Sigma_0 = 6$.

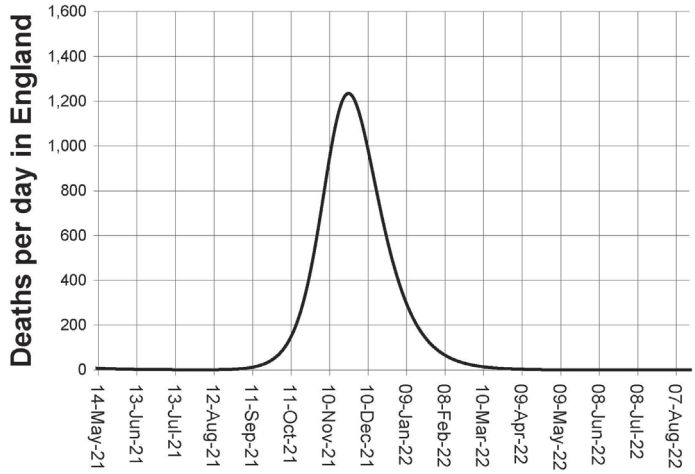

Figure 36. Daily deaths. Two-step strategy, $R = 0.6$ initially. Sensitivity study with $\Sigma_0 = 6$.

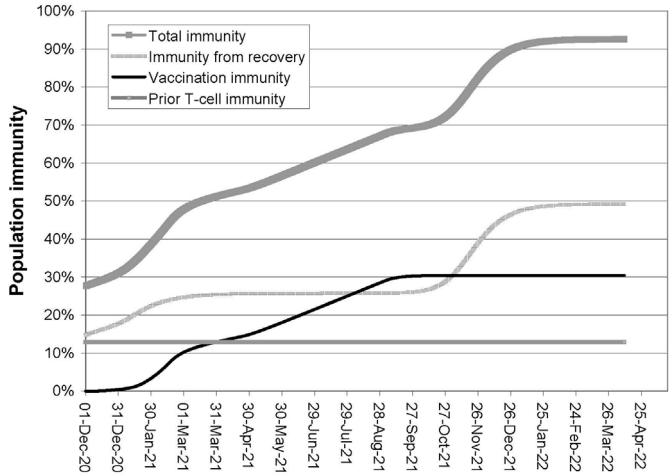

Figure 37. Components of population immunity. Two-step strategy, $R = 0.6$ initially. Sensitivity study with $\Sigma_0 = 6$.

7. Discussion

7.1 Gradualist approach

A key point emerging is that vaccination-generated immunity, while it can make a very valuable contribution to ending the crisis, should be regarded as only one component of the solution. There are two other components: prior T-cell immunity and immunity generated by infection. Scenarios that allow a full escape from restrictions require infection-generated immunity to be greater than vaccine-generated immunity. The latter can contribute from 20% to 30% of immunity, but infection-generated immunity needs to supply at least 35%.

While the Government and its advisers have generally emphasized the desirability of suppressing the virus or at least keeping it as low as possible, the analysis presented here suggests that this policy would prevent England emerging fully from lockdown when a gradualist approach is used. Keeping the R-rate well below 1.0 will lead to restrictions being kept in place indefinitely—an R-rate of about 0.9 represents the cut-off point under the gradualist approach; an R-rate maintained below this value would prevent escape.

This point might be regarded as an unintended consequence of suppressing the virus in a way that many, including scientists, have endorsed as a policy aim. Such behaviours are, however, not untypical of complex systems. It is usually necessary to devise a mathematical model and carry out simulations, as here, in order to discover the presence of what systems engineers often describe as "emergent properties", which are not intuitively obvious.

Although there has been widespread criticism of England's alleged tardiness in locking down, the analysis here suggests that it is necessary for the infection to spread widely at some point in order for the crisis to be terminated. On the other hand, infections acquired after vaccination are to be preferred to those contracted in the absence of vaccination because they incur many fewer deaths; while vaccination does not provide complete immunity from infection and hence does not fully prevent transmission (it is, of course, very helpful in this regard), it does give strong protection against dying from Covid-19.

Leaving the lockdown such that all restrictions can be fully eased while keeping the daily death rate below the high level seen in late January 2021 requires a narrow path to be followed for the six months between February and August 2021, keeping the R-rate in a central band around 1.0. Allowing the level of the virus in circulation to fall too low or to rise too high are both options to be avoided in the gradualist approach. Hence, close control of the R-rate is clearly needed and this will require the R-rate to be measured accurately, continuously and rapidly. Keeping the R-rate close to 1.0 by gradually but continually relaxing restrictions would allow all restrictions to be lifted around the end of August 2021 under the gradualist approach.

7.2 The two-step strategy

The two-step strategy takes advantage of:

(i) the fact that infections after vaccination are much less dangerous that those incurred pre-inoculation, especially for the old and the vulnerable; and

(ii) vaccination continuously decreases the number of susceptible people and, therefore, the potential size of an uncontrolled epidemic.

Controlling the R-rate below 1.0 until the end of May 2021 and then opening up fully provokes a further surge of cases, both when the R-rate is maintained at 0.6 and when it is kept at 0.95. But this large but temporary increase is not accompanied by a huge increase in the number of deaths seen each day—a peak of roughly 350 deaths per day is experienced, but this declines fairly rapidly down to low levels.

The sensitivity study examined the case where the new B.1.1.7 variant becomes fully dominant over the original strain, leading to a higher infection fatality rate and a higher value of Σ_0. As a further test for the two-step strategies, the variant was assumed to possess twice the infectivity of the original strain, so that $\Sigma_0 = 6$. To compensate for this higher value, the final exit from lockdown was delayed by two months, from the end of May to the end of July 2021.

The two-step strategy with an initial R-rate kept constant at 0.95 was largely unaffected, in the sense that the peak daily death rate rose only a little higher. However a much larger effect was seen when the R-rate was maintained at 0.6 initially—the relative lack of prior infections meant that many more were now experienced and the daily deaths rose to the peak level seen in mid January 2021, namely 1200 per day. This pointed to the lack of robustness in the strategy if the country were kept locked down too severely.

8. The accuracy of the results

The PCCF model used in the analysis has demonstrated a good record in measuring the number of active infections in England by reconciling two disparate official measurements: the daily "cases by date recorded" produced by Public Health England and the ONS's coronavirus infection survey.[14] However, the current analysis is projecting forward for a period of a year or more, which removes the feedback inherent in the two data sources: the PCCF is being used in forward prediction rather than in measurement mode.

Models help us comprehend the real world and they need to be simplifications of that world if they are to provide us with an understanding of which features are important to the problem in hand, a point expressed well by Finkelstein: "To treat effectively the complexity of real systems, the models used are highly abstract, that is to say they idealize and omit detail".[15] In this spirit, the figures quoted need be taken as indicative rather than exact. Nevertheless it is hoped and expected that the analysis will have captured the dominant features and modes of the problem of leaving lockdown.

The results are likely to be conservative, in the sense of being more pessimistic, as a result of assuming that the action of the second vaccine dose is merely to consolidate into the longer term the vaccine's effectiveness, both in reducing transmission, by 67%, and in lowering the probability of death by 95%. As described in Appendix E, the effect of the second shot will be to further reduce transmission by a total of 80% and to decrease further the probability of death so that it is 97% less likely than in the unvaccinated state.

9. Conclusions

While vaccination-generated immunity will undoubtedly make a strong contribution to ending the crisis, the other components of the solution are T-cell immunity and immunity generated by infection. Infection-generated immunity needs to be the largest component if all restrictions are to be removed.

Keeping the R-rate below about 0.9 leads to restrictions being kept in place indefinitely if the gradualist approach is adopted, even after all the adult population has been vaccinated. Moreover, maintaining the R-rate too low in the initial phase of the two-step strategy reduces robustness against the possible future dominance of the new B.1.1.7 variant.

Leaving the lockdown to the extent that all restrictions can be fully eased requires a narrow path to be followed during the spring and early summer of 2021, keeping the R-rate in a central band

[14] See *The Spectator* Covid-19 data tracker: https://data.spectator.co.uk/city/national

[15] Finkelstein, L., From technology to wider knowledge, understanding and wisdom, *Measurement Control* **39** (2006) 268–272.

around 1.0. Allowing the level of the virus in circulation to fall too low or to rise too high are both options to be avoided if the spirit of England's policy on Covid-19 is to be retained.

Close control of the R-rate is needed and this will require the R-rate to be measured accurately, continuously and rapidly.

Keeping the R-rate close to 1.0 by gradually but continually relaxing restrictions might allow all restrictions to be lifted by the end of the summer, but the process of leaving lockdown might be speeded up by modifying the approach and using a two step strategy, which might allow full derestriction by the end of May 2021.

Appendix A. Modelling the disease response when the cohorts are divided into groups for vaccination according to age

Let the population of the country be split into two cohorts i, $i = 1, 2$, each of which will be divided into eight age groups j: $j = 1, \ldots, 8$. Anyone in Cohort 1 who contracts Covid-19 will display symptoms and will take a test. People in Cohort 2 contracting Covid-19 will experience either mild or no symptoms; such people will never be tested and hence their infection will never be reported. It is estimated that $\theta_1 = 30\%$ of the population belongs to Cohort 1 while $\theta_2 = 1 - \theta_1 = 70\%$ of the population belongs to Cohort 2.[4] The age groups are listed in Table A.1. The number of people $N_i^{(j)}$ in age group j of cohort i will be:

$$N_i^{(j)} = p^{(j)}\theta_i N \tag{A.1}$$

where $p^{(j)}$ is the fraction of the population in age group j.

Table A.1. Age groups and their identifiers.

Age group identifier, j	Age group (years)	Fraction of English population in age group, $p^{(j)}$	Number in age group across both cohorts, $m^{(j)}(0)$
1	80 – 100	7.56%	4,272,973
2	70 – 79	9.35%	5,282,551
3	65 – 69	5.33%	3,012,633
4	60 – 64	5.59%	3,156,411
5	55 – 59	5.75%	3,251,219
6	50 – 54	5.86%	3,313,718
7	18 – 49	38.60%	21,809,057
8	0 – 17	21.95%	12,401,437
	0 – 100	100%	56,500,000

The social distancing index (SDI) is the number of potentially infective contacts made by the average person between infection and recovery in a fully susceptible population. Infections will be transmitted if the contact is with a susceptible person. Each of the SDIs, Σ_i, and the average time between successive generations, $\tau_{\text{inf},j}$, will taken to be representative of cohort i across all age groups $j = 1, 2, \ldots, 8$.

At the start of vaccination $t = t_{v0}$, and the ratio $n_{si}^{(j)}(t_{v0})/n_{si}(t_{v0})$ of susceptible people in age group j of cohort i to those of all ages across the cohort will be equal to the fraction $N_i^{(j)}(t_{v0})/N_i(t_{v0}) = p^{(j)}$ of people of that age in the cohort, assuming a uniform distribution of infections across ages. Hence

$$n_{si}^{(j)}(t_{v0}) = p^{(j)} n_{si}(t_{v0}) \quad i = 1, 2;\ j = 1, 2, \ldots, 8. \tag{A.2}$$

This equation forms one starting condition for the vaccination exercise.

Clearly the summing equation (A.2) over all j will give the number of susceptible people in the cohort:

$$\sum_{j=1}^{8} n_{si}^{(j)}(t_{v0}) = n_{si}(t_{v0}) \sum_{j=1}^{8} p^{(j)} = n_{si}(t_{v0}) \quad i = 1, 2 \tag{A.3}$$

since $\sum_{j=1}^{8} p^{(j)} = 1$. Moreover, the total number of susceptible people in the population is found, of course, by adding together the contributions from the two cohorts:

$$n_s(t_{v0}) = n_{s1}(t_{v0}) + n_{s2}(t_{v0}). \tag{A.4}$$

Let $n_i^{(j)}(t)$ be the number of people with an active infection in the jth age group in cohort i at time t. At time t_{v0}, just before vaccination starts, the fraction $n_i^{(j)}(t_{v0})/n_i(t_{v0})$ of infectious people in age group j of cohort i will be equal to the fraction $N_i^{(j)}(t_{v0})/N_i(t_{v0}) = p^{(j)}$ of people of that age in the cohort so that:

$$n_i^{(j)}(t_{v0}) = p^{(j)} n_i(t_{v0}) \quad i = 1, 2;\ j = 1, 2, \ldots, 8. \tag{A.5}$$

This equation constitutes a second starting condition.

By analogy with equations (A.4) and (A.5), summation gives the number of people with an active infection in each cohort:

$$\sum_{j=1}^{8} n_i^{(j)}(t_{v0}) = n_i(t_{v0}) \sum_{j=1}^{8} p^{(j)} = n_i(t_{v0}) \quad i = 1, 2 \tag{A.6}$$

and in the whole population:

$$n(t_{v0}) = n_1(t_{v0}) + n_2(t_{v0}). \tag{A.7}$$

The rate at which meetings with the potential to pass on infection are taking place between an infected person in age group j of cohort i and some other individual is:

$$\frac{n_i^{(j)} \Sigma_i}{\tau_{\mathrm{inf},i}} \quad i = 1, 2;\ j = 1, 2, \ldots, 8.$$

The rate at which potentially infectious meetings are taking place between an infected person and someone, anyone, else is the sum over both cohorts and all age groups within them and may be called the common driver, D:

$$D = \sum_{i=1}^{2} \sum_{j=1}^{8} \frac{n_i^{(j)} \Sigma_i}{\tau_{\mathrm{inf},i}}. \tag{A.8}$$

If everyone in the population were susceptible (a so-called "naïve" population), then this would represent the rate at which people were becoming infected. Their infection could come from either of the cohorts and from someone of any age within either cohort. However, as a

result of natural immunity, previous infection and vaccination the number of susceptible people will be less than 100% of the population. Given that one of the potentially infective meetings has occurred, the probability of someone in age group *j* of cohort *i* then being infected is simply the probability that the meeting happens between an infected individual and someone susceptible in age group *j*. The meeting might involve anyone in the population, hence the chance of the encounter being with someone susceptible in age group *j* is the number $n_{si}^{(j)}$ of such people divided by the number of people in the population at large less the infected person, viz. $N-1$. Of course $N-1 \to N$ as N gets very large, as is the case here, where each age group contains millions of people. Hence we may write the probability as $n_{si}^{(j)}(t)/N$.

Utilizing the driver concept introduced in equation (A.8), the rate $\mathrm{d}n_{xi}^{(j)}/\mathrm{d}t$ at which people in age group *j* in cohort *i* are being infected will be

$$\frac{\mathrm{d}n_{xi}^{(j)}}{\mathrm{d}t}(t) = \frac{n_{si}^{(j)}}{N} D, \tag{A.9}$$

which may be re-expressed as

$$\frac{\mathrm{d}n_{xi}^{(j)}}{\mathrm{d}t}(t) = \frac{n_{si}^{(j)}(t)}{N}\left(\Sigma_1 \sum_{j=1}^{8} \frac{n_1^{(j)}(t)}{\tau_{\mathrm{inf},1}} + \Sigma_2 \sum_{j=1}^{8} \frac{n_2^{(j)}(t)}{\tau_{\mathrm{inf},2}} \right). \tag{A.10}$$

Equations (A.8) and (A.9) make the cross-infection between groups explicit.

The rate at which infected people in age group *j* of cohort *i* pass on their infection per day and then recover or die may be called the rate of pure recovery, $\left(\mathrm{d}n_{ri}^{(j)}/\mathrm{d}t\right)\Big|_{pure}$, and given by (cf. equation (A.9) in Thomas (2020)[10])

$$\left.\frac{\mathrm{d}n_{ri}^{(j)}}{\mathrm{d}t}\right|_{pure} = \frac{n_i^{(j)}(t)}{\tau_{\mathrm{inf},i}} \quad i = 1, 2;\ j = 1, 2, \ldots, 8, \tag{A.11}$$

which may be subtracted from the rate at which people are infected to give the net rate of growth of active infections in age group *j* of cohort *i*:

$$\frac{\mathrm{d}n_i^{(j)}}{\mathrm{d}t}(t) = \frac{\mathrm{d}n_{xi}^{(j)}}{\mathrm{d}t}(t) - \left.\frac{\mathrm{d}n_{ri}}{\mathrm{d}t}\right|_{pure} =$$

$$\frac{n_{si}^{(j)}(t)}{N}\left(\Sigma_1 \sum_{j=1}^{8} \frac{n_1^{(j)}(t)}{\tau_{\mathrm{inf},1}} + \Sigma_2 \sum_{j=1}^{8} \frac{n_2^{(j)}(t)}{\tau_{\mathrm{inf},2}} \right) - \frac{n_i^{(j)}(t)}{\tau_{\mathrm{inf},i}} \quad i = 1, 2;\ j = 1, 2, \ldots, 8. \tag{A.12}$$

It is convenient, in the model, to collect under the heading "recovered":

(i) those who had the illness but are now well again—the "pure" recovered;

(ii) those with prior T-cell immunity, estimated to be 12.9% of the population;

(iii) those who have been vaccinated and whose inoculation was long enough ago to be effective;

(iv) those who will succumb to the disease.

It is assumed that, just before vaccination starts, the fraction of people recovered who fall into age group *j* of any cohort *i* will be proportional to the fraction $p^{(j)}$ of people of that age group in the population:

$$n_{ri}^{(j)}(t_{v0}) = p^{(j)} n_{ri}(t_{v0}) \qquad i = 1, 2;\ j = 1, 2, \ldots, 8. \tag{A.13}$$

The rate of change in the number of people recovering will not be affected by the phenomenon of prior T-cell immunity, since this number will not change during the course of the epidemic. However, rate of change in the number of people recovering will depend both the rate of pure recovery, given by equation (A.10), and the rate of vaccination maturity.

Allowing for vaccination

The intervention of vaccination has strong similarities to the event of infection. In this case, however, what results is future immunity, rather than the onset of disease—"future" immunity because protection is given only if the person avoids exposure to infection within the roughly three weeks after inoculation that allow the vaccine shot to become fully effective. This future immunity will not be conferred on a person who is already infected or has already recovered nor on those with prior T-cell immunity. New immunity can only be given if the vaccine is administered to a susceptible person.

An eligible person is one who has not yet been vaccinated. An eligible, susceptible person is a person who is susceptible to the disease but who has not yet been vaccinated. At the start of vaccination, when $t = t_{v0}$, the number of eligible susceptible people is the same as the number of susceptible people:

$$n_{esi}^{(j)}(t_{v0}) = n_{si}^{(j)}(t_{v0}), \tag{A.14}$$

but, while the rate of change $\mathrm{d}n_{si}^{(j)}/\mathrm{d}t$ of susceptible people in age group j in cohort i is simply the rate at which people of that age group and cohort are being infected, viz. $\mathrm{d}n_{si}^{(j)}/\mathrm{d}t = -\mathrm{d}n_{xi}^{(j)}/\mathrm{d}t$, the rate of change of eligible susceptible people will tend to be greater, as the people can leave the ranks of those susceptible and eligible by either (i) becoming infected, when a fraction, $n_{esi}^{(j)}/n_{si}^{(j)}$, of $\mathrm{d}n_{xi}^{(j)}/\mathrm{d}t$ will come from the eligible subset of the susceptible; or else (ii) by being vaccinated at rate $v_{esi}^{(j)}$. Hence

$$\frac{\mathrm{d}n_{esi}^{(j)}}{\mathrm{d}t} = -\frac{n_{esi}^{(j)}}{n_{si}^{(j)}}\frac{\mathrm{d}n_{xi}^{(j)}}{\mathrm{d}t} - v_{esi}^{(j)}. \tag{A.15}$$

Here $v_{esi}^{(j)}$ is the rate of vaccination of eligible, susceptible people in age group j and cohort i. This may be calculated as

$$v_{esi}^{(j)}(t) = p_{vesi}^{(j)}(t) v^{(j)}(t) \tag{A.16}$$

where $v^{(j)}(t)$ is the rate at which people are being vaccinated in age group j. Meanwhile $p_{vesi}^{(j)}$ is the likelihood of selecting an eligible, susceptible person who belongs to age group j and cohort i to be included in the day's age-dependent vaccination batch; that is to say choosing someone who (i) belongs to that grouping, (ii) is susceptible and (iii) has not yet been vaccinated.

The Government specifies and arranges the rates of vaccination, $v^{(j)}(t)$, in age groups first to those aged 80 and over, then 70 to 79 year olds and so on. It is assumed that everyone in the age group j, across both cohorts, who has not yet been vaccinated stands the same chance of being selected for inoculation. Those who are immune through recovery or through prior T-cell protection will be eligible for vaccination *pari passu* with those who are actually susceptible.

Let the number of people yet to be vaccinated in age group j be $m^{(j)}(t)$, which defines the size of the full vaccination pool across both cohorts for age j. (This exaggerates slightly the size of the vaccination pool, since it includes the small number of people in Cohort 1 who not only have an active infection but are also at the symptomatic stage. By contrast, many of those with an active infection in the much larger Cohort 2 are likely to regard themselves as eligible for vaccination anyway, and so need to be included in the vaccination pool. The net effect of including an extra small number of people will be to prolong the vaccination process of each of the seven age groups to be inoculated by up to a day at most.) Let us denote by $n_{esi}^{(j)}(t)$ the current number of eligible susceptible people in age group j of cohort i. The likelihood, $p_{vesi}^{(j)}(t)$, of selecting for the vaccination campaign an eligible, susceptible person who belongs to age group j and cohort i will be the ratio of this number, $n_{esi}^{(j)}(t)$, to the total number of eligible people in the age group:

$$p_{vesi}^{(j)} = \frac{n_{esi}^{(j)}(t)}{m^{(j)}(t)}. \tag{A.17}$$

The starting condition for $m^{(j)}$ before vaccination starts is the number of people in age group j in the population: $m^{(j)}(t_{v0}) = N^{(j)}(t_{v0}) = p^{(j)}N$. It will, however, decrease as more people of age group j are vaccinated:

$$m^{(j)}(t) = m^{(j)}(t_{v0}) - y^{(j)}(t) \tag{A.18}$$

where $y^{(j)}(t)$ is the number of people of age group j who have been vaccinated, found by integrating equation (A.19):

$$\frac{\mathrm{d}y^{(j)}}{\mathrm{d}t}(t) = -v^{(j)}(t). \tag{A.19}$$

The vaccine efficacy at preventing disease and transmission, η_v, will grow from after the first injection and continue further after the second injection 12 weeks later. The process of vaccine maturation may be modelled as an exponential lag, obeying the equation:

$$\eta_v = \eta_{vf}\left(1 - e^{-x/\tau_{mat}}\right) \tag{A.20}$$

where x is the time since first vaccination, η_{vf} is the final vaccine efficiency achieved after the second injection and τ_{mat} is the vaccine maturation time constant. The effect may be simulated by applying the final vaccine efficacy to the flow of vaccinated eligible and susceptible people, $v_{esi}^{(j)}$, and subjecting this to a first-order exponential lag:

$$\frac{\mathrm{d}q_i^{(j)}}{\mathrm{d}t} = \frac{\eta_{vf}v_{esi}^{(j)} - q_i^{(j)}}{\tau_{mat}}. \tag{A.21}$$

Integrating equation (A.21) gives the flow, $q_i^{(j)}(t)$, of people in age group j and cohort i becoming immune at time t as a result of vaccination. This allows the rate of increase in recovered people in age group j and cohort i to be calculated:

$$\frac{\mathrm{d}n_{ri}^{(j)}}{\mathrm{d}t} = \left.\frac{\mathrm{d}n_{ri}^{(j)}}{\mathrm{d}t}\right|_{pure} + q_i^{(j)}(t) = \frac{n_i^{(j)}(t)}{\tau_{\mathrm{inf},i}} + q_i^{(j)}(t) \quad i = 1, 2;\ j = 1, 2, \ldots, 8. \tag{A.22}$$

In this model, a person of age *j* in cohort *i* will belong to one of the categories: susceptible, infected (with an active infection) and recovered. The time-marching integration of equations (A.12) and (A.22) will give the number of people in each of the classifications, "infected" and "recovered", while the total number in the age group and cohort $N_i^{(j)}$ is given by equation (A.1) as $\theta_1 p^{(j)} N$. Hence the number of susceptible people make be found by subtraction:

$$n_{si}^{(j)}(t) = \theta_i p^{(j)} N - n_i^{(j)}(t) - n_{ri}^{(j)}(t) \quad i = 1, 2;\ j = 1, 2, \ldots, 8. \tag{A.23}$$

Vaccine protection against death

In addition to protecting against illness, with efficacy η_v, vaccines will protect against dying from Covid-19, with eventual efficacy η_{ND}. Early evidence suggests that the latter might be as high as 100% for the AstraZeneca vaccine, but in the present study η_{ND} is set more cautiously at 95% . Hence, while some people are protected against both disease and death by vaccination, a further set is protected only against death. The rate at which the number $g_i^{(j)}$ of people in age group *j* and cohort *i* become protected, at time *t*, from dying as a result of vaccination but not against infection may be modelled (cf. equation A.22) as

$$\frac{\mathrm{d}g_i^{(j)}}{\mathrm{d}t} = \frac{\left(\eta_{ND} - n_{vf}\right) v_{esi}^{(j)} - g_i^{(j)}}{\tau_{mat}}. \tag{A.24}$$

Integrating equation (A.24) gives the flow $g_i^{(j)}(t)$ of people protected against dying but still susceptible to infection. Some of them will become infected in the same way as other susceptible people in their age group and cohort. Hence the fraction of the flow of people being infected belonging to this "non-dying" category will be $n_{si}^{(j)}\Big|_{ND} \Big/ n_{si}^{(j)}$, where $n_{si}^{(j)}\Big|_{ND}$ is the number of susceptible people who are protected by vaccination against dying but not against infection. This number, $n_{si}^{(j)}\Big|_{ND}$, will therefore obey the differential equation:

$$\frac{\mathrm{d}}{\mathrm{d}t} n_{si}^{(j)}\Big|_{ND} = g_i^{(j)} - \frac{n_{si}^{(j)}\Big|_{ND}}{n_{si}^{(j)}} \frac{\mathrm{d}n_{xi}^{(j)}}{\mathrm{d}t}. \tag{A.25}$$

The number, $n_{si}^{(j)}\Big|_{D}$, of susceptible people who are not protected from dying may be found as:

$$n_{si}^{(j)}\Big|_{D} = n_{si}^{(j)} - n_{si}^{(j)}\Big|_{ND}. \tag{A.26}$$

The death rate

Let the probability of unvaccinated people in age group *j* dying of the disease if they catch it be $p_{D0}^{(j)}$. At time *t* the number of susceptible people in age group *j* will be the total across both cohorts, $n_{s1}^{(j)}(t) + n_{s2}^{(j)}(t)$. Of those, there will be only $n_{s1}^{(j)}\Big|_{D} + n_{s2}^{(j)}\Big|_{D}$ people who may die if they catch Covid-19, with a probability of death of $p_{D0}^{(j)}$. Hence the overall probability of death once Covid-19 is contracted will be

$$p_D^{(j)}(t) = \frac{0 \times \sum_{i=1}^{2} n_{si}^{(j)}\Big|_{ND} + p_{D0}^{(j)} \sum_{i=1}^{2} n_{si}^{(j)}\Big|_{D}}{\sum_{i=1}^{2} n_{si}^{(j)}} = \frac{n_s^{(j)}\Big|_D}{n_s^{(j)}} p_{D0}^{(j)}. \tag{A.27}$$

The overall probability of dying across all age groups may then be calculated as

$$p_D(t) = \frac{\sum_{j=1}^{8} n_s^{(j)}(t)\, p_D^{(j)}(t)}{\sum_{j=1}^{8} n_s^{(j)}(t)}. \tag{A.28}$$

Appendix B. Modelling the vaccination campaign prioritized according to age

Let the number of unvaccinated people in each age group across both cohorts be $m^{(j)}(t)$: $j = 1, 2, 3, \ldots, 8$. The values at the start of the vaccination process are then $m^{(j)}(t_{v0}) = p^{(j)}N$, where $p^{(j)}$ is the fraction of the population in age group j, $j = 1, 2, \ldots, 8$ (see Table A.1). The number of vaccinations $v(t_n)$ on day t_n across all age groups is regarded as an exogenous variable. It follows the daily rates of first doses reported up to 6 February 2021, and is then set at the constant rate of 400,000 per day for the remainder of the vaccination campaign. From 9 December 2020 to 18 January 2021, 60% of the vaccine doses are assumed distributed to those aged 80 and over and 6.7% each to those in age groups 70–79, 65–69, 60–64, 55–59, 50–54 and 18–49 to account for the vaccination of health workers and those vulnerable with morbidities. From 19 to 28 January 2021, 50% of the vaccine first doses are assumed to go to those of 80 and over and the remainder to those aged between 70 and 79. Vaccination of 92% of those aged 80 and over is completed on 29 January 2021. Thereafter people are vaccinated in ordered age groups, starting with the completion of inoculation of group 2 and ending with group 7, with no vaccinations being given to children, age group 8, in line with government policy. Each successive group is vaccinated until only a fraction, f_{unvac} (set to 8% in this work), is left unvaccinated in each group. Let the cumulative number of vaccinations given to age group j by day t_n be $y^{(j)}(t_n)$, where

$$y^{(j)}(t_n) = \int_{t_{v0}}^{t_n} v^{(j)}(t)\,\mathrm{d}t \tag{B.1}$$

where in turn $v^{(j)}(t)$ is the number of vaccinations made on day, t, to members of age group, j. The number of vaccinations administered to age group j on day t_n is then

$$v^{(j)}(t_n) = \begin{cases} v(t_n) - \sum_{k=2}^{j-1} v^{(k)}(t_n) & \text{if} \quad v(t_n) - \sum_{k=2}^{j-1} v^{(k)}(t_n) < y^{(j)}(t_{n-1}) - f_{unvac} m^{(j)}(t_{v0}) \\ y^{(j)}(t_{n-1}) - f_{unvac} m^{(j)}(t_{v0}) & \text{if} \quad v(t_n) - \sum_{k=2}^{j-1} v^{(k)}(t_n) \geq y^{(j)}(t_{n-1}) - f_{unvac} m^{(j)}(t_{v0}) \end{cases}. \tag{B.2}$$

Appendix C. The death probabilities for different age bands in the absence of

vaccination

Let the number of people in the population be N and the number in age group j be $N^{(j)}$, where the probability of being in age group j is

$$p^{(j)} = \frac{N^{(j)}}{N}. \tag{C.1}$$

Let the number of people in age group j recorded as dying from Covid-19 in England in 2020 be $n_D^{(j)}$, with a total number across all age groups:

$$n_D = \sum_j n_D^{(j)}. \tag{C.2}$$

Let us assume that everyone has the same chance p_{inf} of being infected. Hence the expected value of the (random) number $N_{\text{inf}}^{(j)}$ of people infected in age group j is

$$E\left(N_{\text{inf}}^{(j)}\right) = p_{\text{inf}} N^{(j)} = p_{\text{inf}} p^{(j)} N. \tag{C.3}$$

Let the probability of people in age group j dying after being infected be $p_{D0}^{(j)}$. The expected number of people in age group j dying is therefore:

$$n_D^{(j)} = E\left(N_D^{(j)}\right) = p_{D0}^{(j)} E\left(N_{\text{inf}}^{(j)}\right) = p_{D0}^{(j)} p^{(j)} p_{\text{inf}} N. \tag{C.4}$$

Meanwhile the expected total number of deaths across all age groups may be calculated as

$$n_D = E\left(N_D\right) = p_{D0} E\left(N_{\text{inf}}\right) = p_{D0} p_{\text{inf}} N \tag{C.5}$$

where p_{D0} is the overall probability of dying from Covid-19, given that one has been infected, for the population as a whole. Dividing equation (C.4) by equation (C.5) gives:

$$\frac{p_{D0}^{(j)}}{p_{D0}} = \frac{1}{p^{(j)}} \frac{n_D^{(j)}}{n_D} \tag{C.6}$$

or

$$p_{D0}^{(j)} = \frac{p_{D0}}{p^{(j)}} \frac{n_D^{(j)}}{n_D}. \tag{C.7}$$

Appendix D. Identifying the vaccination maturity time constant, τ_{mat}

Two ways are presented for estimating the time constant associated with the vaccine maturing in the body. The values are roughly similar, but the second method, based on more recent data, is preferred; it suggests that the body is able to mobilize its defences more rapidly.

D.1 Based on Oxford–AstraZeneca trial data

Information provided by Oxford University scientists[1] showed that all infections, both symptomatic and asymptomatic, were reduced by 67% for the period 22 to 90 days after a single dose of the Oxford–AstraZeneca vaccine. Assuming, conservatively, that no immunity builds

up until after 21 days, the measured efficiency in preventing transmission may be modelled as:

$$\eta_{vm}(x) = \begin{cases} 0 & \text{for } 0 < x \le 21 \\ 0.67 & \text{for } 21 < x \le 90 \end{cases} \tag{D.1}$$

where x is the number of days after the first injection. The average efficacy from 0 to 90 days is therefore:

$$\eta_{vmeas}\big|_{ave} = \frac{1}{90}\left(\int_{x=0}^{90} \eta_{vm}\,\mathrm{d}x\right) = \frac{1}{90}\left(\int_{x=0}^{21} 0\,\mathrm{d}x + \int_{x=21}^{90} 0.67\,\mathrm{d}x\right) = \frac{0.67}{90}\times 69. \tag{D.2}$$

Modelling the process as a first order exponential lag produces equation (A.20), here repeated:

$$\eta_v = \eta_{vf}\left(1 - e^{-x/\tau_{mat}}\right). \tag{A.20}$$

The average value of this over the interval from 0 to 90 days will be

$$\eta_v\big|_{ave} = \frac{\eta_{vf}}{90}\int_{x=0}^{90}\left(1 - e^{-\frac{x}{\tau_v}}\right)\mathrm{d}x = \frac{\eta_{vf}}{90}\left(90 + \tau_v\left[e^{-\frac{x}{\tau_v}}\right]_0^{90}\right) = \frac{\eta_{vf}}{90}\left(90 + \tau_v e^{-\frac{90}{\tau_v}} - \tau_v\right). \tag{D.3}$$

Choosing the asymptotic value of η_v as $x \to \infty$ in equation (A.20) as $\eta_{vf} = 0.67$, the two averages of equations (D.2) and (D.3) will be equal if and only if

$$90 + \tau_v e^{-\frac{90}{\tau_v}} - \tau_v = 69, \tag{D.4}$$

which may be rearranged into the form:

$$\tau_v\left(1 - e^{-\frac{90}{\tau_v}}\right) - 21 = 0. \tag{D.5}$$

Inspection of equation (D.5) suggests that the time constant will be close to 21 days (the exponential term becomes very small), and an iterative solution yields:

$$\tau_v = 21.31 \text{ days}. \tag{D.6}$$

D.2 Based on ONS antibody surveys

This section uses as its primary source the ONS antibody surveys for England published on 3 February 2021 and 16 February 2021.[16] The results, which are less conservative, are still fully consistent with AstraZeneca's and they also match very well with data on the reported development of resistance to Covid-19 in practice. The ONS results are summarized in Table D.1. The difference in percentage prevalence of antibodies ΔA_{ONS} between 4 and 18 January 2021 found from the ONS data was matched to the sum of the differences of those calculated by the

[16] ONS, Coronavirus (COVID-19) Infection Survey, antibody data for the UK: 16 February 2021 https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19infectionsurveyantibodydatafortheuk/16february2021#likelihood-of-testing-positive-for-covid-19-antibodies-in-england-wales-northern-ireland-and-scotland

PCCF to be immune as a result of recovery and as a result of vaccination for the two dates:

$$\Delta I_{rec} + \Delta I_{vaxx} \Rightarrow \Delta A_{ONS} \tag{D.7}$$

where equality was ensured by adjusting the vaccine maturity time constant, τ_{mat}. With the original value from §D.1, $\tau_{mat} = 21.31$ days, $\Delta I_{rec} + \Delta I_{vaxx} = 2.93\%$, whereas $\Delta A_{ONS} = 3.2\%$. A solution that satisfies this last equation may be found as

$$\tau_{mat} = 12.26 \text{ days}. \tag{D.8}$$

The development of vaccine maturity is now quicker, as shown in Figure 1. By this model,

Table D.1. ONS antibody surveys.

Date of report	Effective date	Period between effective dates	Percentages in England			Difference in means
			Lower 95% confidence	Mean	Upper 95% confidence	
03-Feb-21	04-Jan-21		14.70%	15.30%	15.90%	
16-Feb-21	18-Jan-21	14	17.90%	18.50%	19.10%	3.20%

the vaccine becomes 29% effective against asymptomatic or symptomatic illness after a week, 46% effective after 2 weeks, 55% after 3 weeks, 60% after 4 weeks and 65% after 6 weeks.

These figures are very much in line with the dynamics of vaccination immunity reported by Prof. Tim Spector based on data from his COVID Symptom Study app.[17] He told Sky News TV's *Sophy Ridge on Sunday*[18] on 14 February 2021 that data collected from 50,000 users vaccinated with either the Pfizer or the Oxford–AstraZeneca jab showed one dose gave 46% protection against symptomatic illness after two weeks, rising to 67% after three to six weeks.

Appendix E. Two-dose model for vaccination

E.1 Basic equations for effectiveness in preventing transmission

The effect of the second dose can be modelled fairly simply by adding a second exponential lag. The vaccine efficacy at preventing disease and transmission, η_v, will grow from after the first injection and continue further after the second injection, which will be administered typically between 8 and 12 weeks later. The process of vaccine maturation may be modelled as two exponential lags, obeying the equations: first for the development of vaccine effectiveness, η_{vA}, after the first jab:

[17] COVID Infections in the UK today, https://covid.joinzoe.com/data

[18] Coles, A., COVID-19: Vaccines giving 67% protection after three weeks, large-scale research shows. *Sky News* (15 February 2021) https://news.sky.com/story/covid-19-vaccines-giving-67-protection-after-three-weeks-large-scale-research-shows-12217943

$$\eta_{vA} = \eta_{vfA}\left(1 - e^{-x/\tau_{matA}}\right); \tag{E.1}$$

and then the additional vaccine effectiveness, $\eta_{v\Delta}$, accruing after the booster, second shot:

$$\eta_{v\Delta} = \eta_{vf\Delta}\left(1 - e^{-x/\tau_{mat\Delta}}\right). \tag{E.2}$$

Here η_{vfA} is the ultimate or final vaccine effectiveness after the first dose, τ_{matA} is the maturity time constant of the first vaccination and x is the time since the first injection was given. Meanwhile $\eta_{vf\Delta}$ is the ultimate (or final) additional vaccine effectiveness achieved through administering the second dose, while $\tau_{mat\Delta}$ is the maturity time constant determining the speed at which the additional effect of the second vaccination comes into force.

At any time after the second shot has been given, the vaccine effectiveness will be the following function of time:

$$\eta_v(t) = \eta_{vA}(t) + \eta_{v\Delta}(t). \tag{E.3}$$

The effect may be simulated by applying each of the final vaccine effectivenesses n_{vfA} and $\eta_{vf\Delta}$ to the flow of vaccinated eligible and susceptible people, $v_{esi}^{(j)}$, and subjecting each resultant flow to a first-order, exponential lag and then integrating and then summing the two results:

$$\frac{\mathrm{d}q_{iA}^{(j)}}{\mathrm{d}t} = \frac{n_{vfA}v_{esi}^{(j)} - q_{iA}^{(j)}}{\tau_{matA}} \tag{E.4}$$

$$\frac{\mathrm{d}q_{iB}^{(j)}}{\mathrm{d}t} = \frac{n_{v\Delta}v_{esi}^{(j)} - q_{iB}^{(j)}}{\tau_{mat\Delta}} \tag{E.5}$$

$$q_{iA}^{(j)}(t) = \int_{t_0}^{t} \frac{\mathrm{d}q_{iA}^{(j)}}{\mathrm{d}t}\mathrm{d}t \tag{E.6}$$

$$q_{iB}^{(j)}(t) = \int_{t_0}^{t} \frac{\mathrm{d}q_{iB}^{(j)}}{\mathrm{d}t}\mathrm{d}t \tag{E.7}$$

$$q_i^{(j)}(t) = q_{iA}^{(j)}(t) + q_{iB}^{(j)}(t). \tag{E.8}$$

$q_i^{(j)}(t)$ is then the flow of people in age group j and cohort i becoming immune at time t as a result of the course of two vaccinating injections.

E.2 Matching to the single shot course

The effectiveness predicted by the model for the two-dose course should match, at least approximately, the effect of a single dose up to the time when the second dose is given. After this point, the vaccine effectiveness will gradually increase to its final level. The assumptions made for the effectiveness of single-dose and two-dose vaccination against symptomatic or asymptomatic transmission are:

(i) The average long-term effectiveness in preventing transmission for a single vaccination may be found by taking a weighted average of the long-term effectivenesses of a single dose of AstraZeneca (67%),[1] and of that of the Pfizer–BioTech vaccine, namely 75%.[19] Applying weightings proportional to the number of doses the UK has ordered (100 M of AstraZeneca, 40 M of Pfizer–BioNtech) gives

$$\eta_{vfA} = 67\% \times \frac{100\times10^6}{140\times10^6} + 75\% \times \frac{40\times10^6}{140\times10^6} \;=\; 69.3\%; \tag{E.9}$$

(ii) The average long-term effectiveness in preventing transmission after a course of two injections of Pfizer–BioNtech is 86%.[20] In the absence of data on the long-term effectiveness of two shots of AstraZeneca vaccine, it is assumed that the 8% differential in favour of Pfizer–BioNtech observed for a single dose carries over to the case of two doses. This would give the AstraZeneca vaccine a long-term transmission effectiveness of 86% – 8% = 78% after two doses.

Making these assumptions, the weighted average long-term effectiveness against transmission, η_{vfB}, after both courses have been administered, of either the AstraZeneca or the Pfizer–BioTech vaccine, will be:

$$\eta_{vfB} = \eta_{vfA} + \eta_{vf\Delta} = 78\% \times \frac{100\times10^6}{140\times10^6} + \;86\% \times \frac{40\times10^6}{140\times10^6} \;=\; 80.3\%. \tag{E.10}$$

Meanwhile the time constant, $\tau_{mat\Delta}$, was chosen as

$$\tau_{mat\Delta} = 70 \text{ days (or 10 weeks)}. \tag{E.11}$$

An optimization exercise determined the two free parameters, η_{vfA} and τ_{matA}, as:

$$\eta_{vfA} = 0.56 \tag{E.12}$$

and

$$\tau_{matA} = 11.5 \text{ days}. \tag{E.13}$$

Note that these values are different from the single dose model, where $\eta_{vf1} = 0.693$ and $\tau_{mat1} = 12.26$ days. The match is shown in Figure E.1, demonstrating that the two models produce similar results up to about 8 weeks, when second vaccinations are assumed to start being given.

E.3. Vaccine protection against death

In addition to protecting against illness, with efficacy η_v, vaccines will protect against dying from Covid-19, with eventual effectiveness η_{ND}.

---

[19] Weekes, M. et al., Single-dose BNT162b2 vaccine protects against asymptomatic SARS-CoV-2 infection. Preprint posted 24 February 2021: https://www.authorea.com/users/332778/articles/509881-single-dose-bnt162b2-vaccine-protects-against-asymptomatic-sars-cov-2-infection?access_token=-hDTQsMUXcCPSpdZV_Lmpg

[20] Hall, V.J. et al., Effectiveness of BNT162b2 mRNA vaccine against infection and COVID-19 vaccine coverage in healthcare workers in England, multicentre prospective cohort study (the SIREN study). Submitted to *The Lancet* (22 February 2021) https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3790399

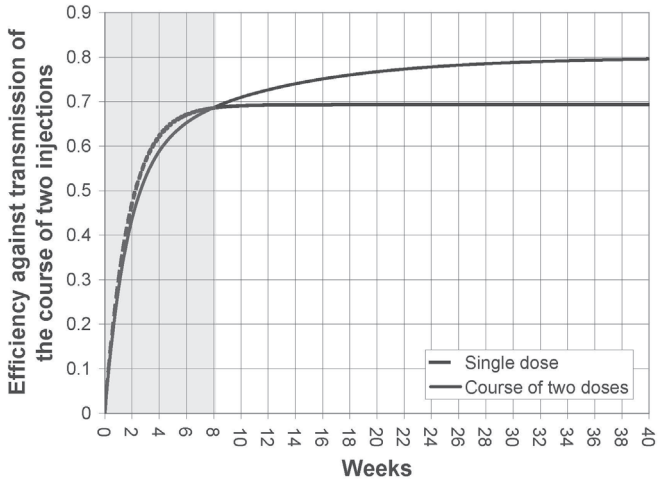

Figure E.1. Development of vaccine maturity after one dose and two doses.

E.3.1 Development of the dynamic equations for vaccine protection against death

In an exact analogy of the procedure laid out in Section E.1, the vaccine efficacy at preventing death η_{ND} will grow from after the first injection and continue further after the second injection, which will be administered between 8 and 12 weeks later. The process of vaccine maturation may be modelled as two exponential lags, obeying the equations, first for the effectiveness, η_{NDA}, of the first jab in preventing death:

$$\eta_{NDA} = \eta_{NDfA}\left(1 - e^{-x/\tau_{matA}}\right) \tag{E.14}$$

and then the additional vaccination effectiveness in preventing death as the booster, second shot matures in the system:

$$\eta_{ND\Delta} = \eta_{NDf\Delta}\left(1 - e^{-x/\tau_{mat\Delta}}\right). \tag{E.15}$$

Thus the total effectiveness, η_{ND}, against death of a course of two shots is

$$\eta_{ND} = \eta_{NDA} + \eta_{ND\Delta}. \tag{E.16}$$

Here x is the time since first vaccination, η_{NDfA} is the final vaccine efficiency achieved after the first injection, $\eta_{NDf\Delta}$ is the additional long-term effectiveness achieved after the second injection, τ_{matA} is the vaccine maturation time constant for a single dose and $\tau_{mat\Delta}$ is the time constant associated with the additional protection afforded by the booster shot.

The long-term effectiveness, η_{NDfB}, in preventing death after both injections have been given may be written:

$$\eta_{NDfB} = \eta_{NDfA} + \eta_{NDf\Delta}. \tag{E.17}$$

The effect may be simulated by applying the final vaccine efficacy to the flow of vaccinated eligible and susceptible people, $v_{esi}^{(j)}$, and subjecting this to two first-order, exponential lags and then integrating and summing the results:

$$\frac{\mathrm{d}G_{iA}^{(j)}}{\mathrm{d}t} = \frac{n_{NDfA} v_{esi}^{(j)} - G_{iA}^{(j)}}{\tau_{matA}} \tag{E.18}$$

$$\frac{\mathrm{d}G_{i\Delta}^{(j)}}{\mathrm{d}t} = \frac{n_{NDf\Delta} v_{esi}^{(j)} - G_{i\Delta}^{(j)}}{\tau_{mat\Delta}} \tag{E.19}$$

$$G_{iA}^{(j)}(t) = \int_{t_0}^{t} \frac{\mathrm{d}G_{iA}^{(j)}}{\mathrm{d}t} \mathrm{d}t \tag{E.20}$$

$$G_{i\Delta}^{(j)}(t) = \int_{t_0}^{t} \frac{\mathrm{d}G_{i\Delta}^{(j)}}{\mathrm{d}t} \mathrm{d}t \tag{E.21}$$

$$G_{i}^{(j)}(t) = G_{iA}^{(j)}(t) + G_{i\Delta}^{(j)}(t). \tag{E.22}$$

$G_{i}^{(j)}(t)$ is then the flow of people in age group *j* and cohort *i* becoming protected against dying at time *t* as a result of the course of two vaccinating injections; $G_{i}^{(j)}(t)$ is then the sum of two flows of people: those protected against all illness, $q_{i}^{(j)}(t)$, including fatal illness, and those, $g_{i}^{(j)}(t)$, who are protected by vaccination from dying but not against some illness:

$$G_{i}^{(j)}(t) = q_{i}^{(j)}(t) + g_{i}^{(j)}(t). \tag{E.23}$$

Thus $g_{i}^{(j)}(t)$ may be found from

$$g_{i}^{(j)}(t) = G_{i}^{(j)}(t) - q_{i}^{(j)}(t). \tag{E.24}$$

E.3.2 Parameter selection

The following considerations apply to effectiveness against death:

(i) a single dose of either the Pfizer–BioNTech or Oxford–AstraZeneca vaccine was found to be 80% effective at preventing hospitalization in over 80s three to four weeks after being administered in a Public Health England study;[21]

(ii) independent research in Scotland[22] suggested that a single dose of the Pfizer–BioNTech vaccine was 85% effective in averting hospitalization, while a single dose of the AstraZeneca vaccine was 94% effective;

(iii) data from Israel[23] suggests that a single dose of the Pfizer–BioNTech vaccine was 74% effective in preventing hospitalization for the period between two and three weeks after the first

---

[21] Bernal, J.L. et al., Early effectiveness of COVID-19 vaccination with BNT162b2 mRNA vaccine and ChAdOx1 adenovirus vector vaccine on symptomatic disease, hospitalisations and mortality in older adults in the UK: a test negative case control study. Preprint posted 2 March 2021: https://www.medrxiv.org/content/10.1101/2021.03.01.21252652v1

[22] Vasileiou, E. et al., Effectiveness of first dose of COVID-19 vaccines against hospital admissions in Scotland: National prospective cohort study of 5.4 million people. Submission to *The Lancet* (19 February 2021) https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3789264

[23] Dagan, N. et al., BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting, *New Engl. J. Med.* **384** (2021) 1412–1423 (https://www.nejm.org/doi/10.1056/NEJMoa2101765).

dose and this effectiveness was augmented by the second dose, which raised the figure to 87% a week after the second jab was given. Thus a course of two doses is at least 10% more effective in preventing hospitalization than just one shot.

In the absence of specific data for the AstraZeneca vaccine for the improvement in preventing hospitalization, the Israeli increment of at least 10% was added to the single-shot effectiveness figure for the AstraZeneca vaccine (80% from PHE and 94% from the Scottish data). Under this assumption, the effectiveness in the long term of two doses of either the Pfizer or the AstraZeneca vaccine in preventing hospitalization would be in excess of 90%.

Since the lowest survival rate of even patients in intensive care in England was just under 60% (and improved significantly thereafter),[24] this suggests that the effectiveness of two doses of either vaccine in preventing death must be 96% or higher. Recent information on the US trials of the AstraZeneca vaccine reported 100%.[25]

On the basis of the above, 97% is chosen as a reasonably cautious estimate of the long-term effectiveness in averting death for a course of two injections of either the Pfizer or the AstraZeneca vaccine. The parameters to be used in a model may thus be selected as:

$$\eta_{NDfB} = 97\% \tag{E.25}$$

$$\eta_{NDfA} = 71\% \tag{E.26}$$

so that

$$\eta_{NDf\Delta} = 26\% \tag{E.27}$$

with the time constants τ_{matA} and $\tau_{mat\Delta}$ retaining the values 11.5 days and 70 days respectively, as used previously.

Appendix F. Allowing for differences in test numbers: development of an alternative method

Appendix D of the fourth J-value coronavirus paper explains the basis for estimating the number of cases there would have been if there had been the same number of tests on a given day as there were on 13 November 2020 (Table F.1).

Test and trace data give weekly estimates in arrears of the fractions p_1 and p_2 of positives in the two pillars, and these have been used to generate an estimate of the number of positive cases standardized to the tests of 13 November 2020 according to the following procedure: the difference in Pillar 1 tests on the day, w_1, and the standardized number, w_{10}, will be

$$\Delta w_1 = w_1 - w_{10}. \tag{F.1}$$

[24] Dennis, J.M., McGovern, A.P., Vollmer, S.J. and Mateen, B.A., Improving survival of critical care patients with coronavirus disease 2019 in England: A national cohort study, March to June 2020. *Crit. Care Med.* **49** (2021) 209–214.

[25] AstraZeneca press release, 2021, AZD1222 US Phase III trial met primary efficacy endpoint in preventing COVID-19 at interim analysis, March 22, https://www.astrazeneca.com/media-centre/press-releases/2021/astrazeneca-us-vaccine-trial-met-primary-endpoint.html

Table F.1. Reference date with reference numbers of tests in Pillars 1 (hospitals) and 2 (general public).

Reference Date	Tests in Pillar 1, w_{10}	Tests in Pillar 2, w_{20}	Total tests across both pillars, w_0
13-Nov-20	71,749	250,067	321,816

The expected excess positives will be

$$E\left(\Delta M_1\right) = p_1\left(w_1 - w_{10}\right). \tag{F.2}$$

Given an actual number of positive tests or cases in Pillar 1 on the day M_1, the standardized number is calculated as

$$M_{1\text{stan}} = M_1 - E\left(\Delta M_1\right). \tag{F.3}$$

Similar equations hold for Pillar 2:

$$\Delta w_2 = w_2 - w_{20} \tag{F.4}$$

$$E\left(\Delta M_2\right) = p_2\left(w_2 - w_{20}\right) \tag{F.5}$$

$$M_{2\text{stan}} = M_2 - E\left(\Delta M_2\right). \tag{F.6}$$

The overall standardized figure is then the summation:

$$M_{\text{stan}} = M_1 + M_2 - E\left(\Delta M_1\right) - E\left(\Delta M_2\right) = M - E\left(\Delta M_1\right) - E\left(\Delta M_2\right) \tag{F.7}$$

or

$$M_{\text{stan}} = M - p_1\left(w_1 - w_{10}\right) - p_2\left(w_2 - w_{20}\right). \tag{F.8}$$

Alternative method

The approach is now adapted to produce an alternative method as follows: calculate the probabilities from the day's figures for cases by date reported and reported tests under each pillar, using the assumption that the new estimated probabilities under the two pillars, p_1^* and p_2^*, are related by

$$\frac{p_1^*}{p_2^*} = r_p = \frac{p_1}{p_2} \tag{F.9}$$

where p_1 and p_2 are the values from test and trace data. There will be an inaccuracy caused by the fact that the figure applies to the previous week, but the change is not likely to be large. The expected value of the number of positives or cases is then

$$E(M) = p_1^* w_1 + p_2^* w_2 = r_p p_2^* w_1 + p_2^* w_2 = \left(r_p w_1 + w_2\right) p_2^*. \tag{F.10}$$

Then using M as an estimator for $E(M)$, it follows that:

$$p_2^* \approx \frac{M}{r_p w_1 + w_2}, \tag{F.11}$$

while applying equation (F.9) to equation (F.11) gives:

$$p_1^* \approx \frac{r_p M}{r_p w_1 + w_2}. \tag{F.12}$$

The standardized figure is then

$$M_{\text{stan}} \approx p_1^* w_{10} + p_2^* w_{20} \tag{F.13}$$

$$M_{\text{stan}} \approx r_p M \frac{w_{10}}{r_p w_1 + w_2} + M \frac{w_{20}}{r_p w_1 + w_2} \tag{F.14}$$

$$M_{\text{stan}} \approx M \frac{r_p w_{10} + w_{20}}{r_p w_1 + w_2}. \tag{F.15}$$

This method has the advantage of relying only on the ratio of the probabilities in Pillars 1 and 2, not on the absolute values of both. This is expected to change more slowly from week to week, thus allowing a smoother set of estimates to develop.