

Annex B: comparison between 1 and 2 dose prioritisation for a fixed number of doses

Published January 2021

Baseline Data

Our starting point is the second wave in the UK (from 1 September 2020, until 21 December 2020), and the age-distribution of mortality compared to the underlying population pyramid for England (Figure 1). From these plots it is abundantly clear that older age groups suffer the greatest mortality, with 60% of deaths due to COVID-19 in the over 80-year olds even though they only comprise 5% of the population.

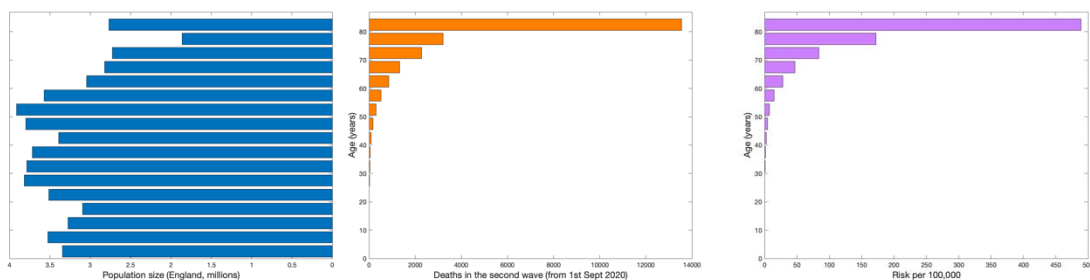


Figure 1. Here we show the population pyramid for England, in 5-year age cohorts up to 80+ years old (blue); we also show the total number of age-dependent deaths (orange) in the same age-groups over the second wave (Sept-Dec 2020) and the associated risk of mortality per 100,000 (purple).

We also take central estimates of vaccine efficacy for the Pfizer and Oxford/AstraZeneca vaccines: Pfizer (89% from first dose; 95% from two doses); AstraZeneca (75% from first dose; 88% from two doses).

Homogeneous strategy

We first examine the simple question of whether, given a limited supply of vaccine, it is better to give as many people one dose or to give two doses to as many people as possible.

If we initially ignore risk-structure and the potential for differential rates of waning immunity, then it is better to prioritise towards one dose if the efficacy from one dose is more than half the efficacy from two doses ($2 \times VE_1 > VE_2$).

As shown above there is considerable risk structure associated with COVID-19 mortality, with older individuals (and people with comorbidities) suffering greater risk of severe disease and death. We examine this question by considering targeting vaccination towards the oldest age-groups first. This brings into the calculation the number of available doses by any given date. There are approximately 3.3 million people over 80 in the UK, therefore if the number of currently available doses is less than 3.3 million we are faced with the choice between giving 1 dose to some proportion of over 80's or 2 doses to only half that number. This is the situation outlined above, which for a (relatively) short duration epidemic favours 1 dose if $2 \times VE_1 > VE_2$.

For larger available amounts of vaccine, we now face the dilemma between giving one dose to ages that are at slightly less risk or giving two doses to those that are most vulnerable. Suppose we have 6.6 million doses of vaccine, we could either give all over 80s two doses, or could give everyone over 75 and some of those in the 70-75 age group one dose. To assess this we need to compare the relative risks in the different age-groups (right-hand graph in Figure 1) and compute the relative number of deaths averted by the two strategies (Figure 2). We note that this is a relative measure, as predicting the scale of the future outbreak is contingent on a number of policy decisions.

From these graphs (Figure 2) we see that when supplies are limited (or alternatively in the early stage of a vaccination programme) a greater number of deaths can be averted by prioritising giving a single dose. The point where it becomes better to switch to giving two doses is governed by both vaccine uptake (higher uptake leads to a later switch) and the relative efficacy from one dose compared to two (higher relative efficacy also leads to a later switch). It is hoped that uptake in the oldest age-groups may exceed 80%, while the relative efficacy from one dose has been estimated as 85% for the Oxford/AstraZeneca vaccine, 94% for the Pfizer vaccine and 96% for the Moderna vaccine.

[Insert title]

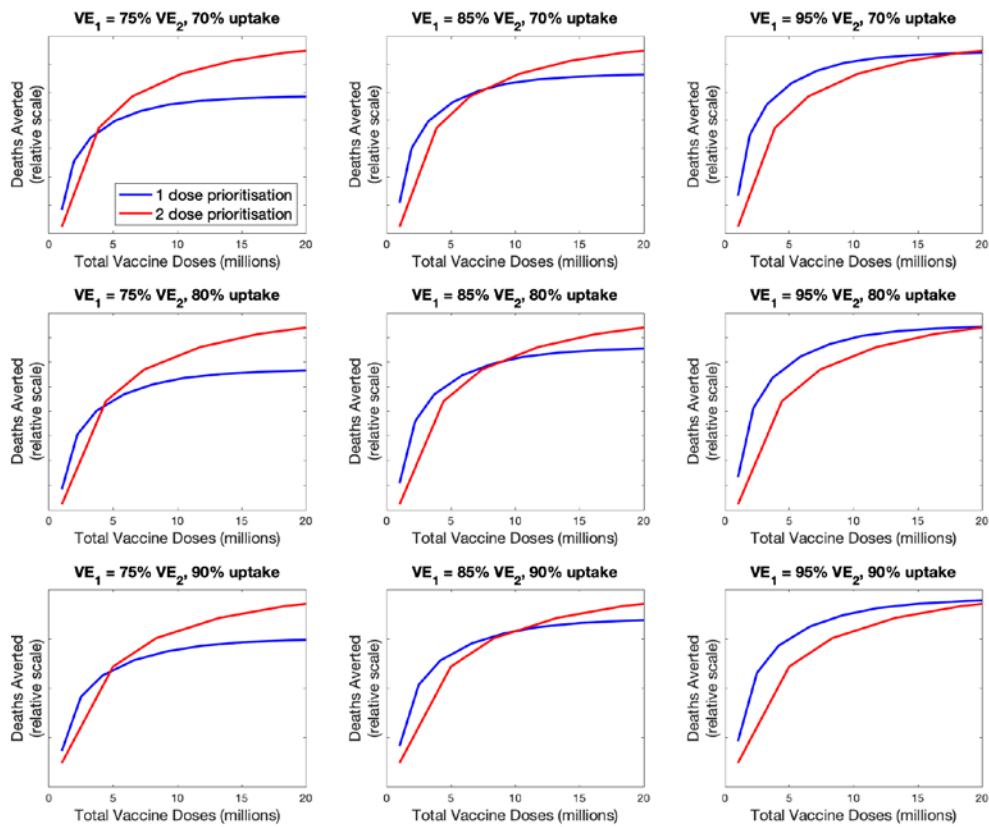


Figure 2. The relative number of deaths averted by a 1-dose (blue) or 2-dose (red) prioritisation strategy, as either the vaccine uptake or the relative vaccine efficacy of 1-dose compared to 2-doses varies.

We expect these simple trade-offs to occur either if there is a limited supply of vaccine, or until that point is reached in an on-going campaign. As such, early vaccine roll-out ought to be targeted towards giving as many people one dose as possible, until the switch-point is reached.

We can explore the two free parameters (total vaccine doses and relative vaccine efficacy) to find in more detail where this switch occurs (Figure 3). For 80% vaccine uptake we observe how low doses or high relative efficacy ($VE_1:VE_2$) favour prioritising giving as many first doses as possible. Higher levels of vaccine uptake extend the parameter space over which one dose is favoured.

Comparison between 1 and 2 dose prioritisation for a fixed number of doses

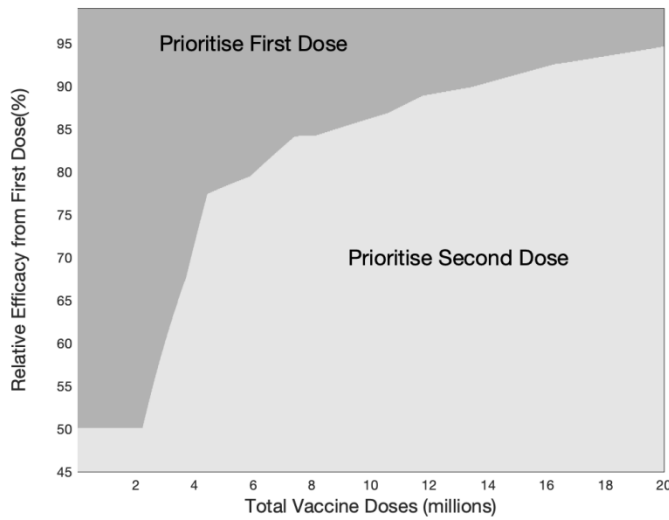


Figure 3. Scanning over the parameter space of the number of doses allocated at any one time and the relative efficacy of the first dose compared to the second, we can calculate if more deaths are likely to be averted from prioritising giving one dose (dark grey) or second doses (light grey). This assumes an 80% uptake in the targeted age-groups.

Heterogeneous strategy

We can extend this simple analysis to consider heterogeneous strategies where, out of a given number of doses, a given percentage are used for first doses and the remainder for second doses. We define the optimal allocation of vaccine between first and second doses, by maximising the relative number of deaths averted when both first and second doses are used to vaccinate the oldest age-groups first (Figure 4).

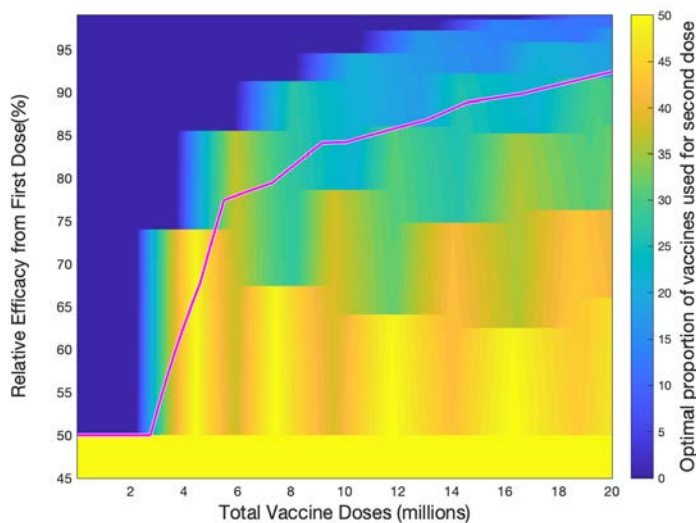


Figure 4. Showing the optimal distribution of a given number of vaccine doses between first and second dose; regions of parameter space in which most doses should be prioritised toward first dose are coloured blue, those in which giving first followed by second doses is optimal is coloured yellow. The pink line shows the boundary between the parameter regions associated with homogenous strategies shown in Figure 3.

To understand Figure 4 in more detail we take a horizontal cross section across a line of 90% relative vaccine efficacy from the first dose compared to two doses (Figure 5). For different numbers of vaccine doses (4 to 12 million) we show the optimal deployment of first and second doses across the age groups. For less than 6 million doses, the optimal strategy is to give first doses to all those over 70 years old. From 6 to 8 million doses, the optimal strategy is to give a second dose to those over 80 years old; even though this only gives a small increase in protection this is balanced by their far greater risk. From 8 to 12 million doses, the optimal strategy returns to prioritising first doses.

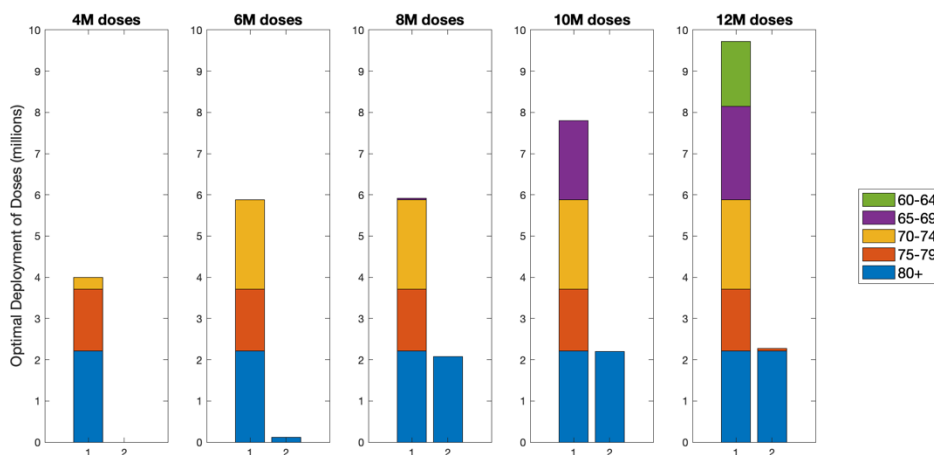


Figure 5. Optimal deployment of a 1-dose versus 2-dose strategy for a given number of doses, assuming that the first dose gives 90% of the efficacy compared to two doses. Effectively, this pulls out the data underlying Figure 4.

Application to the UK

The above calculations all consider the best deployment of a fixed number of vaccine doses, whereas in the UK vaccination is a dynamic process with new supplies of vaccine being manufactured and distributed all the time. In the UK we are also not considering the strict trade-off between one and two doses, but between two doses given at 3 or 12 weeks separation. In addition, the analysis has only considered age-based vaccine targeting, whereas the JCVI priority group list also includes care home residents and workers, health and social care workers and the clinically extremely vulnerable. These two elements both

mean that the theoretical results above need to be interpreted to apply to the situation in the UK.

From Figure 3, we predict that for relatively high protection from the first dose (compared to the efficacy derived from two doses) a substantial number of first doses should be administered before attention switches to giving second doses. For a relative efficacy of 90%, 13.6 million first doses should be prioritised, enough to immunise the first four priority groups; for a relative efficacy of 85%, 8.9 million first doses should be prioritised, which is more than enough to vaccinate the first three priority groups. From Figure 5, the prediction is that first doses should be prioritised until all those over 70 have been offered the vaccine, which again corresponds to the first four priority groups.

One key issue is the speed with which we reach 8.9 or 13.6 million doses administered (or alternatively completing priority groups three or four); if this is achieved in under twelve weeks from the initial start of the vaccination campaign, then it would be worth starting to give second doses to the highest priority groups earlier than the twelve-week deadline. Similar calculations can be performed for other risk groups; it only becomes beneficial to give a second dose to the 75 to 79 age-group (priority group 3) once a first dose of the vaccine has been offered to all those over 60, and a second dose to the 70 to 74 age-group (priority group 3) once those over 55 have been offered their first dose.

In summary there is strong evidence based on the available information on vaccines and the risk stratification in the JCVI priority groups, that a strategy based on maximising the number of primary doses given (while ensuring everyone has their second booster dose within 12 weeks) will lead to a greater number of deaths averted than a strategy which prioritises giving a second dose at 3 weeks.

[Insert title]

© Crown copyright 2021

Published to GOV.UK in pdf format only.

www.gov.uk/dhsc

This publication is licensed under the terms of the Open Government Licence v3.0 except where otherwise stated. To view this licence, visit nationalarchives.gov.uk/doc/open-government-licence/version/3

Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.

OGL