Should We Delay the Second COVID-19 Vaccine Dose?

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February 13, 2021

Abstract

Due to the shortage in COVID-19 vaccine supplies and the alarming sanitary situation engendered by the COVID-19 pandemic, some countries have opted to delay the second dose of the COVID-19 vaccine for some period of time, aiming at getting the first dose of the vaccine to a large number of the population, before proceeding with the second doses [7, 6]. This strategy has sparked some heated debates world-wide for its pros and cons, and no clear consensus is reached among experts [5, 3]. Without taking side in this matter, we tried to answer the following question, from a pure mathematical perspective: should we delay the second dose of the vaccine or not?. We show that the answer to this question depends tightly on the efficacy of the first and the second COVID-19 vaccine doses. In particular, if the first dose is more than 50% efficient, the optimal procedure to maximize the number of effectively vaccinated sub-population is to delay the second vaccine as much as possible (the maximum period between the two doses prescribed by the clinical recommendations). On the other hand, if the efficacy of the first dose is less than 50% and the efficacy of the second dose exceeds a certain threshold, then it would be optimal to administer the second dose as quickly as possible (while respecting the minimum period between the two doses as prescribed by the clinical recommendations). We provide explicitly the expression of this threshold as a function of the efficacy of first dose.

1 Results

In this work, we provide an optimal strategy (in terms of the efficacy of the first and second dose) for the administration of the two doses of the COVID-19 vaccine, in order

NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.
Figure 1: The answer to the question of delaying or advancing the second COVID-19 vaccine dose depends on the efficacies of each of the first and the second doses. This figure depicts the region (in red) where the best scenario would be to delay the second dose and the region (in blue) where the second dose should be advanced for optimal outcomes.

To maximize the number of effectively vaccinated sub-population each day. Of course, by maximizing the immunized population, we aim at saving more lives and containing more quickly the COVID-19 pandemic. Our theoretical findings show that the optimal second vaccine dose scheduling depends on the efficacy of the first and second doses of the vaccine and can be either one of the following scenarios. The first scenario (Scenario 1) consists of delaying the second dose of the vaccine as much as as possible; preferably until the end of the first one-dose campaign or until the maximum period recommended by clinical recommendations is reached. The second scenario (Scenario 2) consists of administering the second dose, as soon as possible, to those who have already taken the first dose.

We derived a simple test formula to check which of the two scenarios is optimal depending on the efficacy of the first and second doses of the vaccine. The formula is given by the following inequality:

$$
\alpha_1 > \frac{\alpha_2}{1 + (\alpha_2/100)}, \quad (1)
$$

where $\alpha_1$ (%) and $\alpha_2$ (%) represent the vaccine efficacy of the first and second dose, respectively. If inequality (1) holds then we should consider Scenario 1 to obtain the best outcomes of the vaccination campaign. Otherwise, the second scenario is preferable. An immediate consequence of this result is that if the efficacy $\alpha_1$ of the first dose is greater than 50%, then Scenario 1 is optimal regardless of the efficacy of the second dose since (1).
must hold. This is a very interesting case since most of the major vaccine companies have announced that their first dose of the COVID-19 vaccine is more than 50% efficient; see Figure 1. However, there is no conclusive evidence on the real efficacy of these vaccines as studies continue throughout the word to adjust the efficacy numbers. Based on the announced numbers, Scenario 1 is the optimal in terms of maximizing the number of the efficiently vaccinated population per day, which is in line with the scenario adopted by the UK authorities [7]. Another way to express inequality (1) is the following:

$$\alpha_2 < \frac{\alpha_1}{1 - (\alpha_1/100)}.$$  

(2)

This shows that, for a given first dose efficacy $\alpha_1$ that is less than 50%, Scenario 2 is optimal if the value of the second dose efficacy exceeds the threshold $\alpha_1/(1 - \alpha_1/100)$, otherwise Scenario 1 is optimal. For instance if we take $\alpha_1 = 40\%$ then a second dose efficacy of more than 67% would imply that the best vaccination strategy is to provide the second dose to those who have taken the first dose as quickly as possible (Scenario 2). In Figure 1 we provide a visual picture of the efficacy intervals for the first and second dose where Scenario 1 or Scenario 2 are optimal. In the same figure, we also provide markers for the officially announced vaccine efficacy of Moderna (mRNA-1273) [1, 4], Pfizer-BioNTech [2], and Oxford-AstraZeneca [8].

2 Methods

We denote by $u_1$ the number of daily sub-population receiving the first dose and by $u_2$ the number of daily sub-population receiving the second dose. The objective function to maximize is the total number of daily susceptible sub-population that is effectively vaccinated which is given by

$$J = \bar{\alpha}_1 u_1 + (1 - \bar{\alpha}_1) \bar{\alpha}_2 u_2,$$  

(3)

where $\bar{\alpha}_1 = \alpha_1/100$ and $\bar{\alpha}_2 = \alpha_1/100$ represents the vaccine efficacy of the first and second dose, respectively. The first term $\bar{\alpha}_1 u_1$ represents the daily effectively vaccinated sub-population due to receiving their first COVID-19 vaccine dose, while the second term $(1 - \bar{\alpha}_1)\bar{\alpha}_2 u_2$ represents the daily sub-population who have not been effectively vaccinated in the first shot but are now effectively vaccinated owing to the second vaccine shot. If we let $u$ be the (total) daily vaccination rate then we have $u_1 + u_2 = u$. This allows to rewrite (3) as

$$J = \left(\bar{\alpha}_1 - \frac{\bar{\alpha}_2}{1 + \bar{\alpha}_2}\right)(1 + \bar{\alpha}_2)u_1 + (1 - \bar{\alpha}_1)\bar{\alpha}_2 u.$$  

(4)

It is clear the maximization of the objective function $J$ depends on the sign of the term $(\bar{\alpha}_1 - \bar{\alpha}_2/(1 + \bar{\alpha}_2))$. If this term is positive then the optimal strategy would be to set $u_1 = u, u_2 = 0$ which corresponds to Scenario 1 of the Results. In the other case, i.e., $(\bar{\alpha}_1 - \bar{\alpha}_2/(1 + \bar{\alpha}_2)) \leq 0$, the optimal strategy would be to set $u_1 = 0, u_2 = u$ which corresponds to Scenario 2 of the Results.
3 Acknowledgements

This research work is supported by the National Research Council of Canada, under the grants NSERC-DG RGPIN-2020-04759 and NSERC-DG RGPIN-2020-0627. Our thoughts are with those who lost their loved ones in this pandemic, and our gratitude and respects go to all the front-line workers across Canada and worldwide for keeping us safe and keeping the world running.

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