Simulation of Covid19 Vaccination Policies in CovidSIMVL

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Introduction

Two vaccines have been approved in Canada, and will be adopted in BC. One is from Pfizer, and the other is from Moderna. They are both two dose protocols, Pfizer being 21 days apart, and Moderna 28 days. Recommendations from The Canadian National Adisory Committee on Immunizations state that they could both be taken 28 days apart, though not interchangeably.

CDC and CNAC feel that Moderna confers immunity at an efficacy level of 80 starting at two weeks after first injection, with Pfizer being recorded as 54% while experts feel it could be as high as 80%, in keeping with Moderna being another MRNA vaccine. It is not formally known how long this immunity might last.

For purposes of the model below, we use the assumption that the immunity starts at 14 days after first injection, for a period of 28 days, then falls to zero. So the first 14 days after the first injection offers no protection. At 28 days, a second injection would confer 95% protection 1 day after injection.

Two policies have been proposed. The first is to hold back half the vaccine supply, so that the 95% protection after 28 days is assured. The second is to use all the vaccine, and either no supply is forthcoming on day 28 or a full second injection is supplied to all.

The question is the extent to which these strategies would protect the public.

METHODOLOGY

We define MODE1 strategy as:

1. Injection at time T=0
2. Protection of 75% after 14 days
3. Continued protection at 75% to day 42 (a 28-day span)
4. At day 42, protection falls to zero.

We define MODE2 strategy as:

1. Injection at time T=0
2. Protection of 75% after 14 days
3. Continued protection of 75% to day 28 (the specified period between injections)
4. On day 29, protection goes to 95% for the entire simulation trial.

We use CovidSIMVL with 100 population of which one is an initial transmitter. Trials are conducted with Mode1 and Mode2 strategies, under varying intensities of the underlying epidemic (different parameters of Hazard Ratio, and contact tracing to reduce the duration of symptomatic agents in circulation from 8 days to 4 days).

The program implements the vaccination strategies in the following way:

1. The user at the start of the trial sets the parameters for Hazard Ratio, symptomatic days, and vaccination strategy
2. During the execution, if a transmission is feasible, the program checks the current day vs the strategy milestones, and where applicable, uses a random number generator to decide whether to execute the transmission or not. Thus, if the random number returns a number less than 0.95, the transmission is bypassed, and the 95% protection has been satisfied.

Initially, we used a population of 50 vaccinations for Mode1 and 25 vaccinations for Mode 2, and this left the situation of the Mode1’s receiving a complete supply as Mode 2 with 50 vaccinations. The initial analysis of this approach led us to conclude that addressing a population in which a part of the population was vaccinated (as In Real Life “IRL”) led to complexities as described below.

In the initial 14 day period, none of those vaccinated are protected, so the natural infection in that period would take in a mix of vaccinated and unvaccinated agents. Then when the protection starts at 75%, some of the vaccinated persons would already have been infected, and this number would vary stochastically with the different instances of the 14-day period. When the protection period falls to zero in the Mode1 case, the population would all be vulnerable. At the end of the 28 day period in Mode2, all those vaccinated who did not get infected in the initial 14 days would have 95% protection, but everyone else would be totally vulnerable. Infections following the second vaccination would then be mixed between the totally vulnerable and those who fell into the 5% window.

Instead, the Eureka moment was to realize that if we modelled the entire population being vaccinated, we could study and compare the different strategies more easily, without the confounding presence of those not vaccinated.

Each trial terminates when there are no more susceptibles, or no more transmitters. The program prints out on the console.log the time of each transmission, which agent transmitted to which recipient, and the probability used in that transmission to determine protection (if applicable).

The input parameter for the vaccination is of the format “M,n” where M is the mode, and n is the % of the population to be vaccinated.

In all trials, we specified all parameters at the start, and used n of 100, to vaccinate everyone.

We present summary results. Detailed tables and console.logs for each trial are available on request.

SUMMARY RESULTS

We used Hazard Ratios of 5, 4.5 and 4 with a Mingle Factor of 1. The latter assures that mobility of agents is high enough that with HzR as above, with no vaccinations and no change in symptomatic days, the trials would run close to 100% infected between 1000 and 2000 hours, or 41 to 80 days.

When the vaccinations are applied, the trials terminate in shorter time, because the transmitting agents only have a finite period of time to reach a susceptible and to meet the probability hurdles, so that running out of transmitters means more survival for the population of vaccinated agents.

So the first and most important metric is the number of survivors at the termination of a trial. Of course, there are trials in which the single infective agent does not find a susceptible to infect, and the trial terminates with no infections, because of the low but finite probability that the initial geometry and stochastic movements finds no successor to the initial transmitting agent.

Discarding the non-starters, here is the ranked list and conditions of the survivors:



Using the feature in Excel called “conditional formatting” we see some tentative relationships. The strongest is in the top box of the data, where the “Red Days” have a count of 15/17 4’s, and on the right hand column, these are the highest survivor trials, ranging from 25 to 85 survivors.

The interpretation is that good contact tracing can reduce the number of days symptomatic cases are circulating in the community, so when this value is reduced from 8 to 4, fewer transmissions will occur, and so there are more survivors.

A weaker relationship might hold between the number of generations (hours) that the trials run, and the strength of survivorship. In the top box of this data, the trials mainly terminate below 1,000 or around the 1,000 value, whereas in the lower box, the higher values for termination pertain.

The bottom trials have lower termination values, near 1,000, but noe that these are all B’s for Mode, or “Baseline” where there are no vaccinations. The values of the Hazard Radius and the default mingling factor of 1 (unchanged in these trials) are sufficiently high that with no vaccination, they run to almost complete population infection within about 1,000 generations.

We can look at the data, sorted by Mode.



The MODE TABLE

This table is sorted by Mode, with the top section the Base (no vaccination) trials. By and large, these result in few survivors, even with reduction in symptomatic days in circulation (“red days” as red is the color used to represent symptomatic cases.

The average number of survivors for Mode2 trials is 46.83, and that for Mode1 is 34.00, so on the face of it, Mode2 results in more survivors. One common feature, highlighted in gray and mauve, is that the combination of 5 for Hazard Radius and 8 for Symptomatic Days leads to fewer survivals in both Modes.

We can contemplate this a bit. The initial 14 days prior to vaccination effects represent the opportunity for the contagion to establish transmitters that will overcome the probability hurdles in Modes1 and 2. Since a large Hazard Radius and more days of transmission favour more infections, this combination ought to produce lower numbers of survivors, and indeed, that matches our findings.

Finally, we can look at the data via the lens of the Hazard Radius.



This serves to accentuate the role that Symptomatic Days play in the way the model unfolds. The shaded areas, with the highest survivors, are all associated with 4’s for Symptomatic Days. However, in the bottom panel, some combination of 5 for Hazard Radius and 8 for Symptomatic Days creep in, with survivor values of 34 and 25, both in Mode2.

The following will serve to illuminate the stochastic nature of “free” vs constrained contact transfers. The console.log shows the time of actual transmissions as well as their number in the order of events.



From these data, for each trial, the time (generation) at which the 10th transmission, 20th transmission etc took place is in the columns to the left. Thus, for the first row, representing a trial with Hazard Radius of 5, and Symptomatic Days of 8, there were 34 survivors, and the 10th infection in this trial was at generation 89, the 20th at gen 180, the 30th at gen 267, etc.

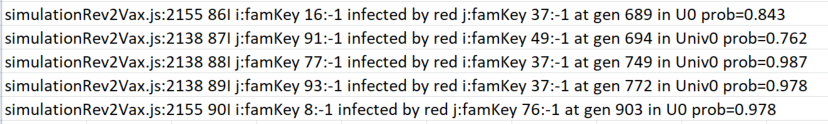
It is important to remember (with the data highlighted in yellow), that Day 14, when the 75% probability barrier starts, is generation 336, and Day 28 up to Day 29, when the efficacy goes to 95%, is at generation 696.

So anything after generation 696 for a Mode2 trial represents a significant difficulty in terms of achieving a transmission, despite contact between a transmitter and a susceptible. The transmitters had to be created and survive the 14 days of 75% probability, and a Symptomatic transmitter only lasts for 8 days.

So in the case of trial 1, top row, 60 infections were reached at generation 578, which leaves 40 susceptibles. We see that by the termination of the trial, 70 infections were not reached. The 40 susceptibles after the 95% barrier kicked in at time 696 proved difficult to surmount. Similarly, the second trial reached 70 infections at gen 632, but after gen 696 and the 95% barrier, was not able to go further.

The third trial had a more aggressive start and so by gen 336, before the 75% barrier started, it had achieved more than 40 and less than 50 infections. In the 75% period, it got more infections, so that it reached the 80 infection level by generation 592. After the 696 generation mark, when the 95% started, it was still able to go from 80 to 91, another 11 infections, within the 95% constraint, to reach 90 infections at 903 generations – taking 408 generations to do so.

The last console.logs for this period reads:



DISCUSSION

The primary question is: which is better? Mode1 with some risks, or Mode2. In the simulation model, we examined the consequences of adopting Mode1 with protection falling to zero after 42 days, versus Mode2 with 95% at day 28 for all.

Clearly Mode2 is superior, with an average of 46,83 survivors compared to 5 for the no vaccine trials. Mode1 considered the effect of giving all the vaccine and not a second dose, and perhaps surprisingly, Mode1 had 34 survivors, on average, because the period from T=14 to T=42 (28 days) was assumed to have 75% protection, a period which outlasted the duration of pre-existing transmitters and dampened the creation of new ones.

IF MODE1 WAS NOT ASSUMED TO HAVE 28 DAYS BUT ONLY 14, THE RESULTS MAY BE QUITE DIFFERENT. WE HAVE NOT MODELED THIS VARIATION.

The other caveat is that it is clear for Mode1 and Mode2 that good contact tracing that could take Symptomatic Days in circulation from 8 to 4 would double the benefit that would otherwise be derived from vaccination. Considering the average of the unshaded vs shaded areas for the Modes Table, we get that the average in Mode2 for the shaded (8’s for symptomatic days) is 25.25 compared to 57.62, or double, and for Mode1, it goes from 10.75 to 44, a factor of 4.

VACCINATION EFFECTIVENESS IS INCREASED SIGNIFICANTLY WITH GOOD CONTACT TRACING, ALMOST BY 100%.

**ADDENDUM. COMPARISON OF PROTOCOL BASED VACCINATION AND HYBRID APPROACH**

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Methodology

We adopted a simplified version of the Pfizer and Moderna protocols, as follows:

1. For Pfizer, at injection T.0 to T.14, we assume no protection. At Time T>14days, protection goes to 54% and at T.21 the second injection causes protection to go to 95%. If the second injection is not given, protection goes to zero after T.22.
2. For Moderna, there is zero protection till T.14 after which time it goes to 80% till day T.28, and the second injection confers 95% protection. If the second injection does not occur, protection falls to zero.

Parameters for the trials of Pfizer and Moderna, using CovidSIMVL, follows the approach in the main body of this note. The parameters for Hazard Radius were 5, 4.5 and 4, combined with a MingleFactor of 1, gives aggressive epidemics in a population of 100 with one initial transmitter, generally going to less than 7 survivors at termination. Each trial ends when there are no more susceptibles, or no more transmitters, having run out their duration as transmitters according to the viral temporal dynamics embedded in CovidSIMVL.

Within the Hazard Radius parameter, Mode 1 was a single injection, and Mode 2 was with two injections. In addition, the additional parameter of Symptomatic Days was used at 8 days, and 4 days, for each such trial. simply called Hazard Radius, and the second “1,100” or “2,100” the syntax referring to one or two injections for 100 persons. The number of survivors (susceptibles) at the termination of a trial is recorded.

Again, we consider what happens to 100 persons who are vaccinated within the context of different intensities of an epidemic (varied by the Hazard Radius), and whether or not contact tracing reduces the number of days that symptomatic cases continue in circulation. The first parameter is

This approach is consistent with the Hybrid approach above in the main body, in which the period between T.14 and T.29 has a protection level of 75%, which rises to 95% with a second injection at T.28, but falls to zero after T.36.

Protection is implemented as described in the main body, by applying a random number generator to make the decision for qualifying potential transmissions between infectives and susceptibles.

The results are as follows. The tables for each candidate strategy follows as an Appendix to this note.

Results

We consider the cases of two injections versus one injection versus none (which we call Baseline).



This table shows that the early (21 days) second injection pays off against the later (T.28) second injection of Moderna and Hybrid, despite the 54% efficacy of the Pfizer partial protection during T.14 to T.21, compared to the 80% protection for 14 days of Moderna and Hybrid.

DISCUSSION

The slightly better result for Hybrid for 1-jab comes from its 75% protection for 35 days compared to Moderna’s 80% for 28 days. The very poor result for Pfizer with 1 jab is due to the shorter period of protection (21days) before it falls to zero, and that during T.14 to T.21 the efficacy is only 54%. Therefore many more transmitter survive or are generated to the time T.21 after which there is no protection, so the trial reverts to Baseline, which is aggressive.

The main reason that the average of 2-jabs in Moderna is less in survivors than the Hybrid is due to contact tracing, which, with a 4-day window for transmission, produces more survivors. In the Moderna Mode 2-jab trials, 3 of 11 trials were contact traced, while the Hybrid trials of Mode 2, none of the 12 trials leading to the average of 46.83 were contact traced to 4 days of symptomatic transmission. If we averaged each class (contact traced and not) and combined them, we get the average survivors for Mode2 in Hybrid to be 38.8 and Moderna to be 42.9. The value for Pfizer stands, as it has an equal number of each class in its Mode2 trials.

A general result that the trials show is that 2-injections is always better than one, as the following detailed data shows for Pfizer. The same relationship holds for the other two strategies.

 **Pfizer Trials**

This table shows first that the Mode 2 survivorship is far better than the Mode 1 (1,100) survivor counts. The second point is that the mauve shaded figures show that in each Hazard Radius class, the contact tracing (4 for Symptomatic Days) is always superior to no contact tracing. This is intuitively obvious, but the quantitative data is shown as experimental results.

The third is that the two lines in blue show that for Mode 1, in which we expect that the trial goes to completion if enough transmitters exist beyond the T.21 time, at which the epidemic reverts to zero protection, the trial should run to terminate with very few survivors. These two are in the Hazard Radius class 4, which means that they are relatively smaller compare to Hazard Radius of 4.5 and 5. The smaller, the less likely to find a susceptible to continue the chain of transmission. These variances are reflective of the stochastic nature of the simulation.

CONCLUDING REMARKS

These trials in the CovidSIMVL simulation sandbox permit us to try a number of different parameters to assess quantitively the differences in protection and infections resulting from the various strategies of vaccination for Pfizer, Moderna and a Hybrid approach similar to what BC is considering.

The interesting observation is that even with only one injection, significantly more survival can come through if the protection between T.14 and T.end of protection is long enough that transmitters at the start of the interim period are extinguished, and the protection is high enough that fewer transmitters are generated.

It should be remembered that an 80% efficacy means that 20 of 100 touches, or 1 out ef 5, can be an effective transmission. This is akin to Russian Roulette with five chambers!

The underlying aggressiveness of the epidemic (as expressed by parameters of Hazard Radius and Mingle Factor) are very important in assessing the impact of vaccination strategies. If the first 14 days have no protection, It does no good to vaccinate 100 persons if 85 of them are infected within the first 14 days! Indeed, if the contagion is intense enough, contact tracing will be less useful, as transmissions would not need more than the first one or two days to succeed in finding the next susceptible in the epidemic.

Thus, to be truly effective, considerations for vaccination strategies should take the aggressiveness of the epidemic, the length of protection after the first injection, and its duration, into account, together with other factors not discussed here, such as whether reducing transmissions take priority over protecting vulnerables.

**APPENDIX**





