Parameters for Vaccination

April 17, 2021

Introduction

Before I do any coding, it would be important to outline the approach, the parameter model, so that the parameter csv file can be produced correctly and the dual routines parse them into the appropriate global and personal variables.

Then we can code the routines with more certainty.

The PROTECTION LEVEL Models

There are two situations that we need to deal with: a single jab, and two jabs. We can differentiate them through timing parameters.

We focus first on the one-jab model, then we will expand the model to accommodate two jabs.

The parameters deal with time in terms of DAYS, and PROTECT-LEVELs of resistance to infection (eg 70%). By 70% we mean algorithmically that if a susceptible person comes into contact with an infective, we generate a random number between 0 and 1, and if the number is greater than 0.7 then the person infection can proceed.

***ONE INJECTION MODEL***

The model looks like this, graphically:

Level.P1

Residual level

T.jab1 T.eff1 T.dec T.res

To explain the diagram above:

T.jab1 day at which the first vaccination takes place

T.eff1 day at which the vaccine reaches maximum effectiveness after one jab

Level.P1 level of protection achieved after one vaccination

protection grows (linearly) from T.jab1 to T.eff

T.dec day at which the Protection-Level starts to decline

T.res day at which the Protection-Level becomes residual

Level.R Residual level of protection (could be zero, could be any +ve percent)

With these parameters, we can model any vaccine (although the changes may not be linear but for want of better evidence, we will use linear as a first approximation.

***TWO INJECTION MODEL-A***

There are two cases for the two injection vaccines. The first is (whether or not following the manufacturer recommendations) when the second vaccination is given before any decline in effectiveness, and the second is after a decline begins.

New effective level level

Level.P1

P.deltata

Residual level

T0 T.eff1 T.jab2 T.eff2 T.dec T.res

Expanding on the ONE INJECTION MODEL, we have the additional parameters:

T.jab2 day on which the second injection is given

T.eff2 day on which the second vaccination protection reaches maximum

P.delta1 the increase in effectiveness due to the second vaccination

In this approach, the T.dec and T.res parameters will not be useful, as long as the new effective level of protection is assumed to be longer than the duration of any simulation.

***TWO INJECTION MODEL-B***

This is the situation in which the second injection is given after the effects of the first have started to decline. We will therefore need the parameters:

T.dec day first vaccine protection starts to diminish

T.res day the decline reaches the residual level of protection

P.res the residual level of protection, needed to calculate the rate of decline

deltata

Effective level

Residual level

T0 T.eff1 T.dec T.jab2 T.eff2 T.res

In addition, the new parameters of:

T.jab2 day of second vaccination

T.eff2 day second vaccination reaches its maximum effect

P.delta2 the additional protection conferred by the second vaccination

this value may or may not be the same as in the MODEL-A

These will be sufficient for the program to calculate the degree of protection that an agent has, given the day of the first vaccination, and the day of the potential infection being considered.

**Disjunctive vs Conjunctive Protection**

The term “disjunctive” here is to interpret **efficacy** as purely population-based. In other words, if the efficacy is 80%, then 80% of the population gets FULL protection, and 20% get NO protection. For the user, it is BINARY, but the vaccinated population as individuals do not know which portion to which they belong.

The term “conjunctive” will interpret efficacy as PERSONAL. In other words, if the efficacy is 80%, then upon a susceptible being challenged by an exposure to an infective, the odds are 80% that this will result in an infection, this being determined through a random( ) function returning a value between 0 and 1.

If the physiological model is that of the vaccinated person responding with a level of antibody to the virus, then the group response is that a certain number will reach a threshold of full resistance, while the rest do not. This is the efficacy for the disjunctive model.

The conjunctive model is somewhat more easily related to the concept of effectiveness, in which other factors may be involved, such as duration of exposure, viral dose of exposure, ambient air circulation, intrinsic physiological factors (stress, fatigue, comorbidity, etc) so that a “level of protection of 80%” means that for every person, there is some chance that an encounter may or may not result in an infection. If the conjunctive probability is high, then the exposure is less likely to happen.

Of course, we could combine the two, and use the disjunctive model to partition the vaccinated population, but apply a conjunctive probability to every exposure. Since this protection is zero for those not infected in our simulation, we could set this to any arbitrary level we wish in the scenario exploration mode, so that the conversation that “if you get it, it will be milder” would translate in our case, to additional persons protected from infective encounters.

**Pfizer EUA and the NEJM Discussion**

The following parameters have been gleaned from the Pfizer EUA [url:] and the NEJM article [ref]. Consider the Pfizer time-line. Dropoff

52.4% 90.5% 94.8%

Dose1 +7 Dose 2(+21) +28 ??

90.5% ???

This represents the parameter set for the Disjunctive model. To assist with implementation, we have changed CovidSIMVL to vaccinate absolute numbers rather than percentages.

THE TRANSMIT LEVEL MODEL

The vaccination models do not integrate viral growth with vaccination, so that viral temporal dynamics continue. Therefore, the converse of becoming infected needs to be taken into account, which is the probability of infecting a susceptible by an agent that has been vaccinated. We do not have biological knowledge of what this probability is with the different vaccines, so we will set this as a parameter.

When a vaccinated infective agent contacts a susceptible, the TRANSMIT-LEVEL is applied in the same way. If we generate a random number, and it is less than the TRANSMIT-LEVEL, then the infection may proceed.

At this time, we will not use a detailed approach as in the PROTECTION-LEVEL models, but we do have some choices.

1. We can assign a fixed number to the T-LEVEL for a vaccinated agent, so that regardless of the P-LEVEL, the T-LEVEL is the same, from the first vaccinated day.
2. Another approach is to use the T-LEVEL as a function of the P-LEVEL, so it can be the complement of the P-LEVEL, or it can be a percentage of the P-LEVEL.

So we will offer two modes: the first is a fixed level of Transmission, the second is a % of the complement of the P-LEVEL.

**POPULATION VS PERSONAL PERSPECTIVE ON THE MODEL**

The classic definition of vaccine efficacy is through comparing a clinical trial in which the infection rate in a vaccinated group is compared with the infection rate in a matching placebo group, at a certain elapsed time from the date of first vaccination, with specifications like no illness in the 7 days preceding the first injection.

For example, the Pfizer EULA gives the efficacy as 95%

We can apply a stochastic variation to the parameters for each calculation using the routine stochast(x,y), without having to individualize each person, except for the day of vaccination, unless different persons get different 2nd vaccination periods.

If the second is true, then it creates some problems in the parameter file approach, which really only sets global variables.

To set individual parameters, we need to resort to the population csv file. We will start with the SINGLE injection, global variable approach, and grow from there.

**TRIALS using the Multiverse and Vaccination Models**

The STAR multiverse permits us to mix populations that are discrete who inhabit universes with possibly different epidemic dynamics.

So one trial we can configure is to have Universes that are age-independent but with different length of effectiveness, so we can see what happens if the 16wk wait for the second injection is too long, and have each Universe have a different P.dec day.

**STAR Configuration**

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Population: 100 per site – 7 Villages, one Mixer, one Generator

Movement – 10 per day to Mixer; stay for 8 hrs synchronous

- in addition, 10 from Mixer to Generator non-overlap for 8 hrs

THE FAST MODEL

The parameter file was established by trial and error to provide a base (no vaccination) of near 100% infection of all Universes within the longest time possible (so that we can use 120 days of pre-jab2). The ages were all set to 0, and the Family Key all set to 2, to neutralize age and family distinctions.

The HzR was set at 3.5 as a global, and expanded by a size factor of 1.5 for the Villages so that they would go to full infection without vaccination.

The generator was set to Mingle Factor (“mF”) of 0.4 and a sizeF of 0.4 to prolong the issue of infectives to the Mixer for as long as possible while going close to full infection for its population.

The Mixer was set to a sizeF of 0.8 as it gets 180 population, and it is desirable to keep it active for as long as possible, but also to ensure that all visitors from Villages eventually get infected.

The Vaccine Parameters

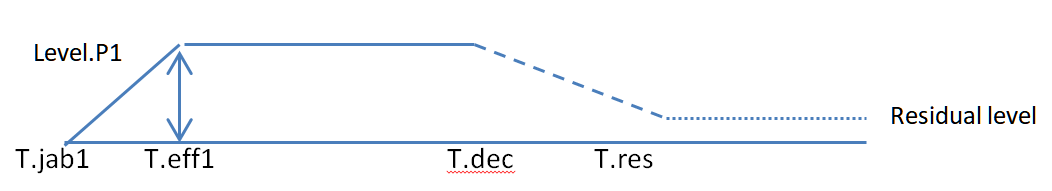
This STAR configuration gives us the option of setting each Village to a different vaccine profile. We used the following profiles, and issued messages for:

- successful infection in a Universe by and to agent IDs with both probabilities (to come)

- Infection prevented in Ux with agent IDs, probabilities, and Vaccination Sector

- Transmission prevented infection with Ux, agent IDs, probabilities and Vaccination Sector

We set the probabilities according to the following model for Universe 2



Current Day CD

--- Sector 1-----| --------------------Sector 2 ---------- | --Sector 3 ------------- | ------- Sector 4 ---------

In this the current BC model, the vaccine takes effect (T.eff1) on Day 14 from the day of vaccination (T.jab1), rising linearly to Level.P1 of 72%.

It stays at this level till T.dec of 120, when the efficacy starts decreasing, again linearly to T.res of 180 days, at which time it reaches a Residual Level of 25%.

This model is decremented for Villages 3,4 and 5 by 20 days for T.dec (time effectiveness starts decreasing) and T.res (time it falls to residual effectiveness). So these are, for T.dec, values of 100, 80 and 60 days. The corresponding T.res would be 160, 140 and 120 days post-vaccination.

For Villages 6,7,8 we decrement by 10 to get T.dec of 50,40 and 30 with T.res of 100, 90 and 80 days. The following is a summary table.

TRIALS of the STAR-FAST Model

CovidSIMVL was run with the following vaccination schedules:

1. No one vaccinated
2. 70% vaccinated at gen=0
3. 80% vaccinated initially
4. 90% vaccinated initially
5. 99% vaccinated initially

We let the trials run to termination, which is the time at which no further infectives exist in any of the Universes – thus, no further changes in state were possible.

The total times, total uninfected in aggregate and in each Universe, were recorded. The details of infections prevented and transmissions prevented due to vaccinations were recorded in console.log but not yet analysed in any detail.

The results were: 700 were vaccinated.



Interpretation

These uninfected numbers are perhaps much lower than expected, given that vaccinations of 70% of the population took place at gen=0.

The following considerations should cause a re-thinking of what it means to be vaccinated at the 70% level.

Protection of one event is 7 times out of 10 ie 70%. The conjoint probability of protection from two successive infection events is 0.7\*0.7 = 0.49 already less than 50%.

The pressure to infect comes from the base activity for the specific epidemic, which was set to high (so all would be infected if no vaccination). This pressure continues, and it does not take many successive 0.7 events to make the breakthrough.

So the right model is that if infection events keep occurring, the analogy is then of a resistance, which is broken over time (a few successive events). It is INEVITABLE, if infection events keep occurring such that the p^n is small.

Only if in the lifetime of an infective, the likelihood of meeting a susceptible is very small, will vaccination make a real difference.

SO THE MAIN POSITIVE RESULT IN FAST EPIDEMICS IS TO SLOW DOWN THE TEMPORAL DYNAMICS BUT NOT THE OUTCOMES OF THE EPIDEMIC BY MUCH (DEPENDING ON THE INTRINSIC RATES).

We can run these trials for slower epidemics, but we will not be starting from a base of full infections. However, we will use WAVE settings for a non-VAX situation and go from there.

Then we can extend this to inject the second vaccine upon some P.jab2 day, as a parameter for each Universe…..so that the parameters will be Universe specific? But if the infection takes place in a MIXING chamber Universe, that will not hold.

What we can do is to initialize each person with the Vaccine characteristics from the Universe they start in, so that the person carries the model, and no matter in what Universe the infection is considered, the models are of the agents themselves.

This method spares our having to define each person in the population.csv file with their vaccination models.

We will then expand this to the other Models, and to the Transmission Models….