github.com/philomaths-org/covid-19/blob/master/conditional_immunity_v1a.pdf.
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Technical Note: CD-3
Notes on Conditional Immunity.

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1 Conditional Immunity

The basic reproduction number, R_0 for COVID-19 is estimated to be 2.5 [1]. Herd immunity is reached when $1 - \frac{1}{R_0}$ have been infected. For an R_0 of 2.5, this is reached with 60% of the population. With the COVID-19 epidemic, governments and the population are varying their behaviours so that the value of R is considerably less than 2.5. This raises the prospect of a population reaching herd immunity with a much smaller percentage infected. This would be conditional herd immunity as it would be conditional on the government and the population maintaining the lower value of R even after the number of infections starts to drop.

We generated the empirical Cumulative Distribution Function (CDF) of the R value for all countries with a tight confidence interval (0.1) for the estimates of R. There were 105 such countries. This data was generated on July 29, 2020, using information from the Johns Hopkins University COVID-19 website [2]. Countries with a tight confidence interval for R generally have a significant incidence of the disease, so it excludes most countries that are in a successful lock-down. It can be seen that the very large majority of countries are maintaining a value of R well below 2.5.

Examining the Wikipedia entry for National Responses to the COVID-19 pandemic [3], it identifies 86 countries that carried out lock-downs, of which, as at July 28, 2020, only 11 were still in lock-downs. An archive of this

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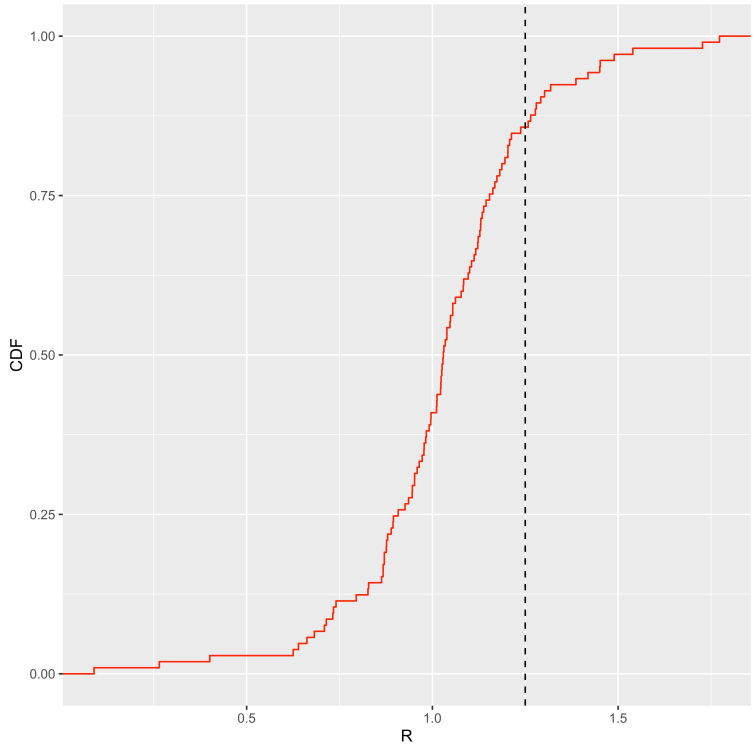
Figure 1: CDF of R values



wikipedia page on this date is stored on the Philomaths github site [4]. The Wikipedia page defines lockdowns as 'a requirement for people to stay where they are'. Although a more details analysis could be carried out, it seems that the large majority of the 105 countries that are analysed in Figure 1 are not under tight lock-down, but are probably under some degree of restriction.

Accordingly the majority of countries are able to maintain much lower value of R without a severe lock-down. Indeed almost 90% of countries have a value of R less than 1.25. Accordingly, it seems reasonable that a target R of 1.25 is achievable without drastic lock-downs. A value of 1.25 means that conditional herd immunity would be reached when 20% of the population have been infected.

2 Reinfection

An important issue with immunity is the rate of reinfection. If this is high, then the immunity is quickly lost and conditional immunity would be transient, if it could be reached at all.

It seems immunity from the COVID-19 disease does last a reasonable length of time. The advice from the Australian Government [5] is that 'There have been reports of apparent re-infection in a small number of cases. However, most of these describe patients having tested positive within 7-14 days after apparent recovery.' The CDR states [6] ''Reinfection with SARS-CoV-2 has not yet been definitively confirmed in any recovered persons to date'. In addition the CDC Planning Scenarios [1] do not include any parameters for reinfection.

The lack of confirmed cases of reinfection is remarkable given in the US as at August 5, 2020, there had be 4,823,890 confirmed cases [2]. Using the Rule of 3, used in clinical trials, the upper 95% confidence limit for the probability of reinfection is 1 in 1.6 million. In the US, there has been infections since late January, so there has been no sign of reinfection for six months. Some insight into the longer term reinfection rate can be done using the Susceptible Infected Recovered Susceptible (SIRS) model [7]

The (SIRS) model [7] allows for an epidemic where immunity is lost over time, so that some recovered individuals return to the Susceptible population. This requires an addition to the standard SIR model, where the recovered individuals re-enter the susceptible population at a rate γ. Accordingly the equations become

$$\begin{cases} \frac{dS(t)}{dt} = -\beta S(t)I(t) + \gamma R(t) \\ \frac{dI(t)}{dt} = \beta S(t)I(t) \ - \ \alpha I(t), \\ \frac{dR(t)}{dt} = \alpha I(t) \quad - \quad \gamma R(t) \end{cases}$$

where γ is the reinfection rate. Note it is still a closed three compartment model so we have

$$S(t) + I(t) + R(t) = N \tag{1}$$

Consider the equation for $R(t)$ in equations 2, but assume there is no inflow to the compartment.

$$\frac{dR(t)}{dt} = -\gamma R(t) \tag{2}$$

If the initial number in the Recovered compartment is R_0, then this can

be solved to yield

$$R(t) = R_0 e^{-\gamma t} \tag{3}$$

Denote $F(t)$ as the number of people who have been reinfected at time t. We have that

$$F_{exp}(t) = R_0 - R_0 e^{-\gamma t} \tag{4}$$

$F_{exp}(t)$ can be interpreted as the Reinfection curve for the epidemic, provided we define $F(t)$ as 0 for $t < 0$. The distribution is an exponential distribution, with a mean of $T_r = \frac{1}{\gamma}$, so T_r is the mean time before being reinfected.

The JHU website provides the number of new cases of infection detected each day. Denote the number of new cases on the kth day as I_k, and suppose that data has been gathered for N days. After N days, the number of reinfected individuals arising from the cases detected on the k^th day with be $I_k F_{exp}(N - k - \tau_r)$, where τ_4 is the average number of days between a person's infected being detected and and the person has recovered and so can be reinfected. The γ used in equation 4 has units of $\frac{1}{\text{days}}$. Accordingly the total number of reinfected individuals occurring during the N days will be

$$N_r = \sum_{k=1}^{N} I_k F_{exp}(N - k - \tau_r) \tag{5}$$

If we apply this equation to the US data from the JHU website as at August 5, 2020, and assume that the value of T_r is 180 days and $\tau_r = 20$days, then the estimated value of N_r is 805,337. The figure of 180 days comes from that length of the pandemic and a τ_r of 20 days corresponds to the time to for a person with severe illness to cease being infectious [6]. It does not need a statistical test to conclude that an exponential distribution with a mean of 180 days is not consistent with the observed zero confirmed reinfections. The result is not sensitive to these parameters, for instance if we assume the value of T_r to be ten years, the value for N_r is still 32,085. This value is lower, but still completely inconsistent with the zero confirmed reinfections.

The actual nature of the reinfection probability curve is not known. However there has been some speculation it might be similar to related viruses that have a reduced risk of infection for several months after the initial infection. Galanti and Shaman [8] estimate the Reinfection curve for two such CoV viruses (HKU1 and OC43). We digitized the Reinfection curve for OC43 from Figure 3 of that paper, and used that with equation 5 to estimate the value of N_r on the JHU data. The result was 167,809, a result which is also

completely inconsistent with observed zero confirmed cases. We expect an estimate of N_r using the Reinfection curve for the HKU1 virus would produce a similar result.

It is possible that a mutation or some other development will change this situation, but at this time believe it is reasonable to assume that immunity will last for a considerable period. In the interest of completeness, in appendix A we explore the effect that such a mutation might have on the effect of an epidemic.

3 Estimation of level of Immunity

Russel et al. [9] describe a method of estimating under reporting of symptomatic cases by use a delay-adjusted case fatality ratio. The method is based on the insight that death from COVID-19 happens many days after initial infection, so the deaths at any time relate to cases that were detected many days earlier. Accordingly, they estimate an corrected Case Fatality Ratio (cCFR) by accounting for the delay from confirmation to death, by estimating the number of cases with known outcomes (recovery or death). The then use estimates for the actual Case Fatality ratio from Wuhan to estimate the Case Detection Ratio (CDR), which is the ratio between the number of detected cases and actual cases. The estimated CDR is given by

$$CDR_{est} = \frac{CFR_{actual}}{cCFR} \tag{6}$$

Russel et. al. also describe a method to estimate the Confidence Interval (CI), i.e CDR_{low} and CDR_{high}, which is partly based on the CI for the CFR_{actual}, i.e. CFR_{low} and CFR_{high}.

Now in some countries, there is wide spread anti-body testing. In such countries, the number of reported cases are are a mix of symptomatic infections, asymptomatic infections or cases where symptoms have yet to develop. However, at any point in time, assuming that the mix is not changing greatly over the time period between detection and death, the same reasoning should be applicable to estimating the Infection Detection Ratio, i.e the ratio of the known cases to the actual number of infections. Accordingly we can use

$$IDR_{est} = \frac{IFR_{actual}}{cCFR} \tag{7}$$

and similarly calculate IDR_{low} and $IDRhigh$, using input from IFR_{low} and IFR_{high}.

We can then estimate the fraction of people with immunity in a country I_{est} that has experienced C cases, with the formula

$$I_{est} = \frac{(\frac{C}{\text{IDR}_{est}} - D)}{N - D} \tag{8}$$

$$a = \tag{9}$$

where N is the total population and D the number of death due to COVID-19. We are ignoring normal births and deaths.

We can also estimate the CI with

$$I_{low} = \frac{(\frac{C}{\text{IDR}_{high}} - D)}{N - D} \tag{10}$$

and

$$I_{high} = \frac{(\frac{C}{\text{IDR}_{low}} - D)}{N - D} \tag{11}$$

If the $D << N$, then I can be approximated by

$$I_{est} \approx \frac{C}{N\text{IDR}_{est}} \tag{12}$$

, with a similar approximation for the CI.

We considered two different estimates of the IFR. The CDC planning scenarios [1] are based on a review paper by Meyerowitz and Lea [10], that give a IFR of (0.0053, 0.0068, 0.0082).

On a daily basis the Philomaths website [11] calculates the level of Immunity for each country in the JHU database [2]. This shows, as at ???, that no country has yet to reach Conditional Immunity, although some are a matter of months off.

A number of researchers at Oxford are hypothesizing that the IFR is considerably lower than this figure. In particular, OK hypotheses a value of IFR_{low} of 0.001 and a value of IFR_{high} of 0.0041. Oke did not give a point estimate, but in order to allow us to make an estimate, we chose an IFR_{est} of 0.0028. We are call the hypothesis that the IFR is given by (0.001, 0.0028, 0.0041) the Oxford Hypothesis.

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On a daily basis the Philomaths website [12] calculates the level of Immunity for each country in the JHU database [2] based on the Oxford Hypothesis. This shows as at ???, two countries have reached Conditional Immunity at the 95% level. The countries are San Marino and Belgium.

Appendices

A Mutation

We built a computer simulation of SIRS equations 2 to explore what would happen if a mutation changed the Reinfection curve. From the CDC planning document [1] we used a value of $R_0 = 2.5$ and the mean serial interval, $T_c = 6$days, with a total population of 1,000. Figure A shows the case of $T_r = \infty$ so there is no reinfection.

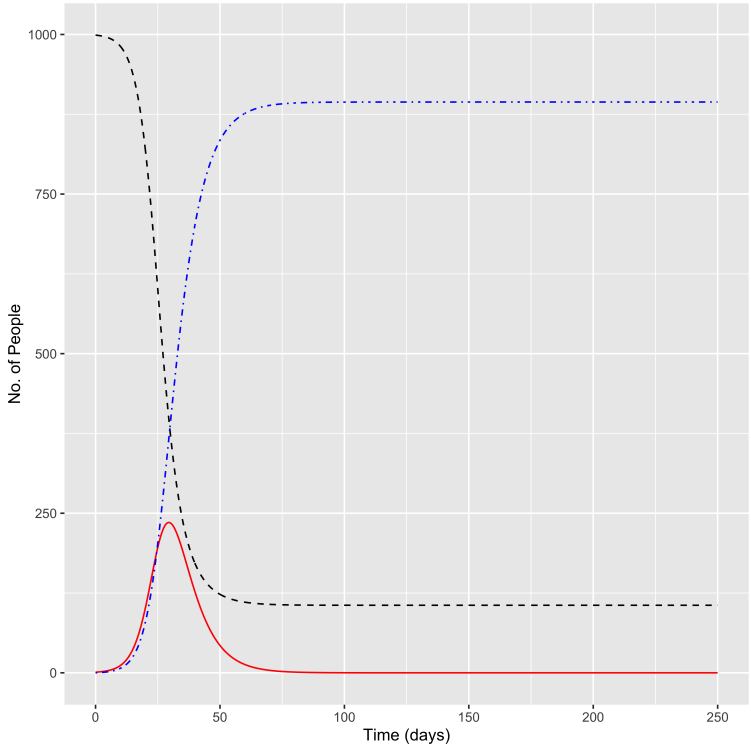
The normal SIR model behaviour can be seen, with the Infected population peaking around 40 days and then slowing reducing to zero, with the Susceptible population monotonically reducing, and the Recovered monotonically increasing.

In Figure A, we have set T_r to 150 days, we do see a different behavior. In the early part of the epidemic ($t < 100$days), the Infected curve looks very similar but from around $t = 50$ the Susceptible curve stops dropping and starts to increase. There is an inverse behaviour in the Recovered population. This is caused by the people who have lost immunity moving from the Recovered compartment back to the Susceptible compartment. This does not immediately cause an appreciable change in the number of Infected individuals because the effective value of R is less than 1 at this point. The Effective Reproduction Number is given by

$$R_{eff} = R_0 \frac{S(t)}{N} \tag{13}$$

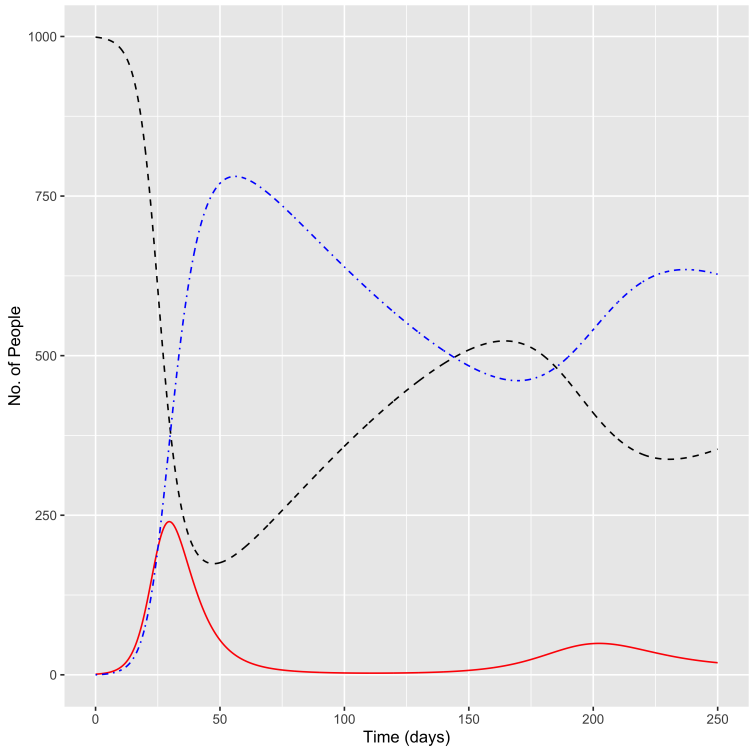
At $t = 50$, the value of $S(t)$ is about 175, so R_eff is 0.44, so there is no effective transmission of the disease. However, by $t = 150$, R_eff is 1.27 and widespread transmission starts again. It is about this time we see the number of Infections rise and keep rising until the R_eff becomes less than one again and so the number of infections drop again towards zero.

Figure 2: Susceptibles (black, dashed), Infected (red, solid), and Recovered (red, dot-dashed) as a function of time.



So a T_r of 150 days has little effect on the first part of the epidemic's trajectory but does cause a small peak around $t = 200$day. The larger T_r the further out this secondary peak is pushed and the smaller its amplitude.

Figure 3: Susceptibles (black, dashed), Infected (red, solid), and Recovered (red, dot-dashed) as a function of time.



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