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Notes on Conditional Immunity. Philomaths Technical Note - TN7

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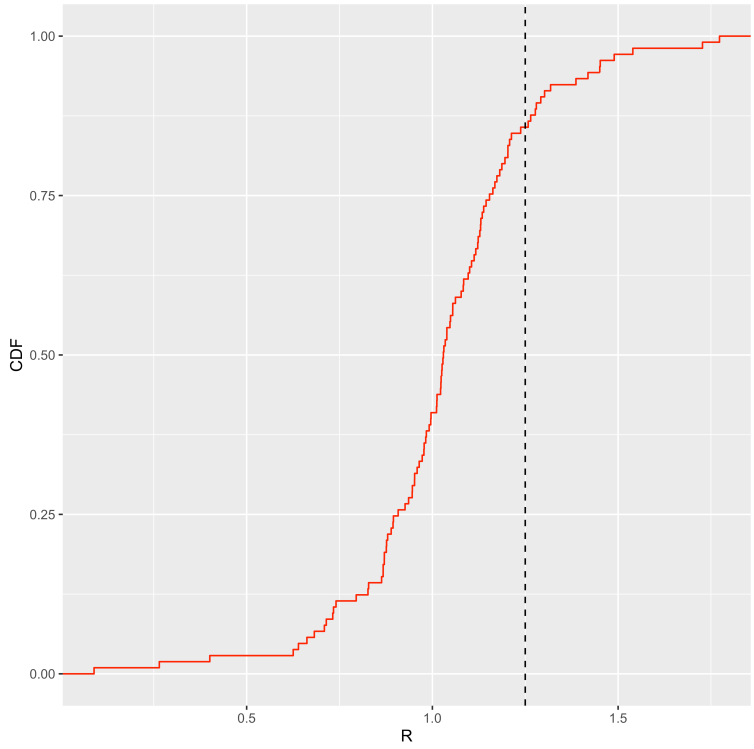
1 Conditional Immunity

The basic reproduction number, $\mathcal{R}_0$ for COVID-19 is estimated to be 2.5 [1]. Herd immunity is reached when $1-\frac{1}{\mathcal{R}_0}$ are infected or have recovered. For an $\mathcal{R}_0$ 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 $\mathcal{R}$ 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 immunity* as it would be conditional on the government and the population maintaining the lower value of $\mathcal{R}$ even after the number of infections starts to drop.

We generated the empirical Cumulative Distribution Function (CDF) of the $\mathcal{R}$ 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 $\mathcal{R}$ 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 $\mathcal{R}$ 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

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 $\mathcal{R}$ without a severe lock-down. Indeed almost 90% of countries have a value of $\mathcal{R}$ less than 1.25. Accordingly, it seems reasonable that a target $\mathcal{R}$ 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 18, 2020, there had be 5,482,416 detected cases [2]. Applying the Rule of 3, used in clinical trials, the upper 95% confidence limit for the probability of reinfection is 1 in 1.8 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_r 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

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

This analysis assumes the IDR remains constant over the period of consideration, so that the detection rate is the same for the initial cases as well as the reinfections.

If we apply equation 5 to the US data from the JHU website as at August 18, 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 1,827,472. 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 61919. 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 205,668 reinfections, 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.

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 partly 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). They 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 IDR_{high}, using input from IFR_{low} and IFR_{high}.

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

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

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

We can also estimate the CI with

$$I_{low} = \frac{(\frac{C}{\text{IDR}_{high}} - D)}{N - D} \tag{9}$$

and

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

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

$$I_{est} \approx \frac{C}{\text{IDR}_{est} N} \tag{11}$$

, 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-Katz 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 August 20, 2020, 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, Oke [12] 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.

On a daily basis the Philomaths website [13] calculates the level of Immunity for each country in the JHU database [2] based on the Oxford Hypothesis. This shows as at August 20, 2020, three countries have reached Conditional Immunity at the 95% level. The countries are San Marino, Belgium and Peru.

4 Comparison of IDR estimates

Hicks et. al. [14] have estimated the IDR based on COVID-19 antibody seroprevalence testing of the population. The found a seroprevalance of 0.28% of the population which they equate to 71,400 infections (95% CI: 0 to 181,050). This testing occured from June 2, 2020 when there were 7387 cases and finished on July 17th, 2020 when there were 11,190 cases. Taking the endpoint of the study, an estimate of the IDR from the seroprevalance data is $\frac{11{,}190}{71{,}400}$ [1]. This provides an estimate of the IDR of 0.16. The lower CI for the IDR can be calculated using $\frac{11{,}190}{181{,}050}$. The value of the lower CI for the number of infections being zero may make sense based on the internal logic used in the paper, but given that there were 11,190 cases actually detected by July 17th, a more reasonable lower CI for our purpose would be 11,190, so that the upper CI for the IDR would be 1. To summarize, using the seroprevalence data, the estimated IDR as at July 17, 2020 for Australia was 16% (95% CI: 6% to 100%). We can compare this with the IDR estimated based on the IFR of Meyerowitz-Katz and Lea. As at September 16, 2020, our estimate of the IDR using the Meyerowitz-Katz IFR is 19% (95% CI: 14% to 28%). At the same date, using Oke's IFR estimate, our estimate of the IDR is 8% (95% CI: 3% to 14%) . This assumes that the IDR in Australia has been constant. A more sophisticated est could be done, but looking at the overlap of confidence intervals, it appears that the IDR using the IFR of Meyerowitz-Katz and Lea is consistent with the seroprevalence estimate, whilse the IDR using Oke is not. However, the lower IFR that Oke hypothesizes may be in part to natural immunity due to past infections/vaccines, which would not show up in a seroprevalence test. This assumes that the IDR has been constant over the period of consideration. Comparing IDR estimates as of July 17 is not possible, because the period from June 2 to early July had a very low number of new cases and then a large increase from early July, that appears to affect the filtering used for IFR based methods.

5 Conclusion

It appears that some countries have already reached Conditional Immunity or are likely to reach this state within a few months. It also appears that

[1] A more sophisticated analysis would weight the detected infections by a function of the detected cases on that day of sampling.

the effects of immunity will be likely to last for a long period of time. Such countries have the option of managing the pandemic by maintaining their value of $\mathcal{R}$ such that the country continues to enjoy herd immunity. If the initial value of $\mathcal{R}$ is 1.25, this can be increased over time, as the fractional level of Susceptible individuals continues to decrease, i.e. $\mathcal{R} = \mathcal{R}_0 \frac{S}{N}$.

A Resources

The resources for this technical note are available for access at https://github.com/philomaths-org/covid-19. The conditional_immunity folder contains the pdf for this paper and relevant code. You can access resources for earlier versions of this note on Github by clicking on the tag corresponding to the earlier technical note's version number.

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