

R₀ We Getting It? Misconceptions and Misinterpretation of the Basic Reproduction Number for CoVID-19.

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1. Introduction

Ever since the outbreak of the COVID-19 pandemic (Hellewell *et al.*, 2020; Wu and McGoogan, 2020), there has been a barrage of epidemiological modelling exercises to inform appropriate policy responses globally. These models project the trajectory of the spread of the disease and develop scenarios under a set of assumptions. From the perspective of transmission of the pandemic, a fundamental and widely used metric is the R₀ (pronounced "R naught"), that has gained currency in the scientific literature as well as popular publications about COVID-19. The R₀ or the basic reproduction number; can be interpreted as the average number of secondary infections (Fine 1993) or the number of secondary cases an infected individual produces when everyone in the population is susceptible (Dietz 1993).

For example, an R₀ of 10 implies that an infected individual will transmit it to 10 other individuals. A value of R₀<1 means that the transmission ends (Diekmann et al. 1990) and the disease attains an endemic status. Despite being a valuable metric for understanding the transmission of COVID-19, a popular understanding of the R₀ as well as how policymakers

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make decisions using the information on the R_0 in the context of COVID-19 seem to have overlooked the established problems of its' misrepresentation, misinterpretation, and misapplication' (Delamater et al. 2019:1).

The concept of the R_0 traces its origins to the field of demography (MacDonald, 1957; Heesterbeek, 2002), there are also differences in the operational definition of the R_0 across different fields; even though the conceptual framework remains the same (Delamater et al., 2019). In the context of the COVID-19 discourse in India, estimates of the R_0 have ranged from 1.23 (Khaitan, 2020) to 4 (Mandal *et al.*, 2020). Many of these estimates have been considerably off in its forecasting estimates (Ioannidis, Cripps and Tanner, 2020) and have given rise to gaps in policy exercises.¹ Given these modelling projections are sensitive to model assumptions, we posit the need to acknowledge the limitations of these assumptions on the model parameters because of an evolving pandemic.

We argue that the model parameter values are not merely a function of the biological characteristics of the virus but are also affected by population as well as environmental factors. Consequently, the complexity involved in the derivation of statistical parameters such as the R_0 (Viceconte and Petrosillo, 2020) highlights the need to interpret them with extreme caution. Furthermore, it is necessary to calibrate these models to a more specific and local context to better account for a pandemic response. In turn, there are considerable public health applications that would benefit from an improved clarity on the R_0 (Ridenhour, Kowalik and Shay, 2014).

2. Making Sense of the R_0 .

Several estimates of the R_0 for COVID-19 are available, ranging from an average of 2.4 to 4.2 (Liu et al., 2020). The WHO has placed the R_0 between 1.4 to 2.5 for COVID-19. What do these numbers mean? As discussed earlier, the value of the R_0 below one implies that the

disease is endemic, while a value above 1, implies an epidemic status of the virus. The R_0 is also utilised in explaining the herd immunity, which goes onto show 'a pattern of immunity' (Fine, Eames and Heymann, 2011) whereby further spread reduces. This occurs not from a reduced virulence of the disease but from an inability to infect a non-infected or previously infected individual (Fine, Eames and Heymann, 2011).

In its most basic formulations in the literature, the R_0 depends on the duration of contagiousness following the infection, the contact rate, and the probability of infection following the contact of an infected person with a susceptible person (Dietz 1993). In popular epidemiological models such as the SIR (susceptible-infectious-recovered) models, this is defined as the ratio of the transmission rate and the recovery rate, typically denoted by the parameters β and γ , respectively. The formulae become more complex as multiple pathways of transmission are added and as we move towards more elaborate epidemiological models. Below we present a few misconceptions about the R_0 .

2.1 Some Misconceptions.

Certain characterisations of the R_0 warrant attention. The R_0 , not only varies for different diseases and hence needs to be accounted for a specific disease, but it varies for the same infectious agent across space and time. This can be attributed to the variations in host-vector, as well as host-host interactions. Besides, numerous socio-behavioural and environmental factors (Delamater et al., 2019) also affect it even when biological characteristics such as those of the virus remain constant (Anderson 1982).

Apart from a dependence on the epidemiologic triad of agent, host, and environment, the disease transmission dynamics depends on several clinical and non-clinical characteristics (Lloyd-Smith *et al.*, 2005). The clinical characteristics include factors such as the degree of seasonal variation in transmissionⁱⁱ and the duration of immunityⁱⁱⁱ. The degree of cross-

immunity between SARS-CoV-2 and other coronaviruses (Kissler et al., 2020), differences in virulent strains in certain places (Biswas, 2020), a plausible presence of the BCG vaccination (Miller *et al.*, 2020; Redelman-Sidi, 2020) are also relevant in the context of Covid-19. With respect to non-clinical characteristics, factors influencing contact rate such as the density of population, intensity and timing of control measures (Kissler *et al.*, 2020), household size^{iv} (Dahab, 2020), usage of face shields and masks, physical distancing (Chu *et al.*, 2020) and handwashing (Bartram and Cairncross, 2010) impact the transmission dynamics. Thus, based on the characteristics as mentioned earlier of the R_0 , using the R_0 from different geographies as a benchmark or as a direct import for the same disease or from a different period for the same or a similar disease is problematic (Delamater et al., 2020; Ridenhour, Kowalik and Shay, 2014).

The following considerations are notable. First, from the perspective of projections of COVID-19, the projections should not largely rely only on the R_0 , but on several other variables: the number of initial cases, the delay from the onset of symptoms to isolation, contact-tracing capability, the proportion of transmission that occurred before symptom onset and the proportion of subclinical infections (Delamater et al., 2019; Bauch et al., 2005 and Hellewell et al., 2020 as cited in Viceconte and Petrosillo, 2020). Thus, calculating a context-specific R_0 is of vital importance.

Second, since the R_0 is a unitless metric, it does not indicate the 'speed' with which new cases arise over a time period. If the R_0 was expressed as a ratio instead of a rate, it is likely to dispense much of this confusion. It should be noted that the speed with which an epidemic reaches certain benchmarks (in terms of having infected a given proportion of the population) is largely determined by the total susceptible population (N), the transmission rate (β) and recovery rate (γ). Of these, the last two play a crucial role in the overall spread of an epidemic.

As the transmission increases, the pace of epidemic spread increases dramatically while the recovery rate decreases to maintain a fixed R_0 (Ridenhour, Kowalik and Shay, 2014).

Third, a misconception about the R_0 is that many a time it is wrongly believed that the R_0 is constant for a disease. For example, values of the R_0 for measles ranges from 3.7 to 203.3 (Guerra et al. 2017). Therefore, one need not be surprised if there are as many R_0 values for COVID-19 as the number of models.

Contrary to conventional wisdom, the R_0 value does not go to indicate the severity of the disease (Viceconte and Petrosillo, 2020). However, it is imperative to determine it since many an outcome depends on it.

For instance, as the reproduction number reduces, the doubling time increases.^v Furthermore, it may seem counterintuitive that the R_0 cannot be reduced by vaccination campaigns alone. This is because of how the R_0 is defined; namely, the R_0 is calculated when the entire population is susceptible. Therefore, over time, with recoveries or deaths in the population and immunity being developed with vaccines, expecting the R_0 to change is misplaced. Instead, the related epidemiologic metric of 'effective reproduction number' (R_e) should be used. The R_e measures the transmission potential without requiring complete susceptibility within a population^{vi}.

Interpreting the R_0 and R_e , however, remains the same, in terms of specifying an endemic or epidemic status. The effective reproduction number is essentially a reflection of how the R_0 alters because of the external intervention (Delamater, 2019). These interventions take the form of social distancing, vaccination or behaviours like the usage of handwash (Ray, 2020) and sanitiser, facemasks and shields (Chu *et al.*, 2020) which reduce the probability of transmission of the infection (β) and in turn the R_e .

This has implications for policy impact evaluation as well, as the intervention efforts will be reflected in the R_e and not R_0 . Both the R_0 and R_e depend on biological properties of the

pathogen, environmental factors, and population behaviour, something often not clarified in the emerging literature on COVID-19. In addition to the misconceptions mentioned above and misrepresentations of R_0 , the readily available values of the R_0 must be considered with caution. Also, another emergent point is, there is an element of historicity in the estimates of the R_0 as they are usually retrospectively calculated rather than prospectively. For instance, the widely accepted R_0 values of measles are based on estimates of the R_0 back in the 1910s-1920s US and 1944-1979 England and Wales (Anderson and May 1982). Recent estimates are nonetheless associated with a wide range of estimate (Guerra et al. 2017). This also raises concerns about obsolescence of the estimates as over such long periods since there are often structural changes in the underlying factors that influence the R_0 . Changes in socio-behavioural factors in particular play an important role in obsolescence of older estimates for contemporary contexts (Markel *et al.*, 2007). Often the calibration of new estimates is done based on older benchmarks, which is a methodological challenge for epidemiological theorists and mathematical modellers. As we learn more about COVID-19, the reliance on limited estimates of R_0 as the basis for important public health policy decisions should be cautiously undertaken. Next, we discuss some concerns about estimating R_0 and related model parameters for epidemiological models in the context of India.

3. Concerns About Estimating Model Parameters for COVID-19.

The ambiguity about the underlying model parameters in the current scenario coupled with issues about the quality of the local data aggravates the estimation. While there are several unofficial dashboards and databases for COVID-19 that may or may not be relying on official sources of data, availability of official raw data (unaggregated data) is a serious concern. There are also discrepancies in data due to the reconciliation of official statistics as well as reassigning of cases to states by the Ministry of Health and Family Welfare (MoHFW), Government of India. There have also been concerns about the credibility of data emerging from different

states. For instance, issues of double-counting of 851 COVID-19 positive patients emerged, raising concerns about the lack of coordination between the Brihanmumbai Municipal Corporation (BMC) and the Government of Maharashtra (Deshpande, 2020).

Similarly, in the case of Delhi, newspapers reported that there was a discrepancy in COVID-19-related deaths reported by the Delhi government and the hospitals (The Hindu, 2020). There have also been changes in the format of the daily reporting of cases across states and the Centre. For instance, the MoHFW, Government of India stopped releasing district-wise statistics on a daily basis since the third week of April 2020. The Delhi government has stopped releasing distribution of COVID-19 deaths across various hospitals and has been under-reporting the number of individuals on ventilators (Mathew, 2020). Supposedly autonomous organisations like the Indian Council of Medical Research (ICMR) also reported data, in decreasing levels of granularity over successive days and did not release consolidated data on test-positivity observed across different states (Mukhopadhyay, 2020). There was inconsistency in the numbers released (at the same time) by the MoHFW and ICMR and disappearance of previously released information from its Archives (Wilson, 2020). There is also a lack of updated information on the production of testing kits, existing capacity and import volumes (Sharma and Premkumar, 2020). On a related note, Gandhi, Yokoe and Havlir (2020) raise the point about patients being classified as asymptomatic at the time test was conducted but being re-classified as pre-symptomatic few days later as they develop symptoms^{vii}. These artefacts of the surveillance systems are likely to influence estimating model parameters and a different set of assumptions will create issues of replication.

The adverse impacts of COVID-19 and the public response to it also affect the healthcare system in a manner that has implications for the hospital capacity, morbidity and the mortality rates as experienced in Italy, for instance, (Manca 2020). These non-linearities rarely get captured in the data collected and presented, let alone being reflected in our parameters.

Another important factor, which has implications for disease spread as well as the intervention is whether the models explicitly account for asymptomatic cases of infection (Cheng *et al.*, 2020), and this figure has implications for several different factors. It has implications for testing, as the latest testing strategy in case of India only focusses on symptomatic individuals or people who are in contact with the infected ones, besides a separate strategy for a high-risk population. While the lack of resources has been touted as the key reason for this testing strategy, it also means that one significant pathway of infection transmission goes completely unnoticed. The asymptomatic transmission is also part of the R_0 calculation, and a failure to account for its in its entirety will also result in under-estimations of the true status of the spread of the epidemic.

4. Concluding Remarks.

In conclusion, we would like to reiterate on the complexity and the interdependence of each of the parameters under consideration for a fundamental understanding of the R_0 . For planners, a social-epidemiological approach might better explain the presence of clusters and hot spots rather than focus on the physical characteristics of the virus alone. The models have not succeeded in explaining things like the concentration of 80 per cent of cases in just five states (MoHFW, 2020). Considering the variations in epidemiological transition amongst the different states of India (Dandona *et al.*, 2017), variations in the R_0 needs to be accounted at the level of each states populace and its health system. However, since the R_0 is usually computed in retrospective using mathematical models after sufficient agent-related data are available, the current estimates should be considered premature but indicative. Model complexities aside, rather than a rush to get the R_0 , the focus should be on understanding whether it is formulated and interpreted correctly – either as model outputs or inputs. Moreover, there are difficulties in public administration of relevant and sufficient data for necessary

calculations (Li and Smith, 2011). Developing countries such as India will offer considerable challenges in such estimation efforts.

Nevertheless, the redundant nature of extant estimates should be frequently reviewed and with improved sero-epidemiologic and mathematical models, estimating the R_0 for COVID-19 is expected to be a fertile area of research with substantial implications on public health policy and pandemic preparedness in the foreseeable future. The rapid reverse migration to states in the aftermath of the lockdown also was a major unknown which most models were not able to account for and expose the sensitivity of model results to these uncertainties.

While we have discussed several misconceptions and misrepresentation of R_0 for COVID-19 as well as the challenges in estimating R_0 given challenges in timely data availability and categorisation, it should be recognised that besides R_0 , other indicators such as case fatality rate (CFR) should also be scrutinised in detail. Due to the high incidence of 'questionable' asymptomatic cases and a long latency period (Cheng *et al.*, 2020), we never have an exact number of cases (Day, 2020; Heneghan, Brassey & Jefferson, 2020). Concerning deaths as well, as the number of complications rise, the causative factors are often missed, either by design^{viii} or as a deliberate strategy to under-report the deaths caused due to COVID-19. Nevertheless, there is a need for an improved understanding of how the R_e is influenced by intervention strategies such as social distancing/physical distancing, mask usage. A complete lockdown of the economy will not by themselves be able to stem the tide of this infection-spread (The Lancet, 2020).

Finally, we acknowledge that there are several challenges to estimating critical model parameters due to challenges of definition and reporting systems. These challenges notwithstanding, are important for subject matter experts to convey the meaning and limitations of our knowledge about the R_0 for COVID-19 to policymakers. Amongst the several challenges

of communicating the science of COVID-19 to the public, bridging the knowledge gap on the R_0 is a step in the right direction.

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ⁱ In a press release by the Ministry of Health and Family Welfare dated 22 May 2020, the estimates made by different independent experts on the lives saved as a result of lockdown range from 1.2-2.1 lakh (1 lakh = 100,000) lives as estimated by Boston Consulting group to 53,773 as estimated by Ministry of Statistics and Programme Implementation & Indian Statistical Institute.

ⁱⁱ Although evidence on seasonality for Covid-19 is limited at the moment, the evidence shows the existence of seasonality for other human coronavirus induced infections (Prem *et al.*, 2020), however in the absence of evidence it is best not to consider for seasonality or latitude (Sajadi *et al.*, 2020).

ⁱⁱⁱ While evidence from China and South Korea has surfaced where patients have been retested positive for the virus.

^{iv} Average household size in India is 4.9 versus 3.1 in China, 2.58 in Italy and 2.52 in the US.

^v Doubling time is the time taken for the cases to double. Some argue that doubling time is a more robust indicator than the R_0 , due to its lower sensitivity than the R_0 to daily fluctuations in number of cases, as its calculation involves only cumulative cases (Basu *et al.*, 2020).

^{vi} R_0 , in the most basic form is defined as ratio of transmission rate to the recovery rate; R_e is defined as $R_e = R_0 * (S/N)$ (Ridenhour, Kowalik and Shay, 2014), where S = Susceptible and N=population.

^{vii} This could possibly arise to the variations in the viral load and the sensitivity of the respective test kits which is seen elsewhere as well (Kucirka *et al.*, 2020).

^{viii} Death certificates generally state only one cause of death.