R_0 and R_e of COVID-19: Can We Predict When the Pandemic Outbreak will be Contained?

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Abstract

 R_0 (R naught) is the basic reproduction number, also known as basic reproduction ratio or rate which is an epidemiological metric used to measure the transmissibility of infectious agents. R_0 is a derivative of the following variables—the duration of infectivity after the patient gets infected, the likelihood of transmission of infection per contact between a susceptible person and an infectious individual, and the contact rate. R_0 is usually estimated retrospectively from serial epidemiological data or using theoretical mathematical models. Epidemiologists can calculate R_0 using contact-tracing data, the most common method is to use cumulative incidence data. When mathematical models are used, R_0 values are estimated using ordinary differential equations. R_0 of COVID-19 as initially estimated by the World Health Organization (WHO) was between 1.4 and 2.4. The forecast is of critical importance as it will help the governments to have an estimate as well as strategize quickly to avoid any unfavorable condition.

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INTRODUCTION

COVID-19 is similar to SARS and MERS coronavirus, which is transmissible from animals to humans, as in it is a zoonotic virus. Most of the affected individuals exhibiting mild or no symptoms are unable to get tested, particularly in developing countries. Therefore, the actual count of cases will be much higher. India's first positive case of COVID-19 was detected in Kerala on January 30, 2020. Initially, the majority of the case had travel history, thus became the primary source of infection to the rest of the population. With the progression of the pandemic, community transmission may have started taking place. Hence, it is important to estimate the transmission dynamics of this pandemic and predict the likely surge of cases.¹

One of the most discussed issues about COVID-19 is R_0 . R_0 (R naught) is the basic reproduction number, also known as basic reproduction ratio or rate which is an epidemiological metric used to measure the transmissibility of infectious agents. Government, public, and mass media are increasingly focusing on this epidemiological value.

HISTORY OF \mathbf{R}_0 and Public Health Importance

In the 1920s, Demographer Alfred Lotka recommended the reproduction number, as an estimate of the rate of reproduction in a select population. Epidemiologist mac Donald used it to describe the transmissibility of malaria. As per his suggestion, if $R_0 < 1$, the disease will perish in the population, and if $R_0 > 1$, the disease will spread faster.

R₀

 R_0 is an estimate of the contagiousness that is a function of human behavior and the biological character of pathogens. R_0 is not a measure of the severity of an infectious disease or the rapidity of a pathogen's spread through a population. It is not

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a biological constant for a specific pathogen.¹ It is estimated when there is zero immunity in the population. R_0 is a derivative of the following variables—the duration of infectivity after the patient gets infected, the likelihood of transmission of infection per contact between a susceptible person and an infectious individual, and the contact rate. The infectivity of the pathogen and duration of contagiousness are biological constants, but the extent of human-to-human interaction will vary and hence R_0 will vary depending on this parameter. This explains the importance of social distancing during the COVID-19 pandemic. It is also to be noted that the R_0 value of COVID-19 is higher than that of SARS and MERS.

R_e

 $\rm R_e$ (effective reproduction number) which also known as $\rm R_t$, is the number of people in a population who can be infected by an individual at any specific time. While measuring the transmissibility of the virus at any given time during an epidemic we use $\rm R_e$. It changes as the population becomes increasingly immunized, either by individual immunity following infection or vaccination and also as people die.

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Factors affecting R_e include the number of people with infection, the number of susceptible people with whom infected people are in contact, and people's behavior such as social distancing.

VACCINATION AND HERD IMMUNITY

 $\rm R_0$ predicts the extent of immunization required to achieve herd immunity. To prevent the sustained spread of infection, the proportion of the population that has to be immunized (Pi) has to be >1–1/R_0. Vaccination campaigns aim to reduce the susceptible population to infection by reducing R_0 to <1 for that event. The removal of susceptible population cuts the transmission by an effective reduction in susceptible contacts between infectious and susceptible persons. While testing the effectiveness of vaccination, we should use effective reproduction number (R_e) which can be used in populations having immune members.

How to Measure R_0 ?

 R_0 is usually estimated retrospectively from serial epidemiological data or using theoretical mathematical models. Epidemiologists can calculate R_0 using contact-tracing data, the most common method is to use cumulative incidence data.

When mathematical models are used, R₀ values are estimated using ordinary differential equations. Two mathematical models are used. The models are a susceptible-infectious-recovered model or susceptible-exposed-infectious-recovered model.

R₀ of COVID-19

 $\rm R_0$ of COVID-19 was initially estimated by the World Health Organization (WHO) and declared in a statement dated January 30, 2020.

The review by Liu et al. compared 12 studies published from January 1 to February 7, 2020, have estimated R_0 ranging from 1.5 to 6.68. They found a final mean and median value of 3.28 and 2.79, respectively, with an interquartile range of 1.16. The reasons behind the low level of accordance between the studies were attributed to the difference in variables considered, methods of modeling, and estimation procedures. According to Liu's findings, the studies using mathematical methods produce estimates that are higher than stochastic and statistic models in determining COVID-19 R_0 . R_0 is proportional to the contact rate and will vary according to the local situation.²

According to a recent review, by Park et al., the mean R_0 range is from 1.9 to 6.5 based on eight published and eight preprint papers. Of 20 estimates, 13 studies were in the range of 2 and 3. The estimates are comparable to that of SARS-CoV in the early phase of an outbreak in Hong Kong (2.7) and Singapore (2.2–3.6).³

Rai et al. conducted a study, showing that reproducibility for COVID-19 in India was 2.56 and herd immunity as 61%, in which an exponential growth model was applied to calculate future cases based on cumulative confirmed cases, recovered cases, and death rate over 21 days period.⁴

A mathematical model for reproduction number and herd immunity

 $It = (R_0) t/SI$

It—the number of cases at the time

R₀—reproduction number.

SI—serial interval—the time between the onset of the primary and secondary case (as per previous studies done in Hong Kong, SI has taken as 4.4).⁵

t-prediction time.

The Imperial College group has estimated R_0 to be between 1.5 and 3.5.³ While the Italian model estimated R_0 between 2.76 and 3.25 and researchers from Lombardy who analyzed the early phase of outbreak in their region reported a reduction in R_0 shortly after the introduction of mitigation measures.⁶

 $\rm R_0$ evaluated on the Diamond Princess Cruise Ship was 2.28 in early February. They estimated that unless $\rm R_0$ decreases by 25–50% by strict infection management and control measures the estimated total cases would be high in the following period. If the R_0 is reduced by 50%, the number of cases would be reduced by half and if the R_0 value is reduced to <1, the infectious cases would gradually die down.⁷

IMPORTANCE OF ESTIMATING Ro

Forecasting R_0 is critical, as it will help the governments to have an estimate as well as strategize quickly to avoid any unfavorable condition. Even though the Government of India has taken many measures, such as, complete lockdown, national and international travel restrictions, mandatory quarantine, etc., to limit the spread, an unforeseen surge within the communities has occurred, which has increased the burden.

Quarantine is an effective measure to alter R_0 . Coordinated global efforts help to curtail the spread of disease by mass quarantine of contacts and isolation of infectious patients. Community measures and social distancing should be proactively implemented to reduce the impact of the epidemic and to delay its peak, allowing healthcare systems to prepare and cope with the increased influx of patients. However, the effectiveness may be hampered by asymptomatic carriers.

Hellewell and colleagues forecasted the potential effectiveness of contact tracing and isolation of COVID-19 cases, using different values of R₀. Accordingly, with R₀ of 1.5, outbreaks would be contained if 50% of contacts will be traced, while with R₀ of 2.5 and 3.5 >70 and 90% of contacts, respectively, have to be traced.⁸

Based on Imperial College COVID-19 response team findings, which used a model assuming R₀ of 2.4, the UK government imposed lockdown as it was estimated that approximately 81% population will be infected with over half a million deaths in the absence of control measures.⁹

The SI shorter than the incubation period implies transmission before symptoms set in. This should be taken into consideration while, strategizing interventions, as it may deter containment efforts. SARS-CoV-2 has shorted SI estimates compared to SARS-CoV (8.4 days) and MERS-CoV (8–13 days), suggestive of challenges that may be faced trying to contain the spread.

In conclusion, the basic reproductive number varies during the course of the disease and is also based on epidemiological factors like susceptible population characteristics, disease transmissibility rate, and control measures adopted. R_0 helps the governments across the world to estimate the future caseloads, to strategize accordingly to accomplish containment goals within the specified time to avoid any unfavorable condition. The pre-symptomatic transmission and asymptomatic patients delay the contact tracing, quarantining, and effectiveness of mitigation measures. Global coercive efforts are required to mitigate the pandemic.



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