A NOTE ON THE BASIC REPRODUCTION NUMBER: NOVEL CORONA VIRUS (2019-nCOV)

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ABSTRACT
The basic reproductive number, R_0, is the expected number of secondary infections produced by a single individual during his or her entire infectious period, in a completely susceptible population. This concept is fundamental to the study of epidemiology and within-host pathogen dynamics. It is often used as a threshold parameter that can predicts whether an infection will spread or not. Since the outbreak of 2019 novel corona virus disease (COVID-19) in Wuhan and other cities of China the growth and spread of this disease is of a growing global concern. Many studies have been carried out and are continued to be carried to model the spread and subsequent control of the disease. In this paper, we give a brief overview of common methods of formulating R_0 from deterministic, non-structured models. Finally, we survey the recent use of R_0 in assessing the spread of novel corona virus.
Keywords: Mathematical Modeling of infectious Diseases, Basic Reproduction ratio, COVID-19, Pandemic

INTRODUCTION
The basic reproductive number, R_0, is the expected number of secondary infections produced by a single individual during his or her entire infectious period, in a completely susceptible population. This concept is fundamental to the study of epidemiology and within-host pathogen dynamics (Rong et *al*., 2020). It is the most important ideas that mathematical thinking has brought to the theory of epidemic and a key concept in bio-mathematics and epidemiology (H o f f ma n n *et al*., 2005; Yong and Owen, 2016; Rong *et al*., 2020). R_0 is also threshold condition used to determine whether an infectious disease will spread or not in a completely susceptible population when disease is introduced into the population (Yong and Owen, 2016).

The basic reproduction number R_0 is a significant indicator in both transmission risks and control of an infectious disease (Rong *et al*., 2020). Since the magnitude of R_0 allows one to determine t h e amount of effort required either to prevent an epidemic or to eliminate an infection from a population, it is therefore, important to estimate R_0 f o r a given disease in a particular population. Such that if one person develops the infection and passes it on to two others, then the R_0 is said to be equal to 2. If the average R_0 in the population is greater than 1, then the infection will spread exponentially, but if R_0 is less than 1, then the infection will spread only slowly, and it will eventually die out. Therefore, the higher the value of R_0, the faster an epidemic will progress (Aronson *et al*., 2020).

The basic reproduction number is affected by: (i) the size of the population and the proportion of susceptible people at the start; (ii) the infectiousness of the organism; and (iii) the rate of disappearance of cases by recovery or death, the first of which depends on the time for which an individual is infective. The larger the population, the more people are susceptible, the more infective the virus and the larger the R_0 w i l l be for a given virus. The faster the rate of removal of infected individuals from the population, by recovery or death, the smaller R_0 will be for a given virus (Aronson *et al*., 2020). The zero in "R zero" means that R_0 is estimated when there is zero immunity in the population, even though not everyone will necessarily be susceptible to infection, which is the usual assumption. Therefore, in an epidemic with a completely new virus, the earlier the measurements are made the nearer the calculated value is likely to be to the true value of R_0, assuming high-quality data (Aronson *et al*., 2020). In demography, R_0 represents the ratio of total p o p u l a t i o n size

from the start to the end of a generation.

So generation in epidemic models are the waves of secondary infection that flow from each previous infection. That is, the first generation of an epidemic is all the secondary infections that results from infectious contact from the index case. Such that, if R_i denotes the reproduction number of ith generation, $R0$ is simply the number of infection generated by index case (zero generation). Therefore, R_0 can also be defined as the expected number of secondary cases produced by generation zero (Heesterbeek, 2002).

As a general definition, R_0 is the expected number of secondary individuals produced by an individual in its lifetime. In demographics and ecology, $R0$ is taken to mean the lifetime reproductive success of a typical member of the species. In epidemiology, $R0$ is used to show the number of individuals infected by a single infected individual during the entire infectious period, in a population which is entirely susceptible. For in-host dynamics, $R0$ gives the number of newly infected cells produced by one infected cell during its lifetime, assuming all other cells are susceptible (Hoffmenn *et al*., 2005).

Therefore, from the definition of $R0$, it is clear that when $R0 < 1$, means that each infected individual produces, on average, less than one new infected individual, and it can be predicted that the infection will be cleared from the population with time. If $R0>1$, the pathogen is able to invade the susceptible population. This threshold behavior is the most important and useful aspect of the $R0$ concept and the infection will increase. Finally, when the $R_0 = 1$ means that, in the absent interventions in a population without immunity, each infected individual will infect another (Viceconte and Petrosilla, 2020).

It is therefore important to determine which control measures, and at what magnitude would be most effective in reducing the $R0$ below one, to avoid reaching the endemic equilibrium. This will provide important guideline to the public health initiatives in order to prevent the possible blown out of the epidemic in the susceptible population. The magnitude of $R0$ is also used to gauge the risk of an epidemic or pandemic in emerging infectious disease (Hoffmenn *et al*., 2005). The basic reproduction number ($R0$) should not be confused with the effective reproduction number (Re), which is sometimes referred to as (Rt
) which is the number of people in a population who can be infected by an individual at any specific time. It changes as the population becomes increasingly immunized, either by individual immunity following infection or by vaccination, and also as people die. Re is affected by the number of people with the infection, the number of susceptible with whom infected people are in contact and people's behaviour such as social distancing (Aronson *et al*., 2020).

The COVID-19 infection, caused by the novel coronavirus SARS-CoV-2, is a transmitted virus causing respiratory infection and highly transmitted from person to another. It is also a contagious disease that can be transmitted through droplets, aerosols, and contact and the symptoms of COVID-19 infection appear after approximately 2 to 5 days also referred to as incubation period, which ranges from most common symptoms (fever, sore throat, cough, and fatigue) to variable ones (loss of smell, sputum production, headache, haemoptysis, diarrhoea, dyspnoea, and lymphopenia) . In severe cases, infected cases may develop pneumonia, bronchitis, severe acute respiratory distress syndrome (ARDS), multi-organ failure, and death (Rahman *et al*., 2020).

The first case of novel corona virus was detected in the city of Wuhan China the capital of Hubei province on December 31, 2019. After developing the pneumonia without a clear case and for which the available vaccine and treatment were found to be ineffective. Currently, the disease has spread globally with the reported case at about and deaths about as at 5th July 2020. Initially, WHO estimated the basic reproduction number for COVID-19 to range between 1.4 and 2.5, as declared in the statement regarding the outbreak of SARS-CoV-2, dated 23th January 2020 (WHO, 2019). Additionally, many studies aim to precisely estimate the COVID-19 R_0. A recent review articles have estimated the R_0 for COVID-19, to range between 1.5 and 6.68 (Viceconte and Petrosilla, 2020; Liu *et al*., 2020). This paper givse an overview of the current methods used in the derivation of $R0$ and assess the use of $R0$ in the newly emerging novel corona virus. Further, we seek to determine to what extent has estimation of $R0$ informed public health policy measures.

DERIVATION AND METHODS OF CALCULATING $R0$

Jones (2007) in his study reported that it was important to note that $R0$ is a dimensionless number and not a rate, which would otherwise have units of time[-1]. Therefore, R_0 can be approximated as:

such that: $_0 =$

Where τ is the transmissibility i.e., the probability of infection given contact between a susceptible and infected individual, is the average rate of contact between susceptible and infected individuals and is the duration of infectiousness. From the above formula using a simple model of SIR (susceptible-infected- removed) model with assumptions that: constant population size exist, constant rates of transmission or removal, no demography i.e., no death and birth within the population and the population is considered to be well-mixed. Considering the SIR model:

$$= \frac{}{} = \quad -$$

Where $\beta = \tau\,c\dot{}$ and is known as the effective contact rate, v is the removal rate. It means that the expected duration of infection is simply the inverse of the removal rate: $d = v^{-1}$. Since the epidemic occurs if the number of infected individuals i nc re a s es that is when $\dfrac{dI}{dt} > 0$ so that:

$$- \quad > 0$$

and

$$>$$

$$\overline{\quad} \quad >$$

At the onset of an epidemic, nearly everyone is susceptible, therefore it can be said that $S \approx 1$. Substituting for S, yields

$$\overline{\quad} \quad > 1$$

Since $beta = \tau\,c\dot{}$ and $d = v^{-1}$, then the expression of $R0$ can be given.

$$0 = \int_0 000$$

In this method it is straight forward to handle situations in which infectivity depends on time since infection, or other transmission probabilities between states vary with time. The method can also be extended to describe models in which a series of states of are involved in the reproduction of infected individuals. This derivative becomes increasingly cumbersome as when this method is extended to infection cycles involving three or more generations. Jones (2007) reported next generation matrix method of finding the $R0$ u s i n g intuitive approach: assuming that a system has a multiple d i screte type of infected individuals. Then, the next generation matrix can be defined as the square matrix **G** in which the i, jth element of **G** is the expected number of secondary infections of type i caused by a single infected individual of type j again assuming that the population of type i is entirely susceptible. That is each element of the matrix **G** **is** a production number. Then the basic reproduction number R_0 c a n be given by the spectral radius of **G** which is the dominant eigenvalue of **G**. To illustrate this, consider a two classes of infected individual. The next generation m a t r i x is :

eigenvalues of **G** is given as:

$$= 1$$

$$\pm = \tbinom{}{} \pm \quad -()()$$

Where: $T = a + d$ is the trace of the matrix G and $D = ad - bc$ is the determinant of the matrix G. Suppose sexually transmitted disease is introduced into a completely heterosexual population. Such that f is the expected number of infected women and m expected number of infected men given contact with a single infected member of the opposite sex in a completely susceptible population. Then, the next generation matrix is given as:

Van den Driessche and Watmough (2002) introduced a more formal of next generation m e t h o d to derive $R0$ in situations where the population is divided into discrete classes, disjoint classes. The next generation operator can thus be used for models with underlying age structure or spatial structure, among other possibilities In this method the $R0$ is defined as the spectral radius of the next generation matrix. The formation of the matrix involves determining two compartments, infected and non-infected from the model. To find the $R0$ using next generation matrix van den Driessche and Watmough (2002) applied the following approach: Let n be the compartments in which m are infected, such that the vector $x^- = x_i$, $i = 1, \ldots n$ where xi denotes the number of individuals in the *ith* compartment. Let $F_i(x)$ be rate of appearance of new infections in compartment i and $Vi(x)=V_i^-(x) - V_i^+(x)$, where $V_i^+(x)$ is the rate if transfer of individuals into

compartment i all other means and $V_i^-(x)$ is the rate of transfer of individual out of the ith compartment, then the next generation matrix is given by FV^{-1} from the matrix of partial derivatives of F_i and V_i.

From the next generation matrix G; Let (0) and (0) . Where x is the disease free equilibrium

$_0$

$= ($ $= ($

state. Then R_0 is the dominant eigenvalue of matrix G=FV. As an example, consider a SEIR epidemic model with four compartments:

$$\begin{aligned} =- \quad + \quad - \\ = \quad -(+) \\ = \quad -(+), \\ = \quad - \end{aligned}$$
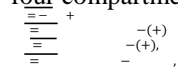
Where β is the effective contact ratio, λ is the birth rate of susceptible, v is the mortality rate, κ is the progression rate from exposed to infected and γ is the removal rate.

The next generation matrix can be calculated by identifying V *and F* such that:

$$= (\qquad)\leftarrow$$

Then $\overline{R_0}$ is the leading eigenvalues of the matrix $F V^{-1}$ given as:
$=(+)(+)$

Diekmann and Heesterbeek, (2005) used the the Jacobian method to find the predictive threshold param-eter. The Jacobian method is widely applied in most of the systems of ordinary differential equations, the predictive parameter is derived from the conditions that all of the eigenvalues of the Jacobian which have negative real parts, using the characteristics polynomials together with the Routh- Hurwitz stability conditions. The Jacobian method allows one to derive a parameter that reflects the stability of the disease free equilibrium. However, the predictive parameter obtained through this method may not be biologically meaning full value for $R0$. Hofferman *et al*., (2005) therefore, suggested that if this threshold parameter does not have the same biological interpretation as the dominant eigenvalue of the next generation matrix, then it should not be called the basic reproductive ratio, nor denoted $R0$.

The basic reproduction number as threshold criteria can also be derived from a condition based on parameter values such that when the condition holds, the endemic equilibrium exists, but when the condition is false, only the disease-free equilibrium exists. Referred mathematically as the transcritical bifurcation, such that at parameter value the condition switches from being false to true at parameter values which give $R0 = 1$ (Hofferman *et al*., 2005). Outbreaks of infectious periods are brief, but continue over the course of the patients' l i f e t i m e , with the virus quiescent at other times. This makes calculating $R0 = 1$ from other methods quite complicated.

Diekmann and Heesterbeek (2000) & Hethcote (2000) calculated the basic reproduction number from the final size equation applicable to closed population, where the infection leads either to immunity or death. Here, the number of susceptibles can only decrease and the $R0$ can be estimated as:

$$= \infty - 1$$

This estimate ho ld s when the disease itself does not interfere with contact process or where contact intensity is proportional to population density.

Nowak *et al*. (1997) and Lloyd (2001a) in their study estimated $R0$ from the intrinsic growth rate of the infected population often denoted as $r0$. From the standard models of viral dynamics, the standard relationship between $R0$ and $r0$ is

$$= 1 + \frac{r0 + a}{v}$$

Where a is the death rate of the infected cells and v is the clearance rate of the virions. If $r0 + a << v$ then, the relation approaches

$$= 1 +$$

This method proves useful since $r0$ can be readily estimated from viral load data for in-host models and from incidence data in epidemiology..

RECENT USE OF $R()$ IN THE S T U D Y OF NOVEL CORONAVIRUS

Okhueso, (2020) conducted a study on a mathematical prediction for Covid-19 as global pandemic when the infected population were quarantined with observatory procedures. In the study, t h e basic reproduction number was found to be $-0.009505 < 1$. This shows that there were 99% chances of secondary infection when an infected population interact by contact with the susceptible population. The study concluded that to attain a disease-free equilibrium there should be a dedicated effort from government, decision makers and stakeholders, Otherwise, the world would hardly get reed of the COVID-19 coronavirus and further spread is eminent.

Mwalili *et al*. (2020) modified susceptible-exposed infectious-recovered (SEIR) compartmental mathemat-ical model for prediction of COVID-19 epidemic dynamics incorporating pathogen in the environment and social distancing. The next generation matrix approach was used to determine the basic reproduction number ($R0$). The model equations are solved numerically using fourth and fifth order Runge Kutta methods. In the study, the basic reproduction number was found to be 2.03, implying that the pandemic will persist in the human p o p ulatio n absent strong control measures. Results after simulating v a r i o u s scenarios indicate that disregarding so c i a l distancing and hygiene measures can have devastating effects on the human population. The model shows that quarantine of contacts a n d isolation of cases can help halt the spread of novel coronavirus.

Maugeri *et al*. (2020) modeled the novel coronavirus (SARS-Cov-2) o utb reak in Sicily. Italy. Incorporating travel restrictions, quarantine and contact precaution as methods used to control the spread of the epidemic. The model a Susceptible-Exposed-Infectious-Recovered-Dead (SEIRD) model to assess SARS- CoV-2 transmission dynamics, working on the number of reported patients in intensive care unit (ICU) and deaths in Sicily (Italy), from 24 February to 13 April. Overall, we obtained a good fit between estimated and reported data, with a small fraction of unreported SARS-CoV-2 cases (19.5%; 95%CI=0%-34.7%) before 10 March lockdown. Interestingly, we estimated that the first set of restrictions reduced transmis- sion rate in the community by 42% (95%CI=38%-46%), and that more stringent measures adopted on 23 March succeeded to drastically curb the transmission rate by 84% (95%CI=80%-88%). They reported that there estimates d elineated the characteristics of SARS-CoV2 epidemic before restrictions taking into account unreported data. Further modeling after the adoption o f control measures, mo reo ver, indicated that restrictions reduced SARS-CoV2 transmission considerably.

Shaikh *et al*. (2020) developed a mathematical model of covid-19 using fractional derivative: outbreak in India with the dynamics of transmission and control In the study, a Bats-Hosts-Reservoir-People trans- mission fractional-order COVID-19 model for simulating the potential transmission by incorporating of individual

social response and control measures by the government. The basic reproduction number R0 was determined using the next generation m a t r i x a n d was found to be 2002283. The study found that in the absence of some treatment, vaccine, preventive measures to reduce the spread of the virus such as social distancing, decreasing number of contacts of susceptible population, mitigation, containment and suppres- sion against the infection recommending self-quarantine of entire populations living in affected areas are crucial with the participation of the public, along with the policy of reducing the transmission period by finding and isolating patients as quickly as possible through efforts by the quarantine authorities would benefit at large towards control of COVID-19.

Rong *et al*. (2020) investigated the effect of delay diagnosis on transmission of Covid-19 using a dynamical model. The basic reproduction number was estimated based on the data of reported cases using next generation matrix method. Sensitivity analyses and numerical simulations of the model revealed that, im- proving the proportion of timely diagnosis and shortening the waiting time for diagnosis can not eliminate COVID-19 but can effectively decrease the basic reproduction number, significantly reduce the transmis- sion risk, and effectively prevent the endemic of COVID-19, e.g., shorten the peak time and reduce the peak value of new confirmed cases and new infection, decrease the cumulative number of confirmed cases and total infection. More rigorous prevention measures and better treatment of patients are needed to control its further spread, e.g., increasing available hospital beds, shortening the period from symptom onset to isolation of patients, quarantining and isolating the suspected cases as well as all confirmed patients.

Anastassopoulou *et al*. (2020) conducted a study on data based analysis, modeling and forecasting of the COVID-19 outbreak, between January 11th to February 10, 2020. On the basis of a Susceptible Infectious-Recovered-Dead (SIDR) model, the study estimated the basic reproduction number ($R0$), the per day infection mortality and recovery rates. By calibrating the parameters of the SIRD model to the reported data, the study attempted to forecast the evolution of the outbreak at the epicenter three weeks ahead, until February 29, 2020. In the study, the number of infected individuals, especially of those with asymptomatic or mild courses, was suspected to be much higher than the official numbers, which could be considered only as a subset of the actual numbers of infected and recovered cases in the total population. They repeated the calculations under
a second scenario that considers twenty times the number of con- firmed infected cases and forty times the number of recovered, leaving the number of deaths unchanged. Based on the reported data, the expected value of $R0$ as computed considering the period from the 11th of January until the 18th of January 2020, using the official counts of confirmed cases was found to be 4.6, while the one computed under the second scenario was found to be 3.2. Thus, b a s e d on the SIRD simulations, the estimated average value of R_0 was found to be 2.6 based on confirmed cases and 2.0 based on the second scenario.

Wang and Yang, (2020) proposed a mathematical model for the novel coronavirus epidemic in Wuhan ,China. The model described multiple t r ans mi ssio n pathways in the infection dynamics, a nd emphasized the role of the environmental reservoir in the transmission and spread of COVID-19. Based on the parameter value the basic reproduction number ($R0$) w a s estimated to 4.25. They reported that based on the current development of COVID-19 it is still being speculated th a t the disease would persist in the human world and become endemic. Therefore, vaccines for the novel corona virus could play an important role in curbing the spread of this virus.

Ivorra *et al*. (2020) developed a mathematical model for the spread of the corona virus disease 2019. The model takes into account the known characteristics of the disease, existence of infectious cases, different sanitary and infectious conditions of hospitalized people. The model also considered the need of beds in hospitals. In the study, the value of the basic reproduction number ($R0$) for covid-19 was found to be 4.225. The study reported that the effective reproduction number decreases, mainly due to the application of control measures, and reached vales lower than 1 after February 2020. They concluded that the magnitude of the epidemic could be drastically reduced when increasing the percentage of detection of covid-19 cases.

Liu *et al*. (2020) developed a mathematical model which covers the data of reported cases, the number of unreported cases for the Covid-19 epidemic in Wuhan China. The model sought to answer fundamental issues regarding the epidemic: How will the epidemic evolve with respect to reported cases and unreported cases? How will the number of unreported cases influence the severity of the epidemic? how will public

health measures such as isolation quarantine, and public closing, mitigate the final size of the epidemic? In the study the basic reproduction number was determined using generation matrix method and was found to be 4.13. They concluded that public health measures, such as isolation quarantine and public closings greatly reduce the size of the epidemic, and make the turning point much earlier than without these measures. They also reported that the number of unreported cases greatly affect the value of ($R0$).

Liu *et al*. (2020) further conducted a review on the basic reproduction number of Covid-19 virus by comparing 12 published articles from January 1, 2020 to February 7, 2020 and they reported that the mean and the median estimates for $R0$ were 3.38 and 2.79 respectively which exceed WHO estimates from 1.4 to 2.5. They further reported that, studies using stochastic and statistical methods for deriving $R0$ reported estimates that are reasonably comparable. However, the studies u s in g mathematical methods produce estimates that were, on average, higher. Some of the mathematically derived estimates fall within the range produced the statistical and stochastic estimates. They concluded that it was important to further assess the reason for the higher $R0$ values estimated by some the mathematical studies.

CONCLUSION
Basic reproduction number of COVID-19 is important parameter during a pandemic which is used to estimate the risk of COVID-19 outbreak and evaluate the effectiveness of implemented measures. Many studies have shown that $R0$ of COVID-19 depends on many factors. In light of this, it is important to thoroughly understand transmission dynamics and implement effective prevention and control programs as well as early diagnosis and timely treatment. It is also crucial and important to establish a joint strategies involving prevention, control, a n d med i cal treatment . The s t rategies should be systematic, scientific, normative, and works perfectly in understanding of COVID-19. To control the spread of this disease it will be highly useful to take care of especially personal hygiene individually, apply social isolation, strengthen the immune system by natural and healthy nutrition, socially support social isolation, scan those with symptoms of COVID-19 infection by laboratory tests and take care especially for those who are at older ages. Finally, current estimates of $R0$ fo r COVID-19 might be biased due to constant change of parameters during the pandemic and accurate a s s u m p t i o n s introduced. Consequently, more reliable $R0$ as more data and information come to light about the COVID-19 will be realised.

FUTURE PROSPECT
More studies are still needed on the spread and mitigation strategies of COVID-19, in order to bring more insight on the policy formulation and control measures. Modeling effort should be expanded t o include temporal an d spatial scale. Finally, validating key modeling assumptions, connecting models with realistic data, tailoring models to practical needs, and leveraging the support from other analytical and computational techniques is required.

CONFLICT OF INTEREST
No conflict of interest

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