



Video Article

A Reduced Serial Interval Can have a Higher Impact on the Spread of Covid-19 Relative to R_0 : An Educational Video Demonstrating the Spread of Flu, Covid-19 and Covid-19 with Early Transmission

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Abstract

In response to the Covid-19 pandemic, there has been widespread focus on the term R_0 to explain the growing numbers of cases and necessity of preventive measures. However, in light of recent evidence supporting early transmission, the resulting shortened serial interval also has a potentially substantial influence on the rapid spread of this disease. We modified an existing educational public video to demonstrate the impact of early transmission on the rapid spread of Covid-19, when R_0 changes and the serial interval is held constant (using established R values for Flu and Covid-19 as an example) and when the R_0 value is constant and the serial interval is changed (using the serial interval for Covid-19 with and without early transmission as an example). This video demonstrates that, in addition to R_0 , the impact of a shortened serial interval on the spread of this disease is substantial. The conditions related to a shortened serial interval may also set the stage for higher transmission; for example, if symptoms are mild or absent during the early transmission stage of this disease, individuals unaware of their infected state may not adhere to risk-mitigating behaviors and be more likely to spread their infection. We hope that drawing attention to the potential role that a shortened serial interval may play on the observed rapid spread of Covid-19 may encourage greater public compliance with much needed preventive measures as well as promote an understanding of public health efforts that sometimes fall behind the rapid spread of Covid-19 outbreaks.

Keywords: COVID-19; SARS-CoV-2; R_0 ; Serial interval; Transmission; Model; Video

Introduction

Until there is a vaccine, mitigating COVID-19 risk will heavily rely on public compliance with preventive measures, such as recommendations for better hygiene, social distancing, and other behavioral changes. These oft repeated messages seem simple enough to understand, and yet changing attitudes and practices can be difficult, especially when they affect livelihoods and lifestyles; furthermore, if the public does comply and outbreaks still cannot be contained, the credibility of those in authority suffers. The rate at which COVID-19 spreads challenges our ability to form a response that effectively mitigates this virus's transmission capabilities. In the current COVID-19 climate, clear and convincing public health messaging may be as important as the original science behind it; in particular, there is one public warning, and supporting scientific concept, about R values that merits modification based on new findings.

With respect to COVID-19, there has been a widespread referral by the media and the public to R naught (R_0) values (i.e., the mean of the total number of infections caused by an infected individual in a completely susceptible population [1-3], before public health control measures have been implemented) to interpret the rapid rate of spread of this disease. For the remainder of this paper, we will instead use R

to represent all values of the total number of newly infected/infectious cases that each case generates over the course of its transmission period that are associated with different, changing capacities for spread (including R_0) as the virus progresses within a population. We argue that focusing only on R values provides an incomplete picture about COVID-19 transmission, which can vary both temporally and among individuals within a given population [4,5].

In general, R values do not include a time component [1,6-8]. Rather, they were initially designed by demographers to focus on replacement number (i.e., the number of daughters each woman birthed and raised to childbearing age over her lifetime) [3]. There was not a great need to look at variations in replication times, since the childbearing period of a woman did not change drastically among communities; further, this period of replication would not be expected to change significantly over time. In contrast, when applied to infectious disease outbreaks, two diseases (e.g., SARS and HIV) may have very different rates and magnitudes of growth, despite having the same R value [9]. We use simplified parameters (see appendix) to illustrate this concept with the following example: suppose symptom onset occurs on day 3 for two viral illnesses. In a 6-day interval, from day 0 (i.e., 3 days before symptom onset) until day 6

(i.e., 3 days after symptom onset), the majority of transmission would occur in the first half of the 6-day interval for Virus A and in the second half of the 6-day interval for Virus B. Although Virus A and Virus B would both have the same R values, Virus A would complete its majority of replication in half the amount of time relative to Virus B. Readers may select any variation of serial intervals (e.g., day 4.5 versus day 7), irrespective of symptom onset, depending on emerging knowledge of COVID-19. We selected simple, hypothetical numbers to convey the concept of early transmission, as the serial interval value of Covid-19 has yet to be fully investigated.

Data have shown that COVID-19 spreads much earlier in the course of an individual's infection than first thought; specifically, there is transmission occurring during the pre-symptomatic stage in the days preceding the onset of symptoms [10-13]. We assume that, for those who remain asymptomatic, transmission may similarly spread earlier in the course of their infection. Furthermore, evidence suggests that a subset of individuals is capable of shedding virus months after contracting COVID-19 [14], although virus shed at this late stage fortunately appears to have very low potential for transmission and thus would not significantly contribute to the R value. We argue that the relatively high transmission occurring in the early, pre-symptomatic stage of this virus may play a relatively large role in the apparent rapid spread of COVID-19 and should be incorporated into existing public materials.

The role that R values play in an outbreak has been previously explained with a public video comparing the outbreak numbers of Flu versus COVID-19 resulting from different R values [15]. This graphic video introduces to the public the concept of R and provides a visual example about how a COVID-19 outbreak can rapidly spread compared with Flu. We argue that this video, and other similar resources, must now be refined in the context of our growing knowledge about the early transmission dynamics of COVID-19. The public health ramifications of these efforts would potentially 1) encourage and elicit greater public compliance with existing preventive measures, and 2) seek greater public forgiveness of health authorities when efforts appear to be thwarted by the virus.

Materials and Methods

Our objective was to refine an existing public video to account for transmission of COVID-19 at an earlier stage (i.e., on day 2 versus day 4 of infection). The original video compared the growth of Flu and Covid-19 virus using different R values and the same replication cycle length (serial interval) [15]. Our new model does not assume the replication cycle lengths to be the same; rather, it compares outbreak growth patterns with replication occurring in half the time (in our model by day 2 versus day 4). While the time for a cycle of replication is shortened by only 2 days, this reduction represents a relatively large proportion (i.e., 50%) of the original proposed cycle length, replicating the same levels in half the time. After a series of growth cycles, the compounding effect of more rapid growth results in an

outbreak where, for every replication of Flu, there are now two of Covid-19. In this new video, we compare three models: the original Flu virus, Covid-19 with the original longer cycle length, and Covid-19 with a shorter cycle length to account for earlier transmission. We illustrate the relative differences in the number of new cases over time, at intervals of 4 days.

In order to investigate the impact of earlier shedding on the spread of COVID-19, we kept the R values the same as those previously used in the original video ($R=1.3$ for Flu and $R=2$ for COVID-19 for both slow and fast replication cycles [15]). As before, when $R<1$, the outbreak declines; when $R=1$, each case merely replaces itself and the outbreak does not grow; when $R>1$, the outbreak grows. When this video was released, late shedding had not yet been documented for COVID-19. Had the virus produced by late shedding turned out to be infectious, this contribution would have been added to the R value.

Our model was built by embedding two videos into a slide and setting them to play back simultaneously. For creating the individual videos, we used a media player (VLC Media Player) that recorded/exported a modified version of a video. We then chose a variable rate for the modified playback output, using the original video as input. Once outputs with the desired modified rates were created, they were embedded into a PowerPoint slide and set to run simultaneously. This allows users to speed up the right column to any multiple (e.g., we used 2), including fractions, of the original replication cycle. The left column represents the Flu ($R=1.7$, replication cycle=4 days), the center column the original COVID-19 model ($R=2$, replication cycle = 4 days), and the right column the updated COVID-19 model ($R=2$, replication cycle=2 days). The left and center columns were shown in the original video [7]. Comparing the case numbers at 4 day intervals, one can see the relative effects of simply having a higher R value (i.e., comparing the left and center columns) versus the compounding effect of a shorter replication cycle (i.e., comparing the center and right columns).

Discussion

Our findings indicate that early transmission may substantially contribute to the rapid spread of COVID-19 by shortening the serial interval of this disease. Independent of the widely discussed R value, the effects of a shortened serial interval are compounding; this can result in different growth rates, even among viruses that have the same R value. In our example, we made day 3 the onset of illness and, if preventive respiratory guidelines were implemented (e.g., covering coughs and self-isolation), there would have been a reduction in R. However, the point of this example was to demonstrate the way in which timing of transmission, independent of R, could impact the growth rate of a virus; we thus kept R values constant to show the effect of earlier transmission.

In particular, early pre-symptomatic transmission is likely to have a critical impact because it not only shortens the replication period of this disease, resulting in

compounding effects shown by this paper, but also precludes opportunities for risk-mitigating behaviors (e.g., personal hygiene, testing, self-isolation, and quarantine measures) that may have otherwise occurred in response to apparent symptoms. Variation in contact rates, competence, and

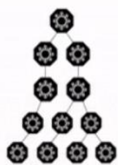
infectivity among individuals, left unchecked, sets the stage for cryptic superspreader events (i.e., when an infected individual causes more infections than expected under homogenous transmission [4]) maintained by highly infectious pre-symptomatic carriers [5].

Replication Rates of Influenza and COVID-19

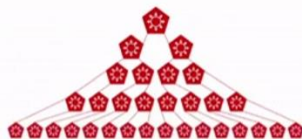
Influenza Replication Rate vs. COVID-19 Replication Rate

Video 1

Influenza



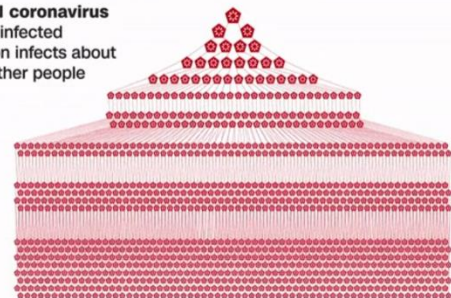
Coronavirus



Original Influenza vs. COVID-19 R_0 Comparison

Video 2

Novel coronavirus
Each infected
person infects about
2-3 other people



COVID-19 Replication with Modified Transmission Rate while Maintaining Original R_0

Video 1: A higher R value results in higher case numbers, when the replication cycle is held constant. Models in the left and right columns were constructed using R values for Flu ($R = 1.7$, replication cycle = 4 days) and the original COVID-19 model ($R = 2$, replication cycle = 4 days), respectively.

Video 2: A shorter replication cycle results in, and has a compounding effect on, higher case numbers. The modified COVID-19 model was constructed using a shorter replication cycle ($R = 2$, replication cycle = 2 days) to account for early COVID-19 transmission.

When an outbreak quickly spreads through a community, it is vital that all steps to control it (e.g., testing, contact tracing, self-isolation, and quarantine) are implemented to reduce its rate of spread. We showed that when an infected individual transmits the virus earlier in the course of illness, this shortened replication cycle may be just as important as the R value with respect to the spread of the virus. We hope that this visual aid helps convey the importance of public compliance with public health strategies (even in the absence of apparent symptoms), as well as stress the fact that if public health authorities cannot organize a response quickly enough to control this rapidly spreading virus, future COVID-19 outbreaks will largely depend upon the public's compliance with other primary preventive measures (e.g., vaccine, social distancing, and hygiene).

Conclusions

In summary, changing the serial interval of a disease can impact its growth rate with each replication cycle,

resulting in compounding effects on its rate of spread that can be even greater than the widely-publicized R_0 term. As we learn more about Covid-19, it has become apparent that early transmission reduces the serial interval of this disease by approximately two days; this relatively large difference in the known transmission period suggests that the rate of growth may be much more rapid than previously thought. Existing models and educational materials communicating concepts about Covid-19 transmission should be recharacterized accordingly. Further, runaway outbreaks should be considered with a greater public understanding, in light of the potential positive impact of a shortened serial interval on Covid-19 transmission. Similarly, preventive recommendations made by public health officials should be taken with greater seriousness, independent of existing outbreak dynamics.

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Appendix

Video instructions: Open the PowerPoint file (accept any conditions that might appear as the yellow header bar). Go to slide show mode, advance to the second slide and the outbreak growth will begin automatically. Click on the hexagon to pause to compare new cases (at 4 day intervals) and the arrow to continue.

The math of replication

R(0) and R are defined as the mean number of infections caused by an infected individual, when the population of interest is susceptible, and once the virus has further progressed over time, respectively. These values add to the cumulative number of cases generated over the entire lifetime of the original case. For example: one case might make two new ones per day. After the first day there is no more reproduction for the original case, but it continues to live. In turn each of the new generation produce two new cases their first day, then behave as the original case, and so on. If each case has only its first day to make new cases (old cases persist but stop generating after the first day) the scheme is as follows:

Time	Number of New Cases	Number of Total cases
Day 0	0	1
Day 1	2	3
Day 2	4	7
Day 3	8	15

Notice the old cases (more than a day old) are no longer generating new cases. By strict definition of R(0) and R, then R = 2 and the number of new cases (per old case) at each time t (in days) is:

$$\# \text{ new cases} = 2^t$$

A convenient way to ignore the old cases is to imagine they die immediately after they reproduce their final new case. In the case of germs which divide (binary), they no longer exist but “turn into” new cases. Finally, the correct way to deal with old cases for disease outbreaks is to ignore those that can no longer spread infection to others. Note this is different from the idea of the banking analogy of accruing interest, since both the original principle and the new interest generates more interest when there is reinvestment and compounding.

One refinement is that the initial number of cases might not be 1. It might be N₀. For each of these N₀ cases there would be a replicating “pyramid” with the total number of new cases being:

$$\# \text{ new cases} = N_0 2^t$$

Now that we have a simple expression the next refinement is easier to convey. In our example we have a case doubling every day and the time we put into the equation as the exponent is also measured in days. In this case it is just a “coincidence” that the units of time (t) which we put into the exponent happens to be in single days which matches the period of replication, a day. It is important to maintain that if R is the number in the next generation created over the period of replication, we need to adjust the value of t in the exponent to reflect this. The following example shows what is intrinsically obvious, but we need it to manipulate the math. Starting with a single germ that doubles every three days. The expression for the new number of germs over time, t (in days), will be:

$$\# \text{ new cases} = 2^{t/3}$$

The exponent has been modified to reflect doubling every 3 days instead of every day.

As a further refinement of the above consider the following example to clarify the algebra of the use of exponents. Suppose there is an R = 2 which remains fixed. The original estimate is that there is replication every 6 days. Then starting from one case for any time t

$$\# \text{ new cases} = 2^{t/6}$$

We then discover that R remains the same, but the replication time is halved, over the first 3 days. The new expression should have a modified exponent of t/3, and it is useful to think of it as equal to (2)(t/6), which is just doubling the number of replication cycles (once for the parent and once for the first generation) during the original 6 day period. With this in mind, can we not simply express our new discovery using as much of the old expression as possible. In other words is there a way to say:

$$R^{t/3} = R^Y \times R^{t/6}$$

from algebra and $R^a \times R^b = R^{a+b}$, the exponents are added together. In this case the original exponent needs to be multiplied by a factor, so it is doubtful that this simple fix to the general form is possible. Again, to retain as much of the old expression ($R^{t/6}$) as possible it would be numerically correct to write the new expression as $(R^a \times R)^b$, but this begins to disrupt the original intent of R [7,16]. The number generated by each generation will still be R. But it occurs so much faster that the new value ($R^a \times R$), this “apparent” R value, really represents numbers over multiple generations. And this value is “forced” to be entered over the original time period. Readers who understand this last paragraph see the limitation of R values, they do impact the speed of an outbreak spread but they are not the only factor [3]. After all, an R value of 2 applies equally to both two children produced over a few decades or two replicants per hour for bacteria.

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