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Commentary

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R, the Reproduction Number, in COVID-19 Epidemic Decision-Making

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Abstract

Background: The COVID-19 pandemic flooded the public discourse and media with a multitude of epidemiological terms. Among them, the Reproduction number (R) was in overabundance. Our aim was to assess the impact of daily R data on the epidemiological analysis of the outbreak in Israel and subsequent decisions.

Methods: The period between September 2020 and January 2022 was included in the study. That corresponded with mass usage of PCR tests, prior to Omicron upsurge and the increasing introduction of antigen tests, with lower sensitivity and specificity. The analysis of COVID-19 incidence involved employing graphical representations of daily R values. These computations, derived from the data encompassing the summation of the preceding 10 days, were compared with the daily case number curve during the study period.

Results: Between September 2020 and January 2022 there were three major waves of COVID-19 morbidity. Study of the incidence and R values presents discrepancies, that are inherent in the process of data collection on the one hand and the computation of R on the other.

Conclusions: Applying R in policymaking is challenging, due to gaps regarding timeliness and actual incident case numbers. Albeit an important biological and epidemiological parameter, R is less suited to support on-going decision-making process, and may have been over-used throughout the COVID-19 pandemic. Alternatively, an in-depth analysis of incidence and trends may provide better approach to public health decision-making.

Keywords: COVID-19; Reproduction number; Disease incidence

Modeling the COVID-19 Outbreaks

The COVID-19 pandemic has been raging for two years with over 700 million cases reported globally and nearly seven million fatalities [1]. Numerous changes occurred in all aspects of life during the pandemic, including incursion of prediction models and epidemiological terms into mass media and public discourse. A colossal amount of energy and funds were invested worldwide, as well as in Israel, into modeling attempts that aim to predict the dynamics of the epidemic and, consequently, provide the decision makers with a helpful tool in order to minimize the effects of forecasted morbidity and mortality. The approach, thus, is accentuating the importance of models in policy, both in the ministry and in discussions by the government. However, as an old English proverb states, "the proof of the pudding is in the eating", and it is not fully clear how the models really perform in correlation to the subsequent incidence data. Waves of the epidemic followed one another and it seems that the main factor that influences this progression is the emergence of new, and more infective, variants of the virus. Certainly, the best health policy requires intelligent forecasts or predictions in order to ameliorate as much as possible the precarious effects of the epidemic. Yet, other important factors are at play when dealing with predictions, especially in a field as sensitive as the health of the nation. These are the costs and consequences of error, or even an inexactitude, as they pertain to the public trust and, subsequently, compliance. Public health choices, based on prediction models, are prone to multiple ambiguities, ranging from the overall model quality to mathematical sensitivity to small changes in its inputs. The impact of people without symptoms on virus transmission, infectiousness and lethality of the virus variant, the probable number of contacts people make in various settings and the estimated success of measures such as masks, social distancing or telling people to work from home, vaccines' effectiveness in preventing infections – these and many other factors just might render the pudding totally inedible. In this article we suggest attending the modeling forecasts with a grain of salt and propose an example by analyzing the extensive use that was applied to the term Reproduction Number (R) during the COVID-19 epidemic in Israel.

The COVID-19 Pandemic and R

Reproduction number (R) became an important and common parameter in analysis and follow-up of the pandemic [2,3]. Previously, R has been used in epidemiology and biostatistics to describe and analyze trends of diseases' transmission. Within the frame of the pandemic, R turned into an iconic term for all. To quote a Nature science journalist David Adam: "In this pandemic, R has leapt from the pages of academic journals into regular discussions by politicians and newspapers, framed as a number that will shape everyone's lives" [4]. R_0, the basic reproduction number, is defined as the predicted average number of cases, infected by a single case in a population, where all are susceptible. Many asymptomatic infections, recoveries, under diagnosing and underreporting, render the universal susceptibility assumption as in accurate. Non-pharmaceutical Protective Measures (NPM), including face-masks, social distancing, lockdowns and quarantines, also decrease likelihood of infection spread. Thus, R_e, the effective reproduction number, relates to current state in a specific population [5,6].

In Israel, R usage by politicians and the media has been extensive, as an important, even major, criterion for public health policy [7]. Policy, that leads to wide implementation of NPM including total and local lockdowns, transportation restrictions and school closures. Concomitantly, the Ministry of Health (MoH) national campaigns utilized R as a major operational estimate. Regarding this use (or abuse) of R, we describe its application during the COVID-19 pandemic in Israel, and assess its appropriateness for the decision-making process.

Data Analysis

Morbidity and mortality data on COVID-19 are published daily by MoH. By the end of December 2021, with over 40 million PCR tests performed, Israel (population 9.3 million) saw approximately 1,390,000 confirmed cases with 8,250 fatalities [8]. We generated a daily database of COVID-19 incidence and mortality in Israel. 7-days' moving averages accounted for fluctuations due to weekends and holidays. R estimates, based upon the national incidence data, were published daily since September 2020 and reflected in the media [9]. The modeling approach has been described by Cori, *et al* and Miller, *et al*. [5,6,10]. Briefly, current incidence data were analyzed, applying additional variables of average infective period, estimated time needed for case identification, percentage of people infected by an index patient per each subsequent day of the infective period. These calculations yielded daily R estimates, as of 10 days previously [10], and were plotted alongside current incident cases, allowing comparative assessment of trends. During the COVID-19 epidemic in Israel, four country-wide waves of infection occurred before 2022. At the height of the third epidemic wave, in late December 2020, a national mass two-dose vaccination campaign was launched; the 3rd (booster) dose was initiated at the beginning of the 4th wave in July 2021. In early 2022, as the new Omicron variant charged around the globe, health systems were overburdened and laboratory-monitoring approaches changed. In Israel the number of PCR tests surpassed 200,000/day with case confirmation based on PCR tests. But beginning in January 2022, mass utilization of antigen tests, with their lower sensitivity and specificity parameters, rendered estimation of R increasingly challenging and probably inaccurate. Consequently, we restricted the analysis to 31/12/2021.

Results

From March 2020, when the epidemic began, there were four major morbidity and mortality waves in Israel. Of these, three were between September 2020 and January 2022 – the period of our data analysis (Figure 1). Afterwards, the Omicron upsurge started in mid-December 2021. The daily epidemic curve for this period, charted together with additional curve for R values, is presented in Figure 2. The dashed line represents the 7-day moving average for the number of cases, aimed at adjusting for the fluctuations associated with weekends and holidays vs. weekdays. The unadjusted incidence is visible in the chart in the background, as solid semitransparent line. R-values curve is presented as the solid red line.

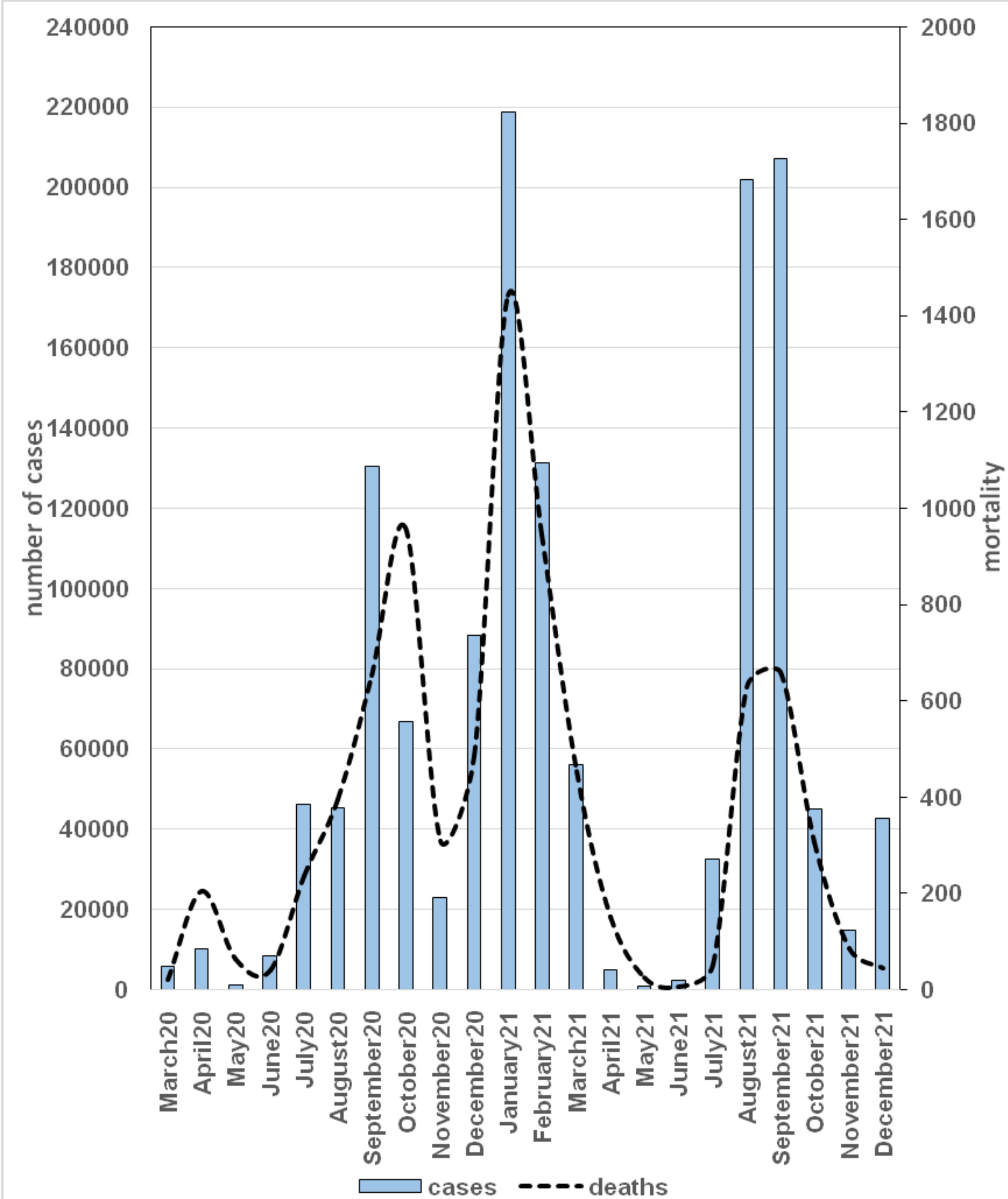

Figure 1: Monthly incidence of COVID-19 in Israel, March 2020-December 2021.

Legend for Figure 1: Epidemic waves are observed for incidence of infections (bars; left y-axis) and mortality (dotted line; right y-axis).

The association between incidence and R curves, albeit inherent in the model for R calculation, is not particularly obvious from visual interpretation of the graph. This may stem from the concept that the R curve is mathematically derived from the incidence data, yet with a 10 days' gap.

Commentary

Reproduction number is an important and useful tool for analysis of biological and epidemiological properties of pathogens' spread in different populations **[4,5,11,12]**. Since the model for R estimation derives values from current incidence data, it lags back and cannot account a timely estimate. Additionally, the estimated R, by definition, does not reflect the actual number of cases, either high or small. Despite being vital for analyzing the outbreaks' dynamics, R is perhaps less suitable as a decision-making measure for constructing real time prevention policy **[4,12]**. A circular argument arises henceforth, wherein incidence data are modeled to estimate R values. Then, same R values are perceived as a basis to interpret and predict future incidence trends. Thus, on December 10 2020, the Israeli Cabinet decided that if the R reaches 1.32 or there are 2,500 new daily cases, a 3-weeks tightened activity-restriction would take place. If after these 3 weeks, the R does not decline to 1, a general lockdown will be imposed **[7]**. As stated previously by Delamater *et al*: "R must be estimated, reported, and applied with great caution because this basic metric is far from simple **[12]**". Basing operational decisions on R seems unfitting the meaning of this parameter and misleading both for decision-makers and the general public. It becomes essential to explain the methodology behind the definition of R and the sequential gap between its construct and the implications that can be derived from it.

Incidence is highly influenced by the testing policy, as well as the population's compliance towards it. In Israel, the ratio of tests-to-population is high, with over 40 million tests performed thus far. As R computation is based upon incident data, it is possible that the estimate is detrimentally affected, with detection bias leading to either under or over-estimation. The hazard of such a bias is clearly present during several outbreak stages, when the numbers of cases dropped low and the R curve became obviously erratic **(Figure 2)**.

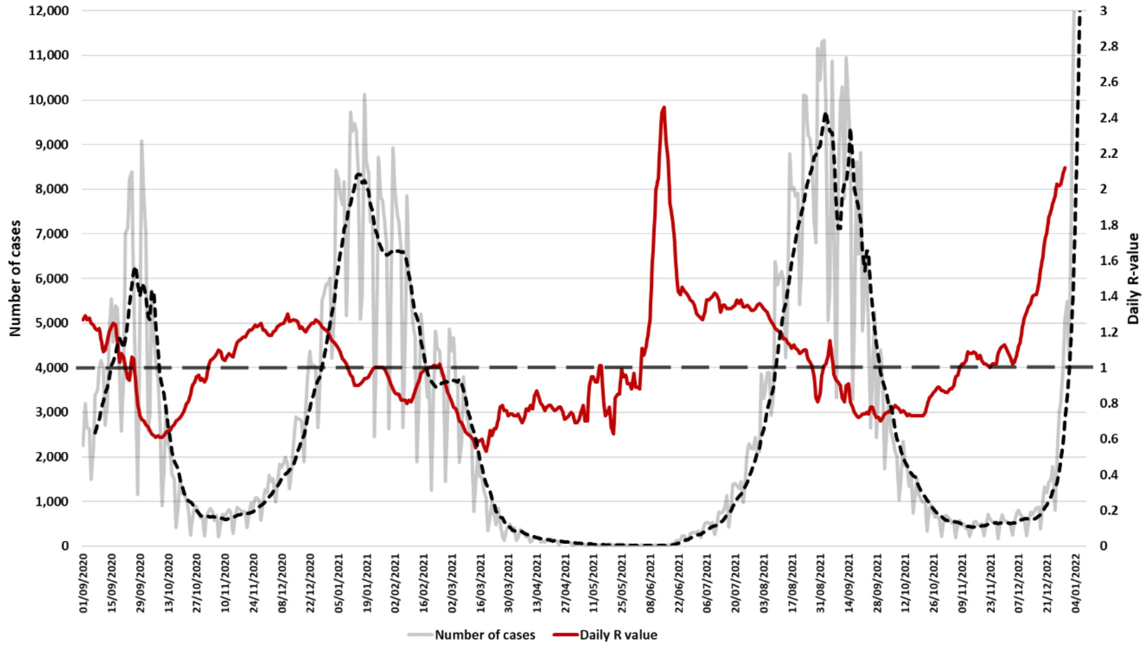

Figure 2: Daily COVID-19 epidemic curve, 7-day moving average and reproduction numbers; Israel, September 2020-December 2021.

Legend for Figure 2: Daily infection incidence (pale blue line; left y-axis) and 7-day moving average of the numbers of cases (dotted blue line; left y-axis) aimed at smoothing the effects of weekends and holidays fluctuations on numbers of tests. The red line represents daily calculated R values (right y-axis). The horizontal dotted line at the value of 1 (right y-axis) denotes the principle of R, with numbers of cases lying over it representing epidemic spread and incidence below the line indicating decrease in the events of COVID-19 infection.

The estimated R is also highly sensitive to rapid fluctuations in disease incidence, such as a local events and outbreaks. For example, in June 2021 COVID-19 cases were detected in a group of Jewish immigrants arriving to Jerusalem from India. Consequently, the estimated national R surged from 0.5 to over 2.4 and then rapidly declined.

Another limitation of R use in decision-making is inaccurate estimation of disease burden. COVID-19 incidence is presented in national data as number of cases, albeit without reference to symptomatology or disease severity. A wide range, 40-80% of infections, are either asymptomatic or very mild [13]. Real-time estimates of disease severity are essential for effective health policy planning, while R is less appropriate for this purpose. We propose an alternative approach, wherein the most valuable hands-on variable for the health services planning and organization is the number of new cases, stratified by severity, with higher emphasis given to the number of severe and critical patients in need of hospitalization and advanced care. These numbers are fully reported, provide a clear and precise view of the situation, and their trends avail the policy makers of understandable and useful operational tools. Morbidity and case-severity data provide clear and precise information. R, being a first-degree derivative of the incidence slope's increase or decrease, is less instructive.

Conclusion

We believe that R, although an important biological and epidemiological parameter, has been over-used throughout the COVID-19 pandemic in Israel and elsewhere. It is neither a timely not an intuitive measure, less suited to support on-going decision-making process. The preferred approach for real-time policymaking, especially during the surge of epidemic, is the "simple" old-fashioned examination of trends with a (digital) magnifying glass over the incidence plot.

References

1. WHO, COVID-19 Weekly Epidemiological Update. Edition 73. 2022.
2. Miller E. Global burden of disease: Part C. Potential and Existing Impact of Vaccines on Disease Epidemiology. The Vaccine Book, Academic Press. 2003;37-50:ISBN 9780121072582.
3. Gallo LG, Oliveira AFM, Abrahão AA, Sandoval LAM, Martins YRA, Almirón M, et al. Ten Epidemiological Parameters of COVID-19: Use of Rapid Literature Review to Inform Predictive Models During the Pandemic. Front Public Health. 2020;8:598547.
4. Adam D. A guide to R - the pandemic's misunderstood metric. Nature. 2020;583(7816):346-348.
5. Cori A, Ferguson NM, Fraser C, Cauchemez S. A new framework and software to estimate time-varying reproduction numbers during epidemics. Am J Epidemiol. 2013;178(9):1505-12.
6. Miller D, Martin MA, Harel N, Tirosh O, Kustin T, Meir M, et al. Full genome viral sequences inform patterns of SARS-CoV-2 spread into and within Israel. Nat Commun. 2020;11(1):5518.
7. Israel Prime Minister's Office Press Releases. PM Netanyahu Convenes Cabinet to Make Decisions on Lowering the Basic Reproduction Number and the Number of New Daily Cases. 2020.
8. MOH website, Israel
9. MOH website, Israel.
10. MOH website, Israel.
11. Linka K, Peirlinck M, Kuhl E. The reproduction number of COVID-19 and its correlation with public health interventions. Comput Mech. 2020;66(4):1035-50.
12. Delamater PL, Street EJ, Leslie TF, Yang YT, Jacobsen KH. Complexity of the Basic Reproduction Number (R0). Emerg Infect Dis. 2019;25(1):1-4.
13. Sturmberg JP, Tsasis P, Hoemeke L. COVID-19 - An Opportunity to Redesign Health Policy Thinking. Int J Health Policy Manag. 2022;11(4):409-413.

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