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## Letter to the Editor

## Timeliness and obsolescence of herd immunity threshold estimates in the COVID-19 pandemic



The term 'herd immunity' has been widely used and abused during the COVID-19 pandemic. Most singularly, the 'herd immunity threshold', a technical concept essential to the understanding of an epidemic, was hijacked early in the pandemic and disseminated with all sorts of distortions, misrepresentations and misunderstandings that prevented the impact of its application by those qualified.

A population invaded by an infectious agent (say a virus) is said to achieve the herd immunity threshold<sup>1</sup> (HIT) when the sum of the immunities acquired by all its individuals is such that the virus cannot cause another epidemic wave. A way to visualise this abstract phenomenon is by imagining a pandemic occurring without mitigation while a record of people infected each day is being kept. Typically, the HIT is the percentage of the population that has been infected (and acquired immunity or died) by the time the epidemic passes its peak.

This representation gave rise to numerous difficulties, which the author tries to summarise:

1. Model-based inference. In a pandemic, people modify their behaviours, making the direct measurement of the HIT impossible. Even if no behavioural changes had occurred, the HIT could only be measured after the epidemic peaked, which would have been too late for it to be useful. Mathematical epidemiologists develop models that enable indirect inference of the HIT from incomplete time series of cases, hospitalisations and deaths. These inferences come with uncertainties difficult to quantify.
2. Differences between individuals. The representation of the HIT as a percentage of the population could only be unambiguous if all immunised individuals contributed the same amount to population immunity. But some individuals are more susceptible than others, and consequently, their immunisation has more weight. Since the epidemic tends to affect more susceptible individuals first, the HIT is attained once a lower percentage of the population has been infected. At the beginning of a pandemic, we do not know how variable susceptibility is. Worse, how to measure individual susceptibility directly is not known much less to build the distribution of susceptibilities among all individuals that constitute the population. To circumvent this obstacle, the authors adapted ideas from demography<sup>2,3</sup> and developed a method to infer these distributions indirectly for use in HIT research.<sup>4,5</sup>
3. Viral evolution. Viruses undergo mutations, and natural selection tends to favour those variants that are more transmissible or less neutralisable by acquired immunity. In general, such variants expand in abundance and become dominant, causing the HIT to increase over time.
4. Seasonality. Respiratory viruses are more transmissible in cold and dry environments, which corresponds to the winter season in temperate climates. Consequently, time series that inform HIT inferences should ideally include at least one winter. Then, what is to be done if the pandemic begins in the spring? Wait until the following winter to estimate the HIT? Of course not! The estimation is begun as soon as possible and updated as the pandemic unfolds. But it cannot stay fixed on the very first estimates especially given the expectation for HIT to increase in the later seasons.
5. Population turnover. It is common for pandemic respiratory viruses to become endemic. The virus continues to circulate, causing seasonal epidemics. So, what happens with herd immunity? Is the HIT unreachable? No, HIT is reached any time there is a seasonal epidemic. But if HIT is reached, why are there any subsequent epidemics at all? Because the population is in constant renewal with elderly ending life trajectories and susceptible babies beginning theirs (waning immunity has a similar effect on susceptibility renewal). This way, the population immunity declines and eventually drops below the HIT again, i.e., conditions to sustain epidemics are restored. Fortunately, the severity tends to be much lower in comparison with initial pandemic waves. In an endemic state, people are naturally exposed early in life, when the infection is mild, and continue to be repeatedly exposed throughout life, maintaining protective immunological memory. This process tends to lose efficacy in older ages, at which point regular vaccination gains importance, such as in the case of influenza.

In conclusion, the use of the HIT concept during the pandemic by policymakers and media has not been consistent with the above population phenomena. Understanding the HIT is useful early in the pandemic, and subsequent use requires a constant update. But the utility of the HIT becomes lower as the pandemic progresses. The utility of the HIT for COVID-19 in the most affected and/or vaccinated regions probably expired during the first semester of 2021.

In European countries, for instance, there seems to be little sense in continuing to aim for herd immunity to the new coronavirus. The situation we are at may be identical to where we will be in 1 year, 2, 3, 4 and so on, and it seems wrong to continue prioritising a disease no longer more important than many others, including those caused by other respiratory viruses that have been suppressed by anti-coronavirus measures and/or competition with SARS-CoV-2 but will most likely return the following winter.

The HIT is fundamental in the cost-benefit analysis of possible measures to mitigate or suppress a pandemic, but its estimation must be early and accurate. Biases that exaggerate the HIT result in exaggerated strategies, while biases that diminish the HIT lead

to insufficient measures. In this pandemic, a complexity of factors has created a powerful tendency for HIT overestimation. The factors and how they interacted to produce such dominant pro-lockdown current seems to be an important topic for transdisciplinary research in years to come.

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