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A Short Path to Coronavirus Herd Immunity?

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This week a number of remarkable articles on herd immunity to Coronavirus COVID-19 (SARS-CoV-2) have been posted without peer review (Britton et al., 2020; Lourenco et al., 2020), and these and other studies have been reviewed by Hamblin (2020). This briefing summarises the main conclusions of these articles.

Until a vaccine is developed, the management of the global pandemic in various regions ranges from elimination (e.g. New Zealand) through effective suppression (e.g. Australia) to reliance on large enough levels of infection to produce herd immunity (e.g. the United States), although as noted at the end of this article it is not clear that immunity is permanent enough to allow herd immunity to develop.

Lourenco et al. (2020) assert that some of the population may already have a high level of immunity to COVID-19 without ever having caught it. They point to evidence suggesting that exposure to seasonal coronaviruses, such as the common cold, may have already provided some with a degree of immunity, and that others may be more naturally resistant to infection. Although it is widely believed that the herd immunity threshold (HIT) required to prevent a resurgence of COVID-19 is more than 50% for any epidemiological setting, their modelling explains how differing levels of pre-existing immunity between individuals could put HIT as low as 20%. These results may help explain the large degree of regional variation observed in infection prevalence and cumulative deaths, and suggest that sufficient herd immunity may already be in place to substantially mitigate a potential second wave.

The effects of the coronavirus are not linear; the virus affects individuals and populations in very different ways. The case-fatality rate varies drastically between adults under 40 and the elderly. This same characteristic variability of the virus - what makes it so dangerous in the early stages of outbreaks - also gives a clue as to why those outbreaks could burn out earlier than initially expected. In countries with uncontained spread of the virus, such as the U.S., exactly what the herd-immunity threshold turns out to be could make a dramatic difference in how many people fall ill and die. Without a better plan, this threshold seems to have become central to the fates of many people around the world.

Gabriela Gomes, professor at the University of Strathclyde in Glasgow, Scotland also believes that the HIT may be much lower than currently thought. She was drawn to the field by frailty variation - why the same diseases manifest so differently from one person to the next. She studies chaos, specifically, patterns in nonlinear dynamics, and uses mathematics to deconstruct the chains of events that can lead two people with the same disease to have wildly different outcomes. For the past few months, she has been collaborating with an international group of mathematicians to run models that incorporate the many variations in how this virus seems to be affecting people. Her goal has been to move as far away from

simple averages as possible, and to incorporate as many of the disparate effects of the virus as possible when making new forecasts.

In normal times, herd immunity is calculated based on a standardized intervention with predictable results: vaccination. Everyone is exposed to the same (or very similar) immune-generating viral components, and it is possible to calculate what percentage of people need that exposure in order to develop meaningful immunity across the population.

This is not the case when a virus is spreading in the real world in the absence of a vaccine. Instead, the complexities of real life create heterogeneity: people are exposed to different amounts of the virus, in different contexts, via different routes. A virus that is new to the species creates more variety in immune responses. Some of us are more susceptible to being infected, and some are more likely to transmit the virus once infected. Even small differences in individual susceptibility and transmission can, as with any chaotic phenomenon, lead to very different outcomes as the effects compound over time on the scale of a pandemic.

In a pandemic, the heterogeneity of the infectious process also makes forecasting difficult. Differences in outcome can grow exponentially, reinforcing one another until the situation becomes, through a series of individually predictable moves, radically different from other possible scenarios. Gomes contrasts two models: one in which everyone is equally susceptible to coronavirus infection (a homogeneous model), and the other in which some people are more susceptible than others (a heterogeneous model). Even if the two populations start out with the same average susceptibility to infection, you do not get the same epidemics. The outbreaks look similar at the beginning, but in the heterogeneous population, individuals are not infected at random. The highly susceptible people are more likely to get infected first, causing selective depletion of their fraction of the population. As a result, the average susceptibility becomes lower and lower over time.

Effects like this selective depletion can quickly decelerate a virus's spread. The compounding effects of heterogeneity seem to show that the onslaught of cases and deaths seen in initial spikes around the world are unlikely to happen a second time. Based on data from several countries in Europe, Gomes's results show a herd-immunity threshold of less than 20%, consistent with Lourenco et al. (2020) but much lower than that of other models. If that proves to be correct, it would be life-altering news. It would not mean that the virus is gone, but if roughly one out of every five people in a given population is immune to the virus, that seems to be enough to slow its spread to a level where each infectious person is infecting an average of less than one other person. Under this condition, the basic reproduction number R0 - the average number of new infections caused by an infected individual, becomes less than 1, causing the number of infections to steadily decline, resulting in herd immunity. It would mean, for instance, that at 25% antibody prevalence, New York City could continue its careful reopening without fear of another major surge in cases.

Gomes admits that, although this does not make intuitive sense, homogenous models do not generate curves that match the current data. Dynamic systems develop in complex and

unpredictable ways, and the best we can do is continually update models based on what is happening in the real world. It is unclear why the threshold in her models is consistently at or below 20%, but if heterogeneity is not the cause, it is unclear what is.

Tom Britton at Stockholm University has also been building epidemiological models based on data from around the globe (Britton et al., 2020). He believes that variation in susceptibility and exposure to the virus clearly seems to be reducing estimates for herd immunity, and thinks that a 20% threshold, while unlikely, is not impossible.

By definition, dynamic systems do not deal in static numbers. Any such herd immunity threshold is context-dependent and constantly shifting. It will change over time and space, depending on R0. During the early stage of an outbreak of a new virus (to which no one has immunity), that number will be higher. The number is skewed by super-spreading events, and within certain populations that lack heterogeneity, such as a nursing home or school, where the herd immunity threshold may be above 70%.

Heterogeneity of behaviour may be the key determinant of our futures, since R0 clearly changes with behaviour. COVID-19 is the first disease in modern times where the whole world has changed its behavior and disease spread has been reduced. Social distancing and other reactive measures have changed the R0 value, and they will continue to do so. The virus has certain immutable properties, but there is nothing immutable about how many infections it causes in the real world. The herd immunity threshold can change based on how a virus spreads. The spread keeps on changing based on how we react to it at every stage, and the effects compound. Small preventive measures have big downstream effects. The herd in question determines its immunity.

There is no mystery in how to drop the R0 to below 1 and reach an effective herd immunity: masks, social distancing, handwashing. It appears that places like New York City, having gone through an initial onslaught of cases and deaths, may be in a version of herd immunity, or at least safe equilibrium.* However, judging by the decisions some leaders have made so far, it seems that few places in the United States will choose to live this way. Many cities and states are pushing backwards into an old way of life, where the herd-immunity threshold is high. Dangerous decisions will be amplified by the dynamic systems of society. There will only be as much chaos as we allow.

All of these models assume that, after infection, people obtain immunity. However, COVID-19 is a new disease, so no one can be sure that infected people become immune reliably, or how long immunity lasts. (Britton et al., 2020) note that there are no clear instances of double infections so far, which suggests that this virus creates immunity for at least some meaningful length of time, as most viruses do. However, earlier this week, an unreviewed pre-print (Seow et al., 2020) suggested that immunity to COVID-19 can vanish within months, which, if true, indicates that the virus could become endemic. They found that 60% of people retained the potent level of antibodies required to resist future infections in the first two weeks of displaying symptoms. However, that proportion dropped to less than 17% after

three months. This prompted Prof Jonathan Heeney, a virologist at the University of Cambridge, to state that the findings had put "another nail in the coffin of the dangerous concept of herd immunity," demonstrating the remarkable state of uncertainty that currently exists among epidemiologists.

*Note that some chaotic systems can have stable equilibria (Wang et al., 2017).

References

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