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Have deaths from COVID-19 in Europe plateaued due to herd immunity?

Transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is currently in marked decline in many countries in Europe, North America, and parts of Asia, following unprecedented governmental interventions aiming to substantially reduce travel and physical contact between individuals. There are two possible and very different explanations for this decline.

First, the observed declines in cases and deaths could be due to lockdowns (taken to include public orders to stay at home, bans on public gatherings with less than ten people, and curfew of all age groups), social distancing, and other interventions. This would imply that the epidemic is still at a relatively early stage and that a large proportion of the population therefore remain susceptible. Under such a scenario, there is a high risk of renewed transmission if interventions or behavioural modifications are completely relaxed. This first explanation also is consistent with a high infection fatality ratio (IFR) in order to explain the number of deaths that have occurred to date.

Second, the observed declines in cases and deaths could be due to the achievement of herd immunity. This would imply that a large proportion of the population are now protected from infection, either through acquisition of immunity following previous infection or through other natural means (such as cross protection from other coronaviruses). Under such a scenario, further declines in cases and deaths are to be expected even in the absence of interventions or behavioural modifications. If one assumes that a large proportion of the population has been infected, this explanation implies a very low IFR to explain the number of deaths that have occurred to date.

Identifying the most probable explanation is key to any future plans to lift social distancing and travel restrictions. It is also critical when considering subsequent public health responses aimed at reducing morbidity and mortality, especially in the context of the wider economic and health impacts of COVID-19 mitigation and suppression strategies.

We took a simple, data-driven approach to establish which of these explanations is better supported by data. Our arguments are based on trends in cumulative deaths over time in a number of countries that went into lockdown at different stages in their epidemics, as reported by the European Centre for Disease Prevention and Control on May 18, 2020. For a subset of countries, we also explore data obtained from serology studies on the proportion of the population that has evidence of prior infection. All data sources for these analyses are listed in the appendix. We find that there is little evidence to support an explantaion that relies on herd immunity for the following reasons.

First, the cumulative per-capita mortality rate from COVID-19 has plateaued at different levels (appendix). The reporting of deaths in different countries with good testing capacity, although not without challenges, is generally considered one of the more reliable statistics on COVID-19 since testing has been prioritised for severe cases. Under herd immunity, the cumulative mortality rate due to COVID-19 per million of the population would be expected to plateau at roughly the same level in different countries (assuming similar basic reproduction numbers). This is not what the data show. For example, in Germany, the Netherlands, and Italy, all countries with good quality health care and testing capacity, the difference in mortality is several fold, with Germany at 95 deaths per million population, the Netherlands at 332 deaths per million population, and Italy at 525 deaths per million population (as of May 17, 2020). Although no data are perfect, it is highly unlikely that differences in mortality reporting across countries could explain this scale of variation. If acquisition of herd immunity was responsible for the drop in incidence in all countries, then disease exposure, susceptibility, or severity would need to be extremely different between populations. Given similar demographics, close geographic proximity, strong genetic similarities, robust health systems, and probable similar previous exposure to other human coronaviruses, there is little evidence to support this. In contrast, if the levelling off of deaths is caused by interventions and associated behavioural changes, then these discrepancies can be explained by the timing and stringency of interventions relative to introduction of the virus.

Second, countries that went into lockdown early experienced fewer deaths in subsequent weeks. Focusing on countries that applied strict suppression measures, we compared the per-capita deaths at the time of lockdown with the per-capita deaths in the following 6 week period (appendix). If herd immunity had already been reached, we would expect no correlation, or even a negative correlation, as lockdown would not alter the herd immunity threshold in the population or the ultimate death rate per capita. A strong linear trend suggests that countries that went into lockdown earlier experienced fewer deaths in the following 6 week period. This trend is therefore inconsistent with the herd immunity explanation; however, it is exactly what one would expect under the explanation that lockdowns are curtailing transmission and deaths, making them most effective when pre-lockdown transmission is low.

Third, and finally, a strong and consistent relationship exists between the prevalence of antibodies to SARS-CoV-2 and mortality from COVID-19 in European populations, consistent with an IFR of 0·5–1·0%. Using data from serology studies (appendix), we compared the proportion of the population that has evidence

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of previous infection, as measured by antibodies (seroprevalence) at a given timepoint, with the proportion of the population that died from COVID-19 up to the same timepoint (appendix). A strong linear relationship between seroprevalence and mortality indicates that disparate regions have experienced a similar mortality per infection.

This result is informative for several reasons. First, if herd immunity had been reached because of a large proportion of the population being infected, then one would expect to see a higher seroprevalence and a correspondingly lower slope (equivalent to a lower IFR). The current data in Europe are consistent with an IFR of 0·5–1·0%, which is many times higher than seasonal influenza (<0·1%). Second, if one conjectures that differences between the European countries in our analysis are caused by differences in severity or death reporting, then one would expect to see very different slopes between countries. The data do not support this explanation. Third, if herd immunity has been reached in all regions, then one would expect to see relatively little variation in seroprevalence. Taking Spain as an example, for the country to have achieved herd immunity, one would have to assume that the herd immunity threshold differs by a factor of ten between regions. In contrast, all of these patterns are easily explained if one assumes that interventions are acting to keep deaths and infections at pre-herd immunity levels. This would, for example, imply that Denmark and Spain have been experiencing a broadly similar IFR but that Denmark has fewer deaths and lower seroprevalence simply because the epidemic did not progress as far as it did in Spain before lockdown came into place. Evidence from outbreaks in confined settings shows the proportion of individuals infected can reach high levels (eg, more than 60%[2]), providing little reason to think the people in these countries who are currently seronegative are not susceptible to infection.

In summary, there are large differences in patterns of per-capita deaths in different countries that are difficult to reconcile with herd immunity arguments but are easily explained by the timing and stringency of interventions. Seroprevalence studies also provide an independent source of information that is highly consistent with mortality data. The herd immunity argument is therefore at odds with both mortality and seroprevalence data, whereas the intervention argument provides a parsimonious explanation for both.

Although the impacts of current control interventions on transmission need to be balanced against their short-term and long-term economic and health impacts on society, epidemiological data suggest that no country has yet seen infection rates sufficient to prevent a second wave of transmission, should controls or behavioural precautions be relaxed without compensatory measures in place.

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