JAMA Insights

Herd Immunity and Implications for SARS-CoV-2 Control

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Herd immunity, also known as *indirect protection*, *community immunity*, or *community protection*, refers to the protection of susceptible individuals against an infection when a sufficiently large proportion of immune individuals exist in a population. In other words, herd immunity is the inability of infected individuals to propagate an epidemic outbreak due to lack of contact with sufficient numbers of susceptible individuals. It stems from the individual immunity that may be gained through natural infection or through vaccination. The term *herd immunity* was initially introduced more than a century ago. In the latter half of the 20th century, the use of the term became more prevalent with the expansion of immunization programs and the need for describing targets for immunization coverage, discussions on disease eradication, and cost-effectiveness analyses of vaccination programs.[1]

Author Audio Interview

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Eradication of smallpox and sustained reductions in disease incidence in adults and those who are not vaccinated following routine childhood immunization with conjugated *Haemophilus influenzae* type B and pneumococcal vaccines are successful examples of the effects of vaccine-induced herd immunity.[1]

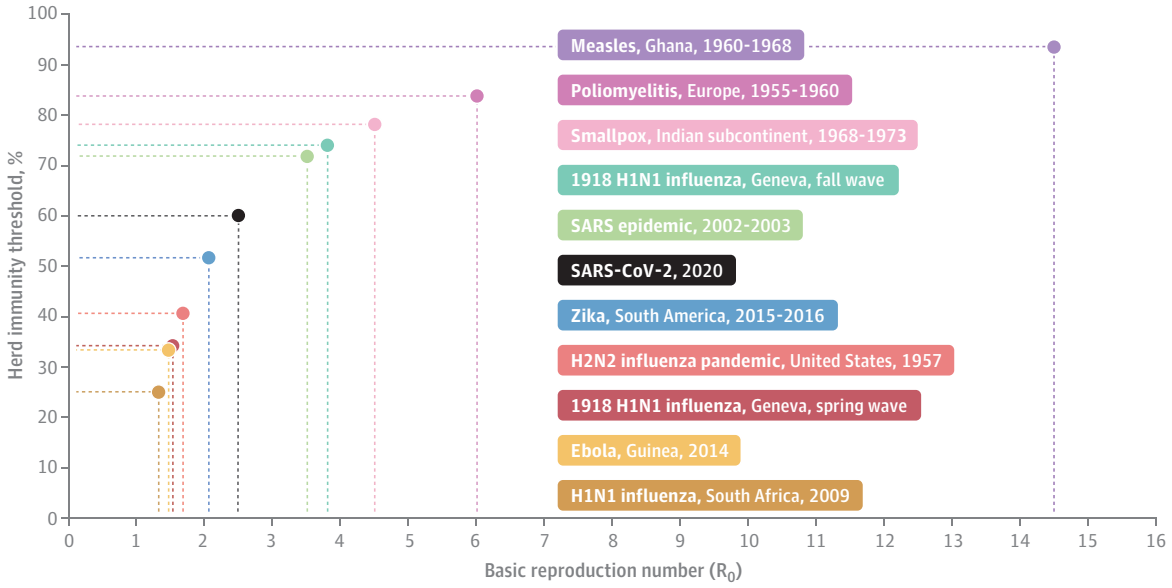
Herd Immunity Threshold

The *herd immunity threshold* is defined as the proportion of individuals in a population who, having acquired immunity, can no longer participate in the chain of transmission. If the proportion of immune individuals in a population is above this threshold, current outbreaks will extinguish and endemic transmission of the pathogen will be interrupted. In the simplest model, the herd immunity threshold depends on the basic reproduction number (R_0; the average number of persons infected by an infected person in a fully susceptible population) and is calculated as $1 - 1/R_0$ (**Figure**).[2,3] The effective reproduction number incorporates partially immune populations and accounts for dynamic changes in the proportion of susceptible individuals in a population, such as seen during an outbreak or following mass immunizations. A highly communicable pathogen, such as measles, will have a high R_0 (12-18) and a high proportion of the population must be immune to decrease sustained transmission. Since the beginning of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, most of the studies estimated the SARS-CoV-2 R_0 to be in the range of 2 to 3.[2] Assuming no population immunity and that all individuals are equally susceptible and equally infectious, the herd immunity threshold for SARS-CoV-2 would be expected to range between 50% and 67% in the absence of any interventions.

Duration of Protection

For both naturally acquired and vaccine-induced immunity, the durability of immune memory is a critical factor in determining population-level protection and sustaining herd immunity. In the case of measles, varicella, and rubella, long-term immunity has been achieved both with infection as well as vaccination. With seasonal coronaviruses, durable immunity has not been observed or has been short lived.[4] For infections that produce transient immunity, the pool of susceptible individuals soon increases in the absence of a vaccine and outbreaks reappear. With an effective vaccine and vaccine program, herd immunity

Figure. Herd Immunity Thresholds by Disease



The locations included are the locations in which the threshold was measured.

can be sustained (even if periodic vaccination is required to do so) and outbreaks can be curtailed as long as the community maintains the necessary levels.

Role of Heterogeneity

Nominal herd immunity thresholds assume random mixing between individuals in a population. However, daily life is more complicated; individuals mix nonrandomly and some individuals have higher numbers of interactions than others. Empirically validated network models have shown that individuals who have higher numbers of interactions get infected earlier in outbreaks.[5] This may contribute to slowing of community spread of an infection before reaching the nominal herd immunity threshold. However, there is uncertainty regarding the precise effect of heterogeneity in social mixing on herd immunity against SARS-CoV-2.

T-Cell Cross-reactivity

T-cells are important mediators of immunity. Recent reports have suggested that cross-reactivity with other coronaviruses may confer relative protection of the population from coronavirus disease 2019 (COVID-19).[6] It is less clear that T-cell cross-reactivity could provide sterilizing immunity (ie, that the host could not carry nor transmit infection) as opposed to reducing the severity of illness.

Infection-Based Herd Immunity as Policy

An infection-based herd immunity approach (ie, letting the low-risk groups become infected while "sequestering" the susceptible groups) has been proposed to slow the spread of SARS-CoV-2. However, such a strategy is fraught with risks. For example, even with modest infection fatality ratios, a new pathogen will result in substantial mortality because most, if not all, of the population would not have immunity to the pathogen. Sequestering the high-risk populations is impractical because infections that initially transmit in low-mortality populations can spread to high-mortality populations. Moreover, so far, there is no example of a large-scale successful intentional infection-based herd immunity strategy.

There are only rare instances of seemingly sustained herd immunity being achieved through infection. The most recent and well-documented example relates to Zika in Salvador, Brazil. Early in the COVID-19 pandemic, as other countries in Europe were locking down in late February and early March of 2020, Sweden made a decision against lockdown. Initially, some local authorities and journalists described this as the *herd immunity strategy*: Sweden would do its best to protect the most vulnerable, but otherwise aim to see sufficient numbers of citizens become infected with the goal of achieving true infection-based herd immunity. By late March 2020, Sweden abandoned this strategy in favor of active interventions; most universities and high schools were closed to students, travel restrictions were put in place, work from home was encouraged, and bans on groups of more than 50 individuals were enacted. Far from achieving herd immunity, the seroprevalence in Stockholm, Sweden, was reported to be less than 8% in April 2020,[7] which is comparable to several other cities (ie, Geneva, Switzerland,[8] and Barcelona, Spain[9]).

The population of the United States is about 330 million. Based on World Health Organization estimates of an infection fatality rate of 0.5%, about 198 million individuals in the United States are needed to be immune to reach a herd immunity threshold of approximately 60%, which would lead to several hundred thousand additional deaths. Assuming that less than 10% of the population has been infected so far,[10] with an infection-induced immunity lasting 2 to 3 years (duration unknown), infection-induced herd immunity is not realistic at this point to control the pandemic. SARS-CoV-2 vaccines will help to reach the herd immunity threshold, but the effectiveness of the vaccine(s) and the vaccine coverage are to be seen.

Conclusions

Herd immunity is an important defense against outbreaks and has shown success in regions with satisfactory vaccination rates. Importantly, even small deviations from protective levels can allow for significant outbreaks due to local clusters of susceptible individuals, as has been seen with measles over the past few years. Therefore, vaccines must not only be effective, but vaccination programs must be efficient and broadly adopted to ensure that those who cannot be directly protected will nonetheless derive relative protections.

ARTICLE INFORMATION

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Published Online: October 19, 2020. doi:10.1001/jama.2020.20892

Conflict of Interest Disclosures: Dr Yildirim reported being a member of the mRNA-1273 Study Group. No other disclosures were reported.

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