COVID-19 – What We Know So Far About... Herd Immunity

Introduction

PHO is actively monitoring, reviewing, and assessing relevant information related to the SARS-CoV-2 virus and Coronavirus Disease 2019 (COVID-19). “What We Know So Far” documents are intended to provide a rapid review of evidence relating to a specific aspect or emerging issue related to COVID-19.

The development of “What We Know So Far” (WWKSF) documents includes a systematic search of the published literature as well as scientific grey literature (e.g., ProMED, CIDRAP, Johns Hopkins Situation Reports and COVID-19 Real Time Learning Network). Relevant results are reviewed and data extracted for synthesis. All WWKSF documents are reviewed by PHO subject-matter experts before posting.

To identify relevant evidence on this topic, systematic searches in MEDLINE and Embase were conducted on January 7, 2020 by PHO Library Services. Search concepts included “herd immunity” and “COVID-19”. It is recognized that there may be additional information not captured in this document. Relevant results are reviewed and data extracted for synthesis.

As the COVID-19 outbreak continues to evolve and the scientific evidence rapidly expands, the information provided in these documents is only current as of the date of posting.

Key Findings

- Herd immunity refers to a state where a significant proportion of the population is immune to an infection leaving few susceptible people who can be infected and transmit the infection. Herd immunity can be achieved through vaccination or infection.
- The herd immunity threshold is achieved when there is sufficient immunity in the population, such that each person who acquires the infection passes it on to less than 1 person on average (i.e., the basic reproduction number (R₀) falls below 1).
- The proportion of the population requiring vaccination to prevent ongoing transmission of a virus is a function of the herd immunity threshold and vaccine effectiveness.
- Estimating the herd immunity threshold for COVID-19, and by extension the proportion of the population that requires vaccination to achieve this threshold, is imprecise given the dynamic nature of virus transmission, presence of immunity due to infection, changes in implementation and adherence to public health measures, and uncertainties in vaccine effectiveness and duration of immunity.
Given these uncertainties, based on a plausible range of $R_0$ estimates in Canada, 56% to 89% of the population of Ontario will require vaccination against COVID-19 to achieve herd immunity.

Herd Immunity and COVID-19

What is “Herd Immunity”?

“Herd immunity”, also known as population immunity or community immunity, refers to a state where a significant proportion of the population is immune to an infection (either through vaccination or natural infection), leaving few people susceptible to being infected and transmitting on the infection.$^{1-3}$ Herd immunity achieved via vaccination breaks the chains of transmission and saves lives by directly protecting those vaccinated and indirectly protecting those with a contraindication to the vaccine (e.g., history of anaphylaxis after vaccine administration), those not eligible for immunization (e.g., infants and children too young to be immunized), and those who may exhibit an impaired immune response despite vaccination (e.g., people with advanced age or immune system compromise).$^{1,4}$ Some examples of the effects of vaccine-induced herd immunity are the global eradication of smallpox, the elimination of measles and rubella in the Americas, and major progress towards the global elimination of polio.$^{5,6}$

How is the Herd Immunity Threshold Calculated?

The herd immunity threshold is achieved when there is sufficient immunity in the population such that each person who acquires the infection passes it on to less than one person on average.$^5$ Surpassing this threshold will result in a decline in the incidence of that infection.$^5$

The threshold of herd immunity is based largely on the transmissibility of the infectious organism.$^5$ Herd immunity (HI) is calculated as follows:$^5$

$$HI = (1 - \frac{1}{R_0})$$

Similarly, the threshold for vaccination ($V_c$) required to achieve herd immunity is as follows and incorporates a measure for vaccine effectiveness:$^5$

$$V_c = (1 - \frac{1}{R_0}) / E$$

$V_c$ = critical vaccination level, which refers to the proportion of the population that must be vaccinated to achieve the threshold of herd immunity.

$R_0$ = basic reproduction number, which refers to the number of transmissions or secondary cases generated by a typical infectious person when the rest of the population is susceptible. $R_0$ can change over time ($R_t$) as a result of immunity due to infection in the population and implemented public health control measures.

$E$ = vaccine effectiveness against transmission.

The formula for herd immunity threshold is built on the following assumptions:

- Infection is transmitted from person-to-person with no animal reservoirs.$^7$
• There is homogeneity in transmission and susceptibility to infection across the population.\(^8\)
  • Herd immunity is impacted by distribution of immunity in the population. If groups at high risk of transmitting an infection attain a high level of immunity through vaccination, herd immunity may still be achieved despite a lower level of vaccine coverage for groups that do not engage in high-risk behaviours. However, this may result in clusters of unvaccinated persons who remain at risk of outbreaks.\(^5\)
• Vaccination prevents transmission in addition to protecting from infection.\(^5\)
  • Herd immunity will depend on the nature of the immunity induced by the vaccine, including the extent to which vaccination prevents transmission\(^5\) and the duration of such protection.\(^5,6\)
• Vaccination protects everyone to the same extent.\(^5\)
• Vaccination is administered uniformly throughout the population.\(^5\)
• Vaccination will be effective against variants that arise from mutations over time.\(^7\)
• Members of a population interact randomly.\(^5\)
• The reproduction rate of the infection remains stable.\(^7\)
• The herd immunity threshold is agnostic to source of immunity, whether it be from infection or immunization.

In the context of COVID-19, many of the above assumptions are imperfect. For example:
• The effectiveness of COVID-19 vaccines in preventing asymptomatic infection remains unknown at this time;
• COVID-19 vaccines may vary in effectiveness depending on the vaccine used and the population receiving vaccination;
• Due to scarcity of doses, the vaccine campaign roll-out targets the highest risk populations first;
• Transmission tends to occur within highly connected groups rather than randomly throughout the population;\(^9\)
• Reproduction rate may be dynamic with changes related to non-pharmacological public health control measures such as contact tracing, quarantining and isolation, physical distancing, public masking, and restrictions on gatherings and travel. As such, herd immunity threshold calculations may be imprecise and only provide an estimated target for vaccination programs based on the information available at any given time; and
• Since vaccinations are being initiated approximately one year after the introduction of COVID-19, a portion of the population may have developed some protection due to infection.

What is the Transmissibility of SARS-CoV-2 in the Absence of a Vaccine?
Transmissibility of infections is often measured by the basic reproduction number (\(R_0\)). The time-dependent reproduction number (\(R_t\)) indicates the number of secondary cases generated by a typical infectious person at a specific point in time, in the context of a susceptible population.\(^10,11\)

\[
R_t = (1 - i_t)(1 - p_t)R_0
\]

\(i_t\) represents the immunity in the population at a specific point in time (t)
\(p_t\) represents the relative reduction in transmission due to other public health control measures at a specific point in time (t).

If \(R_0\) is less than 1, each infected person will on average infect less than 1 additional person and the incidence of the infection will decline. The estimated \(R_0\) for COVID-19 in Canada ranges between 2 and
but will vary over time ($R_t$) based on the proportion of the population with immunity and protection inferred by varied use of public health control measures. Transmissibility will also vary with the variant of SARS-CoV-2 that is locally predominant; for example, the recent Variant of Concern (VOC) lineage B.1.1.7 first identified in the United Kingdom may increase $R_0$ by 0.4 to 0.7, in other words a 1.4 to 1.8 fold increase in $R_0$, bringing the estimated Canadian $R_0$ to between 2.8 to 5.4.

**What is the Estimated COVID-19 Vaccine Efficacy and Duration of Protection for Currently Available COVID-19 Vaccines?**

As of December 23, 2020, Health Canada has authorized two COVID-19 vaccines for use in Canada: Pfizer-BioNTech COVID-19 vaccine and Moderna COVID-19 vaccine. In addition, the Canadian government has advance purchase agreements for five other vaccines from AstraZeneca, Johnson & Johnson, Medicago, Novavax, and combined vaccine development by Sanofi and GlaxoSmithKline for which phase 3 vaccine efficacy data are forthcoming.

Both Pfizer and Moderna vaccines are mRNA-based vaccines and both have been shown to be highly efficacious in the short-term against confirmed symptomatic COVID-19 infection from one to two weeks after receiving two doses. Amongst vaccine trial participants 16 years of age or older who did not have evidence of prior COVID-19 infection, the Pfizer-BioNTech COVID-19 vaccine was 95.0% (95% confidence interval [CI]: 90.3% to 97.6%) efficacious after two doses 21 days apart in preventing symptomatic COVID-19 infection. The efficacy reached 94.7% (95% CI: 66.7% to 99.9%) in those who were 65 years of age or older. In vaccine trial participants 18 years of age or older who did not have evidence of prior COVID-19 infection, the Moderna COVID-19 vaccine was 94.1% (95% CI: 89.3% to 96.8%) efficacious after two doses 28 days apart in preventing symptomatic COVID-19 infection. The efficacy reached 86.4% (95% CI: 61.4% to 95.2%) in those who were 65 years of age or older.

Current evidence is insufficient to inform the duration of protection offered by these vaccines as the median time of follow-up in the primary efficacy analysis for both vaccines was only approximately two months. Available data are also limited in determining whether vaccination reduces the risk of asymptomatic COVID-19 infection and subsequent transmission of the virus, as the primary efficacy indicator was confirmed symptomatic COVID-19 infection. Given the emerging nature of the SARS-CoV-2 infection, further research is needed to determine vaccine effectiveness where immune response may be blunted (e.g., long-term care residents or immunocompromised individuals).

**What is the Estimated Proportion of the Population with Immunity to COVID-19 via Infection in Ontario?**

A total of 208,394 cases have been reported to public health units as of January 7, 2021, translating to a cumulative rate of COVID-19 infection of 1,412 per 100,000 population (1.41%). This may be an underestimate of the actual proportion of the Ontario population with COVID-19 infection due to a variety of factors, including disease awareness and medical care-seeking behaviours, clinical practice, and changes in laboratory testing practices. Estimates from early in the pandemic indicate that only 25.5% of COVID-19 infections in Ontario had been detected.
Another way to estimate the proportion of the Ontario population with SARS-CoV-2 infection is by serologic analysis. Using blood specimens submitted to PHO’s laboratory for non-COVID-19 purposes, PHO estimated that in October 2020, 1.2% of the Ontario population was seropositive (had antibodies against SARS-CoV-2). The estimate was lower than expected considering the increasing COVID-19 incidence in Ontario during that time. While declining levels of antibodies in specimens from persons who were infected earlier in the pandemic could be related to the lower-than-expected estimate, other factors relating to the sensitivity of the assay and the laboratory testing algorithm are being investigated.

The actual proportion of the population infected with SARS-CoV-2 may also be higher than the estimated 1.2% since it takes approximately 2 weeks after infection to produce a measurable antibody response, and the extent to which antibody production translates to immunological protection is uncertain. In addition, individuals who are immunocompromised or at very young or old age may produce a diminished immune response to infection. Further, seroprevalence surveys do not detect cellular immunity (e.g., T cells), which has been documented among COVID-19 contacts who have no detectable antibodies against SARS-CoV-2. Conversely, the 1.2% might be an overestimation due to cross-reaction of the assay with pre-existing antibodies against other strains of human coronavirus.

While most people develop an immune response within a few weeks of infection with SARS-CoV-2, to what extent and for how long this response protects one from re-infection is not fully understood. Likewise, further research is needed to inform how the immune response varies for different people (e.g., after asymptomatic or symptomatic infection).

Can Herd Immunity to COVID-19 be Achieved via Infection?

The suggestion to allow transmission of SARS-CoV-2 in low-risk populations has been raised as an approach to achieve herd immunity. However, uncontrolled transmission in low risk individuals (e.g., young healthy individuals) produces a risk for the entire population. This is because 1) it is challenging to identify those who will suffer from severe or fatal COVID-19 given a large proportion of the population may have a comorbidity that could increase their risk of harm (e.g., cardiovascular disease, diabetes, obesity); 2) even if it was possible to accurately predict risk, it would not be feasible to separate low- and high-risk groups, especially given the ongoing need for caregiving to and health care among those infected. Recent publications from Ontario indicate that the strongest risk factor for a long-term care COVID-19 outbreak is the community incidence of the infection, highlighting the difficulties in protecting this vulnerable population from community transmission.

The consequences of this approach to herd immunity include associated short- and long-term morbidity from symptomatic COVID-19, additional pressures on hospital staff resources and infrastructure that is currently stretched beyond capacity, and a significant increase in mortality. Assuming an infection fatality rate ranging from 0.23% to 2.8% and a conservative herd immunity threshold estimate of 50%, approximately 16,756 to 203,980 lives would potentially be lost to COVID-19 in Ontario before the population reaches the herd immunity threshold. Another challenge with allowing the SARS-CoV-2 infection approach is the uncertainty regarding the magnitude and duration of the protection against recurrent infection, as cases of re-infection have been identified. Early estimates of antibody decline after mild SARS-CoV-2 infection show an IgG half-life of approximately 36 days. It is clear that given the relatively low levels of immunity via immunity acquired through infection with SARS-CoV-2 in Ontario and the potentially short duration of protection post-infection, the herd immunity threshold cannot be safely achieved without the use of a vaccine to prevent mortality and burden to the economy and healthcare system.
What is the Estimated Threshold for Herd Immunity with the Canadian COVID-19 Vaccination Program?

Assuming a reproductive number for SARS-CoV-2 ($R_0$) of 2, and vaccine effectiveness (E) of $95\%$, the herd immunity threshold or vaccination critical level ($V_c$) would be estimated to be $53\%$. On the other hand, assuming a more transmissible variant becomes predominant, with an $R_0$ of 5, the $V_c$ would be estimated to be $84\%$. This means that $53\%$ to $84\%$ of the population would need to be vaccinated against COVID-19 to achieve herd immunity and prevent the continued transmission of the virus. This estimate falls within the range from several publications estimating 40 to $90\%$ vaccination coverage is required to achieve herd immunity for COVID-19 (See Appendix, Table 1 and Table 2).

There are several caveats to these estimates of the herd immunity threshold for SARS-CoV-2:

- Most estimates are simplistic and take into account estimated reproduction numbers and vaccine effectiveness.
- Immunity from SARS-CoV-2 infection is not accounted for in this estimate. However, the proportion of estimated Ontarians with infection is low and duration of immune protection post-infection is uncertain. As a result, Canadian recommendations indicate that those previously infected with SARS-CoV-2 should still receive the COVID-19 vaccine.$^{17}$
- Herd immunity is dynamic and may vary over time and populations. Isolated outbreaks may continue to occur after any herd immunity threshold estimate is reached.
- The SARS-CoV-2 virus may mutate over time, changing its transmissibility and/or vaccine effectiveness.
- While emerging data from clinical trials is becoming available, estimating vaccine efficacy at preventing symptomatic SARS-CoV-2 infection, vaccine effectiveness against asymptomatic infection and viral transmission is largely uncertain, as is the duration of protection.
- Vaccine efficacy estimates from clinical trials is usually higher than real-world vaccine effectiveness and will impact herd immunity threshold estimates.
- Reaching any herd immunity threshold will not result in an immediate end to the pandemic, hence all layers of public health measures for preventing COVID-19 should still continue to be practised at a population level.
Table 1. COVID-19 Herd Immunity Threshold Estimates

<table>
<thead>
<tr>
<th>Publication</th>
<th>Population</th>
<th>$R_0$ or $R_t$</th>
<th>Herd Immunity Threshold</th>
<th>Other Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmad 2020</td>
<td>Saudi Arabia</td>
<td>3.26</td>
<td>69.3%</td>
<td>Modified Susceptible-Exposed-Infectious-Recovered (SEIR) Model in absence of non-pharmacological measures and vaccine</td>
</tr>
<tr>
<td>Altmann 2020</td>
<td>Global</td>
<td>2.2</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td>Anderson 2020</td>
<td>Global</td>
<td>2.5 to 3.5</td>
<td>60 to 72%</td>
<td>Assumes immunity is not short-lived</td>
</tr>
<tr>
<td>Brett 2020</td>
<td>United Kingdom</td>
<td>2.3</td>
<td>53%</td>
<td>Deterministic Age Structured Model Accounts for non-pharmacological measures (e.g., distancing)</td>
</tr>
<tr>
<td>Britton 2020</td>
<td></td>
<td>2.5</td>
<td>43%</td>
<td>Deterministic Age Structured Model accounts for age groups, heterogeneous mixing, and social activity</td>
</tr>
<tr>
<td>Dong 2020</td>
<td>China</td>
<td>2.5</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td>Fontanet 2020, Frederiksen 2020, Randolph 2020</td>
<td>Global</td>
<td>3.0</td>
<td>67%</td>
<td></td>
</tr>
<tr>
<td>Gomes 2020</td>
<td>Global</td>
<td>Variable</td>
<td>&lt;20%</td>
<td>Epidemiological model accounting for heterogeneity in exposure and susceptibility to infection</td>
</tr>
<tr>
<td>Kwok 2020</td>
<td>Canada</td>
<td>2.3</td>
<td>56.5%</td>
<td></td>
</tr>
<tr>
<td>Radwan 2020</td>
<td>Egypt</td>
<td>2.6</td>
<td>52%</td>
<td></td>
</tr>
<tr>
<td>Reilly 2020</td>
<td>Long-Term Care, USA</td>
<td>N/A</td>
<td>60%</td>
<td>Logistic population model</td>
</tr>
<tr>
<td>Neagu 2020</td>
<td>Global</td>
<td>2.0 to 3.0</td>
<td>50 to 67%</td>
<td>In the absence of other interventions</td>
</tr>
<tr>
<td>Omer 2020</td>
<td>Global</td>
<td>1.83</td>
<td>45%</td>
<td>Accounts for non-pharmacological measures (e.g., distancing)</td>
</tr>
<tr>
<td>Syal 2020</td>
<td>United States</td>
<td>Variable</td>
<td>63%</td>
<td>Agent-based simulation model, accounts for non-pharmacological measures (e.g., universal masking)</td>
</tr>
<tr>
<td>Patel 2020</td>
<td>India</td>
<td>5.7</td>
<td>82.5%</td>
<td></td>
</tr>
<tr>
<td>Tatapudi 2020</td>
<td>United States</td>
<td>2.27</td>
<td>56%</td>
<td></td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Publication</th>
<th>Population</th>
<th>$R_0$ or $R_t$</th>
<th>Assumed Vaccine Effectiveness</th>
<th>Vaccine Critical Level</th>
<th>Other Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anderson 2020&lt;sup&gt;42&lt;/sup&gt;</td>
<td>Global</td>
<td>2.5 to 3.5</td>
<td>80%</td>
<td>75 to 90%</td>
<td>Assumes immunity is not short-lived</td>
</tr>
<tr>
<td>Kadkhoda 2020&lt;sup&gt;55&lt;/sup&gt;</td>
<td>Global</td>
<td>2.5 to 3.5</td>
<td>95%</td>
<td>63 to 76%</td>
<td></td>
</tr>
<tr>
<td>Makhoul 2020&lt;sup&gt;56&lt;/sup&gt;</td>
<td>China</td>
<td>3.0</td>
<td>$\geq 70%$</td>
<td>$\geq 80%$</td>
<td>Deterministic Age Structured Model Accounts for non-pharmacological measures (e.g., distancing)</td>
</tr>
<tr>
<td>Moghadas 2020&lt;sup&gt;57&lt;/sup&gt;</td>
<td>United States</td>
<td>1.5</td>
<td>90%</td>
<td>40%</td>
<td>Accounts for non-pharmacological measures (e.g., distancing)</td>
</tr>
<tr>
<td>Park 2020&lt;sup&gt;58&lt;/sup&gt;</td>
<td>South Korea</td>
<td>2.03</td>
<td>50%</td>
<td>62%</td>
<td></td>
</tr>
</tbody>
</table>
References


29. Habib H. Has Sweden’s controversial covid-19 strategy been successful? BMJ [Internet]. 2020;369:m2376. Available from: https://doi.org/10.1136/bmj.m2376


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