A new horizon for COVID-19: Vaccination and herd immunity

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A vaccine to combat the virus responsible for COVID-19 is expected to allow life to begin to return to what it was like pre-pandemic. In this brief article, we consider the performance of select vaccines against other communicable diseases caused by viruses as we anticipate one for COVID-19.

The word vaccine is derived from the Latin word for cow, reflecting its origins during the late 18th century when the relatively milder cowpox virus was used to confer immunity against the devastating smallpox virus.[1] From 1958 to 1977, the World Health Organization (WHO) led a global campaign that eradicated smallpox worldwide (meaning intervention measures such as vaccination are no longer needed).

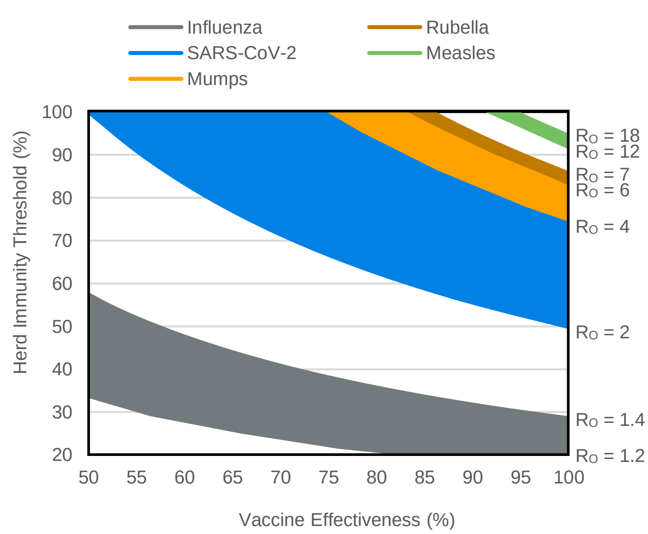
Several highly efficacious vaccines like the one against smallpox exist, though eradication of the diseases they can prevent is complicated by outbreaks caused by insufficient vaccine coverage (proportion of a population that receives vaccination) along with increased opportunities for exposure in a highly mobile era. One example of this is measles, for which WHO reported 863,000 cases globally for 2019, more than twice as many as the nearly 360,000 cases for 2018 and 2011, the two next-highest years over the past decade.[2]

For other communicable diseases, though, vaccines are only moderately effective. Complicated by antigenic drift (small mutations to the virus that make it possible to evade existing immunity) and nonhuman reservoirs (habitats in which the virus normally multiplies), vaccination is far from eliminating the influenza virus at its current effectiveness and coverage levels. Even with relatively predictable seasonality and virulence, a moderately effective vaccine, and multiple antiviral treatment options, WHO estimates 290,000 to 650,000 influenza-related deaths occur annually worldwide.[3]

The novel coronavirus responsible for COVID-19, SARS-CoV-2, has resulted in more than 1.2 million confirmed deaths globally in one year, a figure that continues to rise daily, creating high expectations for the performance of vaccines currently in development.[4] A comparison to viruses for which widespread vaccination is recommended can inform these expectations. We selected influenza, measles, mumps, and rubella here as these viral illnesses vary in terms of how quickly they spread and the impact of vaccination on disease due to infection. We focus on the herd immunity threshold, or the proportion of a population that must demonstrate immunity (through overcoming natural infection or vaccination) to an infectious agent for it to no longer be the cause of large outbreaks. The threshold for SARS-CoV-2 has been a focal point for decisions surrounding containment of the pandemic and will continue to be moving forward.

Vaccine effectiveness, in addition to the basic reproduction number, can be an input for calculation of the threshold. As a vaccine's effectiveness drops below 100%, the threshold to achieve herd immunity increases, as illustrated in Figure 1 for the viruses discussed.[5] The table in Figure 2 contains the epidemiological parameters for SARS-CoV-2 and the viruses selected for comparison. While evidence to more accurately inform how vaccine effectiveness may alter the herd immunity threshold for SARS-CoV-2 is lacking, we can infer from the estimates calculated that the level is higher than that of influenza, but lower than for measles, mumps, and rubella.

FIGURE 1: VACCINE EFFECTIVENESS AND HERD IMMUNITY THRESHOLD* FOR SELECT VIRAL INFECTIONS BY BASIC REPRODUCTION NUMBER (R_O)



* Immunity by vaccination as opposed to from prior infection(s).

Population vaccine coverage indicates progress toward the herd immunity threshold, particularly as vaccination is most effective prior to natural infection. If a recent survey's findings that nearly three-quarters of respondents worldwide would receive a vaccine against SARS-CoV-2 are realized, the herd immunity threshold may be met by vaccination for vaccine effectiveness of 80% or higher.[6] This may vary by location, though. Surveys in the United States suggest coverage may more closely resemble that of influenza, with less than one in two receving vaccination.[7,8] At this rate, herd immunity may not be attainable even with 100% vaccine effectiveness.

Planning for distribution of SARS-CoV-2 vaccine(s) is already underway.[24] For the most recent influenza pandemic, which occurred with a novel H1N1 virus in 2009, the strategy for prioritizing a limited vaccine supply initially was relatively straightforward, vaccinate those who were:

- At high risk for becoming infected or suffering from influenza-related complications
- Likely to come in contact with the virus and expose others in medical care settings
- Close contacts of infants less than six months of age who were too young to be vaccinated[25]

Children and young or middle-aged adults represented the populations most at risk of severe disease from viral infection and for whom H1N1 cases most frequently occurrred.[25]

For SARS-CoV-2, maximum infectivity occurs before or at symptom onset, and the proportion of individuals with mild or no symptomatic illness is high and facilitates undetected transmission.[26] Currently, cases occur most frequently among those who are generally young, healthy, and mobile: while individuals aged 65 years and older comprise nearly 80% of COVID-19-related deaths, they account for only 15% of cases in the United States.[27] Furthermore, it is too early to understand the extent of, and high-risk populations for, long-term health sequelae among survivors of infection.

It will take time, as we have seen with testing, to produce sufficient supplies of vaccine for all who would like to receive one. Vaccine effectiveness and rate of uptake are likely to immediately portend the degree of continued mask-wearing and social distancing practices needed. The potential for cold-chain requirements, the likely need for individuals to receive more than one dose for the earliest vaccines, and the expectation that duration of coverage might be shorter than for other viruses such that repeated vaccination is necessary may lead to additional strain on production and access.[24,28] Although this coronavirus has not demonstrated antigenic properties like those of influenza, there have been more warnings of coronavirus's potential threats to the human population in the first 20 years of the 21st century than in the three decades following its initial identification in the mid-1960s.[29] SARS-CoV-2 may be just a harbinger of more coronaviruses or other pathogens capable of causing severe disease that we may face in the future.

FIGURE 2: DISEASE EPIDEMIOLOGY AND VACCINE EFFECTIVENESS FOR SELECT VACCINATIONS AGAINST PREVENTABLE VIRAL INFECTIONS

VACCINE RECOMMENDATION	VIRUS MODE OF TRANSMISSION	BASIC REPRODUCTION NUMBER	VACCINE EFFECTIVENESS	HERD IMMUNITY THRESHOLD *	POPULATION COVERAGE	DURATION OF COVERAGE
Influenza, annually starting at 6 months of age[9]	Respiratory droplets[10]	1.2-1.4[11]	40% (16-75%)[12]	42-71% (22-100%)	51.8%[8]	1 year[9]
Measles (Me), mumps (Mu), rubella (R), two doses at 12-15 months and 4-6 years; one or two doses after age 19 without evidence of immunity[9]	Me: aerosol[13] Mu & R: respiratory droplets[14,15]	Me: 12-18[16,17,18] Mu: 4-7[16] R: 6-7[16]	Me: 93-97%[13,19] Mu: 78-88%[14,19] R: 97%[15,19]	Me: 95-100% Mu: 85-100% R: 86-88%	91.5%[20]	Me: life-long[13] Mu: >10 years[14] R: >15-20 years[15]
SARS-CoV-2, TBD	respiratory droplets; probably aerosol[21]	2-4[22,23]	TBD	50-75%	TBD; 75%?[6]	TBD

TBD = to be determined. Basic reproduction number = expected number of cases directly generated by one case in a population where all individuals are susceptible to infection. Herd immunity threshold = indirect protection from infectious disease that occurs when a large percentage of a population has become immune to an infection, whether through vaccination or previous infections, thereby providing a measure of protection for individuals who are not immune.

* Calculated here as (1 - 1 / basic reproduction number) / vaccine effectiveness, when available.

It took more than a century, including a dedicated 19-year effort, to eradicate illness caused by smallpox. The incidence of infection from measles has been eliminated (i.e., the disease is no longer occurring naturally) in many defined geographical areas, but continued measures to prevent resurgence of transmission are required. For influenza, on the other hand, we have become accustomed to a level of disease incidence, prevalence, morbidity, and mortality over the past century that varies across seasons and is, at times, unpredictable. Though vaccination is unlikely to be a silver bullet against COVID-19, its role in negating the worldwide burden of the pandemic to allow life to find a normal more similar to what it was pre-2020 remains promising. Time will tell whether vaccination will permit adequate control of SARS-CoV-2 circulation so as to allow for elimination. We should at least anticipate that any vaccine will be accompanied at the outset by obstacles for achieving optimal coverage and that approaches for targeting vaccination to effectively reduce the burden of illness may need to be adapted as we learn more about SARS-CoV-2 disease epidemiology and the vaccine becomes more available.

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ENDNOTES

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