Herd Immunity: The Journey is as Important as the Destination

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We celebrated as the first American received a Coronavirus Disease 2019 (COVID-19) vaccine outside the setting of a clinical trial on December 14, 2020. This unprecedented feat — developing and administering a vaccine against a novel pathogen just 338 days after the genetic sequence was published — was technically possible because of prior knowledge that coronavirus spike protein induces protective neutralizing antibody and the maturation of nucleic acid vaccine technology platforms. The here-to-fore unseen potential of these vaccine technologies fueled innovation and collaboration across the vaccine ecosystem with clinical studies being designed, reviewed, approved, initiated, and enrolled in record time while vaccine manufacturing processes were simultaneously scaled and ready to produce hundreds of millions of doses when confirmatory safety and efficacy data became available. These heroic efforts culminated in dossiers of clinical and manufacturing data supporting safety and efficacy and emergency use authorization of three vaccines (BNT162b, mRNA-1273, and Ad26.COV2.S) in the United States (US). But as Bartsch and colleagues describe in the current issue of *The Journal of Infectious Diseases*, overcoming vaccine hesitancy may be society’s biggest — and most critical — test yet.

To be sure, the Covid-19 vaccine development story of 2020 will be a remarkable chapter in the history of humankind. As of the date of writing this Commentary, 41.8% of the US population have received a single dose and 28.0% are fully vaccinated including 67.1% of individuals 65 years of age and older [1]. This progress is nothing short of extraordinary, yet the pandemic continues to surge, now dominated by the SARS-CoV-2 variant, B.1.1.7 that originally emerged in the United Kingdom. It is sobering to note that despite the great progress on vaccinations, the numbers of COVID-19 cases and deaths have nearly doubled since the day the first vaccine was administered in the US, with cases increasing from 16.6 to 32.0 million and deaths increasing from 305,200 to 571,805 [2]. Whatever the root cause(s), be it a decline in protective behaviors such as handwashing, social
distancing, and mask wearing, the increased transmissibility of emerging variants, or a combination of factors, it is clear that the challenge before us in the US will be to double down on getting vaccines into eligible arms.

Bartsch et al present a computational model showing the number of lives saved and costs avoided for different vaccine coverage levels (30% to 90%) achieved across different periods of time (180, 270, and 360 days) for a range of vaccine efficacies (50% to 90%) [3]. A model isn’t needed to know that a widely used, highly efficacious Covid-19 vaccine that will enable population immunity and end the pandemic will have tremendous clinical and economic benefit. However, this report highlights three important factors that may have previously gone unnoticed and that are important to consider in the US Covid-19 vaccine response. First, even incremental gains of 1% in coverage rates matter, averting millions of cases, tens of thousands of hospitalizations, and thousands of deaths as well as saving billions of dollars in direct medical and indirect costs. Second, coverage rates matter as much as the efficacy of the vaccine. Sensitivity analyses in their study showed that increasing coverage rates can avert more COVID-19 cases than a similar increase in vaccine efficacy, and even at lower vaccine efficacy (e.g. 50%), incremental gains in coverage can provide measurable benefit in terms of cases averted. Third, speed matters. The clinical and economic benefits are significantly greater when time to vaccine coverage occurs over a period of 180 days as compared with 270 days or 360 days.

The limitations of the model to predict the future are also clear. SARS-CoV-2 continues to surprise us with its lack of seasonality and the continued emergence of variants that are more contagious and associated with more severe COVID-19 than that of the original lineage. The magnitude and duration of the efficacies of COVID-19 vaccines in the real-world setting are still being investigated. Further, behavioral changes (or non-pharmaceutical interventions) such as physical distancing and mask wearing vary widely across and within states. Although these factors may affect the threshold
needed for population immunity, they don’t change the need for vaccination. The modeled scenarios were consistent for a broad range of vaccine efficacies and time periods: small incremental gains in vaccine coverage in a short period of time will have a dramatic impact on the health and well-being of citizens in our country. In short, this report provides the quantitative justification for why we must approach COVID-19 vaccination programs with the same or even greater intensity and sophistication as we approached COVID-19 vaccine development.

As Bartsch et al document, vaccine hesitancy in the United States runs strong [4]. And an estimated 80% to 90% of the population will need to be vaccinated to achieve population (herd) immunity. Converting the uncommitted (i.e., vaccine hesitant) to the committed will be our biggest challenge to date in terms of cases averted, lives saved, and financial losses prevented.

Vaccine hesitancy, formally defined as “a delay in acceptance or refusal of vaccination despite availability of vaccine services” was a troubling global phenomenon before the pandemic began with routine vaccination levels plateauing in many countries [5,6]. And the primary factors influencing vaccine hesitancy - complacency, confidence, and convenience - have been magnified even further with the pandemic. Some perceive COVID-19 as a “bad flu” that they can shake off and understandably choose to prioritize work and childcare over making time for vaccination. Studies have shown that confidence in vaccine safety and efficacy has been diminished because of the politicization of vaccine development and because marginalized communities were not engaged early as vaccines were being developed [7]. Further, the very communities that have suffered disproportionate economic and health losses from the pandemic without sufficient resources to control it are now being asked to trust the same system to get vaccinated for the benefit of the wider population [8]. And for them, vaccines have not consistently been readily accessible at a time and in a place and context that is convenient and comfortable [9].
Successful vaccination programs tease out where individuals and communities are along the vaccine hesitancy continuum from refusal to acceptance and develop strategies tailored to the need. As an example, an urban network of hospitals in a racially and ethnically diverse community recently shared their lessons learned from a program to improve equity in COVID-19 vaccinations including the need to answer all vaccine questions without judgment, to respect autonomy and authority allowing people to make decisions aligned with their values and priorities, to identify trusted messengers, i.e., the right healthcare providers that are involved in the community, and to creatively address the functional barriers to access such as misinformation, lack of computer access to make an appointment, and language or health literacy barriers [10].

The US Covid Response aims for a large enough proportion of individuals in the US to be vaccinated by July 4, 2021 to get closer to the normal life that we left behind just over a year ago. Vaccinations were opened to all individuals 16 years of age and older on April 19, 2021. Shipments will be going to more pharmacies and physicians as demand drops at mass vaccination sites. Employers are being incentivized to pay employees for time off work for vaccination and for recovering from side effects. These centralized programs from the federal government are important. Equally important, healthcare providers in local communities must be well supported. The initial strategy of mass vaccination sites was the right one, to rapidly increase vaccination coverage in those individuals committed to vaccination. However, the final victory against COVID-19 will be accomplished in local communities, one individual at a time. The vaccine packaging and presentation need to be fit-for-purpose for small, community-based practices, with vaccine provided in single doses versus the current multi-vial cartons and multi-dose vials. There are also fault lines in our country that course along demographic characteristics. One in five adults in rural areas indicated they will definitely not get the vaccine [4]. Hesitancy also remains strong in communities traditionally underserved or unserved by our health system. Although enthusiasm for vaccines has
increased since December 2020, 24% of Black respondents and 18% of Hispanic respondents recently indicated they would “wait and see” how the vaccine works for others before getting vaccinated themselves [4].

As referenced above, solutions to vaccine hesitancy will be multifaceted from respectfully answering questions to making it easier to get vaccinated. To end on a very practical note, I believe those incremental coverage gains that are so impactful to our health and economy will only be made if we zero-in on each individual’s immediate healthcare setting. Indeed, study after study has shown that the single most powerful tool to increase vaccination is through an individual’s healthcare provider [11]. And it’s not different with COVID-19 vaccines. A recent poll shows that most US adults consider their doctors and nurses their most trusted sources of information about the pandemic and prefer to get vaccinated at their doctor’s office or a local pharmacy [4]. The role that family physicians, nurses, and pharmacists play cannot be overstated. Together, they will be the force that leads to each 1% incremental gain in COVID-19 vaccine coverage. And as Bartsch et al show, these small gains will save millions of lives and billions of dollars on this country’s journey to herd immunity, a journey as important as the destination.

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