When will the COVID-19 pandemic end? An update

Recent news on vaccine and antibody trials has raised hopes worldwide. When will vaccines be available? And is the end of COVID-19 nearer? Here we update our September 21 outlook.

by Sarun Charumilind, Matt Craven, Jessica Lamb, Adam Sabow, and Matt Wilson
Since we published our first outlook, on September 21, the COVID-19 pandemic has raged on, with more than 25 million additional cases and more than 400,000 additional deaths. While the situation looks somewhat better in parts of the Southern Hemisphere, much of Europe and North America is in the midst of a “fall wave,” with the prospect of a difficult winter ahead. Yet the past two weeks have brought renewed hope, headlined by final data from the Pfizer/BioNTech1 vaccine trial and interim data from the Moderna trial, both showing efficacy of approximately 95 percent2; and progress on therapeutics. Is an earlier end to the pandemic now more likely?

The short answer is that the latest developments serve mainly to reduce the uncertainty of the timeline (Exhibit 1). The positive readouts from the vaccine trials mean that the United States will most likely reach an epidemiological end to the pandemic (herd immunity) in Q3 or Q4 2021. An earlier timeline to reach herd immunity—for example, Q1/Q2 of 2021—is now less likely, as is a later timeline (2022). If we are able to pair these vaccines with more effective implementation of public-health measures and effective scale-up of new treatments and diagnostics, alongside the benefits of seasonality, we may also be able to reduce mortality enough in Q2 to enable the United States to transition toward normalcy. (See sidebar, “Two endpoints for the pandemic” for our definitions.)

Exhibit 1

Main effect of recent news is to increase confidence in Q3–Q4 2021 as most likely timeline to achieve herd immunity.

Probability of functional end1 to COVID-19 pandemic in US2 by quarter (illustrative)

<table>
<thead>
<tr>
<th>Quarter</th>
<th>11/23/20 estimate</th>
<th>9/21/20 estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q4 2021</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q2 2022</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q3 2022</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q4 2022</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q2 2023</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q3 2023</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q4 2023</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Early herd immunity if:
- Vaccine rollout and adoption is faster than expected
- Natural immunity is significantly higher than realized
- Peak probability of herd immunity (Q3/Q4 2021) driven by:
  - Emergency use authorization (EUA) of 1+ candidates in Dec 2020/Jan 2021
  - Biologic license application (BLA) (with full approval by March/April 2021)
  - Approximately 6 months for manufacturing, distribution and sufficient adoption to reach herd immunity

Later herd immunity if one or more of the following occur:
- Safety issues delay EUA and/or BLA
- Manufacturing/supply chain issues slow rollout
- Adoption is slower than anticipated
- Duration of immunity is short
- Vaccine prevents disease progression but does not meaningfully reduce transmission

1A functional end to the epidemic is defined as reaching a point where significant, ongoing public-health measures are not needed to prohibit future spikes in disease and mortality (this might be achieved while there are still a number of people in particular communities who still have the disease, as is the case with measles).
2Timeline to functional end is likely to vary somewhat based on geography.
Source: Information compiled from a variety of public statements and sources (ie, Atlantic; CDC; Cell [June 2020]; FDA; MedRxiv; Nature; Nature Reviews [August 2020, July 2020]; NY Magazine; Oxford Academic; PHAS; Science; Science Advances; Science Immunology [June 2020]; WHO); interviews with relevant experts; and surveys conducted by McKinsey and others.

1Pfizer and BioNTech conclude Phase 3 study of COVID-19 vaccine candidate, meeting all primary efficacy endpoints,” Pfizer, November 18, 2020, pfizer.com.
2Moderna’s COVID-19 vaccine candidate meets its primary efficacy endpoint in the first interim analysis of the Phase 3 COVE study,” Moderna, November 16, 2020, modernatx.com.
Two endpoints for the pandemic

An epidemiological end point will be reached when herd immunity is achieved. One end point will occur when the proportion of society immune to COVID-19 is sufficient to prevent widespread, ongoing transmission. Many countries are hoping that a vaccine will do the bulk of the work needed to achieve herd immunity. When this end point is reached, the public-health-emergency interventions deployed in 2020 will no longer be needed. While regular revaccinations may be needed, perhaps similar to annual flu shots, the threat of widespread transmission will be gone.

A second (and likely, earlier) end point, a transition to normalcy, will occur when almost all aspects of social and economic life can resume without fear of ongoing mortality (when a mortality rate is no longer higher than a country’s historical average) or long-term health consequences related to COVID-19. The process will be enabled by tools such as vaccination of the highest-risk populations; rapid, accurate testing; improved therapeutics; and continued strengthening of public-health responses. The next normal won’t look exactly like the old—it might be different in surprising ways, with unexpected contours, and getting there will be gradual—but the transition will enable many familiar scenes, such as air travel, bustling shops, humming factories, full restaurants, and gyms operating at capacity, to resume.

Revelations from vaccine and antibody trials
The world has cheered announcements over the past two weeks by Pfizer and its partner BioNTech, and from Moderna. Their COVID-19 vaccine candidates are showing efficacy rates that are higher than many dared hope for. One is a final result, and the other is an initial result whose sample size is large enough to give reasonable confidence in the data. At about 95 percent, efficacy is higher than expected by most experts.3 It exceeds the optimistic case that we included in our September article. Higher efficacy provides greater benefit to any vaccinated individual and may help to encourage uptake among some segments of the population. It also reduces the fraction of the population required to reach herd immunity. Moderna also announced that its vaccine is more shelf-stable than expected and would need only refrigeration to keep it stable for 30 days—another piece of good news. Finally, there are a number of other vaccines in late-stage trials from which data is expected in the coming months.

Caution is still warranted. The safety records of the Pfizer and Moderna vaccines appear promising so far (no serious side effects reported), but the coming months will provide a fuller picture as the sample size grows. We don’t yet know how long the protection the vaccines offer will last. The Pfizer trial has enrolled some children (ages 12 and older), but efficacy in those under 18 remains unclear.

3 Pfizer vaccine efficacy could be a “game changer,” Cornell University, November 8, 2020, government.cornell.edu.
Beyond vaccines, science is also progressing in therapeutics for COVID-19. For example, Eli Lilly’s antibody bamlanivimab was granted emergency use authorization (EUA) by the US Food and Drug Administration on November 9,4 and Regeneron’s EUA for its antibody cocktail REGN-COV2 for EUA was approved on November 22. Emerging data on these antibodies suggest that they can reduce the need for hospitalization of high-risk patients, and hold potential for post-exposure prophylaxis.5 While they are not recommended for use in hospitalized patients, these antibodies add to the growing armamentarium of treatments and protocols for COVID-19, where every incremental advance could help to reduce mortality. Collectively, these treatments and changes in clinical practice have lowered mortality for those hospitalized by 18 percent or more.6

Looking deep into the data
Research and findings of the past two months have shed light on a number of uncertainties and in some cases have raised new questions. Here we review five implications; each has helped refine our probability estimates for the COVID-19 pandemic timeline.

Vaccine age restrictions elevate coverage requirements to reach herd immunity
It appears that the two vaccines mentioned will be indicated first for use in adults.7 It’s not clear when use in children will be indicated. One consequence is that the vaccines’ contribution to population-wide herd immunity will depend on adults, at least until vaccines are approved for use in younger populations. If vaccines are efficacious, safe, and distributed to all ages, vaccine coverage rates of about 45 to 65 percent—in combination with projected levels of natural immunity—could achieve herd immunity (Exhibit 2).

On the other hand, if vaccines are efficacious but distributed only to adults, who comprise only 76 percent of the US population,8 then higher vaccine coverage rates—approximately 60 to 85 percent—could be required to achieve herd immunity.

Another consequence is that older children, who have twice the COVID-19 incidence of younger children and who have higher viral loads (and therefore greater potential contagiousness) than adults9 may not have immediate access to vaccines.

We recognize that calculating herd immunity thresholds is complex. Basic formulas fail to account for variations in the way populations interact in different places.10 For this reason we include relatively wide ranges.

Unclear impact of vaccines on transmission could raise the bar on coverage
Vaccine trials and regulatory approval will be based on safety and efficacy in reducing virologically confirmed, symptomatic disease among individuals.11 That’s not the same as reducing transmission. This distinction will have much to say about whether the United States reaches normalcy in Q2 or Q3 of 2021. In practice, we have data on whether people who are vaccinated are less likely to get sick with COVID-19 (and less likely to get severe disease), but we won’t have data on how likely they are to transmit to others. It’s an important distinction because what will drive herd immunity is reduction in transmission. If vaccines are only 75 percent effective at reducing transmission, then coverage of about 60 to 80 percent of the population will be needed for herd immunity. And if a vaccine is only 50 percent effective at reducing transmission, coverage of over 90 percent would be required (Exhibit 3).

---

Wide variations in local seroprevalence suggest heterogeneous paths to herd immunity

Improved estimates of seroprevalence are increasingly available for many regions. They vary widely, from as low as 1 to 2 percent in some states like Colorado and Kansas to 14 to 20 percent in New Jersey and New York. Because achieving herd immunity relies in part on a population’s natural immunity, it appears that some locations are closer to herd immunity than others (and have likely also experienced worse impact on public health to date). Based on a range of likely vaccine scenarios and the fact that those with prior exposure to SARS-CoV-2 will still be eligible for vaccination, every ten-percentage-point increase in seroprevalence could roughly translate into a one-month acceleration of the timeline to the epidemiological endpoint.

However, it is possible that areas with higher seroprevalence may also have higher thresholds for herd immunity, because their populations may mix more,¹³ which could have contributed to higher seroprevalence to begin with. If that’s true, then while they are further along, they may also have further to go. Well-executed distribution of effective vaccines will still be paramount.

**Potentially shorter duration of immunity could prolong the path to the ‘end’**

Earlier in the pandemic, it was unclear how long immunity after COVID-19 infection would last. Duration of immunity matters, obviously; for instance, our modeling suggests that if natural immunity to COVID-19 lasts six to nine months, as opposed to multiple years (like tetanus) or lifelong (like measles), herd immunity is unlikely to be achieved unless adult vaccination rates approach 85 percent. While COVID-19 reinfection is documented but rare, there are now population-level studies that question the durability of immunity. Antibody levels may wane after just two months, according to some studies, while a United Kingdom population-monitoring effort reported that antibody prevalence fell by 26 percent over three months.¹⁴

---


The relationship between waning antibodies and reinfection risk remains unclear. Other research suggests that even with waning levels of COVID-19 antibodies, the immune system may still be able to mount a response through other specific B-cell and T-cell immune pathways, where emerging evidence shows much greater durability after six months.¹⁵

**Manufacturing and supply issues are clearer, but have not vanished**

If the initial efficacy data from the Pfizer and Moderna vaccine trials hold up, and if no significant safety issues emerge, then initial demand is likely to be high. Two promising candidates are better than one, but supplies will undoubtedly be constrained in the months following EUA and approval. The situation may be dynamic as vaccines are approved at different times, each with its own considerations in manufacturing and distribution. For example, current data suggest that Moderna’s vaccine is stable at refrigerated temperatures (2 to 8 degrees Celsius) for 30 days and six months at –20 degrees Celsius. Pfizer’s vaccine can be stored in conventional freezers for up to five days, or in its custom shipping coolers for up to 15 days with appropriate handling. Longer-term storage requires freezing at –70 degrees Celsius, requiring special equipment.¹⁶ Both Pfizer’s and Moderna’s would be two-dose vaccines, necessitating rigorous follow-up for series completion. These and other complexities create risk of delay. Timelines to reach the desired coverage threshold will be affected by health systems’ abilities to adapt to changing needs and updated information.

---


¹⁸ *The COVID-19 vaccination program interim operational guidance for jurisdictions playbook*, Centers for Disease Control and Prevention, October 29, 2020, cdc.gov.
Recent developments suggest that herd immunity is less likely to come in early 2021, given that vaccines are arriving roughly on the expected timeline; and the downside scenario stretching into 2022 is also less likely, since efficacy is clearer. The new vaccines may slightly accelerate the timeline—the ongoing surge in cases will likely continue into winter, which would increase natural immunity levels going into Q2. Further, higher-than-expected efficacy may help offset coverage challenges that surveys have suggested. Those two factors could advance the timeline and make Q3 a little more likely than Q4.

Our estimate is based on the widest possible reading of the current scientific literature and our discussions with public-health experts in the United States and around the world. It’s possible that unforeseen developments such as significantly more infections than expected this winter could lead to earlier herd immunity. And real downside risk remains, especially with respect to duration of immunity and long-term vaccine safety (given the limited data available so far). Herd immunity might not be reached until 2022 or beyond.

Even when herd immunity is achieved, ongoing monitoring, potential revaccination, and treatment of isolated cases will still be needed to control the risk of COVID-19. But these would fall into the category of “normal” infectious disease management—not the society-altering interventions we have all lived through this year. The short term will be hard, but we can reasonably hope for an end to the pandemic in 2021.