

Healthcare Systems & Services Practice

# 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*



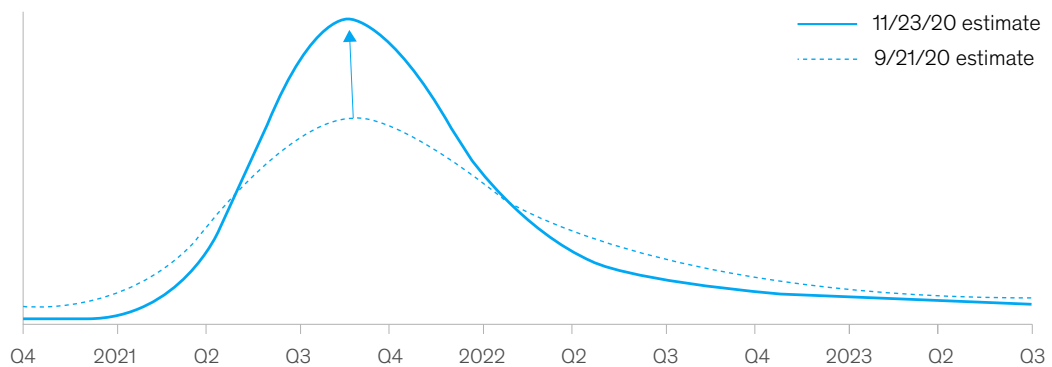
Since we published our first outlook, on September 21, the COVID-19 pandemic has raged on, with more than 25 million additional cases and more than 400,000 additional deaths. While the situation looks somewhat better in parts of the Southern Hemisphere, much of Europe and North America is in the midst 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/BioNTech<sup>1</sup> vaccine trial and interim data from the Moderna trial, both showing efficacy of approximately 95 percent<sup>2</sup>; 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 end<sup>1</sup> to COVID-19 pandemic in US<sup>2</sup> by quarter (illustrative)**



**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

<sup>1</sup>A 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).

<sup>2</sup>Timeline 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*; *PNAS*; *Science*; *Science Advances*; *Science Immunology* [June 2020]; WHO); interviews with relevant experts; and surveys conducted by McKinsey and others

<sup>1</sup> “Pfizer and BioNTech conclude Phase 3 study of COVID-19 vaccine candidate, meeting all primary efficacy endpoints,” Pfizer, November 18, 2020, pfizer.com.

<sup>2</sup> “Moderna’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.

A secondary effect of the recent vaccine trials is to make Q3 2021 more likely for herd immunity than Q4. That said, major questions are still outstanding, even about vaccines, such as long-term safety, timely and effective distribution, and vaccine acceptance by the population, to say nothing of lingering epidemiological questions such as the duration of immunity.

These are estimates for the United States, which is likely to have fast and ready access to vaccines. We will consider timelines for other countries in forthcoming updates; they will vary based on the timing of access and distribution of vaccines and other factors. In this update, we review the most recent findings, look deeper at five implications of the ongoing scientific research, and discuss why our timeline estimates have not shifted meaningfully.

### 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.<sup>3</sup> 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.

<sup>3</sup> "Pfizer vaccine efficacy could be a 'game changer,'" Cornell University, November 8, 2020, [government.cornell.edu](https://www.cornell.edu/govaffairs/newsroom/2020/11/08/pfizer-vaccine-efficacy-could-be-a-game-changer).

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,<sup>4</sup> 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.<sup>5</sup> 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.<sup>6</sup>

### 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.<sup>7</sup> 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,<sup>8</sup> 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 adults<sup>9</sup> 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.<sup>10</sup> 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.<sup>11</sup> 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).

<sup>4</sup> "Coronavirus (COVID-19) update: FDA authorizes monoclonal antibody for treatment of COVID-19," US Food and Drug Administration, November 9, 2020, [fda.gov](https://www.fda.gov).

<sup>5</sup> Laura DeFrancesco, "COVID-19 antibodies on trial," *Nature*, October 2020, [nature.com](https://www.nature.com); "Coronavirus (COVID-19) update," FDA, November 2020.

<sup>6</sup> Leora Horwitz et al., "Trends in COVID-19 risk-adjusted mortality rates," *Journal of Hospital Medicine*, October 2020, [journalofhospitalmedicine.com](https://www.journalofhospitalmedicine.com).

<sup>7</sup> *Development and licensure of vaccines to prevent COVID-19: Guidance for industry*, US Food and Drug Administration, June 2020, [fda.gov](https://www.fda.gov).

<sup>8</sup> *Age and sex composition in the United States: 2019*, US Census Bureau, accessed November 15, 2020, [census.gov](https://www.census.gov).

<sup>9</sup> Rebecca Leeb et al., *COVID-19 trends among school-aged children—United States, March 1–September 19, 2020*, Centers for Disease Control and Prevention, October 2, 2020, [cdc.gov](https://www.cdc.gov); Lael Yonker et al., "Pediatric severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Clinical presentation, infectivity, and immune response," *Journal of Pediatrics*, August 19, 2020, [jpeds.com](https://www.jpeds.com).

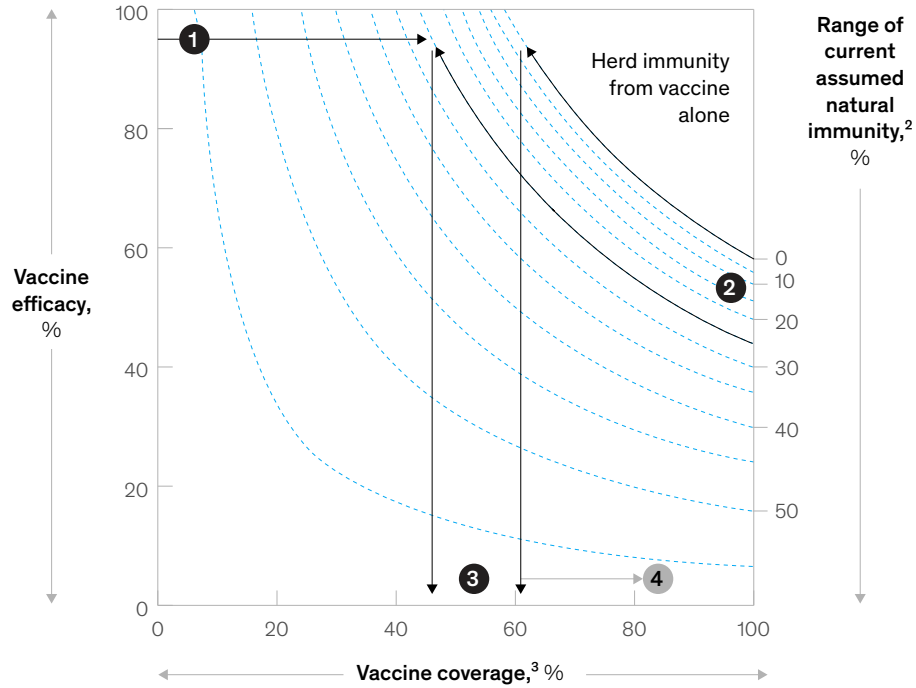
<sup>10</sup> Kevin Hartnett, "The tricky math of herd immunity for COVID-19," *Quanta Magazine*, June 30, 2020, [quantamagazine.org](https://www.quantamagazine.org).

<sup>11</sup> Marc Lipsitch et al., "Understanding COVID-19 vaccine efficacy," *Science*, November 13, 2020, [science.org](https://www.science.org).

Exhibit 2

**Vaccine efficacy and coverage are both important; recent data on efficacy brings clarity to likely coverage targets.**

**COVID-19-immunity scenarios<sup>1</sup>**



- 1** Two new vaccines have shown efficacy of **~95%**
- 2** US seroprevalence (natural immunity) is widely believed to be between **0–25%**<sup>2</sup>
- 3** The intersection of these values for efficacy and seroprevalence suggests that required coverage for the US is **~45–65%**
- 4** The model assumes that vaccines are distributed to adults and children. The new vaccines may not be indicated for children. If only adults are vaccinated, coverage may need to be 30% higher (ie, **58–85%** vaccine coverage)

<sup>1</sup>COVID-19 herd immunity achieved once total immune population reaches 58%, using basic reproductive number (R0) of 2.4; herd-immunity threshold calculated as 1 – (1/R0). The model assumes that each member of a population mixes randomly with all other population members. In reality, people mix mostly with others whose patterns of interaction are similar to their own. Subpopulations with fewer interactions have lower thresholds for herd immunity than do those with more interactions.

<sup>2</sup>Summary statistics, SeroTracker, November 19, 2020, serotracker.com. Our model assumes that test seropositivity correlates with natural immunity. Research is ongoing to validate this. If US seroprevalence continues to rise, then minimum vaccine coverage levels required will decrease.

<sup>3</sup>Assumes that vaccine will be given to entire population, regardless of whether they have had COVID-19.

Source: Moderna; Pfizer; SeroTracker; US Census Bureau

**Wide variations in local seroprevalence suggest heterogeneous paths to herd immunity**

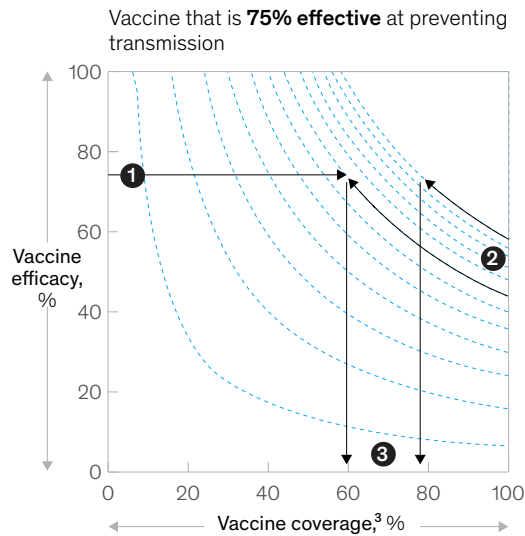
Improved estimates of seroprevalence are increasingly available for many regions. They vary widely, from as low as 1 to 2 percent in some states like Colorado and Kansas to 14 to 20 percent in New Jersey and New York.<sup>12</sup> Because achieving herd immunity relies in part on a population's natural 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.

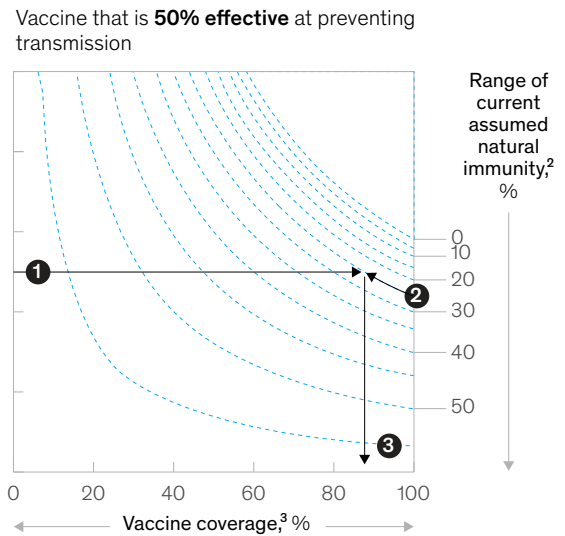
<sup>12</sup> "Nationwide commercial laboratory seroprevalence survey," Centers for Disease Control and Prevention, accessed November 15, 2020, covid.cdc.gov.

## Leaders should be alert to possible scenarios of lower vaccine efficacy.

### Alternative US COVID-19-immunity scenarios<sup>1</sup>



- 1 Vaccine that is **75%** effective at preventing transmission
- 2 Natural immunity is between 0–25%<sup>2</sup>
- 3 These values for efficacy and seroprevalence suggest that required coverage for the US is **60–80%** (or ~78–94% if limited to adults)



- 1 Vaccine that is **50%** effective at preventing transmission
- 2 Natural immunity is between 0–25%<sup>2</sup>
- 3 These values for efficacy and seroprevalence suggest that required coverage for the US is **90% or higher** (or ~100% if limited to adults)

<sup>1</sup>COVID-19 herd immunity achieved once total immune population reaches 58%, using basic reproductive number (R0) of 2.4; herd-immunity threshold calculated as  $1 - (1/R0)$ . The model assumes that each member of a population mixes randomly with all other population members. In reality, people mix mostly with others whose patterns of interaction are similar to their own. Subpopulations with fewer interactions have lower thresholds for herd immunity than do those with more interactions.

<sup>2</sup>Summary statistics, SeroTracker, November 19, 2020, serotracker.com. Our model assumes that test seropositivity correlates with natural immunity. Research is ongoing to validate this. If US seroprevalence continues to rise, then minimum vaccine coverage levels required will decrease.

<sup>3</sup>Assumes that vaccine will be given to entire population, regardless of whether they have had COVID-19.

Source: Moderna; Pfizer; SeroTracker; US Census Bureau

However, it is possible that areas with higher seroprevalence may also have higher thresholds for herd immunity, because their populations may mix more,<sup>13</sup> 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.<sup>14</sup>

<sup>13</sup> Claudio Bozzuto and Anthony Ives, "State-by-state estimates of R0 at the start of COVID-19 outbreaks in the USA," MedRxiv, May 27, 2020, medrxiv.org.

<sup>14</sup> F. Javier Ibarondo et al., "Rapid decay of anti-SARS-CoV-2 antibodies in persons with mild COVID-19," *New England Journal of Medicine*, September 10, 2020, nejm.org; Helen Ward et al., "Declining prevalence of antibody positivity to SARS-CoV-2: A community study of 365,000 adults," MedRxiv, October 27, 2020, medrxiv.org.

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.<sup>15</sup>

**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.<sup>16</sup> 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.

**The pandemic's end is more certain, and may be a little nearer**

Given all of these variables, where do we net out?

While the winter of 2020/2021 in the Northern Hemisphere will be challenging, we are likely to see mortality rates fall in Q2 (or possibly late Q1) of 2021. Seasonality and associated changes in behavior will begin to work again in our favor in the spring, and the combination of early doses of vaccines targeted to those at highest risk (and the benefits of the Pfizer and Moderna vaccines in reducing severe disease), advances in treatment, expanded use of diagnostics, and better implementation of public-health measures should serve to significantly reduce deaths from COVID-19 in the second quarter. At this stage, when monthly mortality from COVID-19 may start to resemble that of flu in an average year, we may see a transition toward normalcy, albeit with public-health measures still in place.

We are as excited as others about the stunning developments in vaccines. We think Q3 or Q4 of 2021 are even more likely to see herd immunity in the United States. This is based on EUA of one or more high-efficacy vaccines in December 2020 or January 2021, as manufacturers are targeting<sup>17</sup>; distribution to people at highest risk (healthcare workers, the elderly, and those with comorbidities) in the early months of 2021<sup>18</sup>; full approval of a vaccine in March or April; and then widespread rollout. Our estimates of three to eight months for manufacturing, distribution, and adoption of sufficient vaccine doses to achieve herd immunity remain unchanged, and suggest that the milestone may be reached between July and December 2021.

<sup>15</sup> Karl Brokstad and Rebecca Cox, "Not just antibodies: B cells and T cells mediate immunity to COVID-19," *Nature Reviews Immunology*, August 24, 2020, nature.com; Jennifer Dan et al., "Immunological memory to SARS-CoV-2 assessed for greater than six months after infection," BioRxiv, November 16, 2020, biorxiv.org.

<sup>16</sup> Katie Thomas, "New Pfizer results: Coronavirus vaccine is safe and 95% effective," *New York Times*, November 18, 2020, nytimes.com.

<sup>17</sup> "Pfizer and BioNTech to submit Emergency Use Authorization request today to the US FDA for COVID-19 vaccine," Pfizer, November 20, 2020, pfizer.com; "Moderna'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, moderna.com.

<sup>18</sup> *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.

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