### The Coronavirus in America: The Year Ahead

**Temperature nytimes.com**/2020/04/18/health/coronavirus-america-future.html

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The coronavirus is spreading from America's biggest cities to its suburbs, and has begun encroaching on the nation's rural regions. The virus is believed to have infected millions of citizens and has killed more than 34,000.

Yet President Trump this week proposed guidelines for reopening the economy and suggested that a swath of the United States would soon resume something resembling normalcy. For weeks now, the administration's view of the crisis and our future has been rosier than that of its own medical advisers, and of scientists generally.

In truth, it is not clear to anyone where this crisis is leading us. More than 20 experts in public health, medicine, epidemiology and history shared their thoughts on the future during in-depth interviews. When can we emerge from our homes? How long, realistically, before we have a treatment or vaccine? How will we keep the virus at bay?

Some felt that American ingenuity, once fully engaged, might well produce advances to ease the burdens. The path forward depends on factors that are certainly difficult but doable, they said: a carefully staggered approach to reopening, widespread testing and surveillance, a treatment that works, adequate resources for health care providers — and eventually an effective vaccine.

Still, it was impossible to avoid gloomy forecasts for the next year. The scenario that Mr. Trump has been unrolling at his daily press briefings — that the lockdowns will end soon, that a protective pill is almost at hand, that football stadiums and restaurants will soon be full — is a fantasy, most experts said.

"We face a doleful future," said Dr. Harvey V. Fineberg, a former president of the National Academy of Medicine.

He and others foresaw an unhappy population trapped indoors for months, with the most vulnerable possibly quarantined for far longer. They worried that a vaccine would initially elude scientists, that weary citizens would abandon restrictions despite the risks, that the virus would be with us from now on.

"My optimistic side says the virus will ease off in the summer and a vaccine will arrive like the cavalry," said Dr. William Schaffner, a preventive medicine specialist at Vanderbilt University medical school. "But I'm learning to guard against my essentially optimistic nature."

Most experts believed that once the crisis was over, the nation and its economy would revive quickly. But there would be no escaping a period of intense pain.

Exactly how the pandemic will end depends in part on medical advances still to come. It will also depend on how individual Americans behave in the interim. If we scrupulously protect ourselves and our loved ones, more of us will live. If we underestimate the virus, it will find us.

# More Americans may die than the White House admits.



Refrigerated trucks were used as mobile morgues on Randall's Island in New YorkCredit...Misha Friedman for The New York Times

Covid-19, the illness caused by the coronavirus, is arguably the leading cause of death in the United States right now. The virus has killed more than 1,800 Americans almost every day since April 7, and the official toll may be an undercount.

By comparison, heart disease typically kills 1,774 Americans a day, and cancer kills 1,641.

Yes, the coronavirus curves are plateauing. There are fewer hospital admissions in New York, the center of the epidemic, and fewer Covid-19 patients in I.C.U.s. The daily death toll is still grim, but no longer rising.

The <u>epidemiological model often cited by the White House</u>, which was produced by the University of Washington's Institute for Health Metrics and Evaluation, originally predicted 100,000 to 240,000 deaths by midsummer. Now that figure is 60,000.

While this is encouraging news, it masks some significant concerns. The institute's projection runs through Aug. 4, describing only the first wave of this epidemic. Without a vaccine, the virus is expected to circulate for years, and the death tally will rise over time.

The gains to date were achieved only by shutting down the country, a situation that cannot continue indefinitely. The White House's "phased" plan for reopening will surely raise the death toll no matter how carefully it is executed. The best hope is that fatalities can be held to a minimum.

Reputable longer-term projections for how many Americans will die vary, but they are all grim. Various experts consulted by the Centers for Disease Control and Prevention in March predicted that the virus eventually could reach 48 percent to 65 percent of all Americans, with a fatality rate just under 1 percent, and would kill up to 1.7 million of them if nothing were done to stop the spread.

A model by researchers at Imperial College London <u>cited by the president</u> on March 30 <u>predicted 2.2 million deaths</u> in the United States by September under the same circumstances.

By comparison, about 420,000 Americans died in World War II.

The limited data from China are even more discouraging. Its epidemic has been halted — for the moment — and virtually everyone infected in its first wave has died or recovered.

China has officially reported <u>about 83,000 cases and 4,632 deaths</u>, which is a fatality rate of over 5 percent. The Trump administration <u>has questioned the figures</u> but has not produced more accurate ones.

Fatality rates <u>depend heavily on how overwhelmed</u> hospitals get and what percentage of cases are tested. China's estimated death rate was 17 percent in the first week of January, when Wuhan was in chaos, according to <u>a Center for Evidence-Based Medicine</u> <u>report</u>, but only 0.7 percent by late February.

In this country, hospitals in several cities, including New York, came to the brink of chaos. Officials in both <u>Wuhan</u> and <u>New York</u> had to revise their death counts upward this week when they realized that many people had died at home of Covid-19, strokes, heart attacks or other causes, or because ambulances never came for them.

In fast-moving epidemics, far more victims pour into hospitals or die at home than doctors can test; at the same time, the mildly ill or asymptomatic never get tested. Those two factors distort the true fatality rate in opposite ways. If you don't know how many people are infected, you don't know how deadly a virus is.

Only when tens of thousands of antibody tests are done will we know how many silent carriers there may be in the United States. The C.D.C. <u>has suggested it might be 25 percent</u> of those who test positive. Researchers in Iceland <u>said it might be double that</u>.

China is also revising its own estimates. In February, a <u>major study</u> concluded that only 1 percent of cases in Wuhan were asymptomatic. <u>New research</u> says <u>perhaps 60 percent</u> were. Our knowledge gaps are still wide enough to make epidemiologists weep.

"All models are just models," Dr. Anthony S. Fauci, science adviser to the White House coronavirus task force, has said. "When you get new data, you change them."

There may be good news buried in this inconsistency: The virus may also be mutating to cause fewer symptoms. In the movies, viruses become more deadly. In reality, they usually become less so, because asymptomatic strains reach more hosts. Even the 1918 Spanish flu virus eventually <u>faded into the seasonal H1N1 flu</u>.

At the moment, however, we do not know <u>exactly how transmissible or lethal the virus is</u>. But refrigerated trucks parked outside hospitals tell us all we need to know: It is far worse than a bad flu season.

## The lockdowns will end, but haltingly.

No one knows exactly what percentage of Americans have been infected so far — estimates have ranged from 3 percent to 10 percent — but it is likely a safe bet that at least 300 million of us are still vulnerable.

Until a vaccine or another protective measure emerges, there is no scenario, epidemiologists agreed, in which it is safe for that many people to suddenly come out of hiding. If Americans pour back out in force, all will appear quiet for perhaps three weeks.

Then the emergency rooms will get busy again.

"There's this magical thinking saying, 'We're all going to hunker down for a while and then the vaccine we need will be available," said Dr. Peter J. Hotez, dean of the National School of Tropical Medicine at Baylor College of Medicine.

In his wildly popular March 19 article in Medium, "<u>Coronavirus: The Hammer and the Dance</u>," Tomas Pueyo correctly predicted the national lockdown, which he called the hammer, and said it would lead to a new phase, which he called the dance, in which essential parts of the economy could reopen, including some schools and some factories with skeleton crews.

Every epidemiological model envisions something like the dance. Each assumes the virus will blossom every time too many hosts emerge and force another lockdown. Then the cycle repeats. On the models, the <u>curves of rising and falling deaths resemble a row of shark teeth.</u>

Surges are inevitable, the models predict, even when stadiums, churches, theaters, bars and restaurants remain closed, all travelers from abroad are quarantined for 14 days, and domestic travel is tightly restricted to prevent high-intensity areas from reinfecting low-intensity ones.

The tighter the restrictions, experts say, the fewer the deaths and the longer the periods between lockdowns. Most models assume states will eventually do widespread temperature checks, rapid testing and contact tracing, as is routine in Asia.

Even the <u>"Opening Up America Again" guidelines Mr. Trump issued on Thursday</u> have three levels of social distancing, and recommend that vulnerable Americans stay hidden. The plan endorses testing, isolation and contact tracing — but does not specify how these measures will be paid for, or how long it will take to put them in place.

On Friday, none of that stopped the president from contradicting his own message by sending out tweets encouraging protesters in Michigan, Minnesota and Virginia to fight their states' shutdowns.

China did not allow Wuhan, Nanjing or other cities to reopen until intensive surveillance found zero new cases <u>for 14 straight days</u>, the <u>virus</u>'s incubation period. Compared with China or Italy, the United States is still a playground.

Americans can take domestic flights, drive where they want, and roam streets and parks. Despite restrictions, everyone seems to know someone discreetly arranging play dates for children, holding backyard barbecues or meeting people on dating apps.

Partly as a result, the country has <u>seen up to 30,000 new case infections each day</u>. "People need to realize that it's not safe to play poker wearing bandannas," Dr. Schaffner said.

Even with rigorous measures, Asian countries have had trouble keeping the virus under control.

China, which has reported about 100 new infections per day, recently <u>closed all the country's movie theaters</u> again. Singapore has <u>closed all schools and nonessential workplaces</u>. Japan recently <u>declared a state of emergency</u>. (South Korea has <u>struggled at times</u>, too, but on Sunday reported only eight new cases, the first single-digit increase in two months.)

Resolve to Save Lives, a public health advocacy group run by <u>Dr. Thomas R. Frieden</u>, the former director of the C.D.C., has <u>published detailed and strict criteria</u> for when the economy <u>can reopen</u> and when it must <u>be closed</u>.

Reopening requires declining cases for 14 days, the tracing of 90 percent of contacts, an end to health care worker infections, recuperation places for mild cases and many other hard-to-reach goals.

"We need to reopen the faucet gradually, not allow the floodgates to reopen," Dr. Frieden said. "This is a time to work to make that day come sooner."

# Immunity will become a societal advantage.

Imagine an America divided into two classes: those who have recovered from infection with the coronavirus and presumably have some immunity to it; and those who are still vulnerable.

"It will be a frightening schism," Dr. David Nabarro, a World Health Organization <u>special</u> <u>envoy on Covid-19</u>, predicted. "Those with antibodies will be able to travel and work, and the rest will be discriminated against."

Already, people with presumed immunity are very much in demand, <u>asked to donate</u> their blood for antibodies and doing risky medical jobs fearlessly.

Soon the government will have to invent a way to certify who is truly immune. A test for IgG antibodies, which are produced once immunity is established, would make sense, said Dr. Daniel R. Lucey, an expert on pandemics at Georgetown Law School. Many companies are working on them.

Dr. Fauci has said the <u>White House was discussing certificates</u> like those <u>proposed in Germany</u>. China <u>uses cellphone QR codes</u> linked to the owner's personal details so others cannot borrow them.

The California adult-film industry <u>pioneered a similar idea a decade ago</u>. Actors use a cellphone app to prove they have tested H.I.V. negative in the last 14 days, and producers can verify the information on a password-protected website.

As Americans stuck in lockdown see their immune neighbors resuming their lives and perhaps even taking the jobs they lost, it is not hard to imagine the enormous temptation to join them through self-infection, experts predicted. Younger citizens in particular will calculate that risking a serious illness may still be better than impoverishment and isolation.

"My daughter, who is a Harvard economist, keeps telling me her age group needs to have Covid-19 parties to develop immunity and keep the economy going," said <u>Dr. Michele Barry</u>, who directs the Center for Innovation in Global Health at Stanford University.

It has happened before. In the 1980s, Cuba <u>successfully contained its small AIDS</u> <u>epidemic by brutally forcing</u> everyone who tested positive into isolation camps. Inside, however, the residents had their own <u>bungalows</u>, food, <u>medical care</u>, <u>salaries</u>, <u>theater troupes and art classes</u>.

Dozens of Cuba's homeless youths <u>infected themselves</u> through sex or blood injections to get in, said Dr. Jorge Pérez Ávila, an AIDS specialist who is Cuba's version of Dr. Fauci. Many died before antiretroviral therapy was introduced.

It would be a gamble for American youth, too. The obese and immunocompromised are clearly at risk, but even slim, healthy young Americans have died of Covid-19.

The virus can be kept in check, but only with expanded resources.

The next two years will proceed in fits and starts, experts said. As more immune people get back to work, more of the economy will recover.

Sign up to receive an email when we publish a new story about the coronavirus outbreak. But if too many people get infected at once, new lockdowns will become inevitable. To avoid that, widespread testing will be imperative.

Dr. Fauci has said "the virus will tell us" when it's safe. He means that once a national baseline of hundreds of thousands of daily tests is established across the nation, any viral spread can be spotted when the percentage of positive results rises.

Detecting rising fevers as they <u>are mapped by Kinsa's smart thermometers</u> may give an earlier signal, Dr. Schaffner said.

But diagnostic testing has been <u>troubled from the beginning</u>. Despite assurances from the White House, doctors and patients <u>continue to complain of delays and shortages</u>.

To keep the virus in check, several experts insisted, the country also must start isolating all the ill — including mild cases.

In this country, patients who test positive are asked to stay in their homes but keep away from their families.

Television news has been filled with recuperating personalities like CNN's Chris Cuomo, sweating alone in his basement while his wife left food atop the stairs, his children waved and the dogs hung back.

But even Mr. Cuomo ended up illustrating why the W.H.O. strongly opposes home isolation. On Wednesday, he <u>revealed that his wife</u> had the virus.

"If I was forced to select only one intervention, it would be the rapid isolation of all cases," said Dr. Bruce Aylward, who led the <u>W.H.O. observer team to China</u>.

In China, anyone testing positive, no matter how mild their symptoms, was required to immediately enter an infirmary-style hospital — often set up in a gymnasium or community center outfitted with oxygen tanks and CT scanners.

There, they recuperated under the eyes of nurses. That reduced the risk to families, and being with other victims relieved some patients' fears. Nurses even <u>led dance and exercise classes</u> to raise spirits, and help victims clear their lungs and keep their muscle tone.

Still, experts were divided on the idea of such wards. Dr. Fineberg co-wrote <u>a New York</u> <u>Times Op-Ed article</u> calling for mandatory but "humane quarantine processes."

By contrast, <u>Marc Lipsitch</u>, an epidemiologist at the Harvard T.H. Chan School of Public Health, opposed the idea, saying: "I don't trust our government to remove people from their families by force."

Ultimately, suppressing a virus requires <u>testing all the contacts</u> of every known case. But the United States is far short of that goal.

Someone working in a restaurant or factory may have dozens or even hundreds of contacts. In China's Sichuan Province, for example, each known case <u>had an average of</u> 45 contacts.

The C.D.C. <u>has about 600 contact tracers</u> and, until recently, state and local health departments <u>employed about 1,600</u>, mostly for tracing syphilis and tuberculosis cases.

China hired and trained <u>9,000 in Wuhan alone</u>. Dr. Frieden <u>recently estimated that the United States will need</u> at least 300,000.

#### There will not be a vaccine soon.

Even though limited human trials of three candidates — two here and one in China — have already begun, Dr. Fauci has repeatedly said that any effort to make a vaccine will take at least a year to 18 months.

All the experts familiar with vaccine production agreed that even that timeline was optimistic. Dr. Paul Offit, a vaccinologist at the Children's Hospital of Philadelphia, noted that the <u>record is four years</u>, for the mumps vaccine.

Researchers differed sharply over what should be done to speed the process. <u>Modern biotechnology</u> techniques using RNA or DNA platforms make it possible to develop candidate vaccines faster than ever before.

But clinical trials take time, in part because there is no way to rush the production of antibodies in the human body.

Also, for unclear reasons, some previous vaccine candidates against coronaviruses like SARS have triggered "antibody-dependent enhancement," which makes recipients more susceptible to infection, rather than less. In the past, vaccines <u>against H.I.V.</u> and <u>dengue</u> have unexpectedly done the same.

A new vaccine is usually first tested in fewer than 100 young, healthy volunteers. If it appears safe and produces antibodies, thousands more volunteers — in this case, probably front-line workers at the highest risk — will get either it or a placebo in what is called a Phase 3 trial.

It is possible to speed up that process with "challenge trials." Scientists vaccinate small numbers of volunteers, wait until they develop antibodies, and then "challenge" them with a deliberate infection to see if the vaccine protects them.

Challenge trials are used only when a disease is completely curable, such as malaria <u>or typhoid fever</u>. Normally, it is ethically unthinkable to challenge subjects with a disease with no cure, such as Covid-19.

But in these abnormal times, several experts argued that putting a few Americans at high risk for fast results could be more ethical than leaving millions at risk for years.

"Fewer get harmed if you do a challenge trial in a few people than if you do a Phase 3 trial in thousands," said Dr. Lipsitch, who recently published a paper advocating challenge trials in the Journal of Infectious Diseases. Almost immediately, he said, he heard from volunteers.

Others were deeply uncomfortable with that idea. "I think it's very unethical — but I can see how we might do it," said Dr. Lucey.

The hidden danger of challenge trials, vaccinologists explained, is that they recruit too few volunteers to show whether a vaccine creates enhancement, since it may be a rare but dangerous problem.

"Challenge trials won't give you an answer on safety," said Michael T. Osterholm, director of the University of Minnesota's Center for Infectious Disease Research and Policy. "It may be a big problem."

Dr. W. Ian Lipkin, a virologist at Columbia University's Mailman School of Public Health, suggested an alternative strategy. Pick at least two vaccine candidates, briefly test them in humans and do challenge trials in monkeys. Start making the winner immediately, even while widening the human testing to look for hidden problems.

As arduous as testing a vaccine is, producing hundreds of millions of doses is even tougher, experts said.

Most American vaccine plants produce only about 5 million to 10 million doses a year, needed largely by the 4 million babies born and 4 million people who reach age 65 annually, said Dr. R. Gordon Douglas Jr., a former president of Merck's vaccine division.

But if a vaccine is invented, the United States could need 300 million doses — or 600 million if two shots are required. And just as many syringes.

"People have to start thinking big," Dr. Douglas said. "With that volume, you've got to start cranking it out pretty soon."

Flu vaccine plants are large, but those that grow the vaccines in chicken eggs are not suitable for modern vaccines, which grow in cell broths, he said.

European countries have plants but will need them for their own citizens. China has a large vaccine industry, and may be able to expand it over the coming months. It might be able to make vaccines for the United States, experts said. But captive customers must pay whatever price the seller asks, and the safety and efficacy standards of some Chinese companies are imperfect.

India and Brazil also have large vaccine industries. If the virus moves rapidly through their crowded populations, they may lose millions of citizens but achieve widespread herd immunity well before the United States does. In that case, they might have spare vaccine plant capacity.

Alternatively, suggested Arthur M. Silverstein, a retired medical historian at the Johns Hopkins School of Medicine, the government might take over and sterilize existing liquor or beer plants, which have large fermentation vats.

"Any distillery could be converted," he said.

## Treatments are likely to arrive first.

In the short term, experts were more optimistic about treatments than vaccines. Several felt that so-called convalescent serum could work.

The basic technique has been used for over a century: Blood is drawn from people who have recovered from a disease, then filtered to remove everything but the antibodies. The antibody-rich immunoglobulin is injected into patients.

The obstacle is that there are now relatively few survivors to harvest blood from.

In the pre-vaccine era, antibodies were "farmed" in horses and sheep. But that process was hard to keep sterile, and animal proteins sometimes triggered allergic reactions.

The modern alternative is monoclonal antibodies. These treatment <u>regimens</u>, which recently <u>came very close to conquering</u> the Ebola epidemic in eastern Congo, are the most likely short-term game changer, experts said.

The most effective antibodies are chosen, and the genes that produce them are spliced into a benign virus that will grow in a cellular broth.

But, as with vaccines, growing and purifying monoclonal antibodies takes time. In theory, with enough production, they could be used not just to save lives but to protect front-line workers.

Antibodies can last for weeks before breaking down — how long depends on many factors, Dr. Silverstein noted — and they cannot kill virus that is already hidden inside cells.

Having a daily preventive pill would be an even better solution, because pills can be synthesized in factories far faster than vaccines or antibodies can be grown and purified.

But even if one were invented, production would have to ramp up until it was as ubiquitous as aspirin, so 300 million Americans could take it daily.

Mr. Trump has mentioned hydroxychloroquine and azithromycin so often that <u>his news</u> conferences sound like infomercials. But all the experts agreed with Dr. Fauci that no decision should be made <u>until clinical trials are completed.</u>

Some recalled that in the 1950s inadequate testing of thalidomide caused thousands of children to be born with malformed limbs. More than one hydroxychloroquine study has been halted after patients who got high doses <u>developed abnormal heart</u> rhythms.

"I doubt anyone will tolerate high doses, and there are vision issues if it accumulates," Dr. Barry said. "But it would be interesting to see if it could work as a PrEP-like drug," she added, referring to pills used to prevent H.I.V.

Others were harsher, especially about Mr. Trump's idea of combining a chloroquine with azithromycin.

"It's total nonsense," said Dr. Luciana Borio, a former director of medical and biodefense preparedness at the National Security Council. "I told my family, if I get Covid, do not give me this combo."

Chloroquine might protect patients hospitalized with pneumonia against lethal cytokine storms because it damps down immune reactions, several doctors said.

That does not, however, make it useful for preventing infections, <u>as Mr. Trump has implied it would be</u>, because it has no known antiviral properties.

Several antivirals, including remdesivir, <u>favipiravir</u> and baloxavir, are being tested against the coronavirus; the latter two are flu drugs.

Trials of various combinations in China are set to issue results by next month, but they will be small and possibly inconclusive because doctors there ran out of patients to test. End dates for most trials in the United States are not yet set.

#### Goodbye, 'America First.'

Previously unthinkable societal changes have taken place already. Schools and business have closed in every state, and tens of millions have applied for unemployment. Taxes and mortgage payments are delayed, and foreclosures forbidden.

Stimulus checks, intended to offset the crisis, began landing in checking accounts this week, making much of America, temporarily, a welfare state. <u>Food banks are opening</u> across the country, and huge lines have formed.

A public health crisis of this magnitude requires international cooperation on a scale not seen in decades. Yet Mr. Trump is moving to defund the W.H.O., the only organization capable of coordinating such a response.

And he spent most of this year antagonizing China, which now has the world's most powerful functioning economy and may become the dominant supplier of drugs and vaccines. China has used the pandemic to extend its global influence, and says it has sent medical gear and equipment to nearly 120 countries.

A major recipient is the United States, through Project Airbridge, an air-cargo operation overseen by Mr. Trump's son-in-law, Jared Kushner.

This is not a world in which "America First" is a viable strategy, several experts noted.

"If President Trump cares about stepping up the public health efforts here, he should look for avenues to collaborate with China and stop the insults," said Nicholas Mulder, an economic historian at Cornell University. He has called Mr. Kushner's project "Lend-Lease in reverse," a reference to American military aid to other countries during World War II.

Dr. Osterholm was even blunter. "If we alienate the Chinese with our rhetoric, I think it will come back to bite us," he said.

"What if they come up with the first vaccine? They have a choice about who they sell it to. Are we top of the list? Why would we be?"

Once the pandemic has passed, the national recovery may be swift. The economy rebounded after both world wars, Dr. Mulder noted.

The psychological fallout will be harder to gauge. The isolation and poverty caused by a long shutdown may drive up rates of <u>domestic abuse</u>, <u>depression</u> and <u>suicide</u>.

Even political perspectives <u>may</u> shift. Initially, the virus heavily hit Democratic cities like Seattle, New York and Detroit. But as it spreads through the country, it will spare no one.

Even voters in Republican-leaning states who do not blame Mr. Trump for America's <u>lack</u> <u>of preparedness</u> or for <u>limiting access to health insurance</u> may change their minds if they see friends and relatives die.

In one of the most provocative analyses in his follow-up article, "<u>Coronavirus: Out of Many, One</u>," Mr. Pueyo analyzed Medicare and census data on age and <u>obesity</u> in <u>states that recently resisted shutdowns</u> and counties that voted Republican in 2016.

He calculated that those voters could be 30 percent more likely to die of the virus.

In the periods after both wars, Dr. Mulder noted, society and incomes became more equal. Funds created for veterans' and widows' pensions led to social safety nets, measures like the G.I. Bill and V.A. home loans were adopted, unions grew stronger, and tax benefits for the wealthy withered.

If a vaccine saves lives, many Americans may become less suspicious of conventional medicine and more accepting of science in general — including climate change, experts said.

The blue skies that have shone above American cities during this lockdown era could even become permanent.

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