

## What Have Been the Biggest Surprises with COVID-19?

The pandemic's effects have been far more wide-reaching than many health officials expected, but COVID has also accelerated some positive trends



### A CONVERSATION WITH ED KELLEY

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*Ed Kelley has been active in the field of global public health at the highest levels for more than 20 yrs.*

*Prior to joining ApiJect, Dr. Kelley served with the World Health Organization for 14 years, most recently as the Director of the Department of Integrated Health Services for the World Health Organization. He also created the WHO's first public-private collaboration working directly with pharmaceutical and the medical device industry to improve health services and patient safety and ran WHO's global injection safety efforts for a decade.*

*From 2003 to 2007 he served as Director of the U.S. National Health Care Reports in the U.S. Department of Health and Human Services, reporting directly to the HHS Secretary. Prior to this, he worked with USAID on several different health systems improvement projects in West and North Africa and Latin America.*

**INTERVIEWER:** Ed, many aspects of COVID-19 and the world's response to it have confounded expectations. Can you outline a few of the major surprises?

**ED KELLEY:** COVID has been a surprise in many ways, including how it works biologically, how it impacts patients, how to detect it, the best ways to treat it, and the complex ways that combatting a pandemic has ripple effects across our entire world's society and across the global economy that many health experts did not anticipate.

COVID comes with both an outbreak side and infection side that are very different from our recent experience with flu epidemics and also clinical management. It has struck every world region and every country. It has strained health systems much more than previous outbreaks going back a century. And, because it arrived during a period of massive world trade and interdependence, COVID has done unprecedented damage to the world's economy.

**In your view, what has been the single biggest surprise associated with this pandemic?**

I certainly did not expect that even after highly effective vaccines became widely available in the first half of 2021, fatalities from COVID would climb from 1.5 million (back in December of 2020), to today where we are on track to hit 5 million fatalities by November of 2021.

That would mean three and a half million people dying of COVID, since we've had these very effective vaccines – way more than half of all fatalities.

## How does COVID-19 compare to the major pandemics of the 20th and early 21st century in terms of fatalities?

COVID is far from the biggest pandemic we've ever had for sheer numbers of deaths. Since the 1980s, some 32 million people have died of HIV over the course of a very prolonged pandemic. With recent previous respiratory pandemics such as H1N1, about 12,000 people died in the U.S., so it was much, much, much milder than COVID has been.



But if we compare COVID to the 1918 Spanish flu, which spread in a rolling fashion across different parts of the world at different times, at that point you had about 1.8 billion people in the world, of whom about 500 million people became infected and estimates are that 50 to 100 million died. It's safe to say that one in three people around the world had this deadly 1918 influenza.

With COVID, right now with a global population of almost eight billion, the current caseload is over 265 million infected. So we're halfway to 1918 levels in absolute numbers, but obviously COVID has not yet infected one in three out of the total world population.

It's worth noting that the 1918 influenza was, quite deadly for young people and not as deadly for older folks. So it's hard to compare COVID to previous outbreaks in terms of biological scale or proportional fatalities. But clearly COVID will go down as having the biggest impact of any pandemic in history.

## Beyond high post-vaccine mortality rates, what have been some other major surprises regarding the biology of COVID?

The Delta variant was a big surprise. According to a CNBC story of Dec. 12, 2021, Delta is now about 99% of cases in the world (“Covid Cases on the Rise Again,” <https://www.cnbc.com/2021/12/04/covid-cases-on-the-rise-again-but-its-still-delta-not-omicron-driving-the-surge.html>). It's just overtaken all the other variants. Now we have the Omicron variant which most scientists believe will eventually take over from Delta. Yes, there was always discussion of potential variants emerging, but even among members of the scientific community who were mapping the mutations, in late 2020 relatively few people were voicing serious concerns about the possibility that a variant would break out that posed an even greater threat to the world's health.

At one point there were over 56 different variants of interests being tracked daily, and they are almost all lineages from the original Delta virus sequence. Today however, there are five variants of concern and two variants of interest. There are many more variants that are not being actively tracked. The scientific community is keenly aware that the longer the pandemic persists, the more variations will have a chance to emerge, and the more in danger we will be in.

### **What about the world's response to COVID, starting with clinical care?**

This has been another major set of surprises, both good and bad. On the plus side, COVID prompted a rate of improvement in clinical care that was simply amazing. At the same time, COVID exposed all of the cracks we have in our different healthcare systems.

On the positive side, we have seen -- and continue to see -- heroic efforts by healthcare workers. Anyone with respiratory knowledge and clinical training just worked 24/7 for weeks and months on end to combat the pandemic and save lives.

The initial fatality rates were high, 35% to 45% in some European countries. But clinical learning about optimal treatment happened quickly, so those fatality rates got under much better control. Clinicians got better at early diagnosis and getting vulnerable patients into intensive care quickly, which makes a difference. The entire world got on a rapid learning curve regarding testing, detection, case management and changes to clinical practice.

Some would say the speed of these changes is a miracle in itself. Medicine is not noted for embracing rapid change. At my old agency at WHO, we used to say that it took at least seven years for good evidence to get into practice. With COVID, we saw the world change its practice and its protocols in a few months. We've gotten much more testing, and on the whole, we do a better job of reliably detecting the virus. We have figured out how to manage patients better.

But the world's medical response to COVID would not have held together in many places, without these truly superhuman efforts by so many healthcare professionals around the world, whether you look at the U.S., Europe, or West Africa. That level of heroic, superhuman effort shouldn't be a necessary piece of your pandemic response. If you're relying on such ongoing sacrifices by health workers, it indicates a system weakness or breakdown. But those heroic efforts really helped the world combat COVID.

**The general consensus is that the world's biggest success in dealing with COVID-19 so far has been the rapid development of effective vaccines. Vaccine development, as we know, can take years if it can be done at all. The world is still waiting for an effective vaccine against HIV, for example, some 35 years or more after the virus first appeared.**



Exactly. And this is why the speed of vaccine development for COVID-19, a virus we've never seen before, using a platform we've never used before -- namely mRNA -- has been nothing short of remarkable.

At the end of January, 2020, at WHO's last in-person meeting on responding to COVID, everybody from the research and development community talked about the challenges of developing a vaccine under those circumstances. Before 2020 ended, this was accomplished by Pfizer, Moderna, and soon AstraZeneca, which uses a different platform.

But it was done with a real collective effort, with collective financing, with the idea that collective results would be shared, and that we would all benefit from the resulting vaccine. All of that adds up to an incredible piece of work.

**What are the biggest failures we've seen in combatting COVID, in your view?**

First, our biggest failure has got to be inequities in vaccine access and immunization rates. Second, the world was relatively late to recognize the true scope and full repercussions of the pandemic, both within the medical realm and across society as a whole.



**Why do such stark disparities in vaccine access and immunization persist, when so many countries and organizations have pledged to provide vaccines for everyone?**

As good as the world is at developing and producing new vaccines, we're very poor at making sure those vaccines are delivered to the point of care, and reach patients with the necessary support. That support includes

transportation, refrigeration, syringes and training for the workers who must administer the injections at population scale. The global health community is very good at the upstream challenges of detection and R&D. But it is very poor at covering "the last mile."

**Why?**

Many of the world's top health officials just assumed that vaccines get developed, they'll get rolled out. Then we produce the vaccines, but we fall short on delivery. That's the story of the past 30 years of immunization, and it's happened again where the COVID vaccine rollout has been extremely inequitable. It means wealthy countries get vaccines but Low- and Middle-Income Countries don't get them at all, or not as fast, and not in a form they can use.

But this inequity also happens in Western countries where we saw ethnic and racial minorities fall behind, and rural populations fall behind, in access and in vaccination rates. It seems we haven't learned anything from past experience.

I used to oversee the National Healthcare Disparities Reports at the U.S. Department of Health and Human Services, so I know we have spent decades publishing and talking about this challenge. Despite that, we've done a very poor job of addressing those issues and coming up with a different approach during this pandemic.

**Addressing some of these inequities is the mission of COVAX, the international vaccine cooperative led by the WHO, Gavi and CEPI (the International Coalition for Epidemic Preparedness Innovations). How do you assess their performance?**

COVAX was created to pool the purchasing power of smaller countries that can't compete on economic terms with the U.S. or China if there is a bidding war for vaccines or medical supplies. That is a reasonable premise, but a recent review commissioned and funded actually by COVAX raised flags for a number of areas of the coalition's work including its funding, its organization and whether it was on track to deliver on its promises.

Of the 6.8 billion COVID doses that were delivered worldwide by September of 2021, only 146 million came through COVAX. They lack unity of command, which may be why they've had three different strategies over the past 18 months. They were so ineffective in obtaining and deploying vaccines that many countries which had hoped to benefit from COVAX, finally went around COVAX and negotiated their own deals. In some cases, these low- or medium-income countries found themselves paying twice as much for vaccines than the prices that the European Union had negotiated for itself.



**Has “vaccine nationalism” played a role in COVAX’s difficulties?**

Yes. It is certainly true that COVAX faces very difficult problems, including insufficient funding. It obviously has not helped that a lot of that early vaccine deals were done by countries with very deep pockets, which reserved much of the original production for their own populations.

At the same time, it’s difficult to deny that there is also a lack of focus and commitment from COVAX board members who cannot override the interests or policies of their own countries. I think at some point when the global health community gets a chance to step back from this pandemic, take a deep breath, and assess the performance of the COVAX strategy for global equity and access, it will be agreed that very serious revisions are needed.

**You also mentioned the failure to see COVID as a “whole of society” problem, rather than just a public health challenge. Can you elaborate?**

Ideally, health experts, scientists and policymakers might have seen more quickly that this was not just a respiratory virus problem; it was a “whole of society problem.”

To begin with, the entire health system was so stressed by COVID that in many times and places, far more people got sick or died from non-COVID issues than should have, because they couldn't get access to care. COVID had taken up all beds and all the time, energy and attention.

Related to that, we really didn't recognize at first that COVID was much more than just a public health problem. For example, think of how many authorities waited until the end of the summer before realizing they faced an issue of reopening schools that fall or not. I don't see how the public health community and other leaders failed to grasp that schools are so much more than just learning centers; they are complex, multi-layered institutions that provide socialization for children, provide childcare for adults, and even provide essential nutrition for countless families. When you close them for any length of time, it leaves a huge gap in our society.

We have had a tremendous object lesson in the basic truth that commerce is connected with health, which is connected with social services, all of which are connected with policy.

**So public health is now recognizing itself as part of a vast ecosystem?**

Yes. Making one change in a seemingly limited, well-defined sphere of life may seem like a small, simple thing. But it can have ripple effects that extend far beyond what was foreseen or intended.

**Now that several effective vaccines have been approved and released to the public, what do you see as the largest challenges that we face in combatting COVID-19?**

Many challenges remain, but two that I'm focused on are public education about science, plus the physical requirements of packaging vaccine into ready-to-use formats and actually getting doses into people's arms around the world, as quickly and efficiently as possible. Both are gigantic undertakings.



**Let's talk first about science education and communication. How do you see this challenge?**

COVID-19 arrived as a novel virus. There was a lot we didn't know at first. We would have been better served to be honest with the public and say, "We're still learning about this. Here is what we think now, but our guidance may change as new information becomes available."

Unsurprisingly, many scientists would develop their opinion -- sometimes backed by science, sometimes not -- about for instance, the effectiveness of masks, or whether the virus spread through airborne transmission or from surface contact, among many other questions. Then they would stake out their favored theory as an immutable position.

Rather than being open to new conclusions from ongoing research, they looked for data to defend their original ideas. Group think and confirmation bias were definitely at work in many cases. Some of this is understandable, but I think it's pretty inexcusable to prolong debates out of pride and concern for professional standing, when lives are at stake.

**What's the cure?**

Scientists and science experts need to go through a learning curve regarding effective public education. This includes providing scientific explanations that the public can follow and trust. It also includes making accommodations for different cultures, even within the same country.

**And, as you mentioned earlier, intellectual humility. In the pandemic's early stages, conflicting forecasts and recommendations were often announced with absolute certainty. Then the guidance changed 180 degrees in some cases. That makes it hard for the public to trust official announcements.**

One of things that keeps me up at night is this education issue.

**And yet the public has not shown itself terribly inclined to trust official statements about COVID anyway, regardless of whether the forecasts are hopeful or scary.**

That's one more factor making public education about science such a challenge. Traditionally, it was possible to persuade people with personal stories in the media: "My dad got his vaccination, and it's been good for him, so now I'm getting it." That approach is not resonating with COVID-19; it is not reducing vaccine hesitancy.

**The second major challenge you identified is the physical requirements to package, distribute and administer individual doses of vaccine.**

As COVID vaccines began rolling out, a Swiss policymaker admitted to me that he thought medical supply chains “just worked,” without anyone having to think about them -- like turning on the light switch and getting power. It’s been a shock to many world leaders to realize that they can’t automatically count on having enough glass vials and enough syringes to vaccinate their populations, certainly not with the speed required to meet global demand.

**Now that we’ve had a year of vaccine availability, have the necessary lessons been learned about the need to strengthen the global supply chain for medical equipment?**

Regrettably, no. In the pandemic’s early stages, when the issue was ventilators or PPE, you would hear someone from WHO say: “There’s a big shipment to Nigeria, but I just talked to our regional person who’s up at then the Northeast part of the country and they don’t have anything. It’s all just sitting in a storehouse in Lagos. They have no way to transport it to the remote corners where it’s needed.”

This story is happening again with vaccine shipments. Sometimes they’re getting to countries, but those doses cannot be administered to people who need them because of cold chain issues, or because of transport issues, or lack of funding for syringes, administrators, fuel and drivers – all the operational costs. The global health community remains very focused on commodities. We buy material, and then it’s up to someone else to make sure it gets delivered and used.

**In October of 2021, the WHO announced that the world may be short as many as two billion vaccine syringes next year. Your own estimate is closer to five billion.**

No question, there is going to be a drastic shortfall for many kinds of syringes. The WHO had already announced that in 2020, an estimated 23 million children around the world were failing to receive routine immunizations each year, because those syringes were being diverted to giving COVID vaccine to adults.

This can be expected to result in many fatalities among children. COVID can be deadly, especially among the elderly and the immuno-compromised, as we know. Unfortunately, it’s much more deadly for kids to be un-vaccinated for measles, than to have adult populations un-vaccinated for COVID.

But if there are only limited number of syringes available, then it’s a zero-sum game out there.

**You have also explained that this shortage of vaccine syringes is the reason why new technology for high-speed, high-volume, high-quality aseptic fill-finish capacity is valuable to global immunization efforts against COVID and against routine diseases.**

Yes, there are innovations coming online in the packaging of injectable drugs and vaccines that we would all have liked to see happening “on the merits,” even without the prod of an historic global emergency.

But now that the emergency is here, governments and industry are realizing how valuable this technology can be. Long-term, I’m optimistic that between the science, the technology and the public policy learning curve, we’ll eventually succeed in making COVID-19 reasonably manageable.

**Thank you, Ed.**