



An elderly man receives the Covid-19 vaccine in Kuala Lumpur on June 7, 2021.
PHOTOGRAPH BY AFIF ABD HALIM, NURPHOTO VIA GETTY

SCIENCE | CORONAVIRUS COVERAGE

Why even fully vaccinated older people are at high risk for severe COVID-19

Many factors weaken the aging immune system. But vaccines—and booster doses—do offer protection from hospitalization and death.

BY AMY MCKEEVER



Mounting data suggest that older people are at higher risk of severe disease from a breakthrough infection of COVID-19—and scientists say that should come as no surprise. After all, older age brackets have been disproportionately at risk throughout the pandemic, and that continues to be true even once someone is fully vaccinated.

Concerns about breakthrough infections bubbled up again this week when news broke on October 18 that former Secretary of State Colin Powell had died after contracting COVID-19. Powell was 84, but his cause of death was more complex: The former statesman suffered from multiple myeloma, a cancer of white blood cells. People with this form of cancer tend not to respond well to vaccines.

But in addition to the immunocompromised, health officials are seeing worrying evidence that older age groups continue to be at higher risk from the pandemic. According to the latest data from the Centers for Disease Control and Prevention, people over 65 account for 67 percent of hospitalizations and 85 percent of deaths from breakthrough cases. And recent media reports citing data from Seattle, Washington, and the United Kingdom show that older vaccinated people face similar—and, in some cases, greater—risks of severe disease than unvaccinated children.

“The huge risk factor is age,” says William Petri, an immunologist at the University of Virginia. That’s why the U.S. prioritized vaccinating older people and those in long-term care facilities when it first rolled out the vaccines, he explains. “If you’re under 45, your chances of dying are almost nonexistent, and then it increases exponentially.”

Concerns over breakthrough infections are also why U.S. regulators have approved booster doses of the Pfizer vaccine for people over 65—and are poised to do the same for the Moderna and Johnson & Johnson jabs. (*Why the CDC and FDA only approved booster shots for some Americans.*)

Here's what scientists know about the aging immune system—and why breakthrough infections don't change the fact that COVID-19 vaccines remain remarkably effective for people at any age.

Aging immune systems

Experts say they still don't have an adequate explanation for why older people were more susceptible to COVID-19 even before vaccines were available. "It's just one of the great mysteries of the virus," says Deepta Bhattacharya, an immunologist at the University of Arizona.

Scientists who study aging say it likely has to do with some of the hallmarks of getting older. For example, the human body normally clears away cells that have become damaged due to disease, injury, or stress. But as the body ages, this process becomes less efficient, and it starts to accumulate so-called senescent cells, which are damaged but won't die. These cells secrete chemicals that damage neighboring healthy cells and trigger inflammation. Senescent cells thus weaken the body and make it harder to fight off infections.

But there's a lot more going on in an aging body, and many elements of aging likely work together to undermine the immune response, says Eric Verdin, president and chief executive officer of the Buck Institute for Research on Aging, a biomedical research group based in California.

Among older people, he says, there are two broad abnormalities of the immune system: a hyperactive innate response, and an underactive adaptive response.

Innate immunity is the defense system you were born with—and the first to respond to invaders. It doesn't target a specific pathogen, but rather mounts a generic inflammatory response. When that response is inappropriately intense, as happens in older people, it can trigger a cascade of damage throughout the body, from the lungs to the heart to the kidneys. ([Here's what the coronavirus does to the body.](#))

The adaptive immune response targets a specific invading pathogen. Vaccines provide a preview of the germ and teach the body how to create antibodies that recognize and latch onto a virus and block it from entering any of the body's cells. If the virus does manage to break through, then T cells join in and kill the infected cell. Verdin likens it to an army that defends the body from attackers. If the amount of virus is small, the antibodies and T cells can easily defeat it.

A larger viral force, however, can overwhelm the adaptive immune system. Older people, who are less able to mount a vigorous adaptive response, may therefore be particularly susceptible to breakthrough infections.

“Everything gets worse with age, is the bottom line,” Bhattacharya says.

Breakthrough infections

Annual flu shot drives have shown that age can dampen the effectiveness of some vaccines. Verdin says a third of people over age 70 don't respond at all to the flu vaccine, which is why it still kills a disproportionate number of older Americans every year.

On the other hand, responses to COVID-19 vaccines have been a lot stronger. “I think one of the more surprising things is how well the mRNA vaccines did with those older populations,” Bhattacharya says. “If you look at the initial immune responses, they weren't very much different at all between people over 65 and those below. So that was a pretty pleasant surprise.”

However, in September the CDC reported that the vaccines are only about 78 percent effective at preventing infection among people of all ages after six months. It's unclear exactly what is responsible for this drop in effectiveness. Bhattacharya says some studies do show that immunity is waning in people over 65, but he points out that it could also be caused by the rise of the Delta variant, which has proven better able to evade the body's immune response.

In late September, *New York* magazine's David Wallace-Wells wrote of "the overwhelming age skew of the disease" even among the vaccinated, citing data from the United Kingdom showing that vaccinated people over 60 died from COVID-19 at higher rates than unvaccinated people under 50. The *New York Times* also recently wrote about hospitalization rates in the Seattle area, which show that the risks for vaccinated people in their 50s are similar to the risks for unvaccinated children under age 15.

Bhattacharya says he doesn't like comparing the two age groups, arguing that it's much more important to compare the risks among unvaccinated versus vaccinated people no matter their age. These data clearly show that everyone benefits from a vaccine: In the U.K., for instance, the death rate for unvaccinated adults is several times higher than it is for vaccinated adults in every age group.

And despite the drop in effectiveness in preventing infection, the Pfizer vaccine remains 90 percent effective at preventing hospitalization, which shows that it remains a solid defense against severe disease and death. A recent report published by the U.S. Department of Health and Human Services said that vaccines "may have helped prevent hundreds of thousands of new COVID-19 infections and tens of thousands of deaths among seniors."

Bhattacharya says that federal regulators in the U.S. have approved boosters for people over 65—and not the general population—because of the extra risks that they face. He and other scientists emphasize that high-profile breakthrough infections and the approval of booster shots should not discourage anyone from getting vaccinated. On the contrary, it should be seen as confirmation that the vaccines work.

“Rest assured, these are the best vaccines we’ve ever had,” Petri says.

Verdin agrees: “Getting vaccinated really puts things on your side. Think about it as a war where you want to have all the ammunition that you can possibly have.” 🟡