Pfizer’s anti-COVID pill Paxlovid shows no benefit for younger adults

Benjamin Mateus
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In its latest guidelines, from August 8, 2022, the US National Institutes of Health (NIH) gave one of its strongest recommendations to Paxlovid for patients at high risk of progressing to severe COVID-19, regardless of vaccination status. The list of underlying medical conditions that raise one’s risk of severe COVID-19 is long and accounts for more than four out of 10 adults (138 million Americans, including 54 million who are 65 or older). Close to 4 million prescriptions have been filled since Paxlovid was authorized.

However, the results of a new retrospective observational study out of Israel published in the *New England Journal of Medicine* (NEJM) seem to place a question mark over the strength of these recommendations, in particular, with the Omicron subvariant.

The report’s authors found that Pfizer’s antiviral medication Paxlovid offered little to no benefit for younger adults. However, it did reduce the risk of hospitalization for high-risk seniors. Notably, supplementary material from the original study of Paxlovid in high-risk non-hospitalized adults with COVID-19 during the Delta wave had demonstrated benefits in those younger than 65, albeit the difference compared to the placebo was much less than in those 65 and older.

The study’s authors utilized the electronic medical records from almost 110,000 patients enrolled in Clalit Health Services, Israel’s largest state-mandated health service organization. Nearly 4 percent, or 3,900 of the patients, had taken Paxlovid (nirmatrelvir) after contracting COVID-19.

Among those over 65, there was a 73 percent decrease in the hospitalization rate and a 79 percent reduction in the risk of death. However, patients between the ages of 40 and 65 saw no benefit in taking the antiviral medication in either category, regardless of previous immunity status.

One of the study’s primary limitations is that it was non-randomized, which can introduce bias in its conclusions. The authors remarked: “Our study showed that only a minority of patients who were identified as high risk and eligible for nirmatrelvir [Paxlovid] therapy received the antiviral therapy. We do not know why other eligible patients did not receive treatment, and there may be some selection mechanism that is not explained by the observed confounders.”

These findings have significant implications, as the use of Paxlovid is rising amidst repeated surges of infections that run roughshod over the population, as COVID-19 is allowed free reign as a matter of policy. People are turning to these medications to reduce their risk of severe disease and lessen their symptoms, without a clear understanding among patients, medical providers and pharmacies of the indication for these drugs. This has consequences for the availability of and access to these medications and raises additional issues, such as the potential development of a Paxlovid-resistant variant.

In the context of potential misuse of Paxlovid, the recent announcement before the US Chamber of Commerce Foundation by White House COVID-19 response coordinator Dr. Ashish Jha that the Biden administration will soon be shifting responsibility for procuring tests and therapeutics to the commercial sector has dire consequences for the working class.

On the near horizon is the lifting of the pandemic emergency measures that cover COVID-related care for all Americans. The implications of returning to the usual business of medicine is that those who are uninsured or underinsured will forgo these life-saving measures when they contract COVID-19 so as to save money for groceries and fuel or pay their rent. Even the new bivalent vaccines will arrive with a price tag. Meanwhile, the more affluent will have no qualms in accessing them, further deepening the class distinctions that the pandemic has exposed.

However, the results of the recent study out of Israel are not surprising. In June, Pfizer announced it was discontinuing enrollment in its EPIC-SR [Evaluation of Protease Inhibition for COVID-19 in Standard-Risk] trial. Preliminary results indicated it had no significant benefits for unvaccinated adults without any risk factors or for previously vaccinated people with at least one risk for progressing to severe disease.

Another critical study from Hong Kong published in *Lancet Infectious Diseases* on the same day as the Israeli study but which went unmentioned in the press offered further evidence of Paxlovid's limited therapeutic role. The authors reviewed their clinical experience with Paxlovid and Lagevrio, Merck's antiviral pill, Molnupiravir, in hospitalized patients. They compared them to hospitalized patients who did not receive those medications during the horrific wave of infections that slammed into the semi-autonomous region in February and March.

Though Lagevrio has been essentially dismissed for its comparatively lower efficacy (30 percent versus 90 percent in initial trials) compared to Paxlovid, a head-to-head test has never been conducted. However, the *Lancet* study found that hospitalized patients receiving either oral antiviral medication had a reduced chance of dying compared to those who did not receive them.

The mortality risk reduction for Lagevrio was 52 percent, and for Paxlovid it was 66 percent. Those receiving antivirals had a lower risk of their disease progressing, but the drugs did not significantly impact their need for mechanical ventilation or ICU admission. The patients in the study averaged in age from mid-70s to early 80s.

The authors wrote: "Results of our subgroup analyses suggested a possible lack of significant benefit in younger patients (aged ? 65 years) and those who had been fully vaccinated, which would support prioritizing the prescription of oral antivirals to older people and those not adequately vaccinated, who are also likely to be at increased risk of progression to severe COVID-19."

Given the results of these studies, it bears mentioning that the Centers for Disease Control and Prevention (CDC) has recently estimated that approximately 95 percent of Americans aged 16 and older have some level of immunity against COVID-19.

Dr. David Boulware, a University of Minnesota physician and researcher, told *MarketWatch*, "Paxlovid will remain important for people at the highest risk of severe COVID-19, such as seniors and those with compromised immune systems. But for the vast majority of Americans who are now eligible, this really doesn't have a lot of benefit."

These studies come on the heels of recent reports that First Lady Jill Biden, who was recently infected with COVID-19, was confirmed to be reinfected, having suffered a rebound infection after completing her Paxlovid course. She is in isolation again. Meanwhile, President Joe Biden is donning his mask for the proscribed 10 days as a close contact, per the new CDC guidelines.

Though it was assumed that rebound was a rare phenomenon, the repetition of the phenomenon first in Dr. Anthony Fauci, then President Joe Biden and now his wife Jill Biden brings to the fore the question of whether rebound is far more common than most had anticipated in an Omicron-dominant pandemic.

The US Food and Drug Administration (FDA) has tasked Pfizer with conducting a trial to be completed by September 30 of next year to see if a second five-day course of the drug would help prevent the "rare" phenomenon. The official request was sent by letter on August 5 during Biden's second convalescence.

Pfizer responded in an email confirming the assignment, saying: "We are working with the FDA to finalize a protocol to study patients who may be in need of retreatment. We will share updates in due course." However, as experts have noted, there do not appear to be any additional benefits from the second course of Paxlovid in regard to preventing severe disease and hospitalization.

In April, *Bloomberg* reported that the Biden administration was "on the hook to pay Pfizer nearly $5 billion for pills it's already ordered to treat COVID-19." The White House was planning to use the $10 billion in COVID-19 funding from the Senate to cover the cost of 20 million courses of the COVID-19 antiviral pills. The other half has been designated for purchasing the bivalent COVID-19 boosters. However, as funding has been exhausted, there has been a decisive shift to commercializing these treatments, leaving millions in the lurch as the fall and winter seasons fast approach.

Meanwhile, Pfizer is teaming up with the Chinese pharmaceutical firm Zhejiang Huahai in a five-year deal to manufacture and sell Paxlovid exclusively in China. Huahai announced the agreement on August 17, though Pfizer has remained publicly silent.

In February, the drug was given emergency use authorization in China, where a large part of the elderly population has remained unvaccinated and at risk of severe COVID-19 should an outbreak reemerge in the only remaining country that has maintained a Zero-COVID policy.