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COVID-19 Vaccines Saved Lives

Richard Simoneaux Steven L. Shafer, MD, FASA
Editor-in-Chief

In a late December 2021 *Nature* article, Mallapaty et al. highlight the impact that the discovery and implementation of vaccines against SARS-CoV-2 have had globally (*Nature* 2021;600:580-3). At the time of the article, they estimated that more than 4.4 billion people worldwide, roughly 56% of the world's population, had received at least one vaccination dose against SARS-CoV-2. As the authors note, the development of dozens of vaccines – including novel platforms, followed by clinical trials, regulatory approval, manufacturing, distributing, and eventually administering doses to 4.4 billion people – represents an amazing "triumph for science and research."

Lives saved in the United States

A study published in *JAMA Network Open* in January 2022 looked at estimated effects of vaccination in the

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Brain Health and the EEG: Toward Personalized Anesthesia Care for Older Patients

Patrick L. Purdon, PhD Daniel J. Cole, MD, FASA

The brain under anesthesia is a marvel to behold. Although the electroencephalogram (EEG) is not a routine part of clinical anesthesia care, there is growing evidence that readily visible changes in the anesthesia-induced EEG are intimately linked to perioperative brain health.

Induction of general anesthesia with propofol produces stereotyped oscillations or waves in the EEG that change form in a dose-dependent manner related to the patient's state of consciousness (*Anesthesiology* 2015;123:937-60). After administering an induction dose of propofol, as a patient becomes sedated,

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Guest Editor: Lilian Kanai, MD, MBA, FASA, FACHE

The Trillion Dollar Six-Pack of Publicly Traded Health Insurance Companies

Thomas R. Miller, PhD, MBA

I wrote this column in February, that exciting time of the year when most publicly traded companies submit Form 10-K to the U.S. Securities and Exchange Commission. The 10-K is a comprehensive report filed each year to inform potential investors about a firm's financial condition. So, I reviewed the 10-Ks of the largest publicly traded health insurance companies as I was curious about their financial health.[1] In 2021, the six largest companies racked up more than $1,102,000,000,000 in revenues, a 23% increase over just two years earlier. These six companies, listed in descending order of 2021 revenue, are CVS Health Corporation, UnitedHealth Group Incorporated, Cigna Corporation, Centene Corporation, Anthem, Inc., and Humana Inc.

Big money, big mission

Table 1 provides summary revenue and income data for the six largest publicly traded (i.e., for-profit) health insurance companies. The $1.1 trillion revenue figure substantially exceeded the U.S. military budget in 2021 (asamonitor.pub/3hGjPuE), and it would place this health insurance "six-pack" in the 17th spot in the gross domestic product (GDP) rankings by country (asamonitor.pub/3hDBEu7).

Figure 1 presents the relative stock price performance of these six companies from January 2, 2020, to March 30, 2022.

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PERIODICALS

In the Know: Vaccines Saved Lives

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U.S. from October 1, 2020 (prior to vaccine emergency use authorization) through June 30, 2021 (*JAMA Netw Open* 2022;5:e214725). The study was based on a model previously published by the authors and expanded to include the transmission dynamics of the Alpha, Gamma, and Delta variants (*MedRxiv* July 2021). The authors compared cases, hospitalizations, and deaths through June 28, 2021, with two alternative scenarios: one in which no vaccines were given, and one in which only half of the administered doses were given.

In the no-vaccination scenario, the authors estimated that vaccination in the U.S. prevented more than 14 million cases, 1,133,617 hospitalizations, and 240,797 deaths. In their scenario in which vaccination uptake in the U.S. was halved, vaccines prevented 336,000 hospitalizations and 77,283 deaths.

The averted deaths speak for themselves. The report does not discuss the implications of such large reductions in hospitalizations. It has been estimated that the median hospital cost in the U.S. for a patient with COVID-19 is $12,000 (*J Med Econ* 2021;24:308-17). The economic savings from fewer hospitalizations is roughly $13.6 billion. Long COVID affects one- to two-thirds of hospitalized patients (*JAMA Netw Open* 2021;4:e2128568). Vaccination averted at least 100,000 cases of long COVID, sparing individuals, and the health care system, the burdens of sustained neurologic impairment, respiratory disorders, psychiatric illness, and impaired mobility and function.

Each state is responsible for implementation of vaccination policies. This creates a natural experiment to evaluate the link between vaccination and deaths. If we graph the percent age of the population vaccinated on the X axis, and the per capita death rates on the Y axis, we can see whether vaccination reduced deaths. The natural experiment is slightly biased because the initial wave of infections and deaths was concentrated in northeastern states, potentially reducing subsequent deaths after the availability of vaccines. Nevertheless, the results seen in the figure are not ambiguous. States with the highest rate of vaccination have reported the lowest per-capita death rates since the introduction of vaccines.

Richard Simoneaux is a freelance writer with an MS in organic chemistry from Indiana University. He has more than 15 years of experience covering the pharmaceutical industry and an additional seven years as a laboratory-based medicinal chemist.

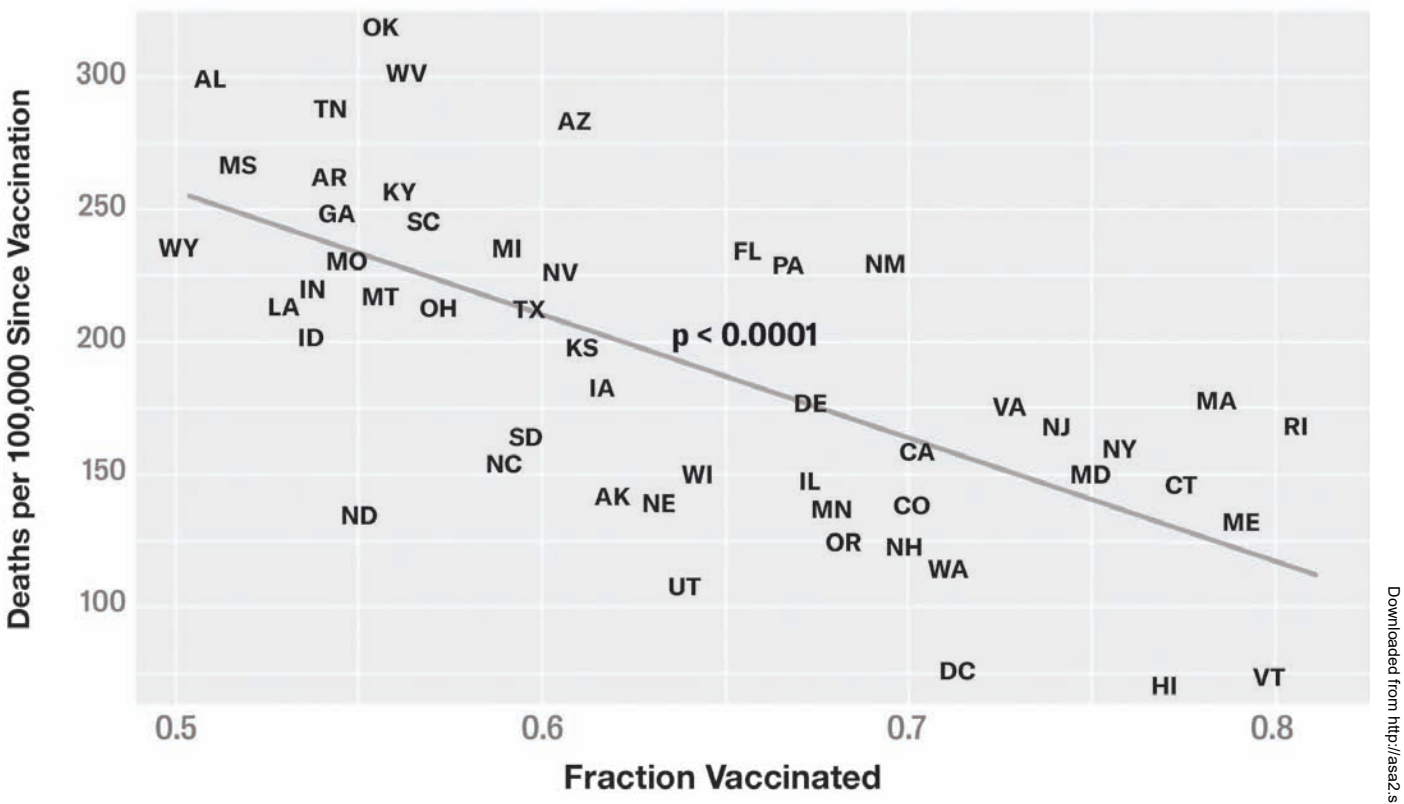

Figure: Deaths per 100,000 population are reduced by more than half with increasing vaccination rates. The deaths are from the Johns Hopkins Coronavirus Resource Center from December 21, 2020 through March 12, 2022 (asamonitor.pub/3MKoSZc; asamonitor.pub/3w94ZFh). Vaccination data are from the CDC (asamonitor.pub/36gol0u).

Lives saved in Europe

The World Health Organization evaluated data from the European Surveillance System to assess the number of deaths averted by vaccination in 33 countries (*Euro Surveil* 2021;26:2101021). The study only considered deaths in patients 60 years of age or older from December 2020 (when vaccines were introduced) through November 2021. These individuals accounted for approximately 90% of the 1.5 million COVID-19-caused deaths in Europe during the study interval.

"The wealthy nations that developed the vaccines have, understandably, prioritized these interventions for their own citizens. However, since the pandemic isn't over anywhere until it is over everywhere, making vaccines available globally would appear to be a priority for all nations to save lives and end this pandemic."

The authors estimated that vaccination averted 469,186 deaths in individuals 60 years or older. Countries with the highest early vaccine uptake, such as Israel, Malta, and the U.K. (England and Scotland), had significantly reduced mortality, particularly in those 80 years or older.

Some countries were noted to have a smaller-than-expected vaccination impact. The authors offered two possible explanations. The first was a slower rollout of vaccines, as was observed in Moldova, Romania, and Ukraine. The second explanation was that vaccination followed a significant wave of SARS-CoV-2 transmission in early 2021, as was observed in Poland, Croatia, and the Czech Republic.

The authors, when discussing possible limitations of their study, noted that "we did not estimate the indirect effect of vaccination or the impact of public health and social measures on mortality by reduction in transmission." In other words, the estimate of lives saved is likely conservative. The authors also noted that their analysis did not differentiate among vaccines, assuming equal efficacy of all vaccines against all variants.

Lives saved in Israel

Some of the best data on vaccine efficacy has come from Israel, which exclusively used the Pfizer BNT162b2 vaccine. A paper in *The Lancet Infectious Diseases* estimated that from December 20, 2020 through April 10, 2021, vaccinations averted 158,665 infections, 24,597 hospitalizations, and 5,532 deaths (*Lancet Infect Dis* 2022;22:357-66). Two-thirds of the averted hospitalizations and 90% of the averted deaths were in individuals 65 years of age or older. The authors concluded that "without the national vaccination campaign, Israel probably would have had triple the number of hospitalizations and deaths compared with what actually occurred during its largest wave of the pandemic to date." Unfortunately, more SARS-CoV-2 waves were in store for Israel and the world.

In late December 2021, two different Israeli studies evaluating the effectiveness of boosters were published in the *New England Journal of Medicine*. Arbel and colleagues modeled the effectiveness of the booster at preventing death over the 54-day period from August 6 to September 29, 2021 in individuals 50 years or older (*N Engl J Med* 2021;385:2413-20). The authors compared the incidence of death in 843,208 individuals, of whom 90% received a booster dose during the study period. Over the 54-day observation interval, the booster dose decreased mortality from 161 per 100,000 individuals to 8.6 per 100,000 individuals. After adjusting for covariates (e.g., age), the authors concluded that booster doses reduced the risk of death by 90% over the observation interval ($P<0.001$) and averted 1,156 deaths among individuals receiving boosters.

Using data from the Israel Ministry of Health, Bar-On and colleagues evaluated booster efficacy in 4,696,865 individuals 16 years of age or older over the interval from July 30, 2021 to October 10, 2021 who had received two doses of the BNT162b2 vaccine (*N Engl J Med* 2021;385:2421-30).

The primary analysis compared two different groups: those who had not received a booster shot (non-booster group) and those who had received a booster shot at least 12 days earlier (booster group).

In all age groups, there was a reduction in the rate of confirmed infection starting six days after administration of the booster dose. In the primary analysis, the booster dose resulted in a 10-fold reduction in infections. The difference in infection rate was greatest in individuals 16-29 years of age (17-fold), and the lowest was in individuals 30-39 years of age (nine-fold). The booster dose reduced the rate of infection 12-fold in individuals 60 years of age or older.

The booster dose resulted in a 22-fold reduction in severe illness among those 40-59 years of age, an 18-fold reduction in severe illness among those 60 years of age or older, and a 15-fold reduction in the rate of death for those 60 years of age or older. Based on these findings, the booster doses are estimated to have saved 236 lives over the study duration in those over 60 years of age.[1]

[1]16,768,943 x (288 / 17,909,789) – 34 (see table 3, page 2427. *N Engl J Med* 2021;385:2421-30)

Vaccine equity

The impact of vaccination could have been greater with a more equitable global sharing of vaccines. Mallapaty and colleagues noted that some countries (e.g., Chile, Cuba, and the United Arab Emirates) administered more than 200 vaccine doses per 100 people, while less affluent countries (e.g., Afghanistan, Papua New Guinea, and Tanzania) administered vaccines to fewer than 20% of the population (*Nature* 2021;600:580-3). The authors lament that "It was expected that poorer nations would get increased supplies once demand fell in wealthy nations, but most rich countries are now administering boosters." The wealthy nations that developed the vaccines have, understandably, prioritized these interventions for their own citizens. However, since the pandemic isn't over anywhere until it is over everywhere, making vaccines available globally would appear to be a priority for all nations to save lives and end this pandemic. As we previously noted, "Nations able to afford vaccination must assist nations that cannot afford mass vaccination to bring the pandemic to an end" (*ASA Monitor* 2021;85:1-7).

Even wealthy countries demonstrate inequity in vaccine availability. A report by the Centers for Disease Control and Prevention (CDC) found that "disparities are associated with socioeconomic status and household composition and disability, particularly in large fringe metropolitan areas" (*MMWR Morb Mortal Wkly Rep* 2021;70:818-24). The figure on page 4 graphically demonstrates these disparities, as the states with low vaccination rates are associated with higher levels of poverty.

The rapid development and administration of SARS-CoV-2 vaccines is a triumph of modern science. It is also a tribute to the ability of scientists, industry, and the government to effectively partner when faced with an existential threat such as the SARS-CoV-2 pandemic. Vaccines altered the course of the pandemic and averted millions of cases, hospitalizations, and deaths. It is worth taking a moment to reflect on this unprecedented scientific achievement and be grateful for the contributions of vaccines to profoundly reduce the burden of many of the most feared communicable diseases, including SARS-CoV-2. ■