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Wither COVID? How the Pandemic Ends

Richard Simoneaux

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

*“This is the way the world ends
This is the way the world ends
This is the way the world ends
Not with a bang but a whimper.”*

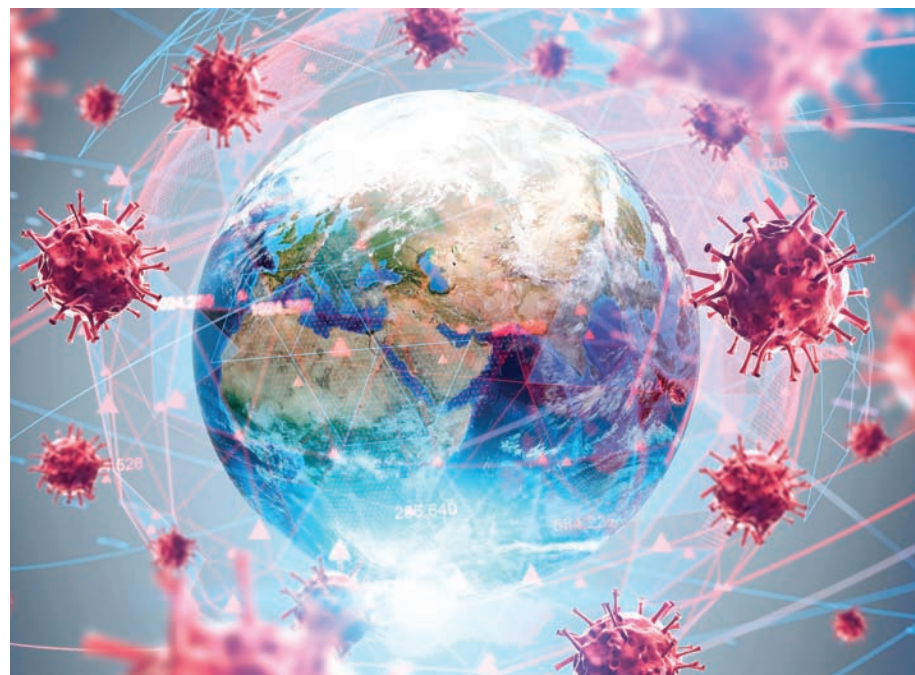
T.S. Eliot

In January 2021, Public Health England initiated a comprehensive strategy to monitor vaccination efficacy and safety (asamonitor.pub/3vnt0G9). Since then, Public Health England has monitored vaccination,

serology (collected from blood donors), and outcomes (hospitalization and death). The serological analysis involved testing 250 samples every week from blood donors for antibodies.

According to the most recent COVID-19 Vaccine Surveillance Report (as of this writing), published on October 14, 2021, 65% of the U.K. population had received one dose of vaccine and 60% had received two doses (asamonitor.pub/30rkWc3).

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Honoring Our Humanitarians

Cheryl K. Gooden, MD, FASA, FAAP

Elizabeth T. Drum, MD, FAAP, FCPP, FASA

Nicholas M. Greene, MD, (1922-2004) joined Yale as Director of Anesthesiology at Yale New Haven Hospital in 1955. He became the founding chair in 1971 at the Yale University School of Medicine in the Department of Anesthesiology. Dr. Greene served as chair of the department until 1973 and continued on as a professor in the department until 1987 when he became professor emeritus.

In the 1980s, Dr. Greene traveled to East Africa, where he observed a need to improve the level of anesthesia care

there. Dr. Greene was able to garner the support of ASA and the Foundation for Anesthesia Education and Research (FAER) for the inaugural funding of the Overseas Teaching Program (OTP). In October 1989, the ASA House of Delegates approved a five-year OTP that would be based in East Africa. This sustainable teaching program, along with other activities, continues within the Committee on Global Humanitarian Outreach (GHO), which is proud to honor this year's humanitarians.

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Catching Up With Warren M. Zapol, MD

The ASA Monitor sat down with Dr. Warren M. Zapol, a key opinion leader in anesthesiology, for his insights on the specialty. Dr. Zapol is the Reginald Jenney Distinguished Professor of Anaesthesia at Harvard Medical School, as well as Anesthetist-in-Chief Emeritus at Massachusetts General Hospital (MGH). As an influential researcher and scientist, Dr. Zapol's successful trials involving the use of inhaled nitric oxide (NO) therapy in newborns are responsible for the adoption of NO therapy for hypoxemic newborns in neonatal intensive units throughout the country.



Warren M. Zapol, MD

in newborns with persistent pulmonary hypertension and adults with primary pulmonary hypertension. Did this come to you in a single “Ah ha!” moment, or was it the culmination of years of investigation into the pulmonary vascular resistance?

Dr. Zapol: After many years investigating the pulmonary vasculature in animals and human ARDS patients, with help from many in our MGH team (pathologists, radiologists), we studied dilating constricted pulmonary vessels with I.V. drugs. Unfortunately, the drugs produced systemic vasodilation, hypotension, and increased pulmonary shunting. One day in 1989, I was at UCLA looking into whether to pursue a position as chief of anesthesiology. There, I met a pharmacologist, Lou Ignarro, PhD, who studied NO. NO is a dilator molecule made in blood vessels from arginine, and Lou would go on to get the Nobel Prize in Physiology and Medicine in 1998 for this

ASA Monitor: *Your insight that inhaled nitric oxide could dilate the pulmonary vessels without causing systemic hypotension has saved countless lives*

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SPECIAL SECTION

Discovering Alignment
(The ‘Burnout’ Issue)

24-30

Guest Editor: Natalya S. Hasan-Hill, MD

In the Know: Pandemic

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Serological surveillance indicates that 95% of the entire U.K. population has antibodies to the spike protein, including 99% of U.K. adults over the age of 60 (asamonitor.pub/2YYZYk6). The U.K. is now in the “end game,” where most adults have antibodies. What does it look like? What does it mean for the United States?

The first observation is that high levels of seropositivity don’t bring either cases or deaths to an end. Figure 1 shows the COVID-19 time series for

“Even though cases and deaths are declining, and immunity is rising, the U.S. picture remains grim. We are still seeing about 1,000 deaths per week.”

England as of this writing (October 17, 2021). Since August, cases and deaths have been remarkably constant. Deaths are averaging about 1,000 per week. That’s almost an order of magnitude less than the number of deaths in December and January, but still horrific. Cases are running about 300,000 per week, which is a considerable health care burden.

As discussed in the October “In the Know” column, the high case numbers in the U.K. reflect offsetting effects of increased infectiousness of the Delta variant and increased resistance to infection conferred by vaccination (ASA Monitor 2021;85:1-13). Every week, the U.K. Health Security Agency publishes the efficacy of the three available vaccines. As shown in Table 1, the Pfizer BNT162b2 vaccine is more efficacious than the AstraZeneca vaccine. The primary utility

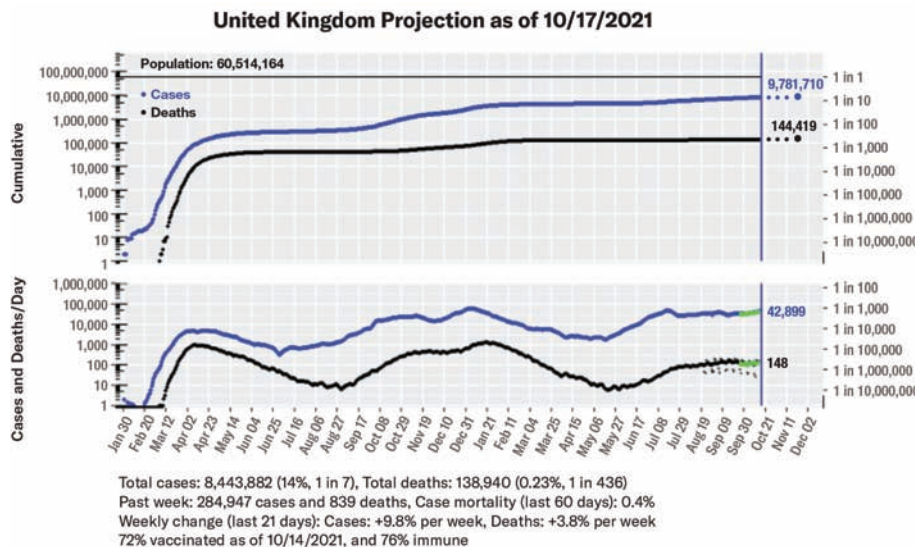


Figure 1: Current time series for the U.K.* Case and death rates are from the archive at Johns Hopkins University. Vaccination data is from Our World in Data (Oxford). Vaccination data are for at least one dose, not full vaccination. * From Steve Shafer’s Weekly Covid Update (see <https://groups.google.com/u/1/a/slsafer.com/g/steves-covid-19-updates>)

of the vaccines is not in preventing cases but in preventing hospitalization and death.

Since adults were vaccinated earlier than adolescents and children in the U.K., it isn’t surprising that most of the current infections are in children and teenagers, as shown in Figure 2. As expected, most of these cases are in unvaccinated kids, as shown in Figure 3.

Figure 3 suggests that vaccination is increasing the rate of infection in those over age 40. Wow – is that possible? Are vaccinations increasing the rate of infection in those over 40?

The answer, of course, is that vaccinations are not raising the rate of infections. As the U.K. Vaccine Surveillance Report suggests, “even with a highly effective vaccine, it is expected that a large proportion of cases, hospitalisations and deaths would occur in vaccinated individuals, simply because a larger proportion of the population are vaccinated than unvaccinated and no vaccine is 100% effective.”

As shown in Figure 4, vaccination provides excellent protection against death. Additionally, nearly all hospitalizations and deaths in vaccinated individuals re-

fect comorbidities (*Clin Microbiol Infect* July 2021). These observations are consistent with the vaccine efficacy reported in Table 1.

As noted by William Haseltine, vaccination is the cornerstone of controlling the pandemic (asamonitor.pub/2Z45MsR). With 95%-99% seropositivity in adults, depending on age, the U.K. provides guidance to what 2022 will look like when (and if) we are able to reach similar vaccination rates in the U.S.

Figure 5 shows the current time series for the U.S. We are getting through the Delta surge. As discussed in the ASA Monitor, if you don’t get vaccinated, you are likely to be infected with COVID (ASA Monitor 2021;85:1,7). That is exactly what happened in the U.K., accounting for 95%-99% seropositivity in their adult population. This is happening in the U.S. Quoting the September 9 policy briefing from the Institute for Health Metrics and Evaluation at the University of Washington, cases in

the U.S. are now declining “likely due to running out of susceptible individuals rather than policy interventions,” (asamonitor.pub/3ASoWyW). Cases may be declining in the U.S. more rapidly than in the U.K. because the Pfizer and Moderna vaccines are more effective than the AstraZeneca vaccine received by most of the U.K. population.

Even though cases and deaths are declining, and immunity is rising, the U.S. picture remains grim. We are still seeing about 1,000 deaths per week. The Institute for Health Metrics and Evaluation expects this death toll to remain nearly constant through the end of 2021.

How will variants affect the pandemic?

A recent paper in *Scientific Reports* explored the linked dynamics of viral evolution and vaccinations during the COVID-19 pandemic (*Sci Rep* 2021;11:15729). The evolutionary advantage of a resistant strain increases sharply as vaccination approaches 100%. The authors show that once a large fraction of the population is vaccinated, the resistant variant has a significant evolutionary advantage relative to the wild type. The authors conclude that it is exceptionally important to maintain non-pharmaceutical interventions (e.g., masks, social distancing) throughout the entire vaccination period to prevent establishing more resistant strains.

This suggests it would be wise to wear masks and follow social distancing for a substantial portion of 2022 as immunity rises to 99%. However, it is worth noting that despite >95% seropositivity, and despite sequencing over 1 million SARS-CoV-2 genomes, the U.K. has not seen the emergence of a variant more infectious than Delta (asamonitor.pub/3vppmv9).

The U.K. Scientific Advisory Group for Emergencies reviewed evolutionary scenarios for SARS-CoV-2 (asamonitor.pub/3vrPtSv). One scenario was an in-

Table 1			
Outcome	Vaccine Effectiveness (2 doses)		
	Pfizer BNT162b2	Moderna mRNA-1273	AstraZeneca ChAdOx1 nCoV-19
Infection	75-85%		60-70%
Symptomatic Disease	80-90%	90-99%	65-75%
Hospitalization	95-99%	95-99%	90-99%
Mortality	90-99%		90-95%

Table 1: Vaccine efficacy data against the Delta variant from the U.K. Health Security Agency as of October 14, 2021 (asamonitor.pub/2YYZYk6).

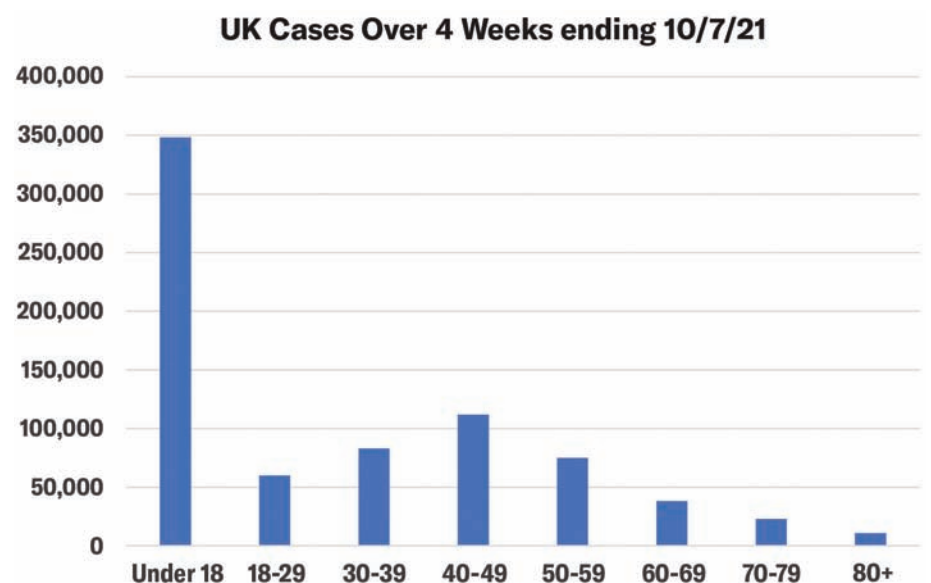


Figure 2: U.K. Cases for the 4 weeks ending October 7, 2021 (asamonitor.pub/2YYZYk6).

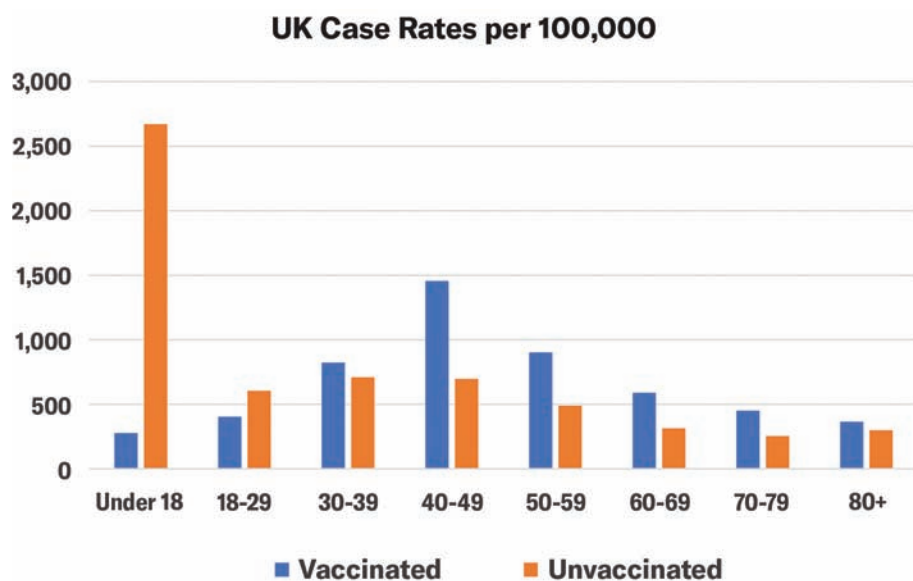


Figure 3: Current U.K. case rates over 4 weeks ending October 7, 2021 (asamonitor.pub/2YZYk6).

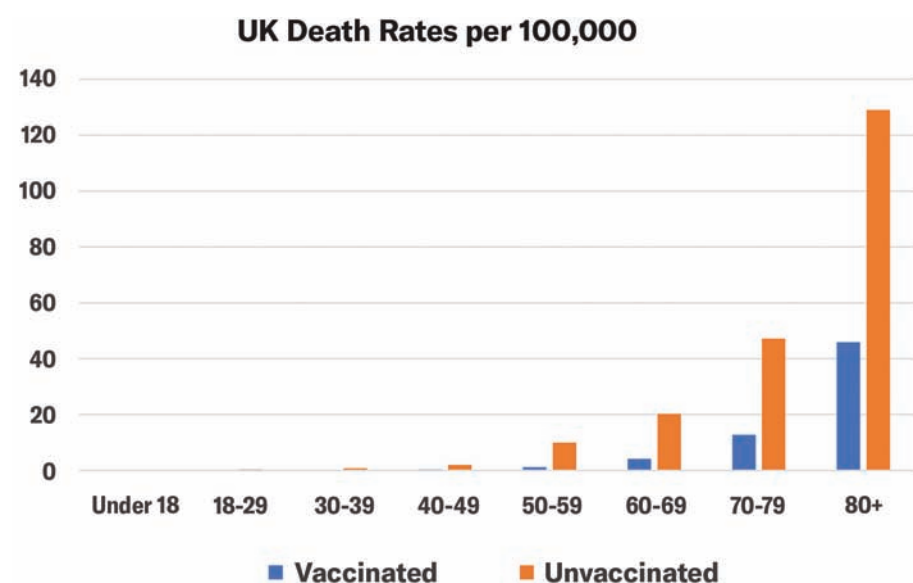


Figure 4: Current U.K. death rates over 4 weeks ending October 7, 2021 (asamonitor.pub/2YZYk6).

crease in lethality, similar to SARS-CoV-1 (10% mortality) or MERS (35% mortality). The authors concluded there was a realistic possibility for the emergence a more lethal variant and suggested increased emphasis on booster vaccinations combined with improved therapeutics (e.g., molnupiravir).

Another scenario was a variant evades current vaccines based on the original SARS-CoV-2 spike protein. The authors suggest the possibility of developing “universal” vaccines that target highly conserved regions of the spike protein (*Science* 2021;373:818-23). It is also possible that “universal” oral therapeutics that target highly conserved SARS-CoV-2 proteins, such as the Mpro protease, will be effective against future variants (*medRxiv* July 2021).

The Delta variant is as infectious as smallpox, which is about as infectious as viruses get. Our existing vaccines are effective in preventing serious illness and death from the Delta variant (Table 1). While there will be new variants, it appears our vaccines will likely remain effective. Thus, it seems unlikely that future variants will extend the pandemic.

What's really going to happen? SARS-CoV-2 is never going away. Two years ago, we had four endemic coronaviruses: HCoV-HKU1, HCoV-OC43, HCoV-50NL63, and HCoV-229E. These viruses infect children without serious sequelae. Re-infections from these coronaviruses occur throughout life roughly every 12 months (*Nat Med* 2020;26:1691-3). We now have five endemic coronaviruses. SARS-CoV-2 will likely behave like the others: infecting young children without consequence and then re-infecting everyone roughly

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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.

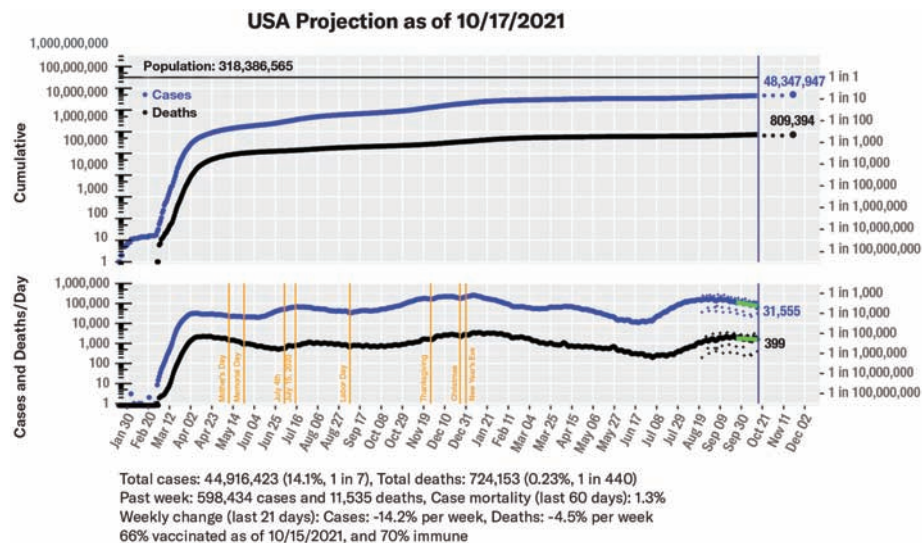


Figure 5: Current time series for the United States. Unlike the U.K. (Figure 1), infections in the U.S. are slowly decreasing, possibly reflecting better efficacy of the mRNA vaccines.* From Steve Shafer's Weekly Covid Update (see <https://groups.google.com/u/1/a/sishafer.com/g/steves-covid-19-updates>)

yearly. The effect will be to boost immunity and minimize the complications of future infections.

Over the next year, immunity will rise to nearly 100% and be further boosted by vaccination or re-infection. As our immunity becomes increasingly robust, we will get to the point where we may still catch SARS-CoV-2, but it will just be another cold.

That is likely at least a year away. The Institute for Health Metrics and

Evaluation projects that we will start 2022 with about 1,000 deaths per week. We know how to minimize this toll: 1) increase vaccination, 2) maintain non-pharmaceutical interventions, 3) develop improved therapeutics, and 4) work globally to end the pandemic. These are exactly the four recommendations from William Haseltine to finally get control over the SARS-CoV-2 pandemic (asamonitor.pub/2Z45MsR). ■

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