A Timeline of COVID-19 Developments in 2020

January 1, 2021
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Coronavirus disease 2019 (COVID-19) dominated 2020. This is a look back at how the pandemic evolved and progressed through the year, which closed with the arrival of vaccines, but also continued challenges.

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As the year ended, the United States surpassed 20 million infections from SARS-CoV-2, and more than 346,000 deaths. Globally, cases rose to 83,832,334 and 1,824,590 deaths.

Cases in some parts of the country began surging again in the weeks after Thanksgiving; the same effect may be seen in January as health officials are gravely concerned about the extent of travel for the Christmas and winter holidays. The Transportation Security Administration said it screened the most passengers (1.3 million) on the Sunday before Christmas, the most since March 15.

While vaccines began to roll out in the last month of the year, distribution challenges became evident and the United States fell short of its goal of providing an initial dose to 20 million people by December 31.

This is an updated look at how the pandemic progressed throughout 2020.

January 9 — WHO Announces Mysterious Coronavirus-Related Pneumonia in Wuhan, China

At this point, the World Health Organization (WHO) still has doubts about the roots of what would become the COVID-19 pandemic, noting that the spate of pneumonia-like cases in Wuhan could have stemmed from a new coronavirus. There are 59 cases so far, and travel precautions are already at the forefront of experts' concerns.

January 20 — CDC Says 3 US Airports Will Begin Screening for Coronavirus

Three additional cases of what is now the 2019 novel coronavirus are reported in Thailand and Japan, causing the CDC to begin screenings at JFK International, San Francisco International, and Los Angeles International airports. These airports are picked because flights between Wuhan and the United States bring most passengers through them.

January 21 — CDC Confirms First US Coronavirus Case

A Washington state resident becomes the first person in the United States with a confirmed case of the 2019 novel coronavirus, having returned from Wuhan on January 15, thanks to overnight polymerase chain reaction testing. The CDC soon after deploys a team to help with

the investigation, including potential use of contact tracing.

January 21 — Chinese Scientist Confirms COVID-19 Human Transmission

At this point, the 2019 novel coronavirus has killed 4 and infected more than 200 in China, before Zhong Nanshan, MD, finally confirms it can be transmitted from person to person. However, the WHO is still unsure of the necessity of declaring a public health emergency.

January 23 — Wuhan Now Under Quarantine

In just 2 days, 13 more people died and an additional 300 were sickened. China makes the

leave without special permission. This means up to 18 million people are under strict lockdown.

January 31 — WHO Issues Global Health Emergency

With a worldwide death toll of more than 200 and an exponential jump to more than 9800 cases, the WHO finally declares a public health emergency, for just the sixth time. Human-to-human transmission is quickly spreading and can now be found in the United States, Germany, Japan, Vietnam, and Taiwan.

February 2 — Global Air Travel Is Restricted

By 5 pm on Sunday, those en route to the United States have to have left China or they can face a 2-week home-based quarantine if they had been in Hubei province. Mainland visitors, however, will need to undergo health screenings upon their return, and foreign nationals can even be denied admittance. Other countries beginning to impose similar air-travel restrictions at this point include Australia, Germany, Italy, and New Zealand.

February 3 — US Declares Public Health Emergency

The Trump administration declares a public health emergency due to the coronavirus outbreak. The announcement comes 3 days after WHO declared a Global Health Emergency as more than 9800 cases of the virus and more than 200 deaths had been confirmed worldwide.

February 10 — China's COVID-19 Deaths Exceed Those of SARS Crisis

The COVID-19 death toll surpasses that of the severe acute respiratory syndrome (SARS) outbreak from 17 years ago, totaling 908 reported deaths in China in the last month compared with 774 deaths in the SARS crisis.

February 25 — CDC Says COVID-19 Is Heading Toward Pandemic Status

Explaining what would signify a pandemic, Nancy Messonnier, MD, director of the CDC's National Center for Immunization and Respiratory Diseases, says that thus far COVID-19 meets 2 of the 3 required factors: illness resulting in death and sustained person-to-person spread. Worldwide spread is the third criteria not yet met at the time.

March 6 — 21 Passengers on California Cruise Ship Test Positive

Twenty-one people of just 46 tested aboard a cruise ship carrying more than 3500 people off the California coast test positive for COVID-19, with 19 being crew members. The ship is held at sea instead of being allowed to dock in San Francisco while testing is conducted. Since the event, 60 passengers have sued the cruise line and parent company, Carnival Corp, for gross negligence in how passenger safety was handled.

March 11 — WHO Declares COVID-19 a Pandemic

In declaring COVID-19 a pandemic, Tedros Adhanom Ghebreyesus, director general of WHO, said at a briefing in Geneva the agency is "deeply concerned by the alarming levels of spread and severity" of the outbreak. He also expressed concern about "the alarming levels of inaction."

March 13 — Trump Declares COVID-19 a National Emergency

President Donald Trump declares the novel coronavirus a national emergency, which unlocks billions of dollars in federal funding to fight the disease's spread.

March 13 — Travel Ban on Non-US Citizens Traveling From Europe Goes Into Effect

The Trump administration issues a travel ban on non-Americans who visited 26 European countries within 14 days of coming to the United States. People traveling from the United Kingdom and the Republic of Ireland are exempt.

March 17 — University of Minnesota Begins Testing Hydroxychloroquine

The University of Minnesota launches a clinical trial to investigate whether hydroxychloroquine can prevent an individual exposed to COVID-19 from becoming ill or reduce the severity of the infection. The trial is limited to those at high risk of exposure and aims to enroll 1500 individuals.

March 17 — CMS Temporarily Expands Use of Telehealth

CMS expands its telehealth rules, permitting use during the COVID-19 pandemic as a means to protect older patients from potential exposure. The relaxation allows Medicare to cover telehealth visits the same as it would regular in-person visits.

March 17 — Administration Asks Congress to Send Americans Direct Financial Relief

Trump asks Congress to expediate emergency relief checks to Americans as part of an economic stimulus package. The proposal comes just as the United States reports its 100th death from COVID-19.

March 19 — California Issues Statewide Stay-at-Home Order

California becomes the first state to issue a stay-at-home order, mandating all residents to stay at home except to go to an essential job or shop for essential needs. The order also instructs health care systems to prioritize services to those who are the sickest.

March 24 — With Clinical Trials on Hold, Innovation Stalls

Overwhelmed hospitals are keeping out everyone who does not need to be there, and that means delaying the start of new clinical trials, according to an interview. The Center for Biosimilars® reported that drugs with fresh FDA approvals are not likely to launch, as their

chances of making it into circulation are dim with hospitals struggling just to find enough personal protective equipment.

March 25 — Reports Find Extended Shutdowns Can Delay Second Wave

Mathematical models based on social distancing measures implemented in Wuhan, China, show keeping tighter measures in place for longer periods of time can flatten the COVID-19 curve.

March 26 — Senate Passes CARES Act

The Senate passes the Coronavirus Aid, Relief, and Economic Security (CARES) Act, providing $2 trillion in aid to hospitals, small businesses, and state and local governments, while including an elimination of the Medicare sequester from May 1 through December 31, 2020.

March 27 — Trump Signs CARES Act Into Law

The House of Representatives approves the CARES act, the largest economic recovery package in history, and Trump signs it into law. The bipartisan legislation provides direct payments to Americans and expansions in unemployment insurance.

March 30 — FDA Authorizes Use of Hydroxychloroquine

FDA issues an emergency use authorization (EUA) for "hydroxychloroquine sulfate and chloroquine phosphate products" to be donated to the Strategic National Stockpile and donated to hospitals to treat patients with COVID-19. The EUA would be rescinded June 15, except for patients in clinical trials, in the wake of reports of heart rhythm problems among some patients.

March 31 — COVID-19 Can Be Transmitted Through the Eye

A report in *JAMA Ophthalmology* creates a stir with the finding that patients can catch the virus that causes COVID-19 through the eye, despite low prevalence of the virus in tears. The coverage of the study involving 38 patients from Hubei Province, China, drew some of AJMC.com's highest readership of 2020, as the findings contradicted assumptions by leading professional societies.

April 8 — Troubles With the COVID-19 Cocktail

"What do you have to lose?" Trump asks when touting the malaria drug hydroxychloroquine or the related chloroquine as possible treatments for COVID-19. With a common antibiotic, azithromycin, the drug cocktail becomes an early candidate to prevent hospitalization or death. But Trump's promotion of the combination, despite known heart risks for some patients, prompts the American Heart Association, the American College of Cardiology, and the Heart Rhythm Society to warn in a joint guidance that the drugs are not for everyone.

April 16 — "Gating Criteria" Emerge as a Way to Reopen the Economy

After Trump briefly entertains the idea of reopening the US economy in time for Easter Sunday, the White House releases broad guidelines for how people could return to work, to church, and to restaurants and other venues. The plan outlines the concept of "gating criteria," which call for states or metropolitan areas to achieve benchmarks in reducing COVID-19 cases or deaths before taking the next step toward reopening.

April 28 — Young, Poor Avoid Care for COVID-19 Symptoms

As the pandemic lingers, the term "deferred care" caught fire in health care circles—referring to the fact that many would avoid a doctor's office or hospital for any procedure that could wait. But a Gallup poll finds a darker side to this phenomenon: 1 in 7 Americans report they would not seek care for a fever or dry cough—the classic symptoms of COVID-19. The reason? Cost concerns. Those most likely to avoid medical treatment for symptoms are younger than age 30 and make less than $40,000 a year. By the end of April, 26.5 million Americans have filed for unemployment since mid-March.

April 29 — NIH Trial Shows Early Promise for Remdesivir

National Institutes of Health (NIH) trial data, which are not peer reviewed, show that remdesivir, made by Gilead Sciences, is better than placebo in treating COVID-19. Patients with advanced COVID-19 and lung involvement who received the antiviral had a 31% faster recovery time, or about 4 days.

May 1 — Remdesivir Wins EUA

Shortly after the trial data are published, FDA grants an EUA to remdesivir after preliminary data from an NIH trial found the treatment accelerated recovery in individuals with advanced COVID-19 and lung involvement.

May 9 — Saliva-Based Diagnostic Test Allowed for At-Home Use

The FDA broadens authorization of a saliva-based test to detect COVID-19 infection; the EUA is granted to Rutgers Clinical Genomics Laboratory. The test makes it possible for those who cannot get to a collection center to get tested, including those who are home because they are ill, quarantined, or at high risk of infection due to their age or comorbidities.

May 12 — Death Toll Likely Underestimated, Fauci Testifies

Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases, testifies before the US Senate that the US death toll of 80,000 is likely an underestimate. He warns against the relaxation of social distancing and says he is "cautiously optimistic" that a vaccine will be effective and achieved within 1 or 2 years.

May 21 — United States and AstraZeneca Form Vaccine Deal

The Trump administration and AstraZeneca announce a collaboration to speed development of a COVID-19 vaccine called AZD1222. HHS says it expects the first doses to be available as early as October 2020; phase 3 clinical studies are underway this summer.

May 28 — US COVID-19 Deaths Pass the 100,000 Mark

The CDC says surpassing 100,000 deaths is a "sobering development and a heart-breaking reminder of the horrible toll of this unprecedented pandemic." It asks that Americans continue following local and state guidance on prevention strategies, such as social distancing, good hand hygiene, and wearing a face mask while in public.

June 4 — *Lancet*, *NEJM* Retract COVID-19 Studies on Hydroxychloroquine

On the same day, *The New England Journal of Medicine* and *The Lancet* both retract 2 studies on the use of hydroxychloroquine in COVID-19, after the authors said they could not vouch for the data used. A private database of medical records compiled by a little-known firm called

Surgisphere was used in both studies. The retractions bring to light the difficulty of publishing vital COVID-19 research while ensuring accuracy.

June 10 — US COVID-19 Cases Reach 2 Million

The number of confirmed cases of COVID-19 hits 2 million in the United States as new infections continue to rise in 20 states. Cases begin to spike as states ease social distancing restrictions.

June 16 — HHS Announces COVID-19 Vaccine Doses Will Be Free for Some

Officials associated with the United States' Operation Warp Speed, a project to rapidly develop and deploy a COVID-19 vaccine, explain that the vaccine would be provided for free to elderly patients and other vulnerable populations who cannot afford it.

June 18 — WHO Ends Study Into Hydroxychloroquine

WHO announces it will stop testing hydroxychloroquine as a treatment for COVID-19. The data from the Solidarity Trial show the drug did not reduce mortality. According to WHO, patients who were previously administered the drug would finish their course or stop based on a supervisor's discretion.

June 20 — NIH Halts Trial of Hydroxychloroquine

Just days after WHO ended its own trial, the NIH announces it is halting a clinical trial examining the safety and effectiveness of hydroxychloroquine as a treatment for COVID-19. The study indicates that the treatment does no harm, but also provides no benefit.

June 22 — Study Suggests 80% of Cases in March Went Undetected

A study in *Science Translation Medicine* suggests that as many as 80% of Americans who sought care for flu-like illnesses in March were actually infected with the virus that causes COVID-19. According to the research, if one-third of these patients sought COVID-19 testing, it may have amounted to 8.7 million infections.

June 26 — White House Coronavirus Task Force Addresses Rising Cases in the South

For the first time in 2 months, the White House Coronavirus Task Force holds a briefing. The focus of the discussion is the rising number of cases and growing positive test rate in some states. As cases rise, Texas and Florida both decide to halt the reopenings as each state records growing numbers of cases.

June 29 — Gilead Sets Price for Remdesivir at $3120

Gilead Sciences sets a price for remdesivir, which can shorten hospitalization stays for patients with COVID-19, at $520 a vial. With a treatment course of 6 vials, the typical treatment course will be $3120 per patient for people covered with private insurance. Critics of the price point are quick to point out that taxpayers funded the COVID-19 remdesivir trial through the National Institute of Allergy and Infectious Diseases.

June 30 — Fauci Warns New COVID-19 Cases Could Hit 100,000 a Day

In his appearance before the Senate Health, Education, Labor, and Pensions Committee, Fauci warns that while the current daily number of new cases in the United States is hovering around 40,000, that could reach as high as 100,000 new cases per day given the outbreak's current

trajectory.

July 2 — States Reverse Reopening Plans

Several states, including California and Indiana, postpone or reverse plans to reopen their economies, as the United States records 50,000 new cases of COVID-19—the largest one-day spike since the pandemic's onset. New Mexico also extends the state's emergency public health order through July 15 and implements a $100 fine for those not adhering to required mask usage.

July 6 — Scientists, Citing Airborne Transmission, Ask WHO to Revise Guidance

Hundreds of scientists call on the WHO to revise recommendations on COVID-19 to better reflect its potential for airborne transmission. Previously, the organization stated that COVID-19 spreads primarily via small droplets from the nose or mouth emitted when an infected individual coughs, sneezes, or speaks.

July 7 — CMS Plans to Pay More for Home Dialysis Equipment

CMS proposes a rule aimed at keeping patients outside of dialysis centers for treatment as the nation faces rising cases. The transitional add-on payment for new and innovative equipment or supplies would allow greater access to home dialysis machines, improving accessibility for Medicare beneficiaries.

July 7 — US Surpasses 3 Million Infections, Begins WHO Withdrawal

The same day that the United States reports 3 million COVID-19 infections, the nation begins its withdrawal from WHO, citing its response to the global pandemic. The Trump administration notifies the United Nations of its decision, which would not take effect until 2021 and could be reversed by President-elect Joe Biden.

July 9 — WHO Announces COVID-19 Can Be Airborne

WHO announces that the novel coronavirus can be transmitted through the air after more than 200 scientists sign a letter urging the agency to revise its recommendations. In an updated scientific brief, WHO notes that the virus may linger in the air in crowded indoor spaces and emphasizes that the virus may be spread by asymptomatic individuals.

July 14 — States With COVID-19 Spikes Report Greatest Health Insurance Coverage Losses

As of May 2020, states with the greatest percentage of nonelderly adults who are currently uninsured included Florida, Texas, Oklahoma, Mississippi, North Carolina, South Carolina, and Georgia, according to an analysis from Families USA. These states also report the highest numbers of new COVID-19 cases per 100,000 residents as of July 12.

July 14 — Early Moderna Data Point to Vaccine Candidate's Efficacy

Data from phase 1/2 trials of Moderna Inc's COVID-19 vaccine show that doses produced immune responses in all 3 groups of 15 volunteers. The company was the first to enter large-scale human trials. Adverse effects of the vaccine candidate, which is administered twice 28 days apart, include injection site pain and chills.

July 15 — New Hospital Data Reporting Protocol Prompts Concern

An announcement mandates that all hospitals must bypass the CDC and send COVID-19–related information to a central database run by HHS Protect. Previously, data were sent to the CDC's National Healthcare Safety Network site. Following the change, questions are raised regarding the future of COVID-19 data transparency and politicization.

July 16 — US Reports New Record of Daily COVID-19 Cases

The United States reported a record 75,600 cases of COVID-19 in a single day, breaking a record set the week prior. At this point, daily cases have seen 11 record totals in the past month alone. Texas, Hawaii, and Montana are among the 10 states reporting new record daily totals.

July 20 — Diagnostic Delays From COVID-19 May Increase Cancer-Related Deaths

The next several years could bear witness to thousands of additional deaths from cancer that could have been prevented through routine diagnostic care that was delayed because of the COVID-19 pandemic. Notably, delays in referrals and screenings for breast, colorectal, esophageal, and lung cancers were indicated in a pair of studies published in *The Lancet Oncology* to potentially lead to almost 10% (n = 3291-3621) more deaths in England over the next 5 years.

July 21 — Vaccines From AstraZeneca, CanSino Biologics Show Promising Results

Two experimental vaccines, one from AstraZeneca and the other from CanSino Biologics, show promising results against COVID-19. The interim results of AstraZeneca's phase 1/2 COV001 trial of AZD1222 show that the vaccine was tolerated and generated robust immune responses against the virus in all participants who were evaluated. In the CanSino Phase 2 trial, the vaccine induced significant neutralizing antibody responses, with as many as 95% of patients showing either cellular or humoral immune responses at day 28 post vaccination.

July 22 — HHS, DOD Announce Vaccine Distribution Agreement With Pfizer and BioNTech

HHS and the Department of Defense (DOD) strike a partnership with biotech giants Pfizer and BioNTech for a December delivery of 100 million doses of their COVID-19 vaccine candidate, BNT162, in a deal that could expand to 600 million doses if the vaccine receives approval or an EUA from the FDA, and even then only if phase 3 clinical trial results confirm that the vaccine is safe and effective.

July 23 — Antibody Levels Drop After First 3 Months of COVID-19 Infection

Findings from a research letter published in the *New England Journal of Medicine* indicate that levels of antibodies against SARS-CoV-2, the virus that causes COVID-19, dropped dramatically across the first 3 months of infection. At this rate, researchers note that antibody resistance would be depleted within a year, although experts note that the possibility of being infected again with the virus is very unlikely.

July 23 — Antibody Cocktail May Treat, Prevent COVID-19

Researchers conceive of an antibody cocktail that uses antibodies directed at different locations on the familiar "spike" on SARS-CoV-2 that gives the virus its "corona." The scientists found the antibodies fell into 2 distinct groups, targeting different regions of the viral spike. Thus, they say, the battle against COVID-19 could be waged on separate fronts, much like those against HIV and some forms of cancer.

July 27 — Moderna Vaccine Begins Phase 3 Trial, Receives $472M From Trump Administration

In beginning the first phase 3 clinical trial to examine a vaccine candidate against COVID-19, Moderna announces that the Trump administration increased funding by $472 million to expand the trial to 30,000 US participants. The move now brings the total investment made by the Biomedical Advanced Research and Development Authority to $955 million.

July 27 — Senate Introduces HEALS Act

Republicans introduce a package of bills known together as the Health, Economic Assistance, Liability Protection, and Schools (HEALS) Act, which provides provisions for another stimulus check, more money for small businesses, and liability protections for companies seeking to bring employees back to the workplace during the pandemic.

July 29 — FDA Grants Truvian EUA for Rapid Antibody Test

FDA grants Truvian Sciences an EUA for its Easy Check COVID-19 IgM/IgG antibody test after it was shown to exceed EUA requirements, including a sensitivity rate of 98.44% and a specificity of 98.9%. The announcement follows the FDA's increased oversight of antibody tests on May 5, requiring them to meet standards of other molecular tests.

August 3 — New US Pandemic Phase; US to Pay Sanofi, GlaxoSmithKline $2B for Vaccine

Coronavirus response coordinator Deborah Birx, MD, says the United States has entered a new phase of the pandemic, as widespread cases nationwide differ from early concentrated outbreaks first reported in March and April. Birx's comments come as the United States agrees to a $2.1 billion deal with GlaxoSmithKline and Sanofi Pasteur in an effort to develop, manufacture, and scale up delivery of a COVID-19 vaccine.

August 4 — Rural Hotspots Face Lack of Intensive Care Unit Beds

Almost 5 months after the pandemic was declared a national emergency in the United States, 49% of low-income areas have no free beds in their intensive care units vs 3% of the wealthiest. Hospitals are now being forced to transfer their sickest patients to care facilities in these wealthier areas, with the Southwest and West facing an especially difficult bed shortage.

August 7 — Talks Stall on Second Relief Package

Stimulus checks from the first package rolled out seemingly quickly, but talks stall between the White House and Democrats on a potential subsequent round of relief, even as jobless claims reach a record high of 1.186 million. Trump continues to claim he will issue executive orders if a deal cannot be reached.

August 11 — Trump Administration Reaches Deal With Moderna

Despite still waiting on final data, the Trump administration reportedly agrees to pay $1.5 billion to Moderna for 100 million doses of its vaccine candidate, mRNA-1273, or an average per-dose price of $15. The vaccine, however, is still under investigation in the joint phase 3 COVE trial Moderna is conducting with the National Institute of Allergy and Infectious Diseases and the Biomedical Advanced Research and Development Authority.

August 12 — Severe Obesity Increases Mortality Risk From COVID-19

Investigators from Kaiser Permanente publish their findings showing that patients with a body

mass index (BMI) of 40 to 44 kg/m^2 have a risk of death from COVID-19 that is more than twice that of individuals whose BMI is 18.5 to 24 mg/m^2. An abundance of comprehensive patient data enabled the team to isolate obesity's effects compared with those resulting from more than 20 comorbidities, health care use, and population density, among others. At the heart of this finding is that excess fat exacerbates the breathing issues brought on by COVID-19.

August 13 — Biden Calls for 3-Month Mask Mandate

Still a presidential nominee, Joe Biden calls on all governors to require their citizens to wear masks anytime they go out in public through November, and he claims he will mandate the practice if elected. At this point, there are a reported 165,000 deaths from COVID-19, and the measure is estimated to save 40,000 lives in the coming months. At this point, mask mandates still vary greatly among the states and regions.

August 15 — FDA Approves Saliva Test

The federal agency issues an EUA for SalivaDirect, a test developed by researchers at the Yale School of Public Health that is less invasive compared with the current standard nasal swabs. With shorter wait times not affecting test sensitivity, labs can reportedly run 90 test samples, which are collected in sterile containers, in under 3 hours. The test is also inexpensive and produces results similar to nasal swabbing.

August 17 — COVID-19 Now the Third-Leading Cause of Death in the US

In just 4 days, there's been a 3.2% uptick in COVID-19–related deaths, to 170,434, giving the disease a No. 3 ranking behind heart disease in the top spot and cancer at No. 2. Deaths now exceed 1000 per day and nationwide cases exceed 5.4 million. Testing has dropped off by an average 68,000 per day, despite death being 8 times more likely in the United States vs in Europe.

August 23 — Convalescent Plasma Is Cleared for Use by FDA

The FDA issues another EUA, this time for convalescent plasma from recovered patients as a therapy to fight COVID-19. There is ongoing debate about the treatment, which is rooted in experts' skepticism that all patient populations will derive benefit from it, due to a lack of efficacy data. Meanwhile, White House Press Secretary Kayleigh McEnany claims it is a therapeutic breakthrough.

August 24 — Remdesivir's Clinical Benefits Questioned

A global, multicenter study finds that the antiviral drug remdesivir had little effect on patients hospitalized with COVID-19. The findings, published in *JAMA*, indicate there were no significant differences in duration of supplemental oxygen or hospitalization between the intervention group given remdesivir and the control group given standard care.

August 25 — CDC Changes Testing Guidance, but Later Reverses Itself

The CDC quietly changes its guidance on who should get tested for COVID-19, saying that individuals who are asymptomatic, but have been exposed, do not need testing. After it is revealed the decision had bypassed CDC's usual scientific review process and without internal review, the changes are reversed.

August 26 — FDA Grants EUA to Abbott's Rapid Test

A portable rapid COVID-19 test that can deliver results in under 15 minutes was cleared by the FDA under an EUA. The test is aimed at places like workplaces and schools.

August 28 — First Known Case of COVID-19 Reinfection Reported in the US

A 25-year-old man from Nevada became reinfected with COVID-19 in late May after recovering from a mild case in April, reports say. It marks the first reported case of reinfection in the United States; the second occurrence resulted in a much more severe case, requiring hospitalization and oxygen. A full study of the case is published in *Lancet Infectious Disease Journal* in October.

September 1 — US Rejects WHO Global COVID-19 Vaccine Effort

The United States says it will not participate in an initiative by the WHO to develop, make, and distribute a COVID-19 vaccine. COVAX, with 172 countries participating, was launched so that an eventual vaccine could be distributed evenly to poor and developing countries.

September 3 — Steroids Reduce Mortality in Severe Cases; Sanofi, GSK Begin Human Vaccine Trials

Three studies report that inexpensive steroids are the most effective treatment to date for serious COVID-19. Results from the studies find that the use of systemic corticosteroids can reduce the risk of death by one-third in individuals hospitalized with COVID-19 compared with usual care or placebo.

Additionally, Sanofi and GlaxoSmithKline (GSK) start a clinical trial of their protein-based vaccine; the COVID-19 vaccine uses the same protein-based technology as one of Sanofi's influenza vaccines and is combined with an adjuvant, or booster, developed by GSK.

September 3 — Bioethicists Weigh In on Equitable Vaccine Distribution

Nineteen bioethicists outline measures for equitable distribution of limited supplies of any COVID-19 vaccine; the plan, called the Fair Priority Model, considers 3 types of harms caused by COVID-19 and 3 values that must be adhered to when considering the allocation of a scarce supply of vaccine.

September 8 — AstraZeneca Halts Phase 3 Vaccine Trial

The phase 3 trial for AstraZeneca's potential COVID-19 vaccine is halted for a safety data review following an unknown adverse reaction in a patient. The patient was part of the United Kingdom arm of the trial. At the time, the nature of the adverse reaction was not known, but the company did say that the participant was expected to recover. AstraZeneca says the hold was initiated as "a routine action."

September 14 — US Airports Stop Screening International Travelers

The government announces it will stop screenings taking place at some airports since January. In March, incoming flights from high-risk countries, including China, Iran, and much of Europe, were funneled through 15 designated airports, but as of September 14, the flights will no longer be redirected and all passenger screenings will be halted. As part of the screening process, passengers had their temperatures taken and were subject to a basic health screening about typical COVID-19 symptoms before they could go through passport control and customs.

September 14 — Pfizer, BioNTech Expand Phase 3 Trial

After initially aiming to recruit 30,000 participants, Pfizer and BioNTech announce they will expand the phase 3 trial of their COVID-19 vaccine by 50% to 44,000. The goal of expanding the trial is to increase data on safety and efficacy and promote a more diverse population, including adolescents as young as 16 years and patients with HIV, hepatitis C, or hepatitis B. The Pfizer/BioNTech vaccine is provided as 2 shots given 3 weeks apart, but the vaccine must be kept at a temperature of –70 degrees Celsius (–94 degrees Fahrenheit), which may make distribution a challenge.

September 14 — NIH Launches Investigation Into Halted Astrazeneca Trial

After AstraZeneca put its phase 3 trial on hold, the NIH announces it is launching an investigation into the adverse reaction before the FDA decides whether or not to resume the trial. The participant suffered spinal cord damage, and there remained some uncertainty about what happened to cause the damage.

September 15 — CDC Reports on Spread of COVID-19 at Restaurants

A study published in *Morbidity and Mortality Weekly Report* finds that people who recently tested positive for COVID-19 were 2.4 times more likely to have dined out. The study considered restaurant dining to include being seated at a patio, being seated outdoors, and being seated indoors. The odds jumped almost 4-fold for participants who had been to a bar or café. The majority of participants (71%) claimed to have worn masks in the 2 weeks before their diagnosis.

September 16 — Trump Administration Releases Vaccine Distribution Plan

A plan devised by HHS and the DOD aims to make a COVID-19 vaccine free for all Americans, with the vaccine being rolled out in January 2021. Once a vaccine is authorized, the plan dictates that 6.6 million kits of supplies needed to administer vaccines will also be distributed. The plan does not include a decision on who would be the first to receive the vaccine.

September 17 — Europe Reports Rising COVID-19 Cases

Europe reports a sharp increase in COVID-19 cases, with numbers growing at a higher rate than they did during the previous peak in March. In the first half of September, more than half of all European countries reported an increase greater than 10%.

September 21 — CDC Pulls Guidance Saying COVID-19 Transmission Is Airborne

The CDC removes guidance from its website that had been posted 3 days earlier saying that the transmission of COVID-19 is airborne. CDC says the document was posted in error and the guidance was a "draft version of proposed changes."

September 21 — Johnson & Johnson Begins Phase 3 Vaccine Trial

Johnson & Johnson announces that it began a large phase 3 clinical trial of its COVID-19 vaccine candidate. This vaccine does not need to be frozen and may require 1 administration instead of 2. The trial is expected to test the vaccine in 60,000 participants, making it the largest phase 3 trial of all vaccines currently being tested.

September 23 — A New, More Contagious Strain of COVID-19 Is Discovered

A study conducted at Houston Methodist Hospital finds a more contagious strain of COVID-19

in a large portion of recent patient samples. Investigators analyzed samples from the earliest phase of the pandemic and a more recent infection wave, finding that nearly all strains from the more recent phase had a mutation that allows the virus to bind and infect more cells.

September 25 — Midwest States See Increase in COVID-19 Cases

Over the course of September, Midwest states experience a dramatic rise in COVID-19 cases, with South Dakota alone having a 166% increase and 10 other states reporting record 1-day increases. The annual Sturgis motorcycle rally, school and university reopenings, and Labor Day weekend celebrations have all been cited as case links.

September 28 — Global COVID-19 Deaths Surpass 1 Million

The number of deaths linked to COVID-19 worldwide crosses the 1 million mark, according to *The New York Times*, surpassing the deaths caused by HIV, dysentery, malaria, influenza, cholera, and measles combined in 2020.

September 29 — HHS to Distribute 100 Million Rapid Tests to States

HHS announces a plan to send 100 million rapid COVID-19 tests, developed by Abbott, to states by the end of the year. The rapid tests are cheaper and faster than laboratory tests and can return results in about 15 minutes. The plan was designed to assist K-12 schools in reopening.

September 29 — Regeneron Announces Positive Results for Monoclonal Antibody Treatment

Regeneron releases study results from its ongoing phase 1/2/3 trial showing that its proposed monoclonal antibody treatment for COVID-19, REGN-COV2, was linked to quicker recovery, reduced viral load, and the need for fewer medical visits. REGN-COV2 is a mixture of 2 monoclonal antibodies (REGN10933 and REGN 10987).

October 2 — Trump, First Lady Test Positive for COVID-19; Trump Enters Hospital

President Trump announces that he and First Lady Melania Trump have tested positive for COVID-19. After experiencing mild symptoms of the disease, Trump was taken to Walter Reed National Military Medical Center, "out of an abundance of caution," said Press Secretary Kayleigh McEnany in a statement.

October 5 — Trump Leaves Hospital, Continues Receiving Treatment

After 3 days, Trump is discharged from the hospital and transported back to the White House, where he would continue to receive treatment for COVID-19 and be monitored. White House physician Sean Conley, DO, says that the president's fever is gone and that his oxygen levels are normal. During his time at the hospital, Trump's treatment consisted of Regeneron's investigational antibody cocktail, remdesivir, and dexamethasone.

October 8 — *NEJM* Criticizes Trump's COVID-19 Response; 39 States See Case Spikes

In an editorial published by the *New England Journal of Medicine* (*NEJM*), 34 editors call out the Trump administration's response of the COVID-19 pandemic, stating that leaders have "taken a crisis and turned it into a tragedy."

Additionally, 39 states report seeing a rise in COVID-19 cases. Nine states set 7-day records for infections, and Wisconsin and Hawaii report a record number for deaths in a 7-day period.

October 8 — More Americans Trust Biden to Lead Health Care System

A poll released on this date by Gallup-West Health, but taken before Trump's COVID-19 diagnosis, finds that more Americans trust Biden to lead the US health care system through the pandemic. The poll notes that Biden had the support of 52% of voters on this issue, compared with 39% who supported Trump, with the remaining undecided. The results leave room for Trump to narrow Biden's wide lead in the national polls.

October 8 — White House COVID-19 Outbreak Grows to 34

By this date, the cluster of people infected by the COVID-19 outbreak connected to the Rose Garden ceremony for Supreme Court Justice Amy Coney Barrett has grown to 34, including several White House staff members, according to *The Washington Post*. CDC experts offer assistance with contact tracing.

October 9 — US Signs Deal With AstraZeneca

The Trump administration signed a $486 million agreement with AstraZeneca to develop an antibody treatment for COVID-19, which would call for HHS and the DOD to work with the company to roll out late-stage development and large-scale manufacturing of AZD7442, a cocktail of 2 monoclonal antibodies with potential to treat or prevent the disease.

October 12 — Johnson & Johnson Halts Vaccine Trial

Johnson & Johnson halts recruitment for its phase 3 ENSEMBLE trial for its COVID-19 vaccine halts vaccine trial over a patient's unexplained illness, a development first reported in POLITICO. The company reports at the time that adverse events that temporarily pause recruitment are not uncommon and mean that clinical trials are being conducted in a safe manner. It later resumes the study of its 1-dose regimen, which is unique among the leading vaccine candidates. The company has also launched ENSEMBLE 2 to study a 2-dose version of the vaccine.

October 15 — US Cases Spike Again; Studies Connect Blood Type and COVID-19 Risk

The United States reports 60,000 new COVID-19 cases, a number not reached since early August. Cases rise countrywide, and 44 states report caseloads surpassing those seen in mid-September. More rural states see numbers even higher than during first waves in the spring.

A pair of studies in *Blood Advance* suggest that the risk of becoming infected with COVID-19 or developing life-threatening complications from the virus might be related to blood type. Researchers caution that the results do not point to any blood type being completely protective or vulnerable to the virus.

October 19 — Global Cases Top 40 Million

Data from Johns Hopkins University indicate that COVID-19 cases have topped 40 million worldwide as the United States and other countries see their highest rates of new cases in months. More than 1.1 million people have been killed by the virus worldwide so far, and nearly 220,000 of those deaths were in the United States, which remains the hardest-hit country in the world.

October 22 — FDA Approves Remdesivir as First COVID-19 Drug

Gilead's remdesivir is the first FDA-approved drug to treat COVID-19 after 3 randomized trials found it to decrease the length of hospital stays and reduce the likelihood that patients will require oxygen. None of the trials showed reduced risk of mortality, however, and a WHO-backed study found that the drug had "little to no effect" on hospitalized patients. The FDA does not mention the WHO trial in its risk-benefit assessment of remdesivir, stating that an NIH-backed trial supporting the approval was better suited to assess time to recovery than the WHO-backed trial.

October 23 — AstraZeneca and Johnson & Johnson Announce Restart of COVID-19 Vaccine Trials

AstraZeneca and Johnson & Johnson announce plans to restart clinical trials for their respective COVID-19 vaccine candidates after they both stopped due to safety concerns. Johnson & Johnson's stalled on October 11, and a patient in the AstraZeneca trial developed neurological symptoms before its study was halted on September 6. An independent monitoring committee determined that the trial for the latter vaccine candidate was safe to continue.

October 28 — CMS Issues Vaccine, Treatment Coverage Rules

CMS provides new rules for insurance coverage, increasing what Medicare pays hospitals for COVID-19 treatments. Trump and Congress had enacted legislation calling for COVID-19 vaccines to be free, but new rules were necessary to fit that policy into the various payment requirements for public and private insurance. The new rules waive co-pays or deductibles on vaccines for seniors with Medicare.

November 4 — US Reports Unprecedented 100,000 Cases in 1 Day

The US hits a grim milestone with 100,000 new COVID-19 cases reported in a single day for the first time. The unprecedented spike in cases leads to a shortage of N95 face masks at health care facilities despite increased production, and workers continue to ration and reuse masks with no end in sight.

November 5 — Study Predicts Difficulties in Nationwide COVID-19 Immunity

An analysis of flu vaccination rates during the 2019-2020 flu season suggests that the path to vaccinating the majority of the country for SARS-CoV-2, thus achieving sufficient immunity, will not be an easy one. Just 52% of the US population received a flu vaccine in the time frame of the analysis, and the study also highlighted disparities: Lower vaccination rates were recorded in Black and Hispanic adults than White adults, and elderly adults were more likely to receive a vaccine.

November 9 — President-Elect Biden Announces COVID-19 Transition Team; Pfizer Publishes Vaccine Results

After former Vice President Joe Biden is determined to be the president-elect on November 7, he announces the names of the scientific, medical, and public health professionals who will serve on his Transition COVID-19 Advisory Board. The same day, Pfizer releases data from its COVID-19 vaccine trial showing that the vaccination was 90% effective.

November 9 — FDA Issues EUA for Eli Lilly's Antibody Treatment

The FDA issues an EUA for Eli Lilly's bamlanivimab, a monoclonal antibody treatment that mimics the immune system's response to infection with SARS-CoV-2 and appears to protect

high-risk patients with COVID-19 from progressing to more severe forms of the disease. Clinical trials showed reductions in COVID-19–related hospitalizations or emergency visits in these patients within 28 days of treatment compared with placebo.

November 11 — Indoor Venues Responsible for Much of COVID-19's Spread

A new study in *Nature* observes that most new cases of COVID-19 originated from indoor gatherings in places like restaurants, gyms, and grocery stores, according to analysis of cell phone mobility data from large cities. The authors suggest that low-income neighborhoods have higher new case burdens because their public venues are more crowded and residents are more likely to work outside their homes.

November 16 — Moderna Reveals Vaccine Efficacy Results

The positive vaccine news continues with Moderna's announcement that its experimental vaccine reduces the risk of COVID-19 infection by 94.5% in participants who received it. Like Pfizer's vaccine, the Moderna vaccine works using mRNA, an innovative approach that has not yet been used in approved vaccines against any disease.

November 16 — FDA to Move Rapidly on EUAs for Pfizer, Moderna Vaccines

On CNBC's "Squawk Box," HHS Secretary Alex Azar says the FDA will move "as quickly as possible" to clear Pfizer's and Moderna's vaccine candidates for emergency use as long as the data support authorization. Both authorization applications are currently being completed, but Azar says that the FDA's teams are working with both companies to "remove any unnecessary bureaucratic barriers."

November 17 — Fauci Highlights the Need for Long-term Follow-up of COVID-19 Effects

During a talk at the American Heart Association Scientific Sessions, Fauci discusses the cardiovascular implications of COVID-19 and highlights the need to follow up with patients to better understand the long-term effects of infection. He points to symptoms like profound fatigue, shortness of breath, muscle aches, sporadic fevers, and an inability to concentrate, which up to one-third of patients live with for weeks or months after contracting COVID-19.

November 18 — Pfizer, BioNTech Vaccine Is 95% Effective

The results of a nearly 44,000-person trial demonstrate that the COVID-19 vaccine from Pfizer and BioNTech is 95% effective, making it as effective as vaccines for shingles and measles. Pfizer also announces that it will seek FDA approval within days so that distribution of the vaccine can happen by the end of the year.

November 20 — Pfizer, BioNTech Submit EUA Application; CDC Warns Against Holiday Travel

Pfizer and BioNTech submit their COVID-19 vaccine to the FDA for an EUA, making them the first companies to seek such an approval in the United States. The EUA submission includes safety data on about 100 children between the ages of 12 and 15 years.

At the same time, the CDC urges Americans to stay home for Thanksgiving amid national spikes in COVID-19 cases and hospitalizations. The agency recommends that people avoid mingling with people who have not resided in their household for the last 14 days. As cases in the United States surpass 11 million, CDC officials worry that the situation could worsen during the holiday season.

November 23 — AstraZeneca Reports Vaccine Is 90% Effective; FDA Grants EUA for Second Antibody Treatment

When AstraZeneca's COVID-19 vaccine is administered as a half dose followed by a full dose at least a month later, it can be approximately 90% effective. This vaccine is easier to distribute and scale up than other vaccines, and the drug maker says it can have as many as 200 million doses by the end of 2020 and 700 million by the end of the first quarter of 2021.

Meanwhile, the FDA grants an EUA for a second COVID-19 antibody treatment. The cocktail, manufactured by Regeneron, was administered to Trump when he was battling COVID-19 at the beginning of October. In a clinical trial of 800 people, the treatment significantly reduced virus levels within days.

December 10 — FDA Advisory Panel Recommends Pfizer, BioNTech COVID-19 Vaccine

An FDA advisory panel endorses the first COVID-19 vaccine. The application for the Pfizer and BioNTech's vaccine is heard in a public, day-long meeting; voting 17-4, with 1 abstention, the Vaccines and Related Biological Products Advisory Committee (VRBPAC) decides the benefits of the vaccine outweigh the risks for those 16 and older.

December 11 — FDA Agrees to EUA for COVID-19 Vaccine From Pfizer, BioNTech

A day after the panel votes, the FDA agrees to an EUA for the Pfizer, BioNTech vaccine, allowing shipments to begin; vaccinations of health care workers begin within days.

December 17 — FDA Panel Backs Moderna COVID-19 Vaccine

A week after hearing the application for the country's first COVID-19 vaccine, the same FDA advisory panel meets and agrees that a second vaccine, from Moderna, will benefit individuals 18 years and older. The vote is 20-0, with 1 abstention. The Moderna vaccine is given 28 days apart; the Pfizer-BioNtech one, 21 days apart.

December 18 — FDA Signs Off on EUA for Moderna's COVID-19 Vaccine

The FDA issues the second EUA allowing shipments of the Moderna COVID-19 vaccine to begin.

December 21 — New COVID-19 Variant Circling the UK

The UK announces that a new strain of the virus that causes COVID-19, B.1.1.7, is spreading across the country. The novel variant is more contagious, but does not appear to be more lethal or lead to more severe disease.

December 23 — US Buys More Pfizer Vaccine

The Trump administration announces it will buy an additional 100 million doses of Pfizer and BioNTech's vaccine.

December 28 — Novavax Starts Phase 3 Trial of COVID-19 Vaccine

Novavax begins a phase 3 clinical trial, PREVENT-19, for its investigational COVID-19 vaccine, NVX-CoV2373, in 30,000 volunteers in Mexico and the United States.

December 29 — First US Case of New COVID-19 Variant Found in Colorado

The recently discovered novel variant found a week prior in the United Kingdom is detected in

a Colorado man in his 20s with no travel history. Scientists say they are concerned, but not surprised, since viruses are known to mutate.

December 30 — UK Approves Emergency Authorization for the AstraZeneca and Oxford COVID-19 Vaccine

As UK cases surge, regulators clear a vaccine from AstraZeneca and Oxford, AZD1222, for individuals 18 years and older.

December 31 —US Falls Short of Goal to Give 20 Million Vaccinations by Year End

As the year closed, the CDC says about 2.8 million people so far have received an initial vaccination. The US says on December 30 that about 14 million doses have been distributed, out of total of 20 million allocated doses.

Radiomics-Based Models Can Accurately Diagnose MM and Bone Metastases, Study Finds

May 21, 2022
Rose McNulty

Differentiation between multiple myeloma (MM) and bone metastases from other cancers can be difficult, but radiomics-based models have potential to improve diagnostic accuracy.

Differentiation between spine multiple myeloma (MM) and bone metastases (BM) related to other cancer types can be difficult given their similar sites of occurrence, clinical traits, and imaging features. To assist traditional methods of classification, a study published in *Frontiers in Medicine* evaluated novel radiomics models based on 18F-fluorodeoxyglucose positron emission tomography/CT (18F-FDG PET/CT) for the classification of spine MM and BM.

Misclassification of bone marrow lesions can affect patient survival and quality of life. Lesions classified incorrectly are also often misdiagnosed as other orthopedic diseases, and treatment options are significantly different for each condition. Reducing the risk of misdiagnosis in this setting is therefore a crucial endeavor.

Although serum markers such as creatinine, globulin, and alkaline phosphatase can help differentiate between BM and MM, patients with certain forms of myeloma tend to have normal or low numbers of these markers. With 18F-FDG PET/CT imaging—the International Myeloma Working Group's recommended imaging method for MM—anatomical and metabolic information are both used to assess bone damage and lesions with high sensitivity and specificity. But some lesions, like osteolytic lesions, are still difficult for even experienced clinicians to identify.

Radiomics uses machine learning to convert imaging features into high-dimensional data, allowing noninvasive evaluation of a tumor's spatial heterogeneity and assisting in personalizing treatment for individual patients. The current study explores the potential for

using radiomics in combination with 18F-FDG PET/CT to identify MM vs BM, given previous research has predominantly evaluated radiomics based on CT and MRI images.

A total of 131 patients were included in the study, 86 with a BM diagnosis and 45 with confirmed MM. In all, 184 lesions were randomly divided into a training group and a validation group at a 7:3 ratio to develop the radiomics models. The training group included 80 BM lesions and 49 MM lesions, and the validation group contained 34 and 21 lesions, respectively.

Ten and 8 texture features were selected from CT and PET, respectively, to build the models after least absolute shrinkage and selection operator regression and 10-fold cross-validation. There were 3 radiomics models: 2 constructed with CT and PET and using multivariate logistic regression and a ComModel using PET plus the maximum standardized uptake value of each lesion. Two experienced physicians evaluated the images in a double-blind format to test accuracy against the radiomics systems.

In both the training and evaluation groups, the 3 radiomics models performed well. The area under the receiver operating characteristic curve (AUC) was 0.909 in the CT training group, 0.949 in the PET training group, and 0.973 in the ComModel training group, and the CT, PET, and ComModel validation group AUCs were 0.897, 0.929, and 0.948, respectively.

The PET and ComModel were significantly better at diagnosing BM and MM vs the expert clinicians, while there was no significant statistical difference between the CT model and physician evaluation.

The study was limited due to its single-center nature. Therefore, more research would determine how the findings' generalizability. Some patients also did not have pathological findings and received their diagnosis based on combined pathological findings and follow-up results, the authors noted. But overall, the study results are promising.

The authors concluded, "Radiomics could transcend subjective visual assessment to provide an objective evaluation of lesion and tissue heterogeneity, which served as a new tool to provide valuable information about the microenvironment of lesions that cannot be observed by the human eyes."

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Biliary Tract Cancer Rates Vary by Country; Prevention Efforts Needed

May 20, 2022
Mary Caffrey

Authors wrote that their analysis was the first to combine incidence and mortality of overall BTC, and its anatomic subtypes, into a single study

Biliary tract cancer (BTC), a category that includes gall bladder cancer and more deadly forms of cholangiocarcinoma, is rising worldwide, a trend likely related to increased incidence of diabetes and obesity, according to new results gleaned from international databases and published in the journal *Gastro Hep Advances*.

Authors wrote that their analysis was the first to combine incidence and mortality of overall BTC, and its anatomic subtypes, into a single study.

Rates of BTC varied by country, with more cases seen in Asia and South America than in Europe or North America. In most countries, gall bladder cancer (GBC) accounted for the highest number of cases, but intrahepatic cholangiocarcinoma (ICC) proved more deadly. Other types included in the study were ampulla of Vater cancer (AVC) and extrahepatic cholangiocarcinoma (ECC).

Study authors said the increased incidence and mortality trends showed a need for better prevention and treatment of all types of BTC. "These findings may provide important public health guidance for intervention strategies and the development of therapeutics related to geographic groups with differing BTC rates," they wrote.

The authors derived their data from the International Agency for Research on Cancer, Cancer Incidence in Five Continents, Volume XI (2008–2012), which included data on 22 countries; and the World Health Organization Mortality Database (2006–2016) which had data from 38 countries. Deaths from BTC rose during the years studied.

BTC incidence, expressed as cases per 100,000 person-years, was highest in Chile, with 14.35 cases, and lowest in Vietnam, at 1.25 cases. Mortality rates were highest for South Korea (11.64) and lowest for Moldova (1.65). Patients who were at least 75 years had morality rates that were 5-10 times higher than overall rates. More women developed and died from GBC, but more men developed and died from ICC, ECC, and AVC.

Geographic differences. Incidence rates were highest in the Asia-Pacific region (1.12–9.00) and in South America (2.73–12.42), compared with those for Europe (2.00–3.59) and North America (2.33–2.35). Within the United States, BTC incidence was 1.3 times higher for Asian Americans than the general population.

The deadliest subtype, ICC, had an incidence rate of 2.18 in South Korea, with the lowest rate in Vietnam (0.16). Higher rates in Asian-Pacific countries have been attributed to infection with the parasite liver flukes in several Asian countries. The authors found that while BTC rates remained higher in this region, the authors also found signs that some prevention efforts are working.

"Although we report the BTC incidence rate in Thailand as one of the highest among the countries included in this analysis, a recent study showed a decrease in cholangiocarcinoma incidence between 2002 and 2013 in a northern Thailand province, which coincided with preventative measures concerning liver flukes," they wrote.

Comorbidities. The authors wrote that rising rates of diabetes, obesity, and non-alcoholic fatty liver disease may be contributing to the rising incidence of BTC. "A meta-analysis of observational studies found that body mass index status of overweight and obese was

associated with increased risk of ECC and GBC,while a different study suggested that diabetes and obesity increased the risk of ICC."

Lifestyle factors may play a role as well. Higher alcohol consumption was linked to ICC, and authors found a dose-repsonse trend. Study results also aligned with recent findings that the different varies of BTC and cholangiocarcinoma may act as very different cancers, with each one affected by specific risk factors. Thus, the authors wrote, the results show the need for "separating epidemiologic data by subtype in order to better understand disease etiology."

The authors acknowledged that their results may be affected by the challenges in getting an accurate BTC diagnosis in some countries; for example, they note that BTC is often classified as hepatocellular carcinoma. Inaccurate or delayed diagnoses can lead to poor treatment and outcomes, because initial treatment with surgery may not be possible once the cancer progresses.

As treatments improve, accuracy diagnosis becomes more important, the authors wrote.

"Improved diagnosis of BTC is also relevant to advances in targeted treatment as BTC subtypes may respond differently to treatments as suggested by studies showing that some subtypes have targetable molecular alterations," they said. "This is especially relevant, since targeted therapies have recently shown remarkable results in biomarker-selected patient populations, potential which could be exploited in combination with the more recent proposed schemas of immunotherapy."

The study was funded by AstraZeneca.

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High Proportions of Deaths Among Infants, Children Linked to RSV, Researchers Find

May 20, 2022
Hayden E. Klein

Researchers also found that 95% of respiratory syncytial virus (RSV)-associated acute lower respiratory infection episodes and more than 97% of RSV-attributable deaths were among children in low– and middle-income countries.

Respiratory syncytial virus (RSV) is linked to 1 in every 50 deaths among children aged 5 years and younger, and 1 in every 28 deaths among children aged between 28 days and 6 months, according to a systematic analysis published in *The Lancet*.

The authors of the analysis also estimated, for each RSV-associated acute lower respiratory infection in-hospital death, approximately 3 more RSV-attributable deaths in the community.

"RSV passive immunisation programmes targeting protection during the first 6 months of life could have a substantial effect on reducing RSV disease burden, although more data are needed to understand the implications of the potential age-shifts in peak RSV burden to older age when these are implemented," the authors wrote.

To come to these findings, the authors conducted a systematic analysis of 481 studies published or unpublished between 2017 and 2020. All studies included data on children aged 5 years or 60 months and younger who had RSV as primary infection with acute lower respiratory infection either in community settings or requiring hospital admission.

Based on these data, the authors said an estimated 33 million RSV-associated acute lower respiratory infection episodes (uncertainty range [UR], 25.4-44.6 million) occurred globally in 2019.

In children younger than 5 years, the authors also estimated 3.6 million RSV-associated acute lower respiratory infection hospital admissions (UR, 2.9-4.6 million) and 26,300 in-hospital deaths (UR, 15,100-49,100), as well as 101,400 RSV-attributable deaths overall (UR, 84,500-125,200).

These numbers were generally lower for infants younger than 6 months, but comparable in some areas.

For this age group, the authors estimated 6.6 million RSV-associated acute lower respiratory infection episodes (UR, 4.6-9.7 million), as well as 1.4 million RSV-associated acute lower respiratory infection hospital admissions (UR, 1.0-2.0 million) and 13,300 in-hospital deaths (UR 6800-28,100), and 45,700 RSV-attributable deaths overall (38,400-55,900).

High mortality rates associated with RSV were estimated for both age groups, with 2% of deaths among children aged 60 months and younger (UR, 1.6-2.4) and 3.6% of deaths among infants aged between 28 days and 6 months (UR, 3.0-4.4) attributable to the virus.

"Based on the estimates for in-hospital and overall mortality above, we further showed that globally, only 26% of RSV-attributable deaths occurred in hospitals in children aged 0–60 months; that is three deaths in the community for every RSV-associated acute lower respiratory infection in-hospital death," the authors said, noting that percentage is much lower than a previously estimated 50%.

It should also be noted that a vast majority of RSV-associated acute lower respiratory infection episodes (95%) and of RSV-attributable deaths (>97%) were among patients in low– and middle-income countries. The authors also discovered pronounced disparities in low-income countries, with 19% of deaths happening in hospitals, reflecting 4 community deaths for every in-hospital death.

"Most of the striking gap between in-hospital and community deaths in low-income settings can be explained by the poor access to care, cost of care, and limited beds in hospitals during an RSV epidemic," the authors wrote. "Another explanation is that some of the RSV deaths might be in children with rapidly progressive illness who, initially, do not appear to be severely ill."

Because of the disproportionately high burden of RSV morbidity and mortality among children younger than 6 months, the authors said further research is needed into immunizations for infants younger than 6 months, as they could potentially significantly reduce the RSV disease burden for these children.

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Study: Sacubitril/Valsartan Led to Fibrosis Improvements in HFrEF

May 20, 2022
Maggie L. Shaw

This study evaluated levels of 4 biomarkers associated with heart failure with reduced ejection fraction (HFrEF) before and after treatment with the angiotensin receptor neprilysin inhibitor sacubitril/valsartan.

Inflammation and fibrosis seen in heart failure with reduced ejection fraction (HFrEF) appeared subdued following treatment with angiotensin receptor neprilysin inhibitor sacubitril/valsartan, which the authors of a new study attribute to the natriuretic peptide system being ramped up and activity of the renin-angiotensin-aldosterone system (RAAS) being subdued.

The authors investigated levels of remodeling biomarkers in patients with HFrEF (N = 26), as well as their clinical and echocardiographic parameters, by comparing data from before administration of sacubitril/valsartan to findings seen at the 30- and 60-day marks post-therapy. The biomarkers were procollagen type 1 C-terminal propeptide (PICP), human cartilage glycoprotein-39 (YKL-40), plasma renin activity (PRA), and aldosterone (Aldo). All participants were receiving care at the Heart Failure Unit of Fondazione Cà Granda Ospedale Maggiore Policlinico, in Milan, Italy, between 2019 and 2020.

Findings from the prospective pharmacological, nonprofit, monocentric interventional pilot study were published recently in *BioMed Central Cardiovascular Disorders*.

"Sacubitril/valsartan is a novel drug combination designed to block the adverse effects of RAAS, to reduce bradykinin potentiation by valsartan, and to inhibit the neprilysin inactivating effect of natriuretic peptides by sacubitril metabolite LBQ657," the authors wrote. "It has been proven to be superior to conventional angiotensin-converting enzyme inhibition in reducing cardiovascular deaths and HF readmission."

Following measurements taken at baseline and at the 30- and 60-day marks, decreases in the means (SD) for all 4 biomarkers and in blood pressure, from baseline to the end of the study, were seen:

- Systolic blood pressure (BP) decreased approximately 10%: 113.4 (3.2) mm Hg from 126 (3.0) mm Hg
- Diastolic BP decreased approximately 6%: 71.9 (1.7) mm Hg from 77.5 (2.1) mm Hg

- Left ventricular ejection fraction rose 22.8%: 36.2% (1.0%) from 29.5% (1.0%)
- LV end-systolic volume dropped 12%: 34.0 (10.0) mL/m2 from 38.6 (8.7) mL/m2
- NT-proBNP dropped 53.7%: 1282 (289) ng/L from 2769 (481) ng/L
- PICP level dropped 42.2%: 85.4 (16.8) ng/mL from 147.8 (16.0) ng/mL
- YKL level dropped 46.8%: 101.9 (13.8) ng/mL from 191.8 (25.8) ng/mL
- PRA level dropped 79.2%: 1.55 (0.40) ng/dL from 7.47 (1.78) ng/mL
- Aldo level dropped 76.7%: 5.19 (3.4) ng/mL from 22.3 (5.12) ng/mL

Especially for the biomarkers, maximum benefit from sacubitril/valsartan was seen within 30 days of initiation ($P < .001$).

Sacubitril/valsartan treatment was begun at a dose of 24/26 mg twice a day. Overall, this dose did not change for 61.5% of patients; however, the dose did increase to 49/51 mg twice a day (the maximum tolerated dose) in 19.2% of patients and to 97/103 mg twice a day (the target dose) in 19.2% of patients.

No adverse events were reported, no patients required hospitalization or had worsening of their HF, and creatinine and electrolyte values remained consistent throughout the study.

Within the study cohort, the mean age was 69.8 (2.3) years, 77% were men, all had New York Heart Association class III disease, 50% had a history of smoking, 62% each had hypertension and hyperlipidemia, and all were on optimal treatment with beta-blockers, mineralcorticoid receptor antagonists, and diuretics before the study protocol initiated treatment with sacubitril/valsartan.

“The major finding of our study was that sacubitril/valsartan treatment in patients with HFrEF was associated with a decrease of circulating markers of fibrosis and inflammation,” the authors wrote. “This effect was already present within 30 days of treatment, persisted during the following 30 days, and was associated with a progressive inhibition of the RAAS.”

Their findings are especially noteworthy because their study is likely the first to find a potential relationship between sacubitril/valsartan treatment and myocardial fibrosis improvement. In turn, these results may add to current knowledge of the mechanism of action of the angiotensin receptor neprilysin inhibitor, particularly because inflammation can worsen HF.

“Our study for the first time documented that sacubitril/valsartan therapy was able to reduce the inflammatory context of HF,” they concluded. “Future studies in larger samples are highly desirable in order to clarify the long-term effect of sacubitril/valsartan on fibrosis in cardiac tissue.”

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FDA Approves Dupilumab as First Therapy for

Eosinophilic Esophagitis

May 20, 2022
Allison Inserro

Eosinophilic esophagitis is a chronic inflammatory disorder in which eosinophils, a type of white blood cell, proliferate in the esophagus, causing difficulties with eating and swallowing.

The FDA Friday approved dupilumab (Dupixent), a biologic, to treat eosinophilic esophagitis (EoE) in adults and children 12 years and older.

It is the first therapy approved specifically for EoE.

EoE was unknown a few decades ago; the chronic inflammatory disorder creates difficulty swallowing, difficulty eating, choking, and food getting stuck in the esophagus.

The monoclonal antibody acts on type 2 inflammation that drives the disease and causes eosinophils, a type of white blood cell, to flourish in the tissue of the esophagus, causing inflammation.

The approval, for patients weighing at least 40 kilograms, or about 88 pounds, was granted to Sanofi and Regeneron about 2 months earlier than expected, and comes at the end of National Eosinophil Awareness Week.

"We have waited a long time for an FDA-approved treatment option for eosinophilic esophagitis–an underdiagnosed and misunderstood disease of the esophagus that can make it extremely challenging and uncomfortable to eat and swallow," said Mary Jo Strobel, Executive Director at the American Partnership for Eosinophilic Disorders (APFED), in a statement provided by the drug companies. "Before today, there were no approved treatments specifically for eosinophilic esophagitis, resulting in many people needing to maintain a strict diet and live in constant fear of food getting stuck in their throat. We welcome therapeutic options that can provide much-needed relief for these patients."

“As researchers and clinicians have gained knowledge about eosinophilic esophagitis in recent years, more cases of the disorder have been recognized and diagnosed in the US,” said Jessica Lee, MD, director of the Division of Gastroenterology in the FDA’s Center for Drug Evaluation and Research. “Today’s approval will fulfill an important unmet need for the increasing number of patients with eosinophilic esophagitis.”

The efficacy and safety of dupilumab in EoE was studied in a randomized, double-blind, parallel-group, multicenter, placebo-controlled trial, that included 2 24-week treatment periods (Part A and Part B) that were conducted independently in separate groups of patients.

In Part A and Part B, patients received either placebo or 300 milligrams of dupilumab every week.

The 2 primary measurements of efficacy were the proportion of patients who achieved a certain level of reduced eosinophils in the esophagus at week 24, as determined by assessing patients’ esophageal tissue under a microscope, and the change in the patient-reported

Dysphagia Symptom Questionnaire (DSQ) score from baseline to week 24. The DSQ is a questionnaire designed to measure difficulty swallowing associated with EoE, with total scores ranging from 0 to 84; higher DSQ scores indicate worse symptoms.

In Part A of the trial, 60% of the 42 patients who received dupilumab achieved the pre-determined level of reduced eosinophils in the esophagus compared to 5% of the 39 patients who received a placebo.

Patients in Part A who received dupilumab experienced an average improvement of 22 points in their DSQ score compared to 10 points in patients who received placebo.

In Part B, 59% of the 80 patients who received dupilumab achieved the pre-determined level of reduced eosinophils in the esophagus compared to 6% of the 79 patients who received a placebo. Patients in Part B who received dupilumab experienced an average improvement of 24 points in their DSQ score compared to 14 points in patients who received placebo.

The most common side effects associated with dupilumab include injection site reactions, upper respiratory tract infections, joint pain, and herpes viral infections.

Dupilumab is also approved to treat atopic dermatitis, moderate to severe asthma or chronic rhinosinusitis with nasal polyposis.

All-Cause Mortality Falling Among People With Type 1 Diabetes

May 20, 2022
Jared Kaltwasser

In some cases, however, the rate of decline is no different than that of the general population, according to new research.

A new analysis of type 1 diabetes (T1D) outcomes from 6 countries shows that mortality rates from the disease have declined since 2000, although excess mortality compared with the general population remains high.

The study was published in *Diabetologia*, and it is based on data from Australia, Denmark, Latvia, Scotland, Spain, and the United States.

Rates of mortality from diabetes have been on the decline for the past 50 years, alongside an overall decrease in age-standardized mortality, explained the authors. Yet, most mortality studies looking specifically at T1D have focused on children and young adults, even though diabetes-related deaths among these age groups are rare.

“Secular mortality trends in middle-aged and older adults, for whom chronic complications dominate the causes of death, and among whom the vast majority of deaths of T1D occur, may differ markedly from younger adults,” the investigators noted. Moreover, they wrote that patients with T1D might also face a higher risk of death from causes not directly related to diabetes.

The investigators decided to use population-based databases in the 6 countries to better understand how all-cause mortality risk among patients with T1D has changed in recent years and how those changes track with variance in all-cause mortality in the general populations of those countries. The data for most of the countries was based on national health care and diabetes databases. In the case of the United States, the data came from Kaiser Permanente Northwest. The years analyzed varied by country, but overall, they cover 2000 to 2016 and include 1.5 million person-years.

The data show that country-by-country annual changes in age- and sex-standardized all-cause mortality among people with T1D dropped by between 2.1% and 5.8% over the study period. Australia had the lowest rate of decline, and Denmark had the largest.

Men and older patients tended to have higher rates of all-cause mortality, the data show, but those factors did not appear to affect the rate of decline. When the investigators used standardized mortality ratios (SMRs) to compare changes in mortality among patients with T1D to the general population, they found the ratio was higher in females than in males and peaked between ages 40 to 70 years.

Still, despite the positive trend in mortality among people with T1D, the investigators said the comparisons to general-population mortality trends provide important nuance. Even though all-cause mortality among T1D dropped in all 6 countries, the SMR—a reflection of excess mortality among people with T1D vs the general population—only declined in Denmark, Scotland, and Spain. That means the rates of decline in Australia, Latvia, and the United States merely tracked with declines in mortality among the general population.

“Despite reductions in absolute all-cause mortality rates, and, in some countries, in the SMR, T1D still confers a higher excess risk of death compared with individuals without diabetes,” the authors wrote.

They said suboptimal glycemic control and the presence of complications are key reasons for the higher risk and concluded that driving down excess mortality in T1D will continue to be a challenge in the coming years and decades.

“Considering the increasing incidence of T1D observed in younger populations in recent years, it is critical to continuously improve the multidimensional management of T1D, particularly among younger populations,” they wrote.

Reference

Ruiz PLD, Chen L, Morton JI, et al. Mortality trends in type 1 diabetes: a multicountry analysis of six population-based cohorts. *Diabetologia*. 2022;65(6):964-972. doi:10.1007/s00125-022-05659-9

Chitosan-Based Gel Found to Lower Risk of Wound Infection, Synechia After Nasal Polyps Surgery

May 20, 2022
Matthew Gavidia

Use of a chitosan-based gel dressing after endoscopic sinus surgery for nasal polyps was found to reduce risk of wound infection and synechia in patients, although no difference was observed regarding granulations.

Use of a chitosan-based gel dressing after endoscopic sinus surgery (ESS) for nasal polyps was found to reduce risk of wound infection and synechia in patients, according to study findings published in *International Wound Journal*.

For patients with chronic rhinosinusitis, septal deviation, or inferior turbinate hypertrophy, ESS has emerged as an effective therapeutic option to address persistent nasal obstruction when standard-of-care intranasal and systemic corticosteroids prove unsuccessful. However, certain limitations regarding the formation of postoperative bleeding and synechia have been knowm to impair recovery and potentially cause reobstruction of the ostiomeatal complex.

"Nasal packing was described to be one common method to stop postoperative bleeding and endorse wound healing.…Although, conventional removable nasal packing was restricted by some inadequacies, for example, nasal airway blockage; bleeding because of extramucosal disorders; headache and pressure; painful mouth, pharynx dryness, and tremendous anxiety," said the study authors.

Prior studies have found conflicting evidence on the use of chitosan-based gel dressing, formed by cross-linking chitosan and dextran derivatives gel, to address postoperative symptoms of ESS for nasal polyps. Acquired by alkaline deacetylation of natural chitins, chitosan has been considered to be an effective hemostatic agent, with a significant capability to quickly clot blood, hypoallergenicity, and antimicrobial influence.

Researchers conducted a meta-analysis of randomized controlled trials to further evaluate the effect of chitosan-based gel dressing on wound infection, synechia, and granulations after ESS of nasal polyps. A total of 6 studies reported between 2010 and 2022 comprising 386 patients who underwent ESS for nasal polyps were included for the analysis, of whom 187 were using chitosan-based gel dressing and 199 were control subjects.

Statistical tools like the dichotomous method were used within a random or fixed-influence model to evaluate the influence of chitosan-based gel dressing on risk of wound infection, synechia, and granulations after ESS of nasal polyps.

Findings indicated that chitosan-based gel dressing significantly lowered risk of postoperative wound infection and synechia by 52% and 75%, respectively (wound infection: odds ratio [OR], 0.48; 95% CI, 0.25-0.92; $P = .03$; synechia: OR, 0.25; 95% CI, 0.13-0.50; $P < .001$), compared with the control group. Conversely, no significant difference was observed in granulations between patients given chitosan-based gel dressing and the control group (OR, 1.57; 95% CI, 0.49-5.00; $P = .45$).

Discussing limitations of the analysis, researchers noted that the pooled data did not consider elements such as group age, ethnicity, and gender because of the lack of data on these variables. They added that further analysis is warranted to confirm findings due to the low

number of selected studies and the low sample size of all of the selected studies found for the meta-analysis.

"This study exhibited a correlation between the effects of chitosan-based gel dressing on wound infection, synechia, and granulations after ESS of nasal polyps," they concluded. "However, more trials are still required to explain the exact clinical difference in the results and closeness."

Reference

Liu R, Gong Z. Effect of chitosan-based gel dressing on wound infection, synechia, and granulations after endoscopic sinus surgery of nasal polyps: a meta-analysis. *Int Wound J.* Published online May 7, 2022. doi:10.1111/iwj.13820

Secukinumab Improved HRQOL, Symptoms in Pediatric Generalized Pustular Psoriasis

May 20, 2022
Allison Inserro

Over 48 weeks, secukinumab was shown to be effective and safe in a small study of 18 children with generalized pustular psoriasis in China.

A recently published case series examined the real-world data of secukinumab when used for pediatric generalized pustular psoriasis (GPP).

Secukinumab is known to be effective in adults with GPP, but the long-term efficacy and safety in children with this rare disease is unknown.

The authors, writing in a letter to the editor in the *Journal of the American Academy of Dermatology*, described 18 patients, seen in China's First Affiliated Hospital of Fujian Medical University, who received secukinumab from July 2019 to August 2020 and were followed for 48 weeks.

Most patients were male, with a mean age (SD) of 7.9 (2.3) years with a mean bodyweight of 29.3 (10.9) kg.

Of the 18 patients:

- 12 had plaque psoriasis before developing GPP
- The mean duration of their GPP was 3.3 years
- Their mean Generalized Pustular Psoriasis Area and Severity Index (GPPASI) score at baseline was 31.7
- Most patients had a mean Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) score at baseline of 3 or 4

Participants received secukinumab 75 mg only via subcutaneous administration at weeks 0, 1, 2, 3, 4 and then every 4 weeks.

Primary outcomes included changes in body temperature, laboratory examination assessments, and the changes in scores of the GPPASI and GPPGA from baseline.

Secondary outcomes included health-related quality of life (HRQOL), assessed by the Children's Dermatology Life Quality Index (CDLQI) and the Pediatric Quality of Life Inventory (PedsQL) scale.

In week 1, there was a rapid drop in body temperature and a reduction in white blood cell count and C-reactive protein.

In week 2, serum albumin levels improved from 36.3 (5.1) at baseline to 44.8 (1.9) at week and to 46.2 (3.8) at week 4.

Pustules subsided rapidly within 3 days of seckinumab treatment and erythema and scale reduced gradually in 2 weeks.

Also in week 2, mean GPPASI score fell from 31.7 to 5.1, and fell further to 1.3 at week 4. The improvement continued to week 48.

At week 48, 13 patients (72%) achieved GPPASI 100 while the other 5 patients achieved GPPASI 90. The GPPGA total score and the GPPGA pustulation subscore fell over time.

Side effects, which included eczema-like reactions, were mild. There were no serious adverse events.

For secondary outcomes, the investigators used the CDLQI and the PedsQL scales.

At the 48-week follow-up, results showed secukinumab improved HRQOL. The mean CDLQI score at baseline was 13.6 (5.5) and by week 48, 100% of the participants had a CDLQI score of 0 or 1. The reduction in the score was correlated with symptom improvement.

The PedsQL score was 25.5 (7.3) at baseline and began improving as early as week 2.

“Taken together, for pediatric GPP patients, the systemic inflammation and skin symptoms did rapidly improve with the treatment of secukinumab, and this effect was maintained up to 48 weeks without any unexpected safety signal,” the authors concluded. “These findings suggest that secukinumab can be a promising therapeutic option for pediatric GPP.”

Reference

Ruan SF, Zhang LI, Liu Z, et al. Real-world data on the clinical use of secukinumab in pediatric generalized pustular psoriasis: a 48-week retrospective study. *J Am Acad Dermatol.* Published online May 16, 2022. doi:10.1016/j.jaad.2022.04.064.

Analysis Underscores Risks of Polypharmacy in Elderly Patients With Cancer

May 20, 2022
Gianna Melillo

Results of a secondary analysis of a randomized controlled trial emphasize the risks of polypharmacy with regard to prescription and nonprescription medications.

Research published in *The Oncologist* highlights the burden of polypharmacy, potentially inappropriate medications (PIMs), and potential drug-interactions (DDIs) and drug–cancer treatment interactions (DCIs) among vulnerable older patients with cancer.

Of note, the study included nonprescription medications (which are often not accounted for in most polypharmacy studies) and found these OTC drugs are frequently PIMs and/or involved in potential DDIs/DCIs, authors wrote.

Polypharmacy is defined as the concurrent use of multiple medications and is common among older adults with cancer, researchers explained, as older individuals are more likely to be prescribed "multiple medications due to age-related multimorbidity, frailty, and other geriatric syndromes" than their younger counterparts.

Care fragmentation across multiple specialties, in addition to prescribing cascades aimed at mitigating adverse effects of other medications, also contribute to high rates of polypharmacy in this population.

Both polypharmacy and PIMs are associated with mortality, falls, and hospitalizations in older adults, and PIMs can even decrease tolerance of cancer treatments and worsen patient outcomes.

To better understand polypharmacy, PIMs, DDIs, and DCIs in an older population with cancer, researchers assessed data from 718 individuals recruited to a national prospective cluster-randomized trial of geriatric assessment (GA), conducted in community oncology practices.

Patients were enrolled between July 2014 and March 2019 and completed a polypharmacy log. All participants were 70 years or older, had a diagnosis of with incurable stage III or IV solid tumor cancer or lymphoma, and were planning to start a new cancer regimen with a high risk of grade 3 to 5 toxicity. Participants also had to be impaired in at least 1 GA domain apart from polypharmacy.

"Polypharmacy was defined as using ≥5 regular medications while excessive polypharmacy was defined using ≥10 regular medications," authors wrote.

Mean patient age was 77.2 years and 43.3% were female; the majority (n = 628) were non-Hispanic White and had stage IV cancer (n = 628).

Analyses revealed:

- Polypharmacy, excessive polypharmacy, and at least 1 PIM were identified in 61.3%, 14.5%, and 67.1% of patients, respectively.
- Cardiovascular medications were the most prevalent (47%), and nonprescription medications accounted for 26% of total medications and 40% of PIMs.
- One-quarter of patients had at least 1 potential major DDI not involving cancer treatment, and 5.4% had at least 1 potential major DCI.
- Each additional medication increased the odds of a potential major DDI and DCI by 39% and 12%, respectively; each additional prescription medication increased these odds by 40% ($P < .01$) and 19% ($P < .01$), respectively.

- Patients with polypharmacy were more likely to be older (mean age, 77.5 vs 76.7 years), have a functional impairment (62.1% vs 50.0%), be physically impaired (94.8% vs 90.1%), have significant comorbidity (78.0% vs 50.7%), and have impaired psychological status (32.7% vs 21.9%).

Hypertension, arthritis, heart diseases, and diabetes were the most common noncancer comorbidities in the cohort, and each patient took a median of 5 medications. Common nonprescription medications included proton pump inhibitors, nonsteroidal anti-inflammatory drugs, and antihistamines.

“Older adults may incorrectly assume that OTC medications are safe for them, and providers may be unaware of the full complement of medications their older patients are taking if a prescription was not generated,” authors wrote.

“This study, therefore, helps delineate the size and shape of a problem underrecognized by both providers and patients, and highlights an opportunity for improved medication reconciliation, patient and caregiver education, deprescribing, and other interventions,” they added.

Around 10% of hospitalizations among older individuals are associated with adverse drug events with most considered preventable, while in those undergoing chemotherapy, polypharmacy has been linked with an up to 114% increased risk of unplanned hospitalization.

The nature of the study, in that it is a secondary analysis of a randomized clinical trial, marks a significant limitation.

“More work is urgently needed to implement and evaluate interventions addressing polypharmacy and PIMs in older adults with cancer, particularly those initiating cancer treatment,” researchers concluded.

Reference:

Ramsdale E, Mohamed M, Yu V, et al. Polypharmacy, potentially inappropriate medications, and drug-drug interactions in vulnerable older adults with advanced cancer initiating cancer treatment. *Oncologist.* Published online March 28, 2022. doi:10.1093/oncolo/oyac053