A surgeon in Tulsa shot by a disgruntled patient. A doctor in India beaten by a group of bereaved family members. A general practitioner in the United Kingdom threatened with stabbing. The reality is grim: Health care workers across the globe experience violence while at work. A new study identifies this trend and finds that 25% of health care workers polled were willing to quit because of such violence.

“That was pretty appalling,” Rahul Kashyap, MD, MBA, MBBS, recalled. Dr. Kashyap is one of the leaders of the Violence Study of Health-care Workers and Systems (ViSHWaS), which polled an international sample of physicians, nurses, and hospital staff. This study has worriyng implications, Dr. Kashyap said. In a time when hospital staff are reporting burnout in record numbers, further deterrents may be the last thing our health care system needs. But Dr. Kashyap hopes that bringing awareness to these trends may allow physicians, policymakers, and the public to mobilize and intervene before it’s too late.

Previous studies have revealed similar trends. The rate of workplace violence directed at U.S. health care workers is five times that of workers in any other industry, according to the Bureau of Labor Statistics. The same study found that intravenous fluids are standard in the early resuscitation of sepsis patients, as are vasopressor agents, but data comparing restrictive or liberal use in these patients are limited, wrote Nathan I. Shapiro, MD, of Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, and colleagues.

In a study published in the New England Journal of Medicine (2023 Jan 21. doi: 10.1056/NEJMoa2212663), the researchers randomized 782 patients to the restrictive fluid group and 781 to the liberal fluid group. Patients aged 18 years and older were enrolled between March 7, 2018, and Jan. 31, 2022, at 60 centers in the United States. The researchers randomized 782 patients to the restrictive fluid group and 781 to the liberal fluid group. Patients aged 18 years and older were enrolled between March 7, 2018, and Jan. 31, 2022, at 60 centers in the United States.

A restrictive fluid strategy had no significant impact on mortality in patients with sepsis-induced hypotension compared to the liberal fluid strategy, based on data from a randomized, controlled trial of 1,563 individuals. Intravenous fluids are standard in the early resuscitation of sepsis patients, as are vasopressor agents, but data comparing restrictive or liberal use in these patients are limited, wrote Nathan I. Shapiro, MD, of Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, and colleagues.
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COVID emergency orders ending: What’s next?

BY DAMIAN MCNAMARA AND KELLY WAIRIMU DAVIS

The Biden administration announced that it will be ending the twin COVID-19 emergency declarations, marking a major change in the 3-year-old pandemic.

The orders spanned two presidencies. Health & Human Services Secretary Alex Azar issued a public health emergency in January 2020. Then-President Trump declared the COVID-19 pandemic a national emergency 2 months later. Both emergency declarations – which remained in effect under President Biden – will expire May 11.

Read on for an overview of how the end of the public health emergency will trigger multiple federal policy changes.

Changes that affect everyone
- There will be cost-sharing changes for COVID-19 vaccines, testing, and certain treatments. One hundred–percent coverage for COVID testing, including free at-home tests, will expire May 11.
- Telemedicine cannot be used to prescribe controlled substances after May 11.
- Enhanced federal funding will be phased down through Dec. 31, 2023. This extends the time states must receive federally matched funds for COVID-related services and products, through the Consolidated Appropriations Act of 2023. Otherwise, this would have expired June 30.
- Emergency use authorizations for COVID-19 treatments and vaccinations will not be affected and/or end on May 11.

Private health insurance
- Many will likely see higher costs for COVID-19 tests, as free testing expires and cost-sharing begins in the coming months.
- COVID-19 vaccinations and boosters will continue to be covered until the federal government’s vaccination supply is depleted. If that happens, you will need an in-network provider.
- You will still have access to COVID-19 treatments – but that could change when the federal supply dwindles.

Medicare recipients
- Medicare telehealth flexibilities will be extended through Dec. 31, 2024, regardless of public health emergency status. This means people can access telehealth services from anywhere, not just rural areas; can use a smartphone for telehealth; and can access telehealth in their homes.
- Medicare cost-sharing for testing and treatments will expire May 11, except for oral antivirals.

Medicaid/CHIP recipients
- Medicaid and Children’s Health Insurance Program (CHIP) recipients will continue to receive approved vaccinations free of charge, but testing and treatment without cost-sharing will expire during the third quarter of 2024.
- The Medicaid continuous enrollment provision will be separated from the public health emergency, and continuous enrollment will end March 31, 2023.

Uninsured people
- The uninsured will no longer have access to 100% coverage for these products and services (free COVID-19 treatments, vaccines, and testing).

Health care providers
- There will be changes to how much providers get paid for diagnosing people with COVID-19, ending the enhanced Inpatient Prospective Payment System reimbursement rate, as of May 11, 2023.
- Health Insurance Portability and Accountability Act (HIPAA) potential penalty waivers will end. This allows providers to communicate with patients through telehealth on a smartphone, for example, without violating privacy laws and incurring penalties.

What the experts are saying
This news organization asked several health experts for their thoughts.

Question: Do you agree with the timing of the end to the emergency order?
Answer: Robert Atmar, MD, professor of infectious diseases at Baylor College of Medicine in Houston: “A lead time to prepare and anticipate these consequences may ease the transition, compared to an abrupt declaration that ends the declaration.”
Answer: Georges C. Benjamin, MD, executive director of the American Public Health Association: “I think it’s time to do so. It has to be done in a great, thoughtful, and organized way because we’ve attached so many different things to this public health emergency. It’s going to take time for the system to adapt. Data collection most likely will continue. People are used to reporting now. The CDC needs to give guidance to the states so that we’re clear about what we’re reporting, what we’re not.”
Answer: Bruce Farber, MD, chief public health and epidemiology officer at Northwell Health in Manhasset, N.Y.: “I would have hoped to see it delayed.”
Answer: Steven Newmark, JD, chief legal officer and director of policy at the Global Healthy Living Foundation: “While we understand that an emergency cannot last forever, we hope that expanded services such as free vaccination, promotion of widespread vaccination, increased use of pharmacists to administer vaccines, telehealth availability and reimbursement, flexibility in work-from-home opportunities, and more continues. Access to equitable health care should never backtrack or be reduced.”

Q: What will the end of free vaccinations and testing mean?
A: Dr. Farber: “There will likely be a decrease in vaccinations and testing. The vaccination rates are very low to begin with, and this will likely lower it further.”
A: Dr. Benjamin: “For people who are uninsured and underinsured, we’ve got to make sure they have access to those. There’s a lot of discussion and debate about what the cost of those tests and vaccines will be, and it looks like the companies are going to impose very steep, increasing costs.”

Q: How will this affect higher-risk populations, like people with weakened immune systems?
A: Dr. Farber: “Without monoclonals [drugs to treat COVID] and free Paxlovid, people with weakened immune systems “may be undertreated.”

A: Dr. Atmar: “The implications of ongoing widespread virus transmission are that immunocompromised individuals may be more likely to be exposed and infected and to suffer the consequences of such infection, including severe illness. However, to a certain degree, this may already be happening. We are still seeing about 500 deaths/day, primarily in persons at highest risk of severe disease.”
A: Dr. Benjamin: “People who have good insurance can afford to get immunized. But lower-income individuals and people who really can’t afford to get tested or get immunized would likely become underimmunized and more infected. So even though the federal emergency declaration will go away, I’m hoping that the federal government will continue to encourage all of us to emphasize those populations at the highest risk – those with chronic disease and those who are immunocompromised.”

A: Mr. Newmark: “People who are immunocompromised by their chronic illness or the medicines they take to treat acute or chronic conditions remain at higher risk for COVID-19 and its serious complications. The administration needs to support continued development of effective treatments and updated vaccines to protect the individual and public health. We’re also concerned that increased health care services – such as vaccination or telehealth – may fall back to pre-pandemic levels while the burden of protection, such as masking, may fall to chronic disease patients alone, which adds to the burden of living with disease.”

Q: What effect will ending Medicaid expansion money have?
A: Dr. Benjamin: Anywhere from 16 to 20 million people are going to lose in coverage. I’m hoping that states will look at their experience over these last 2 years or so and come to the decision that there were improvements in healthier populations.

Q: Will this have any effect on how the public perceives the pandemic?
A: Dr. Farber: “It is likely to give the impression that COVID is gone, which clearly is not the case.”
A: Dr. Benjamin: “I’ll be another argument by some that the pandemic is over. I’m hoping people will realize … that they still need to protect themselves, get vaccinated, and wear a mask when appropriate.”

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Fluid

United States. Participants were randomized within 4 hours of meeting the criteria for sepsis-induced hypotension that was refractory to initial treatment with 1-3 L of intravenous fluid. Baseline characteristics were similar between the groups. At randomization, 21% of patients in the restrictive fluid group and 18% in the liberal fluid group received vasopressors.

The primary outcome was 90-day all-cause mortality, which occurred in 109 and 116 patients in the liberal and restricted groups, respectively (approximately 14% of each group). No significant differences were noted among subgroups based on factors including systolic blood pressure and the use of vasopressors at randomization, chronic heart failure, end-stage renal disease, and pneumonia.

The restrictive fluid protocol called for vasopressors as the primary treatment for sepsis-induced hypotension, with “rescue fluids” to be used for prespecified situations of severe intravascular volume depletion. The liberal fluid protocol was a recommended initial intravenous infusion of 2,000 mL of isotonic crystalloid, followed by fluid boluses given based on clinical triggers such as tachycardia, along with “rescue vasopressors,” the researchers wrote.

The median volume of fluid administered in the first 24-hour period after randomization was 1,267 mL in the restrictive group and 3,400 mL in the liberal group. Adherence to the treatment protocols was greater than 90% for both groups.

Violence

attacks had increased 63% from 2011 to 2018. Other polls that focus on the pandemic show that nearly half of U.S. nurses believe that violence increased since the world shut down. Well before the pandemic, however, a study from the Indian Medical Association found that 75% of doctors experienced workplace violence.

With this history in mind, perhaps it’s not surprising that the idea for the study came from the authors’ personal experiences. They had seen coworkers go through attacks, or had endured attacks themselves, Dr. Kashyap said. But they couldn’t find any global data to back up these experiences. So Dr. Kashyap and his colleagues formed a web of volunteers dedicated to creating a cross-sectional study.

They got in touch with researchers from countries across Asia, the Middle East, South America, North America, and Africa. The initial group agreed to reach out to their contacts, casting a wide net. Researchers used WhatsApp, LinkedIn, and text messages to distribute the survey. Health care workers in each country completed the brief questionnaire, recalling their prepandemic world and evaluating their current one.

Within 2 months, they had reached health care workers in more than 100 countries. They concluded the study when they received about 5,000 results, according to Dr. Kashyap, and then began the process of stratifying the data. For this report, they focused on critical

 Violence continued on following page
Anne C. Coates, MD, FCCP, was born and raised in Montpelier, Vt. She attended the University of Vermont Larner College of Medicine for medical school, completed her pediatric residency at the University of Massachusetts and pediatric pulmonary fellowship at the Lucile Packard Children’s Hospital of Stanford. She returned to Northern New England in 2013 to begin her practice at the Barbara Bush Children’s Hospital in Portland, Maine. She loves being a pediatric pulmonologist and feels honored to serve the community at large where she is passionate about medical education and advocacy. She and her husband, a fellow Vermonter, feel blessed to raise their four young children in such a wonderful community.

Russell Miller, MD, is the Fellowship Program Director for Pulmonary and Critical Care Medicine and Director of Interventional Pulmonology at the Naval Medical Center, San Diego. Dr. Miller is a U.S. Navy physician with extensive experience in both military and academic settings. He has deployed to Afghanistan and served as the officer-in-charge during a COVID-19 domestic assistance deployment. He led the development of the American Association for Bronchology and Interventional Pulmonology’s (AABIP) first consensus guideline on the post-insertion management of indwelling pleural catheters. Dr. Miller has published numerous peer-reviewed articles and book chapters, with a primary focus on interventional pulmonary procedures and lung cancer. He has received numerous military decorations for his service and holds academic appointments as an Assistant Professor of Medicine at the Uniformed Services University of Health Sciences and the University of California, San Diego.

Sreelatha Naik, MD, is the Program Director for Sleep Medicine Fellowship, Regional Director for Sleep Medicine, and attending physician in Pulmonary, Critical Care and Sleep Medicine at Geisinger Health System-Geisinger Wyoming Valley Medical Center and the Geisinger Commonwealth School of Medicine. She manages the Center's home ventilation and chronic respiratory failure clinic. She is Vice-Chair of the Respiratory-Related Sleep Disorders Section of the Sleep Medicine Network. Her clinical expertise is in sleep breathing disorders, neuromuscular respiratory weakness, and noninvasive ventilation for chronic hypotension syndromes.

Dharni Narendra, MD, FCCP, is the Vice-Chair of Bronchiectasis Section, Airway Disorders Network at CHEST. She is an Assistant Professor in the Division of Pulmonary, Critical Care, and Sleep Medicine, Baylor College of Medicine, Houston, Texas. She is the Associate Program Director for Critical Care Medicine Fellowship Program at Baylor. Her clinical and research interests are in critical care, ARDS, airway disorders, and medical education.

Samira Shojaee, MD, MPH, FCCP, is an Associate Professor of Medicine at Vanderbilt University Medical Center and Vanderbilt University College of Medicine. She completed her pediatric residency and pulmonary fellowship at Nationwide Children’s Hospital. Currently, she is an attending in pediatric pulmonology, the Director of the Pulmonary Complex Asthma Clinic, and a collaborating pulmonologist in the Pulmonary Sickle Cell Combined Clinic at Nationwide Children’s Hospital.

Dr. Coates
Dr. Miller
Dr. Naik
Dr. Narendra
Dr. Shojaee

Violence continued from previous page

care, emergency medicine, and anesthesiology, which resulted in 598 responses from 69 countries. Of these, India and the United States had the highest number of participants.

In all, 73% of participants reported facing physical or verbal violence while in the hospital; 48% said they felt less motivated to work because of that violence; 39% of respondents believed that the amount of violence they experienced was the same as before the COVID-19 pandemic; and 36% of respondents believed that violence had increased. Even though they were trained on guidelines from the Occupational Safety and Health Administration, 20% of participants felt unprepared to face violence.

Although the study didn’t analyze the reasons workers felt this way, Dr. Kashyap speculated that it could be related to the medical distrust that grew during the pandemic or the stress patients and health care professionals experienced during its peak.

Regardless, the researchers said their study is a starting point.

Now that the trend has been highlighted, it may be acted on.

Moving forward, Dr. Kashyap believes that controlling for different variables could determine whether factors like gender or shift time put a worker at higher risk for violence. He hopes it’s possible to interrupt these patterns and reestablish trust in the hospital environment. “It’s aspirational, but you’re hoping that through studies like ViSHWaS, which means trust in Hindi ... [we could restore] the trust and confidence among health care providers for the patients and family members.”

LONG COVID

Inflammation and immunity troubles top list of causes

BY SOLARINA HO

Nonstop inflammation and immune problems top the list of potential causes of long COVID, but doctors say it’s growing clear that more than one thing is to blame for the wide swath of often debilitating symptoms that could last months or even years.

“I think that it’s a much more complex picture than just inflammation, or just autoimmune, or just immune dysregulation. It’s probably a combination of all three causing a cascade of effects that then manifests itself as brain fog, or shortness of breath, or chronic fatigue,” said Alexander Truong, MD, a pulmonologist and assistant professor at Emory University, Atlanta, who also runs a long-COVID clinic.

Long COVID, post–COVID-19 condition, and postacute sequelae of SARS-CoV-2 (PASC) are among the terms used by the National Institutes of Health to describe the long-term health issues faced by an estimated 10%-30% of people infected with COVID-19. Symptoms — as many as 200 — can range from inconvenient to crippling, damage multiple organ systems, come and go, and relapse. Long COVID increases the risk of worsening existing health problems.

Long COVID continued on following page
and triggering new ones, including cardiovascular disease and type 2 diabetes.

So far, research suggests there is no single cause, condition, or disease that explains why some people have an extensive range of symptoms long after the early COVID-19 infection has cleared up. Many experts believe some combination of biological processes – including the virus hanging around in our bodies, inflammation, autoimmunity, tiny blood clots, immune system problems, and even the reactivation of dormant viruses such as the Epstein-Barr virus – could be the culprit, a theory also supported by a comprehensive and in-depth review of long-COVID studies published in the journal Nature Reviews Microbiology (2023 Jan 13. doi: 10.1038/s41579-022-00846-2).

"It becomes clear over the last couple of years that there are different [symptoms] of long COVID … that cannot all be lumped together," said Michael Peluso, MD, an assistant professor of medicine and an infectious diseases doctor at the University of California, San Francisco.

Inflammation and a lingering virus

Multiple studies have shown that the virus or pieces of it can remain in many parts of the body, including the kidneys, brain, heart, and gastrointestinal system, long after the early infection. "One major question that I think is the area of most intense investigation now is whether there is viral persistence that is driving immune dysregulation and therefore symptoms," says Dr. Peluso.

A small Harvard University study (Clin Infect Dis. 2022 Sep 2. doi: 10.1093/cid/ciacc722), for example, found evidence that reservoirs of the coronavirus could linger in patients up to a year after they’re first diagnosed.

An earlier German study (Cell Rep Med. 2022 Jun 21. doi: 10.1016/j.xcrm.2022.100663) found that patients with post–COVID-19 symptoms had higher levels of three cytokines – small proteins that tell the body’s immune system what to do and are involved in the growth and activity of immune system cells and blood cells. Researchers said the results supported the theory that there is persistent reprogramming of certain immune cells, and that the uncontrolled “self-fueled hyperinflammation” during the early COVID-19 infection can become continued immune cell disruption that drives long-COVID symptoms.

"Long COVID is more likely due to either an inflammatory response by the body or reservoirs of virus that the body is still trying to clear … and the symptoms we’re seeing are a side effect of that," said Rainu Kaushal, MD, senior associate dean for clinical research at Weill Cornell Medicine in New York.

Australian researchers found (Nat Immunol. 2022 Jan 13. doi: 10.1038/s41590-021-01113-x) that immune system recovery appeared different, compared with those who were infected with other common coronaviruses.

These findings also support concerns that some experts express over the long-term risks of COVID-19 infections in general, but especially repeat infections. "Anything that kind of revs up inflammation in the body can boil that pot over and make the symptoms worse. That’s very easily an infection or some other insult to the body. So that’s the generalized hypothesis as to why insults to the body may worsen the symptoms," said Dr. Truong.


Dr. Truong and his team, for example, have been documenting inflammatory markers in patients at the post–COVID clinic he cofounded more than 2 years ago at Emory Executive Park in Atlanta. When the clinic was first launched, high-dose nonsteroidal anti-inflammatory drugs – including ibuprofen – and prednisone were prescribed to long–COVID patients.

"It didn’t make a difference at all for any of these folks," he said, adding that there are signs that autoimmunity is at play. But he cautioned that it is still too early to suggest treating long-COVID patients with medications used for other autoimmune conditions.

In autoimmune conditions such as rheumatoid arthritis, lupus, and type 1 diabetes, a person’s immune system can’t tell normal cells from foreign pathogens and attacks healthy cells. There is typically no single diagnostic test, and many share similar symptoms, making detection and diagnosis particularly difficult, according to Johns Hopkins Medicine.

A small study published in the journal Science Translational Medicine (2022 Dec 21. doi: 10.1126/scitranslmed.abb8484) found that, among patients who failed to regain their sense of smell long after their initial infection, there was inflammation in the nose tissue where smell nerve cells are found, even though no detectable virus remained. Fewer olfactory sensory neurons were seen, as well – findings that researchers said resembled some kind of “autoimmune-like process.”

Meanwhile, scientists in Canada found signs of autoimmunity in blood samples taken from patients who still had fatigue and shortness of breath after their initial COVID-19 infection. Two specific proteins were present a year after infection in up to 30% of patients, many of whom still had shortness of breath and fatigue, the researchers reported in the Jan. 1 issue of the European Respiratory Journal (2023. doi: 10.1183/13993003.00970-2022). These patients had been healthy and had no autoimmune conditions or other diseases before they were infected.

Immune system problems

A number of studies suggest that a problematic immune response could also explain why symptoms persist for some people.

Researchers in France (J Med Virol. 2022 Oct 13. doi: 10.1002/jmv.28209), for example, found that the immune response problems in those with severe COVID-19 infections caused exaggerated or uncontrolled formation of a type of bug-fighting defense mechanism called a neutrophil extracellular trap (NET), which in turn triggers harmful inflammation that can result in multiorgan damage. These traps are netlike structures made from fibers composed mostly of DNA strings that bind, or trap, pathogens.

Long COVID is not like an acute infectious disease, said Alexander Charney, MD, PhD, the lead principal investigator of the RECOVER adult cohort at Mount Sinai in New York, and an associate professor at Icahn School of Medicine at Mount Sinai. It is more similar to other complex chronic diseases that have taken decades to understand, such as heart disease, mental illness, and rheumatologic diseases, he says.

Biomarkers and blood clots

Scientists are honing in on biomarkers, or detectable and measurable traits – in this case, molecular indicators – that can make diagnosing long COVID easier and give better direction for treatment. These biomarkers are also key to helping sort out the complex biology of long COVID.

In one study, data from blood samples taken from hundreds of hospitalized COVID-19 patients suggest changes are happening at the molecular level during initial severe infections. These changes may be tied to the development of longer-term symptoms, according to the study by Dr. Charney and his team at Mount Sinai published in Nature Medicine (2022 Dec 8. doi: 10.1038/s41591-022-02107-4).

Blood clotting issues have also been detected in long–COVID patients. At least one study (J Med Virol. 2022 Oct 13. doi: 10.1002/jmv.28209) found signs that long-COVID patients had higher levels of a type of auto-antibody linked to the abnormal formation of clots. Researchers suspect that tiny, persistent microclots – undetectable via regular pathology tests – may be cutting off oxygen flow to tissue by blocking capillaries – and could explain many of the post–COVID symptoms described by patients.

While enormous progress has been made toward understanding long COVID, the research is still considered early and faces many challenges, including varying criteria used to define the condition, differences in patient recruiting, the types and quality of data used, and the small size of many studies. Some research also appears to conflict with other studies. And while there are specialized tools for diagnosing some aspects of the condition, standard tests often don’t detect many of the signs seen in long-COVID patients.

"People are suffering now, and they want answers now," said Dr. Charney. "It’s going to be a long haul to figure out what is going on."
LUNG CANCER

Does less invasive surgery compromise outcomes?

BY LIAM DAVENPORT

For patients with early–stage non–small cell lung cancer (NSCLC), the survival outcomes appeared just as good with sublobar resection as with the more invasive lobaresection, suggested results from the CALGB 140503 trial. These new results contrast with those from a previous study from 1995, which found that local recurrence was three times higher and cancer mortality was twice as high with the less invasive procedure.

Those results from nearly 30 years ago established lobectomy as the standard of surgical care in this patient population, but since then advances in imaging and staging have allowed the detection of smaller and earlier tumors, which has “rekindled interest in sublobar resection,” the authors commented. Hence, they conducted the new trial, which involved almost 700 U.S. patients with clinical T1aN0 NSCLC and a tumor size up to 2 cm, who were randomly assigned to lobar or sublobar tumor resection, and followed for 7 years.

“The thoracic surgeons will need to expand their expertise in sublobar resections, especially complex segmentectomies, and will need to collaborate closely with pathologists ...”

The rates of both disease-free and overall survival were similar between the two groups, with no significant differences observed. There were also no substantial differences in rates of distant and locoregional recurrence.

In addition, there was a suggestion of less reduction in pulmonary function following the less invasive procedure.

“These findings affirm that sublobar resection ... is an effective management approach for this subgroup of patients with NSCLC,” said lead author Nasser Altorki, MD, Weill Cornell Medicine, New York–Presbyterian Hospital, New York.

“It is important that these results are interpreted strictly within the constraints of the eligibility criteria mandated by the trial, he emphasizes. “Specifically, the results are applicable only to a highly selected group of patients ... in whom the absence of metastases to hilar and mediastinal lymph nodes is pathologically confirmed.” Nevertheless, Dr. Altorki said that “these results will become increasingly relevant as the proportion of patients with early-stage lung cancer increases with expanded implementation of lung cancer screening, and as the number of older persons with early-stage disease in whom sublobar resection may be the preferred surgical option increases.”


In an accompanying editorial (2023 Feb 9. doi: 10.1056/NEJMe2215647), Valerie W. Rusch, MD, Thoracic Service, Memorial Sloan Kettering Cancer Center, New York, agreed. “As CT screening becomes more widespread, this patient population will increase in clinical practice,” she explained.

However, Dr. Rusch also urged caution around patient selection, underlining that the results do not “provide a license for suboptimal surgical care.” She said that “safeguards” such as the meticulous and strict patient criteria used in the trial “must be preserved in routine practice.”

“Thoracic surgeons will need to expand their expertise in sublobar resections, especially complex segmentectomies, and will need to collaborate closely with pathologists in assessing margins of resection, adequacy of lymph-node staging, and tumor characteristics that may predict recurrence.”

While emphasizing that lobectomy should still be performed when appropriate, Dr. Rusch nevertheless said: “The era of ‘precision surgery for NSCLC has arrived.”

The investigators also point out that their findings are “consistent” with those of a recent Japanese study (Lancet. 2022 Apr 23. doi: 10.1016/S0140-6736(21)02333-3) that compared lobectomy with anatomical segmentectomy, which found that the 5-year overall survival was 91.1% for lobectomy and 94.3% for segmentectomy. The authors suggest that the difference in overall survival rates between the two trials might be due to anatomical segmentectomy being “considered by most surgeons to be more oncologically sound than wedge resection.”

In the current trial, wedge resection was allowed, however, “because it is the most frequently practiced method of sublobar resection in North America and Europe; thus, its inclusion would make the trial more representative of a ‘real world’ setting.”

Another important difference could be that more than 90% of the patients in the Japanese trial had adenocarcinoma, 45% with an associated ground-glass component, which is associated with better survival than a completely solid adenocarcinoma.

Dr. Rusch agrees that there are likely to be various factors related to the survival differences between the two trials, including patient selection, intraoperative management, and tumor characteristics.

“However, these two landmark trials are practice-changing because they establish sublobar resection as the standard of care for a select group of patients with NSCLC,” Dr. Rusch concluded.

Dr. Altorki and colleagues conducted the multicenter, international, randomized, noninferiority, phase 3 trial in patients with clinically staged T1aN0 NSCLC from 83 academic and community-based institutions in the United States, Canada, and Australia.

Patients were required to have a peripheral lung nodule with a solid component of up to 2 cm on preoperative CT, a tumor center in the outer third of the lung, and a tumor location amenable to sublobar resection, whether wedge or segment, or lobaresection, among other criteria.

In all, 697 patients were randomly assigned to undergo either lobaresection or sublobar resection, of whom 59.1% had wedge resection and 37.9% anatomical segmental resection. The median age was 67.9 years, and 57.4% were female. The vast majority (90%) were White. After a median follow-up of 7 years, the 5-year disease-free survival was 63.6% with sublobar resection and 64.1% following lobaresection.

The team found that sublobar resection was not inferior to lobaresection for disease-free survival, at a hazard ratio for disease recurrence or death of 1.01 (90% confidence interval, 0.83–1.24), which adjusted to 0.99 after taking into account the site where the patient was treated.

The 5-year overall survival rate was 80.3% after sublobar resection, and 78.9% following lobaresection, at a hazard ratio for death of 0.95 (95% CI, 0.72–1.26). The results were “generally consistent” when accounting for factors such as age group, sex, tumor location, histologic type, smoking history, tumor size, and ECOG performance status.

The researchers showed that, among 687 patients eligible for assessment, 30.4% of those in the sublobar resection group and 29.3% of those assigned to lobaresection experienced disease recurrence, with 13.4% and 10%, respectively, having locoregional recurrence.

An exploratory analysis indicated that 5-year recurrence-free survival was similar in the two groups, at 70.2% vs. 71.2% or a hazard ratio for recurrence of 1.05 (95% CI, 0.80–1.39). The cumulative incidence of death was also similar. It was also notable that reduction in predictive forced expiratory volume in 1 second from baseline was lower with sublobar than lobaresection, at −4.0 vs. −6.0, as was the reduction in predicted forced vital capacity, at −3.0 vs. −5.0.

“Although this difference is arguably not clinically meaningful in this patient population with normal baseline pulmonary functions,” the team writes, “it may be more clinically relevant in patients with compromised pulmonary functions, or in those with lower-lobe disease in whom lobaresection may be associated with greater impairment of pulmonary function.”

The study was supported by the National Cancer Institute and supported in part by Covidiene and Ethicon. Dr. Altorki reported relationships with AstraZeneca, Genentech, Johnson & Johnson, and Regeneron. Dr. Rusch reported relationships with Genentech, and the National Cancer Institute.
Dapper homolog 2 shows promise for idiopathic pulmonary fibrosis

BY HEIDI SPLETE
MDedge News

Dapper homolog 2 attenuated pulmonary fibrosis development and suppressed glycosis in myofibroblasts, suggesting potential as a therapeutic target for idiopathic pulmonary fibrosis, based on data from mouse models. Idiopathic pulmonary fibrosis (IPF) remains a challenge with poor prognosis, and current therapeutic options are limited, wrote Xiaofan Lai, of Sun Yat-sen University, Guangzhou, China, and colleagues. Previous studies suggest that myofibroblasts are key contributors to fibrosis in IPF, they said.

"We hope this research will lay the theoretical foundation for finding novel therapeutics to alleviate or reverse the development of pulmonary fibrosis."

They found that overexpression of DACT2 was associated with glucose uptake, extracellular acidification rate, intracellular adenosine-triphosphate (ATP) level, and lactate levels of myofibroblasts. The researchers also conducted in vitro experiments in which they treated lung fibroblasts with cycloheximide (CHX), a protein synthesis inhibitor. These experiments showed that DACT2 inhibited differentiation of lung myofibroblasts by downregulating lactate dehydrogenase A (LDHA), which caused suppression of glycosis in myofibroblasts.

"Aerobic glycolysis is an important method of energy generation, and several studies have shown that enhanced glycolysis facilitates the progression of pulmonary fibrosis," the researchers wrote in their discussion.

More research is needed outside of mouse models and in vitro studies, but the current study is the first known to explore the relationship between DACT2 and LDHA in pulmonary fibrosis, and the results provide evidence of the potential benefits of DACT2 in treating lung disorders, the researchers wrote. "We hope this research will lay the theoretical foundation for finding novel therapeutics to alleviate or reverse the development of pulmonary fibrosis and other chronic lung disorders," the researchers concluded.

The study was supported by the National Natural Science Foundation of China and the Regional Joint Fund-Youth Fund projects of Guangdong Province. The researchers had no financial conflicts to disclose.

DACT2 inhibited differentiation of lung myofibroblasts by downregulating lactate dehydrogenase A, which caused suppression of glycosis.
BUSINESS OF MEDICINE

How much is enough for informed consent?

BY LAMBERT HOCWALD

sitting across from a patient explaining a complicated treatment proposal, protocol, or medication may be one of the most complex yet crucial tasks you have as a physician. Although informed consent is at the forefront of shared decisions between you and your patient, there’s a fine line between providing enough information on the risks and benefits of a particular treatment and knowing you’ve explained it well enough to fully educate your patient about their choices.

According to the Medscape “Right and Wrong in Medicine: Life, Death, and Wrenching Choices” report, how you handle the informed consent process can be the difference between a positive outcome and a negative one.

“It is a bit of a fine line because unless your patient happens to be a health care provider, medicine is complicated for patients to understand,” said David L. Feldman, MD, chief medical officer at The Doctors Company, the nation’s largest medical malpractice insurer in New York.

In addition, documenting the interaction is critical, said James Giordano, PhD, MPhil, professor in the departments of neurology and biochemistry and chief of the neuroethics studies program at the Pellegrino Center for Clinical Bioethics at Georgetown University Medical Center, Washington.

“As with anything in medicine, the key rule is that, if it’s not documented, it’s not done,” he said. “This also means diligent documentation in all aspects of the medical record, including the electronic medical record and the written one.”

That said, it’s important to know what’s enough and what’s too granular when you discuss a procedure with your patients, said Erum N. Ilyas, MD, a board-certified dermatologist at Schweiger Dermatology and a bioethicist near Philadelphia.

“One of the most challenging aspects of informed consent, especially for young physicians, is how to discuss a procedure or a medication in a manner that is both relevant and concise,” Dr. Ilyas said. “I’ve had residents ask to perform a skin biopsy spend several minutes covering every aspect of every potential outcome of a routine skin biopsy. The patient is left traumatized and confused as to whether they should proceed with the small procedure.”

Instead, the goal of informed consent is to ensure that the patient has a general overview of the procedure and is empowered, knowing that the decision to proceed is, indeed, part of their decision-making process. How long an informed consent discussion takes depends on the procedure.

“When I was in practice as a plastic surgeon, the conversations varied from the straightforward ‘I’m taking this mole off your cheek, and there’s a risk of scarring and bleeding’ to talking about a mastectomy and breast reconstruction, which could take an hour or more to discuss,” Dr. Feldman said.

To protect yourself, consider using technology to your advantage, especially since lawsuits over informed consent usually happen several years after the procedure.

Ultimately, it’s as essential for doctors to explain the risks associated with a procedure as it is for patients to understand precisely what’s involved, Dr. Ilyas added.

She also recommends creating a flow to the conversation that places the discussion of risks within the context of why the procedure is being performed. This way, clarity about both the risks and the need for the treatment or procedure can be achieved.

When doing so, it’s critical to make sure you’re speaking your patient’s language—literally.

“Have a translator in the room if needed,” Dr. Feldman added. “If your patient is hearing or sight impaired, you need to have every contingency ready to ensure that everyone is in complete communication.”

Document, document, document!

To best protect yourself, the patient must consent to each procedure and intervention via active, informed consent, said Dr. Giordano.

“It’s not enough to hand a patient a piece of paper and say sign it,” he said. “There should be some documented evidence that the patient has not only read the document but that the key parts of the document have been explained and that the patient’s level of comprehension has been assessed and verified.”

It is vital if the patient has a disability, a neurological impairment, or a neurocognitive or psychiatric condition that might impede his or her ability to understand the consent that’s being sought.

In addition, it’s best if a “clinical proxy” handles the consent (for example, a nurse, office worker, or case manager).

“This can be very helpful because it means you’ve had third-party documentation of informed consent,” Dr. Giordano said. “It should then be re-documented with you as the clinician and stated that the patient has affirmatively and actively agreed to treatment.”

What happens when things go wrong?

If you’re sued over informed consent, with the patient claiming that you didn’t fully explain the potential risks, the first thing to consider is why this happened.

“Very often, these situations occur if there was some difficulty or competency of communication,” Dr. Giordano said. “You may have done everything right, but somehow the patient hasn’t gained an understanding of the procedure required.”

Physicians must take a hard look at how they’re explaining risks and possible side effects. For doctors who perform these procedures regularly, the risks may seem small, and they may unconsciously minimize them to the patient. But when something goes wrong, the patient may then feel that they didn’t fully understand the frequency of poor outcomes, or the potential severity.

Next, it’s important to perform a “gap analysis” to assess why something went awry. That means, look at all the potential factors involved to identify which one was the weak link.

“It might be that the patient was on a signing frenzy and signed away but didn’t receive active and informed consent,” Dr. Giordano said. “The goal is to learn how to close the gap for this case and for future cases.”

For protection, consider using technology to your advantage, especially since lawsuits over informed consent usually happen several years after the procedure. This is when a patient might argue that you didn’t tell them about possible complications and that they might have opted out of the procedure if they had known about those issues ahead of time.

“Even before the statute of limitations is up for a lawsuit, it could be 5 years from the time the procedure occurred due to the length of time a lawsuit can take,” Dr. Feldman said. “That’s why it’s important to take a video of your conversation or make a recording of the informed consent conversation. This way if there’s a question of what you said, there’s a video of it.”

For many physicians, this would be a big change—to video record and then store all their informed consent conversations. It could most likely help you if a lawsuit occurs, but some physicians may feel that process to be cumbersome and time-consuming, and they’d rather find another way to ensure that patients understand the risks.

Ultimately, however, if there’s a legal question involved with informed consent, the general thinking is that the effect on the patient must be harmful for it to stand up.

“The question becomes whether the outcome rendered that gap in the consenting process forgivable,” Dr. Giordano said. “The hope is that there was nothing harmful to the patient and that the benefit of the procedure was demonstrable despite any gaps in the informed consent process.”

In the end, informed consent should be a matter of good communication before, during, and after any treatment or procedure.

“When you form a relationship with a patient who needs any procedure, small or large, you’re going to be guiding them through a very scary thing,” Dr. Feldman said. “You want to make patients feel like you care about them and that, while neither you nor the system is perfect, you’ll take care of them. That’s the bottom line.”
The triple overlap: COPD-OSA-OHS. Is it time for new definitions?

BY GORAV SHARMA, MD, AND ALEJANDRA C. LASTRA, MD, FCCP

In our current society, it is likely that the "skinny patient with COPD" who walks into your clinic is less and less your "traditional" patient with COPD. We are seeing in our health care systems more of the "blue bloaters" – patients with COPD and significant obesity. This phenotype is representing what we are seeing worldwide as a consequence of the rising obesity prevalence. In the United States, the pre-pandemic (2017-2020) estimated percentage of adults over the age of 40 with obesity, defined as a body mass index (BMI) of at least 30 kg/m², was over 40%. Moreover, the estimated percentage of adults with morbid obesity (BMI at least 40 kg/m²) is close to 10% (Akinbami, L et al. Vital Health Stat. 2022;190:1-36) and trending up. These patients with the "triple overlap" of morbid obesity, COPD, and awake daytime hypercapnia are being seen in clinics and in-hospital settings with increasing frequency, often presenting with complicating comorbidities such as acute respiratory failure, acute heart failure, kidney disease, or pulmonary hypertension. We are now faced with managing these patients with complex disease.

The obesity paradox does not seem applicable in the triple overlap phenotype. Patients with COPD who are overweight, defined as "mild obesity" have lower mortality when compared with normal weight and underweight patients with COPD; however, this effect diminishes when BMI increases beyond 32 kg/m². With increasing obesity severity and aging, the risk of both obstructive sleep apnea (OSA) and hypoventilation increases. It is well documented that COPD-OSA overlap is linked to worse outcomes and that continuous positive airway pressure (CPAP) as first-line therapy decreases readmission rates and mortality. The triple overlap phenotypic patients, however, are presenting with chronic hypercapnic respiratory failure in a backdrop of morbid obesity, unlike the stable COPD-OSA overlap.

The pathophysiology of hypoventilation in obesity is complex and multifactorial, and, although significant overlaps likely exist with comorbid COPD, by current definitions, to establish a diagnosis of obesity hypoventilation syndrome (OHS), one must have excluded other causes of hypoventilation, such as COPD.

These patients with the triple overlap of morbid obesity, awake daytime hypercapnia, and COPD are the subset of patients that providers struggle to fit into a diagnosis or in clinical research trials.

The triple overlap is a distinct syndrome

Different labels have been used in the medical literature: hypercapnic OSA-COPD overlap, morbid obesity and OSA-COPD overlap, hypercapnic morbidly obese COPD and OHS-COPD overlap. A better characterization of this distinctive phenotype is much needed. Patients with OSA-COPD overlap, for example, have an increased propensity to develop hypercapnia at higher FEV₁ when compared with COPD without OSA – but this is thought to be a consequence of prolonged and frequent apneas and hypopneas compounded with obesity-related central hypoventilation. We found that morbidly obese patients with OSA-COPD overlap have a higher hypoxia burden, more severe OSA, and are frequently prescribed non-invasive ventilation after a failed titration polysomnogram (Htun ZM, et al. Am J Respir Crit Care Med. 2019;199:A1382), perhaps signaling a distinctive phenotype with worse outcomes, but the study had the inherent limitations of a single-center, retrospective design lacking data on awake hypercapnia. On the other side, the term OHS-COPD is contradictory and confusing based on current OHS diagnostic criteria.

In standardizing diagnostic criteria for patients with this triple overlap syndrome, challenges remain: would the patient with a BMI of 70 kg/m² and fixed chronic airflow obstruction with FEV₁ 72% fall under the category of hypercapnic COPD vs OHS? Do these patients have worse outcomes regardless of their predominant feature? Would outcomes change if the apnea hypopnoea index (AHI) is 10/h vs 65/h? More importantly, do patients with the triple overlap of COPD, morbid obesity, and daytime hypercapnia have worse outcomes when compared with hypercapnic COPD, or OHS with/without OSA? These questions can be better addressed once we agree on a definition. The patients with triple overlap syndrome have been traditionally excluded from clinical trials: the patient with morbid obesity has been excluded from chronic hypercapnic COPD clinical trials, and the patient with COPD has been excluded from OHS trials.

There are no specific clinical guidelines for this triple overlap phenotype. Positive airway pressure is the mainstay of treatment. CPAP is recommended as first-line therapy for patients with OSA-COPD overlap syndrome, while noninvasive ventilation (NIV) with bilevel positive airway pressure (BPAP) is recommended as first-line for the stable ambulatory hypercapnic patient with COPD. It is unclear if NIV is superior to CPAP in patients with triple overlap syndrome although recently published data showed greater efficacy in reducing carbon dioxide (PaCO₂) and improving quality of life in a small group of subjects (Zheng et al. J Clin Sleep Med. 2022;18[1]:99-107). To take a step further, the subtypes of NIV set up, such as rise time and minimum inspiratory time, are contradictory:

**How do we get these patients, who do not fit in any of the specified insurance criteria for PAP therapy approved for treatment?**

The goal in ventilating patients with COPD is to shorten inspiratory time, prolonging expiratory time, therefore allowing a shortened inspiratory cycle. In obesity, ventilation strategies aim to prolong and sustain inspiratory time to improve ventilation and dependent atelectasis.

Another area of uncertainty is device selection. Should we aim to provide a respiratory assist device (RAD): the traditional, rent to own bilevel PAP without auto-expiratory positive airway pressure (EPAP) capabilities and lower maximum inspiratory pressure delivery capacity, vs a home mechanical ventilator at a higher expense, life-time rental, and one-way only data monitoring, which limits remote prescription adjustments, but allow auto-EPAP settings for patients with comorbid OSA? More importantly, how do we get these patients, who do not fit in any of the specified insurance criteria for PAP therapy approved for treatment?

A uniform diagnostic definition and clear taxonomy allows for resource allocation, from government-funded grants for clinical trials to a better-informed distribution of health care systems resources and support health care policy changes to improve patient-centric outcomes. Here, we propose that the morbidly obese patient (BMI >40 kg/m²) with chronic airflow obstruction and a forced expiratory ratio (FEV₁/FVC) <0.7 with awake daytime hypercapnia (PaCO₂ > 45 mm Hg) represents a different entity/phenotype and fits best under the triple overlap syndrome taxonomy.

We suspect that these patients have worse outcomes, including comorbidity burden, quality of life, exacerbation rates, longer hospital length-of-stay, and respiratory and all-cause mortality. Large, multicenter, controlled trials comparing the long-term effectiveness of NIV and CPAP: measurements of triple overlap syndrome diagnostic criteria

<table>
<thead>
<tr>
<th>Morbid obesity ≥ 40 kg/m²</th>
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<tbody>
<tr>
<td>COPD</td>
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<tr>
<td>FEV₁/FVC = &lt; 0.7</td>
</tr>
<tr>
<td>Daytime awake hypercapnia PaCO₂ ≥ 45 mm Hg (pH ≥ 7.35)</td>
</tr>
</tbody>
</table>

**Source:** Dr. Sharma, Dr. Lastra

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**Graph:**

**Axes number:**

**Style:**

**Source:**

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**Figures:**

**Caption:**

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**Referenced:**

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respiratory function, gas exchange, blood pressure, and health related quality of life are needed. This is a group of patients that may specifically benefit from volume-targeted pressure support mode ventilation with auto-EPAP capabilities upon discharge from the hospital after an acute exacerbation.

**Inpatient (sleep medicine) and outpatient transitions**

In patients hospitalized with the triple overlap syndrome, there are certain considerations that are of special interest. Given comorbid hypercapnia and limited data on NIV superiority over CPAP, a sleep study should not be needed for NIV qualification. In addition, the medical team may consider the following (Figure 1):

1. **Noninvasive Ventilation:**
   a. Maintaining a high-pressure support differential between inspiratory positive airway pressure (IPAP) and EPAP. This can usually be achieved at 8-10 cm H2O, further adjusting to target a tidal volume (Vt) of 8 mL/kg of ideal body weight (IBW).
   b. Higher EPAP: To overcome dependent atelectasis, improve ventilation-perfusion (VQ) matching, and better treat upper airway resistance both during wakefulness and sleep. Also, adjustments of EPAP at bedside should be considered to counteract auto-PEEP-related ineffective triggering if observed.
   c. OSA screening and EPAP adjustment: for high residual obstructive apneas or hypopneas if data are available on the NIV device, or with the use of peripheral arterial tonometry sleep testing devices with NIV on overnight before discharge.
   d. Does the patient meet criteria for oxygen supplementation at home? Wean oxygen off, if possible.

2. **Case-managers can help establish services with a durable medical equipment provider with expertise in advanced PAP devices.**

3. **Obesity management.** Consider referral to an obesity management program for lifestyle/dietary modifications along with pharmacotherapy or bariatric surgery interventions.

4. **Close follow-up, track exacerbations.** Device download data are crucial to monitor adherence/tolerance and treatment effectiveness with particular interest in AHI, oximetry, and CO2 trends monitoring. Some patients may need dedicated titration polysomnograms to adjust ventilation settings, for optimization of residual OSA or for oxygen addition or discontinuation.

**Conclusion**

Patients with the triple overlap phenotype have not been systematically defined, studied, or included in clinical trials. We anticipate that these patients have worse outcomes: quality of life, symptom and comorbidity burden, exacerbation rates, in-hospital mortality, longer hospital stay and ICU stay, and respiratory and all-cause mortality. This is a group of patients that may specifically benefit from domiciliary NIV set-up upon discharge from the hospital with close follow-up. Properly identifying these patients will help pulmonologists and health care systems direct resources to optimally manage this complex group of patients. Funding of research trials to support clinical guidelines development should be prioritized. Triple overlap syndrome is different from COPD-OSA overlap, OHS with moderate to severe OSA, or OHS without significant OSA.

Dr. Lasta is Program Director, Sleep Medicine Fellowships, Assistant Professor of Medicine, and Associate Medical Director, UChicago Sleep; and Dr. Sharma is a Sleep Medicine Fellow; Section of Pulmonary and Critical Care Medicine, The University of Chicago, Chicago, Illinois.

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**Noninvasive Ventilation Set-Up**

- **Pressure Support**
  - Minimum 8cmH2O
  - Target Vt: 8mL/Kg/IBW
  - Target RR <12 during sleep

- **EPAP**
  - Minimum 8cmH2O
  - Titrated to treat witnessed sleep apneas
  - Adjust for effective triggering (auto-PEEP?)

- **Inspiratory time (Ti)**
  - 0.6-0.8 seconds
  - Monitor for dynamic hyperinflation

- **Monitor CO2 arterial or transcutaneous & adjust further if needed**

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**Join CHEST in Miami, Florida**

**NEWS FROM CHEST**
Tobramycin inhalation; neuromuscular disease; pleural catheters; and more ...
De Marco gift to the CHEST Foundation makes more than one dream possible

As a member of the CHEST Foundation Board of Trustees for years, Bob De Marco, MD, FCCP, ruminated over new, exciting ways to increase support of the philanthropic efforts of the American College of Chest Physicians. Dr. De Marco knows all too well growing the percent of CHEST members who donate to the Foundation in support of CHEST initiatives is – in a word – underwhelming. For those who are involved, they do so greatly and with their whole selves, but Dr. De Marco believed more could be done.

In the months leading up to the CHEST Annual Meeting 2022 in Nashville, Dr. De Marco discussed fundraising with CHEST staff and was already thinking ahead to CHEST 2023 in Hawaii.

"That’s when it hit me – we could leverage Hawaii to get donations and to expose people to the CHEST Foundation,” said Dr. De Marco. "Hawaii is a dream destination and that might be the exact motivation it would take to get that first donation from someone."

Having a good idea is one thing, but making sure it happens requires individual commitment. Dr. DeMarco personally pledged to cover the cost of first-class airfare for two to Hawaii, hotel accommodations, and registration to CHEST 2023 in Honolulu. For a minimum donation of $250 to the CHEST Foundation between September and the end of 2022, each donor would be entered into a drawing for a chance to win this dream trip.

"I thought to myself, who wouldn’t want this prize?”, said Dr. De Marco.

"You get to go to paradise for free – with a guest – and attend a top tier educational conference. Knowing your entry supported an organization as deserving as the CHEST Foundation is the cherry on top,” he added.

In launching the Hawaii trip fundraiser before and during CHEST 2022, attendees from around the world were introduced to the efforts the Foundation supported and its mission to champion lung health. Over $180,000 was donated during this time period, in no small part because of the Hawaii travel reward.

“I’m happy to say that the fundraiser did a lot better than I expected, and I was elated to see all of the new donors,” says De Marco.

"It’s my hope that those first-time donors continue their support for all that we do to provide grants – community, research, and diversity – and support CHEST initiatives that impact patient care and change lives.”

During CHEST 2022, the CHEST Foundation celebrated its 25th anniversary by reflecting on its accomplishments and on its impact over the past 25 years.

Former grant recipients were invited to celebrate with donors and speak to what they were able to accomplish because of the support they received.

The anniversary celebration also introduced the new CHEST initiatives, the First 5 Minutes program and Bridging Specialties: Timely Diagnosis for ILD. The former improves patient care through strengthened patient/clinician relationships and the latter aims to eliminate gaps in diagnosing complex lung diseases like pulmonary fibrosis.

To all who donated to the CHEST Foundation in 2022, Dr. De Marco said, “A sincere thank you to each and every one of you for helping us fulfill our mission. To the first-time donors, hopefully this will inspire you and your friends to be an active part of the CHEST family.”

Congratulations, Noah, and thank you for your faithful giving to support the work of CHEST.

Aloha to our foundation give-away winner

Out of the 150+ donors who gave $250 or more to the CHEST Foundation between September 2022 and the end of 2022, two first-class ticket winners were drawn at the CHEST Annual Meeting 2023 in Honolulu.

Noah donated to the Foundation specifically to the Mark J. Rosen, MD Master FCCP Endowment in honor of his late friend, Dr. Mark Rosen who served as CHEST President from 2006-2007 and died in 2019. "Mark [Rosen] was a remarkable doctor and valued life-long friend," said Noah. "My continued support for CHEST is my way of honoring his memory and how much he meant to me and others."

Dr. DeMarco distinguished career in pulmonary and critical care medicine spanned more than 4 decades, marked by his deep commitments to medical education and patient care. Before serving as President, Dr. Rosen served on the CHEST Board of Regents and the CHEST Foundation Board of Trustees for many years. He held positions as Chair or member on numerous CHEST committees, including Education, Nominations, Membership, Marketing, and Finance.

Following his passing, Dr. Rosen’s wife, Ilene, stayed engaged with the College and the CHEST Foundation by creating the endowment in his name and attending the CHEST Annual Meeting every year to award the Rosen Cup to the winners of the annual CHEST Challenge.

Congratulations, Noah, and thank you for your faithul giving to support the work of CHEST.

The recent TEAM study examined an early mobility approach in mechanically ventilated patients and found no difference in the primary outcome of alive and out-of-hospital at 180 days (N Engl J Med. 2022;387:1747).

Before realizing that the usual care arm included mobilization that was otherwise normally provided. The intervention arm protocolized the early mobility to be done simultaneously with the minimization of sedation. Patients’ assessment occurred in 81% in the usual care arm vs 94% in the intervention arm; both numbers are much higher than reported data in the ICU (Jolley SE et al. Crit Care Med. 2017;45:205).

Revisiting the question of early mobility in the ICU, more data are needed to clarify the best methodology, sedation, timing, amount, and type of patients who will benefit the most. Until then, it should remain a goal for ICUs and part of the daily discussion when caring for critically ill patients.

Mohammed J. Al-Jaghbeer, MBBS, FCCP – Section Member-at-Large
Salim Surani, MD, MPH, FCCP

Networks continued from previous page

CHEST is pleased to recognize the 2022 Distinguished CHEST Educators (DCEs). These individuals have shown great commitment, involvement, and leadership in CHEST education programs and activities.

DCE recipients represent the top 4% of CHEST’s international faculty and are recognized for their achievements and long-term contributions to the design and delivery of CHEST education. DCEs are selected on a yearly basis, based on the past 3 years of CHEST educational activities. It is a 1-year designation and can be received multiple times.

This year’s elite group of 187 recipients include 25 individuals who are receiving the designation for the first time.

Recruiting our 2022 Distinguished CHEST Educators

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Editor’s picks

BY PETER J. MAZZONE, MD, MPH, FCCP
Editor in Chief

By Naveed Saleem, MSc, et al.

Evaluation of an In-Home Virtual Pulmonary Rehabilitation Program for Respiratory Patients Delivered in Response to the COVID Pandemic.
By Virginia Huynh, MSc, PT, et al.

Prolonged Prone Position Ventilation Is Associated With Reduced Mortality in Intubated COVID-19 Patients.
By Daniel Okin, MD, PhD, et al.

Ventilatory Parameters in Obstetric Patients With COVID-19 and Impact of Delivery: A Multicenter Prospective Cohort Study.
By Daniela Vasquez, MD, et al.

How We Escalate Vasopressor and Corticosteroid Therapy in Patients With Septic Shock.
By Bijan Veja, MD, et al.

By Michael J. Falvo, PhD, et al.

Commonly Missed Findings on Chest Radiographs: Causes and Consequences.
By Warren B. Gefter, MD, et al.

Evidence of Advanced Pulmonary Vascular Remodeling in Obstructive Hypertrophic Cardiomyopathy With Pulmonary Hypertension.
By Bradley A. Maron, MD, et al.

Prevalence and Predictors of Sleep-Disordered Breathing in Men Participating in the Multicenter AIDS Cohort Study.
By Naresh M. Punjabi, MD, PhD, et al.

Patient and Clinician Recommendations to Improve Communication and Understanding of Lung Cancer Screening Results.
By Kristina Crothers, MD

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June 8 – 9
Leaders in the field of ultrasonography will share new, cutting-edge EBUS methods. You’ll walk away with increased proficiency in EBUS and greater expertise in lung cancer staging and pathology interpretation.
Introducing CHEST President-Designate, John Howington, MD, MBA, FCCP

John Howington, MD, MBA, FCCP, is a cardiothoracic surgeon currently serving as Chief of Oncology Services and Chair of Thoracic Surgery at Ascension Saint Thomas Health and a professor at the University of Tennessee Health Sciences Center in Nashville, Tennessee.

Dr. Howington received his undergraduate degree from Tennessee Technological University and medical degree from the University of Tennessee. He completed his general surgery residency at the University of Missouri, Kansas City and thoracic surgery residency at Vanderbilt University Medical Center.

Most recently, he received his Physician Executive MBA from the University of Tennessee.

Dr. Howington has participated and published more than 46 research publications and guidelines, numerous book chapters, and has presented hundreds of lectures internationally.

As a passionate thoracic surgeon, he has lent his knowledge to the extensive CHEST lung cancer guideline portfolio for more than a decade. He offers regular leadership in multidisciplinary and executive forums and has spearheaded a series of quality improvement initiatives at Ascension. He has served in a variety of leadership roles with CHEST and with other national thoracic surgery societies.

Dr. Howington began his CHEST leadership journey with the Networks, as a member of the Interventional Chest Medicine Steering Committee and then as the Thoracic Oncology Network Chair (2008-2010).

Other leadership positions include serving as the President of the CHEST Foundation (2014-2016), member of the Scientific Program Committee and Membership Committee, and, recently, as the Chair of the Finance Committee from 2018-2021.

Since 2017, he has served on the Board of Regents as a Member at Large. Dr. Howington will serve as the 87th CHEST President in 2025.

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ASTHMA

Obesity impacts peripheral airway reactivity

BY HEIDI SPLETE

Mededge News

Peripheral airway response to methacholine was similar among obese adults with and without asthma, although forced expiratory volume was lower for those with asthma, based on data from 53 individuals.

Obesity remains a risk factor for asthma, and obese individuals with asthma tend to have worse control and more severe disease, wrote Anne E. Dixon, BM, BCh, of the University of Vermont, Burlington, and colleagues.

Previous studies have shown that airway reactivity can occur in obese individuals without asthma inflammation, but studies characterizing obese asthma based on lung function are lacking, they said. “Combining spirometry and oscillimetry might reveal abnormalities in lung mechanics particularly pertinent to people with obesity and asthma.”

In a cross-sectional study published in the journal Chest (doi.org/10.1016/j.chest.2022.12.030), the researchers reviewed data from 31 obese adults with asthma and 22 obese adults without asthma. The participants were aged 18 years and older, with forced expiratory volume (FEV1) of at least 60% of predicted.

All had class III obesity, with an average BMI of 47.2 kg/m2 for those with asthma and 46.7 kg/m2 for nonasthma controls. Demographic characteristics were similar between the groups.

Airway reactivity was defined as a 20% decrease in FEV1 and/or a 50% change in resistance or reactance at 5 Hz (R5 and X5), at a concentration of 16 mg/mL or less of methacholine. Patients were assessed using spirometry and oscillimetry.

Most obese individuals with and without asthma showed significant changes in peripheral airway resistance. For those with asthma, the resistance at 5 Hz, measured by oscillimetry, increased by 52% in response to 16 mg/mL of methacholine.

This finding suggests that obesity predisposes individuals to peripheral airway reactivity regardless of asthma status, the researchers wrote.

They also identified two distinct groups of asthma patients categorized by respiratory system impedance based on more concordant vs. discordant bronchoconstriction in the central and peripheral airways. The baseline AX for these two groups was 11.8 and 46.7, respectively, with interquartile ranges of 9.9-23.4 and 23.2-53.7, respectively.

The discordant group included only women, and these patients reported significantly more gastrointestinal reflux, increased chest tightness, and more wheezing and asthma exacerbations than the concordant group, which may be related to air trapping, shown on previous studies of obese individuals with asthma.

The findings were limited by several factors, including the measurement of airway impedance only at the peak methacholine dose and the measurement of oscillimetry after spirometry, the researchers noted. Other limitations included the relatively small study population at a single center, and the focus on obese individuals only. More research is needed in larger and more diverse patient populations, but the results support the characterization of a subgroup of obese asthma patients with significant peripheral airway dysfunction, the researchers wrote.

“Oscillimetry testing can reveal a physiologic phenotype of asthma in obesity that may be related to worse symptoms and more severe disease, and also reveal subclinical abnormalities in people with obesity, but without clinically diagnosed lung disease,” they concluded.

The study was supported in by the National Institutes of Health. The researchers reported no conflicts.
Muscle weakness predicts poor outcomes

BY HEIDI SPLETE
MDedge News

Lower muscle mass was significantly associated with more airway obstruction and reduced functional exercise capacity in adults with asthma, based on data from 114 individuals.

Previous studies have shown reduced muscle mass in asthma patients, but the impact on clinical and functional outcomes has not been well studied, wrote Edith Visser, MSc, of Medical Centre Leeuwarden (the Netherlands) and colleagues.

“Many asthma patients, especially those with severe disease, report exercise intolerance and limitations in daily activities, severely affecting their quality of life,” they said. Research into the clinical consequences of low muscle mass and low muscle strength for patients with asthma and the role of inflammation could make muscle function a potential treatment target for those with asthma, they said.

In a study published in the Journal of Allergy and Clinical Immunology: In Practice (2023 Jan 20. doi: 10.1016/j.jaip.2022.12.043), the researchers recruited 114 consecutive adults aged 18 years and older with a diagnosis of moderate to severe asthma who were seen at a single center between Jun. 2019 and Oct. 2022. The mean age of the patients was 51.9 years, 36% were men, 70% were overweight or obese, and 34 were diagnosed with severe asthma.

Participants underwent clinical, functional, and laboratory assessments at one or two visits within a 2-week period. Assessment tools included the Asthma Quality of Life Questionnaire (AQLQ), the Asthma Control Questionnaire (ACQ-6), a questionnaire on health care use (HCU), and the short questionnaire to assess health-enhancing physical activity (SQUASH).

Functional activity was based on the 6-minute walking distance (6MWD), and lung function tests included spirometry and fractional inhaled nitric oxide (FeNO). Muscle mass was based on fat-free mass index (FFMI) and urinary creatinine excretion rate (CER). Muscle strength was measured using hand-grip strength (HGS).

The researchers examined levels of muscle mass and strength and their relation to functional and clinical outcomes.

Overall, the mean measures of muscle mass and strength were higher in males, who had average FFMI, CER, and HGS measures of 20.1 kg/m², 15.3 mmol/day, and 48.8 kg, respectively. These measures in women were 17.3 kg/m², 10.8 mmol/day, and 29.3 kg, respectively.

After adjusting for confounding factors, patients in the lowest tertile for muscle mass based on FFMI had significantly more severe asthma based on postbronchodilator forced expiratory volume in 1 second and FEV₁/forced vital capacity, as well as lower functional exercise capacity based on the 6MWD compared to those in the highest tertile. A similar association appeared between CER and FEV₁, but not FEV₁/FVC.

However, no significant associations appeared between the muscle mass measures of FFMI or CER and scores on the ACQ, AQLQ, emergency department visits, or asthma exacerbations, according to the researchers.

No relationship appeared between muscle strength and functional outcomes. However, patients in the lowest tertile of HGS had worse asthma control, worse quality of life, and a higher probability of at least one visit to the emergency department compared to patients in the highest HGS tertile.

Higher leukocyte levels were significantly associated with lower muscle mass after adjusting for age, sex, weight, and physical activity, but no other inflammatory markers were significantly associated with FFMI.

The association between lower muscle strength and poorer asthma control, lower quality of life, and greater odds of emergency department visits reflect findings from previous studies, the researchers said. The mechanisms behind the loss of muscle strength in asthma remain unclear, but physical inactivity and daily oral corticosteroid use may play a role, they added.

The study findings were limited by the cross-sectional design and the possibility that muscle weakness may instead stem from reduced physical activity associated with poor lung function and asthma control, the researchers noted.

Other limitations included the potential overestimation of FFMI and the lack of statistical power to show a relationship between FFMI and emergency department visits and asthma exacerbations, they said.

However, the current study is the first known to explore the relationship between lower muscle mass and strength and a range of both functional and clinical outcomes in patients with moderate to severe asthma, they said.

“Our findings encourage longitudinal studies into muscle function as a potential target for treatment to improve asthma outcomes,” they concluded.

The study was supported by unrestricted grants from Medical Centre Leeuwarden research fund. Ms. Visser had no financial conflicts to disclose.

Six asthma subtypes may promote personalized therapy

BY HEIDI SPLETE
MDedge News

Six subtypes of asthma that may facilitate personalized treatment were identified and confirmed in a large database review of approximately 50,000 patients, according to a recent study.

Previous studies of asthma subtypes involved age of disease onset, the presence of allergies, and level of eosinophilic inflammation, and have been limited by factors including small sample size and lack of formal validation, Elsie M.F. Horne, MD, of the Asthma UK Centre for Applied Research, Edinburgh, and colleagues wrote.

In a study published in the International Journal of Medical Informatics (2022 Dec 7. doi: 10.1016/j.ijmmedinf.2022.104942), the researchers used data from two databases in the United Kingdom: the Optimum Patient Care Research Database (OPCRD) and the Secure Anonymised Information Linkage Database (SAIL). Each dataset included 50,000 randomly selected nonoverlapping adult asthma patients. The researchers identified 45 categorical features from primary care electronic health records. The features included those directly linked to asthma, such as medications; and features indirectly linked to asthma, such as comorbidities.

The subtypes were defined by the clinically applicable features of level of inhaled corticosteroid use, level of health care use, and the presence of comorbidities, using multiple correspondence analysis and k-means cluster analysis.

The six asthma subtypes were identified in the OPCRD study population as follows: low inhaled corticosteroid use and low health care utilization (30%); low to medium ICS use (36%); low to medium ICS use and comorbidities (12%); varied ICS use and comorbid chronic obstructive pulmonary disease (4%); high ICS use (10%); and very high ICS use (7%).

The researchers replicated the subtypes with 91%-92% accuracy in an internal dataset and 84%-86% accuracy in an external dataset. “These subtypes generalized well at two future time points, and in an additional EHR database from a different U.K. nation (the SAIL Databank),” they wrote in their discussion.

The findings were limited by the retrospective design, the possible inclusion of people without asthma because of the cohort selection criteria, and the possible biases associated with the use of EHRs; however, the results were strengthened by the large dataset and the additional validations, the researchers noted.

“Using these subtypes to summarize asthma populations could help with management and resource planning at the practice level, and could be useful for understanding regional differences in the asthma population,” they noted. For example, key clinical implications for individuals in a low health care utilization subtype could include being flagged for barriers to care and misdiagnoses, while those in a high health care utilization subtype could be considered for reassessment of medication and other options.

The study received no outside funding. Dr. Horne had no financial conflicts to disclose.
COPD

Exacerbation history alone found flawed as risk predictor

BY RICHARD MARK KIRKNER

FROM THE JOURNAL CHEST® • Clinical guidelines recommend use of exacerbation history in choosing therapies to predict the risk for chronic obstructive pulmonary disease exacerbations, but an analysis of data from three different clinical studies has found that exacerbation history alone is not the most accurate risk-prediction tool – and that it may even cause harm in some situations.

“Our results present a cautionary tale for the potential risk of harm to patients when naively applying risk-stratification algorithms across different clinical settings,” lead author Joseph Khoa Ho, PharmD, at the University of British Columbia, Vancouver, told this news organization.

“We show that risk-prediction models have better accuracy than exacerbation history alone for predicting the future risk of COPD exacerbations,” he said. “However, the prediction models required re-evaluation and setting-specific recalibration in order to yield higher clinical utility.”

The study, known as IMPACT, analyzed three trials that enrolled 4,107 patients at varying levels of moderate or severe exacerbation risks: the placebo arm of the Study to Understand Mortality and Morbidity in COPD (SUMMIT; N = 2,421); the Long-term Oxygen Treatment Trial (LOTT; N = 595); and the placebo arm of the Towards a Revolution in COPD Health trial (TORCH; N = 1,091). The exacerbation risks were low, medium, and high in the three respective trials.

The study, published online in the journal CHEST (2022 Dec 8. doi: 10.1016/j.chest.2022.11.041), compared the performance of three risk-stratification algorithms: exacerbation history; the model that Loes C.M. Bertens, PhD, and colleagues in the Netherlands developed in 2013; and the latest version of the Acute COPD Exacerbation Prediction Tool, known as ACCEPT.

Results of the analysis
The study used area under the curve (AUC), a method of evaluating effectiveness or efficiency, to compare performance of the prediction algorithms. ACCEPT outperformed exacerbation history and the Bertens algorithm in all the LOTT (medium risk) and TORCH (high risk) samples, both of which were statistically significant. In SUMMIT (low risk), Bertens and ACCEPT outperformed exacerbation history, which was statistically significant.

The AUC for exacerbation history alone in predicting future exacerbations in SUMMIT, LOTT, and TORCH was 0.59 (95% confidence interval, 0.57-0.61), 0.63 (95% CI, 0.59-0.67), and 0.65 (95% CI, 0.63-0.68), respectively. Bertens had a higher AUC, compared with exacerbation history alone in SUMMIT (increase of 0.10, P < .001), and TORCH (increase of 0.05, P < .001), but not in LOTT (increase of 0.01, P = .84).

ACCEPT had higher AUC, compared with exacerbation history alone in all study samples, by 0.08 (P < .001), 0.07 (P = .001), and 0.10 (P < .001), respectively. Compared with Bertens, ACCEPT had higher AUC by 0.06 (P = .001) in LOTT and 0.05 (P < .001) in TORCH; whereas the AUCs were not different in SUMMIT (change of –0.02, P = .16).

Study rationale
Senior author Mohsen Sadatsafavi, MD, PhD, associate professor of pharmaceutical sciences at the University of British Columbia, told this news organization that this study was inspired by a study in cardiology earlier in 2022 that found that the performance of the multitude of risk-prediction tools used to evaluate cardiovascular disease risk can vary widely if they’re not calibrated for new patient populations.

“The main finding was that exacerbation history alone can be harmful even if it is applied at different risk levels,” Dr. Sadatsafavi said of the IMPACT study. “No algorithm could be universally applicable, but exacerbation history has a very high chance of being worse than not doing any...”
Severe health diagnoses drive suicide risk

BY HEIDI SPLETE
MDedge News

Individuals diagnosed with a severe physical health condition were significantly more likely to commit suicide at 6 months and at 1 year later, based on data from more than 47 million individuals in a national database.

Previous smaller studies have shown a link between increased risk for suicide and a range of health conditions including cancer, coronary heart disease, neurologic conditions, diabetes, and osteoporosis, Vahé Nafilyan, PhD, of the Office for National Statistics, Newport, England, and colleagues wrote.

However, large-scale population-level studies of the association between specific diagnoses and suicide are lacking, they said.

In a study published in The Lancet Regional Health–Europe (2022 Dec 16. doi: 10.1016/j.lanepe.2022.100562), the researchers reviewed a dataset that combined the 2011 Census, death registration records, and the Hospital Episode Statistics. The study population included 47,354,696 individuals aged 6 years and older living in England in 2017. The mean age of the study population was 39.6 years, and 52% were female. The researchers examined deaths that occurred between Jan. 1, 2017, and Dec. 31, 2021.

The primary outcome was the time from the date of a diagnosis or first treatment of a severe physical health condition to a death by suicide. The health conditions included in the analysis were low-survival cancers, chronic ischemic heart disease, chronic obstructive pulmonary disease, and degenerative neurological disease.

The diagnosis of any of these conditions significantly increased the risk for suicide compared with controls. The highest risk appeared within 6 months of a diagnosis or first treatment, but the increased risk persisted at 1 year.

The suicide rate among low-survival cancer patients was 16.6 per 100,000 patients at 6 months, compared with 5.7 per 100,000 controls; at 1 year, these rates were 21.6 and 9.5 per 100,000 patients and controls, respectively.

For patients with COPD, the suicide rate at 6 months after diagnosis was 13.7 per 100,000 patients versus 5.6 per 100,000 matched controls; the suicide rates at 1 year were 22.4 per 100,000 patients and 10.6 per 100,000 matched controls.

The suicide rate at 6 months for individuals diagnosed with chronic ischemic heart disease was 11.0 per 100,000 patients and 4.2 per 100,000 matched controls; at 1 year, the suicide rates were 16.1 per 100,000 patients and 8.8 per 100,000 matched controls.

The 1-year suicide rate was especially high among patients with degenerative neurological conditions (114.5 per 100,000 patients); however, the estimate was considered imprecise because of the rarity of these diseases and subsequent low number of suicides, the researchers noted.

The results support data from previous studies showing links between increased risk of suicide and severe physical conditions, the researchers wrote. Patterns of suicide were similar between men and women and after adjusting for sociodemographic factors.

The findings were limited by the inability to fully control for a history of depression or self-harm, and by the imprecise estimates given the rare occurrence of suicide overall, the researchers noted. Other limitations included the late registration of deaths from external causes and the focus being only on suicides that occurred in England and Wales, meaning that individuals who traveled abroad for assisted suicide were not captured in the dataset.

Further research is needed to understand the mechanisms driving the elevated risk of suicide and help provide the best support to these patients,” the researchers concluded.

However, the current results enhance the literature with a large, population-based review of the elevated suicide risk among individuals newly diagnosed with severe health conditions, and reflect the need for better support for these patients to help with coping, they said.

The study was funded by the Office for National Statistics. The researchers reported no relevant financial relationships.

For patients with COPD, the suicide rate at 6 months after diagnosis was 13.7 per 100,000 patients versus 5.6 per 100,000 matched controls.

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In a study* of individuals with interstitial lung disease (ILD), 41% of patients first had at least one alternate diagnosis, most commonly cardiac or obstructive lung disease. Ubiquitous symptoms make ILDs difficult to diagnose.

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