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Novel obesity medications open door to new era in treatment of OSA

BY KRITHIKA SUBRAMANIAN, PHD

In December 2024, the US Food and Drug Administration (FDA) approved tirzepatide, a dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist previously approved for type 2 diabetes and obesity, as the first prescription medication for adults with moderate to severe OSA and obesity.[1]

The approval was based on the phase 3 SURMOUNT-OSA study, which compared tirzepatide with placebo for improving OSA outcomes in adults with moderate to severe OSA and obesity.[2]

"The approval [of tirzepatide for OSA] is exciting," said Atul Malhotra, MD, FCCP, the global principal investigator on the SURMOUNT-OSA study. "We have a new treatment for sleep apnea. The standard of care first-line treatment is still nasal CPAP. If patients cannot or will not use CPAP therapy, then tirzepatide may be an option. For patients who are on CPAP for OSA who [have obesity], tirzepatide is better than placebo in terms of improving systolic blood pressure, high-sensitivity C-reactive protein levels, patient-reported outcomes, and other parameters assessed in the study." // continued on page 8

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START LEARNING

From the Editor

Dear *CHEST Physician* reader,

As we kick off 2025, I am thrilled to share some major updates that we've made to *CHEST Physician*! This year marks a pivotal moment for our publication. We have been listening closely to your feedback, keeping pace with the rapidly evolving fields of pulmonary, critical care, and sleep medicine, and brainstorming how to make this publication even more useful, engaging, and enjoyable to read. Our evolution is focused on serving you—the dedicated clinicians, researchers, and health care professionals who tirelessly advance the field of chest medicine.

WHAT'S NEW IN 2025?

- **A fresh look:** Starting with this issue, you'll notice a revitalized design. The updated layout is more reader-friendly, with streamlined navigation and enhanced visuals to spotlight the stories that matter most.

- **Improved digital access:** We recently rolled out a newly designed website that's easier to navigate. Articles and recurring columns will now be grouped by clinical topics for seamless access. Plus, the site is optimized for mobile devices, ensuring you can stay connected anytime, anywhere. Be sure to visit chestphysician.org!

- **Updated print cadence:** We're moving to a quarterly print schedule. Each issue will feature in-depth stories, comprehensive coverage of breakthroughs, and richer insights—carefully curated to provide meaningful updates every three months, rather than smaller bites each month.

- **Twice-monthly digital editions:** Every two weeks, you will receive a concise, engaging digital edition packed with clinical updates, research highlights, and practice-changing news. These bimonthly digital editions will keep you up to speed between the quarterly print issues. Together, they're designed to fit your busy schedule and ensure you stay informed no matter how you prefer to read.

- **Interactive fun:** We are bringing a little fun to your reading experience! Starting this year, every print issue will include a crossword puzzle (see page 15) based on articles from the *CHEST*® journal portfolio. These puzzles are a great way to mix learning with leisure, whether it's terminology, guidelines, or history.

None of these changes would have been possible without the dedication, expertise, and creativity of our incredible CHEST publishing team and Editorial Board. Their hard work and commitment to excellence have been the driving force behind this transformation, and I am endlessly grateful for their partnership.

As we embark on this exciting journey in 2025, I encourage you to engage with *CHEST Physician* in new ways. Share your feedback and suggest topics you would like to see covered. Together, we can make this publication an even more vital resource for the global chest medicine community.

Here's to a new chapter for *CHEST Physician*—one that's designed with you, our readers, in mind.

Warm regards,

Angel Coz

Angel Coz, MD, FCCP
Editor in Chief, *CHEST Physician*

CHEST Physician®

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CHEST Physician, an official publication of the American College of Chest Physicians, provides cutting-edge reports on timely news, research, and clinical advances in the world of chest medicine. Regular columns feature the areas of pulmonary, critical care, and sleep medicine, as well as association news and updates from CHEST leadership.

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Inside

In memoriam

CHEST has been informed of the following deaths of CHEST members. We remember our colleagues and extend our sincere condolences.

Charles E. Cernuda, MD
Brian P. Harwood, MD
Richard G. Wood, DO, MS

CRITICAL CARE COMMENTARY

Column

Sepsis order sets good for patients, hospital bottom lines

Is this the future of sepsis treatment?

BY GREG J. EISINGER, MD, MSSW

Sepsis is an enormous public health problem with massive associated morbidity and a staggering cost to the US health care system estimated at $62 billion annually.[1] Although the precise kinetics remain controversial, there is little disagreement that delayed initiation of appropriate therapy leads to measurable increases in mortality.[2]

Sepsis order sets are designed to streamline delivery of guideline-supported interventions to improve the quality and consistency of sepsis care and adherence to metrics such as the SEP-1 bundle. Pressure to ensure comprehensive implementation of SEP-1 bundle components is intense due to public reporting of adherence data and connection to hospital reimbursement. These mandates have been the source of much controversy due to the challenges of early sepsis recognition and rapid implementation of resource-intensive interventions in crowded emergency departments, lack of high-quality data supporting many bundle elements, concern about incentivizing overtreatment, and perceived loss of autonomy in individualizing care.[3,4] While some studies show that timely bundle implementation has a small but significant impact on mortality, others have shown no difference.[5,6]

QUANTIFYING CARE VALUE

Amid this background comes the study by Dale and colleagues published in the November issue of the journal *CHEST*® on the impact of sepsis order set use on care value among hospitalized patients.[7] Care value refers to patient outcomes relative to their cost and, in this study, was operationalized as a composite of hospital mortality, direct costs, and health system reimbursement.

The authors hypothesized that sepsis order sets would improve all three of these component variables, with greater reduction in costs relative to reimbursement, thus increasing the hospital's contribution margin, a measure of financial viability and profitability.

They conducted a large, multicenter, retrospective analysis including 97,249 adult patients receiving a sepsis diagnosis during admission across 51 hospitals between 2021 and 2022. Patients were divided into groups based on whether the institutional sepsis order set was (45.7%) or was not (54.3%) utilized in their care. The order set incorporated most elements of the SEP-1 bundle, as well as increased monitoring, decision support for antimicrobial drug selection, and a real-time view of completion status of various bundle components.

The main analysis conducted after propensity score matching showed that those treated via the order set received antibiotics around 35 minutes faster, despite a negligible (but statistically significant) two-minute shorter time from antibiotic order to administration. They also had shorter duration of hypotension, shorter length of stay, lower readmission rates, and, most importantly, lower mortality (11% vs 15%). Additionally, total cost of care was $1,487 lower, while reimbursement was reduced by only $465, resulting in a net increase in contribution margin of $1,022 per patient. Both the clinical and financial benefits observed were largely driven by the subset of patients with septic shock.

PRESENTING COUNTERPOINTS

Better patient outcomes at a lower cost to the health system may begin to sound like a windfall, but are the findings too good to be true? The authors candidly point out that the mechanism underlying the observed benefits is not clear. The etiology of the cost savings is fairly intuitive—patients treated through the order set had better outcomes and shorter lengths of stay, particularly in the cost-intensive ICU setting, ergo the cost of their care was lower. But what about the mechanism that led to these improved outcomes? Is there face validity to the premise that after decades of negative trials on targeted interventions for sepsis, simply organizing standard-of-care orders into a streamlined package is the panacea we've been waiting for? It seems improbable that two medically equivalent patients treated by the same provider will have a different likelihood of survival if orders are entered through an order set vs being placed ad hoc.

The authors rightly emphasize that despite robust efforts to account for confounders, causation cannot be inferred from their study design. Unfortunately, significant sources of selection bias temper enthusiasm for the results. First, patients with clear-cut manifestations of sepsis are more likely to trigger order set use, whereas those in whom the diagnosis is more obscure are often more complex and may have later initiation of therapy due to delayed recognition. This form of bias is inherent to observational time-to-intervention studies and has been a source of controversy around the dogma of hourly worsening of mortality with delayed antibiotics.[8] Faster receipt of antibiotics despite minimal change in time from order to administration supports earlier recognition as the driver of the improved time to treatment, rather than order set use itself. Additionally, patients in the non-order set group

were less likely to meet sepsis criteria at presentation (88% vs 96%), further supporting the likelihood of atypical presentations delaying recognition in the non-order set group. Some of these patients likely met sepsis criteria after arrival to the wards where order set use may be less common than in the emergency department, the target of many sepsis quality initiatives. Some of these later diagnoses also likely represented hospital-acquired sepsis, a condition with vastly different etiologies and higher mortality than community-acquired sepsis.[9]

Other confounders include overrepresentation of COVID-19 in the non-order set group, a population less likely to trigger use of a sepsis order set but with significant associated morbidity and mortality during the study period. Small but significant differences in baseline characteristics between groups magnified by the large statistical power may also have played a role, especially given that comorbidities were not assessed. While propensity score matching helps to counteract the prognostic imbalance imparted by the above confounders, it is likely that other unmeasured differences remain.

The study time period was also chosen due to increased emphasis at the health-system level on order set use as one component of a broader group of interventions aimed at improving sepsis mortality, including multidisciplinary huddles, focus on early antibiotics, and education on the morbidity of sepsis. As such, order set use may have been a marker for the uptake of a variety of interventions that could have influenced patient outcomes, or perhaps even the Hawthorne effect. It also may have been a marker for individuals who or centers that were more in tune with high-quality sepsis care or generally higher performing in other ways.

USING ORDER SETS, WITH DISCRETION

Despite these limitations, any intervention that proposes to save lives from a devastating disease deserves careful consideration. Use of protocolized care is well-established for other time-sensitive diseases like stroke and myocardial infarction. In sepsis, the benefit of bundled care can be traced back to early goal-directed therapy. The authors of the current study cite numerous others that have demonstrated similar cost savings and outcome benefits associated with components of their intervention, including timely implementation of care bundles, provider education, early detection systems, and decision support for antimicrobial selection. While most of these studies are retrospective and subject to many of the same limitations as the current one, the trend in the literature is clear.

Increased emphasis on order set utilization should be expected after the recent publication of "Hospital Sepsis Program Core Elements" from the Centers for Disease Control and Prevention.[10] This document provides best practices for creating and maintaining high quality sepsis care delivery systems and emphasizes the importance of creating order sets to improve compliance and patient outcomes. Anecdotally, at our own institution, we have observed significant improvement in bundle compliance when the order set is utilized compared with ad hoc order entry.

As we are unlikely to see randomized controlled trials on this topic, we must applaud the authors for undertaking this ambitious and enlightening study. Ultimately, it is hard to argue that sepsis order sets are not a good thing, even if the magnitude of purported benefit may be uncertain. Order sets make it easier to ensure that the right things get done and harder to miss something important due to our human limitations. // continued on page 13

In memoriam: James B.D. Mark, MD, FCCP

On February 7, 2025, the CHEST community lost a great physician and former leader, Past President James B.D. Mark, MD, FCCP. He is survived by his wife, Maxie, five children, seven grandchildren, and nine (soon to be 10) great-grandchildren. Dr. Mark served as CHEST President from 1994 to 1995, and he was extremely active in CHEST throughout his career. He served on the Ethics, Information Delivery, and Nominating Committees, as well as the Community Service Work Group of the CHEST Foundation. Dr. Mark was also a generous donor. The following is a heartfelt obituary written by Dr. Mark's colleague, Joseph Woo, MD, at Stanford Health Care and Stanford Medicine Children's Health.

"It is with a heavy heart and profound sadness that we share the peaceful passing of our esteemed colleague and dear friend, Dr. James B.D. Mark.

Dr. Mark was a dedicated physician, scholar, and mentor who made an extraordinary impact in our field and to the Stanford Medicine community. Since joining Stanford in 1965, he has shaped the field of thoracic surgery, founding Stanford's Division of Thoracic Surgery and serving as its first Division Chief in 1972. He also served as Acting Chair of the Department of Surgery from 1974 to 1977.

Born and raised in Nashville, Tennessee, Dr. Mark earned his BA from Vanderbilt University in 1950 and his MD from Vanderbilt University School of Medicine in 1953. He trained at Yale-New Haven Hospital, completing his residency in surgery and cardiothoracic surgery, including two years of active duty in the United States Public Health Service. He then spent five years at Yale before joining Stanford in 1965 as an Associate Professor of Surgery. He was promoted to Professor in 1970 and later received the Johnson & Johnson Endowed Professorship in 1978.

Beyond his leadership within the department, Dr. Mark served as the Chief of Staff at Stanford University Hospital (1988-1992) and held key roles as Associate Dean for Regional Medical Affairs (1973-1974) and Associate Dean for Student Affairs (1970-1972). His impact extended beyond Stanford, having served in leadership positions in numerous professional organizations, including serving as President of the Halsted Society (1984), President of Western Thoracic Surgical Association (1992-1993), and President of the American College of Chest Physicians (1994-1995).

Dr. Mark's contributions have made a tremendous impact on expanding the thoracic surgery field. He was a pioneer in the early adoption of advancing thoracoscopic and minimally invasive surgery beyond its known diagnostic utility into a therapeutic modality. This set a precedent for ushering in the development and use of video-assisted thoracic surgery in the 1990s, positioning Stanford's role as a leader in minimally invasive thoracic surgery.

Throughout his career, he remained actively involved in scientific research, authoring more than 150 scientific publications and serving on the editorial boards of *The Journal of Thoracic and Cardiovascular Surgery*, *The World Journal of Surgery*, and *The Pharos*.

Dr. Mark touched countless lives not just through his surgical expertise but also through his compassion, mentorship, and unwavering dedication to his colleagues, trainees, and patients. He always greeted you with a smile and a witty remark.

In 2016, Dr. Mark and his family endowed the James B.D. Mark Family Visiting Professorship. Over the years, we have welcomed seven visiting professors who have come to honor Dr. Mark's pioneering work and share how they have brought their contributions to the field of thoracic surgery. The Mark Family Professorship continues to remind us of his lasting contributions to thoracic surgery while celebrating the incredible work of surgeons and scientists from around the world. We are deeply honored to have the privilege of extending his legacy." •

Column

A sticky road: Mucus pathology in COPD

BY ALEJANDRO A. DIAZ, MD, MPH

COPD affects approximately 29 million people and is the fourth leading cause of mortality in the United States. Despite its public health burden, treatment options for COPD remain limited, largely due to several challenges: an incomplete understanding of the disease's underlying mechanisms, difficulties in translating animal model findings into humans, and a lack of sufficient investment in research and drug development. One promising yet understudied area for therapeutic intervention is mucus plugging—a unique form of airway mucus pathology that could offer a new target for treatment.

In individuals with COPD, pathologic changes in the mucociliary system lead to hyperconcentrated and stickier mucus and reduced ability to clear it from the airways. This characteristic hyperconcentrated mucus is primarily due to imbalances in fluid transport in the airway epithelium and heightened levels of mucins—polymers that give mucus its gel-like consistency. Mucin concentrations in sputum correlate closely with COPD severity and chronic bronchitis and can predict future exacerbations in individuals who are symptomatic and exposed to tobacco, even before airflow obstruction becomes apparent.[1] Additionally, cigarette smoke damages cilia and disrupts the function of the cystic fibrosis transmembrane receptor, further impairing mucus clearance. The result is mucus accumulation, plaque formation, and the development of mucus plugs (Figure 1). The occlusion of small airways by mucous content is a key contributor to the obstructive pathophysiology of COPD.

However, translating these mechanistic insights to clinical trials has been challenging, primarily due to the difficulty in accurately measuring mucus pathology. For example, quantifying mucins in sputum requires intricate protocols for sample collection, preservation, transport, and processing, which limits its practical use in clinical practices. Similarly, relying on questionnaires to assess mucus-related symptoms, such as cough and phlegm, is hindered by recall bias and inconsistencies in reproducibility. These challenges have made it difficult to move forward with mucus pathology as a therapeutic target for COPD.

In recent years, chest CT scanning has become an invaluable tool for identifying and quantifying mucus plugs in medium-to-large-sized airways (~2-10-mm lumen diameter). In the COPDGene, Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE), and Subpopulations and Intermediate Outcomes in COPD Study (SPIROMICS) cohorts, it has been found that the prevalence of CT scan-detected mucus plugs varies: 41%, 46%, and 67%, respectively, underscoring the relevance of this pathology.[2-4] CT scan-detected mucus plugs block the airways, increasing airflow resistance and decreasing lung function. In the COPDGene and SPIROMICS cohorts, patients with mucus plugs exhibit lower FEV_1 and more severe disease than those with cleared airways.[4,5]

Mucus plugs vary in appearance: Some are short ("stubby," <12 mm in length), while others are long ("stringy," ≥12 mm in length). The latter tend to contribute more to the total mucus volume observed on CT scans.[6] Mucus plugs mainly localize in airways 2 to 4 mm in lumen diameter.[6] The formation and disappearance of mucus plugs are dynamic; some may resolve quickly, while others can persist over the years. Follow-up data show that 67% of patients with COPD still have mucus plugs after one year, and 73% still have them after five years.[4,5] Interestingly, mucus plugs in the lower lobes tend to be more persistent than in other regions.[5] It is thought that the composition of mucus plugs—comprising dead cells, mucins, fibrin, extracellular DNA, and microbes—and their crosstalk with airway epithelial cells might play a role in the persistence. Regardless of the underlying mechanism, patients with persistent mucus plugs appear to have a faster decline in FEV_1, substantiating their causal role in the obstructive pathophysiology of COPD. A further functional consequence of airway-occluding mucus plugs is a decrease in oxygen saturation. Notably, this drop in oxygen saturation is more pronounced in patients without emphysema, likely due to the ventilation/perfusion mismatch caused by the lung parenchyma destruction.[4]

Despite the well-established link between cough, sputum production, and mucociliary dysfunction, up to 36% of people with COPD who have mucus plugs on CT scan report no cough or phlegm. These "silent mucus plugs" might be particularly concerning, as they have been linked to reduced FEV_1 and oxygen saturation, lower exercise capacity (as measured by a 6-minute walk distance test), and poorer quality of life (as measured by the St. George's Respiratory Questionnaire), supporting mucus plugs as a unique form of pathology.[7]

Patients with mucus plugs are at higher risk for adverse outcomes, including exacerbations, all-cause mortality, and respiratory deaths.[2-4,7,8] Recent studies in the COPDGene and ECLIPSE cohorts have shown that patients with mucus plugs experience more frequent moderate to severe exacerbations and severe exacerbations (ie, those requiring hospitalizations). Over time, these patients have a 7% to 15% higher risk of moderate to severe episodes and a 5% to 37% higher risk of episodes requiring hospitalization compared with those without mucus plugs.[3] The association holds across various patient groups—women and men, patients with a BMI below and ≥30, individuals who formerly smoked, those with mild to moderate and severe or very severe COPD, and individuals with and without a history of exacerbations. Furthermore, a separate study found that mucus plugs are linked to higher all-cause mortality in patients with COPD. Specifically, the mortality risk increased by up to 26% in patients with mucus plugs affecting three or more lung segments.[2] A subsequent study of the same cohort revealed that mucus plugs also contribute to respiratory deaths, with a 13% and 36% increased risk when one to two and three or more lung segments

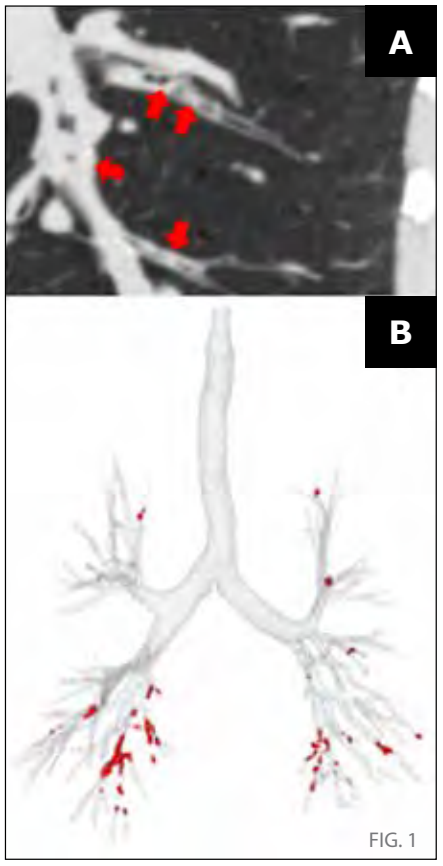


Figure 1. Cigarette smoke damages cilia and disrupts the function of the cystic fibrosis transmembrane receptor, further impairing mucus clearance. The result is mucus accumulation, plaque formation, and the development of mucus plugs. Photo courtesy of Dr. Diaz.

were involved with mucus plugs.[8] The potential mechanisms underlying these associations may include plugs being a nidus of infection and inflammation, potentiating microbial growth. Moreover, these airway-occluding mucus plugs can worsen ventilation/perfusion mismatch, which may lead to respiratory failure.

Current CT scan-based studies rely on time-consuming visual methods to identify and quantify mucus plugs, including counting affected lung segments or individual plugs. However, recent advances in artificial intelligence (AI)-based approaches seem promising in overcoming these limitations, improving the efficiency and accuracy of mucus plug detection (Figure 1). Regardless of the methodology used, airway mucus plugs on CT scans are linked to functional measures of COPD and clinically relevant outcomes, supporting them as a potential therapeutic target.

Several therapies have the potential to treat mucus pathology, including biologics and muco-active drugs and more broadly accessible COPD treatments, including nebulized saline and positive expiratory pressure devices (flutter valves). These therapies can reduce the burden of mucus plugs in the airways, but they have yet to undergo rigorous testing in COPD-specific clinical trials. Encouraging results from a trial in moderate to severe asthma suggest that biologics, such as those blocking the thymic stromal lymphopoietin receptor—which activates interleukin-13 and interleukine-5 signaling—can decrease mucus plugs and improve lung function.[9] Additionally, muco-active drugs have shown efficacy in reducing airway mucus plugs in animal models.[10] Regardless of the treatment approach, removing accumulated airway mucus could have wide-ranging benefits. It may lower airway microbial load, increase expiratory airflow, improve the function of the ciliated epithelial cells, and potentially promote a more uniform airway distribution of inhaled medications, thereby improving overall treatment effectiveness.

Designing clinical studies to test interventions targeting mucus plugs presents several challenges. First, mucus plug scores are generally not utilized in routine clinical practice, meaning that this information is rarely available in medical records, making it challenging to identify potential patients for clinical trials. Second, there is a clear need for a standardized approach to define, quantify, and report this imaging biomarker. Third, identifying and quantifying mucus plugs requires training, which can be a barrier for widespread implementation. Lastly, while AI-based algorithms have shown promise in detecting mucus plugs, the widespread adoption of this technology is limited, hindering their potential to streamline and improve the detection process in clinical settings.

While substantial progress has been made, there is still much to uncover about the nature of mucus pathology. The content of mucus plugs is assumed to be just "mucus," yet a deep characterization of their components is still lacking. It remains unclear whether CT scan-detected mucus plugs truly reflect small airways pathology and why some persist over time. Emerging fields like omics science—proteomics, metabolomics—hold promise to discover the molecular pathways that drive mucus pathology. Most studies of mucus plugs have focused on older individuals, individuals with chronic airway diseases, and those exposed to tobacco; however, we have little understanding of how mucus pathology manifests in the broader community-dwelling population. Additionally, the potential role of environmental and lifestyle factors—such as indoor and outdoor air pollution, cannabis use, vaping, and physical activity—on mucus plug formation remains largely unexplored. Addressing these gaps could lead to new insights into how mucus plugs develop and how we can better treat them in diverse patient groups.

Targeting mucus pathology could fulfill an unmet therapeutic need in managing patients with COPD, providing a novel approach to addressing the underlying mechanisms contributing to airway obstruction. By focusing on clearing sticky, mucus-laden airways, we could modify disease course and improve patient outcomes. ●

All references are available online at chestphysician.org.

FDA proposal would eliminate addicting power of cigarettes, combustible tobacco products

BY FRED GEPHARDT

On January 15, the US Food and Drug Administration (FDA) published its first-ever proposed rule to limit nicotine content in tobacco products. The proposed nicotine limit of 0.70 mg/g of tobacco is intended to render cigarettes and most other combustible tobacco products incapable of inducing or maintaining addiction. If the rule is finalized, tobacco manufacturers would have two years to comply with the new nicotine limit.

Sven-Eric Jordt, PhD

"Clinical studies have shown that people who exclusively have access to these low-nicotine cigarettes slowly reduce tobacco consumption," said Sven-Eric Jordt, PhD, Associate Professor in Anesthesia, Pharmacology, and Cancer Biology at Duke University School of Medicine. "This [proposed rule] is based on scientific findings."

There are currently no limits on nicotine content in cigarettes or any other form of tobacco sold in the United States. According to the FDA, the average nicotine content in the top 100 US cigarette brands in 2017 was 17.2 mg/g of total tobacco. The agency first announced its intention to propose limits on nicotine content in cigarettes in 2018.

"Cigarettes are the only legal consumer product that, when used as intended, will kill half of all long-term users," said Scott Gottlieb, MD, who was FDA Commissioner when the proposal was released. "Approximately 5 million additional [adults who smoke] could quit smoking within one year of implementation. Smoking rates could drop from the current 15% to as low as 1.4%."

The agency reported that despite declines in tobacco use in recent decades, tobacco use—largely cigarette smoking—still kills more than 480,000 Americans annually and costs nearly $300 billion in direct health care and lost productivity each year.

The 0.70 mg/g nicotine limit would apply to combustible tobacco products, cigarettes, cigarette tobacco, roll-your-own tobacco, most cigars and cigarillos, and pipe tobacco sold in the United States.

The limit would not apply to premium cigars, noncombustible cigarettes such as e-cigarettes and other electronic nicotine delivery systems, oral tobacco, or water pipe tobacco.

The proposed rule says that cigarette manufacturers have long designed cigarettes to precisely control nicotine delivery and provide nicotine doses to create and sustain addiction. The new maximum limit is intended to produce cigarettes and other tobacco products that can no longer create or sustain nicotine addiction in those who smoke cigarettes and other covered tobacco products.

At least one low-nicotine cigarette brand, VLN, is currently available in the United States. // continued on page 11

Novel obesity medications and OSA treatment // continued from cover

Participants received tirzepatide at the maximum tolerated dose (10 mg or 15 mg weekly, via subcutaneous injection) for 52 weeks or placebo. Tirzepatide improved the apnea-hypopnea index (AHI) at week 52, with an estimated treatment difference of −23.8 and −20.0 events per hour in patients who were or were not receiving concomitant CPAP therapy, respectively. Notably, these improvements were accompanied by a significant decrease (17.7% to 19.6%) in body weight in patients who received tirzepatide, compared with placebo (1.6% to 2.3%).

THE BIDIRECTIONAL OBESITY-OSA RELATIONSHIP

The prevalence of obesity is increasing globally, with more than 40% of adults and nearly 20% of children in the United States reported to have obesity.[3-5] Clinicians are tasked with a truly Sisyphean endeavor—tackling this growing epidemic of obesity and associated complications.

A significant comorbidity of obesity is OSA, with 60% to 70% of individuals with obesity developing the sleep disorder.

"Obesity and sleep problems and apnea are closely interrelated, and this relationship is bidirectional," said Rizwana Sultana, MD, Pediatric Sleep Medicine Specialist, Division of Pulmonary Critical Care and Sleep Medicine at the University of Texas Medical Branch. "We do know that the initiating step is a physiological process driven by slowed metabolism, concomitant with lower activity, due to different factors, leading to weight gain, which then affects sleep."

She added, "Once people develop sleep apnea, the resulting difficulty staying asleep and daytime sleepiness can trigger abnormalities in leptin and ghrelin—hormones that regulate hunger, energy balance, and food intake. Sleep deprivation is associated with higher levels of ghrelin, the hunger/appetite regulator, causing increased food intake, especially calorie-dense food, particularly at night. The increased food intake, coupled with other lifestyle factors, can in turn lead to further weight gain, which exacerbates sleep disturbances."

> *"If patients cannot or will not use CPAP therapy, then tirzepatide may be an option."*
>
> — ATUL MALHOTRA, MD, FCCP

Dr. Malhotra characterized the obesity-OSA relationship as complex, stating, "The interconnectedness between obesity and OSA is not fully understood, and although there certainly are mechanical effects, there are other effects, such as how the body controls breathing. In addition, the dilator muscles in the upper airway that are important for maintaining airway patency may be affected in people with sleep apnea plus obesity, compared [with] people with obesity alone."

TACKLING OBESITY TO TREAT OSA

There has been a significant shift in the clinical approach to obesity, with clinicians considering multimodal and multidisciplinary management of this serious disease, Dr. Sultana said. There must be a similar shift in perception among patients, she added. The stigma associated with obesity and the multifactorial barriers to lifestyle modification-mediated weight loss are the biggest challenges in managing obesity and complications like obesity-related OSA.

"Until recently, we were focusing on asking the patient to change their lifestyle and eat healthier. In my opinion, we must treat obesity as a disease, akin to how we treat other conditions," Dr. Sultana said. "For instance, while a low-salt diet is a key principle for managing hypertension, clinicians consider and use other components, including medication, to ensure that the patient meets their blood pressure goals."

Significant reliance on the patient's ability to implement and sustain a range of lifestyle modifications may set some patients up for failure, she noted, as systemic factors and circumstances beyond their control may impede or limit the patient's progress on their weight-loss journey.

PRACTICE IMPLICATIONS FOR TREATING OSA

The approval of tirzepatide for OSA comes at a time when GLP-1 receptor agonists, especially semaglutide, have already captured significant public attention, resulting in intermittent shortages of this class of medications.

The good news is that the FDA formally reported resolution of these shortages in late 2024, though many clinicians report that the drug is still difficult to obtain.[6]

> *"Using anti-obesity medications is a game changer, not only for diabetes and obesity but also for treating obesity-associated OSA and comorbidities."*
>
> — RIZWANA SULTANA, MD

"Obesity is the mother of all diseases," Dr. Sultana said. "Once we start treating obesity, it is easier for people to lose weight, which can improve not just their OSA but allow for opportunities to improve their overall health. Using anti-obesity medications is a game changer, not only for diabetes and obesity but also for treating obesity-associated OSA and comorbidities. I am a big advocate of obesity-targeted treatments, including GLP-1 medications and bariatric surgery."

Dr. Sultana acknowledged that clinicians and their patients need to be aware of the side effects. She added that GLP-1 medications may not be appropriate for every patient.

Dr. Malhotra framed the practice implications, stating, "The standard of care has not changed. The first-line treatment for sleep apnea is CPAP. The standard of care in OSA management has always been to address both obesity and sleep apnea, rather than either one alone; and, we now have more effective treatments for obesity, which could be coupled with treatment of sleep apnea to optimize results. While diet, exercise, and lifestyle modifications have been core components of OSA management in patients with obesity, these approaches are not always effective or sustained in the long term. This is an exciting time."

THE NEXT PHASE

The story of novel obesity medications in OSA is still unfolding. The phase 3 SURMOUNT-MMO study is evaluating the impact of tirzepatide on long-term outcomes in adults with obesity.[9] Additional randomized studies are needed to clarify the role of GLP-1 receptor agonist medications in the comanagement of obesity, OSA, and cardiovascular complications.

Dr. Sultana expressed confidence and optimism about the emerging role of medications in managing obesity and OSA, noting, "Sleep medicine is a multidisciplinary field. Physicians are now able to utilize this medication as part of their patient management." •

All references are available online at chestphysician.org.

Disclaimer: The SURMOUNT-OSA trial was sponsored by Eli Lilly.

Exploring the evolving landscape in combination therapies for EGFR-mutated advanced NSCLC

BY HALEIGH BEHRMAN

Recent findings from the phase III MARIPOSA trial revealed promising results for a combination of amivantamab and lazertinib as a first-line therapy for patients with epidermal growth factor receptor (EGFR)-mutant non-small cell lung cancer (NSCLC). The combination therapy demonstrated a statistically significant improvement in median progression-free survival (PFS) in the amivantamab-lazertinib group compared with the osimertinib group, from 23.7 vs 16.6 months.[1] Overall survival was a secondary endpoint, and although the result was not statistically significant, there was a trend toward improved overall survival at both 18 and 24 months compared with osimertinib monotherapy. The hazard ratio for death was 0.80 (95% CI, 0.61 to 1.05).[2]

Susan Scott, MD

Thoracic medical oncologist, Susan Scott, MD, Assistant Professor of Oncology at Johns Hopkins University School of Medicine, recently spoke with CHEST Physician about the implications of MARIPOSA in light of previous data from the FLAURA2 study of osimertinib with or without chemotherapy in EGFR-mutated advanced NSCLC.[2]

CHEST Physician: Could you provide an overview of the primary focus of the phase III MARIPOSA trial?

Dr. Scott: The phase III MARIPOSA study compared first-line treatments for lung cancer driven by a classical EGFR mutation, comparing first-line treatment with osimertinib to treatment with a combination of amivantamab and lazertinib. The primary outcome measured was progression-free survival, while secondary outcomes included response rates and overall survival.

CHEST Physician: What do you think the success of the MARIPOSA trial means for the field of lung cancer?

Dr. Scott: I think the finding that amivantamab and lazertinib improved overall survival compared with osimertinib alone is truly exciting. This is great news for patients. We are always looking for more effective combinations to offer additional options. Hopefully, this will allow for further personalization of treatment for each patient.

I believe it remains to be seen who will benefit from which treatment regimen, as they haven't been directly compared. FLAURA2 and MARIPOSA are two separate combination regimens, both of which demonstrate improved progression-free survival in the frontline setting. Certainly, an improvement in overall survival is exciting news for patients and providers. How we will incorporate this into clinical practice remains to be seen.

Each new drug introduces new side effects. So we would expect that a combination of amivantamab and lazertinib would have more side effects than osimertinib alone. We always have to balance these potential side effects with the expected benefits, as well as consider patient and disease characteristics, along with patient goals and preferences.

There will be a population of patients who may be more interested in or who could benefit more from a combination like amivantamab and lazertinib, and there may be others who benefit more from an osimertinib-chemotherapy combination.

CHEST Physician: Would you consider overall survival to be the gold standard in your practice when determining first-line treatments for patient therapy?

Dr. Scott: Yes, overall survival is undoubtedly the gold standard. It is what we hope to see because it reflects the entire patient course rather than just the first treatment. However, this does need to be considered in the context of when the trial was done, what other therapies the patients received, and what sequential options are available when we think about how to incorporate it into practice in the coming years.

CHEST Physician: Are there any patients for whom you would consider osimertinib as a standalone therapy?

Dr. Scott: Yes, I would still consider osimertinib alone for select patients with lower-risk disease with classical mutations, without brain metastases, and who may have a limited burden of disease. It may be a better option for patients who wish to be more conservative with their therapy, who don't want to have IV treatments, or who can't tolerate chemotherapy or the blood thinners that we recommend with the combination of amivantamab and lazertinib.

CHEST Physician: Can you explain your therapeutic algorithm for selecting a first-line therapy for a newly diagnosed patient with a sensitive EGFR mutation in stage IV lung cancer?

Dr. Scott: This is evolving as we gather more data from FLAURA2 and MARIPOSA. I consider all three regimens when I see a patient with newly diagnosed EGFR lung cancer. A patient who seems to have low-risk disease features or is averse to combination therapies due to the additional toxicity and risks that come with that. That would be a patient I would consider appropriate for osimertinib monotherapy.

I'm considering combination therapies more and more, particularly for patients with brain metastases, patients with positive circulating tumor DNA at diagnosis, those with a high burden of disease, or those who are very symptomatic. These are the patients for whom I would prefer a combination regimen.

I'm reviewing additional data to determine which combination regimen is best for which high-risk patient. I think we'll gain more insights in the coming years. It's always good to have options, and I believe that treatment is an individualized decision. Some of it comes down to patient preferences, their risk factors for additional combination therapies, as well as specific disease features, which may lean me toward one or the other.

Overall, I think it's exciting to see the overall survival outcomes from MARIPOSA. I'm hopeful that we'll see similar results for FLAURA2. More choices are always better for our patients.

CHEST Physician: What are the next steps for this research following these results?

Dr. Scott: We need more data on specific risk subgroups to determine who can safely receive osimertinib monotherapy, and we need more precision in distinguishing between the two combination regimens. I think there is a group of patients who specifically benefit from dual inhibition of EGFR, as well as the addition of the MET inhibition.

I think there are patients who need immediate cytoreduction with the addition of chemotherapy. Additional studies are needed to examine these higher-risk subgroups, ideally comparing the treatment regimens. I know that's a big ask in the frontline setting when both regimens are approved. But hopefully that data will become available in the coming years as we gain more experience with these different treatment regimens.●

All references are available online at chestphysician.org.


Reexamining treatment for RLS: What do the new AASM guidelines teach us?

BY LAUREN A. TOBIAS, MD, FCCP; BRIAN B. KOO, MD

Restless legs syndrome (RLS) is a common neurological disorder characterized by an uncomfortable urge to move one's legs, often with significant impact on sleep quality and overall well-being. The American Academy of Sleep Medicine (AASM) recently released updated clinical practice guidelines for management of this prevalent disorder.[1] In this article, we review RLS as a disorder relevant to not only sleep providers but also those across pulmonary medicine and provide an overview of these updated guidelines, highlighting key clinical recommendations to enhance patient care.

BACKGROUND

The development of RLS appears to be driven by a mix of genetic susceptibility, iron deficiency, and dopamine dysregulation. Certain conditions including chronic kidney disease, diabetes, and pregnancy are linked to a higher prevalence of RLS. Some studies have suggested that the prevalence of RLS may also be increased among patients with certain pulmonary disorders, including COPD, asthma, cystic fibrosis, and idiopathic pulmonary fibrosis.[2-6]

RLS is a clinical diagnosis that is neither defined by nor requires sleep testing. Its diagnosis rests on eliciting a characteristic history of an urge to move one or both legs during rest, which is relieved with movement and predominates in the evening or nighttime. If a patient with RLS does undergo sleep testing for whatever reason, period limb movements during sleep are often observed, particularly early in the night, but this finding is neither necessary nor sufficient to make an RLS diagnosis. The severity of RLS ranges broadly in the population, with some having infrequent symptoms, occurring once every few months, while others experience symptoms on a nightly basis. Sleep disruption caused by RLS is often cited by patients as the most troublesome aspect of the disorder. At its mildest, sleep disturbance may consist of brief leg repositioning over seconds to minutes that provides sufficient relief to allow sleep. In the most severe of cases, pacing the floors in the middle of the night for hours can be required to relieve the unrelenting urge to move before a patient can finally sleep.

As might be expected given this broad severity range in RLS, not all patients need treatment. The decision to initiate therapy depends on symptom severity and patient preference. A patient with only occasional symptoms that don't impact their ability to fall asleep may be content handling the occasional nuisance of their symptoms on their own. These patients usually do not come to medical attention, but a mild history of RLS may be discovered on a sleep intake history completed for the assessment of another sleep-related symptom. On the other hand, for patients with RLS whose nightly symptoms impede sleep initiation and who get less sleep as a result, thereby experiencing daytime impairment, a trial of therapy is clearly recommended.

TREATMENT OPTIONS

Even before embarking on a treatment program, it is important to recognize some common RLS triggers consistent with the good clinical practice statement outlined in the AASM RLS Treatment Guidelines. Cutting down on alcohol, tobacco use, and caffeine can help better control symptoms. Several commonly used over-the-counter medications including antihistamines and antiemetics (dopamine-blocking) can precipitate or worsen RLS symptoms, and their withdrawal can improve RLS symptoms significantly. Nearly all antidepressants have the potential to worsen RLS symptoms; however, the impetus to discontinue these medications should be especially strong when RLS is severe and the antidepressant has antihistaminergic properties (mirtazapine, doxepin, or other tricyclic antidepressants).

Assessment of iron status, and repletion when appropriate, is a cornerstone of the proper evaluation and treatment of RLS. All patients should be tested for iron stores, ideally in the morning after avoidance of iron-containing supplements and meals for the prior 24 hours. Either oral or intravenous iron can be used when the ferritin levels are below 75 µg/L. Only intravenous iron is recommended when the ferritin is between 75 µg/L and 100 µg/L, based on low absorption of oral iron when ferritin is in this range. The assessment and appropriate treatment of OSA is critical in the management of RLS. OSA and RLS often co-occur, and the treatment of OSA itself may be sufficient to eliminate RLS when symptoms are infrequent. Moreover, the control of RLS is more difficult when OSA is left untreated.

If RLS symptoms persist despite addressing triggers, or if RLS symptoms are so severe that simultaneous treatment initiation is warranted, practitioners can reference the new 2024 AASM RLS Treatment Guidelines. The initial choice when medical therapy is warranted, given that iron and ferritin have been properly addressed, should almost always be a gabapentinoid.

Gabapentin enacarbil, gabapentin, and pregabalin were all given strong recommendations, based on evidence that they result in clinically significant improvement in disease severity, sleep quality, and quality of life and should be considered first-line for the treatment of RLS. Most of the supporting studies used the validated International RLS Study Group Severity Scale to quantify response to therapy. These medications do have the potential to cause somnolence and dizziness, sometimes to a point limiting their use, and patients should be counseled about these potential side effects.

Several iron formulations were given strong or conditional recommendations for the treatment of RLS. Based on five randomized clinical trials that showed efficacy, intravenous ferric carboxymaltose received a strong recommendation for the treatment of RLS. However, this formulation is often unavailable in infusion centers. Other intravenous formulations that were given conditional recommendations include low molecular weight iron dextran and ferumoxytol. It bears noting that intravenous iron has long been considered dangerous, but this is largely based on anaphylaxis associated with high molecular weight iron dextran that is no longer available in the US. In circumstances

when serum ferritin is below 75 µg/L, oral ferrous sulfate can be given.

Opioid medications received a conditional recommendation for the treatment of RLS in this newest guideline. Randomized clinical trial data testing extended-release oxycodone-naloxone formed the basis of this recommendation. There is some complication here, however, as this formulation is not available in the US. Furthermore, long-acting oxycodone, while effective in treating RLS, may present resource issues for patients. Based on a class effect and overwhelming clinical experience with the use of other µ-opioid agonists, the task force felt it was warranted to extend the conditional recommendation to include other opioids. This recommendation comes with the acknowledgement of additional risks of abuse and chemical dependence, which by most accounts in RLS appear to be low.[7]

DEVIATION FROM 2012 GUIDELINES

The most striking departure of the 2024 RLS treatment guidelines from the prior 2012 version relates to the use of dopamine agonists (pramipexole, ropinirole, rotigotine, and carbidopa-levodopa). Previously considered standard treatment, and indeed adopted as first-line for most patients, the current 2024 guidelines provide a conditional recommendation against the standard use of each of these medications. The rationale driving this shift relates to mounting evidence for the past decade suggesting higher rates of augmentation with these agents.[8]

Augmentation refers to the paradoxical, iatrogenic worsening of RLS symptoms that can occur after prolonged use of dopaminergic medications. This phenomenon is characterized by an earlier onset of RLS symptoms in the day, increased intensity, and sometimes even spread of symptoms to other body parts such as the arms. Augmentation should be considered any time a dose increase in a dopamine agonist or levodopa is being considered. When the dose is at or exceeds the maximum recommended dose for RLS (4.0 mg for ropinirole, 0.75 mg for pramipexole, 3 mg for rotigotine), then augmentation almost definitely is occurring. Treating augmentation requires that the offending dopaminergic medication be tapered to off while an alternative nondopaminergic therapy is initiated. (For details of the treatment of augmentation, please refer to other previously published recommendation statements.[9,10])

Patients on dopamine agonists who are not experiencing augmentation and are on submaximum recommended doses can be safely continued on these medicines. It is important that they be monitored for signs of augmentation and development of other dopamine agonist-related adverse events such as impulse control problems. Maintaining the dose below the recommended maximum is critical. Practitioners still have the option of prescribing dopamine agonists for RLS but should do so only after following good practice and considering or trying a gabapentinoid.

Because very few clinical trials have evaluated RLS treatment in pediatric populations, recommendations were limited only to favoring the use of oral iron when stores are low. Similarly, in pregnant women, a paucity of studies led to a general recommendation to consider the safety profiles of the various medication options, without recommending a specific agent.

UPDATING CURRENT PRACTICES

For most clinicians, the key clinical takeaway from the new guidelines is that dopamine agonists are no longer first-line therapy for RLS and, rather, gabapentinoids should be used as primary therapy for the vast majority of patients. Although major RLS expert organizations have advocated for the use of gabapentinoids for nearly a decade, clinical practice has been slow to reflect this shift away from dopamine agonists.[10] In fact, a recent retrospective analysis found that more than half of patients with RLS were being treated with dopamine agonists, and, of these, nearly 20% were on a dose exceeding the maximum recommended by the US Food and Drug Administration.[11] Treatment of RLS falls within the scope of multiple specialties, including primary care, neurology, psychiatry, sleep medicine, and others. It is our hope that these guidelines will promote broad dissemination of the message that augmentation is a critical outcome in RLS—and one that we can usually avoid by steering clear of dopamine agonists.

The relevance of the guidelines for our patients is clear. RLS leads to significant distress and disrupts not only sleep but also next-day activities

for a large number of patients. An emerging literature even shows increased rates of suicidal intent and self-harm.[12,13] The 2024 updated clinical practice guidelines for RLS provide a robust framework for managing this complex condition. In the systematic review that accompanies the guidelines, the authors reflect upon the last 40 years with "some pride at our progress, some disappointment at our naïveté, but some optimism that continued research will translate into better treatments for RLS in the future."[14] ●

All references are available online at chestphysician.org.

FDA proposal

// continued from page 7

"There is evidence from tightly controlled studies that this could work," Dr. Jordt said. "There has been concern that people would try to compensate and smoke more to get their usual levels of nicotine, [but, in studies,] that only happened very early on. People went back to smoking their regular number of cigarettes and eventually tapered down their smoking."

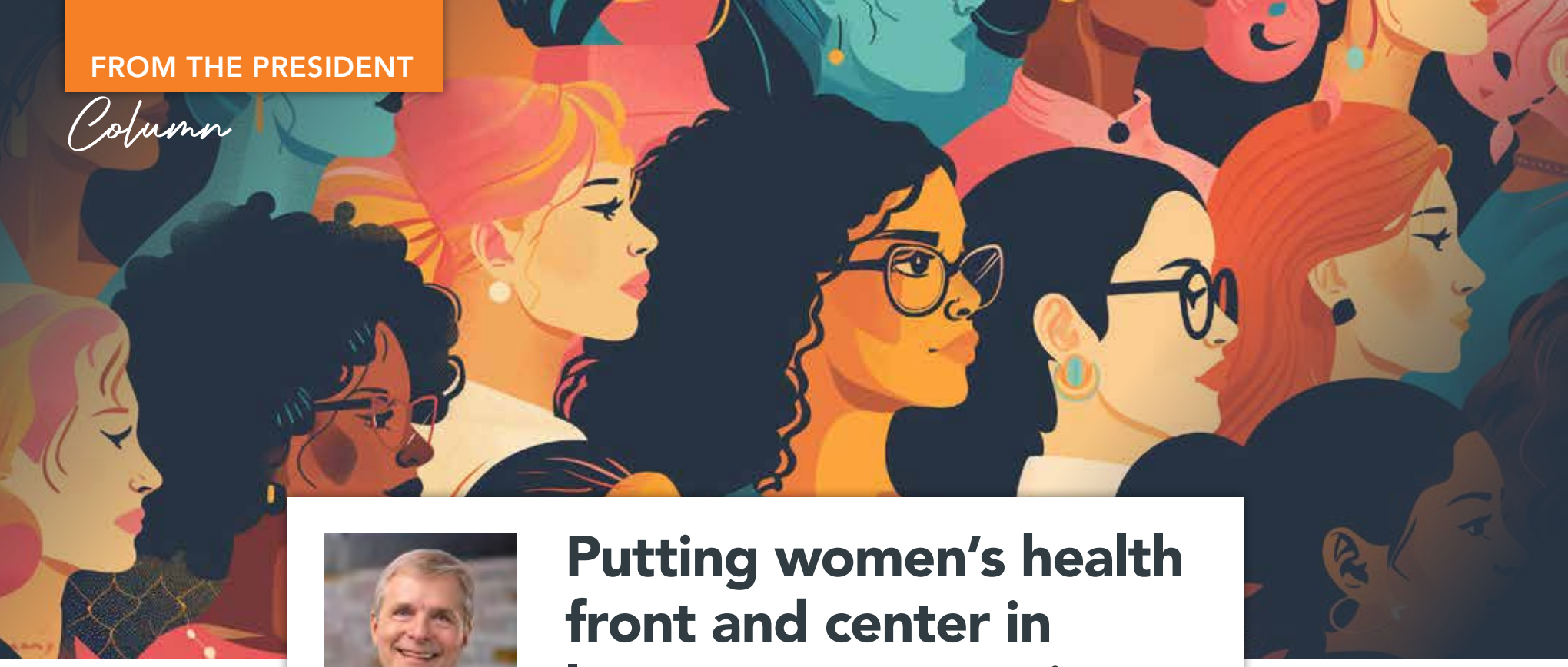
There is also the ethical question of whether respiratory medical groups should, or even could, support any form of smoking regardless of the nicotine content. Low-nicotine products may not trigger or sustain nicotine addiction, but the smoke is not harmless.

"Many of the carcinogens in tobacco are derived from nicotine," Dr. Jordt said. "However, when you burn organic matter, you still get all these highly toxic combustion products other than nicotine that you inhale. As a chest physician, you need to consider if you can support people using these highly toxic products."

Indeed, the proposed rule addresses nicotine but not the other toxic compounds produced during tobacco combustion. There is no evidence that inhaling smoke containing nonaddictive levels of nicotine carries a lower risk of cardiopulmonary and other complications of tobacco use.

The medical community has been slow to react to the proposed nicotine limit, but that is likely to change. The FDA is actively seeking comment on the proposed rule, Dr. Jordt said, and typically gives greater weight to comments from individual medical practitioners and medical organizations. The proposed rule is open for public comment until September 15, 2025. ●

All references are available online at chestphysician.org.



Putting women's health front and center in lung cancer screening

BY JOHN HOWINGTON, MD, MBA, FCCP

We are only a few months into the new year, and it already feels like so much has been accomplished. We recently wrapped up the meeting of the Scientific Program Committee at CHEST Headquarters, where hundreds of sessions for CHEST 2025 were selected and slotted into a tentative schedule. It was a grueling two days for those on the committee, but it will be a strong educational program because of their hard work.

I am very much looking forward to CHEST 2025 in Chicago, October 19 to 22—to see my friends and colleagues, to learn with some of the best and brightest in the field, and to celebrate the 90th anniversary of the American College of Chest Physicians. This is a pivotal year for the organization to step back and ask ourselves, "Where are we now compared with where we started, and where do we want to be at 100 years?"

It's a thrill to be at the helm of the CHEST Board of Regents at such an exciting time, and I look forward to celebrating 90 years with all of you.

Before I talk too much about the meeting happening in October, I want to bring us back to the present. And for my column this quarter, I thought it fitting to focus on women's health, with March being Women's History Month and home to International Women's Day (March 8). In my clinical practice, when I think of women's health, I am reminded of the staggering gender disparities that are present in lung cancer, specifically, and want to raise awareness of these troubling statistics.

Lung cancer is the number one cancer killer in women, claiming the lives of more women than breast, ovarian, and cervical cancers combined. While statistics for overall lung cancer are decreasing due to smoking interventions, we are seeing that the decline is much slower in women. For the last several years, more women were diagnosed with lung cancer than men each year in the United States. When polled, about 30% of men say they have been counseled by their clinicians about lung cancer screening, whereas only 15% of women have been counseled. It is unfortunate that women are not always given the opportunity to have these conversations because research shows that women seem to have a higher risk for lung cancer for the same level of smoking as men.

I'm an optimist at heart, so the good news is that the more we elevate these issues and bring them to the forefront of our conversations, the more interventions we can encourage. The fact is that we need more women to get screened for lung cancer, and, to do this, we need more clinicians recommending women get screened for lung cancer.

Throughout the month of March, I ask that you share these numbers with your colleagues and help celebrate women by improving their care and helping to curb these statistics.

John Howington, MD, MBA, FCCP
President, American College of Chest Physicians

P.S. Please use **#CHEST90** on all social media platforms throughout the year to help us celebrate CHEST's 90th anniversary. •

Column

Advanced practice respiratory therapist: The new advanced practice provider

BY MINDY CONKLIN, MRT, RRT, RRT-ACCS

With the physician shortage continuing to increase across the nation, the need for trained providers continues to be a void in the health care system. Advanced practice providers (APPs) have played an integral part in filling this gap for years. The success of these providers has, in turn, opened the door for a new role within the respiratory care profession: the advanced practice respiratory therapist (APRT).

The implementation of this new role is bringing forth a major shift in the profession of respiratory care. The APRT is a skilled and qualified practitioner trained by academic and clinical education to provide a scope of practice that exceeds that of the registered respiratory therapist (RRT). The pathway to becoming an APRT includes obtaining a baccalaureate degree in respiratory care, obtaining the National Board for Respiratory Care (NBRC) RRT credential, completing one year of experience as an RRT, and completing a graduate APRT education program where students focus on adult or neonatal/pediatric populations. The current Commission on Accreditation for Respiratory Care (CoARC) accredited APRT graduate program requires a minimum of 1,200 clinical hours.

As with other APPs, APRTs work in a physician-led team to provide diagnosis and treatment to patients with cardiopulmonary disease in multiple areas of a hospital setting, including acute care, critical care, and long-term care. APRTs are also prepared to provide outpatient services such as pulmonology, sleep medicine, interventional pulmonology, cardiology, pulmonary rehab, and neuromuscular patient management. APRTs can be integrated into the interdisciplinary team in the ICU to help manage patients suffering from COPD exacerbations to sepsis to respiratory failure. APRTs bring significant value to the team with proficiency in management and liberation of patients on mechanical ventilation. APRTs are a great asset to the team by adding their expertise in point-of-care ultrasound, line placements, airways, bronchoscopy, and overall knowledge of pulmonary diseases and disorders.

Having an APP who is specialized in cardiopulmonary care is valuable to patients and facilities alike. APRTs have demonstrated the determination and knowledge needed to provide excellent medical care to patients. As a result, patients value the expertise these specialized APPs display in pulmonology, and they have confidence they are receiving outstanding care. Daniel Thacker, MRT, RRT, RRT-ACCS, a practicing APRT at the VA Maryland Health Care System, states, "We are seeing a myriad of patients in various stages of pulmonary diseases and disorders. From tobacco treatment programs to sleep medicine clinics, our expertise as APRTs has made our treatment and care of patients very successful. Beyond direct patient care, we are also proving ourselves beneficial to the research conducted within our facility, thus further utilizing our education and expertise to the highest potential."

The rise of the APRT marks a pivotal advancement in respiratory care, addressing the growing need for specialized providers in health care. With advanced training and expertise in cardiopulmonary care, APRTs are enhancing patient outcomes across diverse settings and becoming integral members of health care teams. As physician shortages continue, APRTs are well-positioned to fill critical gaps, improving both patient care and team efficiency for the future of health care. •

All references are available online at chestphysician.org.

Sepsis // continued from page 5

Automating the mundane components of care delivery allows us to focus our intellect on the nuances of individualized evaluation and personalized care, where it performs best, rather than making sure we remember to order the repeat lactate or calculate the fluid bolus correctly.

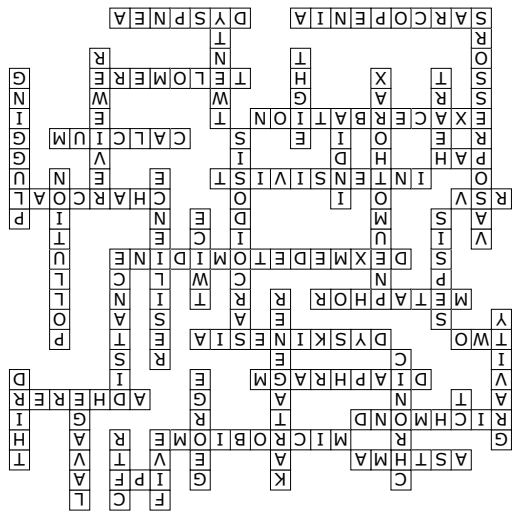
While the downsides of order set use are likely negligible, several potential pitfalls should be noted. First, caution is warranted against incorporation of mandated order set use into reportable metrics such as SEP-1 in the absence of strong evidence to support them. Second, the onus remains on providers to ensure that order set components are selected thoughtfully rather than automatically out of fear of reprisal for nonadherence to mandated bundles. While it is easy to click through boxes, we must remember that each click represents an important clinical decision with downstream effects. Perhaps the fluid bolus should be decreased in the floridly hypervolemic dialysis patient and broad-spectrum antibiotics should be withheld for the tachycardic, febrile college student with the flu.

The future of sepsis care is personalized precision medicine targeting distinct phenotypes rather than a blanket, one-size-fits-all approach. As we adapt to the increasing integration of human and artificial intelligence, we must embrace the areas where technology enhances and extends our capabilities, while clinging to those where our personal touch will always make the practice of medicine a human endeavor. •

All references are available online at chestphysician.org.

CHEST PUZZLER KEY

Answer key to crossword puzzle on page 15



COPD program aims to close gaps in diagnosis and treatment

BY ANDREA BROWN

COPD is one of the most prevalent yet underdiagnosed respiratory diseases. Research shows that two-thirds of patients with COPD miss the opportunity for an early diagnosis, often due to overlapping symptoms with other lung conditions, variability among individuals, and delayed symptom onset. Unfortunately, this delay can result in higher rates of exacerbation, increased comorbidities, and elevated health care costs compared with cases diagnosed early.

Recognizing these challenges, CHEST launched the Bridging Specialties®: Timely Diagnosis and Treatment for COPD program, an initiative focused on enhancing collaboration between primary care physicians (PCPs) and pulmonologists.

Megan Conroy, MD, MAEd, FCCP

"We created a suite of educational materials to address learning objectives for both PCPs and pulmonologists," said Steering Committee Chair, Megan Conroy, MD, MAEd, FCCP. "Our goal is to bridge the gap between primary and pulmonary care to improve patient outcomes."

CLOSING THE GAP

Patients with COPD often first present their symptoms in primary care settings, where initial diagnosis and treatment are established. PCPs face the challenge of managing and diagnosing a wide range of diseases; given the complexity of COPD, this can lead to delayed referrals to pulmonologists, particularly for patients who fail to respond to first-line therapies.

"Our primary care colleagues are managing an incredible breadth of conditions while navigating high patient volumes," Dr. Conroy said. "A close relationship between PCPs and pulmonologists ensures timely interventions and streamlines the transition of care for patients who need specialized treatment."

Geography can also hinder access to pulmonology care, further underscoring the importance of an integrated approach. "When there's a strong connection between PCPs and pulmonologists, it reduces delays in care and optimizes outcomes for patients," Dr. Conroy said. That was why it was so important to have Nate Falk, MD, MBA, CPE, CAQSM, FAAFP, a family medicine physician, on the Bridging Specialties team. "It was critical to have a PCP's perspective when developing these tools," Dr. Conroy said.

Sharren Smith, MAHRD, Manager of e-Learning and Instructional Design at CHEST and the lead for the Bridging Specialties program, reinforced this sentiment. "It takes a medical team to walk a patient through their disease management," she said. "The PCP often has an established relationship with the patient, which helps bridge the gap to pulmonology. These clinicians can improve outcomes and enhance quality of life for patients."

EARLY DIAGNOSIS AND TREATMENT

While data on whether early diagnosis changes the long-term trajectory of COPD are limited, earlier detection and intervention can significantly reduce symptom burden. For instance, patients diagnosed early are more likely to participate in smoking cessation programs, which can mitigate symptom progression.

"Connecting patients to the correct diagnosis sooner decreases symptom burden and improves their quality of life," Dr. Conroy said. "It's all about timely interventions that make a meaningful difference."

CLINICIAN RESOURCES

To empower clinicians, the Bridging Specialties program offers an array of tools designed to streamline care and improve decision-making. The toolkit includes:

- Two self-paced e-learning modules on early detection and decision-making for COPD
- A CME-eligible interactive infographic summarizing COPD diagnosis and staging
- Podcasts exploring emerging treatment strategies
- Patient materials, such as a questionnaire and inhaler device guide in both English and Spanish
- Checklists and management guides to aid clinical workflows

These resources are tailored for busy PCPs and pulmonologists, providing concise, practical information to enhance care delivery. For example, the patient questionnaire helps PCPs identify potential COPD cases early and determine when a referral to a pulmonologist is warranted.

"This toolkit serves as an additional resource in clinicians' toolboxes," Dr. Conroy said. "It's designed to help PCPs dive deeper into symptoms like shortness of breath and guide next steps for diagnosis and management."

IMPACT ON CLINICAL PRACTICE

The Bridging Specialties toolkit has garnered positive feedback for its practical application in clinical settings. "Learners have praised its effectiveness in enhancing decision-making skills through interactive, scenario-based content," said Martha Zaborowski Pascale, CPM, Director of Learning Products at CHEST. "It provides valuable insights into early diagnosis, treatment options, and strategies for managing disease progression."

Specific areas where the toolkit has proven beneficial include refining prescreening processes, understanding lung volume reduction surgeries, and improving staging and management protocols. CHEST continues to gather user feedback to refine and expand the educational experience.

ACCESSING RESOURCES

Clinicians can access these resources through the Bridging Specialties section on CHEST's website under Learning and Events. Additional content, including new podcasts, webinars, and e-learning modules for nontuberculous mycobacteria and bronchiectasis, will be available later this year.

BETTER PATIENT OUTCOMES

Dr. Conroy reflected on the personal fulfillment she's found in this initiative: "Collaborating with colleagues across the country to develop these resources has been incredibly rewarding. They provide essential knowledge to help clinicians deliver the highest level of care to their patients."

By bridging the gap between primary and pulmonary care, CHEST's Bridging Specialties program is paving the way for earlier diagnoses, more effective treatments, and better outcomes for patients with COPD. This initiative exemplifies the power of collaboration and education in transforming the landscape of respiratory care. •

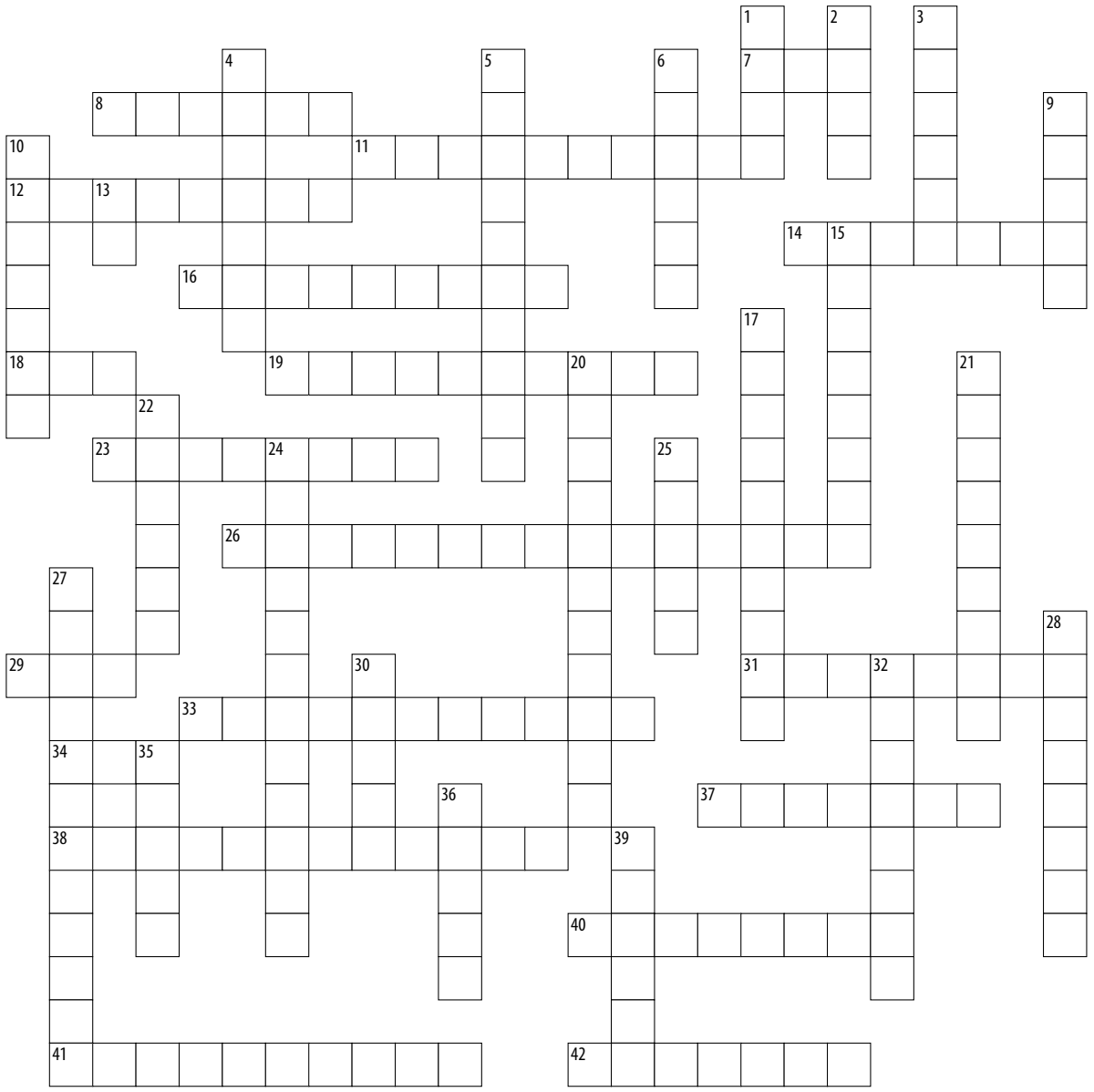
CHEST gratefully acknowledges the following supporters of Bridging Specialties: Timely Diagnosis and Treatment for COPD.
Supported by Regeneron Pharmaceuticals Inc. and Sanofi

CHEST Puzzler

Test yourself with these clues from the October, November, and December 2024 issues of the journal *CHEST*®—compiled by William Kelly, MD, FCCP.

Snap a picture of your completed crossword puzzle and post it on X to be entered to win CHEST swag! You MUST tag **@accpchest** and include **#CHESTpuzzler** in your posted picture for your entry to count. Entries will be accepted until 11:59 PM CT on **Friday, March 28**.

No purchase necessary to enter. Only open to 18+, with a US shipping address. Entries must be submitted by 11:59 PM CT on 3/28/25. This giveaway is not affiliated with X. Void where prohibited.



Answer key on page 13

ACROSS

7. In pulmonary conditions, patients with COPD and *this* ILD were more likely to receive ICU care instead of palliative care at the end of life, compared to patients with lung cancer (Dec p.1488)
8. Affects up to 15% of children worldwide, persisting to adulthood in 30%-50% (Oct p.653)
11. "The forgotten organ"—a personal ecosystem integral to health and disease (Nov p.925)
12. A "_____ agitation and sedation scale score" (RASS) of 4 to 5 is deep sedation (Oct p.659)
14. The healthy _____ effect explains why CPAP users are also more likely to get vaccinated (Oct p.671)
16. Ultrasound can assess blood flow to this muscle of respiration (Oct p.665)
18. Diagnostic delay for pulmonary arterial hypertension is often _____ years (Nov p.916)
19. Primary ciliary _____ should be considered in patients with bronchiectasis who are younger, with upper airway disease and pseudomonas (Nov p.948)
23. Linguistic tool used to facilitate abstract understanding ("my mom is a fighter") (Nov p.1162)
26. Sedative, highly selective alpha-2-adrenoreceptor agonist can reduce heartrate in sepsis (Dec p.1264)
29. Single-stranded RNA virus, discovered in 1957. Vaccine recommended for patients who are pregnant and age >60. (Nov p.963)
31. Production of the fuel source _____ requires carbonization of wood by pyrolysis at very high temperatures—and workers have 2x to 3x the risk for COPD (Dec p.1335)
33. Improving over 25 years, _____ coverage is now present in 85% of ICUs (Oct p.661)
34. Asymptomatic carriers of BMPR2 mutation had 2.3% annual risk of developing _____ (Nov p.916)
37. Pulmonary artery to aorta diameter ratio and coronary artery _____ score are CT findings that may predict cardiovascular events and COPD exacerbations (Dec p.1360)
38. One severe COPD _____, or two moderate ones, increased MI risk by 50% (Dec p.1262)
40. Measuring _____ length changed ILD treatment in 32% of patients (Nov p.909)
41. Progressive loss of skeletal muscle mass, impairing physical performance and adding to dyspnea in the aging population (Dec p.1275)
42. Pulmonary sensation in 36% of people over 65, half the time due to cardiorespiratory disease (Dec p.1259)

DOWN

1. In TNM lung cancer classification, T3 is tumor larger than _____ cm and less than 7 cm (Nov p.923)
2. Overall health has significantly improved with _____ modulators for cystic fibrosis, but women may benefit relatively less (Nov p.951)
3. Bronchoscopic _____ was originally a research technique (1970s) but is now essential and safe for infection, ILD evaluations (Oct p.794)
4. _____ cough is defined as duration for more than eight weeks—it affects 4%-12% of world population (Nov p.1125)
5. Syndrome of primary ciliary dyskinesia plus laterality defects (Nov p.939)
6. Respiratory questionnaire named after this saint (Dec p.1259)
9. Chronic respiratory disease is the _____ leading cause of death worldwide (Nov p.901)
10. The GRAVITAS randomized trial showed suction during thoracentesis was as safe and three minutes faster than _____ drainage (Dec p.1279)
13. Only 5%-18% of those eligible get an annual ____ screening, even though it reduces lung cancer mortality by 20%-25% (Nov p.1250)
15. In March 2023, United States lung transplant allocation policy minimized importance of _____ between recipient and donor hospital (Dec p.1272)
17. _____, or an individual's capacity to resist, adapt, recover, or grow from adversity, is a modifiable trait that may improve ICU survivorship (Dec p.1432)
20. Significant sexual dysfunction was noted in a cross-sectional study of patients with this granulomatous disorder, and was correlated with depression and fatigue (Dec p.1473)
21. Up to half of COPD attributable risk may be associated with air _____ (Nov p.899)
22. Leading cause of hospital mortality—and $45 billion cost per year (Nov p.1046)
24. Patients with ILD who have had a recent _____ should wait at least four weeks after resolution to start an exercise program (Nov p.1109)
25. Asthma prevalence for Black children is _____ that of White children (Dec p.1310)
27. Surviving Sepsis Campaign recommends initial fluid resuscitation within three hours and consideration of _____ within one hour if hypotensive (Dec p.1269)
28. Mucous _____ on CT, even if silent, may be associated with worse COPD outcomes (Nov p.1010)
30. South Africa has the highest COVID-19 vaccine hesitancy (52%); this country has the lowest (1.7%) (Oct p.656)
32. The December issue thanked each _____, who expertly evaluated manuscripts this past year (Dec p.1583)
35. The Framingham _____ Study established 29 mm as mean pulmonary artery size in men. By echo, 25 mm has been proposed. (Nov p.919)
36. VV-ECMO transfusion guidelines are restrictive, but one study saw lower mortality with _____ g/dL hemoglobin threshold instead of 7 (Dec p.1266)
39. 2022 ESC/ERS guide defines pulmonary hypertension as above *this* resting mean pressure (Oct p.668)

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