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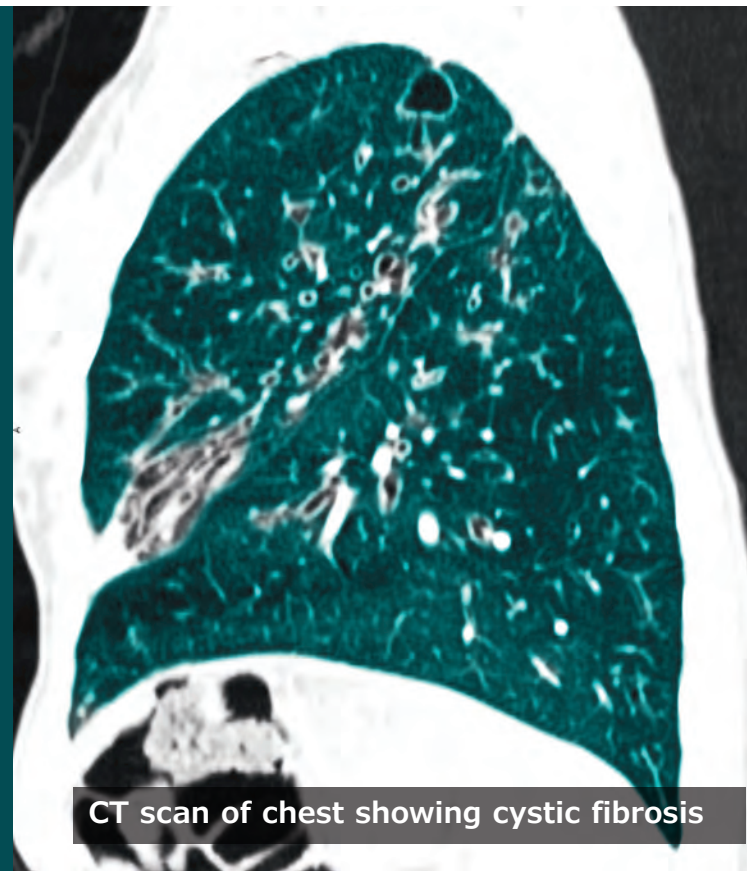
Advances in cystic fibrosis treatment bring new challenges to clinical care



CT scan of chest showing cystic fibrosis

Callista Images/Image Source/Getty Images

BY WALTER ALEXANDER

After Rena Barrow-Wells, an African American mother, fought mightily to prevent a repeat of her experience of two decades earlier when her first child's cystic fibrosis (CF) took 4 years to diagnose, her story became the subject of a *New York Times* feature covering disparities in diagnostic CF screening. The article highlighted not only her struggles, but also the utter transformation of the CF landscape since the introduction of small molecule mutation-specific drugs. These drugs restore function to defective CF transmembrane conductance regulator (CFTR) proteins. By the time Ms. Barrow-Wells' son was treated, lung and pancreatic scarring were already significant. So when the 39-mutation variant screening test available in Ms. Barrow-Wells' Lawrenceville, Georgia, clinic turned out negative for CF, her pediatrician told her to stop worrying despite her new son's inherent genetic risk, telltale salty skin, foul-smelling diapers, and her pleas to test for sweat chloride. It took 3 months for a confirmed diagnosis and the initiation of treatment.

Current genetic tests, based largely on older clinical trials enrolling mostly White children, are highly accurate for identifying CF in white babies (95%), but may fail to identify mutations originating in Africa, Asia, and Latin America. They miss CF in Asian (44%), Black (22%), and Hispanic, Native American and Alaskan Native babies (14%), the Times article stated. In the United States, the number of CF variants tested for falls into a wide range: from the one variant found mostly in White populations in Mississippi (with a 38% Black populace) to 689 variants in Wisconsin.

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Ensifentrine for COPD: Out of reach for many?

BY NEIL OSTERWEIL

Ensifentrine (Ohtuvayre™), a novel medication for the treatment of COPD recently approved by the Food and Drug Administration, has been shown to reduce COPD exacerbations and may improve the quality of life for patients, but these potential benefits come at an unreasonably high annual cost, authors of a cost and effectiveness analysis say.

Ensifentrine is a first-in-class selective dual inhibitor of both phosphodiesterase 3 (PDE-3) and PDE-4, combining both bronchodilator and nonsteroidal anti-inflammatory effects in a single molecule. The drug is delivered through a standard jet nebulizer. In the phase 3 ENHANCE 1 and 2 trials, ensifentrine significantly improved lung function based on the primary outcome of average forced expiratory volume in 1 second within 0-12 hours of administration, compared with placebo (Am J Respir Crit Care Med. 2023 Aug 15;208[4]:406-416). In addition, patients were reported to tolerate the inhaled treatment well, with similar proportions of ensifentrine- and placebo-assigned patients reporting treatment-emergent adverse events. The most common treatment-emergent adverse events were

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INSIDE HIGHLIGHT

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AI's ability to improve care

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nasopharyngitis, hypertension, and back pain, reported in < 3% of the ensifentrine group.

High cost barrier

But as authors of the analysis from the Boston-based Institute for Clinical and Economic Review (ICER) found, the therapeutic edge offered by ensifentrine is outweighed by the annual wholesale acquisition cost that its maker, Verona Pharma, has established: $35,400, which far exceeds the estimated health-benefit price of $7,500-$12,700, according to ICER

ICER is an independent, nonprofit research institute that conducts evidence-based reviews of health care interventions, including prescription drugs and diagnostic tests. "Current evidence shows that ensifentrine decreases COPD exacerbations when used in combination with some current inhaled therapies, but there are uncertainties about how much benefit it may add to unstudied combinations of inhaled treatments," said David Rind, MD, chief medical officer of ICER in a statement.

Dr. Rind noted the high price of ensifentrine may lead payers to restrict access to an otherwise promising new therapy. "Obviously many drugs in the US are overpriced, and this one, too, looks like it is overpriced. That causes ongoing financial toxicity for individual patients and it causes problems for the entire US health system, because when we pay too much for drugs we don't have money for other things. So I'm worried about the fact that this price is too high compared to the benefit it provides."

As many as one in six persons with COPD in the United States miss or delay COPD medication doses because of high drug costs (BMC Public Health. 2024 Mar 20. doi: 10.1186/s12889-024-18333-z). "I think that the pricing they chose is going to cause lots of barriers to people getting access and that insurance companies will throw up barriers. Primary care physicians like me won't even try to get approval for a drug like this given the hoops we will be made to jump through, and so fewer people will get this drug," Dr. Rind said. He pointed out that a lower wholesale acquisition cost could encourage higher-volume sales, affording the drugmaker a comparable profit with the higher-cost but lower-volume option.

Good drug, high price

An independent appraisal committee for ICER determined that "current evidence is adequate to demonstrate a net health benefit for ensifentrine added to maintenance therapy when compared to maintenance therapy alone."

But ICER also issued an access and affordability alert "to signal to stakeholders and policymakers that the amount of added health care costs associated with a new service may be difficult for the health system to absorb over the short term without displacing other needed services."

ICER recommends that payers should include coverage for smoking cessation therapies, and that drug manufacturers "set prices that will foster affordability and good access for all patients by aligning prices with the patient-centered therapeutic value of their treatments."

"This looks like a pretty good drug," Dr. Rind said. "It looks quite safe and I think there will be a lot of patients, particularly those who are having frequent exacerbations, who this would be appropriate for, particularly once they've maxed out existing therapies, but maybe even earlier than that. And if the price comes down to the point that patients can really access this and providers can access it, people really should look at this as a potential therapy."

Drug not yet available?

However, providers have not yet had direct experience with the new medication. "We haven't been able to prescribe it yet," said Corinne Young, MSN, FNP-C, FCCP, director of Advance Practice Provider and Clinical Services for Colorado Springs Pulmonary Consultants, president and founder of the Association of Pulmonary Advance Practice Providers, and a member of the *CHEST Physician* Editorial Board.

She learned "they were going to release it to select specialty pharmacies in the 3rd quarter of 2024. But all the ones we call do not have it and no one knows who does. They haven't sent any reps into the field in my area so we don't have any points of contact either," she said.

Verona Pharma stated it anticipates ensifentrine to be available in the third quarter of 2024 "through an exclusive network of accredited specialty pharmacies."

Funding for the ICER report came from nonprofit foundations. No funding came from health insurers, pharmacy benefit managers, or life science companies. Dr. Rind had no relevant disclosures. ■

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Few who smoke and want to quit seek provider help

BY HEIDI SPLETE

Approximately half of US adults who smoke tried to quit in 2022, but fewer than 40% used counseling or medication, and half received assistance or advice about quitting from clinicians, based on a review in the Centers for Disease Control and Prevention's *Morbidity and Mortality Weekly Report*.

Previous research has shown that clinician intervention and evidence-based treatment increase the odds that people who smoke can quit successfully, but the extent to which these interventions are applied in practice has not been well studied, the researchers noted.

Although progress has been made in reducing cigarette smoking in the US, an estimated 28.8 million adults reporting cigarette smoking in 2022, said lead author Brenna VanFrank, MD, MSPH. "Cigarette smoking remains the leading preventable cause of death and disease in the United States," said Dr. VanFrank, Senior Medical Officer, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion.

In a new review (Morb Mortal Wkly Rep 2024;73:633-641), the researchers examined data from the 2022 National Health Interview Survey. The study population included 27,651 adults aged 18 years and older. Current smoking was defined as currently smoking each day or some days and ever having smoked at least 100 cigarettes. The survey assessed the individuals' interest in quitting, past-year quit attempts, recent quitting success, receipt of HCP advice about quitting, and use of counseling or medication to help quit.

In 2022, approximately two-thirds (67.7%) of the 28.8 million adults who smoke in the US wanted to quit, half (53.3%) tried to quit, and 8.8% were successful. Of those who reported trying to quit, 38.3% used counseling or medication. Of these, 36.3% used medication, 7.3% used counseling, and 5.3% used both. The highest prevalence of attempts to quit smoking in the past year were among adults aged 18-24 years and the lowest among those aged 45-64 years (74.4% vs 47.5%). Rates of successful quitting

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CYSTIC FIBROSIS

// *continued from page 1*

Not long ago, CF was thought of as an inherited childhood disease leading to childhood or adolescent mortality. Now, life expectancy approaches the normal range for those who can be and are appropriately treated — given that less than 10% of individuals with CF have genetic variants that the triple treatment (Trikafta: elexacaftor/ivacaftor/tezacaftor) leaves out.

Today's CF challenges

Still, ongoing research is needed to find treatments for other variants, and better care for adult populations living with treated CF and the disease's multisystem manifestations. "As people with CF live longer, we need to be very focused on optimized adult medical care for this population," Marc A. Sala, MD, assistant professor of medicine, Adult CF Program, Northwestern University Feinberg School of Medicine, Chicago, said. "For example, we need higher vigilance for liver, microvascular, coronary artery disease, and various cancer screenings. We do not know exactly how these will manifest differently from the way they do in non-CF populations, so this is where more work needs to be done."

Emphasis on monitoring

The authors of "Future therapies for cystic fibrosis" (Allen et al. Nature Communications, 2023 Feb 8), after citing the ongoing transformative change for people with CF since the introduction of CFTR drugs, gave voice to important cautions (doi: 10.1038/s41467-023-36244-2). "Disease will progress, albeit more slowly, and will be more challenging to monitor. Effective CFTR modulators will likely slow or, at best, halt disease progression, but will not reverse a disease that has already become fixed." They cited pancreatic destruction in the majority, bronchiectasis, and absence of the vas deferens, with still recurring pulmonary exacerbations along with chronic infections and persistent airway inflammation. "It is essential that we do not become complacent about disease progression in this population," the researchers stated.

They cautioned that effective surveillance for infection is critical in asymptomatic patients, emphasizing that it underpins the management of young healthy children with CF who demonstrate disease progression despite a lack of symptoms. Among the ~90% for whom Trikafta is suitable and approved (those with least one copy of F508del or other responsive mutations), improvements include increased percent predicted FEV_1 by 10%-15% or more, decreased exacerbations, and improved quality of life," Dr. Sala said. "Subsequent 'real world' experience shows dramatic reductions in sputum production and decreased frequency of lung transplant."

"Adult CF care in general is a completely new frontier. It's fairly new to have separate pediatric and adult CF centers. There's been a shift."
– Meilinh Thi, DO

Mutation agnostic therapy

Unfortunately, CF mutants, outside the population eligible for Trikafta, are prodigious in number and do not fall into just a few major groups. "Although CF is a monogenic disease, it has variable phenotypes even for two individuals with the same mutations," Dr. Sala said. "Current CFTR modulators act on the dysfunctional CFTR protein (either as channel gating potentiators or molecular chaperones to improve misfolding). That leaves about 10% of the CF population, those with little to no protein production ineligible for treatment with CFTR modulators. The ideal "would be to develop a 'mutation agnostic' strategy — such as with mRNA or gene delivery. Here you could imagine that regardless of the type of mutation, a patient would then be able to receive the technology to increase CFTR channel function," Dr. Sala said.

Strategies in testing phases

"For patients with class I (nonsense) mutations there is hope that small molecules will be identified that can facilitate premature truncation codon (PTC) read-through and/or impede mRNA decay allowing for clinically relevant levels of functional CFTR," the researchers noted. While the most extensively developed, ataluren, an oxadiazole, failed in phase 3 trials after initial promise, other ribosomal read-through drugs are in preclinical and early phase clinical trials. Also, early encouraging results support an alternative strategy, engineered transfer RNAs (tRNAs) that introduce an amino acid to an elongating peptide in place of the termination codon.

While these will address specific mutations, DNA or mRNA replacement strategies would be "mutation agnostic," the researchers stated. The major challenge: delivery to the respiratory epithelium. Approaches currently in early testing include an inhaled aerosolized, lipid-based nanoparticle carrier for mRNA delivery, viral and non-viral DNA transfer, lipid-mediated CFTR gene transfer, pseudotyped lentiviral vector and adeno-associated vector transfer of CFTR DNA.

Adult CF care

"Adult CF care in general is a completely new frontier," Meilinh Thi, DO, director of the adult cystic fibrosis program and assistant professor at University of Texas Health at San Antonio, said in an interview. "It's fairly new to have separate pediatric and adult CF centers. There's been a shift," she said. "We're encountering diseases in CF that we have not in the past had to deal with: diabetes that has features of both type 1 and type 2, increased colon cancer risk, bone disease, and mental health issues. Also, while pregnancy was previously discouraged for women with CF because of lung disease, now many are giving birth without complications and living normal lives," Dr. Thi said.

The lifetime health issues conferred by CF, Dr. Thi noted, include lung disease with chronic inflammation, infection, respiratory failure (still the most common cause of death), gastrointestinal disorders (including of the pancreas) , colon obstruction and colon cancer, sinus disease, and reproductive system effects.

Their permanence, she said, depends on how far their disease has progressed. "So the earlier you can provide these newer therapies, the modulators, for example, or the gene therapy whenever that comes out, then the less damage these organ systems will have, and the patients, we hope, will then do better." ■

COPD

Are beta-blockers safe?

BY AARON B. HOLLEY, MD

Everyone takes a pharmacology class in medical school that includes a lecture on beta receptors. They're in the heart (beta-1) and lungs (beta-2), and drug compounds agonize or antagonize one or both. The professor will caution against using antagonists (beta blockade) for patients with COPD lest they further impair the patient's irreversibly narrowed airways. Obsequious students mature into obsequious doctors, intent on "doing no harm." For better or worse, you withhold beta-blockers from your patient with COPD and comorbid cardiac disease.

Perhaps because the pulmonologist isn't usually the one who decides whether a beta-blocker is prescribed, I've been napping on this topic since training. Early in fellowship, I read an *ACP Journal Club* article about a Cochrane systematic review that concluded that beta-blockers are fine in patients with COPD. The summary appealed to my bias towards evidence-based medicine (EBM) supplanting physiology, medical school, and everything else. I was more apt to believe my stodgy residency attendings than the stodgy pharmacology professor. Even though COPD and cardiovascular disease share multiple risk factors, I had never reinvestigated the relationship between beta-blockers and COPD. Turns out that while I was sleeping, the debate continued. Just last month a prospective, observational study published in *JAMA Network Open* found that beta-blockers did not increase the risk for cardiovascular or respiratory events among patients with COPD being discharged after hospitalization for acute myocardial infarction. Although this could be viewed as a triumph for EBM over physiology and a validation of my decade-plus of intellectual laziness, the results are actually pretty thin. These studies, in which patients with an indication for a therapy (a beta-blocker in this case) are analyzed by whether or not they received it, are problematic. The fanciest statistics — in this case, they used propensity scores — can't control for residual confounding. What drove the physicians to prescribe in some cases but not others? We can only guess.

This might be okay if there hadn't been a randomized controlled trial (RCT) published in 2019 in *The New England Journal of Medicine* that found that beta-blockers increase the risk for severe COPD exacerbations. In EBM, the RCT trumps all. Ironically, this trial was designed to test whether beta-blockers reduce severe COPD exacerbations. Yes, we'd come full circle. There was enough biologic plausibility to support a positive effect, or so thought the study authors and the Department of Defense (DOD) — for reasons I can't possibly guess, the DOD funded this RCT. The RCT did leave beta-blockers some wiggle room. The authors purposely excluded anyone with a cardiovascular indication for a beta-blocker. The intent was to ensure beneficial effects were isolated to respiratory and not cardiovascular outcomes. Of course, the reason I'm writing and you're reading this is that COPD and cardiovascular disease co-occur at a high rate. The RCT notwithstanding, we prescribe beta-blockers to patients with COPD because they have a cardiac indication, not to reduce acute COPD exacerbations. So, it's possible there'd be a net beta-blocker benefit in patients with COPD and comorbid heart disease. That's where the *JAMA Network Open* study comes in, but as discussed, methodologic weaknesses preclude its being the final word. That said, I think it's unlikely we'll see a COPD with comorbid cardiac disease RCT performed to assess whether beta-blockers provide a net benefit, unless the DOD wants to fund another one of these. In the meantime, I'm calling clinical equipoise and punting. Fortunately for me, I don't have to prescribe beta-blockers. I suppose I could consider stopping them in my patient with severe COPD, the one I can't keep out of the hospital, but I'm not convinced that would make much difference. ■

Dr. Holley is professor of medicine at Uniformed Services University in Bethesda, Maryland, and a pulmonary/sleep and critical care medicine physician at MedStar Washington Hospital Center in Washington, DC. He reported conflicts of interest with Metapharm, the American College of Chest Physicians, and WebMD.

CESSATION *continued from previous page*

were highest among individuals with higher levels of education and income, and use of smoking cessation treatment was highest among White adults (42.7%), followed by non-Hispanic adults of another race, Black adults, and Hispanic adults (33.6%, 32.6%, and 28.8%, respectively). People who smoke menthol cigarettes had low success rates for quitting (< 10%), although they were significantly more likely than people who smoke nonmenthol cigarettes to express interest in quitting (72.2% vs 65.4%). People who smoke menthol cigarettes also had significantly lower prevalences than those who smoke nonmenthol cigarettes of receiving clinician advance to quit and using treatment strategies (both $P < .05$). The study findings were limited by several factors, including the use of self-reports and a lack of data on institutionalized adults or adults in the military. However, the results suggest that opportunities exist to increase smoking cessation across public health and health care sectors by expanding access to and use of services.

Ensuring support for tobacco cessation

"It is important to ensure everyone has an opportunity to quit smoking and has access to proven treatments to help them be successful," Dr. VanFrank said. Strategies including behavioral counseling, cessation medications, and advice and support from HCPs can increase quit success. Quitting successfully often takes multiple tries, and those trying to quit may need long-term support and repeated treatment. "Health systems changes, such as adoption of treatment protocols and standardized clinical work flows, can systematize clinical treatment delivery, and such changes might also serve to increase treatment access for the 75% of adults who smoke who see a health care professional in a given year," Dr. VanFrank said.

As for additional research, "continued surveillance of tobacco use and cessation-related behaviors will help us monitor progress and identify continued opportunities to eliminate tobacco product use and tobacco-related disparities," Dr. VanFrank said. Including equitable opportunities in all commercial tobacco prevention and control efforts has the potential to reduce tobacco-related health disparities.

The results of the review were not surprising, and reflect where tobacco treatment has been for the past 20 years, said David M. Mannino, MD, a pulmonologist and professor of medicine at the University of Kentucky, Lexington, who was not involved in the study. The good news is that smoking prevalence has continued to drop in the United States over the past 15 years. However, some bad news is that use of e-cigarettes/vaping is still increasing, especially in younger populations, and new nicotine delivery systems are addicting a new generation.

Always ask about smoking

In practice, "clinicians should always ask patients about cigarette smoking, as well as vaping and other nicotine use, advise them to quit, and refer them to tobacco treatment experts," Dr. Mannino said. The bottom line is that better treatments are needed for tobacco/nicotine addiction, Dr. Mannino said. "Although we have come a long way, we have a long way to go as millions of [people who smoke] in the US and globally would like to quit."

Behavioral counseling helps, as does pharmacotherapy, and the two together are more effective than either alone, said Jamie Garfield, MD, professor of thoracic medicine and surgery at the Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, who was not involved in the study.

Cessation services need to be tailored to the many demographic groups who use tobacco products, Dr. Garfield said. "Just as marketing campaigns directed to older adults will be different from those directed to young adults, so too must cessation resources. Providers need better options to choose from with regard to cessation resources and behavioral counseling sessions. They need to be aware of what motivates one group of people to smoke and how they can be inspired to quit, including which pharmacotherapies are affordable, available, and will work; the same strategies will not work for all people"

The study was supported by the Centers for Disease Control and Prevention's National Center for Chronic Disease Prevention and Health Promotion. The researchers had no financial conflicts to disclose. Dr. Mannino disclosed serving as an expert witness for on tobacco use and tobacco-caused disease on behalf of people suing the tobacco and vaping industries. Dr. Garfield had no financial conflicts to disclose. ■

Wearable may confirm sleep disruption impact on chronic disease

BY HEIDI SPLETE

Rapid eye movement (REM) sleep, deep sleep, and sleep irregularity were significantly associated with increased risk for a range of chronic diseases, based on a new study of > 6000 individuals.

"Most of what we think we know about sleep patterns in adults comes from either self-report surveys, which are widely used but have all sorts of problems with over- and under-estimating sleep duration and quality, or single-night sleep studies," said corresponding author Evan L. Brittain, MD, of Vanderbilt University, Nashville, Tennessee.

The single-night study yields the highest quality data but is limited by extrapolating a single night's sleep to represent habitual sleep patterns, which is often not the case, he said. In the current study, published (2024 Jul 19. doi: 10.1038/s41591-024-03155-8) in *Nature Medicine*, "we had a unique opportunity to understand sleep using a large cohort of individuals using wearable devices that measure sleep duration, quality, and variability. The All of Us Research Program is the first to link wearables data to the electronic health record at scale and allowed us to study long-term, real-world sleep behavior," Dr. Brittain said.

The timing of the study is important because the American Heart Association now recognizes sleep as a key component of heart health, he added. The researchers reviewed objectively measured, longitudinal sleep data from 6785 adults who used commercial wearable devices (Fitbit) linked to electronic health record data in the All of Us Research Program. The median age of the participants was 50.2 years, 71% were women, and 84% self-identified as White individuals. The median period of sleep monitoring was 4.5 years.

REM sleep and deep sleep were inversely associated with the odds of incident heart rhythm and heart rate abnormalities. Each percent increase in REM sleep was associated with a reduced incidence of atrial fibrillation (odds ratio [OR], 0.86), atrial flutter (OR, 0.78), and sinoatrial node dysfunction/bradycardia (OR, 0.72). A higher percentage of deep sleep was associated with reduced odds of atrial fibrillation (OR, 0.87), major depressive disorder (OR, 0.93), and anxiety disorder (OR, 0.94).

Increased irregular sleep was significantly associated with increased odds of incident obesity (OR, 1.49), hyperlipidemia (OR, 1.39), and hypertension (OR, 1.56), as well as major depressive disorder (OR, 1.75), anxiety disorder (OR, 1.55), and bipolar disorder (OR, 2.27). The researchers also identified J-shaped associations between average daily sleep duration and hypertension (P for nonlinearity = .003), as well as major depressive disorder and generalized anxiety disorder (both $P <$ .001).

The study was limited by several factors including the relatively young, White, and female study population. However, the results illustrate how sleep stages, duration, and regularity are associated with chronic disease development, and may inform evidence-based recommendations on healthy sleeping habits, the researchers wrote.

Findings support need for sleep consistency

"The biggest surprise for me was the impact of sleep variability of health," Dr. Brittain told this news organization. "The more your sleep duration varies, the higher your risk of numerous chronic diseases across the entire spectrum of organ systems. Sleep duration and quality were also important but that was less surprising," he said.

The clinical implications of the findings are that sleep duration, quality, and variability are all important, Dr. Brittain said. "To me, the easiest finding to translate into the clinic is the importance of reducing the variability of sleep duration as much as possible," he said. For patients, that means explaining that they need to go to sleep and wake up at roughly the same time night to night, he said.

"Commercial wearable devices are not perfect compared with research grade devices, but our study showed that they nonetheless collect clinically relevant information," Dr. Brittain added. "For patients who own a device, I have adopted the practice of reviewing my patients' sleep and activity data which gives objective insight into behavior that is not always accurate through routine questioning," he said.

As for other limitations, the cohort included only those who already owned a Fitbit.

Device data will evolve to inform patient care

"With the increasing use of commercial wearable devices, it is crucial to identify and understand the data they can collect," said Arianne K. Baldomero, MD, a pulmonologist and assistant professor of medicine

CHRONIC *continued on following page*

Irregular sleep patterns increase type 2 diabetes risk

BY MARILYNN LARKIN

Irregular sleep duration was associated with a higher risk for diabetes in middle-aged to older adults in a new UK Biobank study. The analysis of more than 84,000 participants with 7-day accelerometry data suggested that individuals with the most irregular sleep duration patterns had a 34% higher risk for diabetes compared with their peers who had more consistent sleep patterns.

"It's recommended to have 7-9 hours of nightly sleep, but what is not considered much in policy guidelines or at the clinical level is how regularly that's needed," said Sina Kianersi, PhD, of Brigham and Women's Hospital in Boston, Massachusetts. "What our study added is that it's not just the duration but keeping it consistent. Patients can reduce their risk of diabetes by maintaining their 7-9 hours of sleep, not just for 1 night but throughout life." The study was published online in *Diabetes Care* (2024 Jul 17. doi: 10.2337/dc24-0213).

Modifiable lifestyle factor

Researchers analyzed data from 84,421 UK Biobank participants who were free of diabetes when they provided accelerometer data in 2013-2015 and who were followed for a median of 7.5 years (622,080 person-years).

Participants had an average age of 62 years, 57% were women, 97% were White individuals, and 50% were employed in non–shift work jobs. Sleep duration variability was quantified by the within-person standard deviation (SD) of 7-night accelerometer-measured sleep duration. Participants with higher sleep duration SD were younger and more likely to be women, shift workers, or people who currently smoke; those who reported definite "evening" chronotype (natural preference of the body to sleep at a certain time); those having lower socioeconomic status, higher body mass index, and shorter mean sleep duration; and were less likely to be White individuals. In addition, a family history of diabetes and of depression was more prevalent among these participants.

A total of 2058 incident diabetes cases occurred during follow-up.

After adjustment for age, sex, and race, compared with a sleep duration SD ≤ 30 minutes, the hazard ratio (HR) was 1.15 for 31-45 minutes, 1.28 for 46-60 minutes, 1.54 for 61-90 minutes, and 1.59 for ≥ 91 minutes. After the initial adjustment, individuals with a sleep duration SD of > 60 vs ≤ 60 minutes had a 34% higher diabetes risk. However, further adjustment for lifestyle, comorbidities, environmental factors, and adiposity attenuated the association — ie, the HR comparing sleep duration SD of > 60 vs ≤ 60 minutes was 1.11. Furthermore, researchers found that the association between sleep duration and diabetes was stronger among individuals with lower diabetes polygenic risk score.

"One possible explanation for this finding is that the impact of sleep irregularity on diabetes risk may be less noticeable in individuals with a high genetic predisposition, where genetic factors dominate," Dr. Kianersi said. "However, it is important to note that these sleep-gene interaction effects were not consistently observed across different measures and gene-related variables. This is something that remains to be further studied." Nevertheless, he added, "I want to emphasize that the association between irregular sleep duration and increased diabetes risk was evident across all levels of

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at the University of Minnesota, Minneapolis. "This study specifically analyzed sleep data from Fitbit devices among participants in the All of Us Research Program to assess sleep patterns and their association with chronic disease risk," said Dr. Baldomero, who was not involved in the study.

The significant relationships between sleep patterns and risk for chronic diseases were not surprising, Dr. Baldomero said. The findings of an association between shorter sleep duration and greater sleep irregularity with obesity and sleep apnea validated previous studies in large-scale population surveys, she said. Findings from the current study also reflect data from the literature on sleep duration associated with hypertension, major depressive disorder, and generalized anxiety findings, she added.

"This study reinforces the importance of adequate sleep, typically around 7 hours per night, and suggests that insufficient or poor-quality sleep may be associated with chronic diseases," Dr. Baldomero said. "Pulmonologists should remain vigilant about sleep-related issues, and consider further investigation and referrals to sleep specialty clinics for patients suspected of having sleep disturbances," she said. "What remains unclear is whether abnormal sleep patterns are a cause or an effect of chronic diseases," Dr. Baldomero noted. "Additionally, it is essential to ensure that these devices accurately capture sleep patterns and continue to validate their data against gold standard measures of sleep disturbances," she said.

The study was based on work that was partially funded by an unrestricted gift from Google, and the study was supported by National Institutes of Health. Dr. Brittain disclosed research funds unrelated to this work from United Therapeutics. Dr. Baldomero had no financial conflicts to disclose.

IRREGULAR *continued from previous page*

diabetes polygenic risk scores."

The association also was stronger with longer sleep duration. The authors suggested that longer sleep duration "might reduce daylight exposure, which could, in turn, give rise to circadian disruption." Overall, Dr. Kianersi said, "Our study identified a modifiable lifestyle factor that can help lower the risk of developing type 2 diabetes."

The study had several limitations. There was a time lag of a median of 5 years between sleep duration measurements and covariate assessments, which might bias lifestyle behaviors that may vary over time. In addition, a single 7-day sleep duration measurement may not capture long-term sleep patterns. A constrained random sampling approach was used to select participants, raising the potential of selection bias.

Regular sleep routine best

Ana Krieger, MD, MPH, director of the Center for Sleep Medicine at Weill Cornell Medicine in New York City, commented on the study. "This is a very interesting study, as it adds to the literature," she said. "Previous research studies have shown metabolic abnormalities with variations in sleep time and duration."

"This particular study evaluated a large sample of patients in the UK which were mostly White middle-aged and may not be representative of the general population," she noted. "A similar study in a Hispanic/Latino group failed to demonstrate any significant association between sleep timing variability and incidence of diabetes. It would be desirable to see if prospective studies are able to demonstrate a reduction in diabetes risk by implementing a more regular sleep routine [Sleep. 2021 Apr 9. doi: 10.1093/sleep/zsaa218]."

The importance of the body's natural circadian rhythm in regulating many physiological processes was highlighted by the 2017 Nobel Prize of Medicine, she pointed out. "Alterations in the circadian rhythm are known to affect mood regulation, gastrointestinal function, and alertness, among other factors," she said. "Keeping a regular sleep routine will help to improve our circadian rhythm and better regulate many processes, including our metabolism and appetite-controlling hormones."

Notably, a study published online in *Diabetologia* (2024 Jun 27. doi: 10.1007/s00125-024-06202-8) in a racially and economically diverse US population also found adults with persistent suboptimal sleep durations (< 7 or > 9 hours nightly over a mean of 5 years) were more likely to develop incident diabetes.

This study was supported by the National Institutes of Health (grant number R01HL155395) and the UKB project 85501. Dr. Kianersi was supported by the American Heart Association Postdoctoral Fellowship. Drs. Kianersi and Krieger reported no conflicts of interest.

Could resistin predict severity and death in PAH?

BY HEIDI SPLETE

Increased levels of the cytokine resistin were associated with an increased risk for death in adults with PAH, based on data from more than 1000 individuals. Resistin, a cytokine expressed in adipocytes, has been associated with poor clinical outcomes in heart failure and cardiovascular disease, Li Gao, MD, of Johns Hopkins University, Baltimore, Maryland, and colleagues wrote. In a study published in *Respiratory Research* (2024 Jun 6. doi: 10.1186/s12931-024-02861-8), the researchers reviewed biospecimens and clinical and genetic data from 1121 adults with PAH, 808 with idiopathic PAH (IPAH), and 313 with scleroderma-associated PAH (SSc-PAH). They examined the associations between serum resistin levels and PAH outcomes in multivariate regression models, using machine-learning algorithms to develop models to predict mortality.

Resistin levels were significantly higher in all patients with PAH and patients with the two subtypes than in control participants (all $P <$ .0001). Resistin was also associated with significant discriminative properties, with area under the curve (AUC) measures of 0.84, 0.82, and 0.91 for PAH overall, IPAH, and SSc-PAH, respectively. Elevated resistin levels (defined as > 4.54 ng/mL) were significantly associated with an increased risk for death (hazard ratio, 2.6; $P <$ .0087), with older age and shorter distance on the 6-minute walk test (P = .001 for both) and reduced cardiac capacity based on the New York Heart Association functional class ($P <$ .014).

Survival models derived from machine learning confirmed the prognostic value of resistin for mortality in PAH as seen in the random forest model, with an AUC of 0.70. The researchers also evaluated three *RETN* genetic variants (rs7408174, rs3219175, and rs3745367) for a specific association with serum resistin levels and measures of PAH severity. Resistin levels were highest among individuals who were carriers of either the rs3219175 or rs3745367 mutation, the researchers noted.

"It is a dynamic time in PAH research and clinical management, given the recent approval and use of the BMP/TGF beta balancing agent sotatercept (Winrevair) as an effective agent to target the molecular origins of this disease," said Stephen Chan, MD, professor of medicine and director of the Vascular Medicine Institute at the University of Pittsburgh, Pittsburgh, Pennsylvania. The growing number of PAH medications will likely be more effective if patients are identified and treated early, said Dr. Chan, who was not involved in the study. However, "there is an unmet need to develop effective and preferably noninvasive tools to aid in early diagnosis of PAH," Dr. Chan added.

The power of the study is in the number of patients included, as much of previous PAH research has involved small studies of patients, Dr. Chan said. The use of the PAH Biobank allows researchers to access a larger population of patients with PAH. "Currently, we do not have a reliable blood-based biomarker that we use in clinical PAH practice, although there are emerging studies that suggest other markers such as metabolites, RNA molecules, and proteins that may serve in the same capacity. If these studies turn out to be reproducible, generalizable, and specific to PAH in larger populations, measuring resistin could be helpful in making early diagnosis, particularly in areas that do not have invasive catheterization facilities (and globally) and for nonspecialists who are puzzled about the nonspecificity of initial symptoms of PAH," Dr. Chan said. However, resistin is not specific to PAH, which makes interpretation of the results more complicated, Dr. Chan said. "In this study, the authors used a smaller healthy control cohort of 50 patients as a comparison to their PAH cohort. However, they did not compare their PAH cohort with other cohorts that represent these other 'resistin-relevant diseases' and thus do not know whether they can distinguish PAH from any of these other diseases based on simply the resistin levels." The frequency of comorbidities in patients with PAH, such as obesity, other inflammatory diseases, and cardiovascular disease, could confound the resistin levels. The study was supported by the National Institutes of Health. Researchers and Dr. Chan had no financial conflicts to disclose. ■

Will hospital-at-home go mainstream?

BY KEN TERRY

Jordan Stohler, a 42-year-old nurse in Knoxville, Tennessee, was readmitted to Fort Sanders Medical Center in June 2023 with sepsis following surgery. She spent 5 days in the hospital to clear up the infection. Then she was offered a choice: She could either stay in the hospital while she received IV antibiotics, or she could go home and have the antibiotics given to her there under the Advanced Care at Home program of Covenant Health, the nine-hospital system to which Fort Sanders belongs.

She opted to go home, where she knew she'd be more comfortable and would be close to her beloved dog. In the end, she was very glad she did. "I received great care in the hospital, but to be allowed to be in the comfort of your own home, to be around my dog, who I think is therapeutic, to be able to cook my own meals, and to have the same one-on-one nursing care that I would have gotten in the hospital was great," Ms. Stohler said.

Being cared for at home helped her heal, she said. "I probably would have gotten a little stir crazy if I'd stayed in the hospital any longer. I received excellent care at home."

Covenant's Advanced Care at Home program is an example of the hospital-at-home trend that has been growing rapidly since Medicare began reimbursing hospitals for this approach during the COVID pandemic. Currently, 322 hospitals in 37 states have Medicare waivers for these kinds of programs, although not all of them are currently functioning.

A recent survey published in *JAMA* found that nearly half of consumers would accept hospital-at-home, and more than a third were neutral on it. Only 17% said they'd rather be cared for in a brick-and-mortar hospital.

The findings of the *JAMA* survey confirm those of earlier studies, said Bruce Leff, MD, a professor at Johns Hopkins Medical School in Baltimore, who has researched hospital-at-home since the 1990s. Like the new study, those trials found that the results had no relationship to individual traits, such as socioeconomic status, medical conditions, age, gender, or race.

Whether a person felt comfortable with the idea of hospital-at-home boiled down "to a preference for receiving care at home or in the hospital," he said. Some people distrust hospitals, and others feel insecure about receiving care at home, even if it is provided by qualified health care professionals.

How patients are selected

While the details of hospital-at-home vary from program to program, the basic scenario is that patients who need certain kinds of acute care can be sent home from hospitals, emergency departments, or clinics to receive that care at home. Among the kinds of conditions that make stable patients eligible are heart failure, COPD, pneumonia, cellulitis, and COVID-19, said John Busigin, MD, a hospitalist and medical director of Covenant Advanced Care at Home.

When a patient is admitted to hospital-at-home, the hospital will send along whatever equipment and medications that person needs. In some cases, this may include a hospital bed, although Ms. Stohler used her own. An IV line was put into her arm, and the IV stand was placed next to the bed.

Ms. Stohler received a computer tablet that she used to communicate with doctors and nurses in Covenant's "command center" in Knoxville. She also wore a watch with a button she could push in case of an emergency. And she had a telephone line that went directly to her medical team, in case she had an issue and the tablet didn't work.

Twice a day, or as needed, specially trained paramedics came to Ms. Stohler's home. They checked on the IV line, changed the IV bag, performed tests, and uploaded vital signs from monitoring equipment to Ms. Stohler's tablet so it could be transmitted to the command center. A physician assistant came in on the second and fourth days of her week-long stay in the program, and she saw a hospitalist remotely every day.

While some hospital-at-home programs have RNs visit patients at home, RNs are in short supply. To fill this gap, Covenant's program uses community paramedics who have been in the field for at least 5 years, doing everything from intubating patients and placing them on ventilators to providing advanced cardiac

HOSPITAL-AT-HOME *continued on following page*

HOSPITAL-AT-HOME *continued from previous page*
life support, Dr. Busigin said. To get certified as community paramedics, they go through a 3-month training program.

Shortly after Ms. Stohler went into hospital-at-home, she had another crisis. Excess fluid had built up in her body because of all the IV fluids she'd received in the hospital while fighting the sepsis. As a result, she became short of breath. If she had been discharged to home rather than hospital-at-home, she said, she would have had to go to the emergency room. Instead, she sent out a distress call. One of the paramedics rushed to her house and gave her an IV diuretic medication, which helped her urinate to get rid of the excess fluid.

A small number of the estimated 300 people who have gone through the program had to be admitted to the hospital, Dr. Busigin said. Nationally, he said, about 5%-10% are admitted. But readmissions among the patients in the Covenant program have been 25% lower than for patients who received conventional hospital care and had the same conditions as those in hospital-at-home.

Studies have shown that these programs not only reduce readmissions, but also cost less, on average, and create a better patient experience than traditional hospital care does. And, according to the *JAMA* survey, most consumers like the idea. Fifty-six percent of people who took the survey agreed with the statement that people recover faster at home than in the hospital. Fifty-nine percent agreed they'd feel safe being treated at home, and 49% said they'd be more comfortable if treated at home.

The 1134 people who took the survey were also asked about their comfort level with providing various kinds of care to their loved ones during a hospital-at-home episode. The results varied with the type of task: For example, 82% of the respondents agreed or strongly agreed they could manage a patient's medications, while just 41% said they'd be willing to change a feeding tube. Smaller percentages were willing to change an IV bag or a catheter or do wound care.

However, hospital-at-home programs don't allow caregivers to take part in clinical care, which is prohibited by Medicare waivers and state licensing regulations. None of the 22 health systems that use the hospital-at-home services of Medically Home, including Covenant, ask caregivers to do anything along this line, said Pippa Shulman, DO, medical director of the company, which provides equipment, technology, and protocols for hospital programs

The only exception at Covenant, Dr. Busigin said, is that the hospital may train family members to do wound care when a patient is discharged from the hospital to Advanced Care at Home. They may also prepare meals for their loved ones, although the program provides balanced meals to patients if they want them. Ms. Stohler had some of these meals, which just had to be heated up, for the first few days of hospital-at-home, and later her relatives brought meals to her house.

Challenges for the future

The number of Medicare hospital-at-home waivers has nearly doubled since 2021. A year earlier, when Medicare began reimbursing hospitals for acute care at home to help them cope with the overflow of COVID patients, there were only about 15-20 programs in the United States, said Dr. Leff of Johns Hopkins.

A big reason for the lack of use before the pandemic, Dr. Leff said, is that there was no payment system for hospitals that offered hospital-at-home. Now, they can get paid by

Medicare and 10 state Medicaid programs, and a number of private payers are also coming on board. Ms. Stohler's private insurer covered her hospital-at-home stay, and Dr. Busigin said several plans that contract with Covenant will pay for it.

Dr. Leff said he's cautiously optimistic Congress will extend the Medicare waiver program, which is scheduled to end in December, for another 5 years. A couple of key House committees have signed off on a bill to do that, he said, and a Congressional Budget Office report found that the program did not cost Medicare more money.

But even if the waiver is renewed, some health systems may find it tough to deliver the service. The current version of this model depends a lot on technology, because telemedicine is used and reliable communication is needed. That's why many of the hospitals hire outside vendors like Medically Home to provide the infrastructure they need.

Medically Home manages the tablets given to patients and all connection and networking services, including internet and cellphone connections. It also provides technical services in the command centers that hospitals set up for the doctors and nurses who provide care remotely.

And the firm figures out how to deliver the standard care for each condition in each hospital-at-home. "We need to make sure that

HOSPITAL-AT-HOME *continued on following page*

HOSPITAL-AT-HOME *continued from previous page*
the patient is going to get what they need in the time frame it needs to be delivered in, and that it's safe and effective for the patient," Dr. Shulman said. "So we've developed logistical protocols for a multitude of disease states that allow us to provide high-acuity care in the home to a variety of complex patients."

The health care workers use the hospital electronic health record for hospital-at-home patients, and vital signs uploaded from patient tablets flow directly into the electronic health record, she said.

Rural areas need help

The use of hospital-at-home in rural areas holds a lot of promise, Dr. Leff said. "A lot of rural hospitals have been closing, and hospital-at-home could be a mechanism to create hospital-level care where facilities have closed down. It's easier to do this in urban areas, but it can be done in rural environments as well."

Rami Karjian, CEO of Medically Home, agreed. The firm services hospital-at-home programs in rural areas of Oklahoma and California, using cellphones and paramedics in areas that lack broadband connections and nurses, he pointed out. "Hospital-at-home can't just be available to people who live in big cities," he said. "The access problems in health care are pervasive, and this is part of how we solve access problems in rural areas." ■

Rheumatoid arthritis may raise lung cancer risk

EDITED BY VINOD RANE

Rheumatoid arthritis (RA) is linked with more than a 50% increased risk for lung cancer, according to a new study. Those with RA-associated interstitial lung disease (RA-ILD) were found to be particularly vulnerable, facing nearly a threefold higher risk.

Researchers conducted a retrospective matched cohort study to evaluate the risk for lung cancer in participants with RA, including those with RA-ILD, within Veterans Affairs (VA) from 2000 to 2019.

A total of 72,795 participants with RA were matched with 633,937 participants without RA on the basis of birth year, sex, and VA enrollment year. Among those with RA, 757 had prevalent RA-ILD and were matched with 5931 participants without RA-ILD.

The primary outcome was incident lung cancer, assessed using the VA Oncology Raw Domain and the National Death Index.

Higher lung cancer risk in patients with RA

Over a mean follow-up of 6.3 years, 2974 incidences of lung cancer were reported in patients with RA, and 34 were reported in those with RA-ILD.

The risk for lung cancer was 58% higher in patients with RA than in those without RA (adjusted hazard ratio [aHR], 1.58; 95% CI, 1.52-1.64), with this association persisting even when only those who never smoked were considered (aHR, 1.65; 95% CI, 1.22-2.24).

Participants with prevalent RA-ILD had 3.25-fold higher risk for lung cancer than those without RA (aHR, 3.25; 95% CI, 2.13-4.95).

Both patients with prevalent and those with incident RA-ILD showed a similar increase in risk for lung cancer (aHR, 2.88; 95% CI, 2.45-3.40).

Study did not include those who smoke

Limitations included that the study was made up of a predominantly male population, which may have affected the generalizability of the study. Although the study considered smoking status, data on the duration and intensity of smoking were not available. Restriction to those who never smoked could not be completed for comparisons between patients with RA-ILD and those without RA because of insufficient sample sizes.

The study was led by Rebecca T. Brooks, MD, Department of Internal Medicine, Mayo Clinic, Rochester, Minnesota. It was published online in *Arthritis & Rheumatology* (doi: 10.1002/art.42961).

This study did not receive funding from any source. Some authors reported receiving research funding or having ties with various pharmaceutical companies and other sources. ■

This article was created using several editorial tools, including AI, as part of the process. Human editors reviewed this content before publication.

NETWORKS

Nutritional management in the ICU, HALT recognition, home tracheostomy care, and more

CRITICAL CARE NETWORK

Nonrespiratory Critical Care Section

Advancements in nutritional management for critically ill patients

Nutrition plays an important role in the management and recovery of critically ill patients admitted to the ICU. Major guidelines recommend that critically ill patients should receive 1.2 to 2.0 g/kg/day of protein, with an emphasis on early (within 48 hours of ICU admission) enteral nutrition.

In a randomized controlled trial involving 173 critically ill patients who stayed in the ICU in Zhejiang, China, Wang and colleagues studied the impact of early high protein intake (1.5 g/kg/day vs 0.8 g/kg/day). The primary outcome of 28-day mortality was lower among the high protein intake group (8.14% vs 19.54%). Still, this intention-to-treat analysis did not reach a statistical significance (P = .051). However, a time-to-event analysis using the Cox proportional hazard model showed that the high protein intake group had a significantly lower 28-day mortality rate, shorter ICU stays, and improved nutritional status, particularly in patients with sepsis (P = .045).

Dr. Ho

Dr. Al-Jaghbeer

In a systematic review and meta-analysis involving 19 randomized controlled trials and 1,731 patients, there was no definitive evidence that higher protein intake significantly reduces mortality. However, it may improve specific clinical outcomes like muscle mass retention and shorter duration of mechanical ventilation. Similarly, a post hoc analysis on the EFFORT Protein Trial focusing on critically ill patients with acute kidney injury (AKI) showed that higher protein intake did not significantly impact the duration of kidney replacement therapy but was associated with higher serum urea levels and slower time-to-discharge-alive among patients with AKI.

For critically ill patients, increasing early protein intake to 1.5 g/kg/day is safe and may be beneficial. We still need more data to guide the

NETWORKS *continued on page 22*

Top reads from the CHEST journal portfolio

Covering the frailty scale in ILD, diagnosis of peripheral pulmonary nodules, and platelet mitochondrial function in sepsis

Journal CHEST®

The Clinical Frailty Scale for Risk Stratification in Patients With Fibrotic Interstitial Lung Disease

By Sabina A. Guler, MD, and colleagues

Life expectancy is a very important factor for patients with interstitial lung disease (ILD) and their caregivers. The discussion surrounding prognosis is often wrought with uncertainty and is inherently painful for both patients and clinicians when faced with nonmodifiable traits. This study illustrates the significance of employing a method that succinctly and systematically communicates the degree of functional impairment in patients with fibrotic lung disease. The authors have highlighted the importance of identifying and improving health factors associated with frailty to enhance the survival and quality of life of patients with chronic noncurable fibrotic lung disease. It also presents hope that interventions aimed at improving functional capacity may improve frailty and thus modify prognosis. In the future, longitudinal trends of frailty assessments following interventions aimed at improving both exercise and functional capacity, like pulmonary rehab, should be explored.

Dr. Balakrishnan

– Commentary by Priya Balakrishnan, MD, MS, FCCP, Member of the *CHEST Physician* Editorial Board

CHEST® Pulmonary

The Diagnostic Yield of Cone Beam CT Combined With Radial-Endobronchial Ultrasound for the Diagnosis of Peripheral Pulmonary Nodules

By Michael V. Brown, MD, and colleagues

Brown and colleagues provide a systemic review and meta-analysis of the diagnostic yield of cone beam computed tomography (CBCT) scan combined with radial-endobronchial ultrasound (r-EBUS) for the diagnosis of peripheral pulmonary nodules. They included 14 studies (865 patients with 882 lesions) with pooled diagnostic yield from CBCT scan and r-EBUS for peripheral pulmonary nodules of 80% (95% CI, 76% to 84%) with complication rates of 2.01% for pneumothorax and 1.08% for bleeding. Amongst the studies selected, confounders (including study design, definition of diagnostic yield, use of ROSE, additional equipment, etc) existed. The important takeaway is that 3D imaging guidance with CBCT scan can corroborate "tool in lesion" and thus potentially improve the outcomes of the different bronchoscopic modalities utilized to diagnose peripheral pulmonary nodules. Future prospective investigations with less heterogeneity in study design and outcomes, as well as comparison with newer technologies such as robotic bronchoscopy, are necessary to corroborate these findings.

Dr. Faiz

– Commentary by Saadia A. Faiz, MD, FCCP, Member of the *CHEST Physician* Editorial Board

CHEST® Critical Care

Platelet Bioenergetics and Associations With Delirium and Coma in Patients With Sepsis

By Chukwudi A. Onyemekwu, DO, and colleagues

The study by Onyemekwu and colleagues explores the link between platelet mitochondrial function and acute brain dysfunction (delirium and coma) in patients with sepsis. The investigators measured various parameters of platelet mitochondrial respiratory bioenergetics and found that increased spare respiratory capacity was significantly associated with coma but not delirium. These findings suggest that systemic mitochondrial function could influence brain health and indicate a potential link between mitochondrial bioenergetics and coma during sepsis. The study did not find a significant association between platelet bioenergetics and delirium, suggesting that coma and delirium may have different underlying pathophysiologic mechanisms. We must interpret the results with caution, as the associations identified in this observational study do not prove causation. It is possible that the changes seen in platelet mitochondria may be a result of coma rather than a mechanism. Nonetheless, the study provides a foundation for future research to explore the mechanistic role of mitochondria in acute brain dysfunction during sepsis and the potential for developing mitochondrial-targeted therapies as a possible treatment approach for patients with sepsis-induced coma.

Dr. Coz

– Commentary by Angel Coz, MD, FCCP, Editor in Chief of *CHEST Physician*

NETWORKS *continued from page 20*
best approach to determining the protein intake.

All references available online at chestphysician.org.

– Kam S. Ho, MD
Fellow-in-Training
– Mohammed J. Al-Jaghbeer, MD, MBBS, FCCP, Member-at-Large

DIFFUSE LUNG DISEASE AND LUNG TRANSPLANT NETWORK

Lung Transplant Section

HALT early recognition is key

Hyperammonemia after lung transplantation (HALT) is a rare but serious complication occurring in 1% to 4% of patients with high morbidity and mortality. Typically presenting within 2 weeks post transplant, HALT manifests as elevated serum ammonia levels with symptoms ranging from encephalopathy to seizures and cerebral edema. Early recognition is crucial, as mortality rates can reach 75%.

HALT arises from excess ammonia production or decreased clearance and is often linked to infections by urea-splitting organisms, including mycoplasma and ureaplasma. Prompt, aggressive treatment is essential and typically includes dietary protein restriction, renal replacement therapy (ideally intermittent hemodialysis), bowel decontamination (lactulose,


Dr. Turner


Dr. Frye

rifaximin, metronidazole, or neomycin), amino acids (arginine and levocarnitine), nitrogen scavengers (sodium phenylbutyrate or glycerol phenylbutyrate), and empiric antimicrobial coverage for urea-splitting organisms. Given concerns for calcineurin inhibitor-induced hyperammonemia, transition to an alternative agent may be considered.

Given the severe risks associated with HALT, vigilance is vital, particularly in intubated and sedated patients where monitoring of neurologic status is more challenging. Protocols may involve routine serum ammonia monitoring, polymerase chain reaction testing for mycoplasma and ureaplasma at the time of transplant or with postoperative bronchoscopy, and empiric antimicrobial treatment. No definitive ammonia threshold exists, but altered sensorium with elevated levels warrants immediate and more aggressive treatment with levels >75 µmol/L. Early testing and symptom recognition can significantly improve survival rates in this potentially devastating condition.

All references available online at chestphysician.org.

– Grant A. Turner, MD, MHA,
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– Laura K. Frye, MD
Member-at-Large

SLEEP MEDICINE NETWORK

Home-Based Mechanical Ventilation and Neuromuscular Section

Hospital to home tracheostomy care

Patients with tracheostomies require comprehensive planning to avoid adverse events. Technological improvement has enhanced our ability to support these patients with complex conditions in their home settings. However, clinical practice guidelines are lacking, and current practice relies on a consensus of expert opinions.


Dr. Munoz


Dr. Sahni

Once a patient who has had a tracheostomy begins transitioning care to home, identifying caregivers is vital. Caregivers need to be educated on daily tracheostomy care, airway clearance, and ventilator management. Protocols to standardize this transition, such as the "Trach Trail" protocol, help reduce ICU readmissions with new tracheostomies (P = .05), eliminate predischarge mortality (P = .05), and may decrease ICU length of stay (P = 0.72). Standardized protocols for aspects of tracheostomy care, such as the "Go-Bag" from Boston Children's Hospital, ensure that a consistent approach keeps providers, families, and patients familiar with their equipment and safety procedures,

NETWORKS *continued on following page*

SLEEP STRATEGIES

OSA in pregnancy: Who to test and how to screen?

BY SEEMA AMIN, MD, AND GHADA BOURJEILY, MD, FCCP

The estimated prevalence of OSA in pregnancy ranges from 4% to 27% compared with 0.7% to 6.5% in nonpregnant, reproductive-age females, with an even higher prevalence in complicated pregnancies. The increased prevalence in pregnancy can be explained by physiologic changes impacting the upper airway such as increases in maternal blood volume and reductions in oncotic pressure, as well as increases in circulating levels of estrogen and progesterone. OSA in pregnancy is associated with adverse perinatal outcomes such as hypertensive disorders of pregnancy, gestational diabetes, severe maternal morbidity abnormalities in fetal growth, preterm birth, and congenital abnormalities in the offspring.

Despite this evidence, guidelines on the screening, diagnosis, and treatment of OSA in pregnancy have only recently been published and will be reviewed here.

The obstetric subcommittee of the Society of Anesthesia and Sleep Medicine that produced these guidelines had expertise in obstetric anesthesiology, sleep medicine and sleep research, high-risk obstetrics, and obstetric medicine. The guideline aimed to answer 3 questions: 1) Who should be screened in pregnancy for OSA, 2) how to make a diagnosis of OSA in pregnancy and the postpartum period, and 3) what is the treatment for OSA in pregnancy and the postpartum period. As sleep disordered breathing (SDB) has been associated with many conditions linked to maternal mortality, better management of

PREGNANCY *continued on following page*

NETWORKS *continued from previous page*

improving outcomes and decreasing tracheostomy-related adverse events.

Understanding the landscape surrounding which equipment companies have trained field respiratory therapists is crucial. Airway clearance is key to improving ventilation and oxygenation and maintaining tracheostomy patency. Knowing the types of airway clearance modalities used for each patient remains critical.

Trach care may look substantially different for some populations, like patients in the neonatal ICU. Trach changes may happen more frequently. Speaking valve times may be gradually increased while planning for possible decannulation. Skin care involving granulation tissue and stoma complications is particularly important for this population. Active infants need well-fitting trach ties to balance enough support to maintain their trach without causing skin breakdown or discomfort. Securing the trach to prevent pulling or dislodgement as infants become more active is crucial as developmental milestones are achieved.

We hope national societies prioritize standardizing care for this vulnerable population while promoting additional high-quality, patient-centered outcomes in research studies. Implementation strategies to promote interprofessional teams to enhance education, communication, and outcomes will reduce health care disparities.

All references available online at chestphysician.org.

– Caroline Skolnik, MD
– Tomas I. Munoz, MD
– Ashima S. Sahni, MD, MBBS, FCCP, Member-at-Large

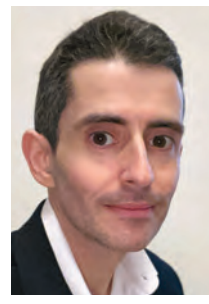
PULMONARY VASCULAR AND CARDIOVASCULAR NETWORK

Cardiovascular Medicine and Surgery Section

New developments on the forefront of intermediate-risk pulmonary embolism

Patients with intermediate-risk pulmonary embolism (IRPE), or those with right ventricular dysfunction without overt hemodynamic instability, represent a heterogenous population with short-term mortality ranging from 2% to 17%. While systemic anticoagulation is the

Dr. Ohlsson



Dr. Yuriditsky

mainstay therapy, select individuals may benefit from more immediate reperfusion. Catheter-based therapies (CBT), including thrombus aspiration, fragmentation, or catheter-directed thrombolysis, have seen rapid uptake over the last decade, with promising retrospective data. Unfortunately, only small, randomized trials exploring surrogate outcomes are available to guide modality and patient selection.

To better define which patients with IRPE are best managed with which therapy, several large-scale randomized controlled trials are underway. PE-TRACT, a study funded by the National Institutes of Health, aims to randomize 500 patients with IRPE to anticoagulation alone vs one of several modalities of CBT with a focus on long-term functional outcomes, including peak oxygen consumption at 3 months and functional class at 1 year. Aspiration thrombectomy with the FlowTriever® device is being compared with anticoagulation alone in a study of 1,200 patients examining short-term composite end points.

While full-dose thrombolysis may decrease the composite outcome of death or hemodynamic deterioration in this population, the benefit is counterbalanced by the risk of significant bleeding. Whether reduced-dose thrombolysis is associated with improved outcomes has been questioned in several small studies. The PEITHO-3 trial plans to randomize 650 patients with IRPE to reduced-dose thrombolytics vs placebo, exploring several outcomes at 30 days. With multiple large trials ongoing, we anticipate important changes to the landscape of IRPE care over the coming years.

All references available online at chestphysician.org.

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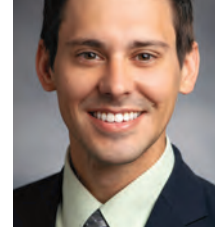
AIRWAYS DISORDERS NETWORK

Bronchiectasis Section

Bronchiectasis: A call to action

Bronchiectasis is an extremely heterogeneous airways disease, making it difficult to study. For years, the noncystic fibrosis (CF) bronchiectasis community has been trying to organize to provide better care for more than half a million adults with bronchiectasis in the United States. Internationally, the Europeans created the European Bronchiectasis Registry, which has been a powerful tool including nearly 20,000 patients, to answer important epidemiologic and management questions. We must do more for the bronchiectasis community.

Clinicaltrials.gov indicates that there are 8 international phase 3 or 4 clinical trials that are currently enrolling; 3 of those have enrollment sites in the United States.



Dr. Swiatek

One such study from University of North Carolina at Chapel Hill is looking at the use of nebulized hypertonic saline in patients with non-CF bronchiectasis to understand the effect it has on mucociliary clearance. Emory University is looking at the use of elexacaftor/tezacaftor/ivacaftor (Trikafta) in patients with non-CF bronchiectasis; these patients have only 1 targetable mutation and a phenotype that resembles CF. This 8-week, open-label, single-center study aims to measure both clinical and biomarker outcomes after treatment with Trikafta. Finally, a phase 3 trial out of Florida, the ICoN-1 study, is examining the efficacy and safety of inhaled clofazimine in the treatment of nontuberculous mycobacteria (NTM). This double-blind, randomized trial will look at culture conversion and quality of life measures. Additionally, the COPD Foundation has created the Bronchiectasis and NTM Research Registry, an American cohort containing more than 5,000 patients and data from 22 different sites, to answer some of the most important questions for clinicians and patients.

We have made significant progress in bronchiectasis research; however, there is still much to learn. Together, we must make a concerted effort to enroll patients in clinical trials. Doing so will allow us to define our epidemiologic profile more precisely and explore new treatments and airway clearance techniques.

– Kevin M. Swiatek, DO, FCCP
Member-at-Large

FROM THE PRESIDENT

The countdown to CHEST 2024 begins

BY JACK D. BUCKLEY, MD, MPH, FCCP

As we find ourselves in September, I cannot help but dedicate my column to the upcoming CHEST Annual Meeting quickly approaching, October 6 to 9, in Boston.

If you haven't yet been to a CHEST Annual Meeting, it's an unmatched experience. We have top-notch experts in the field delivering content and materials in a variety of learning formats—lectures, interactive sessions, case-based scenarios, simulations, etc—and there's an atmosphere unlike any other that's welcoming to any level of practice.

For those who have attended, there's always something new to see. Every year is different, with the culture of the location guiding the way and new opportunities to network while engaging in activity. No matter how many times you have been, attending the CHEST Annual Meeting never gets old.

Leveraging CHEST 2024's location, we'll be hosting a Grand Rounds event days before the meeting starts with pulmonary and critical care medicine fellows from the regional Boston programs to learn from visiting CHEST leadership on a variety of influential topics. These fellowship programs held events like this prepandemic, so I'm truly excited we could help restart the tradition and give the local fellows an opportunity to interact with each other from both an academic and social perspective. Personally, I am very much looking forward to meeting and getting to know the fellows from the Boston area.

The meeting has a lot of notable opportunities lined up (see my official "President's checklist"), including the third year of CHEST After Hours (Monday, October 7)—a unique storytelling event focusing on the humanities of medicine in partnership with The Nocturnists podcast. And for the first time in recent years, CHEST 2024 will feature a 5K run/walk (Tuesday, October 8) in support of CHEST philanthropy and its work to fuel breakthroughs, empower innovation, and drive toward a future where every patient's well-being is safeguarded. I encourage you to register in advance of the meeting to secure your space and snag a souvenir T-shirt.

First thing Sunday morning (October 6), the meeting kicks off with the Opening Session where we will be celebrating the new fellows of the college (FCCP), honoring trailblazers in chest medicine, and welcoming this year's keynote speaker.

This year's keynote address will come from Vanessa Kerry, MD, who will speak on environmental issues and her work to raise awareness of the impact of climate change on health.

With so many things to look forward to, this meeting will be one to remember for all in attendance.

I look forward to seeing you in Boston,

Jack

PREGNANCY *continued from previous page*
SDB in this population is key.

Screening for OSA in the pregnant population

The guideline does not support universal screening of all people who are pregnant, but rather suggests that people who are pregnant and at high risk for OSA, such as those with a body mass index (BMI) ≥30 kg/m2 and those with hypertensive disorders of pregnancy, or diabetes, in the index pregnancy or a prior pregnancy, be screened for OSA in the first or second trimester. Screening for OSA in pregnancy in limited populations is recommended due to the lower yield of universal screening and its potential burden on the health care system.

Furthermore, screening for OSA in early pregnancy is suggested given the practical challenges of arranging testing, initiating, and allowing time for patients to become acclimated to therapy in later stages of pregnancy. However, even when timing of diagnosis may not allow for appropriate treatment of OSA during pregnancy, knowing a person's OSA status before delivery is beneficial, particularly for patients at risk for Cesarean delivery who may require intubation and exposure to sedative medications, as well as those receiving epidural anesthesia, as OSA is a risk factor for respiratory depression.

Although screening was thought to be beneficial in specific populations, there is insufficient evidence to recommend any one screening tool. The guideline made recommendations against the use of the Berlin questionnaire, STOP-BANG questionnaire, Epworth Sleepiness Scale, or the ASA checklist. These screening tools were developed and validated in nonpregnant patient populations and their pooled sensitivity and specificity to detect OSA in pregnancy is low. Individual components of these screening tools, such as prepregnancy BMI, frequency and volume of snoring, hypertension, and neck circumference ≥16 inches have, however, been associated with OSA status.

Pregnancy-specific OSA screening tools have been proposed. The guideline suggests these pregnancy-specific tools may be considered for screening for OSA in pregnancy but still require external validation, especially in high-risk populations. The committee agreed that individuals with BMI >30kg/m2, hypertension, diabetes, and those with a history of difficult intubation or Mallampati score III or IV are considered at risk for OSA in pregnancy.

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Diagnosis of OSA in the pregnant population

In the general population, in-laboratory polysomnogram (PSG) is the gold standard diagnostic test. However, for patients in whom uncomplicated OSA is suspected with a moderate to high pretest probability, unattended home sleep apnea testing (HSAT) is a reasonable initial study. On the other hand, in-lab PSG is recommended in mission-critical workers and when coexisting respiratory sleep disorders, or nonrespiratory sleep disorders, are suspected. For individuals who are pregnant and suspected of having OSA, the guideline suggests that HSAT is a reasonable diagnostic tool, as many level III devices have demonstrated good agreement between the respiratory disturbance index (RDI) and apnea-hypopnea index (AHI) measured by PSG. Notably, most studies have examined the performance of level III devices in late pregnancy in populations with obesity; hence, the performance of these devices in early pregnancy when risk for OSA is lower, or more subtle forms of SDB may be more common, is less clear but may be an acceptable first-line test.

PREGNANCY *continued on following page*

CHEST releases new guideline on management of central airway obstruction

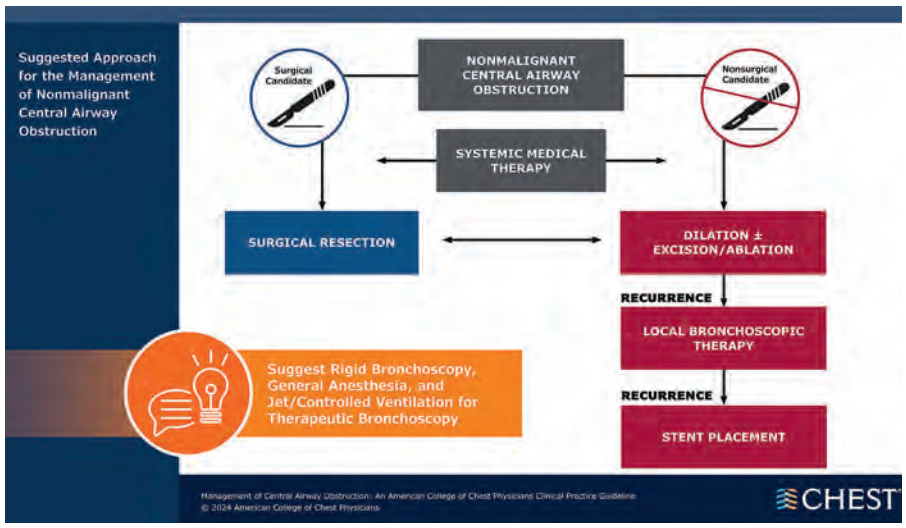
CHEST recently released a new clinical guideline on central airway obstruction (CAO). Published in the journal CHEST®, the guideline contains 12 evidence-based recommendations to guide the management of both malignant and nonmalignant CAO.

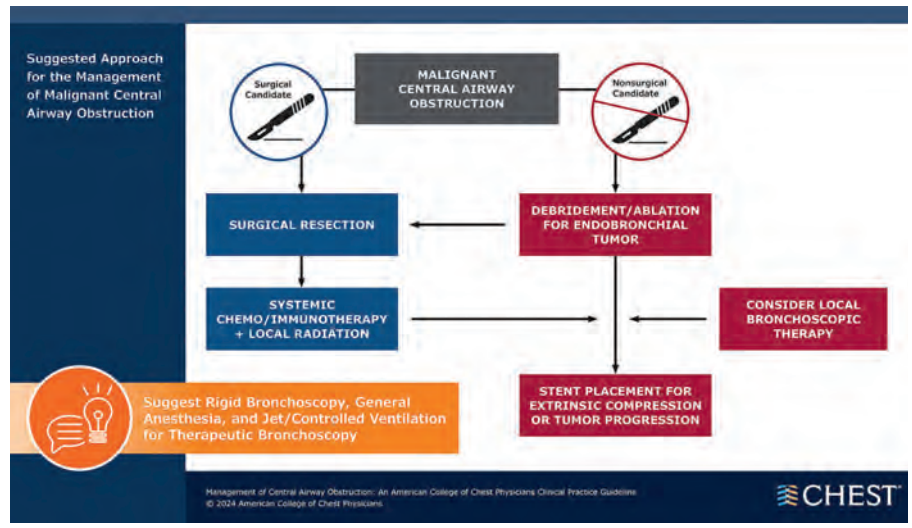
"Central airway obstruction is associated with a poor prognosis, and the management of CAO is highly variable dependent on the provider expertise and local resources. By releasing this guideline, the panel hopes to standardize the definition of CAO and provide guidance for the management of patients to optimize care and improve outcomes," said Kamran Mahmood, MD, MPH, FCCP, lead author on the guideline. "The guideline recommendations are developed using GRADE methodology and based on thorough evidence review and expert input. But the quality of overall evidence is very low, and the panel calls for well-designed studies and randomized controlled trials for the management of CAO."

CAO can be caused by a variety of malignant and nonmalignant disorders, and multiple specialists may be involved in the care, including pulmonologists, interventional pulmonologists, radiologists, anesthesiologists, oncologists, radiation oncologists, thoracic surgeons, and otolaryngologists, etc. The panel recommends shared decision-making with the patients and a multidisciplinary approach to manage CAO.

Below, you'll find flowcharts outlining the suggested treatments for patients with a malignant or nonmalignant CAO.

Visit **www.chestnet.org/CAO-guideline** to download the flowcharts and access the complete guideline. ■





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The guideline did not provide recommendations for next steps following an inconclusive, technically inadequate, or negative HSAT. However, recommendations to proceed with in-lab PSG in individuals with clinical suspicion for OSA and a negative HSAT is a reasonable approach, keeping in mind the time restrictions of pregnancy. The more delayed the diagnosis, the less time there will be for initiation of and acclimation to therapy to maximize potential benefits during pregnancy. HSAT is especially practical and convenient for individuals with young families. The guideline does not recommend the use of overnight oximetry for diagnostic purposes.

The postpartum period is usually associated with weight loss and reversal of pregnancy physiology. Generally, the decision to perform a repeat sleep study following weight loss is individualized, based on factors such as improved symptoms or sustained, significant weight loss. Though data show improvement in AHI following delivery, small studies show persistent OSA in nearly half of individuals diagnosed in pregnancy. Hence, as pregnancy increases the risk for OSA, and given that the postpartum status is not always associated with resolution of OSA, the guideline recommends considering repeat diagnostic testing in the postpartum period. The decision to repeat testing also depends on whether OSA or OSA symptoms predated pregnancy, on the persistence of symptoms, and the degree of weight loss with delivery and the postpartum body habitus.

Treatment of OSA in the pregnant population

The guideline recommends behavior modification in OSA similarly to individuals who are not pregnant (avoidance of sedatives, smoking, and alcohol). However, weight loss is not recommended in pregnancy due to the potential for harm to the fetus.

The gold standard treatment for people who are pregnant and have OSA is continuous positive airway pressure (CPAP). Treatment of OSA in pregnancy is complicated by the fact that very few women are referred to sleep practices due to time restrictions and logistical reasons, and that data demonstrating improved pregnancy outcomes with CPAP are scarce, limiting the prioritization of OSA management.

However, expert consensus considers a theoretical benefit in the context of lack of current evidence of harm from treatment. Hence, at this point, the guideline recommends counseling around CPAP therapy be aimed at improvement in symptoms, AHI, and quality of life, rather than pregnancy-specific outcomes. This recommendation was based on observations from small case series that demonstrated improved breathing parameters during sleep and symptoms, and small randomized controlled trials (RCT), limited by short-term exposure to the intervention.

However, since the publication of this guideline, a large RCT that randomized pregnant women with SDB to CPAP or usual care has demonstrated significantly lower diastolic blood pressure, an altered diastolic blood pressure trajectory, and a lower rate of preeclampsia in the group treated with CPAP compared with usual care.

This guideline provides helpful insight on who to screen and how to manage OSA in pregnancy but additional research is needed to elucidate benefits of treatment and its effects on maternal and neonatal outcomes.

Multidisciplinary collaborations between obstetric and sleep teams are necessary to ensure that screening and diagnostic strategies result in management change for improved outcomes. ■

All references available online at chestphysician.org.

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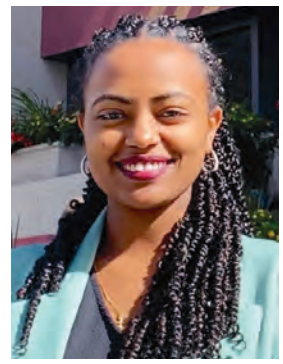
CRITICAL CARE COMMENTARY

The language of AI and its applications in health care

BY HEAVEN Y. TATERE, MD, MSC, MPH, AND CRAIG M. LILLY, MD, FCCP



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The respiratory community is interested in artificial intelligence (AI) because it can improve the effectiveness of our care delivery processes. AI is a group of nonhuman techniques that utilize automated learning methods to extract information from datasets through generalization, classification, prediction, and association. In other words, AI is the simulation of human intelligence processes by machines. The branches of AI include natural language processing, speech recognition, machine vision, and expert systems. AI can make clinical care more efficient; however, many find its confusing terminology to be a barrier. This article provides concise definitions of AI terms and is intended to help physicians better understand how AI methods can be applied to clinical care. The clinical application of natural language processing and machine vision applications are more clinically intuitive than the roles of machine learning algorithms.

Machine learning and algorithms

Machine learning is a branch of AI that uses data and algorithms to mimic human reasoning through classification, pattern recognition, and prediction. Supervised and unsupervised machine-learning algorithms can analyze data and recognize undetected associations and relationships.

Supervised learning involves training models to make predictions using data sets that have correct outcome parameters called labels using predictive fields called features. Machine learning uses iterative analysis including random forest, decision tree, and gradient boosting methods that minimize predictive error metrics (see Table 1). This approach is widely used to improve diagnoses, predict disease progression or exacerbation, and personalize treatment plan modifications.

Supervised machine learning methods can be particularly effective for processing large volumes of medical information to identify patterns and make accurate predictions. In contrast, unsupervised learning techniques can analyze unlabeled data and help clinicians uncover hidden patterns or undetected groupings. Techniques including clustering, exploratory analysis, and anomaly detection are common applications. Both of these machine-learning approaches can be used to extract novel and helpful insights.

The utility of machine learning analyses depends on the size and accuracy of the available datasets. Small datasets can limit usability, while large datasets require substantial computational power. Predictive models are generated using training datasets and evaluated using separate evaluation datasets. Deep learning models, a subset of machine learning, can automatically readjust themselves to maintain or improve accuracy when analyzing new observations that include accurate labels.

Challenges of algorithms and calibration

Machine learning algorithms vary in complexity and accuracy. For example, a simple logistic regression model using time, date, latitude, and indoor/outdoor location can accurately recommend sunscreen application. This model identifies when solar radiation is high enough to warrant sunscreen use, avoiding unnecessary recommendations during nighttime hours or indoor locations. A more complex model might suffer from model overfitting and inappropriately suggest sunscreen before a tanning salon visit.

Complex machine learning models, like support vector machine (SVM) and decision tree methods, are useful when many features have predictive power. SVMs are useful for small but complex datasets. Features are manipulated in a multidimensional space to maximize the "margins" separating two groups. Decision tree analyses are useful when more than two groups are being analyzed. SVM and decision tree models can also lose accuracy by data overfitting.

Consider the development of an SVM analysis to predict whether an individual is a fellow or a senior faculty member. One could use high gray hair density feature values to identify senior faculty. When this algorithm is applied to an individual with alopecia, no amount of model adjustment can achieve high levels of discrimination because no hair is present. Rather than overfitting the model by adding more nonpredictive features, individuals with alopecia are analyzed by their own algorithm (tree) that uses the skin wrinkle/solar damage rather than the gray hair density feature.

Decision tree ensemble algorithms like random forest and gradient boosting use feature-based decision trees to process and classify data. Random forests are robust, scalable, and versatile, providing classifications and predictions while protecting against inaccurate data and outliers and have the advantage of being able to handle both categorical and continuous features. Gradient boosting, which uses an ensemble of weak decision trees, often outperforms random forests when individual trees perform only slightly better than random chance. This method incrementally builds the model by optimizing the residual errors of previous trees, leading to more accurate predictions.

In practice, gradient boosting can be used to fine-tune diagnostic models, improving their precision and reliability. A recent example of how gradient boosting of random forest predictions yielded highly accurate predictions for unplanned vasopressor initiation and intubation events 2 to 4 hours before an ICU adult became unstable.

Machine Learning Methods (Table 1)

Method	Description	Common uses	Limitations
Decision tree	Branching sequence of feature-based decisions that produce label at the terminal branch	Classification or regression-based predictions	Short trees are prone to errors of bias and deep ones are prone to overfitting
Random forest	Labels derived from collections (ensembles) of decision trees	Classification or regression-based predictions	Prone to overfitting error and can produce weak prediction
Gradient boosting	The use of ensembles of weak decision trees to produce labels	Classification or regression-based predictions	Can produce stronger estimation than random forest models

Assessing the accuracy of algorithms

The value of the data set is directly related to the accuracy of its labels. Traditional methods that measure model performance, such as sensitivity, specificity, and predictive values (PPV and NPV), have important limitations. They provide little insight into how a complex model made its prediction. Understanding which individual features drive model accuracy is key to

AI *continued on following page*

Feds may end hospital system's noncompete contract for part-time docs

BY ALICIA GALLEGOS

Mount Sinai Health System in New York City is forcing part-time physicians to sign employment contracts that violate their labor rights, according to a June 2024 complaint by the National Labor Relations Board (NLRB). The complaint stems from no-poaching and confidentiality clauses in the agreements required as a condition of employment, NLRB officials alleged.

The contracts state that, for 1 year following termination, part-time physicians may not recruit, solicit, or induce to terminate the employment of any hospital system employee or independent contractor, according to a copy of the terms included in NLRB's June 18 complaint.

By requiring the agreements, NLRB officials claimed, Mount Sinai is "interfering with, restraining, and coercing employees" in violation of the National Labor Relations Act. The health system's "unfair labor practices" affect commerce as outlined under the law, according to the NLRB. The Act bans employers from burdening or obstructing commerce or the free flow of commerce.

Mount Sinai did not respond to requests for comment.

The NLRB's complaint follows a landmark decision by the Federal Trade Commission (FTC) to ban noncompete agreements nationwide. In April 2024, the FTC voted to prohibit noncompetes indefinitely in an effort to protect workers.

"Noncompete clauses keep wages low, suppress new ideas, and rob the American economy of dynamism, including from the more than 8500 new startups that would be created a year once noncompetes are banned," FTC Chair Lina M. Khan said in a statement. "The FTC's final rule to ban noncompetes will ensure Americans have the freedom to pursue a new job, start a new business, or bring a new idea to market."

Business groups and agencies have since sued to challenge the ban, including the Chamber of Commerce. The Chamber and other business groups argue that noncompete agreements are important for companies to protect trade secrets, shield recruiting investments, and hide confidential information. The lawsuits are ongoing.

A physician blows the whistle

An anonymous physician first alerted the NLRB to the contract language in November 2023. The complaint does not say if the employee is still employed by the hospital system.

To remedy the unfair labor practices alleged, the NLRB seeks an order requiring the health system to rescind the contract language, stop any actions against current or former employees to enforce the provisions, and make whole any employees who suffered financial losses related to the contract terms.

The allegation against Mount Sinai is among a rising number of grievances filed with the NLRB that claim unfair labor practices. During the first 6 months of fiscal year 2024, unfair labor practice charges filed across the NLRB's field offices increased 7% — from 9612 in 2023 to 10,278 in 2024, according to a news release.

NLRB, meanwhile, has been cracking down on anticompetitive labor practices and confidentiality provisions that prevent employees from speaking out.

In a February 2023 decision, for instance, NLRB ruled that an employer violates the National Labor Relations Act by offering severance agreements to workers that include restrictive confidentiality and nondisparagement terms. In 2022, the NLRB and the Federal Trade Commission forged a partnership to more widely combat unfair, anticompetitive, and deceptive business practices.

"Noncompete provisions reasonably tend to chill employees in the exercise of Section 7 rights when the provisions could reasonably be construed by employees to deny them the ability to quit or change jobs by cutting off their access to other employment opportunities that they are qualified for," NLRB General Counsel Jennifer Abruzzo said in a 2023 release.

An administrative law judge is scheduled to hear the case on September 24. ■

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fostering trust in model predictions. This can be done by comparing model output with and without including individual features. The results of all possible combinations are aggregated according to feature importance, which is summarized in the Shapley value for each model feature. Higher values indicate greater relative importance. SHAP plots help identify how much and how often specific features change the model output, presenting values of individual model estimates with and without a specific feature (see Figure below).

Promoting AI use

AI and machine learning algorithms are coming to patient care. Understanding the language of AI helps caregivers integrate these tools into their practices. The science of AI faces serious challenges. Algorithms must be recalibrated to keep pace as therapies advance, disease prevalence changes, and our population ages. AI must address new challenges as they confront those suffering from respiratory diseases. This resource encourages clinicians with novel approaches by using AI methodologies to advance their development. We can better address future health care needs by promoting the equitable use of AI technologies, especially among socially disadvantaged developers. ■

All references available online at chestphysician.org.