The utility of artificial intelligence in pulmonology has focused mainly on using image datasets to detect and diagnose lung malignancies, but now a growing number of AI models are emerging that apply machine learning to improve predictability for other pulmonary conditions, including pulmonary infections, pulmonary fibrosis, and chronic obstructive pulmonary disease (COPD).

These applications are moving beyond the traditional AI model of collecting data from a multitude of images to cast a wider data net that includes electronic health records.

Also on the horizon, ChatGPT technology is poised to have an impact. But pulmonologists and their practices have a number of barriers to clear before they feel a meaningful impact from AI.

The imperative, said AI researcher Ishanu Chattopadhyay, PhD, is to create transformative models that can detect lung disease early on. Dr. Chattopadhyay, an assistant professor of medicine at the University of Chicago and its Institute for Genomics and Systems Biology, and fellow researchers developed an AI algorithm that uses comorbidity signatures in electronic health records to screen for idiopathic pulmonary fibrosis (IPF) (Nature Med. 2022 Sep 29. doi: 10.1038/s41591-022-02010-y).

Researchers in Texas are developing a “green light” technology they hope will solve a crucial problem highlighted by the pandemic: the limits of pulse oximeters in patients with darker skin.

A recent study adds weight to earlier findings that their device works.

“It is a new, first-in-class technology,” said Sanjay Gokhale, MD, the bioengineer who is leading this research at the University of Texas at Arlington. “The team conducted extensive preclinical work and carried out phase 1 studies in human volunteers, demonstrating sensitivity and accuracy.”

It’s one of several projects underway to update pulse oximetry, a technology based on research in lighter-skinned people that has not changed much in 50 years.

The pulse oximeter, or “pulse ox,” measures the saturation of oxygen in your hemoglobin (a protein in red blood cells). But it tends to...
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Overestimate the oxygen saturation in patients with darker skin by about 2%-3%. That may not sound like a lot, but it’s enough to delay major treatment for respiratory issues like COVID-19.

“Falsely elevated readings from commercial oximeters have delayed treatment of Black COVID-19 patients for hours in some cases,” said Divya Chander, MD, PhD, an anesthesiologist in Oakland, Calif., and chair of neuroscience at The Singularity Group. (Dr. Chander was not involved in the UT Arlington research.)

“The team conducted extensive preclinical work and carried out phase 1 studies in human volunteers, demonstrating sensitivity and accuracy.”

Early research happening separately at Brown University and Tufts University aims to redesign the pulse oximeter to get accurate readings in patients of all skin tones.

University of California, San Diego, researchers are looking into a method that measures blood oxygen using sound in combination with light. Other solutions try to correct for skin tone with algorithms.

The device from UT Arlington uses an algorithm too, but its main innovation is that it replaces red light with green light.

Red light, green light

Traditional oximetry devices, which typically clip on to the patient’s fingertip, use LEDs to beam light through the skin at two wavelengths: one in the red part of the spectrum, the other in the infrared. The light transmits from one side of the clip to the other, passing through arterial blood as it pulses – thus the name pulse oximetry.

The device calculates a patient’s oxygenation based on how much light of each wavelength is absorbed by hemoglobin in the blood. Oxygenated hemoglobin absorbs the light differently than deoxygenated hemoglobin, so oxygenation can be represented as a percentage; 100% means all hemoglobin is completely oxygenated. But the melanin in skin can interfere with the absorption of light and affect the results.

The green-light method measures not absorption but reflectance – how much of the light bounces back. As with traditional oximetry, the green-light method uses two wavelengths. Each is a different shade of green, and the two forms of hemoglobin reflect them differently.

Using an algorithm developed by the researchers, the device can capture readings in patients of all skin tones, the researchers say.

And because it works on the wrist rather than a finger, the device also eliminates issues with cold fingers and dark nail polish – both known to reduce accuracy in traditional oximetry.

In the latest experiments, the researchers tested the technology on synthetic skin samples with varying amounts of melanin, Dr. Gokhale said. The device picked up changes in blood oxygen saturation even in samples with high melanin levels.

In a study published last year, the technology was tested in 16 people against an invasive handheld blood analyzer and a noninvasive commercial pulse oximeter, and found to be comparable to the invasive method.

A drawback

The green-light approach could be “game changing,” Dr. Chander said. But there is a drawback.

Since green light doesn’t penetrate as deeply, this approach measures blood oxygen saturation in capillary beds (small blood vessels very close to the skin surface). By contrast, traditional oximetry measures oxygen saturation in an artery as it pulses – thus the name pulse oximetry.

Valuable information can be obtained from an arterial pulse.

Changes in arterial pulse, known as the waveforms, “can tell us about a patient’s hydration status [for instance],” Dr. Chander said. “In a mechanically ventilated patient, this variation with a patient’s respiratory cycle can give us feedback about how responsive the patient will be to fluid therapy and the research if their blood pressure is too low.”

Given such considerations, the green light method may be useful as an adjunct, not a full replacement, to a standard pulse oximeter.
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“If you could do this when somebody walks into a primary care setting and they are barely suspecting something is going on with them or when they don’t have the typical risk factors, there is a certain fraction of these people who do have IPF and they will almost invariably be diagnosed late and/or misdiagnosed,” Dr. Chattopadhyay said, citing a study that found 55% of patients with IPF have had at least one misdiagnosis and 38% have two or more misdiagnoses (BMC Pulm Med. 2018 Jan 17. doi: [10.1186/s12890-017-0560-x](https://doi.org/10.1186/s12890-017-0560-x)).

**Harnessing massive data sets**

AI models cull data sets, whether banks of radiographic images or files in an EHR, to extract telltale signatures of a disease state. Dr. Chattopadhyay and his team’s model used three databases with almost 3 million participants and 54,247 positive cases of IPF. Hospitals in Scotland have deployed what they’ve claimed are the first AI models to predict COPD built with 55,000 patient records from a regional National Health Service database. Another AI model for staging COPD, developed by researchers in the United States and Romania, used more than 18,000 medical records from 588 patients to identify physiological signals predictive of COPD (Advanced Sci. 2023 Feb 19. doi: [10.1002/advs.202203485](https://doi.org/10.1002/advs.202203485)).

Said Dr. Chattopadhyay: “If I can bring in AI which doesn’t just look at radiological images but actually gets it back where someone walks into primary care using only the information that is available at that point in the patient files and asking for nothing more, it raises a flag reliably that gets you a pulmonary referral that will hopefully reduce the misdiagnosis and late diagnosis.”

Victor Tseng, MD, medical director for pulmonology at Ansible Health in Mountain View, Calif., who’s researching the potential of AI in pulmonology, speculated on what functions AI can perform in the clinic. “I think you will start to see much more interventional sort of clinically patient care–facing applications,” he said. That would include acting as a triage layer to direct patient queries to a nurse, physician, or another practitioner, providing patient instructions, serving as therapeutic software, coordinating care, integrating supply chain issues,” he said.

**AI vs. spirometry for COPD**

Researchers in the United States and Romania, led by Paul Bogdan, PhD, at the University of Southern California Viterbi School of Engineering, developed a model that predicted COPD with an accuracy of almost 99% (98.66%) and avoids many of the shortcomings of spirometry, Dr. Bogdan said.

The models developed by Dr. Bogdan and collaborators use a different principle than existing AI platforms, Dr. Bogdan said. They analyze the properties of the data. As he explained it, they exploit what he called the “geometry of these data” to make inferences and decisions on a patient’s risk for COPD.

“Deep learning is very good for images, for videos, but it doesn’t work that well for signals,” said Mihai Udrescu, PhD, one of the Romanian collaborators. “But if we process the data with the technique brought up by Paul [Bogdan] and his team at USC, deep learning also works well on physiological signals.”

Said Dr. Bogdan, “Nobody thought about using physiological signals to predict COPD before this work.

They used spirometry, but spirometry is cumbersome and several steps have to be performed in order to have an accurate spirometry.” His team’s AI models extract and analyze risk data based on 10 minutes of monitoring.

This technology also has the potential to improve accessibility of COPD screening, Dr. Udrescu said. “It can democratize the access to the health care because you don’t need to travel for 100 or 200 miles to see a specialist,” he said. “You just send an app to the mobile phone of a patient, the person puts on a smart watch and wears it for a couple of minutes, and the data is either recorded locally or is transmitted and it is analyzed.” The computations can be done locally and in a matter of minutes, he said.

In Scotland, a 12-month feasibility study is underway to evaluate an AI model to identify COPD patients at greatest risk for adverse events. A

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FDA warns AstraZeneca over ‘misleading claims’ about COPD drug

BY LUCY HICKS

The U.S. Food and Drug Administration has issued a warning letter to AstraZeneca over the pharmaceutical company’s advertising of the efficacy of a treatment for chronic obstructive pulmonary disease (COPD). Promotional materials for the drug Breztri (budesonide/formoterol fumarate/glycopyrrholate inhaled) suggest that the drug has a positive effect on all-cause mortality for COPD patients, but the referenced clinical trial does not support that claim, the letter states. The FDA issued the warning letter on Aug. 4 and published it online on Aug. 15. (https://tinyurl.com/4zp2bpy).

“The sales aid highlights a 49% observed relative difference in time to all-cause mortality (ACM) over 1 year between Breztri and long-acting muscarinic antagonist/long-acting beta agonist (LAMA/LABA) inhalers. Because of ‘statistical testing hierarchy failure’ as well as confounding factors such as the removal of patients from inhaled corticosteroids (ICS) prior to entering the treatment arm of the trial, ‘no conclusions about the effect of Breztri on ACM can be drawn from the [clinical] trial,’ the FDA wrote.

“To date, no drug has been shown to improve ACM in COPD,” the FDA added.

“The Breztri sales aid also states that there was a 20% reduction of severe exacerbations in patients using Breztri compared with patients using ICS/LABA. However, in the cited clinical trial, ‘the reduction in severe exacerbations was not statistically significant for patients treated with Breztri relative to comparator groups,’ according to the FDA.

AstraZeneca was given 15 working days from the receipt of the letter to respond in writing with ‘any plan for discontinuing use of such communications, or for ceasing distribution of Breztri,’ the agency wrote.

As a result of the warning, FDA will be overseeing care that involves removing patients from inhaled corticosteroids (ICS) prior to entering the treatment arm of the trial, and the sales aid also states that there was a 20% reduction of severe exacerbations in patients using Breztri compared with patients using ICS/LABA. However, in the cited clinical trial, the reduction in severe exacerbations was not statistically significant for patients treated with Breztri relative to comparator groups, according to the FDA.

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The physicians and researchers interviewed for this report had no relevant relationships to disclose.

AI continued from previous page

press release from Lenus, the company developing the technology, said the study will use a COPD multidisciplinary team to consider real-time AI model outputs to enable proactive patient encounters and reduce emergency care visits.

Researchers in Paris built an AI model that showed a 68% accuracy in distinguishing people with asthma from people with COPD in administrative medical databases (BMJ Pulmon Med. 2022 Sep 20. doi: 10.1186/s12890-022-02144-2). They found that asthma patients were younger than those with COPD (a mean of 49.9 vs. 72.1 years) and that COPD occurred mostly in men (68% vs. 33%). And an international team of researchers reported that an AI model that used chest CT scans determined that ever-smokers with COPD who met the imaging criteria for bronchiectasis were more prone to disease exacerbations (Radiology. 2022 Dec 13. doi: 10.1148/radiol.221109).

AI in idiopathic pulmonary fibrosis

The AI model that Dr. Chattopadhay and collaborators developed had an 88% accuracy in predicting IPF. Researchers at Nagoya University in Japan also reported on an AI algorithm for predicting IPF that used 646,800 high-resolution CT images and medical records data from 1,068 patients. Their algorithm had an average diagnostic accuracy of 83.6% and, they reported, demonstrated good accuracy even in patients with signs of interstitial pneumonia or who had surgical lung biopsies (Respirology. 2022 Dec 13. doi: 10.1111/resp.14310).

ChatGPT: The next frontier in AI

Dr. Tseng last year led a group of researchers that fed questions from the United States Medical Licensing Exam to a ChatGPT model, which found it answered 60%-65% of questions correctly (PLOS Digit Health. 2023 Feb 9 doi: 10.1371/journal. pdgh.000198). As Dr. Tseng pointed out, that’s good enough to get a medical license.

It may be a matter of time before ChatGPT technology finds its way into the clinic, Dr. Tseng said. A quick ChatGPT query of how it could be used in medicine yielded 12 different answers, from patient triage to providing basic first aid instructions in an emergency.

“People who don’t have all the risk factors still get IPF. So we have to step back from the raw EHR data from where the features are being generated automatically, and then you can apply standard ML tools.”

The AI model that Dr. Chattopadhay and collaborators developed had an 88% accuracy in predicting IPF.

Dr. Novak

Dr. Novak, PhD, reported (JAMIA Open. 2023 May 3. doi: 10.1093/jamiaopen/ooad028). But it’s coming nonetheless, Dr. Novak, an associate professor of biomedical informatics at Vanderbilt University Medical Center in Nashville, Tenn., said in an interview.

“In the near future, managers in clinics and inpatient units will be overseeing care that involves numerous AI-based technologies, including predictive analytics, imaging tools, language models, and others,” she said. “Organizations need to support managers by implementing capabilities for algorithm-vigilance.”

That would include dealing with what she called “algorithmic drift” – when the accuracy of an AI model wanes because of changes in the underlying data – and ensuring that models are unbiased and aren’t used in a way that contributes to inequities in health care.

“These new organizational capabilities will demand new tools and new competencies,” she said. That would include policies and processes drawing guidance from medical societies for legal and regulatory direction for managers, staff training, and software documentation.

Dr. Tseng envisioned how AI would work in the clinic. “I personally think that, at some time in the near future, AI-driven care coordination, where the AI basically handles appointment scheduling, patient motivation, patient engagement and acts as their health navigator, will be superior to any human health navigator on the whole, only for the reason that AI is indefatigable.” Dr. Tseng said.

“It doesn’t get tired, it doesn’t get burned out, and these health navigation care coordination roles are notoriously difficult.”

The physicians and researchers interviewed for this report had no relevant relationships to disclose.
Two newly approved respiratory syncytial virus (RSV) vaccines for adults aged 60 years and older may be able to prevent illness in those at risk for severe RSV disease. Most adult RSV illness occurs among the older age group and results in an estimated 60,000-160,000 hospitalizations and 6,000-10,000 deaths per year among people aged at least 65 years.

Older adults deciding whether to get the vaccines should weigh risks and their own preferences and decide in consultation with their clinicians, said authors of a Centers for Disease Control and Prevention report.

Michael Melgar, MD, with the Coronavirus and Other Respiratory Viruses Division at the CDC, was lead author on the report, published in the Morbidity and Mortality Weekly Report (2023 Jul 21;72[29]:793-801).

**Two new vaccines**
In May, the U.S. Food and Drug Administration approved the first of two vaccines for preventing RSV lower respiratory–tract disease for adults aged at least 60 years. On June 21, the Advisory Committee on Immunization Practices (ACIP) recommended that people in that age group receive a single dose of RSV vaccine using shared decision-making.

The recommendation for shared decision-making makes the ACIP decision different from routine and risk-based vaccine recommendations. Rather than targeting all in a particular age group or risk group, the decision calls for consideration of a patients’ risk for disease and their characteristics, preferences, and values; the health care professional’s clinical discretion; and performance of the vaccine.

Dr. Melgar and colleagues reported that vaccination with one dose of the GSK or Pfizer RSV vaccines has proved moderately to highly effective in preventing symptomatic RSV-associated lower respiratory tract disease over two consecutive RSV seasons among people aged 60 and older.

The trials that led to approval weren’t powered to gauge efficacy against RSV-associated hospitalization and death. However, the authors wrote, the prevention of lower respiratory tract disease, including medically attended illness, suggests that the shots might prevent considerable morbidity from RSV disease among those aged 60 and older.

Both vaccines were generally well tolerated with a good safety profile. However, six cases of inflammatory neurologic events (including Guillain-Barre Syndrome, acute disseminated encephalomyelitis, and others) were reported in clinical trials after RSV vaccination.

“Whether these events occurred due to chance, or whether RSV vaccination increases the risk for inflammatory neurologic events, is currently unknown,” they wrote.

Postmarketing surveillance may help clarify the existence of any potential risk, but until those results are clearer, the CDC researchers said, RSV vaccinations should be targeted to older adults at highest risk for severe RSV and those most likely to benefit from the shots.

**At higher risk**
Some adults with certain medical conditions have a higher risk for RSV-associated hospitalization, according to the report.

Those conditions include chronic obstructive pulmonary disease, asthma, heart failure, coronary artery disease, cerebrovascular disease, diabetes mellitus, and chronic kidney disease. People who are frail and of advanced age also are at higher risk for RSV hospitalization. That risk increases with age and the highest risk is for people aged at least 75 years.

The researchers added that RSV can cause severe disease in those with compromised immunity, including people who have received hematopoietic stem cell transplants and patients taking immunosuppressive drugs such as those used with solid-organ transplants, cancer treatment, or other conditions.

For the 2023-2024 season, the report states, clinicians should offer RSV vaccination to adults aged at least 60 years using shared clinical decision-making as early as vaccine supply is available and should continue to offer vaccination to eligible adults who remain unvaccinated.

RSV vaccines can be administered with other adult vaccines during the same visit, the authors confirmed.

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**Heat waves plus air pollution tied to doubling of fatal MI**

The combination of heat waves and poor air quality is associated with double the risk of fatal myocardial infarction (MI), with women and older adults at greatest risk, according to a new study. Researchers estimate that up to 3% of all deaths due to MI could be attributed to the combination of extreme temperatures and high levels of ambient fine-particle matter (PM2.5).

“Our findings provide evidence that reducing exposure to both extreme temperatures and fine-particle pollution may be useful to prevent premature deaths from heart attack,” senior author Yuwei Liu, MD, PhD, with Sun Yat-sen University in Guangzhou, China, said in a statement. The study was published online in Circulation (2023 Jul 24. doi: 10.1161/CIRCULATIONAHA.122.063504).

There is “long-standing evidence” of the harmful cardiovascular effects of air pollution, Jonathan Newman, MD, MPH, cardiologist at NYU Langone Heart in New York, who wasn’t involved in the study, said in an interview. However, this study found an interaction between extreme hot temperatures and air pollution, “which is worrisome with global warming,” said Dr. Newman. Data was analyzed on 202,678 adults (mean age, 77.6 years; 52% male) who suffered fatal MI between 2015 and 2020 in Jiangsu province, a region with four distinct seasons and a wide range of temperatures and ambient PM2.5.

They evaluated the association of exposure to extreme temperature events, including both hot and cold spells, and PM2.5 with MI mortality, and their interactive effects. Among the key findings:

- **The risk of fatal MI was 18% higher during 2-day heat waves with heat indexes at or above the 90th percentile (ranging from 82.6° to 97.9° F) and 74% higher during 4-day heat waves with heat indexes at or above the 97.5th percentile (ranging from 94.8° to 109.4° F), compared with control days.**

- **The risk of fatal MI was 4% higher during 2-day cold snaps with temperatures at or below the 10th percentile (ranging from 33.3° to 40.5° F) and 12% higher during 3-day cold snaps with temperatures at or below the 2.5th percentile (ranging from 27.0° to 37.2° F).**

  - The risk of fatal MI was twice as high during 4-day cold snaps with temperatures at or below PM2.5 above 37.5 mcg/m³. Days with high levels of PM2.5 during cold snaps did not have an equivalent increase in the risk of fatal MI.

- **Up to 2.8% of MI deaths during the 5-year study period may be attributable to the combination of extreme temperature exposure and PM2.5 at levels exceeding World Health Organization air-quality guidelines (37.5 mcg/m³).**

- **The risk of fatal MI was generally higher among women than men during heat waves and was higher among adults 80 years old and older than in younger adults during heat waves, cold snaps, or days with high levels of PM2.5.**

The finding that adults over age 80 are particularly susceptible to the effects of heat and air pollution and the interaction of the two is “notable and particularly relevant given the aging of the population,” Dr. Newman said.

“To improve public health, it is important to take fine-particle pollution into consideration when providing extreme temperature warnings to the public,” Dr. Liu added in the statement.

The authors and Dr. Newman reported having no financial conflicts.
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SLEEP MEDICINE

Smart-bed technology reveals insomnia, flu risk link

BY MEGAN BROOKS

Insomnia may increase vulnerability to influenza-like illness, a novel finding that was revealed by the passive collection of biometric data from a smart bed.

The study of smart-bed sleepers found that there was a statistically significant correlation between a higher number of episodes of influenza-like illnesses (ILI) per year with longer duration compared with people without insomnia.

However, more research is needed to determine causality and whether insomnia may predispose to ILI or whether ILI affects long-term sleep behavior, the researchers noted.

“Several lines of evidence make me think that it’s more likely that insomnia makes one more vulnerable to influenza through pathways that involve decreased immune function,” study investigator Gary Garcia-Molina, PhD, with Sleep Number Labs, San Jose, Calif., said in an interview. Sleep disorders, including insomnia, can dampen immune function and an individual’s ability to fight off illness, he noted.

The findings were presented at the annual meeting of the Associated Professional Sleep Societies.

**Smart, connected devices**

Pathophysiological responses to respiratory viral infection affect sleep duration and quality in addition to breathing function. “Smart” and “connected” devices that monitor biosignals over time have shown promise for monitoring infectious disease.

In an earlier study presented at SLEEP 2021, Dr. Garcia-Molina and colleagues found that real-world biometric data obtained from a smart bed can help predict and track symptoms of COVID-19 and other respiratory infections. They showed that worsening of COVID-19 symptoms correlated with an increase in sleep duration, breathing rate, and heart rate and a decrease in sleep quality.

In the new study, the researchers evaluated vulnerability to ILI in people with insomnia.

They quantified insomnia over time using the insomnia severity index (ISI). They quantified ILI vulnerability using an established artificial intelligence model they developed that estimates the daily probability of ILI symptoms from a sleep number smart bed using ballistocardiograph sensors.

Smart-bed data — including daily and restful sleep duration, sleep latency, sleep quality, heart rate, breathing rate, and motion level — were queried from 2019 (pre-COVID) and 2021.

A total of 1,680 smart sleepers had nearly constant ISI scores over the study period, with 249 having insomnia and 1,431 not having insomnia.

Data from both 2019 and 2021 show that smart sleepers with insomnia had significantly more and longer ILI episodes per year, compared with peers without insomnia.

For 2019, individuals without insomnia had 1.2 ILI episodes on average, which was significantly less (P < 0.01) than individuals with insomnia, at 1.5 episodes. The average ILI episode duration for those without insomnia was 4.3 days, which was significantly lower (P < 0.01) in those with insomnia group, at 6.1 days.

The data for 2021 show similar results, with the no-insomnia group having significantly fewer (P < 0.01) ILI episodes (about 1.2), compared with the insomnia group (about 1.5).

The average ILI episode duration for the no-insomnia group was 5 days, which was significantly less (P < 0.01) than the insomnia group, at 6.1 days.

The researchers said their study adds to other data on the relationship between sleep and overall health and well-being. It also highlights the potential health risk of insomnia and the importance of identifying and treating sleep disorders.

“Sleep has such a profound influence on health and wellness, and the ability to capture these data unobtrusively in such an easy way and with such a large number of participants paves the way to investigate different aspects of health and disease,” Dr. Garcia-Molina said.

**Rich data source**

In a comment, Adam C. Powell, PhD, president of Payer+Provider Syndicate, a management advisory and operational consulting firm, said “smart beds provide a new data source for passively monitoring the health of individuals.”

“Unlike active monitoring methods requiring self-report, passive monitoring enables data to be captured without an individual taking any action. These data can be potentially integrated with data from other sources, such as pedometers, smart scales, and smart blood pressure cuffs, to gain a more holistic understanding of how an individual’s activities and behaviors impact their well-being,” said Dr. Powell, who wasn’t involved in the study.

“There are some methodological limitations to the study, he noted. “While the dependent variables examined were the duration and presence of episodes of influenza-like illness, they did not directly measure these episodes. Instead, they calculated the daily probability of influenza-like illness symptoms using a model that received input from the ballistocardiograph sensors in the smart beds,” Dr. Powell noted. “The model used to calculate daily probability of influenza-like illness was created by examining associations between individuals’ smart-bed sensor data and population-level trends in influenza-like illness reported by the Centers for Disease Control and Prevention,” he explained.

Nonetheless, the findings are “consistent with the literature. It has been established by other researchers that impaired sleep is associated with greater risk of influenza, as well as other illnesses,” Dr. Powell said. Funding for the study was provided by Sleep Number. Dr. Garcia-Molina and five coauthors are employed by Sleep Number. Dr. Powell reported no relevant financial relationships.
Neutropenia affects clinical presentation of pulmonary mucormycosis

BY HEIDI SPLETE

FROM THE JOURNAL CHEST® • Neutropenia and radiological findings affected the presentation and diagnosis of pulmonary mucormycosis in adult patients, based on data from 114 individuals.

Diagnosis of pulmonary mucormycosis (PM), an invasive and potentially life-threatening fungal infection, is often delayed because of its variable presentation, wrote Anne Coste, MD, of La Cavale Blanche Hospital and Brest (France) University Hospital, and colleagues.

Improved diagnostic tools including molecular identification and image-guided lung biopsies are now available in many centers, but relations between underlying conditions, clinical presentations, and diagnostic methods have not been described, they said.

In a study published in the journal Chest (2023 Jul 5. doi: 10.1016/j.chest.2023.06.039), the researchers reviewed data from all cases of PM seen at six hospitals in France between 2008 and 2019. PM cases were based on European Organization for Research and Treatment of Cancer and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) criteria. Diabetes and trauma were included as additional host factors, and positive serum or tissue PCR (serum qPCR) were included as mycological evidence. Participants also underwent thoracic computed tomography (CT) scans.

The most common underlying conditions among the 114 patients were hematological malignancy (49%), allogeneic hematopoietic stem cell transplantation (21%), and solid-organ transplantation (17%), Among the 40% of the cases that involved dissemination, the most common sites were the liver (48%), spleen (48%), brain (44%), and kidneys (37%).

Among the 40% of the cases that involved dissemination, the most common sites were the liver (48%), spleen (48%), brain (44%), and kidneys (37%).

A review of radiology findings showed consolidation in a majority of patients (58%), as well as pleural effusion (52%). Other findings included reversed halo sign (RHS, 26%), halo sign (24%), vascular abnormalities (26%), and cavity (23%). Bronchoalveolar lavage (BAL) was present in 46 of 96 patients (50%), and transthoracic lung biopsy was used for diagnosis in 8 of 11 (73%) patients with previous negative BALs.

Seventy patients had neutropenia. Overall, patients with neutropenia were significantly more likely than were those without neutropenia to show an angioinvasive presentation that included both RHS and disease dissemination (P < .05).

In addition, serum qPCR was positive in 42 of 53 patients for whom data were available (79%). Serum qPCR was significantly more likely to be positive in neutropenic patients (91% vs. 62%, P = .02). Positive qPCR was associated with an early diagnosis (P = .03) and treatment onset (P = .01).

Possible reasons for the high rate of disseminated PM in the current study may be the large number of patients with pulmonary involvement, use of body CT data, and availability of autopsy results (for 11% of cases), the researchers wrote in their discussion.

Neutropenia and radiological findings influence disease presentation and contribution of diagnostic tools during PM. Serum qPCR is more contributive in neutropenic patients and BAL examination in nonneutropenic patients. Lung biopsies are highly contributive in case of non-contributive BAL.

The findings were limited by several factors including the retrospective design, the inability to calculate sensitivity and specificity of diagnostic methods, and lack of data on patients with COVID-19, the researchers noted. However, the results provide real-life information for clinicians in centers with current mycological platforms, they concluded.

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

Observation recommended as first-line therapy in select cases of primary spontaneous pneumothorax

BY WALTER ALEXANDER

FROM THE JOURNAL CHEST® • Observation should be considered the first-line treatment of choice in appropriately selected primary spontaneous pneumothorax patients, according to a recent review.

Observation was the dominant choice, based on economic modeling showing it to offer both the highest utility and the lowest cost, according to the review published in the journal CHEST (2023 May 18. doi: 10.1016/j.chest.2023.05.017), which encompassed 20 years of relevant publications.

While current guidelines are shifting toward either aspiration or observation and away from recommending chest tube placement, chest tube placement remains quite common in physicians’ clinical practices, Gilgamesh Eamer, MD, MSc, FRCS, of Children’s Hospital of Eastern Ontario, Ottawa, and colleagues wrote. While prior systematic reviews have examined various primary spontaneous pneumothorax management techniques, no reviews encompass more recently published high-quality studies comparing aspiration to other interventions such as observation or Heimlich valve devices.

The authors identified 22 articles for systematic review and meta-analysis after screening an initial list of 5,179 potentially relevant articles (Jan. 1, 2000, to April 10, 2020). They compared observation, needle aspiration, and chest tube placement, and created an economic model for these three treatment pathways based on Canadian medical cost data. The primary outcome measure was resolution following the initial intervention. Secondary outcomes included primary spontaneous pneumothorax recurrence, length of hospital stay, and treatment complications.

The analysis revealed that, compared with observation, chest tube and aspiration had higher resolution without additional intervention (relative risk for chest tube, 0.81; P < .01; RR for aspiration, 0.73; P < .01). Compared with a chest tube, observation and aspiration had shorter length of stay (mean difference for observation, 5.17; P < .01; MD for aspiration, 2.72; P < .01). Two-year recurrence rates did not differ between management strategies.

Cost utility modeling found a cost of $14,658 (Canadian dollars [CAD]) with 1.2535 = 1 U.S. dollar for chest tube placement, $13,126 CAD for aspiration, and $6,408 CAD for observation.

The utility (a measure including both quantity and quality of life) for each management arm was 0.77 for CT placement, 0.79 for aspiration, and 0.82 for observation. “The observation arm dominates the other two arms meaning it results in a more desirable (higher) utility with lower cost and results in a negative ICER [incremental cost-effectiveness ratio],” the authors stated.

They observed further that it is not typical for a medical intervention to improve patient outcomes, compared with standard care, and at the same time to bring costs down. “Given this, and the increasing evidence that observation is safe and effective in appropriately selected patients presenting with primary spontaneous pneumothorax,” they concluded that “observation should be considered in all patients presenting with primary spontaneous pneumothorax who meet predefined criteria.” They added that, because aspiration is favored over chest tube placement, it should be considered second-line therapy in well-selected primary spontaneous pneumothorax patients presenting with recurrence or who have failed a trial of observation.

“This review sheds light on ‘less is better’ for primary spontaneous pneumothorax management,” commented Dharani K. Narendra, MD, of the department of medicine, Baylor College of Medicine, Houston. Neither Dr. Eamer nor Dr. Narendra reported any conflicts.
The presence of a positive fungal culture in patients with bronchiectasis does not appear to correlate with disease severity or any increased risk of an adverse outcome, according to data pulled from the Bronchiectasis and NTM Registry and presented at the 6th World Bronchiectasis & NTM Conference.

"The question we were asking is whether there is some signal that suggests we need to take care of these patients differently, and the answer is no," reported Pamela J. McShane, MD, a pulmonologist on the faculty at the University of Texas Health Science Center at Tyler.

When compared for outcome over time, those with a positive fungal culture at initial evaluation did not have more exacerbations, more hospitalizations, or other signs of a more severe disease or more complex course than did those without a positive fungal culture.

When fungal infections are detected in an initial microbiologic evaluation of patients with bronchiectasis or other lung diseases, first-line clinicians generally assume that coverage is needed. Dr. McShane noted that many of the patients referred to her with bronchiectasis and a positive fungal culture were already on an antifungal.

These data are not supportive of treatment in the absence of fungal-related complications. Dr. McShane suggested they even raise questions about the value of culturing beyond bacterial pathogens in the absence of suspicion that fungal organisms are playing a role in symptoms. She cautioned, however, that more studies specifically studying this possibility are needed.

**Study details**

The data were drawn in December 2022 from the U.S.-based Bronchiectasis and NTM Registry, which at that time had 22 participating sites. Of the more than 5,000 patients enrolled, the study looked at 2,230 after several exclusions, such as a diagnosis of allergic bronchopulmonary aspergillosis (ABPA).

Of these 2,230 patients, 949 had a fungal infection at the time of diagnosis and 1,281 did not. Those with a fungal infection were further subdivided into those with an aspergillosis (331 patients) and those with a nonaspergillosis fungal infection (751 patients). The total of these two numbers is greater than the total number of fungal infections because these were not mutually exclusive.

At enrollment into the registry, there were no statistical differences between groups for age. Some statistical differences were observed among groups stratified by race, but Dr. McShane doubted that these were clinically significant with the exception of a potential disparity among Asians that might deserve further analysis.

**Infection results**

Of clinical features evaluated for their association with fungal infection, there was no correlation with either body mass index or history of asthma. Eosinophilia was associated...
Create a foundation based on clinical results
CAN CHANGE THE OUTCOME
WHAT YOU START WITH

In the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to reduce the risks of disease progression and hospitalization for PAH.

arterial hypertension (PAH, WHO Group I) to reduce the

following: a sustained ≥15% decrease from baseline

in 6MWD,† worsening of PAH symptoms,‡ and need

for additional PAH treatment) during double-blind
treatment plus 7 days.

■ 25%
■ Mean patient age was
■ Etiologies included IPAH/HPAH (31%)
■ Patients had predominantly WHO FC II (

36%)
■ 36%
■ 52%

64% of patients were not using PAH-specific
background therapy at baseline*

were previously diagnosed (≥6 months)

were recently diagnosed (<6 months)

were using background therapy with PDE-5
inhibitors or inhaled/oral prostanoids at baseline*

were predominantly WHO Functional Class II-III

HA-HIV (1%)

connective tissue disorders (31%), and PAH caused

by congenital heart disease with repaired shunts (8%).

The beneficial effect of OPSUMIT® was primarily attributable to a reduction in clinical worsening events (defined as all of the following: a sustained ≥15% decrease from baseline in 6MWD,† worsening of PAH symptoms,‡ and need for additional PAH treatment).

The SERAPHIN trial design and demographics

OPSUMIT® significantly reduced the risk of disease progression by

1.0% in 6- to 2-year treatment after 1 year of treatment.

A primary endpoint event was experienced by

25.5% of patients in the OPSUMIT® 10 mg treatment group

and 37.2% of patients in the placebo group.

The risk of worsening PAH treatment (defined as all of the following: a sustained ≥15% decrease from baseline (or no change in WHO FC IV) and signs of right heart failure that does not respond to oral diuretic treatment.

†Confirmed by a second 6-minute walk test performed on a different day within 2 weeks.

‡Worsening of PAH included at least one of the following: Advancing to a higher FC [a decline in WHO FC], and need for additional PAH treatment).

3% of patients experienced an event of lung transplantation or atrial septostomy in the placebo or OPSUMIT® 10 mg treatment groups.

§No patients experienced an event of lung transplantation or atrial septostomy in the placebo (n=250), 10 mg (n=242), or 2.4% (n=23) of placebo-treated patients vs

2.4% (n=21) of OPSUMIT® 10 mg (n=116) and 2.4% (n=16) of OPSUMIT® 37.2% (n=93) treated patients vs placebo (n=1).

mortality event, defined as atrial septostomy, lung transplantation, initiation of IV or SC prostanoids, or clinical worsening of PAH (defined as all of the following: a sustained ≥15% decrease from baseline in 6MWD,† worsening of PAH symptoms,‡ and need for additional PAH treatment).

The risk of disease progression was reduced by 1.0% in 6- to 2-year treatment after 1 year of treatment.

The risk of disease progression was reduced by 1.0% in 6- to 2-year treatment after 1 year of treatment.

The risk of disease progression was reduced by 1.0% in 6- to 2-year treatment after 1 year of treatment.

...continued on following page
BRONCHIECTASIS continued from previous page

infection, but these are what the data say.

Steroid use was associated with a statistically significant risk of fungal infection, but Dr. McShane said it is unclear whether steroid use drives the risk or is an epiphenomenon. "We looked at this a lot of different ways: oral vs. inhaled and oral vs. inhaled and oral, and it did not make much difference. Generally speaking, the fungal cultures were more likely to be positive in patients on any kind of steroid," she said.

Finally, with the exception of the slightly lower FEV₁ in patients with fungal infections, Dr. McShane said that there was no discernible relationship between the presence of a fungal infection and severity of bronchiectasis.

Because of this evidence, Dr. McShane concluded that the presence of fungus in the culture of patients with bronchiectasis does not appear to correlate with outcome or severity. Since completing the study, she said she is now using these data to reassure patients who have a positive fungal culture.

While these data do not affect the need to diagnosis fungal infections in patients who are not responding typically to therapy or otherwise have an abnormal course of bronchiectasis, raising suspicion that fungal infection is participating in
the disease course, the data provide a basis for questioning whether routine cultures are needed, according to the discussion that followed Dr. McShane's presentation.

**Expert opinion**

Several of the experts at the presentation provided an opinion. Some reported that they would continue to order fungal cultures on a routine basis, while others said that they now, on the basis of these data, plan to order cultures only at the first visit or when fungal infection is suspected of exacerbating the disease.

Of this latter group, which seemed to be dominant, Juzar Ali, MD, professor of medicine, Louisiana State University, New Orleans, said that he has not been ordering fungal cultures on every visit. Rather, he has been doing so selectively. Examples include those who are on steroids or those with an unusual pattern of exacerbations.

“The value of these data is that they have now provided some data to support this approach,” Dr. Ali said in an interview. Noting that this is the first large study to address this question in a systematic way, he considers this to be a valuable contribution for approaching a common clinical issue.

Dr. McShane reports no relevant financial relationships. Dr. Ali reports a financial relationship with Inamed. 

Enacting a hypoglossal nerve stimulation program

BY KIRAT GILL, MD

It is estimated that almost one billion people globally are affected by obstructive sleep apnea (OSA) (Benjafied A, et al. Lancet Respir Med. 2019;7[8]:687-98). Despite such high prevalence, the treatment options for OSA are somewhat limited. Continuous positive airway pressure (CPAP), the gold standard therapy, is not viable for many due to difficulties tolerating the device or mask, and thus may not be a realistic long-term solution. As per certain estimates, nearly 50% of CPAP users discontinue treatment by the fifth year (Schoch O, et al. Respiration. 2014;87[2]:121-8). Furthermore, alternative options such as mandibular advancement devices, positional therapy, weight loss, and maxillofacial or palate surgery, also have unique challenges and limitations.

First described in 2001, hypoglossal nerve stimulation (HGNS) is a relatively new and emerging technology for the treatment of OSA (Schwartz A, et al. Arch Otolaryngol Head Neck Surg. 2001 Oct;127[10]:1216-23). HGNS therapy was approved by the U.S. Food and Drug Administration in 2014 for the treatment of moderate to severe OSA. The therapy involves surgical implantation of the HGNS device, optimization of device settings, and evaluation for treatment response. A physician-led multidisciplinary Hypoglossal Nerve Stimulation Clinic involves collaboration from essential stakeholders, most importantly sleep medicine providers, clinic staff, sleep technologists, and ENT sleep surgeons. Goals of the multidisciplinary program are to ensure timely follow-up, optimization of device settings, and maximizing treatment efficacy. This review describes steps involved in developing a successful multidisciplinary HGNS program within a sleep medicine practice.

**Patient selection and evaluation**

There is growing interest in HGNS relative to conventional CPAP therapy, with many patients presenting to clinic to inquire about this therapy. However, not all patients are candidates for HGNS therapy. Prioritizing appropriate patient selection and education are key first steps. The initial assessments usually occur with a sleep medicine specialist. It begins with confirmation of the diagnosis of OSA in all patients and a concerted effort to trouble-shoot and address any barriers to CPAP use before consideration of surgery. Patients who are unwilling to use or unable to tolerate CPAP therapy undergo further evaluation for HGNS therapy. It is important to ensure that patients are also screened for other sleep disorders,
A complete concentric collapse of the soft palate is updated polysomnography if a recent study is not Surgery, and drug-induced sleep endoscopy is available. If the polysomnography reveals central and mixed apneas comprising less than 25% of such as insomnia or restless leg syndrome, to rule out their contribution to daytime (or nighttime) symptoms.

Other salient inclusion criteria include an apnea-hypopnea index (AHI) between 15 and 100 events per hour (previously 65), at least 18 years of age, and a body mass index (BMI) less than 40 kg/m² (previously 32). Qualifying patients undergo an updated polysomnography if a recent study is not available. If the polysomnography reveals central and mixed apneas comprising less than 25% of the total AHI, patients are referred to ENT Sleep Surgery, and drug-induced sleep endoscopy is offered to examine upper airway anatomy. When a complete concentric collapse of the soft palate is seen on drug-induced sleep endoscopy, surgery is contraindicated. Prior palate surgery or maxillo-mandibular advancement (MMA) are not contraindications to HGNS therapy.

The patients receive comprehensive information on the nature of the surgery, expected recovery course, and device activation timeline. Perhaps most importantly, the patients receive structured education on HGNS therapy and potential outcomes to set realistic expectations. In the STAR trial, patients experienced a reduction in the AHI of approximately 70% (Strollo P, et al. N Engl J Med. 2014;370[2]:139-49). It is important to note that a response to therapy was defined as a reduction in the AHI by at least 50% and a value less than 20 events/hour (Strollo P, et al. Sleep. 2015;38[10]:1593-8). Therefore, patients who are expecting complete resolution of snoring and/or OSA may not be ideal candidates for surgery. Furthermore, patients who continue to experience fatigue and sleepiness on CPAP despite control of OSA may not experience amelioration of these symptoms with HGNS therapy.

**Surgery and device management**

The surgery, performed under general anesthesia, lasts approximately 3 hours, and may be followed by an overnight hospital stay depending on patient’s comorbidities. The device implantation involves placement of an implantable pulse generator (IPG) in the chest wall and leads to the hypoglossal nerve. The IPG is similar to a pacemaker and functions to stimulate the ipsilateral hypoglossal nerve innervating the tongue during sleep. The most common postoperative complications noted in the STAR trial data include incision site pain and swelling as well as temporary tongue weakness or paresthesia. Postoperative restrictions are minimal and include no heavy lifting for 1 month after surgery.

One week postsurgery, patients return to the ENT Sleep Surgery Clinic for follow-up, at which time the incisions, as well as tongue strength and sensation are evaluated. In a subsequent visit, between 4 and 6 weeks postsurgery, patients are evaluated in a joint Sleep Medicine and ENT clinic. They undergo device education and activation of the IPG using a dedicated programmer obtained from the device manufacturer. Device comfort features such as start delay and pause time, are also programmed. Furthermore, appropriate tongue movement, lead placement, and voltage range settings are assessed during the visit. The ENT surgery team reevaluates the incision sites and assesses for tongue function and sensation. Patients are instructed to increase the voltage incrementally every week as tolerated with the goal of using the device nightly for the entirety of sleep. If patients tolerate the therapy well during the 2- to 3-month follow-up, a sleep study is scheduled to evaluate treatment effectiveness at the peak tolerated voltage. For those struggling with the therapy, adjustments to electrode configurations should be considered, pulse width, and rate. Occasionally, patients may require awake endoscopy and/or an advanced HGNS titration while asleep to determine the most appropriate settings to optimally control sleep apnea.

Until recently, patients implanted with an early version of the HGNS were limited to magnetic resonance imaging (MRI) scans of the head, neck, and extremities only. However, patients with the latest model IPGs can now undergo full-body MRI scans. It is important to note that the MRI’s Tesla cannot exceed 1.5T, necessitating specific imaging centers. Other constraints include the inability to adjust device settings remotely, which could mean long travel for minor setting adjustments such as altering start delay or pause times. Furthermore, provider education on operating and managing the device can be time consuming and may also be a barrier to implementation in a clinic. Also challenging may be the availability of an ENT surgery, which plays a critical role in the implantation of the devices and follow-up.

Currently, Inspire Medical Systems is the only FDA-approved hypoglossal nerve stimulation device available in the United States, and globally, more than 45,000 patients have had implants. However, the field of neurostimulation is rapidly growing. Companies like LivaNova have secured Investigational Device Exemption for their HGNS device. The Genio system by Nyxoah is evaluating the use of bilateral hypoglossal nerve stimulation in patients with OSA and complete concentric collapse of the palate. A multidisciplinary Hypoglossal Nerve Stimulation Clinic is an important component of a comprehensive sleep medicine clinic for patient care and medical education. In the appropriate patient, this emerging technology may provide improvement in OSA severity and symptoms.
changes on the airway in patients hyperreactive. Cold air can remove of temperature and humidity impactful on our patients. matic airways that are already encencies may have been especially not unusual, but their recent occurrences may have been especially impactful on our patients. Earlier works investigating effects of temperature and humidity changes on the airway in patients with asthma are insightful (Strauss, et al. 1978). Heat can irritate asthmatic airways that are already inflamed and can affect patients with COPD. Seasonal variation in COPD exacerbations was demonstrated by the TORCH study, where a two-fold increase in COPD exacerbations and hospitalizations was noted during the winter months in both northern and southern regions of the world. This trend was not observed in tropical countries with average annual temperatures of >18 °C (64 °F). Factors accounting for this variation may include greater risk of viral infections, increased host susceptibility, and more time spent indoors, along with impact of temperature variation on lung function (Jenkins, et al. 2012). This effect was accompanied by variation in the treatment choices with antibiotics alone or in combination with steroids. A trend towards combined antibiotics and steroids was noted during winters. Ideal conditions for patients with COPD to minimize risk for exacerbation would be home humidity between 30% and 50% with indoor temperature of 21°C at least 9 hours per day in living areas (Osman, et al. 2008). Outdoor activities during extreme temperatures should be avoided. Air conditioning and/or humidifiers can be helpful in modifying influences.

References

Asthma/COPD, sepsis cardiomyopathy, and more....
inotropic support. (L’Heureux, Sternberg et al. 2020).

In patients who fail to improve with therapy, including a potential role for mechanical circulatory support, LV apical ballooning with preserved contractility of the basal segments. A movement toward a standard definition of SICM would allow a more rigorous evaluation of risk factors and future directions for therapy, including a potential role for mechanical circulatory support in patients who fail to improve with inotropic support.

Tarun Kapoor MD
Section Fellow-in-Training
Andrew Petrilli, MD
Guest Author

Looking for more information on sepsis? Visit CHEST’s Sepsis Topic Collection Page at chestnet.org/Topic-Collections/Sepsis for research, infographics, and more developed by the CHEST Sepsis Resources Steering Committee.

THORACIC ONCOLOGY AND CHEST IMAGING NETWORK
Lung Cancer Section
Environmental and occupational risk factors for lung cancer
Lung cancer is the third most prevalent cancer in United States, with the highest mortality (Oliver, 2022)(Siegel et al, 2023). The factors contributing to its occurrence have become more complex due to increased industrialization and worsening environmental pollution. Air pollution is a well-established environmental risk factor for lung cancer (Lu et al. 2019). On average, a full-time worker spends around 90,000 hours at work over their lifetime. It is crucial to control environmental and occupational exposures to decrease the risk of developing lung cancer. Occupations like asbestos-related work, mining, and transportation are well-known to be at risk for lung cancer (Li et al. 2021). With worsening air pollution, occupations such as firefighters, outdoor delivery workers, and forest rangers are facing an increased risk as well. Many of these carcinogens independently increase lung cancer risk (Li et al. 2021). Smoking combined with these exposures, causes a synergistic effect on lung cancer incidence. They also have a cell subtype differential risk favoring squamous and small cell lung cancer (Christiani, 2020). It is essential for workers in these high-risk occupations to use proper PPE, have regular check-ups and screenings and follow occupational safety regulations and guidelines. As air pollution continues to worsen, individuals living in these areas should reduce outdoor activities during AQI alerts, and use air purifiers and masks. Public health efforts to decrease air pollution with cleaner transportation and energy production, and better local and national air quality regulations will decrease risk in the general population (Rice et al. 2021).

Amaraja Kanitkar, MD, MBBS
Guest Author

References


Are you ready for CHEST 2023 in Hawai‘i?

just a few weeks ahead of CHEST 2023, we’re sharing the can’t-miss opportunities available on site at the meeting.

With double the abstract submissions of previous meetings, CHEST 2023 – taking place October 8 to 11 in Honolulu – will offer the highest caliber of educational content covering pulmonary, critical care, and sleep medicine. Beyond the top-tier education, CHEST 2023 has a lot to offer attendees in the way of networking, development, and unique experiences that will all make for a memorable meeting.

We’re sharing a preview of the many opportunities that will be available over the 4 days of the meeting. For more specifics on these events, including locations, scan the QR code to visit the CHEST 2023 website. You can also download the CHEST 2023 mobile app, which will be available in mid-September.

Networking and development

• For those who want to get more involved with the CHEST community, the Networks Mixer (Monday, October 9, 4 PM HST) is open to all who would like to learn more about the seven CHEST Networks and the 21 clinically-focused Sections within them.

• The annual Women in Chest Medicine Luncheon (Monday, October 9, 12:45 PM HST) will feature a panel of three women speaking about their experiences, their advice, how to support other women in the field, and more. This event is free, but preregistration is required.

• The first-ever Ohana Mixer (Tuesday, October 10, 6 PM HST) is an opportunity for CHEST attendees to celebrate the spirit of community that unites us across our differences. Attendees can network with each other, meet the members of our newly formed Interest Groups – including the leaders of our Women in Chest Medicine Interest Group and Respiratory Care Interest Group – and socialize with presenters from our three local CHEST Community Connections organizations.

• The Trainee Lounge will feature activities like speed mentoring, a lunch and learn with the Keynote Speaker, Dr. Cedric “Jamie” Rutland, financial wellness presentations, and more.

CHEST experiences

• The Opening Session (Sunday, October 8, 3:15 PM HST) will showcase traditional Hawaiian performances and the Keynote Address from Dr. Rutland. Immediately following, the CHEST Welcome Reception will feature live music and a traditional Hawaiian luau.

• For the second year, CHEST After Hours (Monday, October 9, 3 PM HST) will feature clinicians sharing stories of their personal triumphs, tribulations, and more experiences within medicine.

• Each year, the CHEST Challenge Championship (Tuesday, October 10, 7 PM HST) gives pulmonary and critical care medicine fellows-in-training an opportunity to compete in a live Jeopardy-style game – with bragging rights and cash prizes on the line.

• The Wellness Zone has a packed schedule of events, including beachy workouts, food demonstrations, meditation, and more.

Exhibit hall activities

• Opportunities to network with and hear presentations from local Hawaiian organizations, such as the Waianae Coast Comprehensive Health Center

• Hands-on, experiential education escape rooms

• Live educational games, including Hocus POCUS Diagnosis, PulmMemory, Peer Pressure, and more

• Simulation experiences, including Aspirated POCUS Diagnosis, PulmMemory, Peer Pressure, and more

Mark your calendars now to participate in all that CHEST 2023 has to offer. We’ll see you in Hawai‘i!

CHEST SEEK releases key points feature and new print edition

two exciting updates have come to the CHEST SEEK® portfolio this summer.

The latest book, CHEST SEEK® Pulmonary Medicine: 33rd Edition, was released in August. And in this newest book and certain CHEST SEEK Library collections, a feature called key points is included in the recently published 150 pulmonary medicine questions.

Key points are concise summaries of the most important takeaways of SEEK questions. Knowing the key point can help learners focus their studies.

“SEEK questions can be quite robust and intentionally detailed in their response as to why the answer options are correct or incorrect. But because of the level of detail, it can be difficult at times for the learner to correctly hone in on the author’s teaching point,” said CHEST Director, Product Strategy and Evaluation, Martha Zaborowski Pascale, CPM.

“Key points concisely summarize each question’s most important details, potentially saving the learner study time.”

CHEST SEEK® Pulmonary Medicine: 33rd Edition was developed from the pulmonary medicine board subspecialty examination content blueprints. It tests recall, interpretation, and problem-solving skills. Rationales provide thorough explanations and reasoning for the correct and incorrect answers. Key points are easy to find at the bottom of the pages and in a tab within SEEK Library questions.

For 3 decades, SEEK has been a trusted resource for chest medicine clinicians. From a printed booklet to the classic book and subscription-based library, learners have engaged with case-based questions in multiple ways. As SEEK has transformed through the years, it’s continued to be a timeless, reliable study partner.

“SEEK has evolved in many ways over its 30-year history. As technologic involvement has permitted greater advances in imaging and data presentation, SEEK has sought to make such advances from the bedside as part of the SEEK experience,” said Pascale.

“The strength of peer-reviewed, expert-written content has remained the same, but modalities such as digital flash cards and behind-the-scenes peer review discussions have enhanced this enduring product in ways that help it stand the test of time.”

Based on CHEST evaluation data, more than 90% of SEEK learners said their practice will change based on content found in the library. Plus, more than 95% of SEEK learners agreed that SEEK question authors are effective instructors.

“The success of SEEK in the past and the ability of this tool to be adapted to the changing needs of learners makes one excited about the editions to come,” said Jesse B. Hall, MD, FCCP, SEEK Editor-in-Chief and Chair of CHEST SEEK® Pulmonary Medicine: 33rd Edition. Looking toward the future, SEEK will continue to develop and serve the needs of chest medicine clinicians.

“One of the joys of our professional lives is the constant new discoveries and trials that change the way we practice,” said SEEK Pulmonary Medicine Vice-Chair and Deputy Editor, Jess Mandel, MD.

“However, with this comes the challenge of keeping up and staying current as the field evolves. SEEK is a terrific resource for keeping up with changes in practice and the underlying data that justify them.”

Subscribe to the SEEK Library and find CHEST SEEK® Pulmonary Medicine: 33rd Edition at chestnet.org/Learning-and-Events/Learning/Seek-App or by scanning the QR code at left.
This advertisement is not available for the digital edition.
COPD

LAMA-LABA surpasses corticosteroid combination

BY HEIDI SPLETE
MDedge News

Use of inhalers with long-acting muscarinic antagonists and long-acting beta-agonists reduced COPD exacerbations and pneumonia hospitalizations compared with inhalers with corticosteroids and long-acting beta-agonists (LABAs), based on data from more than 30,000 individuals.

Current guidelines for COPD patients recommend inhalers with long-acting muscarinic antagonists (LAMAs) and LABAs over those with inhaled corticosteroids (ICSs) and LABAs, but data comparing the two formulations have been inconsistent, wrote William B. Feldman, MD, of Brigham and Women’s Hospital, Boston, and colleagues.

In a study published in JAMA Internal Medicine (2023;183[7]:685-95), the researchers reviewed data from a commercial insurance claims database of individuals diagnosed with COPD who filled a new prescription for a LAMA-LABA inhaler or ICS-LABA inhaler between Jan. 1, 2014, and Dec. 31, 2019. Patients with asthma and those younger than 40 years were excluded. The study population included 137,833 individuals with a mean age of 70.2 years; 50.4% were female. Of the 107,004 ICS-LABA users and 30,829 LAMA-LABA users, 30,216 matched pairs were included in a 1:1 propensity score–matched study. The primary outcomes were effectiveness, based on the rate of first moderate or severe COPD exacerbation, and safety, based on the rate of first pneumonia hospitalization.

Use of LAMA-LABA inhalers was associated with an 8% reduction in the rate of first moderate or severe COPD exacerbation and a 20% reduction in the rate of first pneumonia hospitalization compared with use of ICS-LABA (hazard ratios 0.92 and 0.80, respectively). The absolute rate reductions with LAMA-LABA inhalers for first moderate or severe COPD exacerbations and for first pneumonia hospitalizations were 43.0 events per 1,000 person-years and 91.8 events per person-years, respectively.

The overall rates of total moderate to severe COPD and pneumonia hospitalizations were 5% and 17% lower, respectively, among patients who used LAMA-LABA than those treated with ICS-LABA. The results were consistently robust in subgroup and sensitivity analyses, the researchers wrote in their discussion. However, the results must be interpreted cautiously in comparison to other large studies because of the significant differences in the cohorts of patients studied, notably that most patients in the current study had not received previous inhaler therapy.

The study findings were limited by several factors including the relatively short follow-up time and reliance on prescription fills as an indicator of medication use, the researchers noted. Other limitations included notable differences between the LAMA-LABA patients and ICS-LABA patients, such as...
therapy for COPD patients, the researchers concluded. 

"This study was required to provide clarity regarding the optimal choice of treatment for COPD given conflicting data from other recent trials," Suman Pal, MBBS, of the University of New Mexico, Albuquerque, said in an interview. 

"The study findings reinforce the benefits of combined LAMA-LABA in improving clinical outcomes in COPD in a real-world setting," and the data provide further support for choosing LAMA-LABA over ICS-LABA in COPD patients, said Dr. Pal, who was not involved in the study. Availability and affordability of LAMA-LABA inhalers may be barriers to expanding their use in clinical practice, he noted.

Dr. Feldman disclosed fees from Alosa Health and Aetion and serving as an expert witness in litigation against inhaler manufacturers. Dr. Pal had no financial conflicts to disclose.
Sometimes we get what we pay for. Other times we pay too much. That's the message of a study published in Annals of Internal Medicine (2023 Aug 8. doi: 10.7326/M23-0615), which finds that a generic maintenance inhaler is as effective at managing symptoms of chronic obstructive pulmonary disorder (COPD) as a pricier branded alternative. In 2019, the U.S. Food and Drug Administration approved Wixela Inhub (the combination corticosteroid/long-acting beta2 adrenergic agonist fluticasone-salmeterol; Viatris) as a generic dry-powder inhaler for managing symptoms of COPD. This approval was based on evidence of the generic's effectiveness against asthma, although COPD also was on the product label.
The study authors compared Wixela’s effectiveness in controlling symptoms of COPD with that of the brand name inhaler Advair Diskus (fluticasone-salmeterol; GlaxoSmithKline), which uses the same active ingredients.

The result: “The generic looks to be as safe and effective as the brand name. I don’t see a clinical reason why one would ever need to get the brand name over the generic version,” said study author William Feldman, MD, DPhil, MPH, a health services researcher and pulmonologist at Harvard Medical School and Brigham and Women’s Hospital, both in Boston. Dr. Feldman and colleagues compared the records of 10,000 patients with COPD who began using the branded inhaler to the records of another 10,000 patients with COPD who opted for the generic alternative.

Participants in the two groups were evenly matched by age, sex, race, and ethnicity, region, severity of COPD, and presence of other comorbidities, according to the researchers.

Participants were all older than age 40. The average age in both groups was 72 years.

The researchers looked for a difference in a first episode of a moderate exacerbation of COPD, defined as requiring a course of prednisone for 5-14 days. They also looked for cases of severe COPD exacerbation requiring hospitalization in the year after people began using either the generic or brand name inhaler. And they looked for differences across 1 year in rates of hospitalization for pneumonia.

For none of those outcomes, however, did the type of inhaler appear to matter. Compared with the brand-name drug, using the generic was associated with nearly identical rates of moderate or severe COPD exacerbation (hazard ratio, 0.97; 95% confidence interval, 0.90-1.04. The same was true for the proportion of people who went to the hospital for pneumonia at least once (HR, 0.99; 95% CI, 0.86-1.15).

As a general matter, having a single generic competitor will not lower costs much, Dr. Feldman noted, pointing to 2017 research from Harvard that found a profusion of generic competitors is needed to significantly lower health care costs (N Engl J Med. 2017;377:2597-8). “I don’t want to in any way underestimate the importance of getting that first generic onto the market, because it sets the stage for future generics,” he added.

“There are very few generic options for patients with COPD,” said Surya Bhatt, MD, director of the Pulmonary Function and Exercise Physiology Lab at the University of Alabama at Birmingham.

“The results are quite compelling,” said Dr. Bhatt, who was not involved in the research. Dr. Bhatt noted that the FDA’s 2019 approval – given that the agency requires bioequivalence studies between branded and generic products – was enough to cause him to begin prescribing the generic inhaler.

The fact that this approval was based on asthma but not also COPD is not a concern.

“There are so many similarities between asthma, COPD, and some obstructive lung diseases,” Dr. Bhatt noted.

Dr. Feldman reported funding from Arnold Ventures, the Commonwealth Fund, and consulting relationships with Alosa Health and Aetion. Dr. Bhatt reported having no conflicts.
Study suggests protective role for vitamin D

BY WALTER ALEXANDER
MDedge News

A potentially protective role for vitamin D in the pathogenesis of chronic obstructive pulmonary disease (COPD) is suggested by the finding that serum 25-hydroxyvitamin D (25(OH)D) concentrations are inversely associated with COPD incidence and mortality. COPD risk was 23% higher in people within the lowest quintile vs. the fourth quintile of 25(OH)D concentrations, according to research appearing in BMJ Open Respiratory Research (2023 Jun 23. doi: 10.1136/bmjresp-2023-001684).

While low vitamin D status has been linked to increased inflammatory diseases risk and to the regulation of pathogenic mechanisms in COPD, epidemiological evidence regarding the associations of 25(OH)D concentrations with COPD incidence and survival remains inconclusive, Zheng Zhu, MD, of Jiangsu Provincial Center for Disease Control and Prevention, Nanjing, China, and colleagues wrote.

From UK Biobank data recorded from 403,648 participants (mean age 56.4 years; 54% women) who were free of COPD at baseline and had 25(OH)D measurements, researchers estimated hazard ratios and 95% confidence intervals for the associations of 25(OH)D concentrations with COPD risk and survival. After median follow-up of 12.3 years (ending Sept. 30, 2021), with 11,008 COPD cases recorded, beyond the COPD and mortality increase (HR, 1.23; 95% CI, 1.16-1.31) in the lowest quintile of 25(OH)D concentrations, risk for overall death was 38% higher, as well (HR, 1.38; 95% CI, 1.22-1.56). Serum concentrations were greater than 64.6 nmol/L in the highest (quintile 5) and less than 31.7 nmol/L in the lowest (quintile 1). Also, men and current smokers had higher COPD and mortality risk (P interaction for both: < .05).

While event rates tracked generally inversely with 25(OH)D concentrations, overall the event curves were non-linear. Dr Zhu and associates reported that the decreasing risk of COPD appeared to be lowest at 55 nmol/L of 25(OH)D within quintile 4 (51.8 to < 64.6 nmol/L). Furthermore, lower prediagnostic 25(OH)D concentrations were associated with a significant decrease in overall and COPD-specific survival.

Smoking is the most commonly encountered risk factor for COPD, the researchers noted, and their findings indicated that 25(OH)D concentrations were inversely associated with COPD risk in both smokers and never-smokers. In a fully adjusted model, compared with quintile 4, the quintile 1 increase in COPD risk was 25% in never-smokers and 23% in smokers.

“Our findings imply that vitamin D might play a role in progression of COPD,” the authors stated. They added, “Whether lower concentrations of 25(OH)D are causal or contributory to COPD risk may spur future long-duration and large-scale RCTs.”

“Vitamin D has an important function in the immune system and lower serum levels have been implicated in a variety of inflammatory diseases,” commented associate professor of medicine Diego J. Maselli, MD, FCCP, who is chief of the division of pulmonary diseases & critical care at UT Health San Antonio and a member of the CHEST Physician Editorial Board.

“Patients with COPD often have lower levels of vitamin D compared to healthy individuals. COPD patients with low serum levels of vitamin D may have a higher risk of exacerbations and worse lung function.”

He added, “The research by Zhu and colleagues adds to the field of study and highlights the potential role of vitamin D in the pathophysiology of COPD. It is important to remember that these associations do not establish causality, as patients with chronic and debilitating diseases may have limited sunlight exposure, poor nutritional intake, and other behaviors that may affect vitamin D levels. There are mixed results in studies evaluating the role of supplementing vitamin D in COPD with regards to disease progression and exacerbation reduction. While there are some studies that report that supplementation of vitamin D can reduce COPD exacerbations, there is still a need for randomized controlled studies that explore if the supplementation of vitamin D can prevent the development of COPD, particularly in those who actively smoke. Yet, it is reasonable to evaluate the serum vitamin D levels in COPD patients who have had exacerbations and supplement when there is a severe deficiency.”

No disclosures were reported by Dr. Zhu or by Dr. Maselli.

COPD plus PRISm may promote frailty progression

BY HEIDI SPLITZ
FROM THE JOURNAL CHEST® • Chronic obstructive pulmonary disease and a new phenotype of lung function impairment predicted progression of frailty in older adults, based on data from more than 5,000 individuals.

Longitudinal data on the association of COPD with progression of frailty are limited, as are data on the potential association of preserved ratio impaired spirometry (PRISm) with frailty progression, wrote Di He, BS, of Zhejiang University, China, and colleagues.

PRISm has been defined in recent studies as “proportional impairments in FEV₁ and FVC, resulting in the normal ratio of FEV₁ and [FVC].” Individuals with PRISm may transition to normal spirometry or COPD over time, the researchers wrote.

In a study published in the journal CHEST (2023 Jul 20. doi: 10.1016/j.chest.2023.07.020), the researchers reviewed data from 5,901 adults aged 50 years and older who were participating on the English Longitudinal Study of Ageing (ELSA), a prospective cohort study. Of these, 3,765 were included in an additional analysis of the association between transitions from normal spirometry to PRISm and the progression of frailty. The mean age of the participants was 65.5 years; 54.9% were women.

The median follow-up period for analysis with frailty progression was 9.5 years for PRISm and COPD and 5.8 years for PRISm transitions. Lung function data were collected at baseline. Based on spirometry data, participants were divided into three lung function groups – normal spirometry, PRISm, and COPD – and each of these was classified based on severity. Frailty was assessed using the frailty index (FI) during the follow-up period.

Frailty progression based on FI was significantly accelerated in patients with PRISm and COPD, compared with individuals with normal spirometry, with additional annual increases of 0.301 and 0.172, respectively (P < .001 for both).

When stratified by severity, individuals with more severe PRISm and with more COPD had higher baseline FI and faster FI progression, compared with those with mild PRISm and COPD.

PRISm transitions were assessed over a 4-year interval at the start of the ELSA. Individuals with normal spirometry who transitioned to PRISm during the study had accelerated progression of frailty, as did those with COPD who transitioned to PRISm. However, no significant frailty progression occurred in those who changed from PRISm to normal spirometry.

The mechanisms behind the associations of PRISm and COPD with frailty remain unclear, but the results were consistent after controlling for multiple confounders, “suggesting PRISm and COPD had independent pathophysiological mechanisms for frailty,” the researchers write in their discussion. Other recent studies have identified sarcopenia as a complication for individuals with lung function impairment, they noted. “Therefore, another plausible explanation could be that PRISm and COPD caused sarcopenia, which accelerated frailty progression,” they say.

The findings were limited by several factors, including the observational design and the potential underestimation of lung function in participants with reversible airflow obstruction because of the use of prebronchodilator spirometry in the cohort study, the researchers noted.

However, the results were strengthened by the large sample size and high-quality data from the ELSA, as well as by the repeat measures of FI and lung function. The results were consistent after controlling for multiple confounders, and support the need for more research to explore the causality behind the association of PRISm and COPD with frailty, the researchers concluded.

The researchers reported having no relevant financial relationships.
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AI scribes: Just how good are they?

LORRAINE L. JANECZKO, MPH

A ndrea Partida, DO, an obste-
trician and gynecologist in
Enid, Okla., loves her new
assistant.

The 15 or 20 minutes she used to
spend on documentation for each
patient visit is now 3. The 2-3 hours
she’d spend charting outside clinic
hours is maybe 1.

All that time saved allows her to
see two to five more patients a day,
provide better care to each patient,
and get more involved in hospital
leadership at Integris Health, where
she works.

“I have a better work-life balance
with my family,” Dr. Partida said. “I
leave work at work and get home
earlier.”

You’ve probably figured out the
plot twist: Dr. Partida’s assistant is
not a person – it’s artificial intelli-
gence (AI).

Dr. Partida uses IRIS, a tool from
OnPoint Healthcare Partners, part
of a fast-growing niche of AI med-
ical scribes designed to automate
onerous data entry. The evolution
of generative AI – specifically, large
language models, such as ChatGPT
– has led to a rapid explosion of
these tools. Other companies in the
space include Abridge, Ambience
Healthcare, Augmedix, DeepScribe,
Nuance (part of Microsoft), and
Suki. The newest kid on the block,
Amazon Web Services, announced
the launch of HealthScribe in July.

These tools – some of which are
already on the market, with more on
the way – record patient visits and
generate notes for treatment and
billing. Earlier iterations combine
AI with offsite human scribes who
provide quality control. But more
and more are fully automated: no human
required. Some also offer video
recording and foreign language
translation.

The promise is alluring: Ease your
workload and reclaim hours in your
day so you can spend more time
with patients or try that “work-life
balance” thing you’ve heard so much
about.

But do these tools fulfill that
promise?

According to Dr. Partida and
other doctors who spoke with this
news organization, the answer is a
resounding yes.

A tech solution for a tech problem

“I believe a lot of doctors see
patients for free. They get paid to
do paperwork,” said Anthony J.
Mazzarelli, MD, JD, MBE, co-presi-
dent and CEO of Cooper University
Health Care, in Camden, N.J.

Indeed, for every hour U.S. cli-
nicians spend with their patients,
they may spend 2 more hours docu-
menting in electronic health records
(EHRs), estimates show. About half

“I think within a matter of 2 or 3
years, these tools will be pervasive
throughout health care.”

Since introducing these tools at
Cooper, “our doctors’ paperwork
burden is significantly lighter,” said
Dr. Mazzarelli, who decides which
 technologies Cooper should invest
in and who monitors their results.

What’s it like to use an AI medical scribe?

The scribes feature hardware (typ-
ically a smartphone or tablet) and
software built on automatic speech
recognition, natural language pro-
cessing, and machine learning.

Download an app to your device,
and you’re ready to go. Use it to
record in-person or telehealth visits.

In the first week, a company may
help train you to use the hardware
and software. You’ll likely start by
using it for a few patient visits per
day, ramping up gradually. Dr. Par-
tida said she was comfortable using
the system for all her patients in 6
weeks.

Each day, Dr. Partida logs in to
a dedicated smartphone or tablet,
opens the app, and reviews her
schedule, including details she needs
to prepare for each patient.

At the start of each patient visit,
Dr. Partida taps the app icon to
begin recording and lays the device
nearby. She can pause as needed. At
the end of the visit, she taps the icon
again to stop recording.

The AI listens, creates the note,
and updates relevant data in the
EHR. The note includes patient
problems, assessment, treatment
plan, patient history, orders, and
tasks for staff, along with medica-
tions, referrals, and preauthoriza-
tions. A human scribe, who is also a
physician, reviews the information
for accuracy and edits it as needed.

By the next morning, the data are
ready for Dr. Partida to review.

Fully automated versions can
generate notes much faster. Jack
Shilling, MD, MBA, an orthope-
dic surgeon at Cooper University
Health Care, in Voorhees, N.J., uses
DAX. A new feature called DAX
Express – which uses OpenAI’s
GPT-4 but no humans – provides
him with a draft of his clinical notes
in just seconds.
How accurate are AI notes?
The accuracy of those notes remains an open question, Dr. Garcia said – mostly because accuracy can be hard to define.

“If you asked five docs to write a note based on the same patient encounter, you’d get five different notes,” Dr. Garcia said. “That makes it hard to assess these technologies in a scientifically rigorous way.”

Still, the onus is on the physician to review the notes and edit them as needed, Dr. Garcia said. How light or heavy those edits are can depend on your unique preferences.

Dr. Shilling said he may need to lightly edit transcripts of his conversations with patients. “When someone tells me how long their knee hurts, slight variability in their transcribed words is tolerable,” he said. But for some things – such as physical exam notes and x-ray readings – he dictates directly into the device, speaking at a closer range and being less conversational, more exact in his speech.

Should you let patients know they’re being recorded?
The federal Health Insurance Portability and Accountability Act (HIPAA) does not require providers to inform patients that their face-to-face conversations are being recorded, said Daniel Lebovic, JD, corporate legal counsel at Compliance Group, in Greenlawn, N.Y., a company that helps providers adhere to HIPAA rules.

But make sure you know the laws in your state and the policies at your health care practice. State laws may require providers to inform patients and to get patients’ consent in advance of being recorded.

All the doctors who spoke to this news organization said their patients are informed that they’ll be recorded and that they can opt out if they wish.

How much do AI scribes cost?
As the marketplace for these tools expands, companies are offering more products and services at different price points that target a range of organizations, from large health care systems to small private practices.

Price models vary, said Dr. Garcia. Some are based on the number of users, others on the number of notes, and still others on minutes. Amazon’s HealthScribe is priced at 10 cents per minute. For 1,000 consultation transcripts per month, with each call averaging 15 minutes, it would take 15,000 minutes at a total cost of $1,500 for the month.

In general, the rapidly growing competition in this space could mean prices become more affordable, Dr. Garcia said. “It’s good that so many are getting into this game, because that means the price will come down and it will be a lot more accessible to everybody.”

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