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THE NEWSPAPER OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS



Corinne R. Young, MSN, FNP-C, FCCP, is founder and president of the Association of Pulmonary Advanced Practice Providers.

## Advanced practice providers – an evolving pulmonary medicine role

BY CHRISTINE KILGORE  
*MDedge News*

**T**he integration of advanced practice providers (APPs) into pulmonology practice is in flux and deepening across numerous settings, from outpatient clinics to intensive care and inpatient pulmonary consult services – and as it evolves, so do training issues.

Some institutions are developing pulmonary fellowship programs for APPs. This is a good indication that team-based pulmonology may be moving toward a time in the future when nurse practitioners (NPs) and physician assistants (PAs) join pulmonologists in practice after having undergone formal education in the

subspecialty, rather than learning solely on the job from dedicated mentors.

Neither NPs nor PAs, who compose almost all of the APP workforce in pulmonology, currently have a pulmonary tract for training. “Weight falls on the employer’s shoulders to train and educate their APPs,” said Corinne R. Young, MSN, FNP-C, FCCP, director of APP and clinical services at Colorado Springs Pulmonary Consultants and founder and president of the Association of Pulmonary Advanced Practice Providers (APAPP), which launched in 2018.

The role and scope of practice of these providers are determined not only by state policies and regulations – and by their prior experience,

**PROVIDERS** // *continued on page 4*

## OSA overlap impairs functional performance in COPD

BY HEIDI SPLETE  
*MDedge News*

**O**bststructive sleep apnea (OSA) was associated with both impaired functional performance during exercise and overall worse outcomes in patients with chronic obstructive pulmonary disease (COPD), based on data from 34 adults.

Individuals with COPD are at increased risk for hospital readmissions and disease exacerbations, Patricia Faria Camargo, PhD, of Federal University of São Carlos (Brazil), and colleagues wrote. These patients often have concomitant OSA, which itself can promote adverse cardiovascular events, but the impact of the overlap of these two conditions on clinical outcomes has not been explored.

In a study published in *Heart & Lung* (2022 Oct 28. doi: 10.1016/j.hrtlng.2022.10.007), the researchers recruited 17 adults with COPD only and 17 with OSA and COPD. At baseline, patients underwent pulmonary function tests,

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knowledge, and motivation – but by “how much work a practice puts into [education and training],” she said.

An estimated 3,000-8,000 APPs are working in pulmonology, according to an analysis done by a marketing agency that has worked for the American College of Chest Physicians, Ms. Young said.

A 2021 APAPP survey of its several hundred members at the time showed them

working in hospital systems (41%), private practice (28%), university systems (10%), and other health care systems (21%). They indicated practicing in pulmonary

medicine, sleep medicine, or critical care – or some combination of these areas – and the vast majority (82%) were seeing both new and established patients in their roles.

“Nobody knows exactly how many of us are out there,” Ms. Young said. “But CHEST and APAPP are making great efforts to be beacons to APPs working in this realm and to bring them together to have a voice.”

The APAPP wants to “close the education gap” and to “eventually develop a certification program to vet our knowledge in this area,” she said. “Right now, the closest we can get to vetting our knowledge is to become an FCCP through CHEST.”

### Earning trust, seeking training

Omar Hussain, DO, has been practicing with an NP for over a decade in his role as an intensivist and knows what it’s like to train, supervise, and grow together. He and his private practice colleagues have a contract with Advocate Condell Hospital in Libertyville, Ill., to cover its ICU, and they hired their NP primarily to help care for shorter-stay, non-critically ill patients in the ICU (for example, patients receiving postoperative monitoring).

The NP has been invaluable. “We literally sit next to each other and in the mornings we make a game plan of which patients she will tackle first and which ones I’ll see first,” Dr. Hussain said. “When we’re called by the nurse for an ICU evaluation [on the floor], we’ll decide in real time who goes.”

The NP ensures that all guidelines and quality measures are followed in the ICU and, with a Monday-Friday schedule, she provides

valuable continuity when there are handoffs from one intensivist to another, said Dr. Hussain, who serves as cochair of the Joint CHEST/American Thoracic Society Clinical Practice Committee, which deals with issues of physician-APP collaboration.

After working collaboratively for some time, Dr. Hussain and his partners decided to teach the NP how to intubate. It was a thoughtful

*“Nobody knows exactly how many of us are out there. But CHEST and APAPP are making great efforts to be beacons to APPs working in this realm and to bring them together to have a voice.”*

and deliberate process, and “we used the same kind of mindset we’ve used when we’ve supervised residents at other institutions,” he said.

Dr. Hussain and his partners have been fortunate in having such a long-term relationship with an APP. Their NP had worked as a nurse in the ICU before training as an adult gerontology-acute care NP and joining Dr. Hussain’s practice, so she was also “well known to us.”

Rachel Adney, CPNP-PC, a certified pediatric NP in the division of pediatric pulmonology at Stanford (Calif.) Medicine Children’s Health,



Ms. Adney

is an APP who actively sought advanced training. She joined Stanford in 2011 to provide ambulatory care, primarily, and having years of prior experience in asthma management and

education, she fast became known as “the asthma person.” After a physician colleague one day objected to her caring for a patient without asthma, Ms. Adney, the first APP in the division, approached John D. Mark, MD, program director of the pediatric fellowship program at Stanford, and inquired about training “so I could have more breadth and depth across the whole pulmonary milieu.”

Together they designed a “mini pediatric pulmonary fellowship” for Ms. Adney, incorporating elements of the first year of Stanford’s pediatric fellowship program as

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Angel Coz, MD, FCCP, is Editor in Chief of CHEST Physician.

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well as training materials from the University of Arizona's Pediatric Pulmonary Center, Tucson, one of six federally funded PCCs that train various health care providers to care for pediatric patients with chronic pulmonary conditions (<https://mchb.hrsa.gov/training/projects.asp?program=15>). (Dr. Mark had previously been an educator at the center while serving on the University of Arizona faculty.)

Ms. Adney's curriculum consisted of 1,000 total hours of training, including 125 hours of didactic learning and 400 hours of inpatient and outpatient clinical training in areas such as cystic fibrosis, sleep medicine, bronchopulmonary dysplasia (BPD), neuromuscular disorders, and general pulmonary medicine. "Rachel rotated through clinics, first as an observer, then as a trainee ... and she attended lectures that my fellows attended," said Dr. Mark, who has long been a preceptor for APPs. "She became like a 1-year fellow in my division."

Today, Ms. Adney sees patients independently in four outreach clinics along California's central coast. "She sees very complicated pediatric pulmonary patients now" overall, and has become integral to Stanford's interdisciplinary CRIB (cardiac and respiratory care for infants with BPD) program, Dr. Mark said. "She follows these patients at Stanford along with the whole CRIB group, then sees them on her own for follow-up."

As a result of her training, Ms. Adney said, "knowing that I have the knowledge and experience to take on more complex patients, my colleagues now trust me and are confident in my skills. They feel comfortable sending [patients] to me much earlier. ... And they know that if there's something I need help with I will go to them instantly."

Pulmonology "really spoke to my heart," she said, recalling her pre-Stanford journey as an in-hospital medical-surgical nurse, and then, after her NP training, as an outpatient primary care PNP. "For the most part, it's like putting a puzzle together, and being able to really impact the quality of life these patients have," said Ms. Adney, who serves on the APAPP's pediatric subcommittee.

It's clear, Dr. Mark said, that "things are changing around the country" with increasing institutional interest in developing formal APP specialty training programs. "There's no way [for an APP] to walk into a specialty and play an active role without additional

training," and institutions are frustrated with turnover and the loss of APPs who decide after 6-9 months of on-the-job training that they're not interested in the field.

Stanford Medicine Children's Health, in fact, has launched an internal Pediatric APP Fellowship Program that is training its first cohort of six newly graduated NPs and PAs in two clinical



Dr. Mark

tracks, including a medical/surgical track that incorporates rotations in pulmonary medicine, said Raji Koppolu, CPNP-PC/AC, manager of advanced practice professional development for Stanford Medicine Children's Health.

APP fellowship programs have been in existence since 2007 in a variety of clinical settings, she said, but more institutions are developing them as a way of recruiting and retaining APPs in areas of high need and of equipping them for successful transitions to their APP roles. Various national bodies accredit APP fellowship programs.

Most pulmonary fellowship programs, Ms. Young said, are also internal programs providing postgraduate education to their own newly hired APPs or recent NP/PA graduates. This limits their reach, but "it's a step in the right direction toward standardizing education for pulmonary APPs."

### Defining APP competencies

In interventional pulmonology, training may soon be guided by newly defined "core clinical competencies" for APPs. The soon-to-be published and distributed competencies – the first such national APP competencies in pulmonology – were developed by an APP Leadership Council within the American Association of Bronchology and Interventional Pulmonology (AABIP) and cover the most common disease processes and practices in IP, from COPD and bronchoscopic lung volume reduction to lung cancer screening.

Rebecca Priebe, ACNP-BC, who cochairs the AABIP's APP chapter, organized the effort several years ago, bringing together a group of APPs and physician experts in

advanced bronchoscopy and IP (some but not all of whom have worked with APPs), after fielding questions from pulmonologists at AABIP meetings about what to look for in an AAP and how to train them.

Physicians and institutions who are hiring and training APPs for IP can use any or all of the 11 core competencies to personalize and

*It's clear that "things are changing around the country" with increasing institutional interest in developing formal APP specialty training programs.*

evaluate the training process for each APP's needs, she said. "Someone looking to hire an APP for pleural disease, for instance, can pull up the content on plural effusion."

APP interest in interventional pulmonology is growing rapidly, Ms. Priebe said, noting growth in the AABIP's APP chapter from about 7-8 APPs 5 years ago to at least 60 currently.



Ms. Priebe

their inpatient pleural disease service and a bronchoscopic lung volume-reduction program.

For the inpatient IP service, after several months of side-by-side training with an IP fellow and attending physicians, she began independently evaluating new patients, writing notes, and making recommendations.

For patients with pleural disease, she performs ultrasound examinations, chest tube insertions, and bedside thoracentesis independently. And for the bronchoscopic lung volume-reduction program, she evaluates patients for candidate status, participates in valve placement, and sees patients independently through a year of follow-up.

"Physician colleagues often aren't sure what an APP's education and scope of practice is," said Ms. Priebe, who was an ICU nurse before training as an acute care NP and then worked first with a private practice

inpatient service and then with the University of Michigan, Ann Arbor, where she established and grew an APP-run program managing lung transplant patients and a step-down ICU unit.

"It's a matter of knowing [your state's policies], treating them like a fellow you would train, and then using them to the fullest extent of their education and training. If they're given an opportunity to learn a subspecialty skill set, they can be an asset to any pulmonary program."

### 'We're here to support,' not replace

In her own practice, Ms. Young is one of seven APPs who work with nine physicians on a full range of inpatient care, outpatient care, critical care, sleep medicine, and procedures. Many new patients are seen first by the APP, who does the workup and orders tests, and by the physician on a follow-up visit. Most patients needing routine management of asthma and COPD are seen by the physician every third or fourth visit, she said.

Ms. Young also directs a 24-hour in-house APP service recently established by the practice, and she participates in research. In a practice across town, she noted, APPs see mainly established patients and do not practice as autonomously as the state permits. "Part of that difference may [stem from] the lack of a standard of education and variable amounts of work the practice puts into their APPs."

The American Medical Association's #StopScopeCreep social media messaging feels divisive and "sheds a negative light on APPs working in any area," Ms. Young said. "One of the biggest things we want to convey [at APAPP] is that we're not here for [physicians'] jobs."

"We're here to support those who are practicing, to support underserved populations, and to help bridge gaps" created by an aging pulmonologist workforce and real and projected physician shortages, Ms. Young said, referring to a 2016 report from the Health Resources and Services Administration (<https://bhwh.hrsa.gov/sites/default/files/bureau-health-workforce/data-research/internal-medicine-subspecialty-report.pdf>) and a 2017 report from Merritt Hawkins indicating that 73% of U.S. pulmonologists (the largest percentage of all subspecialties) were at least 55 years old (<https://www.merrithawkins.com/uploadedFiles/mhwhitepaperspecialties2017.pdf>).

Dr. Hussain said he has "seen

# COPD care bundle curbs all-cause readmissions

BY HEIDI SPLETE

MDedge News

A multidisciplinary care bundle for chronic obstructive pulmonary disease (COPD) significantly reduced all-cause hospital readmissions at 30, 60, and 90 days, based on data from approximately 300 patients.

COPD remains a leading cause of mortality and a leading contributor to health care costs, but data suggest that adoption of an interdisciplinary care bundle

*Notably, pharmacists consulted with 68.5% of patients overall and assisted with access to outpatient medications for 45.7% of those in the care bundle arm.*

could reduce hospital readmission for COPD patients, Sibyl Cherian, PharmD, BCPS, of Overlook Medical Center, Summit, N.J., and colleagues wrote. The Centers for Medicare & Medicaid Services has introduced both penalties and bundled payments for hospitals with excess all-cause readmission rates after hospitalizations, but more data are needed on the ability of a COPD care bundle to reduce readmission for COPD.

In a study published in the *Journal of the American Pharmacists Association* (2022 Oct 10. doi: 10.1016/j.japh.2022.10.002), the researchers assigned 127 individuals with COPD to a COPD care bundle arm and 189 to a control arm for treatment at a single center. The standard of care group was admitted between Jan. 1 and Dec. 31, 2017; the COPD care bundle group was admitted between Jan. 1 and Dec. 31, 2018. The mean age of the participants across both groups was 72 years, and more than 70% of patients in each group were White. The COPD care bundle was managed by a team including pulmonologists, hospitalists, care managers, advanced practice nurses, pharmacists, respiratory care

practitioners, physical therapists, documentation specialists, quality improvement experts, social workers, and dietitians.

The primary outcome was 30-day all-cause readmission among adults with acute exacerbation of COPD.

Overall, the rate of 30-day all-cause readmissions was significantly lower in the COPD care bundle arm versus the control arm (11.8% vs. 21.7%;  $P = .017$ ). Similar differences appeared between the care bundle group and control group for all-cause readmissions at 60 days (8.7% vs. 18%;  $P = .013$ ) and 90 days (4.7% vs. 19.6%;  $P < .001$ ).

Reasons for reduced readmissions after implementation of the COPD care bundle included pulmonary follow-up appointments of 7 days or less, significantly increased physical therapy consultations, and significant escalation of COPD maintenance therapy, the researchers wrote.

Notably, pharmacists consulted with 68.5% of patients overall and assisted with access to outpatient medications for 45.7% of those in the care bundle arm, the researchers wrote. Patients in the COPD care bundle group were significantly more likely to have an escalation in maintenance therapy versus the control patients (44.9% vs. 22.2%;  $P < .001$ ), which illustrates the importance of interventions by pharmacists in escalating therapy to reduce readmissions.

The study findings were limited by several factors including the retrospective design and use of data from a single center, the researchers noted. Other limitations included the lack of data on the need for therapy escalation in the control group and the lack of controlling for socioeconomic status, which is a known risk factor for hospital readmission.

However, the results support the value of a COPD care bundle for reducing readmissions, and that such a bundle can be replicated at other hospitals, although more research is needed to evaluate the impact of other COPD care strategies, they emphasized.

The study received no outside funding. The researchers had no financial conflicts to disclose. ■

## OSA AND COPD // continued from page 1

echocardiography, and polysomnography to confirm their OSA and COPD diagnoses.

The primary endpoint was the impact of OSA on functional performance and cardiac autonomic control in COPD patients, based on measures of heart rate variability and the 6-minute walk test (6MWT). Participants were followed for 1 year, with telephone contacts every 3 months. A secondary endpoint was the number of exacerbations, hospitalizations, and deaths. At baseline, OSA-COPD patients had worse polysomnographic function, compared with COPD patients; they also tended to be older and have higher body mass index, but other demographics were similar between the groups.

Overall, patients in the OSA-COPD group had significantly greater functional impairment, compared with the COPD group ( $P = .003$ ), as measured by the 6MWT. The OSA-COPD patients also showed significantly worse autonomic response during exercise, compared with the COPD group.

A lower work load during exercise and the interaction between group and time factors suggests that OSA impacts the exercise capacity of COPD patients, the researchers said. Notably, however, neither age nor body mass index was associated

with functional performance in the OSA-COPD group.

Patients in the OSA-COPD group also were significantly more likely to experience exacerbations during the study period, compared with the COPD-only group (67.4% vs. 23.5;  $P = .03$ ). However, the severity of COPD was similar between the groups, which further illustrates that OSA can impair functional performance in COPD patients, the researchers said.

The findings were limited by several factors including the small sample size and restricted collection of follow-up data during the pandemic, the researchers noted. However, the results support previous studies, and suggest that overlapping OSA and COPD produces worse outcomes.

“Future studies can confirm our findings, providing new clinical evidences to the assessment of sleep quality in COPD patients and its implications for the general health status of these individuals. In addition to contributing to more assertive clinical and therapeutic alternative support, [there is] the need for more research into the mechanisms behind this overlap in larger samples to develop treatment alternatives,” they concluded.

The study was supported by the Federal University of São Carlos. The researchers had no financial conflicts to disclose. ■

### PROVIDERS continued from previous page

scope creep” first-hand in his hospitals, in the form of noncollaborative practices and tasks performed by APPs without adequate training – most likely stemming from poor decisions and oversight by physicians. But when constructed thoughtfully, APP-physician teams are “serving great needs” in many types of care, he said, from follow-up care and management of chronic conditions to inpatient rounding. “My [colleagues] are having great success,” he said.

He is watching with interest – and some concern – pending reimbursement changes from the Centers for Medicare & Medicaid Services that will make time the only defining feature of the “substantive” portion of a split/shared visit involving physicians and APPs in a facility setting. Medical decision-making will no longer be applicable.

For time-based services like critical care, time alone is currently the metric. (And in the nonfacility setting, physician-APP teams may still apply “incident to” billing practices). But in the facility setting, said Amy

M. Ahasic, MD, MPH, FCCP, a pulmonologist in Norwalk, Conn., who coauthored a 2022 commentary on the issue (*Chest*. 2022;162[3]:514-6), the change (now planned for 2024) could be problematic for employed physicians whose contracts are based on productivity, and could create tension and possibly lead to reduced use of APPs rather than supporting collaborative care.

“The team model has been evolving so well over the past 10-15 years,” said Dr. Ahasic, who serves on the CHEST Health Policy and Advocacy Reimbursement Workgroup and cochairs the CHEST/ATS Clinical Practice Committee with Dr. Hussain. “It’s good for patient safety to have more [providers] involved ... and because APP salaries are lower health systems could do it and be able to have better care and better coverage.”

The pulmonology culture, said Dr. Hussain, has been increasingly embracing APPs and “it’s collegial.” Pulmonologists are “coming to CHEST meetings with their APPs.

The article sources reported they had no relevant conflicts. ■



# OSA tied to risk of atrial fibrillation and stroke

BY HEIDI SPLETE

MDedge News

Undiagnosed atrial fibrillation (AFib) was significantly more common among adults with obstructive sleep apnea (OSA), compared with controls, based on data from 303 individuals.

OSA has become a common chronic disease, and cardiovascular diseases including AFib also are

*The researchers noted that no guidelines currently exist for systematic opportunistic screening for comorbidities in OSA patients.*

known independent risk factors associated with OSA, Anna Hojager, MD, of Zealand University Hospital, Roskilde, Denmark, and colleagues wrote. Previous studies have shown a significant increase in AFib risk in OSA patients with severe disease, but the prevalence of undiagnosed AFib in OSA patients has not been explored.

In a study published in Sleep Medicine (2022 Oct 7. doi: 10.1016/j.sleep.2022.10.002), the researchers enrolled 238 adults with severe OSA (based on apnea-hypopnea index of 15 or higher) and 65 with mild or no OSA (based on an AHI of less than 15). The mean AHI across all participants was 34.2, and ranged from 0.2 to 115.8.

Participants underwent heart rhythm monitoring using a home system or standard ECG for 7 days; they were instructed to carry the device at all times except when showering or sweating heavily. The primary outcome was the detection of AFib, defined as at least one period of 30 seconds or longer with an irregular heart rhythm but without

detectable evidence of another diagnosis. Sleep was assessed for one night using a portable sleep monitoring device. All participants were examined at baseline and measured for blood pressure, body mass index, waist-to-hip ratio, and ECG.

Overall, AFib occurred in 21 patients with moderate to severe OSA and 1 patient with mild/no OSA (8.8% vs. 1.5%,  $P = .045$ ). The majority of patients across both groups had hypertension (66%) and dyslipidemia (77.6%), but the severe OSA group was more likely to be dysregulated and to have unknown prediabetes. Participants who were deemed candidates for anticoagulation therapy were referred for additional treatment. None of the 22 total patients with AFib had heart failure with reduced ejection fraction, and 68.2% had normal ejection fraction and ventricle function.

The researchers noted that no guidelines currently exist for systematic opportunistic screening for comorbidities in OSA patients, although the American Academy of Sleep Medicine recommends patient education as part of a multidisciplinary chronic disease management strategy. The high prevalence of AFib in OSA patients, as seen in the current study, “might warrant a recommendation of screening for paroxysmal [AFib] and could be valuable in the management of modifiable cardiovascular risk factors in patients with OSA,” they wrote.

The study findings were limited by several factors including the observational design and absence of polysomnography to assess OSA, the researchers noted. However, the study has the highest known prevalence of silent AFib in patients with moderate to severe OSA, and supports the value of screening and management for known comorbidities of OSA.

The study received no outside funding. The researchers had no financial conflicts to disclose. ■

**Jonathan Ludmir, MD, comments:** This small study highlights the strong known association between atrial fibrillation (AFib) and OSA. The European Society of Cardiology AFib guidelines provide a 2a recommendation to screen for AFib in patients with OSA. As a cardiologist, I think it is crucial to consider OSA screening for new-onset AFib, as optimal OSA management can ameliorate AFib symptoms.



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*“It made a big difference for us to be able to use our clinic more fully [and] more comfortably...” he said. “It’s been roughly 10 years, and that equipment is still in use today.”*



### REMOVING LANGUAGE BARRIERS TO CARE | 2017

*“The learners really appreciated having up-to-date, peer-reviewed, high-quality written material for them to refer to and take home from the course because that’s so rare,” says Dr. Silverman. “Even to this day, [to] go to different pediatric facilities around Haiti and see those manuals still dog-eared and coffee-stained, but well-used, is really a testament to how much impact putting on these courses and having French materials available for the learners really provided.”*



### OFFERING A HAND UP, NOT A HAND OUT | 2021

*“They just need a helping hand. They need a friendly face. They need someone who they trust,” Andrews said. “So me, as a community supporter—I just feel compelled to help out. To be that conduit between them and their doctor.”*

In 2022, the CHEST Foundation awarded more than \$600,000 in clinical research and community service grants to 23 individuals.



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# Targetable patients with NSCLC miss treatments

BY LIAM DAVENPORT

**N**early two-thirds of patients with advanced non-small cell lung cancer (NSCLC) who are eligible for targeted therapy are not receiving these drugs because of gaps in clinical practice all along the cancer care spectrum, reveals a new analysis of data from U.S. practices.

For some of these patients, it could mean missing the chance for long-term survival or even cure.

Patients who have lung cancer with mutations that can be targeted with drug therapies – but who do not receive them – are missing this opportunity. The new study suggests that there are many such patients. The researchers analyzed data on more than 38,000 patients with actively managed advanced NSCLC. They found that about half did not receive biomarker test results for a variety of reasons. But even among the half who were successfully tested, 30% of these did not receive the appropriate targeted therapies.

Overall, around 64% of eligible patients with advanced NSCLC are not benefiting from the most appropriate therapies, the team concludes.

The research was published online in JCO Precision Oncology (2022 Oct 31. doi: 10.1200/PO.22.00246).

The high rate of failure points to clinical practice gaps in “many areas” across the cancer care spectrum, lead author Daryl Pritchard, PhD, from the Personalized Medicine Coalition, Washington, told this news organization.

“There’s various steps along the way that affect clinicians, laboratories, payers, the health providers [and] even patients,” he said. He added that product manufacturers also “have a role.”

“So it’s not an individual group that’s causing the problem. It’s a systemic awareness and systemic need to improve the delivery process,” he said. “We need to work as a community to demonstrate the value of this care and improve education and awareness to providers and payers. That will encourage value-based practice coverage and reimbursement policies, and then also incentivize utilization in validated cases.”

Sandip P. Patel, MD, an oncologist at the Precision Immunotherapy Clinic at the University of

California, San Diego, in La Jolla, wondered whether the issue is lack of education among physicians or whether there are potential financial problems. “Is there a financial risk to patients, for example, that is not being captured?” he mused.

It could also be a question of urban vs. rural centers, language barriers in communicating to patients, or other social determinants of health, he added.

At his institution (UCSD), there are “multiple choices” of molecular tests, each with “little nuances that differ among the tests that folks sometimes will take a look at in terms of picking the best.” But the best test is the one that gets done, and here we’re seeing no testing at all” for many patients, he said. Referring to the relatively high proportion of patients who didn’t receive targeted therapy even after being tested, he said, “For me, this study leaves more questions than answers.” The researchers noted that more than 90 targeted therapies have been approved by the U.S. Food and Drug Administration for use in eligible cancer patients. An estimated 55% of recent oncology trials involved the use of biomarkers.

Predictive biomarker testing to identify patients who may benefit from targeted therapies “is a cornerstone of personalized medicine in cancer care, allowing for more rapid diagnosis while informing treatment decisions that could lead to better patient outcomes and systemic efficiencies,” the researchers emphasized.

However, providers “face several challenges” when integrating biomarker testing and targeted therapeutics into cancer care, and the use of biomarker testing varies widely across tumor types, biomarkers, and practice settings.

For their study, the team examined the use of targeted therapy in advanced NSCLC using data from the Diagnostics Data Repository, which includes commercial and Medicare claims, as well as laboratory data.

They focused on 38,068 patients with actively managed advanced NSCLC. Of those patients, 50.80% were women, and 64.6% were aged 71 years or older. The vast majority (84.50%) were non-Hispanic White patients.

The team examined the impact of seven clinical practice gaps on the timeline from ordering a biopsy to delivering targeted treatment.

They then normalized the results to a standard patient population of 1,000.

In 6.6% of cases, an initial tissue or liquid biopsy was never performed, meaning that 66 of the 1,000 patients could not progress toward targeted therapy.

Among those who underwent a biopsy, for 4.0%, there was insufficient tissue on the initial biopsy, while for a further 0.97%, there was insufficient tissue on re-biopsy. Moreover, 9.6% could not undergo biopsy testing because of a lack of tumor tissue. Consequently, a further 136 of the 944 remaining patients were lost.

For the third clinical practice gap, the tumor cell content was overestimated in 1.7% of patients. As a result, their biopsy specimen could not be tested because it did not meet the threshold requirements.

Moreover, for a further 17.5% of patients, biomarker testing was not ordered at all, owing to cost concerns, a lack of access to testing, a lack of awareness of testing options, and low confidence in the results, among other reasons. An additional 0.6% began treatment before any testing was ordered. Even among patients who underwent biomarker testing, 14.5% had uninformative or inconclusive results, and 3.9% had false-negative results.

In another 4.0% of cases, the results of biomarker testing did not arrive within the treatment decision window, because of delays in reporting the results, and so for these patients, treatment began without the results being taken into consideration.

The final clinical practice gap was not choosing the appropriate targeted treatment on the basis of test results. The researchers found that of 27,186 patients who underwent biomarker testing and received a timely result, 29.2% were not given the corresponding therapy.

Overall, the team calculated that 64.4% of patients newly diagnosed with advanced NSCLC “are not benefiting from precision oncology care options appropriate for their diseases and will likely have suboptimal outcomes.”

The research was supported in part by the Personalized Medicine Coalition, a nonprofit 501c3 organization dedicated to the advancement of personalized medicine.

Dr. Pritchard is an employee of the Personalized Medicine Coalition. ■

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# Newer agents for nosocomial pneumonia: The right drug for the right bug

BY WALTER ALEXANDER

MDedge News

**FROM CHEST 2022** ■ “The right drug at the right time with the right dose for the right bug for the right duration.” That, said professor Kristina Crothers, MD, is the general guidance for optimizing antibiotic use (while awaiting an infectious disease consult). In her oral presentation at the annual meeting of the American College of Chest Physicians, “Choosing Newer Antibiotics for Nosocomial Pneumonia,” Dr. Crothers asked the question: “Beyond the guidelines: When should novel antimicrobials be used?”

Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) are the most common nosocomial infections at 22%, and are the leading cause of death attributable to hospital-acquired infections. They increase mortality by 20%-50%, with an economic burden of about \$40,000 per patient. The incidence of multidrug-resistant (MDR) organism infections varies widely by locality, but several factors increase the likelihood: prior broad-spectrum antibiotic exposure within the past 90 days; longer hospitalization; indwelling vascular devices; tracheostomy; and ventilator dependence. The Centers for Disease Control and Prevention lists as “Serious Threat” the HAP/VAP MDR organisms methicillin resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa* (PSA) with difficult-to-treat-resistance, and beta-lactamase producing *Enterobacterales* (ESBL). In the category of “Urgent Threat” the CDC lists carbapenemase-resistant *Enterobacterales* (CRE) (carbapenemase producing or non-carbapenemase producing), and carbapenem-resistant *Acinetobacter* (CRAB), according to Dr. Crothers of the University of Washington Veterans Affairs Puget Sound Health Care System, Seattle.

Newer antibiotics for HAP/VAP that are still beyond the guidelines include telavancin and tedizolid as gram-positive agents, and as gram-negative ones: ceftazidime-avibactam, ceftolozane-tazobactam, cefiderocol, imipenem-cilastatin-relebactam, and meropenem-vaborbactam, she added.

**Tedizolid**, Dr. Crothers stated, is a novel oxazolidinone, and is an alternative to vancomycin and linezolid for gram-positive HAP/VAP. In the VITAL noninferiority study versus linezolid with 726 patients, it was noninferior to linezolid for 28-day all-cause mortality (28% vs. 26%), but did not achieve noninferiority for investigator-assessed clinical cure (56% vs. 64%).

**Televancin**, a semisynthetic derivative of vancomycin, in the ATAIN studies vs. vancomycin had overall similar cure rates. It is FDA-approved for *S. aureus* HAP/VAP but not other bacterial causes. It should be reserved for those who cannot receive vancomycin or linezolid, with normal renal function, according to Dr. Crothers.



Excluded from first-line treatment of gram-positive HAP/VAP are daptomycin, ceftaroline, ceftobiprole, and tigecycline.

**Ceftazidime-avibactam**, a third-generation cephalosporin-plus novel beta-lactamase inhibitor has wide activity (*Klebsiella pneumoniae*, *Enterobacter cloacae*, *Escherichia coli*, *Serratia marcescens*, *Proteus mirabilis*, PSA, and *Haemophilus influenzae*). It is also active against some extended-spectrum beta-lactamases, ampC beta-lactamases (AmpCs), and *K. pneumoniae* carbapenemase (KPC)-producing *Enterobacterales*, but not with metallo-beta-lactamases. Ceftazidime-avibactam is also indicated for HAP/VAP, and has a toxicity profile including nausea, vomiting, and diarrhea.

In the REPROVE trial of ceftazidime-avibactam vs. meropenem for 7-14 days with 527 evaluable patients (37% *K. pneumoniae*, 30% *P. aeruginosa*, and 33%-35% VAP), the clinical cure at 21-25 days post randomization was 69% vs. 73%, respectively, with similar adverse events.

**Ceftolozane-tazobactam**, a novel fifth-generation cephalosporin plus a beta-lactamase inhibitor has activity against PSA including extensively drug-resistant PSA, AmpC, and ESBL-E, but it has limited activity against *Acinetobacter* and *Stenotrophomonas*. It is indicated for HAP/VAP, has reduced efficacy with creatine clearance of 50 mL/min or less, increases transaminases and renal impairment, and causes diarrhea. In ASPECT-NP (n = 726) ceftolozane-tazobactam versus meropenem for 8-14 days (HAP/VAP), showed a 28 day-mortality of 24% vs. 25%, respectively, with test

of cure at 54% vs. 53% at 7-14 days post therapy. Adverse events were similar between groups.

**Imipenem-cilastatin-relebactam**, a novel beta-lactamase inhibitor plus carbapenem, is indicated for HAP/VAP and has activity against ESBL, CRE, KPC-producing *Enterobacterales*, and PSA including AmpC. It can cause seizures (requires caution with central nervous system disorders and renal impairment). It increases transaminases, anemia, and diarrhea, and reduces potassium and sodium. In RESTORE-IMI 2 (n = 537 with HAP/VAP) it was noninferior for 28-day all-cause mortality vs. piperacillin and tazobactam (16% vs. 21%), with similar adverse events.

**Cefiderocol**, a siderophore cephalosporin, is indicated for HAP/VAP. It has a wide spectrum of activity: ESBL, CRE, CR PSA, *Stenotrophomonas maltophilia*, *Acinetobacter baumannii*, *Streptococcus*. It increases transaminases, diarrhea, and atrial fibrillation, and it reduces potassium and magnesium.

In APEKS-NP versus linezolid plus cefiderocol or extended meropenem infusion (HAP/VAP n = 292; gram-negative pneumonia = 251; 60% invasive mechanical ventilation) it was noninferior for 14-day all-cause mortality (12.4% vs. 11.6%) with similar adverse events. In CREDIBLE-CR vs. best available therapy for carbapenem-resistant gram-negative infections, clinical cure rates were similar (50% vs. 53% in 59 HAP/VAP patients at 7 days), but with more deaths in the cefiderocol arm. Adverse events were > 90% in both groups and 34% vs. 19% died, mostly with *Acinetobacter*.

**Meropenem-vaborbactam**, a novel beta-lactamase inhibitor plus carbapenem, is approved and indicated for HAP/VAP in Europe. It has activity against MDR, *Enterobacterales* including CRE. Its toxicities include headache, phlebitis/infusion-site reactions and diarrhea. In TANGO-2 versus best available treatment for CRE (n = 77, 47 with confirmed CRE), clinical cure was increased and mortality decreased compared with best available therapy. Treatment- and renal-related adverse events were lower for meropenem-vaborbactam.

In closing, Dr. Crothers cited advice from the paper by Tamma et al. (“Rethinking how antibiotics are prescribed” JAMA. 2019; 32[2]:139-40) about the need to review findings after therapy has been initiated to confirm the pneumonia diagnosis: Novel agents should be kept in reserve in the absence of MDR risk factors for MRSA and gram-negative bacilli; therapy should be deescalated after 48-72 hours if MDR organisms are not detected; and therapy should be directed to the specific organism detected. Most HAP and VAP in adults can be treated for 7 days, she added.

“Know indications for new therapeutic agents approved for nosocomial pneumonia,” she concluded.

Dr. Crothers reported having no disclosures. ■

# Study affirms shorter regimens for resistant TB

BY KATE JOHNSON

**T**wo short-course treatments containing bedaquiline for rifampicin-resistant tuberculosis showed “robust evidence” for superior efficacy and less ototoxicity compared to a 9-month injectable control regimen, researchers report.

The findings validate the World Health Organization’s current recommendation of a 9-month, bedaquiline-based oral regimen, “which was based only on observational data,” noted lead author Ruth Goodall, PhD, from the Medical Research Council Clinical Trials Unit at University College London, and colleagues.

The study was published in *The Lancet* (2022 Nov 8. doi: 10.1016/S0140-6736(22)02078-5).

The Standard Treatment Regimen of Anti-tuberculosis Drugs for Patients With MDR-TB (STREAM) stage 2 study was a randomized, phase 3, noninferiority trial conducted at 13 hospital clinics in seven countries that had prespecified tests for superiority if noninferiority was shown. The study enrolled individuals aged 15 years or older who had rifampicin-resistant TB without fluoroquinolone or aminoglycoside resistance.

The study’s first stage, STREAM stage 1, showed that a 9-month injectable regimen was noninferior to the WHO’s 2011 recommendation of a 20-month injectable regimen. The 9-month regimen was recommended by the WHO in 2016. That recommendation was superseded in 2020 when concerns of hearing loss associated with aminoglycosides prompted the WHO to endorse a 9-month bedaquiline-containing, injectable-free alternative, the authors write.

## Seeking shorter treatment for better outcomes

STREAM stage 2 used a 9-month injectable regimen as its control. The investigators measured it against a fully oral 9-month bedaquiline-based treatment (primary comparison), as well as a 6-month oral bedaquiline regimen that included 8 weeks of a second-line injectable (secondary comparison).

The 9-month fully oral treatment included levofloxacin, clofazimine, ethambutol, and pyrazinamide for 40 weeks; bedaquiline, high-dose isoniazid,

and prothionamide were given for the 16-week intensive phase.

The 6-month regimen included bedaquiline, clofazimine, pyrazinamide, and levofloxacin for 28 weeks, supplemented by high-dose

isoniazid with kanamycin for an 8-week intensive phase.

For both comparisons, the primary outcome was favorable status at 76 weeks, defined as cultures that were negative for *Mycobacterium*

*tuberculosis* without a preceding unfavorable outcome (defined as any death, bacteriologic failure or recurrence, or major treatment change).

Among 517 participants in the

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modified intention-to-treat population across the study groups, 62% were men, and the median age was 32.5 years.

For the primary comparison, 71% of the control group and 83% of the oral regimen group had a favorable outcome.

In the secondary comparison, 69% had a favorable outcome in

the control group, compared with 91% of those receiving the 6-month regimen.

Although the rate of grade 3 or 4 adverse events was similar in all three groups, there was significantly less ototoxicity among patients who received the oral regimen, compared with control patients (2% vs. 9%); 4% of those taking the 6-month

regimen had hearing loss, compared with 8% of control patients.

Exploratory analyses comparing both bedaquiline-containing regimens revealed a significantly higher proportion of favorable outcomes among participants receiving the 6-month regimen (91%), compared with patients taking the fully oral 9-month regimen (79%). There were

no significant differences in the rate of grade 3 or 4 adverse events.

The trial's main limitation was its open-label design, which might have influenced decisions about treatment change, note the investigators.

"STREAM stage 2 has shown that two short-course, bedaquiline-containing regimens are not only

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non-inferior but superior to a 9-month injectable-containing regimen,” they conclude.

“The STREAM stage 2 fully oral regimen avoided the toxicity of aminoglycosides, and the 6-month regimen was highly effective, with reduced levels of ototoxicity. These two regimens offer promising

treatment options for patients with MDR or rifampicin-resistant tuberculosis,” the authors write.

Dr. Goodall added, “Although both STREAM regimens were very effective, participants experienced relatively high levels of adverse events during the trial (though many of these were likely due to the close laboratory monitoring of the trial).

“While hearing loss was reduced on the 6-month regimen, it was not entirely eliminated,” she said. “Other new regimens in the field containing the medicine linezolid report side effects such as anemia and peripheral neuropathy. So more work needs to be done to ensure the treatment regimens are as safe and tolerable for patients as possible. In

addition, even 6 months’ treatment is long for patients to tolerate, and further regimen shortening would be a welcome development for patients and health systems.”

**A ‘revolution’ in MDR tuberculosis**

“The authors must be commended on completing this challenging

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high-quality, phase 3, randomized controlled trial involving 13 health care facilities across Ethiopia, Georgia, India, Moldova, Mongolia, South Africa, and Uganda ... despite the COVID-19 pandemic,” noted Keertan Dheda, MD, PhD, and Christoph Lange, MD, PhD, in an accompanying comment titled, “A revolution in the management of

multidrug-resistant tuberculosis” (Lancet. 2022; Nov 8. doi: 10.1016/S0140-6736[22]02161-4). Although the WHO recently approved an all-oral 6-month bedaquiline, pretomanid, and linezolid plus moxifloxacin (BPaLM) regimen, results from the alternate 6-month regimen examined in STREAM stage 2

“do provide confidence in using 2 months of an injectable as part of a salvage regimen in patients for whom MDR tuberculosis treatment is not successful” or in those with extensively drug-resistant or pre-XDR TB, “for whom therapeutic options are few,” noted Dr. Dheda, who is from the University of Cape Town (South Africa) and

the London School of Hygiene and Tropical Medicine, and Dr. Lange, from the University of Lübeck (Germany), Baylor College of Medicine, and Texas Children’s Hospital, both in Houston. Both the study authors and the commentators stressed that safer and simpler treatments are still

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needed to use for MDR TB.

“The search is now on for regimens that could further reduce duration, toxicity, and pill burden,” according to Dr. Dheda and Dr. Lange.

However, they also noted that “substantial resistance” to bedaquiline is already emerging.

“Therefore, if we are to protect key drugs from becoming functionally redundant, drug-susceptibility testing capacity will need to be rapidly improved to minimize resistance amplification and onward disease transmission.”

The study was funded by USAID and Janssen Research and Development. Dr. Goodall has disclosed no

relevant financial relationships. Dr. Dheda has received funding from the EU and the South African Medical Research Council for studies related to the diagnosis or management of drug-resistant tuberculosis.

Dr. Lange is supported by the German Center for Infection Research and has received funding from the European Commission for

studies on the development of novel antituberculosis medicines and for studies related to novel diagnostics of tuberculosis; consulting fees from INSMED; and speaker’s fees from INSMED, GILEAD, and Janssen; and is a member of the data safety board of trials from Medicines sans Frontiers, all of which are unrelated to the current study. ■

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# Nitrogen test predicts decline in lung function

BY HEIDI SPLETE  
*MDedge News*

The slope of the alveolar plateau on the single-breath nitrogen test (SBN<sub>2</sub>) was a significant

predictor of lung function decline and of chronic obstructive pulmonary disease (COPD), based on data from 907 adults.  
In recent years, interest in small-airways disease has renewed, with

research suggesting a link between SAD pathology and COPD progression, wrote Francesco Pistelli, MD, of the University of Pisa (Italy) and colleagues.  
The SBN<sub>2</sub> has been used to

detect early SAD, but few studies have examined the relationship between SBN<sub>2</sub> measures and lung function decline over time, they said.

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In a study published in *Pulmonology* (2022 Oct 7. doi: 10.1016/j.pulmoe.2022.09.001), the researchers reviewed data from adults aged 20 years and older who were enrolled in the Po River Delta prospective study in Italy. The study population included 907 individuals, with a

mean age of 37.4 years; 56% were male.

The primary outcome was a change in lung function and incidence of COPD during an 8-year follow-up period. COPD was defined using either the Global Initiative for Chronic Obstructive Lung Disease (GOLD) or American

Thoracic Society/ European Respiratory Society criteria.

In a multinomial regression model, one SBN<sub>2</sub> index, the slope of alveolar plateau (N<sub>2</sub>-slope) was significantly associated with rates of forced expiratory volume in 1 second (FEV<sub>1</sub>) decline, with a decrease of 7.93 mL/year for each

one-unit change in N<sub>2</sub>-slope.

The N<sub>2</sub>-slope also was significantly associated with an increased risk of COPD, with a relative risk of 1.81 for mild obstruction and 2.78 for severe obstruction based on GOLD criteria. The association was similar for COPD based on the ATS-ERS criteria, with a relative risk of 1.62 for mild obstruction and 3.40 for moderate to severe obstruction.

*“Pulmonologists could rediscover an ‘old’ test, which could provide important information on their patients at risk for developing COPD.”*

Age was associated with an increased COPD risk using the GOLD criteria, but not the ATS-ERS criteria; neither sex nor current or former smoking were associated with increased COPD risk for either measure.

The results are consistent with some previous longitudinal studies, but not others, possibly because of differences in sampling procedures, test techniques, or statistical approaches, the researchers wrote in their discussion.

The study findings were limited by several factors, including incomplete data on closing capacity and vital capacity, and by the lack of bronchodilator for performing baseline spirometry, since bronchodilator testing was not recommended at the time of the study, the researchers noted.

However, the results support the role of SAD as a contributor to COPD, and the potential value of the SBN<sub>2</sub> test, they said. “Large prospective studies are needed to evaluate whether new proposed functional or imaging tests that measure small airways impairment may be useful in the early detection of COPD,” they noted. In the meantime, “pulmonologists could rediscover an ‘old’ test, which could provide important information on their patients at risk for developing COPD,” they concluded.

The study was supported in part by the National Research Council Targeted Project and the Italian Electric Power Authority. The researchers had no financial conflicts to disclose. ■

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# 2023 GOLD Report: Important updates and revisions

BY WALTER ALEXANDER

MDedge News

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) Report is revised annually and is used widely throughout the world as a tool for implementing effective management.

Among the updates in the 2023 GOLD Report, the section on diagnostic criteria added a proposed new category “PRISm,” denoting “preserved ratio impaired spirometry,” encompassing individuals who present with structural lung lesions (for example, emphysema) and/or other physiological abnormalities such as low-normal forced expiratory volume in 1 second (FEV<sub>1</sub>), gas trapping, hyperinflation, reduced lung diffusing capacity, and/or rapid FEV<sub>1</sub> decline, but without airflow obstruction (FEV<sub>1</sub>/FEV<sub>0.7</sub> ≥ 0.7 post bronchodilation). Some of these “pre-COPD” (chronic obstructive pulmonary disease) individuals, who have a normal ratio but abnormal spirometry are at risk over time of developing airflow obstruction. The best treatment for them, beyond smoking cessation, needs to be determined through research, the report states.

## Clinical updates

The 2023 GOLD Report also offers proposed clinical guidance, in the absence of high-quality clinical trial evidence, on initial pharmacologic management of COPD. The proposal is based on individual assessment of symptoms and exacer-

*“The new 2023 GOLD recommendations represent a meaningful change for the treatment of COPD by prioritizing the utilization of a fixed LAMA/LABA combination.”*

bation risk following use of the ABE Assessment Tool, a revised version of the ABCD Assessment Tool that recognizes the clinical relevance of exacerbations independent of symptom level.

These updates to information and figures pertaining to initial pharmacological treatment and follow-up pharmacological treatment revise the positioning of LABA (long-acting beta<sub>2</sub> agonists) plus LAMA (long-acting muscarinic agonists) and LABA/ICS (inhaled corticosteroids). Among GOLD group A patients with 0 or 1 moderate exacerbations that do not lead to hospital admission, a bronchodilator is recommended.

The recommendation for group B patients is LABA/LAMA with the caveat that single-inhaler therapy may be more convenient and effective than multiple inhalers. For group E patients with two or more moderate exacerbations or one or more leading to hospitalization, LABA/LAMA is recommended (with the same inhaler therapy caveat). With blood eosinophil levels at 300 or higher, LABA/LAMA/ICS may be considered.

Commenting on the combination

recommendations in a press release, Antonio Anzueto, MD, professor of medicine, pulmonary critical care, University of Texas Health, San Antonio, stated: “From a physician’s perspective, we are always grateful to receive well-vetted and informed recommendations on how we can best utilize available treatment options to provide the most benefit to our patients. The new 2023 GOLD recommendations represent a meaningful change for the treatment of COPD by prioritizing the utilization of a fixed LAMA/LABA combination.”

## More interventions

In a section on therapeutic interventions to reduce COPD mortality, the report lists studies showing mortality benefits for fixed-dose inhaled triple combinations (LABA + LAMA + ICS) versus dual inhaled long-acting bronchodilators, and for smoking cessation and pulmonary rehabilitation.

Also new is a strong emphasis on inhaler choice, education, and technique training with assessment of inhaler technique and adherence urged as a prerequisite to judging whether current therapy as insufficient. The report summarizes principles guiding inhaler type selection.

The report also added a section on chronic bronchitis, defining it as a common but variable condition in COPD patients with cough and expectorated sputum on a regular basis over a defined period in the absence of other conditions plausibly causing symptoms.

The fact that chronic bronchitis is sometimes found in never-smokers suggests the involvement of other factors such as exposure to inhaled dusts, biomass fuels, chemical fumes, or domestic heating and cooking fuels, according to the report. Gastroesophageal reflux may also be associated with chronic bronchitis.

The report discusses various taxonomic terms for different types of COPD, such as COPD-G for genetically determined COPD, COPD-D for those with abnormal lung development, and COPD-C for COPD associated with cigarette smoking.

## Change in exacerbations

The report also revises the definition of a COPD exacerbation as “an event characterized by increased dyspnea and/or cough and sputum that worsens in less than 14 days which may be accompanied by tachypnea and/or tachycardia and is often associated with increased local and system inflammation caused by infection, pollution, or other insult to the airways.” To overcome limitations conferred by the current grading of COPD exacerbations, the 2023 report proposes a four-step point-of-contact diagnosis and assessment tool.

## Telemedicine

Given the constraints brought on by COVID-19 on top of the generally sparse availability of programs and facilities for delivering well-proven pulmonary rehabilitation methods, tele-rehabilitation has been proposed as an alternative to traditional approaches. While the evidence base is

still evolving and best practices have not yet been established, the GOLD Report calls for better understanding of barriers to tele-rehabilitation success.

## Comorbidities update

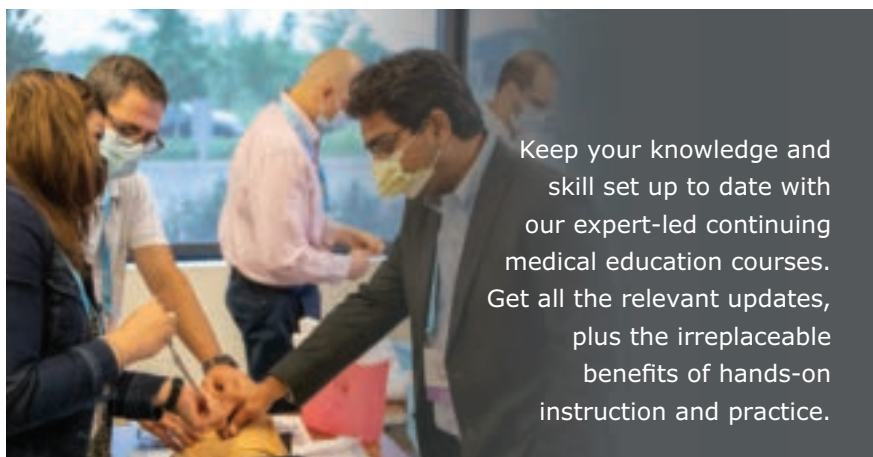
The GOLD Report chapter on COPD and comorbidities was also updated, and lists cardiovascular disease, lung cancer, osteoporosis, depression/anxiety, and gastroesophageal reflux disease as



common comorbid conditions which may affect prognosis and, in the case of cancer, mortality. The report urges simplicity of treatment to minimize polypharmacy. While annual low-dose CT is recommended for COPD caused by smoking, it is not recommended for COPD not caused by smoking; data are insufficient to establish benefit over harm.

While the GOLD Report “COVID-19 and COPD” chapter summarizes current evidence stating that individuals with COPD do not seem to be at substantially greater risk of infection with SARS-CoV-2, it underscores that they are at higher risk of hospitalization for COVID-19 and may be at higher risk for developing severe disease and death.

Many other topics are included in the updated report, among them screening, imaging, vaccinations, adherence to therapy, and surgical and bronchoscopic interventions. In its closing section, the 2023 GOLD Report reiterates its mission, stating: “The GOLD initiative will continue to work with National Leaders and other interested health care professionals to bring COPD to the attention of governments, public health officials, health care workers, and the general public, to raise awareness of the burden of COPD and to develop programs for early detection, prevention and approaches to management. ■



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# CHEST President shares inside look at priorities, plans for 2023

Attendees at the CHEST 2022 Opening Session on October 16 got a sneak peek into plans and priorities for CHEST President Doreen J. Addrizzo-Harris, MD, FCCP, in 2023 – and some insights into her own path to the role.

A longtime leader at CHEST, she shared how members' pandemic response reminded her of the great impact the organization can have. In March 2020, Dr. Addrizzo-Harris was overseeing ICU staffing at NYU Langone Health's Bellevue Hospital Center and organizing dozens of volunteer physicians to help meet the pandemic care burden.

"I knew all too quickly that we wouldn't have enough intensivists," said Dr. Addrizzo-Harris. "It was a quick call very late one night, probably around 1 am, that I made to CHEST CEO, Bob Musacchio, that helped materialize a monumental effort ... many of these physicians were CHEST members themselves. They were fearless and unselfish, and they came to help us in our time of need."

She saw this same spirit of dedication and drive in CHEST's leadership and staff, she said – one she will continue and expand upon during her presidency.

"I've watched our last three presidents lead by great example ... with innovation and nimbleness, in a time when we were so isolated from each other and so tired from the long hours that we worked each day," she said. "They, along with the Board of Regents, the CEO, and our phenomenal staff, were able to keep CHEST amazingly alive and vibrant and more connected than ever. They are truly inspiring. For 2023, I hope



Dr. Doreen J. Addrizzo-Harris

to take this incredible energy to the next level."

As CHEST president, Dr. Addrizzo-Harris plans to expand and strengthen the CHEST community by supporting greater cooperation and collaboration with sister societies in the United States and advancing international outreach initiatives launched by CHEST Past President David Schulman, MD, MPH, FCCP. This also includes supporting and building upon CHEST's ongoing commitment to diversity, equity, and inclusion initiatives to encourage greater representation in the field and improve patient care.

"Whether it's through supporting our clinical research grants, expanding patient education and advocacy, or programs like the First 5 Minutes™ and the Harold Amos scholarship program, we want to train our leaders for the future," she said.

Revisit the September issue of *CHEST Physician*, and watch future issues to learn more about Dr. Addrizzo-Harris and her plans for the presidency. ■



## In memoriam

CHEST has been informed of the following deaths of CHEST members.

We remember our colleagues and extend our sincere condolences.

- Desmond R. Del Giacco, MD, FCCP
- Walter H. Herbert, MD
- Donald C. Zavala, MD





Nina Dietzel/Getty Images

## CHEST Challenge returned to the stage in the Music City

BY DANIELLE LEBER

Managing Editor, CHEST News Channels

After several years of virtual competitions, the CHEST Challenge Championship returned to the stage at CHEST 2022 in Nashville, where outstanding fellows from Brooke Army Medical Center, Mayo Clinic, and NewYork Presbyterian Brooklyn Methodist battled to compete in unconventional skills challenges and clinical trivia.

After an excellent showing from all three institutions, Mayo fellows, Amjad Kanj, MD; Paige Marty, MD; and Zhenmei Zhang, MD, won the day, earning their training program \$5,000 (not to mention, the ultimate bragging rights and the chance to raise the coveted Rosen Cup). Runner-up Brooke Army Medical Center received \$3,000, and NewYork-Presbyterian Brooklyn Methodist received \$1,000.

This year's Jeopardy-style championship included a variety of category types, including everything from straightforward clinical answers in "Asthmalogic" about asthma-related issues and "Under a Microscope" for topics related to histopathology, to brain-boggling alternate options, such as "Rhyme Time," which twisted answers in rhyming phrases.

The competition also included timed skills challenges that tested the competitors physically – and presented some very special guests.

In "Bugs and Drugs," Team Methodist sprinted to grab and then matched unlabeled pathogen photographs with their appropriate therapeutic agents in less than 35 seconds. In another, Team Brooke aced the challenge of performing timed procedures on three different body parts in Dr. Frankenstein's laboratory, while the monster himself (played by Board of Regents member Victor J. Test, MD, FCCP) worked to distract them.

Mayo Clinic was already in the lead by the time the Final Challenge wager was presented by William Kelly, MD, FCCP, so the team responded to the answer "This disease is inherited as an autosomal recessive trait and is a variant in the *SCL34A2* gene" with their own unique reply: "Thank you, CHEST," and a symbolic wager of \$22.

Drs. Kanj, Marty, and Zhang credited their success to their training program back home, as well as the support of friends and colleagues on-site, including Program Director, Darlene Nelson, MD, FCCP. The team also prepared with mock sessions days before the championship and had a strong fan base cheering them on in the audience.

Want to join rising stars in pulmonary, critical care, and sleep medicine for next year's championship in Hawai'i? Watch CHEST's social media in the spring for the first phase of CHEST Challenge. ■



## CHEST 2023 Hawaii

### Call for Honor Lectures & Annual Awards Now Open

Each year, we honor individuals advancing chest medicine, providing mentorship and training, and furthering the mission of CHEST. Nominate a colleague or mentor for an honor lecture or annual award today.



**DEADLINE:**

**January 31, 2023**



**Submit a nomination**



### Save the Date

Join CHEST, October 8 - 11, in Hawai'i, at the Hawai'i Convention Center in Honolulu.

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# CHEST 2022 award winners

**E**ach year, CHEST recognizes members who make an impact – through dedication to the organization, by contributions to research and practice, through their commitment to educating the next generation, and so much more.

## MASTER FELLOW AWARD

**Gerard A. Silvestri, MD, MS, Master FCCP**

## DISTINGUISHED SERVICE AWARD

**Aneesa M. Das, MD, FCCP**

## COLLEGE MEDALIST AWARD

**William R. Auger, MD, FCCP**

## ALFRED SOFFER AWARD FOR EDITORIAL EXCELLENCE

**Todd W. Rice, MD, FCCP**

## EARLY CAREER CLINICIAN EDUCATOR AWARD

**Mauricio Danckers, MD, FCCP**

## More award winners

**Please Note:** Award winners from the following categories will be listed in the February issue of *CHEST Physician*.

CHEST Foundation Grant Awards  
Scientific Abstract Awards  
Alfred Soffer Research Award Winners  
Young Investigator Award Winners  
Abstract Rapid Fire Winners  
Case Report Session Winners  
Case Report Rapid Fire Winners

## MASTER CLINICIAN EDUCATOR AWARD

**Neil R. MacIntyre, MD, FCCP**

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**CHEST Staff**

## EDWARD C. ROSENOW III, MD, MASTER FCCP/MASTER TEACHER ENDOWED HONOR LECTURE

**Alexander S. Niven, MD, FCCP**

## THOMAS L. PETTY, MD, MASTER FCCP MEMORIAL LECTURE

**Sandra G. Adams, MD, FCCP**

## 2021 DISTINGUISHED SCIENTIST HONOR LECTURE IN CARDIOPULMONARY PHYSIOLOGY

**Kenneth I. Berger, MD, FCCP**

## PRESIDENTIAL HONOR LECTURE

**Jack D. Buckley, MD, MPH, FCCP**

## PASQUALE CIAGLIA MEMORIAL LECTURE IN INTERVENTIONAL MEDICINE

**Nicholas J. Pastis, MD, FCCP**

## ROGER C. BONE MEMORIAL LECTURE IN CRITICAL CARE

**E. Wesley Ely, MD, MPH, FCCP**

## MURRAY KORNFELD MEMORIAL FOUNDERS AWARD

**Marin H. Kollef, MD, FCCP**

## OM P. SHARMA, MD, MASTER FCCP MEMORIAL LECTURE

**Daniel A. Culver, DO, FCCP**

## RICHARD S. IRWIN, MD, MASTER FCCP HONOR LECTURE

**Nneka O. Sederstrom, PhD, MS, MA, FCCP**

## 2022 DISTINGUISHED SCIENTIST HONOR LECTURE IN CARDIOPULMONARY PHYSIOLOGY

**Martin J. Tobin, MBBCh, FCCP**

## MARK J. ROSEN, MD, MASTER FCCP ENDOWED MEMORIAL LECTURE

**Stephanie M. Levine, MD, FCCP**

## MARGARET PFROMMER ENDOWED MEMORIAL LECTURE IN HOME-BASED MECHANICAL VENTILATION

**Lisa Wolfe, MD, FCCP**

## CHEST CHALLENGE FINALISTS

### 1st Place – Mayo Clinic

Amjad Kanj, MD

Paige Marty, MD

Zhenmei Zhang, MD

Program Director: Darlene Nelson, MD, FCCP

### 2nd Place – Brooke Army Medical Center

Joshua Boster, MD

Tyler Campbell, DO

Daniel Foster, MD

Program Director: Robert Walter, MD, PhD

### 3rd Place – NewYork-Presbyterian Brooklyn Methodist

Albina Guri, DO

Jahrul Islam, MD

Sylvana Salama, MD

Program Director: Anthony Saleh, MD, FCCP

# CHEST simulation courses support learning for every career stage

**O**ne mark of an excellent clinician is their commitment to lifelong learning, and CHEST's hands-on simulation courses offer the chance for practitioners of all experience levels to enhance their knowledge.

A variety of interactive courses are offered at CHEST's state-of-the-art Innovation, Simulation, and Training Center in Glenview, Illinois, covering topics like ultrasonography, bronchoscopy, and mechanical ventilation. And this year, our simulation schedule will offer several new sessions on advances in invasive and noninvasive ventilation, critical care transesophageal echocardiography, master-level EBUS practice, and mechanical circulatory support.

Each course is led by expert instructors and includes attendees from a full range of career stages,

from trainees and mid-career clinicians to long-time CHEST faculty members.

At a fall 2022 session of the Ultrasonography: Essentials in Critical Care course, Adil Ahmed, MD, an intern at the University of Texas Health Science Center at San Antonio, shared his perspective attending as a resident.

"CHEST has lots of specialized resources and renowned faculty members, and they're doing an exceptional job," he said. "A lot of the things I've learned in the first workshop alone are completely brand new to me. I think more programs should start sending residents to these courses."

Trainees don't just attend simulation courses – they teach them, too. Carmen Mei, MD, a pulmonary and

critical care fellow at Rutgers University, was a faculty member at the recent ultrasound course. She taught attendees representing a wide array of ages.

"It's a learning environment. Everybody's very engaged, no matter where they are in their career," she said.

As a mid-career clinician, Yonatan Y. Greenstein, MD, FCCP – who serves as a co-chair of the ultrasonography course – appreciates the diversity of experiences among attendees.

"Over the years, we've found that the wide breadth enhances the course because learners appreciate the questions that are brought up from different angles," he said.

For experienced clinicians like CHEST Immediate Past President

David Schulman, MD, MPH, FCCP, the interactive courses provide an opportunity to continue expanding his expertise. At the ultrasound course, Dr. Schulman said he enjoyed the chance to extend and refine his skillset alongside clinicians with a broad range of experience levels.

"Ultrasound is one of those skills that many clinicians, even in their forties and older, have never trained in. It's great to see how the more junior learners approach this with a very excited mindset, and they're learning right beside mid-career faculty who didn't have the exposure to ultrasound when they were young," he said.

To find the simulation course that's the best fit for your practice, visit [chestnet.org/simulation](https://chestnet.org/simulation). ■



# Screening raises lung cancer survival rate to 80%

BY MARCIA FRELICK

MDedge News

CHICAGO – Discovering lung cancer early with annual low-dose computed tomography greatly improves long-term survival rates to 80%, findings from a 20-year international study indicate.

Claudia Henschke, MD, PhD, professor of radiology and director of the Early Lung and Cardiac Action Program at the Icahn School of Medicine at Mount Sinai, New York, presented research results at the annual meeting of the Radiological Society of North America.

The researchers studied lung-cancer-specific survival (LCS) of 87,416 participants enrolled in an international, prospective study named the International Early Lung Cancer Action Program.

Lung cancer is the leading cause of cancer death. The American Lung Association states the average 5-year survival rate is 18.6%. Only



cancer instead of CT at the beginning of the second half of the life cycle,” Dr. Henschke said.

“The study raises the power of prospective data collection in the context of clinical care as recommended by the Institute of Medicine long ago,” she said.

## Findings ‘very promising’

Ernest Hawk, MD, MPH, head of the division of cancer prevention and population sciences at the University of Texas MD Anderson Cancer, Houston, told this news organization the findings look “very promising.” Dr. Hawk was not involved in the study.

“This was one of the earliest studies to evaluate low-dose CT scanning. Their report that the initial benefits seem to be holding up over a longer period of observation is great,” he said.

16% of the cancers are caught early and more than half of people with lung cancer die within a year of diagnosis.

## Participants’ 20-year survival rate 80%

Results of this large international study showed the overall 20-year

survival rate for the 1,285 screening participants diagnosed with early-stage cancer was 80% (95% confidence interval, 77%-83%). Among the 1,285 diagnosed, 83% had stage 1 cancer, Dr. Henschke said.

LCS was 100% for the 139 participants with non-solid nodule consistency and for the 155 participants with part-solid consistency. LCS was 73% (95% CI, 69%-77%) for the 991 with solid consistency, and for clinical stage IA participants LCS was 86% (95% CI, 83%-89%), regardless of consistency.

For participants with pathologic stage IA lung cancer 10 mm or less in average diameter, the 20-year survival rate with identification and resection was 92% (95% CI, 87%-96%).

No lung cancer deaths were identified in the part-solid and nonsolid cancers, the researchers report.

These results show the 10-year findings from 2006 published in the New England Journal of Medicine (2006 Oct 26. doi: 10.1056/NEJMoa060476), which also showed 80% survival rates with low-dose CT, have persisted, she said.

At the time of the 2006 paper, 95% of Americans diagnosed with lung cancer died from it, Dr. Henschke said.

Dr. Henschke notes that, by the time symptoms appear, lung cancer is often advanced, so the best tool for detecting early-stage lung cancer is enrolling in an annual screening program.

When cancer is small enough and can be surgically removed, patients can be effectively cured long term, she said.

“In the future, perhaps blood markers will allow us to detect it in the first half of the life cycle of lung

*By the time symptoms appear, lung cancer is often advanced, so the best tool for detecting early-stage lung cancer is enrolling in an annual screening program.*

“This bolsters the data that lung cancer screening is beneficial over a longer period of observation,” he said, noting that most of the randomized controlled trials have been shorter.

Lung cancer screening is now recommended for high-risk individuals – those with at least a 20-pack-year history of tobacco use who are between 50 and 80 years old.

So far, screening is still limited to people at high risk, Dr. Hawk said, though there’s discussion about whether benefit would extend to people exposed to asbestos, for instance, or secondhand smoke.

“The biggest challenge right now is getting the screening to those who actually meet the criteria,” Dr. Hawk said.

Medscape reported earlier this month that less than 6% of high-risk smokers have the recommended annual lung cancer screening, according to a new report from the American Lung Association.

Dr. Henschke is on the Advisory Board for LungLifeAI and is on the board for the Early Diagnosis and Treatment Research Foundation. Dr. Hawk reported no conflicts. ■

## NEWS FROM CHEST

# This month in the journal *CHEST*®

## Editor’s picks

BY PETER J. MAZZONE, MD, MPH, FCCP

Editor in Chief

**Extracorporeal Membrane Oxygenation for Refractory Asthma Exacerbations With Respiratory Failure.**

By Jonathan K. Zakrajsek, MS, et al.

**Long-term Azithromycin in Children With Bronchiectasis Unrelated to Cystic Fibrosis Treatment Effects Over Time.**

By Don Vicendese, PhD, et al.

**Association of Inhaled Corticosteroids With All-Cause Mortality Risk in Patients With COPD: A Meta-analysis of 60 Randomized Controlled Trials.**

By Hong Chen, MD, et al.

**A 30-Minute Spontaneous Breathing Trial Misses Many Children Who Go On to Fail a 120-Minute Spontaneous Breathing Trial.**

By Kelby E. Knox, MS, et al.



**Psychological Morbidity After COVID-19 Critical Illness.**

By Keerthana Sankar, MD, et al.

**Feasibility of a New Lung Ultrasound Protocol to Determine the Extent of Lung Injury in COVID-19 Pneumonia.**

By Giovanni Volpicelli, MD FCCP, et al.

**“No Escalation of Treatment” Designations: A Multi-institutional Exploratory Qualitative Study.**

By Jason N. Batten, MD, et al.

# Buzz kill: Lung damage looks worse in pot smokers

BY DONAVYN COFFEY

**S**cans of the lungs of pot users have turned up an alarming surprise: Regular smokers of marijuana appear to be at greater risk for lung damage than are people who smoke tobacco alone.

“There’s a public perception that marijuana is safe,” said Giselle Revah, MD, a radiologist at the University of Ottawa. “This study is raising concern that this might not be true.”

Dr. Revah said she can often tell immediately if a CT scan is from a heavy or long-time cigarette smoker. But with the legalization and increased use of marijuana in Canada and many U.S. states, she began to wonder what cannabis use does to the lungs and whether she would be able to differentiate its effects from those of cigarette smoking.

She and her colleagues retrospectively examined chest CT scans from 56 marijuana smokers and compared them to scans of 57 nonsmokers and 33 users of tobacco alone (*Radiology*. 2022 Nov 15. doi: 10.1148/radiol.212611).

Emphysema was significantly more common among marijuana smokers

(75%) than among nonsmokers (5%). When matched for age and sex, 93% of marijuana smokers had emphysema, vs. 67% of those who smoked tobacco only ( $P = .009$ ).

Without age matching, rates of emphysema remained slightly higher among the marijuana users (75% vs. 67%), although the difference was no longer statistically significant. Yet more than 40% of the marijuana group was younger than 50 years, and all of the tobacco-only users were 50 or older – meaning that marijuana smokers may develop lung damage earlier or with less exposure, Dr. Revah said.

Marijuana smokers also showed higher rates of airway inflammation, including bronchial thickening, bronchiectasis, and mucoid impaction, with and without sex- and age-matching, the researchers found.

The findings are “not even a little bit surprising,” according to Alan Kaplan, MD, a family physician in Ontario who has expertise in respiratory health. He is the author of a 2021 review on cannabis and lung health (*Pulm Ther*. 2021 Oct 25. doi: 10.1007/s41030-021-00171-8).



Cabezon/istock/Getty Images

Marijuana smokers “take a big breath in, and they really push it into lungs and hold pressure on it, which may actually cause alveoli to distend over time.”

Because most marijuana smokers in the study also smoked cigarettes, whether the observed damage was caused by marijuana alone or occurred through a synergy with tobacco is impossible to discern, Dr. Revah said. Still, the results are striking, she said, because the marijuana group was compared to tobacco users who had an extensive smoking history – 25-100 pack-years – and who were from a high-risk lung cancer screening program.

“The message to physicians is to ask about cannabis smoking,” Dr. Kaplan said. In the past, people have been reluctant to admit to using cannabis. Clinicians should still try to identify frequent users, especially those who are predisposed for lung conditions. If they intend to use the drug, the advice should be, “There are safer ways to use cannabis,” he said.

Dr. Revah and Dr. Kaplan have disclosed no relevant financial relationships. ■

In an editorial accompanying the journal article by Dr. Revah and colleagues (*Radiology*. 2022 Nov 15. doi: 10.1148/radiol.222745), pulmonary experts noted that the new data give context to a recent uptick in referrals for nontraumatic pneumothorax. The authors said they had received 22 of these referrals during the past 2 years but that they had received only 6 between 2012 and 2020. “Many, but not all, of these patients have a documented history of marijuana use,” they wrote.

One reason for the additional damage may be the way marijuana is inhaled, Dr. Kaplan said.

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# Persistent asthma linked to increased carotid plaque

BY BATYA SWIFT YASGUR, MA, LSW

Persistent asthma is associated with increased carotid plaque burden and higher levels of inflammation, putting these patients at risk for atherosclerotic cardiovascular disease (ASCVD) events, new research suggests.

Using data from the Multiethnic study of atherosclerosis (MESA), investigators analyzed more than 5,000 individuals, comparing carotid plaque and inflammatory markers in those with and without asthma.

They found that carotid plaque was present in half of participants without asthma and half of those with intermittent asthma but in close to 70% of participants with persistent asthma. Moreover, those with persistent asthma had higher interleukin-6 (IL-6) levels, compared with those without asthma or those with intermittent asthma.

“The take-home message is that the current study, paired with prior studies, highlights that individuals with more significant forms of asthma may be at higher cardiovascular risk and makes it imperative to address modifiable risk factors among patients with asthma,” lead author Matthew Tattersall, DO, MS, of the University of Wisconsin School of Medicine and Public Health, Madison, told this news organization.

The study was published online Nov. 23, 2022 in the Journal of the American Heart Association (doi: 10.1161/JAHA.122.026644).

Asthma and ASCVD are “highly prevalent inflammatory diseases,” the authors write. Carotid artery plaque detected by B-mode ultrasound “represents advanced, typically subclinical atherosclerosis that is a strong independent predictor of incident ASCVD events,” with inflammation playing a “key role” in precipitating these events, they note.

Serum inflammatory markers such as C-reactive protein (CRP) and IL-6 are associated with increased ASCVD events, and in asthma, CRP and other inflammatory biomarkers are elevated and tend to increase during exacerbations.

Currently, there are limited data looking at the associations of asthma, asthma severity, and atherosclerotic plaque burden, they note, so the researchers turned to the MESA study – a population of individuals free of prevalent ASCVD at baseline.

They also wanted to explore “whether these associations would be attenuated after adjustment for baseline inflammatory biomarkers.”

Dr. Tattersall said the current study “links our previous work studying the manifestations of asthma,” in which he and his colleagues demonstrated increased cardiovascular events among MESA participants with persistent asthma, as well as late-onset asthma participants in the Wisconsin Sleep Cohort. His group also showed that early arterial injury occurs in adolescents with asthma.

However, there are also few data looking at the association with carotid plaque, “a late manifestation of arterial injury and a strong predictor of future cardiovascular events and asthma,” Dr. Tattersall added.

He and his group therefore “wanted to explore the entire spectrum of arterial injury, from the initial increase in the carotid media thickness to plaque formation to cardiovascular events.”

To do so, they studied participants in MESA, a study of close to 7,000 adults that began in the year 2000 and continues to follow participants today. At the time of enrollment, all were free from CVD. The analysis looked at 5,029 MESA participants (mean age 61.6 years, 53% female, 26% Black, 23% Hispanic, 12% Asian), compared to those with persistent asthma, defined as “asthma requiring use of controller medications,” intermittent asthma, defined as “asthma without controller medications,” and no asthma.

Participants underwent B-mode carotid ultrasound to detect carotid plaques, with a total plaque score (TPS) ranging from 0 to 12.

Participants with persistent asthma were more likely to be women, have higher body mass index (BMI), and higher high-density lipoprotein (HDL) cholesterol levels, than those without asthma.

Participants with persistent asthma had the highest burden of carotid plaque ( $P \leq .003$  for comparison of proportions and  $.002$  for comparison of means).

Moreover, participants with persistent asthma also had the highest systemic inflammatory marker levels – both CRP and IL-6 – compared with those without asthma. While participants with intermittent asthma also had higher average CRP, compared with those without asthma, their IL-6 levels were comparable.

## Carotid plaque burden by asthma status

Type of participant	% with carotid plaque	Total plaque score (standard deviation)
No asthma	50.5	1.29 (1.80)
Intermittent asthma	49.5	1.25 (1.76)
Persistent asthma	67	2.08 (2.35)

Note: The analysis involved 5,029 participants in the Multi-Ethnic Study of Atherosclerosis.  
Source: J Am Heart Assoc. 2022 Nov 23:e026644

## Inflammatory marker levels by asthma status

Marker	No asthma (SD)	Intermittent asthma (SD)	Persistent asthma (SD)
CRP (mg/L)	3.61 (5.50)	4.54 (6.80)	6.49 (11.20)
IL-6 (pg/mL)	1.52 (1.21)	1.60 (1.21)	1.89 (1.61)

Note: The analysis involved 5,029 participants in the Multi-Ethnic Study of Atherosclerosis.  
Source: J Am Heart Assoc. 2022 Nov 23:e026644

In unadjusted models, persistent asthma was associated with higher odds of carotid plaque presence (odds ratio, 1.97; 95% confidence interval, 1.32-2.95) – an association that persisted even in models that adjusted for biologic confounders (both  $P < .01$ ). There also was an association between persistent asthma and higher carotid TPS ( $P < .001$ ).

In further adjusted models, IL-6 was independently associated with presence of carotid plaque ( $P = .0001$  per 1-SD increment of 1.53), as well as TPS ( $P < .001$ ). CRP was “slightly associated” with carotid TPS ( $P = .04$ ) but not carotid plaque presence ( $P = .07$ ).

There was no attenuation after the researchers evaluated the associations of asthma subtype and carotid plaque presence or TPS and fully adjusted for baseline IL-6 or CRP ( $P = .02$  and  $P = .01$ , respectively).

“Since this study is observational, we cannot confirm causation, but the study adds to the growing literature exploring the systemic effects of asthma,” Dr. Tattersall commented.

“Our initial hypothesis was that it was driven by inflammation, as both asthma and CVD are inflammatory conditions,” he continued. “We did adjust for inflammatory biomarkers in this analysis, but there was no change in the association.”

Nevertheless, Dr. Tattersall and colleagues are “cautious in the interpretation,” since the inflammatory biomarkers “were only collected at one point, and these measures can be dynamic.”

Robert Brook, MD, professor and

director of cardiovascular disease prevention, Wayne State University, Detroit, said the “main contribution of this study is the novel demonstration of a significant association between persistent (but not intermittent) asthma with carotid atherosclerosis in the MESA cohort, a large multi-ethnic population.”

These findings “support the biological plausibility of the growing epidemiological evidence that asthma independently increases the risk for cardiovascular morbidity and mortality,” added Dr. Brook, who was not involved with the study. “The main take-home message for clinicians is that, just like in COPD (which is well-established), asthma is often a systemic condition in that the inflammation and disease process can impact the whole body,” he said.

“Health care providers should have a heightened awareness of the potentially increased cardiovascular risk of their patients with asthma and pay special attention to controlling their heart disease risk factors (for example, hyperlipidemia, hypertension),” Dr. Brook stated.

Dr. Tattersall and co-authors and Dr. Brook declared no financial conflicts. ■

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