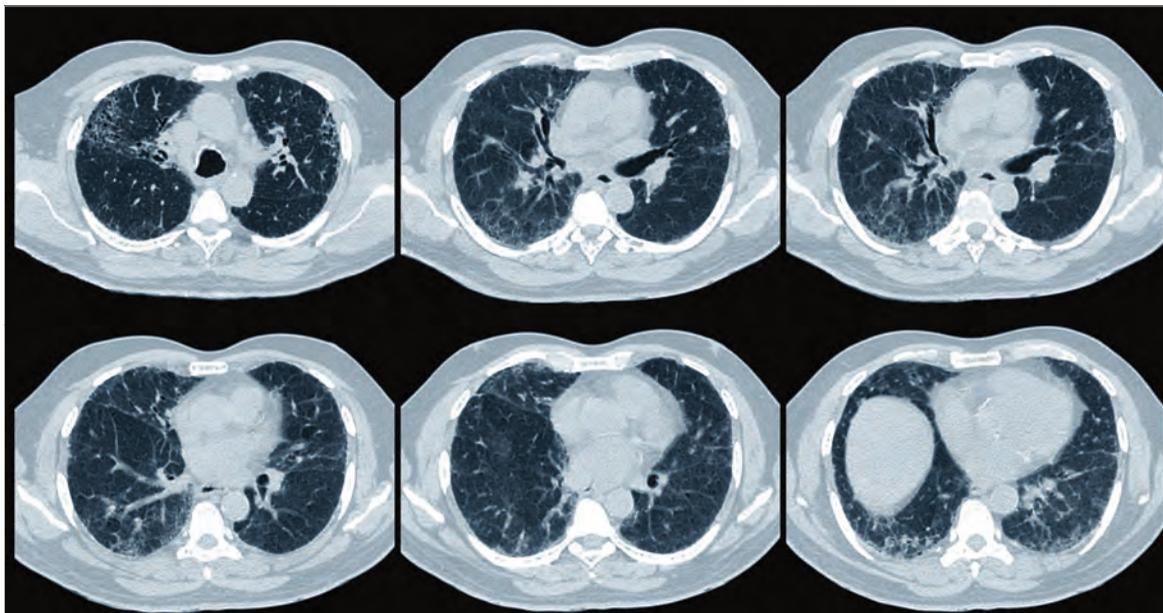


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Computed tomography scans of axial sections through the chest of a 68-year-old patient with interstitial lung disease (diffuse parenchymal lung disease, DPLD): Various microcystic lesions can be seen, along with evidence of localized, irreversible dilation of part of the bronchial tree (bronchiectasis).

Science Source

Race-specific lung function values may skew IPF testing

BY NEIL OSTERWEIL
MDedge News

FROM CHEST 2023 ■ Old habits die hard, especially when it comes to pulmonary function testing in a diverse population of patients with interstitial lung disease (ILD).

Specifically, pulmonary care clinicians may be habitually relying on outdated and inaccurate race-specific reference values when evaluating respiratory impairment in persons of African and Hispanic/Latino ancestry, which can result in underrecognition, underdiagnosis, and undertreatment, reported Ayodeji Adegunsoye, MD, from the University of Chicago, and colleagues. “Our results make a compelling case for

re-evaluating the use of race as a physiological variable, and highlight the need to offer equitable and optimal care for all patients, regardless of their race or ethnicity,” Dr. Adegunsoye said in an oral abstract session at the annual meeting of the American College of Chest Physicians (CHEST).

Flawed assumptions

In an interview, Dr. Adegunsoye noted that race-specific notions, such as the automatic assumption that Black people have less lung capacity than White people, are baked into clinical practice and passed on as clinical wisdom from one generation of clinicians to the next.

IPF // continued on page 2

Tezepelumab found effective in asthma with GERD

BY JIM KLING
MDedge News

FROM CHEST 2023 ■ Among patients with asthma and comorbid gastroesophageal reflux disease (GERD), the biologic tezepelumab (Tezspire, Amgen) had similar efficacy at reducing exacerbations, improving lung function, and symptom control as observed in patients with asthma alone, according to a new post hoc analysis of the phase 2b PATHWAY and phase 3 NAVIGATOR clinical trials. GERD occurs in about 60% of asthma patients, and the comorbidity is associated with a greater risk of asthma exacerbations. “As we start doing subgroup analyses, we are looking at different comorbidities and reflux is one that’s very common and very impactful on asthma outcomes in a negative way, so it became an area of interest,” said Njira Lugogo, MD, who presented the study during a poster session at the annual meeting of the American College of Chest Physicians (CHEST). She is a professor of internal medicine and pulmonary critical care at the University of Michigan, Ann Arbor.

The analysis confirmed other findings, with GERD // continued on page 4

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Pulmonary function reference values that are used to make a diagnosis of idiopathic pulmonary fibrosis in Black or Hispanic/Latino patients “appear flawed when we use race-specific values. And beyond the diagnosis, it also appears to impact eligibility for key interventional strategies for managing the disease itself,” he said.

The use of race-specific equations can falsely inflate percent-predicted pulmonary function values in non-White patients, and make it seem as if a patient has normal lung function when in fact he may have impaired function.

For example, using race-based reference values a Black patient and a White patient may appear to have the same absolute forced vital capacity readings, but different FVC percent predicted (FVCpp), which can mean a missed diagnosis.

Investigators who studied the association between self-identified race and visually identified emphysema among 2,674 participants in the Coronary Artery Risk Development in Young Adults study found that using standard equations to adjust for racial differences in lung function measures appeared to miss emphysema in a significant proportion of Black patients.

Pulmonary Fibrosis registry

In the current study, to see whether the use of race-neutral equations for evaluating FVCpp could change access to health care in patients with ILD, Dr. Adegunsoye and colleagues used both race-specific and race-neutral equations to calculate FVCpp values among separate cohorts of Black, Hispanic/Latino, and White patients enrolled in the Pulmonary Fibrosis Foundation Patient Registry who had pulmonary functions test within about 90 days of enrollment.

The race-specific equations used to calculate FVCpp was that published in 1999 by Hankinson and colleagues in American Journal of Respiratory and Critical Care Medicine (doi: 10.1164/ajrccm.159.1.9712108). The race-neutral Global Lung Function Initiative (GLI) equations by Bowerman and colleagues were developed in 2022 and published in March 2023 in the same journal (doi: 10.1164/rccm.202205-0963OC).

The investigators defined access to care as enrollment in ILD clinical trials for patients with FVCpp greater than 45% but less than 90%, and US payer access to antifibrotic therapy for patients with FVCpp of greater than 55% but less than 82%.

They found that 22% of Black patients were misclassified in their eligibility for clinical trials in each of two scenarios – those who would be excluded from trials using the 1999 criteria but included using the 2022 criteria, and vice versa, that is included with 1999

criteria but excluded by the 2022 GLI criteria. In contrast, 14% of Hispanic Latino patients and 12% of White patients were misclassified.

Using the 1999 criteria to exclude patients because their values were ostensibly higher than the upper cutoff meant that 10.3% of Black patients who might benefit would be ineligible for clinical trial, compared with 0% of Hispanic/Latinos and 0.1% of Whites.

Similarly, 11.5% of Black patients but no Hispanic/Latino or White patients would be considered eligible for clinical trials using the old criteria but ineligible under the new criteria.

Regarding antifibrotic therapy eligibility, the respective misclassification rates were 21%, 17%, and 19%.

“Our study showed that use of race-specific equations may confound lung function tests, potentially leading to misclassification, delayed diagnosis, and inadequate treatment provision. While our study suggests potential disparities in access to health care for patients with interstitial lung disease facilitated by race-specific equations, further research is required to fully comprehend the implications,” the investigators wrote.

ATS statement

In an interview, Juan Wisniewsky, MD, DrPH, from Mount Sinai Medical Center, New York, who also chairs the Health Equity and Diversity Committee for the American Thoracic Society, pointed to a recent ATS statement he coauthored citing evidence for replacing race- and ethnicity-specific equations with race-neutral average reference equations (Am J Respir Crit Care Med. 2023 Apr 15;207[8]:978-95).

IPF continued on following page

“Our results make a compelling case for re-evaluating the use of race as a physiological variable.”

-Ayodeji Adegunsoye, MD

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

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Sputum microbiome may augur treatment success

BY NEIL OSTERWEIL

MDedge News

FROM CHEST 2023 ■ The diversity of species in the sputum of patients undergoing therapy for nontuberculosis mycobacterial pulmonary disease (NTM-PD) could be a marker for treatment efficacy, authors of a small prospective study suggest.

Among 14 patients treated for NTM-PD, 7 of whom had treatment-refractory disease and 7 of whom had microbiological cures after antibiotic therapy, the diversity of the microbiome in sputum was greater for patients who were cured, indicating the variety of species found in sputum could help clinicians evaluate the efficacy of therapy and guide patient management, said Noeul Kang, MD, PhD, from Samsung Medical Center in Seoul, South Korea.

“What we found was that in NTM-PD patients the sputum of the patients who remained in long-time stabilization without recurrence exhibited higher microbiome diversity than that of treatment-refractory patients, and several genera were identified in the samples of the cured group. We hope to do more research on this, and we are planning to compare the patients who have never been treated with those who respond to treatment,” she said at

the annual meeting of the American College of Chest Physicians (CHEST).

NTM-PD on the rise

The incidence and prevalence of NTM-PD in both South Korea and the United States have been rising steadily since 2007, with the highest incidence occurring among those 65 and older. “NTM-PD is becoming a global burden,” Dr. Kang said. Across the world, the most commonly occurring organisms in NTM-PD patients are *Mycobacterium avium* complex (MAC), with other mycobacteria species varying in frequency by region.

Outcomes of treatment differ according to the etiologic organism, with *M. avium* complex infections being successfully treated in about 60% of patients, compared with 70% of patients’ infections with the *M. abscessus massiliense*, and 30%-40% of infections yielding to antibiotics in patients with *M. abscessus abscessus*, Dr. Kang said.

To compare the characteristics of the sputum microbiota of NTM-PD patients based on their treatment outcomes, Dr. Kang and colleagues looked at sputum from all patients with NTM-PD who agreed to provide samples at their center from 2018 through 2022.

SPUTUM continued on following page



Dr. Kang

IPF continued from previous page

“This use of race and ethnicity may contribute to health disparities by norming differences in pulmonary function. In the United States and globally, race serves as a social construct that is based on appearance and reflects social values, structures, and practices. Classification of people into racial and ethnic groups differs geographically and temporally. These considerations challenge the notion that racial and ethnic categories have biological meaning and question the use of race in PFT interpretation,” the statement authors wrote.

“There is some agreement that race-based equations shouldn’t be used, but all the potential

consequences of doing that and which equations would be the best ones to use to replace them is a bit unclear,” Dr. Wisniewsky said.

He was not involved in the study by Dr. Adegunsoye and colleagues.

Data used in the study were derived from research sponsored by F. Hoffman–La Roche and Genentech. Dr. Adegunsoye disclosed consultancy fees from AbbVie, Inogen, F. Hoffman–La Roche, Medscape, and Patient-Mpower; speaking/advisory fees from Boehringer Ingelheim; and grants/award from the CHEST Foundation, Pulmonary Fibrosis Foundation, and National Institutes of Health. Dr. Wisniewsky had no relevant disclosures. ■

ACORN: No excess AKI with pip-tazo vs cefepime

BY NEIL OSTERWEIL

MDedge News

Two antibiotics, both alike in efficacy, are commonly prescribed for empirical treatment of infection in hospitalized adults.

Yet each drug – cefepime and piperacillin-tazobactam (PTZ) – has its own baggage in terms of suspected associated toxicities: Cefepime has been implicated in neurologic dysfunction, and PTZ has been associated with acute kidney injury (AKI).

The true nature of toxicities associated with each agent in clinical practice has been unclear, however – until now. As results of the randomized ACORN (Antibiotic Choice on Renal Outcomes) trial showed, PTZ was not associated with a higher incidence of AKI, compared with cefepime, but cefepime was indeed associated with a higher incidence of neurologic dysfunction as measured by freedom from delirium and coma.

The findings, by Edward T. Qian, MD, MSc, and colleagues at Vanderbilt University Medical Center, Nashville, Tenn., were published in JAMA (2023 Oct 24;330[16]:1557-67).

Questioning a common practice

In an interview, Dr. Qian said that he and his colleagues conducted the pragmatic trial to seek answers to an important issue.

“We noticed a change in practice patterns as people were afraid of using [PTZ] as empiric antibiotic therapy because they were afraid of the risks of AKI,” he said. “And as that practice shifted with a lower quality of evidence, just from observational studies, we started using more cefepime and we started seeing more patients with this rare phenomenon called ‘cefepime neurotoxicity.’”

To see whether the choice of one antibiotic over the other would affect the risk for either AKI or neurologic dysfunction, the investigators enrolled adults for whom a clinician ordered antipseudomonal antibiotics within 12 hours of when they were seen in the ED or medical ICU.

The patients were randomized on a 1:1 basis to receive either cefepime or PTZ.

A total of 2,511 patients treated from Nov. 10, 2021, to Oct. 7, 2022, were included in the primary analysis. A large majority of the patients (94.7%) were enrolled in the ED,

and 77.2% of patients were also receiving vancomycin at the time of enrollment.

No added AKI risk

The investigators found that there was no significant difference between the drugs for the primary outcome of the highest stage of AKI or death within 14 days of the start of treatment.

In the cefepime arm, 85 of 1,214 patients (7.0%) had stage 3 AKI, and 92 (7.6%) died.

In the PTZ arm, 97 of 1,297 patients (7.5%) had stage 3 AKI, and 78 (6%) died. As noted, the difference was not statistically significant.

In addition, there was no significant difference between the groups in the secondary endpoint of the incidence of major adverse kidney events at day 14, with 10.2% in the cefepime arm and 8.8% in the PTZ arm having an event.

As noted before, however, there was a significant difference in the secondary outcome of the number of days alive and free of delirium and coma within 14 days.

Patients on cefepime had a mean 11.9 days free of delirium and coma, compared with 12.2 days for patients on PTZ. This difference translated into an odds ratio of 0.79 (95% confidence interval, 0.65-0.95).

Dr. Qian said that he and his colleagues stop short of calling the neurologic dysfunction that they observed “cefepime neurotoxicity,” but added that it warrants further study.

Risk factors examined

The investigators plan to evaluate those patients who developed neurologic dysfunction while on the drug to see whether there were predisposing factors that might be a contraindication for cefepime in some cases.

“I think the big takeaway is you should feel comfortable starting or using pip-tazo for your patients who are coming into the hospital and receiving empiric antibiotics for acute infection,” Dr. Qian said.

The ACORN investigators are supported by grants from the National Heart, Lung, and Blood Institute; National Institutes of Health; National Center for Advancing Translational Science; US Defense Department; and Vanderbilt University. Dr. Qian had no conflicts of interest to disclose. ■

comorbid GERD associated with more exacerbations, use of maintenance steroids, and high-dose inhaled steroids. “They had more disease activity, and the effect [of tezepelumab treatment] was similar whether you had reflux or didn’t have reflux. It did seem like the people without reflux had a slightly higher reduction in exacerbations, so maybe there is a slight difference, but overall it looked like both groups were really improving,” Dr. Lugogo said.

Tezepelumab is a newer biologic, having received Food and Drug Administration approval in 2021. It targets the epithelial cytokine thymic stromal lymphopoietin (TSLP), which contributes allergic inflammatory responses by acting on various innate immune cells, including dendritic cells, mast cells, and CD34+ progenitor cells. It is upregulated in the airways of asthma patients, with higher levels linked to more severe disease. A single-nucleotide polymorphism in the gene that codes TSLP has also been found to be protective against asthma, atopic asthma, and airway hyper-responsiveness.

Dr. Lugogo noted that TSLP could be a factor in how GERD may worsen triggers or worsen asthma. It is produced in the epithelium of the upper airway in response to injury, which could include aspiration into bronchial tubes attributable to GERD, and this could lead to a downstream inflammatory and immune response. “Reducing the production of or at least blocking TSLP from an epithelium that’s being irritated by acid reflux could have potential benefits. On the reverse side, could the continued presence of reflux blunt the expected response [to tezepelumab]? If someone has very severe reflux, maybe you’ve treated their asthma with tezepelumab, and they’re still having symptoms. Could it be a masquerading issue [where] you have untreated reflux contributing to ongoing symptoms, which you’re attributing to not being related to asthma? So it’s looking at

it in two different ways,” Dr. Lugogo said.

Tezepelumab is the only biologic available to treat patients with non-type 2 inflammation, which includes about 10% of adult patients, according to Dr. Lugogo. Its mechanism also influences eosinophilic and allergic asthma. When tezepelumab first became available, Dr. Lugogo noticed that physicians tended to switch to it from another biologic rather than starting it up front, but that may be changing. “I feel like more and more people are starting it up front as a therapeutic intervention, so there seems to be more and more people embracing its use in the treatment of severe asthma,” she said.

The analysis included 294 patients with asthma and GERD and 1,040 with asthma alone. Patients in the GERD comorbidity group were older (55.0 versus 48.6 years), had a higher mean body mass index (30.8 kg/m² versus 27.8 kg/m²), and were more likely to be female (67.3% versus 63.0%).

Maintenance oral corticosteroid use was higher in the GERD group (17.0% versus 6.9%), as was use of high inhaled corticosteroid dose (78.2% versus 67.0%), frequency of nasal polyps in the previous 2 years (21.4% versus 13.8%), and experience of more than two exacerbations in the previous year (42.2% versus 34.6%).

There was a 65% reduction (95% confidence interval, 50%-76%) in annualized asthma exacerbation rate versus placebo with tezepelumab treatment in the GERD group, compared with a 58% reduction in the asthma-only group (95% CI, 48%-66%). The drug led to a 0.10 increase in forced expiratory volume in 1 second versus placebo (95% CI, 0.00-0.19) at week 52 in the GERD group, versus 0.15 (95% CI, 0.10-0.20) in the asthma-only group. Tezepelumab also improved week 52 ACQ-6 scores in the GERD group (-0.39 versus placebo; 95% CI, -0.63 to -0.14) and the asthma-only group (-0.32 versus placebo; 95% CI, -0.45 to -0.19).

The study adds to the evidence supporting tezepelumab as a promising new therapy, said Muhammad Adrish, MD, who attended the

Diego Maselli, MD, FCCP, comments:

These findings will not have a significant change in practice yet but generate discussion and awareness on the importance of comorbid conditions in asthma. In particular, GERD has been linked to poor outcomes in asthma, and addressing this comorbid condition has been found to improve asthma control in randomized controlled studies.



Dr. Maselli is a member of the CHEST Physician Editorial Board.

poster session and was asked to comment on the study. “I think this is a very interesting analysis in the sense that gastric reflux disease is a frequent comorbid condition we see in patients with asthma, and a lot of these patients can have poor outcomes. When you look at the results from the data, you see regardless of how sick they were and how much medication utilization these patients have at baseline, they still had a pretty decent response to tezepelumab. That speaks to the efficacy of that drug along a wide spectrum of patients,” said Dr. Adrish, who is an associate professor of pulmonary, critical care, and sleep medicine at Baylor College of Medicine, Houston.

The PATHWAY (N Engl J Med. 2017. doi: 10.1056/NEJMoa1704064) and NAVIGATOR (N Engl J Med. 2021. doi: 10.1056/NEJMoa2034975) studies were funded by Amgen. Dr. Lugogo has advised or consulted for AstraZeneca, Amgen, Regeneron, TEVA, Avillion, Sanofi, Novartis, Genentech, GSK, and Janssen. Dr. Adrish has no relevant financial disclosures. ■

SPUTUM continued from previous page

After excluding those who did not receive antibiotics, those who were on treatment but did not have refractory disease, and those who were lost to follow-up or whose samples did not pass quality control, they identified seven patients who had microbiological cures, and seven whose disease remained refractory to treatment.

They defined culture conversion at three or more consecutive negative sputum cultures after treatment, collected at least 4 weeks apart, and microbiological cures at maintenance of multiple consecutive negative cultures without any positive cultures of the causative species from respiratory samples.

Infections were deemed to be refractory if there were sustained positive cultures from respiratory samples of causative NTM species

after at least 1 year of antibiotic therapy.

Microbial diversity

Samples from 8 of the 14 participants had *M. abscessus*-PD, with the proportion higher among those who had a sustained microbiological cure (71.4% vs. 42.9%). At baseline, patients with refractory disease were found to have significantly lower alpha-diversity, a measure of microbial diversity within a single sample, compared with those whose infections were cured ($P = .025$).

In addition, samples at 6-month follow-up from those with baseline

refractory infections had differences in the species level of beta-diversity (that is, differences among samples), compared with both baseline and follow-up samples from the cured group ($P = .022$ and $.024$, respectively).

The sputum of the patients who remained in long-time stabilization without recurrence exhibited higher microbiome diversity than that of treatment-refractory patients.

The investigators also used linear discriminant analysis to look at taxonomic biomarkers, and observed that several species were more abundant in samples from the microbiological cure group than

from the refractory disease group ($P < .05$). These species included organisms in the *Streptococcus pneumoniae* group, *Prevotella melaninogenica*, and *Haemophilus*

parahaemolyticus group.

Promising start

A pulmonologist who was not involved in the study commented in an interview that, although the findings need further study, the microbiome of sputum samples has the potential for predictive value.

“I think this will be clinically useful, if we’re able to identify and diagnose patients with MAC disease and then we identify their sputum microbiome, it might give us an idea whether these patients are more sensitive or refractory to treatment,” said Muhammad U. Khawar, MD, from the University of Cincinnati.

Dr. Khawar moderated the session where Dr. Kang reported her data.

The investigators did not report a funding source. Dr. Kang and Dr. Khawar reported no relevant disclosures. ■

In advanced ILD, ECMO linked to good outcomes as bridge to transplant in meta-analysis

BY JIM KLING

MDedge News

FROM CHEST 2023 ■ Extracorporeal membrane oxygen support appears to be beneficial in patients with advanced interstitial lung disease (ILD), according to a meta-analysis. Specifically, among patients undergoing ECMO as a bridge to transplant, mortality was lower with venoarterial (VA) ECMO than with venovenous (VV) ECMO, although confidence in the finding was low.

ECMO has been used increasingly in ILD patients over the past 10-15 years for acute decompensation and as a bridge to lung transplant, according to Prasanth Balasubramanian, MD, but clinical evidence for its use is limited to case series or short-term retrospective studies. “We don’t have robust evidence on whether it really helps with the outcome, and which mode is better,” said Dr. Balasubramanian, who is a fellow in pulmonary critical care at Mayo Clinic in Jacksonville, Fla. He presented the new research at the annual meeting of the American College of Chest Physicians (CHEST).

The results were encouraging, according to the study’s lead author Pramod Guru, MD. “I think what we take from this analysis is ECMO should not be considered as a contraindication for people you are considering for lung transplant. If we have this

population of people who are very sick, but we have the opportunity to solve them with VA ECMO and then give the transplantation possibly, that may be the way,” said Dr. Guru, a critical care specialist at Mayo Clinic, Jacksonville. He acknowledged more work needs to be done to determine whether VA

“A patient might say, ‘Why am I going to go through all this? Is it just prolonging my death, or is there a chance of saving my life?’ I think what this study shows is it does have potential of saving their life.”

-Chris Carroll, MD

or VV is best in specific patient populations.

The meta-analysis included 18 studies with a total of 1,341 patients (mean age, 55.89; 61.08% male). Most procedures (75.3%) were VV. The overall mortality was 52.6%, including 59.7% for VV ECMO and 34.2% for VA ECMO. The survival difference did not reach statistical significance (odds ratio, 0.48; $P = .11$). There was also no significant difference in survival between patients who underwent ECMO and those who did not (OR, 0.48; $P = .43$).

The researchers also analyzed 13

studies with 1,002 patients with ECMO as a bridge to transplant (mean age, 52.1; 52.2% male; 49.3% VV, 31.1% VA, 32.4% cardiopulmonary bypass). Mortality was lower in the VA group than in the VV group (odds ratio, 0.62; $P = .04$).

“VA ECMO is generally for sicker patients, so it’s odd the patients who are on the more aggressive support had lower mortality. But it’s good; it says it works,” said Chris Carroll, MD, an intensivist at the University of Florida, Jacksonville, who was asked to comment on the study.

The finding may also be an artifact of bias in the retrospective data, according to Joshua Diamond, MD, who co-moderated the session where the study was presented.

He noted age, physical function, and illness severity, among other factors can play a role in decision-making. “I have a feeling what you’re seeing is a very carefully selected patient population as opposed to a true mortality benefit with VA versus VV ECMO,” said Dr. Diamond, who is associate medical director of the Penn Lung Transplant Program in Philadelphia.

Another weakness of the study is ECMO techniques and devices have changed over time, making older data less relevant to current practice. Dr. Diamond described the study as interesting, but he’d “like to see a bit more granularity of data to figure

out who makes or doesn’t make a good candidate.”

Patients with ILD undergoing ECMO as a bridge to transplant had higher 1-year posttransplant mortality than patients with other causes for transplant (OR, 1.78; $P < .01$). This finding relied on two retrospective studies using the UNOS database at different intervals (2001-2012 and 2015-2020), leading to potential confounders and risk of bias.

Dr. Balasubramanian recognized the limitations of the analysis. “We do think further prospective studies comparing various modalities would be essential, although it would be challenging,” he said.

Nevertheless, Dr. Guru said his own center is changing its patient selection criteria for ECMO and will begin to collect prospective data: “I would say in 12 months we’ll have our own data to support what we are doing.”

The study could inform potential end-of-life decisions about pursuing aggressive ECMO therapy. “This study says if you choose to pursue more aggressive therapy, you may still have a good outcome. A patient might say, ‘Why am I going to go through all this? Is it just prolonging my death, or is there a chance of saving my life?’ I think what this study shows is it does have potential of saving their life,” Dr. Carroll said.

Dr. Balasubramanian, Dr. Guru, and Dr. Carroll have no relevant financial disclosures. ■

Nirmatrelvir-ritonavir ineffective with most post-COVID conditions

BY BECKY ELLIS

Nirmatrelvir-ritonavir doesn’t reduce the incidence of most post-COVID conditions, according to a new study. Thromboembolic events are the exception.

Post-COVID conditions

A retrospective study of 9,593 veterans older than 65 years examined the impact of nirmatrelvir-ritonavir compared with no treatment on post-COVID-19 conditions (PCCs). Researchers coded 31 conditions, including cardiac, pulmonary, renal, thromboembolic, gastrointestinal, neurologic, mental health, musculoskeletal, and endocrine categories.

The incidence of PCCs was analyzed 31-180 days after treatment.

Key takeaways

The combined incidence of venous thromboembolism and pulmonary embolism was reduced among patients given nirmatrelvir-ritonavir. No statistically significant reduction of other conditions was found. “Our results suggest considerations about PCCs may not be an important factor in COVID-19 treatment decisions,” the authors write.

Results of the study differ from a smaller study that found the incidence of 10 of 13 PCCs was lower.

Limitations

Because of a large number of outcomes, the association between treatment and reduced incidence of thromboembolic events may have occurred by chance. PCC Long-term effects may not have

been fully captured by the ICD-10 diagnosis codes. Electronic health records did not accurately capture symptom burden or onset date. Patients treated may have had more symptoms than matched controls.

Veteran cohort

The study was funded by the Department of Veterans Affairs and was published in *Annals of Internal Medicine* (2023 Oct 31. doi: 10.7326/M23-1394). George Ioannou, MD, hepatology director at VA Puget Sound Health Care System in Seattle, led the study.

The authors reported relationships with Korean Diabetes Association, American Diabetes Association, International Society for the Diabetic Foot, Quality Insights, Brown University, and Society for Women in Urology, among others. ■

mRNA vaccine cuts COVID-related Guillain-Barré risk

BY KELLI WHITLOCK BURTON

The risk for Guillain-Barré syndrome (GBS) is six times higher in people with COVID-19 in the 6 weeks following infection, according to a new study.

Methodology

- The nested-case control study analyzed data for 3.2 million patients aged 16 years and older, with no history of GBS.
- GBS cases (n = 76) were identified based on hospital discharge data from January 2021 to June 2022.
- For every GBS case, investigators chose 10 controls at random, matched for age, gender, and follow-up duration (n = 760).
- Investigators examined the association between GBS and SARS-CoV-2 infection, through documentation of prior positive SARS-CoV-2 test (polymerase chain reaction or antigen), and any COVID-19 vaccine administration.

Among those diagnosed with GBS, 8 were exposed to SARS-CoV-2 infection only, 7 were exposed to COVID-19 vaccination only, and 1 patient was exposed to both SARS-CoV-2 infection and COVID-19 vaccination in the prior 6 weeks, leaving 60 GBS patients without exposure to either infection or vaccination. All COVID-19 vaccine doses administered in GBS cases within 6 weeks of the index date, and all but two doses administered in controls in the same timeframe, were Pfizer-BioNTech vaccines. Compared with people without GBS, those with the condition were more than six times as likely to have had SARS-CoV-2 infection within 6 weeks of GBS diagnosis (adjusted odds ratio, 6.30; 95% confidence interval, 2.55-15.56).

People who received the COVID-19 vaccine were 59% less likely to develop GBS than those who did not get the vaccine (aOR, 0.41; 95% CI, 0.17-0.96).

“While Guillain-Barré is extremely rare, people should be aware having a COVID infection can increase their risk of developing the disorder, and receiving an mRNA vaccine can decrease their risk,” study author Anat Arbel, MD, of Lady Davis Carmel Medical Center and the Technion-Israel Institute of Technology, both in Haifa, said.

Co-lead author of the study, which was published in the journal

Neurology, is Haya Bishara, MD, of Lady Davis Carmel Medical Center.

Study limitations include a possibility of misclassification of SARS-CoV-2 infection, which could lead to an overestimation of the

magnitude of association between infection and GBS. The diagnosis of GBS relied solely on ICD-9 coding, which has been shown in prior studies to contain errors.

The study was unfunded.

Dr. Bishara and Dr. Arbel report no relevant financial relationships. Co-author, Eitan Auriel, MD, has received lecturer fees from Novo Nordisk, Pfizer, Boehringer Ingelheim, and Medison. ■

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No cerebrospinal fluid abnormalities in long COVID

BY LISA O'MARY

A pair of new studies about long COVID have shed light on the sometimes-disabling condition affecting millions of people.

In the first study, 31 adults underwent lumbar puncture and blood draws to look for changes in their immune systems and in the nerve cells that transmit signals to the brain.

Among participants, 25 people had neurocognitive symptoms of long COVID, such as memory loss or attention problems. Six participants had fully recovered from COVID, and 17 people never had

COVID. Those who had COVID were diagnosed between March 2020 and May 2021, and fluid samples were drawn at least 3 months after their first symptoms.

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The results were published in the *Journal of Infectious Diseases* (2023 Oct 24. doi: 10.1093/infdis/jiad395). Results showed long COVID does not appear to be linked to the SARS-CoV-2 virus invading the brain or causing active brain damage.

According to a study summary from the University of Gothenburg

(Sweden), “there were no significant differences between the groups when analyzing blood and cerebrospinal fluid for immune activation or brain injury markers.”

In the second study, Norwegian researchers compared the likelihood of having 17 different long COVID symptoms based on prior COVID infection. The analysis included

53,846 people diagnosed with COVID between February 2020 and February 2021, and over 485,000 people who were uninfected. Results, published in the journal *BMC Infectious Diseases* (2023 Oct 25. doi: 10.1186/s12879-023-08727-6), showed those who had COVID were twice as likely to experience shortness of breath or fatigue, and more

likely to experience memory loss or headache, compared with those uninfected. Hospitalization increased the risk for long COVID symptoms of shortness of breath, fatigue, and memory loss. The authors noted not all symptoms reported during a visit with a general practice provider are recorded in Norway, potentially affecting the results. ■

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Patient contact time vs admin: Is your contract fair?

BY BATYA SWIFT YASGUR,
MA, LSW

What's in a day's work? For doctors, it's typically a mix of seeing patients and

completing paperwork and follow-up. Often it extends well past the standard workday.

Dennis Hursh, JD, managing partner of Physician Agreements Health Law, a Pennsylvania-based law firm

that represents physicians, describes one overwhelmed physician who recently consulted him for this problem.

"My client had accepted a position in a group practice where his

contract stated he would be working during normal office hours, Monday through Friday, from 8 a.m. to 5 p.m. – in other words, a 40-hour workweek," Mr. Hursh said.

But the distressed physician discovered that actually, he was working almost twice as many hours. "He'd get to work early to do charting, then see patients during the 40 hours, perhaps grabbing a quick sandwich for a few minutes – and then stay after 5 [p.m.] for a few more hours when he'd work on charts or other administrative tasks. Then he'd get something to eat, work on more charts, then go to bed, get up in the morning, and repeat."

It turned out the 40-hour workweek included in the contract referred to patient-facing hours, not all of the ancillary tasks that are part of practicing medicine. "Unfortunately, this is far from an isolated story," Mr. Hursh said.

Be aware of what's in the contract

"The first draft of many standard physician employment contracts often omits mention of patient contact hour requirements and rather uses vague verbiage such as 'full-time' employment or '1.0 FTE' – or full-time equivalent – without defining that term," Mr. Hursh said. Typically, the 40 hours exclude call coverage, but most physicians understand that and, at least at first glance, it all sounds very reasonable.

But once charting, hours on the phone, argument with managed care companies, prescriptions, administrative meetings, and other tasks are thrown in, the work hours expand dramatically.

Amanda Hill, JD, owner of Hill Health Law based in Austin, Tex., told this news organization that this predicament isn't unique to physicians. Exempt employees who don't clock in and out are often expected to work overtime – that is, to "work as long as it takes to get the job done." It can affect nurse practitioners, physician assistants, and many others in the health care space. But the number of tasks that fall upon a doctor's shoulders and the fact that patients' health and lives are at stake up the ante and make the situation far more difficult for doctors than for employees in other industries.

So it's important to nail down precise terms in the contract and, if possible, negotiate for a more

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Medicare 2024 rate cut prompts calls for overhaul

BY KERRY DOOLEY YOUNG

Physicians in 2024 can expect a 3.4% drop in the conversion factor that determines their base Medicare pay, according to federal officials, but they also will receive more money for primary care and treating complex conditions.

The Centers for Medicare & Medicaid Services on Nov. 2 released its 2024 final physician fee schedule, triggering renewed concerns from doctors' groups, who protested CMS's cuts when they were first previewed earlier in 2023.

The 2024 conversion factor, or base rate for clinician pay, will be \$32.74, a decrease of \$1.15, or 3.4%, from 2023's level. The pay cuts come as costs of providing health care are expected to rise as much as 4.6% in 2024, the American Medical Association said.

The new rule follows a 2% payment reduction in 2023, AMA president Jesse M. Ehrenfeld, MD, MPH, said in a statement.

The 2024 conversion factor, or base rate for clinician pay, will be \$32.74, a decrease of \$1.15, or 3.4%, from 2023's level.

"This is a recipe for financial instability," Dr. Ehrenfeld said. "Patients and physicians will wonder why such thin gruel is being served."

The AMA is among the many physician groups pressing Congress to change its approach to paying clinicians and consider inflation rates in determining future payments.

Medicare already includes automatic inflation adjusters in other payment rules, such as the ones for care provided in hospitals. But Congress in 2015 eliminated this feature for the physician fee schedule when it passed the Medicare Access and CHIP Reauthorization Act.

A pending House bill, the bipartisan Strengthening Medicare for Patients and Providers Act (H.R.2474), would return to permanently including a broader inflation adjuster in the Medicare physician fee schedule.

"This long-overdue change would not only help provide greater stability within the Medicare payment system, but it would also help

physicians' practices – many of whom operate as small business owners – more effectively navigate the ever-changing economic factors that impact their practices, including rising medical costs, workforce and labor challenges, administrative burdens, office rental prices and more," Larry Bucshon, MD (R-Ind.), Ami Bera, MD (D-Calif.), Raul Ruiz, MD (D-Calif.), and Mariannette Miller-Meeks, MD (R-Iowa), wrote in an opinion article in the newspaper *The Hill*.

Major changes to determining Medicare physician pay remain unlikely this year. Still, Congress has softened or blocked slated cuts in physician pay in recent years, passing temporary "doc fixes" as add-ons to spending packages.

E/M add-on payment

"We're encouraged to see that CMS listened to our concerns and extended telehealth flexibilities as well as implemented the G2211 code, which will help Medicare beneficiaries and their physicians better manage complex and chronic rheumatic diseases," said Douglas White, MD, PhD, president of the ACR. ■

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humane schedule by specifying how the working hours will be used.

"It's true that a 1.0-FTE definition is too vague," Ms. Hill said. "I've negotiated a lot of contracts where we nail down in writing that the in-office schedule equals 34 hours per week, so the physician is guaranteed an additional 6 hours for administrative time."

Mr. Hursh usually asks for 32 hours of patient contact per week, which leaves 1 full day per week to catch up on basic administrative tasks. "It's important for employers to recognize that seeing patients isn't the only thing a doctor does and there's a lot of work in addition to face-to-face time," he said.

But he hasn't always been successful. One physician client was seeking a workweek consisting of 36 patient contact hours, "which is 90% of the usual FTE of a 40-hour week," Mr. Hursh said. "But the employer called it 'part-time,' as if the doctor were planning to be lying in the sun for the other 4 hours."

The client decided to accept a 10% pay cut and 10% less vacation to guarantee that she had those extra hours for administrative tasks. "She's probably working way more than 36 hours a week, but maybe closer to 50 or 60 instead of 70 or more," he said.

Clarify call coverage

Call coverage is typically not included in the hours a physician is contracted to work on a weekly

basis. "Most contracts have call, and it's usually evenly distributed among parties in a practice, but call can expand if another doctor is out sick, for example," Ms. Hill said.

Sometimes the language in the contract is vague regarding call coverage. "I ask, how many shifts per year is the doctor is expected to work? Then, I try to negotiate extra pay if more shifts arise," she said. "The hospital or practice may not demand extra call because they don't want to pay extra money to the physician."

On the other hand, some physicians may be eager to take extra call if it means extra income.

Ms. Hill stated one of her clients was being paid as a "part-time, 2-day-a-week provider" but was asked to be on call and take night and weekend work. When you added it all up, she was putting in almost 30 hours a week.

"This is abusive to a provider that works so hard for patients," Ms. Hill said. "We have to protect them through the contract language, so they have something hard and fast to point to when their administrator pushes them too hard. Doctors should get value for their time."

Ms. Hill and her client pushed for more money, and the employer gave in. "All we had to do was to

point out how many hours she was actually working. She didn't mind all the extra call, but she wanted to be compensated." The doctor's salary was hiked by \$25,000.

Differences in specialties and settings

There are some specialties where it might be easier to have more defined hours, while other specialties are more challenging. Anu Murthy, Esq., an attorney and associate contract review specialist at Contract Diagnostics (a national firm that reviews physician contracts) told this news organization that the work of hospitalists, intensivists, and emergency department physicians, for example, is done in shifts, which tend to be fixed hours.

"They need to get their charting completed so that whoever takes over on the next shift has access to the most recent notes about the patient," she said. By contrast, surgeons can't always account for how long a given surgery will take. "It could be as long as 9 hours," she said. Notes need to be written immediately for the sake of the patient's postsurgical care.

Dermatologists tend to deal with fewer emergencies, compared with other specialists, and it's easier for their patients to be slotted into an organized schedule. On the other

hand, primary care doctors – internists, family practice physicians, and pediatricians – may be seeing 40-50 patients a day, 1 every 15 minutes.

Practice setting also makes a difference, Ms. Murthy said. Veterans Administration (VA) hospitals or government-run clinics tend to have more rigidly defined hours, compared with other settings, so if you're in a VA hospital or government-run clinic, work-life balance tends to be better.

Physicians who work remotely via telehealth also tend to have a better work-life balance, compared with those who see patients in person, Ms. Murthy said. But the difference may be in not having to spend extra time commuting to work or interacting with others in the work environment, since some research has suggested that telehealth physicians may actually spend more time engaged in charting after hours, compared with their in-person counterparts.

Using scribes to maximize your time

Elliott Trotter, MD, is an emergency medicine physician, associate clinical professor of emergency medicine at Texas Christian University Medical Schools, and founder of the ScribeNest, a Texas-based company that trains health care scribes. He told this news organization that there are ways to maximize one's time

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84-year-old MD contests employer's mandatory cognitive tests for older docs

BY RANDY DOTINGA

Should older physicians be forced to undergo cognitive tests to stay on the job? One 84-year-old ophthalmologist is suing her Michigan employer to stop the practice.

Lylas G. Mogk, MD, recently sued Henry Ford Health and Henry Ford Medical Group in federal court, alleging the mandatory cognitive test violates the Americans With Disabilities Act, the Age Discrimination in Employment Act, and two Michigan laws.

Dr. Mogk's lawsuit follows a widely watched 2020 case in which the U.S. Equal Employment Opportunity Commission sued Yale New Haven (Conn.) Hospital, the teaching hospital of Yale University, for age discrimination.

According to that lawsuit, the hospital illegally required neuropsychological and eye examinations of physicians aged 70 or older who sought to gain or renew staff privileges.

As for the present lawsuit, Dr. Mogk is a member of Henry Ford Medical Group, which in 2017 required all members aged 70 and older to undergo cognitive screening tests. The tests would be repeated every 5 years thereafter, the lawsuit said, and anyone who refused would have to resign or be fired. Dr. Mogk completed the screening, although no information about the results or outcome was mentioned in the lawsuit. It's not clear whether Henry Ford's cognitive test mandate remains in place; a spokesperson for Henry Ford Health and attorneys for Dr. Mogk declined to comment.

By the numbers

The number of practicing physicians in their 70s and beyond is rising. A 2021 report found that 12% of U.S. licensed physicians in 2020 were least 70 years old, up from 9% in 2010 and an increase from 75,627 to 120,510. The percentage of doctors aged 60-69 grew to 19% from 16% in

2010. The number of health systems requiring testing of older physicians isn't known, although various reports suggest at least a dozen have had mandates.

The University of California, San Diego, offers a physical and mental screening program that health organizations can use to evaluate "late-career physicians," and a 2021 report (Neurol Clin Pract. 2021 Apr;11[2]:167-74) noted that "Nebraska's Children's Hospital requires physicians aged 70 years and older to undergo an assessment by several peers, a complete physical, and unspecified cognitive screening." Another system, Hartford HealthCare, mandated an annual reappointment process for clinicians aged 70 or older, requiring them to undergo various exams.

There's evidence that physician performance declines with age. However, age-based cognitive testing can run afoul of federal and state laws against age discrimination, said Sharona Hoffman, JD, professor of law and bioethics at Case Western Reserve University, Cleveland. Federal law prohibits age-related restrictions on employment but allows exceptions in areas like public safety, Ms. Hoffman said. Pilots, law enforcement officers, firefighters, and air controllers can be forced to retire at specific ages. It's not clear how many physicians took the cognitive tests required by Henry Ford Medical Group.

Policies in place

However, details are available about the policy at Yale New Haven Hospital: According to the EEOC lawsuit, from 2016 to 2019, 145 physicians aged 70 or older took the mandatory test. Of those, seven individuals failed either or both

of the exams, 14 were listed as "borderline deficient," and 1 was listed as "deficient." Another five refused testing and either resigned or changed their status. The EEOC case against the hospital is still pending.

"You can make an argument that health care is like a public safety job because people put their lives in the hands of doctors," Ms. Hoffman said.

In defending mandatory cognitive tests, she said, health care systems could say, "it's not really discrimination; we're not forcing them to retire; we're not limiting their work in any way. We're just doing testing to make sure they perform competently, and the ADA allows us to conduct testing that is job-related."

Indeed, a Yale New Haven Hospital spokesman made an argument along these lines in a statement regarding the 2020 lawsuit: The "policy is designed

to protect our patients from potential harm while including safeguards to ensure that our physicians are treated fairly. The policy is modeled on similar standards in other industries, and we are confident that no discrimination has occurred and will vigorously defend ourselves in this matter."

However, Ms. Hoffman herself doesn't buy these arguments. Requiring tests only for older physicians does appear to be discrimination based on age, she said. As an alternative, "employers can do close supervision of people. As soon as there are performance problems or patient complaints, you need to see a doctor or get testing done."

Another option is to mandate tests at specific ages via licensing boards. "I don't think that would be legally problematic," Ms. Hoffman said.

Ms. Hoffman has no disclosures. ■

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during shifts so that much of the charting can be accomplished during working hours.

"About 28 years ago, I realized that the documentation load for physicians was enormous and at that time I developed the Modern Scribe, using premed students for 'elbow support' to help with the workload by documenting the ED encounters in real time during the encounter so I wouldn't have to do so later."

Over the years, as EHRs have become more ubiquitous and onerous, the role of the scribe has "evolved from a luxury to a necessity," Dr. Trotter said. The scribes can actually record the encounter directly into the EHR so that the physician doesn't have to do so

later and doesn't have to look at a computer screen but can look at the patient during the encounter.

"This enhances communication and has been shown to improve patient care," he said.

Dr. Trotter said he rarely, if ever, needs to do documentation after hours. "But one of my physician colleagues had over 500 charts in his in-basket on a regular basis, which was overwhelming and untenable."

The use of AI in health care is rapidly growing. Many doctors are interested in using AI-generated summaries to help hasten the process of taking notes. Ms. Hill warned physicians to "be careful not to rely so heavily on AI that you trust it over your own words."

She noted it can make mistakes, and the liability always remains with the clinician.

Creating time-efficient strategies

Wilfrid Noel Raby, PhD, MD, a psychiatrist in private practice in Teaneck, N.J., was formerly a psychiatrist in the substance abuse unit at Montefiore Hospital, New York. He developed a system whereby he rarely had to take work home with him. "I was working only 20 hours a week, but I was usually able to do my charting during those hours, as well as seeing patients," he said. "I scheduled my appointments and structured a little 'buffer time' between them so that I had time to document the first appointment

before moving on to the next one."

There were days when this wasn't possible because there were too many patients who needed to be seen back-to-back. "So I developed my own template where I could take rapid, very standardized notes that fit into the format of the EHR and met those expectations." Then, when he had finished seeing patients, he could quickly enter the content of his notes into the EHR. If necessary, he completed his charting on a different day.

"At the end of the day, doctors are people," Ms. Hill said. "They are not machines. Maybe in residency and fellowship they may grind out impossible shifts with little sleep, but this pace isn't tenable for an entire career." ■

CDC: Student use of tobacco, vape products drops

BY LISA GILLESPIE

Use of e-cigarettes among U.S. teens was down sharply, dropping from 14.1% in 2022 to 10% in 2023, government figures show, but the majority of these youth still used flavored products, which have been shown to both entice teens and keep them vaping.

Web-based questionnaire

The MMRW report from the United States Centers for Disease Control and Prevention presented data from an annual survey of U.S. middle and high school students of their use of tobacco products, including vapes. The survey queried students on their use of e-cigarettes, traditional cigarettes, cigars, smokeless tobacco, nicotine pouches, hookahs, pipe tobacco, and other oral nicotine products.

The survey was a cross-sectional, school-based, self-administered web-based questionnaire that used a stratified, three-stage cluster sampling procedure to generate a nationally representative sample based off the responses of 22,069 students in 2023.

The overall response rate was 30.5%. “Ever use” was defined as using a product once or twice and

“current use” was defined as use in the past 30 days.

Tobacco use down

The use of tobacco products by high school students decreased by 540,000 people from 2022 to 2023 (2.51 million versus 1.97 million students). From 2022 to 2023, current e-cigarette use among high school students declined from 14.1% to 10.0%.

Among middle and high school students, e-cigarettes were the most commonly used nicotine product in 2023 (7.7%; 2.13 million), followed by cigarettes (1.6%), cigars (1.6%), nicotine pouches (1.5%), smokeless tobacco (1.2%), other oral nicotine products (1.2%), hookahs (1.1%), heated tobacco products (1.0%), and pipe tobacco (0.5%).

Prevention efforts

“Sustained efforts to prevent initiation of tobacco product use among young persons and strategies to help users quit are critical to reducing U.S. youth tobacco product use,” the report states.

Among students reporting current e-cigarette use, 89.4% said they used flavored products, and 25.2% said they used an e-cigarette daily. The most commonly

Lisa Ulrich, MD, comments: This article highlights the decline in e-cigarette use among U.S. teens. While this is overall a positive trend, it also highlights that 10% of the population studied continued to use. This can have significant impact on the health of the pediatric population. It’s also important to note that the most common products were flavored with either fruit or candy flavors.

Past concerns about marketing to children remains a very relevant issue today. Despite the limitations discussed, this article emphasizes the continued need for advocacy in pediatrics to try to prevent the use of all tobacco products, including e-cigarettes.

Dr. Ulrich is a member of the CHEST Physician Editorial Board.



reported brands were Elf Bar, Esco Bar, Vuse, JUUL, and Mr. Fog. Fruit (63.4%) and candy (35%) were the most commonly reported flavors.

Self-reporting limitations

Data were obtained by students self-reporting their tobacco use, which can result in social desirability and recall biases, the report states.

In addition, the responses were from students enrolled in school settings and may not be representative of teens who are in detention centers, are in alternative

schools, have dropped out of school, or who are homeschooled.

The response rate for the 2023 survey was also lower than in the previous year (30.5% in 2023 vs. 45.2% in 2022), increasing the potential for higher standard errors and reducing the power to detect significant differences.

Disclosures

The report was produced by the CDC and published in the *Morbidity and Mortality Weekly Report* for Nov. 3, 2023.

No potential conflicts of interest were disclosed. ■

Nasal ventilation function may factor into children’s OSA

BY HEIDI SPLETE

MDedge News

Children with obstructive sleep apnea (OSA) showed significantly reduced nasal ventilation function (NVF), compared with healthy controls, based on data from more than 200 individuals.

Previous research has shown an increased risk of OSA in patients with compromised nasal respiration, but the association between increased nasal resistance (NR) and OSA in children is controversial and remains unclear, wrote Ying Pang, MD, of Children’s Hospital of Chongqing (China) Medical University, and colleagues.

In a study published in the *Ear, Nose & Throat Journal* (2023 Oct 20. doi: 10.1177/01455613231205991), the researchers enrolled 109 children aged 6-12 years with OSA and 116 healthy control children, with the goal of examining the role of NVF on OSA.

Participants underwent acoustic rhinometry (AR) following polysomnography, and measurements of the nasal minimal cross-sectional area (NMCA) were taken in 3 segments, as were nasal cavity volume (NCV) from 0 cm to 5 cm, nasopharyngeal volume (NPV) from

6 cm to 8 cm, and distance of the minimal cross-sectional area to the nostril (DCAN). The children also underwent NR testing in both nostrils while awake and lying in a supine position.

Overall, the NR of children with OSA were significantly higher than that of controls ($P < .05$). For AR, children with OSA had sig-

Results suggest that NVF plays a role in the pathogenesis of OSA in children and suggest a need to improve NVF in treating these patients.

nificantly lower measures of NMCA, NCV, and NPV, but DCAN values were between the groups. Both AR and NR measures were similar among children with mild, moderate, or severe OSA.

A subset of 90 children with mild or moderate OSA were treated with intranasal corticosteroids (ICS) and oral montelukast for

12 weeks. Of these, 69 completed the study and were divided into three groups: effectively cured (group A), successfully treated (group B), and treatment failure (group C). The researchers compared the size of the tonsil adenoids, the polysomnography, NR, and AR before and after treatment and found significant differences in NR, NMCA, and NCV for the A and B groups but no significant changes in DCAN following treatment.

For group A, treatment was associated with a significant reduction in adenoid size and increase in NPV, but these changes did not occur in group B.

The findings were limited by several factors, including the small sample size and measurement of NR when patients were awake and sitting upright, and larger studies are needed to confirm the results, the researchers noted.

However, the results suggest that NVF plays a role in the pathogenesis of OSA in children and suggest a need to improve NVF in treating these patients, they concluded.

This study was supported by the Medical Project of Chongqing Municipal Science and Health Bureau of China. The researchers had no financial conflicts to disclose. ■

No effect of endoscopic sinus surgery on asthma with rhinosinusitis

BY HEIDI SPLETE

Endoscopic sinus surgery (ESS) has no significant impact on asthma symptoms for patients with chronic rhinosinusitis up to a year after the procedure, a study of 64 patients shows.

Although ESS is effective in relieving chronic rhinosinusitis, whether it leads to improvement of asthma severity for patients with both conditions remains unclear, Anyull Dayanna Bohórquez Caballero, IMG, said in a presentation at the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) 2023 annual meeting.

The study “offers a unique approach to explore the effects of endoscopic sinus surgery in a real-world context, with valuable insights that differ from previous research,”

Dr. Bohórquez Caballero, an international medical graduate and research fellow of the Mayo Clinic, Jacksonville, Fla., said in an interview.

Under the leadership of senior author Angela Donaldson, MD, Dr. Bohórquez Caballero and colleagues at the Mayo Clinic analyzed data from 185 adults with both asthma and chronic rhinosinusitis who underwent ESS at the clinic between 2013 and 2023. Asthma severity was evaluated up to 3 months before and 1 year after surgery. Patients’ asthma severity was classified as mild, moderate, or severe on the basis of current Global Initiative for Asthma guidelines using medication requirements.

The final study population included 64 patients; 42 of these (66.7%) had chronic rhinosinusitis with nasal polyps. Outcomes included differences in asthma severity, asthma medication doses, and the number of medications.

Overall, there was no significant difference in measures of mild, moderate, or severe asthma before and after ESS in a McNemar paired test ($P = .130, .999, \text{ and } .288,$

respectively). Similarly, no difference was found before and after ESS in terms of total inhaled corticosteroid dose ($P = .999$), number of medications prescribed ($P = .157$), or control of the disease ($P = .078$).

The findings were limited by the relatively small number of patients. The study is the first known to assess the real-world impact of ESS on asthma severity, Dr. Bohórquez Caballero said.

Expected reduction in asthma severity not seen

Past studies have suggested that ESS improves parameters such as pulmonary function test results or sinonasal outcomes, Dr. Bohórquez Caballero told this news organization. “Our findings indicate that ESS does not significantly impact asthma severity or trends in treatment, including the number and/or dose of medications, in

everyday practice.

Our study also identified crucial opportunities to reinforce interdisciplinary follow-up after ESS,” she noted, and it provides a comprehensive depiction of the outcomes experienced by patients with chronic rhinosinusitis and asthma who undergo ESS.

“We were expecting a reduction in severity or a decrease in the dose of inhaled corticosteroid therapies, and we expected to see a translation from previous evidence into clinical practice; however, we did not,” Dr. Bohórquez Caballero said.

“The take-home message is that, while there is a strong correlation between [chronic rhinosinusitis] and asthma, it does not appear that ESS alone improves real-world treatment based on asthma severity,” she said. “However, our findings have shown that patients may experience a longer period without the need for a reliever medication in the early postoperative period.”

Looking ahead, “We want to explore what happens 5 or 6 months after sinus surgery that would explain

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“Our findings indicate that ESS does not significantly impact asthma severity or trends in treatment, including the number and/or dose of medications.”

- Anyull Dayanna Bohórquez Caballero, IMG



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Asthma with EoE linked to earlier hospitalization

BY JIM KLING

MDedge News

FROM CHEST 2023 ■ Hospitalized patients with both asthma and eosinophilic esophagitis (EoE) were younger on average than those hospitalized with asthma alone, according to a new analysis of data from HCA Healthcare.

Not much work has been done on the overlap between the two conditions, both of which are believed to be driven by the action of both eosinophils and helper T cells, according to Linda Pham, DO, who presented the research at the annual meeting of the American College of Chest Physicians (CHEST).

“I have a colleague who is interested in GI and he’s really interested in EoE. We thought it would be nice to look at those populations of patients to see if there’s a correlation between them aside from just the atopic disease,” said Dr. Pham. She is an internal medicine resident at Riverside (Calif.) Community Hospital.

The findings underscore the need for assessing individual patient risk. “Having another concomitant disease like EoE, or maybe like atopic dermatitis, might cause you to have more severe [asthma] exacerbations causing you to go into the hospital more. I think if patients have more of these diseases, doctors can be more cognizant that they need to really be on top of treatment and make sure that [their patients] are aware of themselves so that if their symptoms exacerbate, they can go to the hospital and seek care,” Dr. Pham said.

The study was a retrospective analysis of 3,678,812 patients with asthma and 5,823 patients with both EoE and asthma. The data were drawn from 185 HCA hospitals, with records between 2016 and 2021.

The incidence of both asthma and asthma with EoE remained stable between 2016 and 2021. Dr. Pham pointed out that there are good methods to diagnose both conditions, which suggests that existing treatments are effective enough to be limiting the need for emergency treatment, according to Dr. Pham.

Among patients hospitalized with asthma alone, 72.55% were female, while 27.45% were male ($P < .001$). The numbers were much more evenly split among

those with asthma and EoE, at 51.78% and 48.22%, respectively. The differing gender statistics aren’t easy to explain. “It’s not quite clear whether it’s because they just have more severe symptoms, or if it is other factors causing women to seek care more than their male counterparts. It could be personal biases, or it could be the asthma itself that is more severe in women,” Dr. Pham said.

When they broke down the analysis by sex, the researchers found that male EoE patients without asthma were a mean value of 5.517 years older than male EoE patients with asthma, and the mean difference was 5.480 years in female patients ($P < .001$ for both).

Although the direct cause of earlier hospitalization among patients with concomitant EoE and asthma is unclear, Dr. Pham speculated the combination of atopic diseases may be leading to a stronger inflammatory response. It remains to be seen if a similar relationship occurs with other atopic diseases, and future research could examine other factors. “I think it’d be good to look at not just age and gender, but [body mass index] and occupation, things like that,” Dr. Pham said.

The study was of particular interest to Michelle Robertson, MD, who was in the audience. She is the director for clinical services at the Airborne Hazards and Burn Pits Center of Excellence at the New Jersey War-Related Illness and Injury Study Center. “We see a significant number of [veterans] who have been diagnosed with both asthma and eosinophilic esophagitis,

Diego Maselli, MD, FCCP, comments: As the understanding of the spectrum of eosinophil-driven diseases increases, clinicians should be cognizant that addressing comorbidities remains an integral part of asthma care, particularly in those who have severe or uncontrolled disease.



Dr. Maselli is a member of the CHEST Physician Editorial Board.

and our thinking is that that is likely related to some of the military exposures: in particular, [what the] deployed veterans encountered in the Gulf War, [such as] the smoke from burn pits, sand and dust storms, and smoke from oil well fires. Our thinking is that the particulate matter, the PM 2.5, the very, very tiny particles, may be either sensitizing the lung area and/or esophagus and predisposing them to having those symptoms when they return home,” Dr. Robertson said.

Particles of this size may be able to bypass the protected areas of the nose and lungs to reach the alveoli, where they could potentially interfere with the transfer of air between the lungs and the rest of the body, which could in turn lead to a variety of inflammatory conditions, according to Dr. Robertson. She noted particle exposure varies with a soldier’s wartime occupation, with higher exposures among mechanics and burn pit managers, for example. However, the highest levels of exposure do not predict later illness, which is a natural prompt for future research. “The second part of this pathophysiology is susceptibility. Is there something about those people that do get sick that makes them more susceptible than folks that don’t, even though they both have the same jobs?”

Dr. Pham and Dr. Robertson have no relevant financial disclosures. ■



Marines dispose of trash in a burn pit in Afghanistan in 2012.

PUBLIC DOMAIN/U.S. MARINE CORPS/ALFRED LOPEZ

SINUS *continued from previous page*

the sudden need for a reliever medication,” she added. “Future studies are warranted to investigate the long-term effects of ESS on asthma severity as it relates to modifications of asthma regimens.”

Data important for patient discussions

The current study is important

because of the frequency of comorbid asthma among patients with chronic rhinosinusitis, Megan Durr, MD, of the University of California, San Francisco, said in an interview.

“When we are considering functional endoscopy sinus surgery with patients, we are often asked if the surgery will impact the severity of their asthma symptoms,” said Dr.

Durr, who served as a moderator for the session in which the study was presented.

“I am surprised the study did not see any difference in asthma severity after sinus surgery, as we often talk to patients about the unified airway that refers to the shared epidemiologic and pathophysiologic relationship between the upper and lower airways,” she said.

“This study will allow us to have a more informed evidenced-based discussion with patients and their primary care providers and/or pulmonologists” about what to expect for asthma outcomes following surgery, Dr. Durr said.

The study received no outside funding. Dr. Durr has disclosed no relevant financial relationships. ■

ASTHMA

Phytoestrogen-based hormonal replacement therapy may ease late-onset asthma in older women

BY HEIDI SPLETE

MDedge News

Phytoestrogens show potential as a treatment for menopausal women with late-onset asthma that may relieve symptoms of both conditions, according to a new review.

Fluctuations in female sex steroid hormones during menstrual periods have been linked to asthma exacerbations, and the absence of these hormones during childhood and menopause has been associated with fewer and less severe asthma episodes, wrote Bettina Sommer, PhD, of the Instituto Nacional de Enfermedades Respiratorias, Mexico City, and colleagues.

Late-onset asthma (LOA) has been categorized as a specific asthmatic phenotype that includes menopausal women, and research is needed to explore therapeutic alternatives that might provide relief to older women suffering from LOA, they said.

In a review published in the *International Journal of Molecular Sciences* (2023 Oct 19. doi: 10.3390/ijms242015335), the researchers outlined the potential of phytoestrogens to manage LOA as well as symptoms of menopause.

LOA is often nonatopic and distinguished by a lack of eosinophilic inflammation; it is also associated

Fluctuations in female sex steroid hormones during menstrual periods have been linked to asthma exacerbations.

with obesity and pollutants such as cigarette smoke. LOA is more common in women versus men, and develops between ages 27 and 65 years, the researchers wrote. Very late-onset asthma, which develops in women aged 65 years and older, is related to low levels of total lack of circulating estrogens.

Previous studies have shown that hormone therapy reduces the risk of LOA in menopausal women, but concerns about side effects persist. Phytochemicals offer a low-risk alternative, but phytoestrogen-based



fewer side effects than other options, the researchers wrote. “They may also contribute to more efficient responses to infection and inflammation leading menopausal women to a much better quality of life.”

The absence of female sex steroid hormones during childhood and menopause has been associated with fewer and less severe asthma episodes.

hormone therapy and its role in LOA have not been well studied, the researchers wrote.

Estrogen receptors (ERs) have two intracellular isoforms, alpha and beta. “Notably, the literature sustains that ERs expression differs between asthmatics and nonasthmatics,” and mainly the beta-ERs are upregulated in asthma or during inflammations, the researchers said. Phytoestrogens activate ER and benefit postmenopausal women, especially those with asthma, in addition to their anti-inflammatory and antioxidant properties.

Studies using mouse models have shown that E2 phytoestrogen supplementation in mice both increases the expression of antioxidant enzymes and reduces inflammation, according to the researchers. Age-related changes in hormonal statuses, immunology, and systemic inflammation may predispose older adults to more infections and asthma exacerbations, but also might drive the development of LOA.

As another example of potential connections between phytoestrogen and asthma, phytoestrogen’s action on an estrogen receptor, notably the beta-ER, was associated with lowered airway hyperresponsiveness in a mouse model, and beta-ER knockout mice showed reduced lung function, compared with wild-type and alpha-ER knockout mice.

More research is needed, but novel

therapies using phytoestrogens offer an added advantage to older women with LOA by potentially easing some menopause symptoms with

The study was funded by the Instituto Nacional de Enfermedades Respiratorias, Consejo Nacional de Ciencia y Tecnología, Programa de Apoyo a Proyectos de Investigación e Innovación Tecnológica, and the Universidad Nacional Autónoma de México. The researchers had no financial conflicts to disclose. ■

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Laura Riordan
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PRESIDENTIAL CITATION

Scott Manaker, MD, PhD, FCCP
The Presidential Citation is awarded on behalf of the CHEST President to individuals who have shown their dedication to the chest medicine field and for their contributions to CHEST. ■

For a comprehensive list of Distinguished CHEST Educators, new FCCP designees, and scientific abstract award winners, visit chestnet.org/awards.

“A physician’s secret weapon”: Why the world needs more RTs

BY KENDRA BENNER

CHEST and the National Board for Respiratory Care (NBRC) are continuing their longstanding partnership to raise awareness about the MoreRTs initiative, which addresses the alarming shortage of respiratory therapists (RTs) in the United States.

The COVID-19 pandemic intensified the shortage of RTs, but the problem predated the 2020 crisis. A survey from the American Association for Respiratory Care showed several factors driving the need for more RTs, including an aging US population, growing incidences of respiratory disorders, and advances in pulmonary medical devices.

But the squeeze is coming from both internal and external forces. Retirements of RTs are outpacing new growth, while, at the same time, the need for quality respiratory care is increasing. Simply put, demand for RTs is high, but the supply of RTs is dangerously low.

Lori Tinkler, Executive Officer of the NBRC, said physicians can make a difference in increasing the number of RTs and championing their success on the clinical care team. Tinkler recently shared her insights on the initiative and how

physicians can get involved.

CHEST: Respiratory therapists are extremely valuable members of the clinical care team. Can you share why RTs are so important?

Lori Tinkler: I like to say respiratory therapists are a physician’s secret weapon. Respiratory therapists work under the direction of a medical director.

They really carry out the orders of physicians and help the physician determine the best pathway for patients using protocols. They [serve as] experts when it comes to ventilators and treating the patients for their pulmonary issues under the physician’s orders.

CHEST: How can physicians get more done with more RTs on the clinical team?

Tinkler: By working with protocols and relying on their respiratory therapists. Listen to what they’re saying when it comes to patient care since respiratory therapists are spending much more time with the patients than the physicians are.

It’s really the whole health care team working together with the patient. What [physicians can] keep in mind is, how are they going to treat that patient the best and utilize the expertise that

respiratory therapists bring to the table? They probably have the most diverse skillset, but they are highly trained and specialized in lung diseases and treatment of asthma and COPD.

CHEST: How can physicians help integrate RTs into the clinical team?

Tinkler: It’s really ensuring that their institutions recognize the value of respiratory therapists and what they bring to the table. Ensuring that their departments are adequately staffed and championing that effort, speaking up, and being a voice for the respiratory therapist and what they bring to the bedside.

CHEST: How else can physicians get involved?

Tinkler: We’re always looking for physician stories about how they utilize and champion their respiratory therapist. And, of course, we’re always looking for physicians to get involved in the credentialing process by being a consultant or board member, or by being a content expert and helping write the test questions for the respiratory therapy credentialing exams.

Additional information is available at MoreRTs.com. ■

Networks at CHEST 2023

BY CASSIE KENNEDY, MD, FCCP – CHAIR, COUNCIL OF NETWORKS AND MARGARET PISANI, MD, MPH, FCCP – VICE-CHAIR, COUNCIL OF NETWORKS

CHEST 2023 in Honolulu kicked off for Network Leadership during the Council of Networks meeting. Leadership from the seven Networks presented their plans for CHEST 2023, participation in proposed guidelines, CHEST projects completed over the past year, and other accomplishments.

We congratulated our Network leaders – Margaret Pisani, Council of Networks Vice-chair, who was awarded the Roger C. Bone Memorial Lecture in Critical Care; and Jean Elwing, Chair of the Pulmonary Vascular & Cardiovascular Network, for being awarded the Distinguished Scientist Honor Lecture in Cardiopulmonary Physiology. CHEST 2023 included excellent educational content by the Networks, including two Network

highlights per each of the seven Networks, as well as an Experience CHEST submission from each of the 22 sections.

We also had the opportunity to meet face-to-face at the Network Open Forums, the Network Mixer, and the inaugural Fellow-in-Training Mixer in the Trainee Lounge. We saw a lot of familiar faces at these events, and 182 new individuals also signed up to become Network members.

There will be one final Council of Networks leadership meeting in December prior to our leadership transition in January.

We thank outgoing Network chairs, Dr. Marcos Restrepo of the Chest Infections & Disaster Response Network, Dr. Christopher Carroll of the Critical Care Network, Dr. Debbie Levine of the Diffuse Lung Disease & Lung Transplant Network, and Dr. Carolyn D'Ambrosio of the Sleep Medicine Network, for their leadership and hard work dedicated to the Networks that have greatly benefited from their service. ■

This month in the journal CHEST®

Editor's picks

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

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By Alexis Maillard, MD, et al.

The Economic Burden of Bronchiectasis: A Systematic Review
By Jack M. Roberts, et al.

Indicators of Neighborhood-Level Socioeconomic Position and Pediatric Critical Illness
By Carlie N. Myers, MD, et al.

Restrictive Visitation Policies and Related Post-Traumatic Stress Among of Families of Critically Ill Patients With COVID-19
By Katherine R. White, MD, et al.



Central and Peripheral Hemodynamics in Young Water-Pipe Users and the Acute Effects of Water-Pipe Use

By Hassan A. Chami, MD, et al.

Emotional Distress, Anxiety, and General Health Status in Patients With Newly Identified Small Pulmonary Nodules: Results From the Watch the Spot Trial

By Michael K. Gould, MD, et al.

Antithrombotic Therapy in Arterial Thrombosis and Thromboembolism in COVID-19: An American College of Chest Physicians Expert Panel Report

By Tatjana Potpara, MD, PhD, et al.



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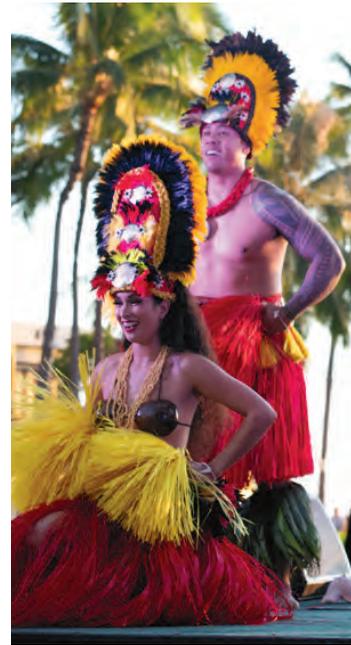
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Scenes From CHEST 2023





IMAGES COURTESY CHEST

Get to know President-Elect John “Jack” D. Buckley

Starting January 1, 2024, current President-Elect John “Jack” D. Buckley, MD, MPH, FCCP, will become the new President of CHEST. Dr. Buckley is a pulmonologist and critical care physician with an extensive background in education, and he has served on the Board of Regents for the College for 8 years collectively.

Before Dr. Buckley steps into the role of President, he spoke with CHEST for a glimpse into what he is looking to bring to the organization.

What would you like to accomplish as President of CHEST?

I mentioned this in my address during the CHEST Annual Meeting in Honolulu, but the role of President is to guide the Board of Regents as we provide governance and direct the organization to fulfill our mission. With that in mind, my job is to advance CHEST by following our strategic plan, continuing the great work already being done, and preparing for what comes next.

As our world changes around us, we must not only adapt to the



Dr. Buckley

current environment but anticipate the future and take the lead by influencing the direction we believe to be important. This is the role of the Board of Regents, and we need input from CHEST’s members.

In 2023, with the guidance of an advisory board, and a tremendous amount of time and effort encompassing input from a wide range of CHEST members, leaders and staff, the organization defined its core

values. The values – Community, Inclusivity, Innovation, Advocacy, and Integrity – are reflective of the CHEST organization and will guide decisions for years to come.

“I cannot stress enough that every person reading this should join the conversation. Meant to represent the whole of pulmonary, critical care, and sleep medicine clinicians, CHEST is stronger with every voice.”

*-John D. Buckley,
MD, MPH, FCCP*

While looking forward, it’s also important to reflect on the past. CHEST started as an organization centered on preventing and treating tuberculosis. As progress was made, the entire pulmonary field evolved from tuberculosis experts and, from there, critical care emerged and continues to evolve. Now we’re seeing tremendous growth in the roles of advanced practice providers in our ICUs and, most recently, a resurgence of cardiology-critical care. We are excited to welcome these colleagues into CHEST as we move forward.

What do you consider to be CHEST’s greatest strength, and how will you build upon this during your presidency?

The strength of CHEST is in our community and our educational programs. Our emphasis is on delivering relevant information to our members in ways that are immediately clinically applicable – something I think we do better than anyone – to improve the care we’re able to provide to our patients. Through expanding our community and continuing to produce quality medical education, this will continue to be a focus for years to come.

What are some challenges facing CHEST, and how will you address them?

The challenges facing CHEST are the same challenges facing the whole of health care. Predominantly, providers and patients are both caught navigating complex health

systems and insurance programs, costs of care, and access. The latter is particularly concerning for us as the burnout of health care providers has worsened, and people are leaving the clinical setting.

While there is no simple solution, CHEST has demonstrated commitments to making an impact through initiatives like First 5 Minutes[®], which was created to address implicit bias, establish trust, and form a stronger connection between patients and their clinicians more quickly.

This will be a growing focus for CHEST, and it is reflected in the formal addition of social responsibility to our organizational pillars. The work being done in philanthropy and through our diversity, equity, inclusion, and belonging efforts will continue to develop and are now a core element of the organization.

And finally, what do you ask of the members and Fellows of CHEST to support you during your presidency?

I cannot stress enough that every person reading this should join the conversation. Meant to represent the whole of pulmonary, critical care, and sleep medicine clinicians, CHEST is stronger with every voice.

“The strength of CHEST is in our community and our educational programs. Our emphasis is on delivering relevant information to our members.”

*-John D. Buckley,
MD, MPH, FCCP*

Conveniently, an email address exists for this very purpose. The address president@chestnet.org is a direct way to communicate with me, and I very much encourage you to take me up on this.

Let me know what you would like to see change in 2024 or what you think we’re doing well. I’d also like to hear if there is something neat you’re doing for the field; beyond my personal interest, CHEST loves to celebrate the accomplishments of its members.

I look forward to elevating your voice and am truly elated to serve as the next President of CHEST. ■

CHEST Career Connection

CHEST is here to help you in every step of your career, including your job search. Career Connection, powered by the HEALTHe CAREERS Network, is your resource for employment opportunities in pulmonary, sleep, and critical care medicine. With a wide breadth of clinical and academic opportunities to choose from, you can feel confident as you make the next move in your career.



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The double-edged sword of virtual pulmonary rehabilitation

BY GRANT A. CAGLE, MD;
AND ERIC J. GARTMAN, MD,
FCCP

Pulmonary rehabilitation (PR) is an invaluable program typically set in structured in-person environments for individuals living with chronic respiratory conditions. It offers a comprehensive approach to improving lung health and overall quality of life using a combination of tailored exercise routines, educational sessions, and emotional support. It empowers our patients to better manage their conditions, improve their fitness level, and regain a sense of control over their lives. However, the response to the COVID-19 pandemic increased the use of telemedicine as a method for providing health care (Shaver J. *Prim Care*. 2022;49[4]:517).

Many patients have welcomed the convenience offered by virtual care, and studies have demonstrated high levels of patient satisfaction (Polinski JM, et al. *Gen Intern Med*. 2016;31[3]:269). Geography also drives telehealth use. In urban areas in the United States, the median travel distance is 7.5 miles one way with a resulting travel time of 3 to 25 minutes. In rural areas, the estimated travel distance is three times as long. Distance and travel time have been recognized as major barriers to attending PR (Keating A, et al. *Chron Respir Dis*. 2011;8[2]:89).

Access to PR is also hindered by lack of program availability. As of 2019, there were only 831

pulmonary rehab centers in the United States serving roughly 24 million patients with COPD. Only 561 of these centers are certified by the American Association of Cardiovascular and Pulmonary Rehabilitation, leaving only one certified center for every 43,000 patients with COPD (Chan L, et al. *J Rural Health*. 2006;22[2]:140). As such, virtual PR is one option for augmenting availability and accessibility.

While virtual PR programs offer numerous advantages, including accessibility and convenience, there are inherent risks and challenges. There is also concern that they are inferior to in-person PR. They offer less supervision by trained health care professionals and no immediate access to medical assistance. Combined with the absence of real-time monitoring of vitals or symptoms, there may be a higher risk of adverse events despite the incorporation of safety measures. Furthermore, the lack of accountability forces an increased reliance on self-motivation, which may hinder progress (Spruit MA, et al. *Am J Respir Crit Care Med*. 2013;188[8]:e13).

Although the digital divide is narrowing rapidly, reliable access to technology, combined with poor internet connections or computer literacy, will prevent adoption by some patients. Even in well-resourced areas, technical issues can disrupt continuity. Finally, virtual PR lacks the intangible benefits from in-person group sessions. Social interactions in this already isolated subset of patients are lost



Dr. Cagle and Dr. Gartman are with the Warren Alpert Medical School of Brown University and Providence VA Medical Center, Division of Pulmonary, Critical Care, and Sleep Medicine, Providence, RI.

in virtual PR, and the cultivation of motivation and support to seek a common goal goes unrealized.

While these concerns are appreciated, PR is currently highly underutilized and essentially unavailable to most pulmonary patients. As such, further study is needed to shape the future design of quality virtual PR programs. In the March 2023 issue of the journal CHEST, Huynh and colleagues published an observational cohort study comparing virtual with traditional PR programs (Huynh VC, et al. *Chest*. 2023; Mar;163[3]:529). Of the 554 participants in the study, 171 were enrolled in virtual and 383 to in-person PR. Attendance and drop-out rates did not differ, CAT scores significantly improved in both programs, and there were no adverse events during virtual PR. Participants in the virtual group received a TheraBand and were required to have a sturdy chair, three large step-lengths of empty space surrounding their chair, and access to internet/Zoom. They had one-on-one Zoom meetings but relied mostly on staff-made or online videos.

These results replicate past investigations that have demonstrated low adverse event rates, positive overall patient satisfaction, and noninferiority in patient-centered outcomes with PR. The total volume of data remains limited though (Cox NS, et al. *Cochrane Database Syst Rev*. 2021;Issue 1;Art No: CD013040).

PR is an essential resource for the management of chronic lung diseases. Given existing barriers and the growing number of eligible patients, we must embrace alternative delivery strategies, all the while ensuring that a quality and useful product is deployed (Rochester CL, et al. *Am J Respir Crit Care Med*. 2015;192[11]:1373). Additional study is needed to standardize and validate the implementation of virtual PR. Ultimately, virtual and alternative methods of care delivery may help optimize outcomes for our patients where more traditional methods fall short. ■

The views and opinions of authors expressed herein do not necessarily reflect those of the Department of Veterans Affairs or the US government.

University of Washington fellowship director announced as mentor for medical educator scholarship

BY KENDRA BENNER

It wasn't until Başak Çoruh, MD, FCCP, was a mentee herself that she realized the value of structured mentoring. And now, she has more to give.

Dr. Çoruh, Associate Professor of Pulmonary, Critical Care, and Sleep Medicine and Director of the Pulmonary and Critical Care Medicine fellowship program at the University of Washington, was named as the mentor for the Medical Educator Diversity Scholarship Fellowship.

This mentorship opportunity is part of a joint program sponsored by CHEST and the Association of Pulmonary and Critical Care Medicine Program Directors (APCCMPD). It was created to



Dr. Çoruh

support a fellow who intends to pursue a career in medical education but who may have limited resources to train in teaching, formal medical education curricula, and medical education research.

"The fellowship is an incredible opportunity to increase the diversity of our medical education community," Dr. Çoruh said. The fellowship also closely aligns with CHEST's newly established philanthropic pillar of "Support of the profession." CHEST is devoted to elevating the field of chest medicine through top-notch clinical education and empowering early career clinicians from diverse backgrounds with the latest knowledge.

"I'm particularly excited to serve as a mentor for an aspiring medical educator without access

to resources for coursework, teaching activities, or scholarship at their home institution," Dr. Çoruh said. "I am fortunate to be a part of a large and welcoming education community at the University of Washington that I'm excited to share with my mentee." The importance of mentorship cannot be overstated, as it can shape the rest of a clinician's career. There is immense value in not only the funding and research aspect but in the wisdom-sharing and motivational side, as well.

"It wasn't until my own fellowship that I experienced the value of structured mentoring, and the mentoring I have received has impacted my career in countless ways. I look forward to helping [the fellow] achieve their goals."

The fellowship recipient will be announced in early 2024. ■

Amivantamab comes of age in NSCLC

BY LIAM DAVENPORT

MADRID – New data from three trials evaluating the bispecific antibody amivantamab (Rybrentamab) in epidermal growth factor receptor (EGFR)-mutated advanced non-small cell lung cancer (NSCLC) have revealed a clear benefit, experts said at the annual meeting of the European Society for Medical Oncology (ESMO).

The results of the three trials – PAPILLON, MARIPOSA, and MARIPOSA-2 – are “really exciting” for patients harboring EGFR mutations, said Silke Gillessen, MD, head of the department of medical oncology, Università della Svizzera Italiana in Lugano, Switzerland, and the ESMO 2023 scientific chair.

Presenting findings from PAPILLON, Nicolas Girard, MD, PhD, highlighted outcomes among patients with EGFR exon 20 insertion-mutated advanced NSCLC. These patients, who represent about 2%-3% of NSCLC cases, have “historically poor” outcomes, with a 5-year overall survival rate of just 8%. Tumors harboring exon 20 insertions are largely insensitive to

targeted and immune checkpoint therapies, explained Dr. Girard, from Curie-Montsouris Thorax Institute, Institut Curie, Paris. That leaves platinum-based chemotherapy as the standard of care, which has “limited efficacy,” he noted.



Dr. Gillessen

In the trial, 308 treatment-naive patients with locally advanced or metastatic NSCLC and documented exon 20 insertions were randomly assigned to amivantamab

plus chemotherapy or chemotherapy alone. The median age was about 62 years, approximately half were female, and just over 60% were Asian – a similar patient profile as MARIPOSA and MARIPOSA-2.

The results, showed amivantamab plus chemotherapy significantly increased progression-free survival (PFS). After a median follow-up of 14.9 months, patients receiving the combination had a median PFS of 11.4 months vs. 5.7 months with

chemotherapy alone (hazard ratio, 0.395; $P < .0001$). This benefit consistently occurred across predefined subgroups.

Amivantamab plus chemotherapy was associated with a lower risk of a second progression, with the median not reached vs. 17.2 months with chemotherapy alone (HR, 0.493; $P = .001$). A higher proportion of patients receiving the combination had an objective response – 73% vs. 47% – and these patients had a longer duration of response – 9.7 months vs. 4.4 months. The overall survival data were immature but showed a trend toward a reduced risk of death for those on the combination (HR, 0.675; $P = .106$).

The rates of grade ≥ 3 adverse events were 75% with amivantamab plus chemotherapy and 54% with chemotherapy alone, and adverse events leading to discontinuation of amivantamab occurred in 7% of patients. Pneumonitis/interstitial lung disease (ILD) was reported in 3% of patients in the combination therapy arm.

Dr. Girard concluded that, with a safety profile “consistent” with that seen for the individual agents,

amivantamab plus chemotherapy “represents a new standard of care” for first-line treatment of EGFR exon 20 insertion-mutated advanced NSCLC.

The MARIPOSA trials

The two MARIPOSA trials also demonstrated amivantamab, in combination with other agents, improved PFS among patients with EGFR-mutated advanced NSCLC.

Byoung Chul Cho, MD, PhD, Yonsei Cancer Center, Seoul, South Korea, presented results from MARIPOSA, which focused on patients with any kind of EGFR mutation.

Early clinical data suggest combining amivantamab with the highly selective third-generation EGFR TKI lazertinib leads to clinical activity and durable responses. For the phase 3 MARIPOSA trial, 1,074 patients with treatment-naive locally advanced or metastatic EGFR-mutant NSCLC were randomly assigned to amivantamab plus lazertinib ($n = 429$), osimertinib alone ($n = 429$), or lazertinib alone ($n = 216$).

After a median follow-up of 22 months, the median PFS among patients on the combination was

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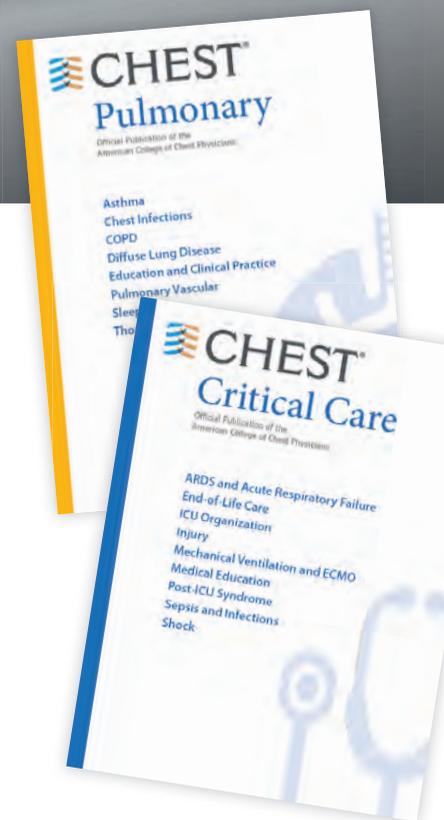
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Marijuana increases risk of heart problems, stroke

BY LISA O'MARY

Regularly using marijuana can significantly increase a person's risk of heart attack, heart failure, and stroke, according to a pair of new studies. People who use marijuana daily have a 34% increased risk of heart failure, compared with people who don't use the drug, according to one of the new studies.

The findings leverage health data from 157,000 people in the National Institutes of Health "All of Us" research program. Researchers analyzed whether marijuana users were more likely to experience heart failure than nonusers over the course of nearly 4 years. The results indicated that coronary artery disease was behind marijuana users' increased risk.

The research was conducted by a team at Medstar Health, a large Maryland health care system that operates 10 hospitals plus hundreds of clinics. The findings were presented at the American Heart Association's Scientific Sessions 2023 in Philadelphia.

"Our results should encourage more researchers to study the use of marijuana to better understand its health implications, especially on cardiovascular risk," said researcher Yakubu Bene-Alhasan, MD, MPH, at Medstar Health in

Baltimore. "We want to provide the population with high-quality information on marijuana use and to help inform policy decisions at the state level, to educate patients, and to guide health care professionals."

About one in five people in the U.S. use marijuana, according to the Centers for Disease Control and Prevention. The majority of U.S. states allow legal use of marijuana for medical purposes, and more than 20 states have legalized recreational marijuana, a tracker from the National Conference of State Legislatures shows.

A second study showed older people with any combination of type 2 diabetes, high blood pressure, and high cholesterol who use marijuana have an increased risk for a major heart or brain event, compared with people who never used the drug. The researchers analyzed data for more than 28,000 people age 65 and older who had health conditions that put them at risk for heart problems and whose medical records showed they were marijuana users but not tobacco users. The results showed at least a 20% increased risk of

heart attack, stroke, cardiac arrest, or arrhythmia (irregular heartbeat). The findings are significant because medical professionals have long said that research on the long-term health effects of using marijuana are limited.

"Smoking and inhaling cannabis increases concentrations of blood carboxyhemoglobin [and tar] similar to the effects of inhaling a tobacco cigarette."

-Robert L. Page II, PharmD, MSPH

"The latest research about cannabis use indicates smoking and inhaling cannabis increases concentrations of blood carboxyhemoglobin (carbon monoxide, a poisonous gas), tar (partly burned combustible matter) similar to the effects of inhaling a tobacco cigarette, both of which have been linked to heart muscle disease, chest pain, heart rhythm disturbances, heart attacks and

other serious conditions," said Robert L. Page II, PharmD, MSPH, chair of the volunteer writing group for the 2020 American Heart Association Scientific Statement: Medical Marijuana, Recreational Cannabis, and Cardiovascular Health. "Together with the results of these two research studies, the cardiovascular risks of cannabis use are becoming clearer and should be carefully considered and monitored by health care professionals and the public." ■

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23.7 months vs. 16.6 months for those on osimertinib alone (HR, 0.70; $P < .001$) and 18.5 months for those on lazertinib alone.

The PFS benefit observed with amivantamab plus lazertinib occurred across subgroups, including among patients with brain metastases. The combination reduced the risk for extracranial progression or death by 32% and improved median PFS by 9 months, compared with osimertinib alone (HR, 0.68; $P < .001$). The risk for a second progression was also lower with the combination (HR, 0.75).

Interim overall survival data suggested a benefit with the combination therapy, compared with osimertinib alone (HR, 0.80; $P = .11$).

Grade 3 or higher adverse events were more common among patients treated with the combination vs. osimertinib alone – 75% vs. 43%. Higher rates of treatment-related discontinuation of any agent were observed in the combination group – 35% vs. 14% – though rates of adverse events leading to death were similar between the groups – 8% and 7%, respectively.

As in PAPILLON, rates of ILD/pneumonitis were "low," Dr. Cho said, at approximately 3% in both treatment arms. However, he noted, rates of venous thromboembolism were higher with the combination, with

grade ≥ 3 events occurring in 11% vs. 3.7% of patients on osimertinib.

Based on the findings, amivantamab plus lazertinib "represents a new standard of care in first-line EGFR-mutant advanced NSCLC," Dr. Cho said.

MARIPOSA-2 evaluated patients with EGFR-mutated locally advanced or metastatic NSCLC who had progressed on or after osimertinib. In this trial, 657 patients were randomly assigned to amivantamab plus lazertinib and chemotherapy ($n = 263$), amivantamab plus chemotherapy ($n = 263$), or chemotherapy alone ($n = 131$).

Given the increased risk for hematologic toxicities, the study protocol was adjusted in the triple-therapy arm so that patients received lazertinib after completing carboplatin. The findings, presented by study investigator Antonio Passaro, MD, PhD, were published in *Annals of Oncology* (2023 Oct 23. doi: 10.1016/j.annonc.2023.10.117).

After a median follow-up of 8.7 months, the triple therapy reduced the risk for progression or death by 56% (HR, 0.44) and amivantamab plus chemotherapy reduced the risk

for progression or death by 52% (HR, 0.48). Overall, the median PFS was 8.3 months in the triple-combination arm, 6.3 months in the amivantamab plus chemotherapy arm, and 4.2 months in the chemotherapy arm.

This PFS benefit was observed across prespecified subgroups with both combination therapies. The combinations also reduced the risk for intracranial progression (HR, 0.58 in the triple-therapy arm; HR, 0.55 in the amivantamab plus chemotherapy arm). The current interim analysis did not show an overall survival benefit with either combination therapy vs. chemotherapy alone, although the survival curve hinted at a benefit in the amivantamab plus chemotherapy arm.

The median duration of response was 9.4 months for triple therapy, 6.9 months for the double combination, and 5.6 months for monotherapy.

Rates of grade ≥ 3 adverse events were notably higher in the combination groups – 92% of patients on triple therapy, 72% on double, and 48% on chemotherapy alone. But the treatment duration was longer in the combination groups and adverse

events leading to death were low, as was discontinuation.

Amivantamab plus chemotherapy or plus lazertinib and chemotherapy are the "first regimens to demonstrate improved PFS versus chemotherapy in EGFR-mutated NSCLC after disease progression on osimertinib," concluded presenter Dr. Passaro, from the European Institute of Oncology IRCCS, Milan. Given the consistent efficacy and more favorable safety profile, "we can say amivantamab plus chemotherapy is the new standard of care for patients progressing after osimertinib," although more follow-up is required to understand its "real impact" in the clinic, Dr. Passaro said.

PAPILLON, MARIPOSA, and MARIPOSA-2 were funded by Janssen Pharmaceuticals. Dr. Girard declared relationships with AstraZeneca, Boehringer-Ingelheim, Bristol-Myers Squibb, Hoffmann La Roche, Lilly, Merck Sharp & Dohme, Novartis, Pfizer, and others. Dr. Cho declared relationships with Novartis, AstraZeneca, Boehringer-Ingelheim, Roche, BMS, Onegene Biotechnology, Pfizer, Eli Lilly, and others. Dr. Passaro declared relationships with AstraZeneca, Bristol-Myers Squibb, Eli Lilly, Janssen, Pfizer, Roche, Bayer, Boehringer-Ingelheim, Merck Sharp & Dohme, Mundipharma, Daiichi Sankyo, Medscape, and eCancer. ■

"[Amivantamab plus lazertinib] represents a new standard of care in first-line EGFR-mutant advanced NSCLC."

-Byoung Chul Cho, MD, PhD



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