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# Underinsurance impedes access to care for patients with COPD, asthma

BY THOMAS R. COLLINS

MDedge News

**FROM THE JOURNAL CHEST** • Over the past 20 years, patients with asthma and chronic obstructive pulmonary disease (COPD) have seen next to no improvement in problems of delayed care because of cost or unaffordable medications, despite wider insurance coverage since the passage of the Affordable Care Act, a new analysis shows.

The long-view analysis illuminates the ongoing problem for people with these chronic diseases despite health care legislation that was considered historic.

"That long-term scope puts recent improve-

ments in better context – whereas we have made improvements in coverage in recent years due to the Affordable Care Act, the longer-term picture is that people with asthma and COPD are struggling to obtain needed medical care and medications despite a substantial reduction in the uninsurance rate," said Adam Gaffney, MD, MPH, assistant professor of medicine at Harvard Medical School, Boston, in an interview. Dr. Gaffney authored the paper with David Himmelstein, MD, professor of public health at City University of New York–Hunter College. The findings were published in Chest (2021 Jan 23. doi: 10.1016/j.chest.2021.01.035).

Researchers examined data from 1997 to

COPD // continued on page 4

# Physician burnout may start with the workload

BY CALEB RANS, PHARMD

MDedge News

orkload, not personal vulnerability, may be at the root of the current physician burnout crisis, a recent study has concluded

The cutting-edge research utilized cognitive theory and workload analysis to get at the

source of burnout among practitioners. The findings indicate that, although some institutions continue to emphasize personal responsibility of physicians to address the issue, it may be the amount and structure of the work itself that trigger burnout in doctors.

"We evaluated the cogni-



Dr. Harry

tive load of a clinical workday in a national sample of U.S. physicians and its relationship with burnout and professional satisfaction," wrote Elizabeth Harry, MD, of the University of Colorado at Denver, Aurora, and

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## INSIDE HIGHLIGHT



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## Patients with asthma and COPD delay care because of cost // continued from page 1

2018 for 76,843 adults with asthma and 30,548 adults with COPD, from the National Health Interview Survey, an annual survey by the Centers for Disease Control and Prevention that is based on in-person interviews and health

questionnaires completed by an adult in each family.

**Insurance coverage up, patients losing ground**During 1997 and 2018, there was an overall 9.3% decrease in the rate of

adults with asthma who were uninsured, a significant improvement (P < .001). Between the pre- and post-ACA years, there was modest improvement in those putting off care because of cost, a drop of 3.8%, or going without prescriptions, a drop

of 4.0%. But those improvements didn't correspond to the 7.2% drop in the uninsured rate after the ACA, contributing to the finding that there was no significant improvement over the 20 years.

For adults with COPD, it was a

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slightly different story. Over those 2 decades, the uninsured rate dropped by 9.5%. But the number of patients foregoing care because of cost actually rose by 3.4%, which wasn't statistically significant, but the rate of those unable to afford needed medications rose significantly by 7.8%.

Researchers found there was im-

provement between the pre- and post-ACA years among COPD patients putting off care and going without medications (decreases of 6.9% and 4.5%, respectively). That adhered fairly closely with the improvement in the uninsured rate, which fell by 7.1%. But over the 20-year study period, the percentage

of those needing medications they couldn't afford increased significantly by 7.8%. The rate of those delaying or foregoing care also increased, though this amount was not statistically significant.

After the ACA was created, Blacks and Hispanics with asthma had greater improvement in obtaining

insurance, compared with other racial and ethnic groups. But over the 20 years, like all racial and ethnic groups, they saw no statistically significant improvement in rates of "inadequate coverage," defined in this study as either being uninsured, having to delay care because of cost, or being unable to afford needed medications.

For those with COPD, only Whites had statistically significant improvement in the number of patients with inadequate coverage after the ACA, researchers found.

So despite obtaining insurance, patients lost ground in managing their disease because of the growing cost of care and medication.



"Medication affordability has actually

Dr. Ouellette

worsened for those with COPD – a worrisome development given that medication nonadherence worsens outcomes for these vulnerable patients," Dr. Gaffney said. "Policy makers should return to the issue of national health care reform. Both uninsurance and underinsurance undermine pulmonologists' ability to care for their patients with chronic disease. A health care system without financial barriers, in contrast, might well improve these patients' outcomes, and advance health equity."

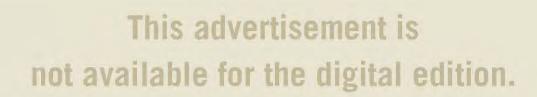
## Insurance is no guarantee to access

Daniel Ouellette, MD, FCCP, a pulmonary and critical care specialist at Henry Ford Health System in Detroit, said it's not surprising that access to care remains a problem despite the Affordable Care Act.

"It covers the hospitalizations and ER visits – patients in this segment of society were getting cared for there anyway," he said. "And what the ACA didn't always do was provide adequate prescription coverage or cover these outpatient gaps. So even though the patients have the ACA they still have unaffordable prescriptions, they still can't buy them, and they still can't pay for their outpatient clinic if they have a \$500 or \$1,000 deductible." These patients also continue to struggle with more fundamental issues that affect access to care, such as lack of transportation and poor health literacy.

At Henry Ford, pharmacists work with patients to identify medications

Continued on following page





## **COVID** cases severely undercounted

BY CAROLYN CRIST

arge numbers of COVID-19 cases have been undetected and unreported, which has resulted in severe undercounting of the total number of people who have been infected during the pandemic, according to a new study published in the journal PLOS ONE (2021 Feb 8. doi: 10.1371/journal.pone.0246772).

In the United States, the number of COVID-19 cases is likely three times that of reported cases. According to the study, more than 71 million Americans have contracted the virus during the pandemic, and 7 million were infected or potentially contagious last week.

Public health officials rely on case counts to guide decisions, so the undercounting should be considered while trying to end the pandemic.

"The estimates of actual infections reveal for the first time the true severity of COVID-19 across the U.S. and in countries worldwide," Jungsik Noh, PhD, a bioinformatics professor at the University of Texas Southwestern Medical Center, said in a statement.

Dr. Noh and colleague Gaudenz Danuser, PhD, created a computational model that uses machine-learning strategies to estimate the actual number of daily cases in the United States and the 50 most-infected countries.

The model pulls data from the Johns Hopkins University database and the COVID Tracking Project, as well as large-scale surveys conducted by the Centers for Disease Control and Prevention and several states. The algorithm uses the number of reported deaths, which is thought to be more accurate than the number of lab-confirmed cases, as the basis for

In 25 of the 50 countries, the "actual" cumulative cases were estimated to be 5-20 times greater than the confirmed cases. In the United States, Belgium, and Brazil, about 10% of the population has contracted the coronavirus, according to the model. At the beginning of February, about 11% of the population in Pennsylvania had current infections, which was the highest rate of any state.

"Knowing the true severity in different regions will help us effectively fight against the virus spreading," Dr. Noh said. "The currently infected population is the cause of future infections and deaths. Its actual size in a region is a crucial variable required when determining the severity of COVID-19 and building strategies against regional outbreaks.

A version of this article first appeared on WebMD.com.

Continued from previous page

covered by their insurance and work to find discounts and coupons, he said. As for the ACA, "it's a good first start, but we really need to identify what its limitations are." Locally driven, less expensive solutions



Dr. Seay

might be a better way forward than costly federal initiatives.

Brandon M. Seay, MD, a pediatric pulmonologist and sleep specialist at Children's Healthcare of Atlanta, said the findings

dovetail with what he has seen in the pediatric population.

"From my experience, the ACA has helped patients get their foot in the door and has helped patients decrease the possibility of serious financial burden in emergency situations, but the ability to afford

medications has not changed very much," he said. When patients struggle with sufficient prescription coverage, he helps patients fight for coverage and connects them with prescription assistance programs such as GoodRx.

"Instead of focusing on the access of insurance to patients, the goal of the system should be to make care as affordable as possible," Dr. Seay said. "Access does not meet the needs of a patient if they cannot afford what they have access to. Transition to a nationalized health system where there is no question of access could help to drive down prescription drug prices by allowing the government to negotiate with pharmaceutical companies more adequately by removing the 'middle man' of the private insurance industry."

The investigators reported no financial conflicts. Dr. Ouellette and Dr. Seay reported no financial

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## Specialties with higher workload had higher rates of burnout // continued from page 1

coauthors. The results were reported in the Joint Commission Journal on Quality and Patient Safety (2021 Feb. doi: 10.1016/j.jcjq.2020.09.011).

The researchers investigated whether task load correlated with burnout scores in a large national study of U.S. physicians from October 2017 to March 2018.

As the delivery of health care becomes more complex, physicians are charged with ever-increasing amount of administrative and cognitive tasks. Recent evidence indicates that this growing complexity of work is tied to a greater risk of burnout in physicians, compared with workers in other fields. Cognitive-load theory, pioneered by psychologist Jonathan Sweller, identified limitations in working memory that humans depend on to carry out cognitive tasks. Cognitive load refers to the amount of working memory used, which can be reduced in the presence of external emotional or physiological stressors. While a potential link between cognitive load and burnout may seem self-evident, the correlation between the cognitive load of physicians and burnout has not been evaluated in a large-scale study until recently.

Physician task load (PTL) was measured using the National Aeronautics and Space Administration Task Load Index (NASA-TLX), a validated questionnaire frequently used to evaluate the cognitive load of work environments, including health care environments. Four domains (perception of effort and mental, physical, and temporal demands) were used to calculate the total PTL score.

Burnout was evaluated using the Emotional Exhaustion and Depersonalization scales of the Maslach Burnout Inventory, a validated tool considered the gold standard for measurement.

The survey sample consisted of physicians of all specialties and was assembled using the American Medical Association Physician Masterfile, a record of all nearly U.S. physicians independent of AMA membership. All responses were anonymous and participation was voluntary.

#### **Results**

Among 30,456 physicians who received the survey, 5,197 (17.1%) responded. In total, 5,276 physicians were included in the analysis.

The median age of respondents was 53 years, and 61.8% self-identified as male. Twenty-four specialties

were identified: 23.8% were from a primary care discipline and internal medicine represented the largest respondent group (12.1%).

Almost half of respondents (49.7%) worked in private practice, and 44.8% had been in practice for 21 years or longer.

Overall, 44.0% had at least one symptom of burnout, 38.8% of participants scored in the high range for emotional exhaustion, and 27.4% scored in the high range for depersonalization. The mean score in task-load dimension varied by specialty.

The mean PTL score was 260.9 (standard deviation, 71.4). The specialties with the highest PTL score were emergency medicine (369.8), urology (353.7), general surgery subspecialties (343.9), internal medicine subspecialties (342.2), and radiology (341.6).

Aside from specialty, PTL scores also varied by practice setting, gender, age, number of hours worked per week, number of nights on call per week, and years in practice.

The researchers observed a dose-



Dr. Shanafelt

response relationship between PTL and risk of burnout. For every 40-point (10%) reduction in PTL, there was 33% lower odds of experiencing burnout (odds ratio, 0.67; 95%

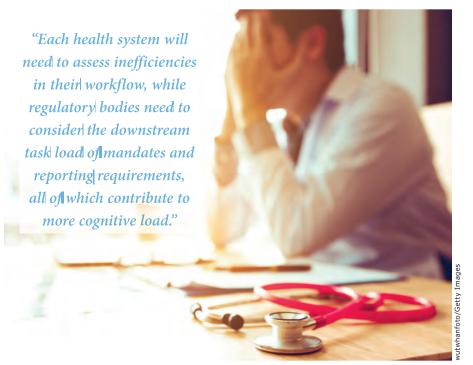
confidence interval, 0.65-0.70; *P* < .0001). Multivariable analyses also indicated that PTL was a significant predictor of burnout, independent of practice setting, specialty, age, gender, and hours worked.

## Organizational strategies to reduce physician burnout

Coauthors of the study, Tait D. Shanafelt, MD, professor of medicine at Stanford (Calif.) University and Colin P. West, MD, PhD, of the Mayo Clinic in Rochester, Minn., are both experts on physician well-being and are passionate about finding new ways to reduce physician distress and improving health care delivery.

"Authentic efforts to address this problem must move beyond personal resilience," Dr. Shanafelt said in an interview. "Organizations that fail to get serious about this issue are going to be left behind and struggle in the war for talent.

"Much like our efforts to im-



prove quality, advancing clinician well-being requires organizations to make it a priority and establish the structure, process, and leadership to promote the desired outcomes," said Dr. Shanafelt.

One potential strategy for improvement is appointing a chief wellness officer, a dedicated individual within the health care system that leads the organizational effort, explained Dr. Shanafelt. "Over 30 vanguard institutions across the United States have already taken this step."

Dr. West explained that conducting an analysis of PTL is fairly straightforward for hospitals and individual institutions. "The NA-SA-TLX tool is widely available, free to use, and not overly complex, and it could be used to provide insight into physician effort and mental, physical, and temporal demand levels," he said in an interview.

"Deeper evaluations could follow to identify specific potential solutions, particularly system-level approaches to alleviate PTL," Dr. West explained. "In the short term, such analyses and solutions would have costs, but helping physicians work more optimally and with less chronic strain from excessive task load would save far more than these costs overall."

Dr. West also noted that physician burnout is very expensive to a health care system, and strategies to promote physician well-being would be a prudent financial decision long term for health care organizations.

Dr. Harry, lead author of the study, agreed with Dr. West, noting that "quality improvement literature has demonstrated that improvements in inefficiencies that lead to

increased demand in the workplace often have the benefit of reduced cost.

"Many studies have demonstrated the risk of turnover due to burnout and the significant cost of physician turnover," she said in an interview. "This cost avoidance is well worth the investment in improved operations to minimize unnecessary task load."

Dr. Harry also recommended the NASA-TLX tool as a free resource for health systems and organizations. She noted that future studies will further validate the reliability of the tool

"At the core, we need to focus on system redesign at both the micro and the macro level," Dr. Harry said. "Each health system will need to assess inefficiencies in their workflow, while regulatory bodies need to consider the downstream task load of mandates and reporting requirements, all of which contribute to more cognitive load."

The study was supported by funding from the Stanford Medicine WellMD Center, the American Medical Association, and the Mayo Clinic department of medicine program on physician well-being. Coauthors Lotte N. Dyrbye, MD, and Dr. Shanafelt are coinventors of the Physician Well-Being Index, Medical Student Well-Being Index, Nurse Well-Being, and Well-Being Index. Mayo Clinic holds the copyright to these instruments and has licensed them for external use. Dr. Dyrbye and Dr. Shanafelt receive a portion of any royalties paid to Mayo Clinic. All other authors reported no conflicts of interest.

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# COVID-19: Peginterferon lambda may prevent clinical deterioration, shorten viral shedding

BY WALTER ALEXANDER

MDedge News

n outpatients with COVID-19, peginterferon lambda has the potential to prevent clinical deterioration and shorten the duration of viral shedding, according to results of a double-blind, placebo-controlled trial (NCT04354259).

Reductions in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA were greater with peginterferon lambda than with placebo from day 3 onward in the phase 2 study led by Jordan J. Feld, MD, of the Toronto Centre for Liver Disease. The findings were reported in The Lancet Respiratory Medicine (2021 Feb 5. doi: 10.1016/S2213-2600[20]30566-X).

#### **Fewer side effects**

To date in randomized clinical trials, efficacy in treatment of COVID-19 has been shown only for remdesivir and dexamethasone in hospitalized patients, and in an interim analysis of accelerated viral clearance for a

monoclonal antibody infusion in outpatients.

Activity against respiratory pathogens has been demonstrated for interferon lambda-1, a type III interferon shown to be involved in innate antiviral responses. Interferons, Dr. Feld and coauthors stated, drive induction of genes with antiviral, antiproliferative, and immunoregulatory properties, and early treatment with interferons might halt clinical progression and shorten the duration of viral shedding with reduced onward transmission. In addition, interferon lambdas (type III) use a distinct receptor complex with high expression levels limited to epithelial cells in the lung, liver, and intestine, leading to fewer side effects than other interferons, including avoiding risk of promoting cytokine storm syndrome.

The researchers investigated peginterferon lambda safety and efficacy in treatment of patients with laboratory-confirmed, mild to moderate COVID-19. Sixty patients (median age 46 years, about 60% female, about 50% White) were recruited from

outpatient testing centers at six institutions in Toronto, and referred to a single ambulatory site. Patients were randomly assigned 1:1 to a single subcutaneous injection of peginterferon lambda 180 mcg or placebo within 7 days of symptom onset or, if asymptomatic, of their first positive swab. Mean time from symptom onset to injection was about 4.5 days, and about 18.5% were asymptomatic. The primary outcome was the proportion of patients negative for SARS-CoV-2 RNA on day 7 after the injection.

## Benefit greater for higher baseline load

A higher baseline SARS-CoV-2 RNA concentration found in the peginterferon-lambda group was found to be significantly associated with day 7 clearance (odds ratio, 0.69; 95% confidence interval, 0.51-0.87; P = .001). In the peginterferon-lambda group, also, the mean decline in SARS-CoV-2 RNA was significantly larger than in the placebo group across all time points (days 3, 5, 7, and 14). While viral load decline was 0.81-log greater in the treatment group (P =.14) by day 3, viral-load decline increased to 1.67-log copies per mL by day 5 (P = .013) and 2.42-log copies per mL by day 7 (P = .0041). At day 14, the viral decline was 1.77-log copies per mL larger in the peginterferon-lambda group (P = .048). The investigators pointed out that the difference in viral-load decline between groups was greater in patients with high baseline viral load (at or above 10<sup>6</sup> copies per mL). In the peginterferon-lambda high-baseline viral load group, the reduction was 7.17log copies per mL, versus 4.92-log copies per mL in the placebo group (P = .004).

## More patients SARS-CoV-2-RNA negative

By day 7, 80% of patients in the peginterferon-lambda group were negative for SARS-CoV-2 RNA, compared with 63% in the placebo group (P = .15). After baseline load adjustment, however, the peginterferon-lambda treatment was significantly associated with day 7 clearance (OR, 4.12; 95% CI, 1.15-16.73; P = .029).

## Respiratory symptoms improved faster

Most symptoms in both groups were mild to moderate, without

difference in frequency or severity. While symptom improvement was generally similar over time for both groups, respiratory symptoms improved faster with peginterferon lambda, with the effect more pronounced in the high–baseline viral load group (OR, 5.88; 95% CI, 0.81-42.46; P=.079).

"Peginterferon lambda has potential to prevent clinical deterioration and shorten duration of viral shedding," the investigators concluded.

"This clinical trial is important" because it suggests that a single intravenous dose of peginterferon lambda administered to outpatients



Dr. Bowton

with a positive SARS-CoV-2 nasopharyngeal swab speeds reduction of SARS-CoV-2 viral load, David L. Bowton, MD, FCCP, professor emeritus, Wake Forest Baptist Health, Win-

ston-Salem, N.C., said in an interview. He observed that the smaller viral load difference observed at day 14 likely reflects host immune responses. Dr. Bowton also noted that two placebo-group baseline characteristics (five placebo-group patients with anti-SARS-CoV-2 S protein IgG antibodies; two times more undetectable SARS-CoV-2 RNA at baseline assessment) would tend to reduce differences between the peginterferon-lambda and placebo groups. He added that the study findings were concordant with another phase 2 trial of hospitalized COVID-19 patients receiving inhaled interferon beta-1a (Lancet Respir Med. 2021;9[2]:196-206).

"Thus, interferons may find a place in the treatment of COVID-19 and perhaps other severe viral illnesses," Dr. Bowton said.

The study was funded by the Toronto COVID-19 Action Initiative, University of Toronto, and the Ontario First COVID-19 Rapid Research Fund, Toronto General & Western Hospital Foundation.

Dr. Bowton had no disclosures. Disclosures for Dr. Feld and coauthors are listed on the Lancet Respiratory Medicine website (doi: 10.1016/S2213-2600[20]30566-X).

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## **ColCORONA:** More questions than answers

#### BY PATRICE WENDLING

cience by press release and preprint has cooled clinician enthusiasm for the use of colchicine in nonhospitalized patients with COVID-19, despite a pressing need for early treatments.

As previously reported by this news organization, a Jan. 22 press release announced that the massive ColCORONA study missed its primary endpoint of hospitalization or death among 4,488 newly diagnosed patients at increased risk for hospitalization.

It also touted that use of the anti-

inflammatory drug significantly reduced the primary endpoint in 4,159 of those patients with polymerase chain reaction-confirmed COVID and led to reductions of 25%, 50%, and



Dr. Tardif

44%, respectively, for hospitalizations, ventilations, and death.

Lead investigator Jean-Claude Tardif, MD, director of the Montreal Heart Institute Research Centre, deemed the findings a "medical breakthrough."

When the preprint released a few days later (MedRxiv. 2021 Jan 27. doi: 10.1101/2021.01.26.21250494), however, newly revealed confidence intervals showed colchicine did not meaningfully reduce the need for mechanical ventilation (odds ratio, 0.50; 95% confidence interval, 0.23-1.07) or death alone (OR, 0.56; 95% CI, 0.19-1.66).

Further, the significant benefit on the primary outcome came at the cost of a fivefold increase in pulmonary embolism (11 vs. 2; P = .01), which was not mentioned in the press release.

"Whether this represents a real phenomenon or simply the play of chance is not known," Dr. Tardif and colleagues noted later in the preprint.

"I read the preprint on colchicine and I have so many questions," Aaron E. Glatt, MD, spokesperson for the Infectious Diseases Society of America and chief of infectious diseases, Mount Sinai South Nassau, Hewlett, N.Y., said in an interview. "I've been burned too many times with COVID and prefer to see better data.

"People sometimes say if you wait

for perfect data, people are going to die," he said. "Yeah, but we have no idea if people are going to die from getting this drug more than not getting it. That's what concerns me. How many pulmonary emboli are going to be fatal versus the slight benefit that the study showed?"

The pushback to the non-peer-reviewed data on social media and via emails was so strong that Dr. Tardif posted a nearly 2,000-word letter responding to the many questions.

Chief among them was why the trial, originally planned for 6,000 patients, was stopped early by the investigators without consultation



Dr. Glatt

with the data safety monitoring board (DSMB).

The explanation in the letter that logistical issues like running the study call center, budget constraints, and a perceived

need to quickly communicate the results left some calling foul that the study wasn't allowed to finish and come to a more definitive conclusion.

"The press release really didn't help things because it very much oversold the effect. That, I think, poisoned the well," said David Boulware, MD, MPH, professor of medicine in infectious diseases at the University of Minnesota, Minneapolis.

"The question I'm left with is not whether colchicine works, but who does it work in," he said. "That's really the fundamental question because it does seem that there are probably high-risk groups in their trial and others where they benefit, whereas other groups don't benefit. In the subgroup analysis, there was absolutely no beneficial effect in women."

According to the authors, the number needed to treat to prevent one death or hospitalization was 71 overall, but 29 for patients with diabetes, 31 for those aged 70 years and older, 53 for patients with respiratory disease, and 25 for those with coronary disease or heart failure.

Men are at higher risk overall for poor outcomes. But "the authors didn't present a multivariable analysis, so it is unclear if another factor, such as a differential prevalence of smoking or cardiovascular risk facColCORONA: Composite of death or hospitalization in 30 days

	Colchicine (%)	Placebo (%)	Odds ratio	95% CI
Overall cohort	4.7	5.8	0.79	0.61-1.03
PCR-confirmed patients	4.6	6.0	0.75	0.57-0.99
Men	5.8	8.4	0.67	0.48-0.95
Women	3.7	3.5	1.07	0.70-1.65

**Note:** Based on data for 4,488 newly diagnosed patients at increased risk for hospitalization. **Source:** medRxiv. 2021 Jan 27. doi: 10.1101/2021.01.26.21250494

tors, contributed to the differential benefit," Rachel Bender Ignacio, MD, MPH, infectious disease specialist, University of Washington, Seattle, said in an interview.

Importantly, in this pragmatic study, duration and severity of symptoms were not reported, observed Dr. Bender Ignacio, who is also a STOP-COVID-2 investigator. "We don't yet have data as to whether colchicine shortens duration or severity of symptoms or prevents long COVID, so we need more data on that."

The overall risk for serious adverse events was lower in the colchicine group, but the difference in pulmonary embolism (PE) was striking, she said. This could be caused by a real biologic effect, or it's possible that persons with shortness of breath and hypoxia, without evident viral pneumonia on chest x-ray after a positive COVID-19 test, were more likely to receive a CT-PE study.

The press release also failed to include information, later noted in the preprint, that the MHI has submitted two patents related to colchicine: "Methods of treating a coronavirus infection using colchicine" and "Early administration of low-dose colchicine after myocardial infarction."

Reached for clarification, MHI communications adviser Camille Turbide said in an interview that the first patent "simply refers to the novel concept of preventing complications of COVID-19, such as admission to the hospital, with colchicine as tested in the ColCO-RONA study."

The second patent, she said, refers to the "novel concept that administering colchicine early after a major adverse cardiovascular event is better than waiting several days," as supported by the COLCOT study, which Dr. Tardif also led.

The patents are being reviewed by authorities, and "Dr. Tardif has waived his rights in these patents and does not stand to benefit financially at all if colchicine becomes used as a treatment for COVID-19," Ms. Turbide said.

Dr. Tardif did not respond to interview requests for this story. Dr. Glatt said conflicts of interest must be assessed and are "something that is of great concern in any scientific study."

Cardiologist Steve Nissen, MD, of the Cleveland Clinic said in an interview that, "despite the negative results, the study does suggest that colchicine might have a benefit and should be studied in future trials. These findings are not sufficient evidence to suggest use of the drug in patients infected with COVID-19."

"Stopping the trial for administrative reasons is puzzling and undermined the ability of the trial to give a reliable answer," Dr. Nissen said. "This is a reasonable pilot study that should be viewed as hypothesis generating but inconclusive."

Several sources said a new trial is unlikely, particularly given the cost and 28 trials already evaluating colchicine. Among these are RECOVERY and COLCOVID, testing whether colchicine can reduce the duration of hospitalization or death in hospitalized patients with COVID-19.

"We have already learned the lesson in the pandemic that early adoption of potentially promising therapies can negatively impact our ability to study and develop other promising treatments," she said.

The trial was coordinated by the Montreal Heart Institute and funded by the government of Quebec; the National Heart, Lung, and Blood Institute of the National Institutes of Health; Montreal philanthropist Sophie Desmarais; and the COVID-19 Therapeutics Accelerator launched by the Bill & Melinda Gates Foundation, Wellcome, and Mastercard. CGI, Dacima, and Pharmascience of Montreal were also collaborators. Dr. Glatt reported no conflicts of interest.

A version of this article first appeared on Medscape.com.

## Loss of smell lingers post COVID-19

#### BY PAULINE ANDERSON

ore than 50% of health care workers infected with SARS-CoV-2 report that their sense of smell has not returned to normal an average of 5 months post infection, new research shows.

The findings illustrate that olfactory problems are common not only during the acute COVID-19 phase but also "in the long run" and that these problems should be "taken into consideration" when following up these patients, study investigator Johannes Frasnelli, MD, professor, department of anatomy, Université du Québec à Trois-Rivières, said in an interview.

Loss of the sense of smell can affect quality of life because it affects eating and drinking, and may even be dangerous, said Dr. Frasnelli. "If your sense of smell is impaired, you may unknowingly eat spoiled food, or you may not smell smoke or gas in your home," he said. In addition, Dr. Frasnelli noted that an impaired sense of smell is associated with higher rates of depression. The findings will be presented at the annual meeting of the American Academy of Neurology in April.

### 'Striking' finding

Research shows that about 60% of patients with COVID-19 lose their sense of smell to some degree during the acute phase of the disease. "But we wanted to go further and look at the longer-term effects of loss of smell and taste," said Dr. Frasnelli.

The analysis included 813 health care workers in the province of Quebec. For all the patients, SARS-CoV-2 infection was confirmed through testing with a nasopharyngeal viral swab.

Participants completed a 64-item online questionnaire that asked about three senses: olfactory; gustatory, which includes tastes such as sweet, sour, bitter, salty, savory, and umami; and trigeminal, which includes sensations such as spiciness of hot peppers and "coolness" of mint.

They were asked to rate these on a scale of 0 (no perception) to 10 (very strong perception) before the infection, during the infection, and currently. They were also asked about other symptoms, including fatigue.

Most respondents had been infected in the first wave of the virus in March and April of 2020 and responded to the questionnaire an average of 5 months later.

The vast majority of respondents (84.1%) were women, which Dr. Frasnelli said was not surprising because women predominate in the health care field.

The analysis showed that average smell ratings were 8.98 before infection, 2.85 during the acute phase, and 7.41 when respondents answered the questionnaire. The sense of taste was less affected and recovered faster than did the sense of smell. Results for taste were 9.20 before infection, 3.59 during the acute phase, and 8.05 after COVID-19.

Among 580 respondents who indicated a compromised sense of smell during the acute phase, the average smell rating when answering the

questionnaire was 6.89, compared to 9.03 before the infection. More than half (51.2%) reported not regaining full olfactory function.

The fact that the sense of smell had not returned to normal for half the participants so long after being infected is "novel and quite striking," said Dr. Frasnelli.

However, he noted, this doesn't necessarily mean all those with a compromised sense of smell "have huge problems." In some cases, he said, the problem "is more subtle."

#### **Further study**

Respondents also completed a chemosensory dysfunction home test (CD-HT). They were asked to prepare common household food items, such as peanut butter, sugar, salt, and vinegar, in a particular way – for example, to add sugar or salt to water – and provide feedback on how they smell and taste.

"From the questionnaires, roughly 50% said their sense of smell is still not back to normal, and when we look at the [chemosensory dysfunction] home test, we see that almost 20% of subjects indeed have pretty strong impairment of their sense of smell,"

For this CD-HT analysis, 18.4% of respondents reported having persistent loss of smell. This, Dr. Frasnelli said, adds to evidence from self-reported responses and suggests that in some cases the problem is more than senses not returning to normal.

"From the questionnaires, roughly 50% said their sense of smell is still not back to normal, and when we look at the CD home test, we see that almost 20% of subjects indeed have pretty strong impairment of their sense of smell," he said.

The results showed no sex differences, although Dr. Frasnelli noted that most of the sample were women. "It's tricky to look at the data with regard to sex because it's a bit skewed," he said.

Male respondents were older than female participants, but there was no difference in impairment between age groups. Dr. Frasnelli said this was "quite interesting," inasmuch as older people usually lose some sense of smell.

The researchers have not yet examined whether the results differ by type of health care worker.

They also have not examined in detail whether infection severity affects the risk for extended olfactory impairment. Although some research suggests that the problem with smell is more common in less severe cases, Dr. Frasnelli noted this could be because loss of smell is not a huge problem for patients battling grave health problems.

As for other symptoms, many respondents reported lingering fatigue; some reported debilitating fatigue, said Dr. Frasnelli. However, he cautioned that this is difficult to interpret, because the participants were health care workers, many of whom returned to work during the pandemic and perhaps had not fully rested.

He also noted that he and his colleagues have not "made the link" between impaired smell and the degree of fatigue.

The COVID-19 virus appears to attack supporting sustentacular cells in the olfactory epithelium, not nerve cells.

"Right now, it seems that the smell problem is not a central nervous system problem but a peripheral problem," said Dr. Frasnelli. "But we don't know for sure; it may be that the virus somehow gets into the brain and some symptoms are caused by the effects of the infection on the brain."

The researchers will extend their research with another questionnaire to assess senses 10-12 months after COVID-19.

Limitations of the study include the subjective nature of the smell and taste ratings and the single time point at which data were collected.

## **Confirmatory findings**

Commenting on the research in an interview, Thomas Hummel, MD, professor, smell and taste clinic, department of otorhinolaryngology, Technische Universität Dresden (Germany), said the new results regarding loss of smell after COVID-19 are "very congruent" with what he and his colleagues have observed.

Research shows that up to one in five of those infected with SARS-CoV-2 experience olfactory loss. "While the numbers may vary a bit from study to study or lab to lab, I think 5%-20% of post-COVID-19 patients exhibit long-term olfactory loss," Dr. Hummel said.

His group has observed that "many more are not back to normal," which conforms with what Dr. Frasnelli's study reveals, said Dr. Hummel.

Also commenting on the research, Kenneth L. Tyler, MD, professor of neurology, University of Colorado at Denver, Aurora, and a fellow of the American Academy of Neurology, said the study was relatively large and the results "interesting."

Although it "provides more evidence there's a subset of patients with symptoms even well past the acute phase" of COVID-19, the results are "mostly confirmatory" and include "nothing super surprising," Dr. Tyler said in an interview.

However, the investigators did attempt to make the study "a little more quantitative" and "to confirm the self-reporting with their validated CD home test," he said.

Dr. Tyler wondered how representative the sample was and whether the study drew more participants with impaired senses. "If I had a loss of smell or taste, maybe I would be more likely to respond to such a survey," he said.

He also noted the difficulty of separating loss of smell from loss of taste.

"If you lose your sense of smell, things don't taste right, so it can be confounding as to how to separate out those two," he noted. The study was supported by the Foundation of the Université du Québec à Trois-Rivières and the Province of Quebec. Dr. Frasnelli has received royalties from Styriabooks in Austria for a book on olfaction published in 2019 and has received honoraria for speaking engagements. Dr. Hummel and Dr. Tyler have disclosed no relevant financial relationships.

A version of this article first appeared on Medscape.com.

# Health care workers not immune to vaccine hesitancy

BY DOUG BRUNK

early 60% of those working in a large health care system expressed their intent to roll up their sleeves to receive the COVID-19 vaccine, but about onethird were unsure of doing so.

Moreover, 54% of direct care providers indicated that they would take the vaccine if offered, compared with 60% of non-care providers.

The findings come from what is believed to be the largest survey of health care provider attitudes toward COVID-19 vaccination, published online Jan. 25 in Clinical Infectious Diseases (2021. ciab054. doi: 10.1093/cid/ciab054).

"We have shown that self-reported willingness to receive vaccination against COVID-19 differs by age, gender, race, and hospital role, with physicians and research scientists showing the highest acceptance," Jana Shaw, MD, MPH, State University of New York, Syracuse, the study's corresponding author, told this news organization. "Building trust in authorities and confidence in vaccines is a complex and time-consuming process that requires commitment and resources. We have to make those investments as hesitancy can severely undermine vaccination coverage. Because health care providers are members of our communities, it is possible that their views are shared by the public at large."

For the study, Dr. Shaw and her colleagues emailed an anonymous survey to 9,565 employees of State University of New York Upstate Medical University, Syracuse, an academic medical center that cares for an estimated 1.8 million people. The survey, which contained questions intended to evaluate attitudes, belief, and willingness to get vaccinated, took place between Nov. 23 and Dec. 5, 2020, about a week before the U.S. Food and Drug Administration granted the first emergency use authorization for the Pfizer-Bio-NTech BNT162b2 mRNA vaccine.

Survey recipients included physicians, nurse practitioners, physician assistants, nurses, pharmacists, medical and nursing students, allied health professionals, and nonclinical ancillary staff.

Of the 9,565 surveys sent, 5,287

responses were collected and used in the final analysis, for a response rate of 55%. The mean age of respondents was 43, 73% were female, 85% were White, 6% were Asian, 5% were Black/African American, and the rest were Native American, or Native Hawaiian/Pacific Islander, or from other races. More than half of respondents (59%) reported that they provided direct patient care, and 32% said they provided care for patients with COVID-19.

Of all survey respondents, 58% expressed their intent to receive a COVID-19 vaccine, but this varied by their role in the health care system. For example, in response to the statement, "If a vaccine were offered free of charge, I would take it," 80% of scientists and physicians agreed that they would, while colleagues in other roles were unsure whether they would take the vaccine, including 34% of registered nurses, 32% of allied health professionals, and 32% of master's-level clinicians. These differences across roles were significant (P less than .001).

The researchers also found that direct patient care or care for COVID-19 patients was associated with lower vaccination intent. For example, 54% of direct care providers and 62% of non–care providers indicated they would take the vaccine if offered, compared with 52% of those who had provided care for COVID-19 patients vs. 61% of those who had not (*P* less than .001).

"This was a really surprising finding," said Dr. Shaw, who is a pediatric infectious diseases physician at SUNY Upstate. "In general, one would expect that perceived severity of disease would lead to a greater desire to get vaccinated. Because our question did not address severity of disease, it is possible that we oversampled respondents who took care of patients with mild disease (i.e., in an outpatient setting). This could have led to an underestimation of disease severity and resulted in lower vaccination intent."

The authors have disclosed no relevant financial relationships. Dr. Milstone disclosed that he has received a research grant from Merck, but it is not related to vaccines.

A version of this article first appeared on Medscape.com.

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## Short sleep predicts dementia and all-cause mortality

BY HEIDI SPLETE

MDedge News

ore evidence has emerged linking sleep deficiency, dementia, and mortality.

"Sleep disturbance and insufficiency have been shown to be associated with both the development and progression of Alzheimer's disease and with all-cause mortality," wrote Rebecca S. Robbins, PhD, of Brigham and Women's Hospital, Boston, and colleagues. However, research on this topic has yielded conflicting results, and "few studies have included a comprehensive set of sleep characteristics in a single examination of incident dementia and all-cause mortality."

In a study published in Aging (2021 Feb 11;13[3]:3254-68. doi: 10.18632/aging.202591), the researchers identified 2,812 adults aged 65 years and older from the National Health and Aging Trends Study (NHATS), a nationally representative longitudinal study of Medicare beneficiaries aged 65 years and older in the United States.

Participants completed surveys about sleep disturbance and duration in 2013 (1,575 individuals) and in 2014 (1,237 individuals), and the researchers examined the relationship between sleep disturbance and deficiency and incident dementia and all-cause mortality over the next 5 years. The average age of the study participants was 76.9 years, 60% were women, and 72% were White.

Overall, approximately 60% of the participants reported never or rarely having problems with alertness, approximately half said that they rarely or never napped, and more than half said they fell asleep in 15 minutes or



less. Approximately 70% rated their sleep quality as good or very good, and more than 90% said they rarely or never snored.

"Short sleep duration was a strong predictor of both incident dementia and all-cause mortality, suggesting this may be a sleep characteristic that is important - over and above the other predictors – of adverse outcomes among older adults."

The researchers examined the relationships between sleep characteristics and the development of incident dementia over 5 years. In a fully adjusted Cox multivariate analysis, individuals who slept 5 hours or less per night had approximately twice the risk for incident dementia as those who slept longer (hazard ratio, 2.04); risk of dementia also was higher among those who took

30 minutes or longer to fall asleep (HR, 1.45).

In addition, the risk of all-cause mortality was significantly higher among individuals who reported difficulty maintaining alertness some days or most days/every day (HR, 1.49 and HR, 1.65, respectively), routinely napping some days or most days/every day (HR, 1.38 and HR, 1.73, respectively), poor or very poor sleep quality (HR, 1.75), and sleeping 5 hours or less each night (HR, 2.38).

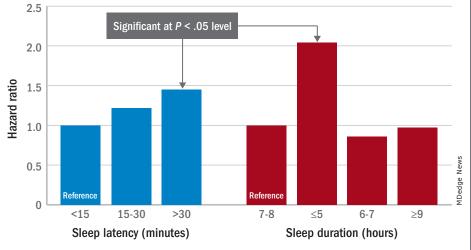
The study findings were limited by several factors including a population representing only one-quarter of the NHATS cohort, which prevented nationally representative estimates, the availability of only 2 years of sleep data, and small sample size for certain response categories, the researchers noted.

However, "our study offers a contribution to the literature on sleep among aging populations in its assessment of incident dementia and all-cause mortality and a range of sleep characteristics among older adults," they said. In particular, "short sleep duration was a strong predictor of both incident dementia and all-cause mortality, suggesting this may be a sleep characteristic that is important – over and above the other predictors - of adverse outcomes among older adults," and future areas for research include the development of novel behavioral interventions to improve sleep in this population.

The study was supported in part by the National Institute for Occupational Safety and Health; the National Heart, Lung, and Blood Institute; the National Institute on Aging; and the Brigham Research Institute Fund to Sustain Research Excellence. Lead author Dr. Robbins disclosed fees from Denihan Hospitality, Rituals Cosmetics, Dagmejan, Asystem, and SleepCycle. Several coauthors disclosed relationships with multiple pharmaceutical companies, and support from various philanthropic organizations.

chestphysiciannews@chestnet.org

#### Association between sleep disturbance and incident dementia



Note: Based on data for 2,812 Medicare beneficiaries included in the 2013 and 2014 National Health and Aging Trends Study surveys.

Source: Aging. 2021 Feb 11;13(3):3254-68. doi: 10.18632/aging.202591

## \_ NEWS FROM CHEST \_

## This month in the journal *CHEST*®

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BY PETER J. MAZZONE, MD, MPH, FCCP

Editor in Chief

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**Long-term Benefits of Pulmonary Rehabilitation in COPD Patients:** A 2-Year Follow-up Study. By Dr. A. Yohannes, et al.

Impact of Corticosteroids in **COVID-19 Outcomes: Systematic** Review and Meta-Analysis.

By Dr. E. Cano, et al.

Leadership Essentials for the Chest Physician: Models, Attributes, and Styles.

By Dr. J. K. Stoller.

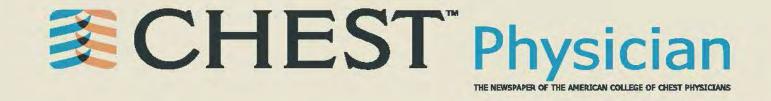
Incidence of Venous Thromboembolism and Bleeding Among Hospitalized Patients With **COVID-19: A Systematic Review** and Meta-Analysis.

By Dr. D. Jiménez, et al.

Disparities in Sleep Health and **Potential Intervention Models: A** Focused Review.

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## President's report

BY STEVEN Q. SIMPSON, MD, FCCP

s I write, it is 1 degree Fahrenheit and dreary in Kansas City, where I live. That's minus 17 degrees Celsius for many of you. I hope that it is cheerier and bordering on springtime when you're reading. You'll understand, though, why I say Happy 2021! 2020 was a humdinger in many ways.

One of those ways, of course, was the COVID-19 pandemic, which wrought so many things – face masks, social distancing, steep learning curves, over 300,000 excess deaths, and new vaccines. For CHEST, it meant that two of our most important educational opportunities of the year, board review and the annual meeting, were held virtually. Dr. Levine has already written about the board reviews, so I'll focus on the annual meeting, held in late October.

In many ways, the meeting was a success. We had over 6,800 attendees. There were 88 live online sessions, 22 that were semi-live, and 160 prerecorded sessions. For presenters, this was simultaneously both easy and difficult. They had to ensure that their recording equipment and their Internet access were of sufficient quality, and if prerecorded, the sessions had to be finished weeks ahead of time. But the presentations could be given from presenters' homes or from their normal work offices. For attendees, the ability for nonsimultaneous playback allowed for fitting the meeting into a work-life schedule. In fact, at least one friend related that he watched sessions with a grandchild on his lap.

However, it meant a lack of opportunities to ask clarifying questions of the presenters, which is a common activity at the end of a session, and the opportunity to see and catch up with old friends and colleagues was missing. Simulations, of course, could not be hands-on, but virtual educational games matured significantly. The satisfaction scores from both attendees and faculty were good, if slightly below our usual scores for live meetings. They told us that we all prefer our in-person meetings, but that content is deliverable and receivable in an online format. Overall, we have to consider the CHEST 2020 online platform to be a successful endeavor.

Which brings me to our plans for future meetings. The Board of Regents discussed the alternatives for CHEST 2021. Should we hold a live meeting in Vancouver, as planned? Should we hold another online meeting like the one we just discussed? None of us has the crystal ball that tells us exactly how COVID-19 is going to develop. We don't know exactly how many people will be vaccinated either north or south of the US-Canada border.

While those of us who care for patients in the United States have had the opportunity to be vaccinated, we don't know if the professional staff from CHEST headquarters who travel to the annual meeting will be vaccinated, even though that prospect is currently looking very reasonable. We don't know if the Canadian government will be allowing US residents to visit Canada without

quarantine. There are just quite a few things that we can't know. However, convention centers need to know if we will be there, and we needed to decide.

In the end, a couple of things swayed us—the unexpected availability of a US convention center and uncertainty about travel to Canada. We



Dr. Simpson

are planning to hold CHEST 2021 in Orlando, Florida, during our usual late October time frame. CHEST 2021 is slated to be the first in-person pulmonary, critical care, and sleep conference to be held in the United States in 2 years.

The Executive Program Committee has met, and program selections have been made. Very soon, invitations

will go to our prospective faculty, and we will be underway. We are planning CHEST 2021 as what we call a "hybrid" meeting, a meeting that will provide an excellent experience whether one attends in person at the Orlando Convention Center or partakes of the meeting from home. Some sessions will be broadcast live and others will be prerecorded. Needless to say, the experience will not be equal for in-person and at-home learners, but it will be equitable. Regardless of how you choose to partake, CHEST 2021 will have excellent content to suit your needs. This plan also allows us the ability to convert to a fully online meeting, should the COVID-19 circumstances dictate that we must. Having sat in on the program committee meetings, I am excited about what we have to offer. So, dig around and find your old mouse ears or your red forehead scar. CHEST 2021 will be a dynamite experience for us

Our board review sessions, which are also among the most highly valued of CHEST activities, will be different out of necessity. Again, decisions had to be made many months ahead of time, and we have chosen to hold our board reviews online again this year. COVID-19 uncertainties certainly play into our decision to not put attendees in a room together. However, the ability to play and replay, slow down and speed up video content, and ability to watch any session any time are all well suited to reviewing for an examination. We think this is the appropriate decision for 2021, but we may be back together again for future sessions. Frankly, we are listening to hear which format our attendees like more. And, we are plotting how to make the online platform review even better.

The Board of Regents has been hard at work on a lot of fronts, but I want to focus on one of them, for now. It is important to the Board of Regents and to me, personally, that CHEST be the single most inclusive and diverse professional medical society, bar none. It is of utmost importance that we remove any barriers that might have inadvertently been put into place that would hamper the success of any of our members or their patients. In other words, we hope to find

any implicit biases in attitude and behavior and to illuminate and remedy them. We have begun the process by focusing on what CHEST is all about – making a difference with our patients and corporate self and being an inclusive and diverse professional organization.

We believe that we must look at ourselves in three separate, but related, ways. We must examine our patient-facing side and the ways in which we help our members to serve their patients. We must examine our headquarters and our hiring, working, and promoting practices to ensure an inclusive and welcoming environment for the staff who do our day to day business. Finally, we must examine ourselves and our member-based organization, to ensure that all can participate freely in CHEST opportunities and, for those who aspire to lead our organization, to ensure that there are no implicit biases that hold them

We began the process with a series of regional listening sessions across the United States, sponsored by the CHEST Foundation, in which we heard from both patients and community leaders of color. We learned of challenges that our patients face in accessing care, communicating with their doctors, and obtaining the medications they need for their illness. Our professional staff has organized an anti-racism task force and is working to ensure that we can be proud of a diverse and inclusive work environment. For our members, we have held two board development sessions, so that our Board of Regents can examine us and our attitudes toward race and toward inclusiveness in our organization. We will soon be holding a listening session with CHEST members of color with the express purpose of allowing those of us who are not persons of color to better understand the challenges faced by our members and to understand where organizational changes could be necessary to help make their professional lives better. As a long time CHEST member, I believe that CHEST is not purposefully exclusive of anyone. We are, nevertheless, a part of the larger fabric of society, and because of that, we are subject to having implicit biases and practices as an organization. Our best path to be aware of them and to deal with them is to hear from our members who experience them, and we shall.

I will end on a note that is somber but important. In the past year, we have all lost friends and colleagues with whom we worked side by side, to COVID-19. Many of them have been CHEST members. Because of the pandemic, we have often not been able to mourn those we have cared about in the same ways that we normally would, in the company of friends and family. Yet, it is important for us to remember our colleagues and to share our memories. So, we established CHEST Remembers, a memorial wall on the CHEST website where we can post the news of our friends' passing, along with our remembrances of them. If your friend or colleague has died of COVID-19, please feel free to share with the CHEST community. You can find the link to do that at www.chestnet.org.

## Introducing President-Designate Doreen J. Addrizzo-Harris, MD, FCCP

oreen J. Addrizzo-Harris, MD, FCCP, is a pulmonary/critical care physician with an extensive background in bronchiectasis and non-tuberculous mycobacterial infection and medical education.

Dr. Addrizzo-Harris is currently a Professor of Medicine at the NYU Grossman School of Medicine. She serves as the Associate Division Director for Clinical and Faculty Affairs, is the Director of the NYU Bronchiectasis and NTM Program, and is Co-Director of the NYU Pulmonary Faculty Practice. She is now serving in her 20th year as the Program Director of NYU's Pulmonary and Critical Care Medicine Fellowship.

Dr. Addrizzo-Harris received her medical degree and completed her residency and fellowship training at New York University School of Medicine. Since completing her training, she was recruited to stay as a faculty member at NYU, where she has been a critical presence over the past 25 years. She has been instrumen-

tal in educating the next generation of pulmonary/critical care physicians and has won a number of awards for her teaching skills, most recently, the 2021 Outstanding Educator Award from the APCCMPD.

Dr. Addrizzo-Harris has served on the board of the Association of Pulmonary and Critical Care Medicine Program Directors (APCCMPD), including serving as President from 2006-2007. Academically, she au-

thored 44 peer-reviewed publications and 57 scientific abstracts presented at international conferences. She has participated in numerous clinical trials, many as PI. Dr. Addrizzo-Harris

has been recognized as a Distinguished CHEST Educator each year since its inception in 2017 and received the Distinguished Service Award in 2019.

During her leadership tenure with CHEST, Dr. Addrizzo-Harris has served on the Marketing Committee, the Health and Science Policy Committee (Chair from 2007-2009), Government Relations Committee, Scientific Program Committee, Education Committee, Governance Committee, Editorial Board for CHEST Physician, Professional Standards Committee (Chair 2016-2018), Board of Regents, and CHEST Foundation Board of Trustees. Most recently, Dr. Addrizzo-Harris served as the President of the CHEST Foundation from 2018-2019 and Co-Chair of the Foundation Awards Committee from 2015-2020. She will serve as the sixth woman to lead the American College of Chest Physicians.



Dr. Addrizzo-Harris

## CHEST 2021 moves to Orlando and online - your choice

CHEST is excited to announce that CHEST 2021 will be held in Orlando, Florida, from October 17-21 at the Orange County Convention Center. CHEST 2021 will be offered as both an in-person and online experience. Since travel restrictions remain unknown, CHEST is working to ensure that everyone has access to the same top-tier learning – wherever they are.

"Learning together as a community is an important aspect of the CHEST annual meeting. Whether we are face-to-face or online, the knowledge gained from expert presenters, simulations and games, and talking with one another can't be duplicated elsewhere. In whatever way you can attend, join us at CHEST 2021 to discuss the critically relevant topics affecting our patients and chest medicine," said CHEST President Steven Q. Simpson, MD, FCCP.

It is also essential that those who cannot travel can still avail themselves of the engaging and interactive learning offered at the CHEST conference. Everyone – whether online or in-person – will be able to experience the meeting in real-time, including expert faculty presentations, simulated learning experiences, gaming, and more.

#### What to expect

Through bite-sized, immersive learning, experts in the field will



cover the latest updates in pulmonary, critical care, and sleep medicine. CHEST 2021 offers you the opportunity to learn from a diverse set of knowledgeable educators representing different viewpoints and experiences.

Team-based learning is an indispensable component of the annual meeting. The activities support collaborative discovery and help you build relationships with your peers. Known for its development of simulation courses, at CHEST 2021, you can take part in the latest in "handson" learning. In addition, gaming will allow for friendly competition among colleagues, whether playing from home or on-site.

#### **Getting involved**

Make your mark by submitting your original abstracts and case reports to be presented at CHEST 2021. Because of the past year's challenges, new discoveries were made in the treatment and approaches to managing chest medicine diseases. This work is important and will inform the way patients receive care in the future.

Showcase COVID-19 research,

among other topics you are working on, for a chance to share your findings with colleagues, gain feedback from expert faculty, collaborate with other professionals in the field, and expand your professional portfolio. The deadline to submit is April 28. [https://bit.ly/3qXgytH]

### **Keeping safe**

It's been a long time since in-person conferences were possible. CHEST is closely monitoring the status of the pandemic throughout the planning process. The Orange County Convention Center was selected because the venue

is large enough to support social distancing. The CHEST team is establishing protocols that limit the number of individuals in a space, promote good traffic flow, require the wearing of masks, and other safety measures. All on-site participants and CHEST support staff will be required to attest to having received a COVID-19 vaccination to attend.

Continue to watch for more information. Registration for CHEST 2021 will open in May. We've missed you, and we look forward to seeing you in Orlando, Florida, October 17-20.

## CHEST to offer research matching service

CHEST Analytics has announced its new resource for members interested in serving as investigators in industry-sponsored clinical trials.

The new program, CHEST Clinical Trials Solutions, will pair members who have indicated their interest in specific research topics with companies seeking investigators. According to CHEST President Steven Q. Simpson, MD, FCCP: "For members who would like to be involved in research and

for companies that have defined distinct criteria for their studies, CHEST Analytics can pair qualifying parties to facilitate communication between researcher and sponsor. It's a great way for young investigators to get started or accomplished members to share their experience while helping industry expedite introducing new products that improve patient care." More information regarding enrollment will be available at info.chestnet. org/clinical-trials.

### **SLEEP STRATEGIES**

## Home noninvasive ventilation in hypercapnic COPD: Progress but important unanswered questions

BY JEREMY E. ORR, MD

atients with COPD may develop sustained hypercapnia, often defined as an awake arterial Pco<sub>2</sub> of >45 mm Hg. Other synonymous terms include alveolar hypoventilation or chronic hypercapnic respiratory failure, noting that the specific terminology used may reflect local practice, an assessment of patient severity, or specific insurance requirements. Regardless, available data suggest that hypercapnic COPD patients are at high risk for adverse health outcomes (Yang H, et al. BMJ Open. 2015;5[12]:e008909). Moreover, there appears to have been a growing interest in this population driven by a focus on reducing COPD hospitalizations, increasing recognition of sleep-disordered breathing, and progress in potential therapeutic strategies.

There are a number of factors that might drive COPD patients to develop hypercapnia. Lower airway obstruction, expiratory flow limitation, and air trapping cause mechanical load on breathing, as well as a trade-off between time spent in inspiration vs prolonged expiration. The function of the diaphragm is impacted by hyperinflation leading to mal-positioning, as well as possibly by local and/or systemic myopathy. The net result is often decreased overall minute ventilation. In terms of gas exchange, increased dead space and ventilation-perfusion mismatching leads to reduced efficiency of ventilation toward CO2 removal. Breathing changes during sleep play an important role, as evidenced by worsened hypercapnia during sleep that can drive chronic CO<sub>2</sub> retention (O'Donoghue FJ, et al. Eur Respir J. 2003;21[6]:977). The pathogenesis includes reduced central respiratory drive, increased upper airway resistance and/or obstructive hypopneas and apneas, and respiratory muscle atonia, particularly during REM

sleep. The extent to which each of these factors contributes to hypercapnia varies across individual patients, in accordance with the known substantial heterogeneity of COPD.



Dr. Orr

Regardless of underlying traits, patients with COPD who develop hypercapnia have sufficiently severe perturbations to disrupt the normally tight control over CO, homeostasis.

Nocturnal home noninvasive ventilation (NIV) has been examined as a potential therapeutic strategy for patients with hypercapnic COPD. While older studies have not shown consistent benefits, more recent evidence suggests that NIV can reduce hospitalizations, improve quality of life, and potentially reduce mortality among those with hypercapnic COPD. Accordingly, the American Thoracic Society recently released a clinical practice guideline regarding the use of NIV in patients with chronic stable hypercapnic COPD (Macrea M, et al. Am J Respir Crit Care Med. 2020;202[4]:e74-e87). Recommendations from the guideline included:

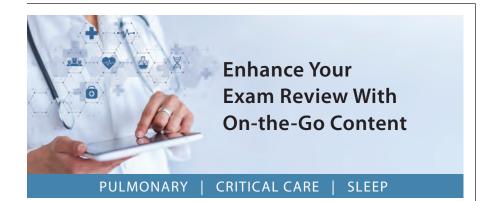
- 1. The use of nocturnal NIV for patients with chronic stable hypercapnic COPD
- 2. Screening for OSA before initiation of long-term NIV
- 3. Not using in-hospital initiation of long-term NIV after an episode of acute or chronic hypercapnic respiratory failure, favoring instead reassessment for NIV at 2-4 weeks after resolution
- 4. Not using an in-laboratory overnight PSG to initially titrate NIV
- 5. Targeting normalization of

Although it now seems clear that efforts should be made to use NIV in COPD to decrease chronic hypercapnia, there are a number of important questions that remain, particularly surrounding the topic of concurrent OSA, titration, and devices:

• What is the appropriate approach toward patients with suspected concurrent OSA? Most studies of NIV have excluded patients with OSA, or otherwise at higher risk

of OSA. Nonetheless, such patients may be common, both based on continued high prevalence of obesity, as well as the potential role that upper airway obstructive events may play toward elevations in CO<sub>2</sub> (Resta O, et al. Sleep Breath. 2002;6[1]:11-18). COPD epidemiologic studies indicate obesity as a risk factor for several poor outcomes, including severe COPD exacerbation (Lambert AA, et al. Chest. 2017;151[1]:68-77), while studies of COPD and OSA suggest that the presence of hypercapnia defines a high-risk group (Jaoude P., Lung. 2014;192:215). Recognizing the potential importance of OSA in this group, ATS guidelines recommend that a general questionnaire-based screening be performed. If screening is positive, the implication would be to perform diagnostic polysomnography to confirm the diagnosis of OSA. However, this may be a challenge for chronically ill patients, and likely would result in delays in NIV initiation. Of note, emerging evidence suggests that home sleep apnea testing (HSAT) might have reasonable accuracy in this group, which may facilitate formal diagnosis. Other concerns in this area include the lack of questionnaire validation in COPD patients.

- Should patients with OSA be managed differently than those without OSA? A diagnosis of OSA might impact several subsequent management decisions related to appropriate NIV therapy and titration. Patients with OSA have increased upper airway collapsibility, which might necessitate higher EPAP support than the minimal EPAP used in NIV trials with non-OSA patients (often fixed at 4 cm water). Potential strategies for optimizing EPAP include use of an NIV device with auto-titrating EPAP, titration in the sleep laboratory (discussed below), or outpatient titration based on clinical parameters and subsequent device download follow-up. On the other hand, one might consider all patients to be at risk for upper airway obstruction and need for additional EPAP titration, which would obviate the need for OSA diagnostic testing.
- What is the role of the sleep laboratory toward successful titration?





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The inpatient hospital setting has been the traditional site to initiate home NIV in some institutions but is highly resource-intensive and increasingly impractical in many health systems. On the other hand, advances in home remote device monitoring now provide the clinician with the ability to examine daily usage, estimated leak, tidal volumes, respiratory rate, and other parameters - often reported as recently as the prior night. In addition, setting changes can be made via these remote monitoring tools (for nonventilator devices), allowing titration to be performed over time on outpatients. Several studies support the effectiveness of this approach over hospital titration in neuromuscular disease and now in COPD (Duiverman ML, et al. Thorax. 2020;75[3]:244-52). Similarly, data suggest that titration under polysomnographic guidance might not be necessary (Patout M, et al. Polysomnography versus limited respiratory monitoring and nurseled titration to optimize non-invasive ventilation set-up: a pilot randomised clinical trial. Thorax. 2019;74:83-86).

• Limitations toward the sleep lab as the site of initial titration include waiting time, cost and insurance coverage, and the need to accommodate issues such as impaired mobility or reliance on a caretaker. In addition, titration goals must be clearly outlined in protocols and via staff training specific to NIV. The sleep laboratory may be most appropriately utilized in the minority of patients in whom outpatient titration is unsuccessful. Relatively common issues that might be best addressed in the lab setting include excessive mask leaks, residual apneas and hypopneas, failure to control CO<sub>2</sub>, or other sleep complaints. In general, studies should probably be focused primarily on titrating EPAP to alleviate upper airway obstructive events. The goals in terms of IPAP titration (or ventilation titration, in the case of "VAPS" modes) are less clear, and overly aggressive increases may complicate the picture with excessive leaks or airway obstruction due to glottic closure. Attempting to accomplish "too much" often leads to a study with limited utility. In contrast, simply performing the study in the patient's home settings can provide useful diagnostic information regarding the problem one is trying to solve.

- When and where should one initiate NIV following a severe COPD exacerbation? In contrast to the ATS guidelines, the European Respiratory Society guidelines suggest that patients recovering from severe COPD exacerbations be initiated on NIV during that hospitalization, noting that this is a group at high risk for early rehospitalization and mortality (Ergan B, et al. Eur Respir J. 2019;54[3]:1901003). ATS guidelines had the concern of unnecessary start of NIV in those who might normalize their CO<sub>2</sub> after recovery, and the possibility of prolonging hospitalizations for titration. For the clinician, the decision will probably be individualized based on risk and available resources. For patients with frequent ICU admissions and/or difficulty with close outpatient follow-up, earlier NIV initiation is certainly a reasonable approach, but adherence and effectiveness remains a concern and, thus, more data are needed.
- Which patients should receive a bedside respiratory assist device (RAD, ie, BiPAP machine) vs. a noninvasive ventilator? Two classes of devices can be used for home NIV. While both can provide similar positive pressure ventilation, ventilators are designed as life support with alarms and batteries, and may have modes not otherwise available (auto-titrating EPAP). On the other hand, RAD devices are more convenient for patients and less expensive, but difficult qualification requirements (particularly for devices capable of bilevel ST or VAPS) have likely resulted in their underutilization. CHEST is spearheading an effort to reconsider Medicare coverage determinations (current rules are from 1998), which will hopefully better align device qualification requirements with emerging evidence regarding patient needs and preferences.

Home noninvasive ventilation can improve outcomes in these high-risk patients with hypercapnic COPD, and the new clinical practice guidelines are an important step in outlining appropriate management. Further progress is needed to delineate an individualized approach based on underlying patient pathophysiology, COPD manifestations/ phenotypes, and systems-based practice considerations.

Dr. Orr is Assistant Professor, Division of Pulmonary, Critical Care, and Sleep Medicine, UC San Diego.







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#### **NETWORKS**

## Disaster response and global health. Interstitial and diffuse lung disease. Practice operations. Transplant.

## Disaster response and global health

One step forward, two back...

No adult alive today will live to see global gender parity. The 2020 World Economic Forum Global Gender Gap Report, published December 2019, assessed four dimensions of gender inequality – health, economic opportunities, educational advancement, and political empowerment.

The report stated that despite some advances, overall global gender parity would not be reached for 99 years. The gender gap is not solely a developing nation's problem. The US standing as the 51st in gender parity fell to 53rd during the previous 2-year period. And these numbers were before COVID-19.

Disasters, including pandemics, negatively affect female subjects disproportionately. COVID-19 has unmasked and exacerbated both gender and minority disparity. Global health care workers (HCW) are overwhelmingly female, exposing them to

a higher risk of contagion. This risk was exceptionally high among Black, Asian, and minority ethnic HCW (Nguyen et al. *Lancet Public Health*. 2020;5[9]:E475). The gender pay gap, where women are paid 80% of their male counterparts and women

90

Dr. Reed

of color make 63%, has led to a greater financial burden among female HCW during Covid COVID-19. Women, including HCW, provide the majority of the unpaid work, ie, child-

care, elder care, and home care. 2020 saw an unprecedented loss of women in the workplace, including health care. Both clinical practice and research have been affected. The long-term effect on women HCW careers is unknown at present. Global gross domestic product growth loss due to

this decline in the female workforce is estimated at 1 trillion USD over the next decade.

Disaster and gender parity are entwined. COVID-19 has revealed the persistence of inequalities that needs to be considered in future disaster planning.

Mary Jane Reed, MD, FCCP Steering Committee Ex-Officio

## Interstitial and diffuse lung disease

Emergence and benefits of home monitoring and telemedicine for patients with ILD

Patients with interstitial lung disease (ILD) require regular monitoring with outpatient clinic visits and pulmonary function tests.

The emergence of COVID-19 forced an unprecedented transition to telemedicine and a new reliance on home monitoring. Home spirometry enables quick detection of rapidly progressive disease and is more sensitive than hospital-based spirom-

etry in predicting prognosis (Russel, et al. *Am J Respir Crit Care Med*. 2016;194[8]:989). Patients with idiopathic pulmonary fibrosis randomized to a home monitoring program had improved psychological wellbeing and higher patient satisfaction

with individually tailored treatment decisions (Moor, et al. *Am J Respir Crit Care Med.* 2020;202[3]:393). However, there are some inaccuracies in home monitoring. For instance, pulse



Dr. Gersten

oximetry is less reliable in African American patients receiving supplemental oxygen (Sjoding, et al. *N Engl J Med.* 2020;383:2477). It is critical to protect ILD patients from potential COVID-19 exposure given the high risk of serious complications. Telemedicine should be offered to all



## CHEST Clinical Trial Opportunities

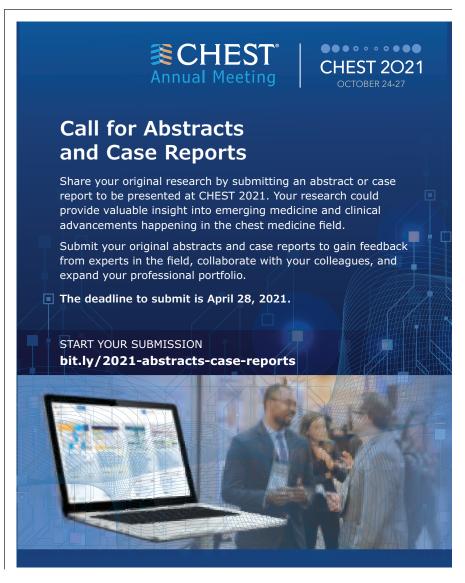
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patients and may actually increase access to care in ILD patients, a population with disabling dyspnea and supplemental oxygen needs that require specialist care unavailable in many geographic regions. African American patients, those older than 65, and patients with lower socioeconomic status are less willing to engage in videoconferencing (Fischer, et al. JAMA Netw Open. 2020;3[10]:e2022302). It is essential that telephone visits be offered to minimize disparities in access to care. Many telemedicine platforms enable caregivers and family members to attend visits from separate locations and provide a unique opportunity to address advance care planning. In-person visits should be arranged for patients with no access to internet or telephone or those with poor medical literacy or insufficient social support to conduct a productive remote visit. Telemedicine and home monitoring have proved invaluable during the COVID-19 pandemic and have the potential to continually increase access to and quality of care.

> Rebecca Anna Gersten, MD Steering Committee Member

## **Practice operations**

Use of media platforms to eliminate the COVID-19 infodemic
We were shocked when we read a tweet in December 2020 from a health care worker stating, "My biggest concern is the lack of data and the quick development time. Feels like we are a bunch of guinea pigs" in reference to the new COVID-19 vaccine.

We reflected back on the last pandemic in 2009, H1N1, and remembered when the new vaccine developed in 174 days was first released to pregnant women and children after phase 3 trials. How did we get here? What do we do to fix it?

This misinformation is labeled as the "COVID-19 infodemic." In the last year, we have seen the media, more specifically social platforms, quickly spread medical misinformation. In the book "Made to Stick: Why Some Ideas Survive and Some Die," the authors described core elements that make an idea "sticky." Use of those exact same sticky techniques can be used to circulate accurate information and to halt the spread of this infodemic. Although, numerous media companies, including Twitter, are making an effort to remove the false content from their platforms, their efforts require a lengthy process and are delayed. Therefore, it is crucial for the

public health figures and community at large in partnership with various national organizations to establish a robust connection with the social platforms in a dynamic and timely fashion to help spread the verified information across social media, digital





Dr. Khan

Dr. Anjum

and traditional media outlets.

The UN has launched an initiate called "Verified." This is a world-wide effort to help individuals spread reliable information regarding COVID-19 to their friends and families via social platforms as various media platforms and businesses have partnered with Verified. Also, we encourage our members to access the CHEST COVID-19 resource center and benefit from the various clinical and practice management tools along with validated patient information materials.

Roozera Khan, DO, FCCP Steering Committee Member Humayun Anjum, MD, FCCP

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#### **Transplant**

#### **COVID-19 + lung transplant**

The COVID-19 pandemic has created a dilemma for lung transplantation, with a new group of patients with refractory respiratory failure secondary to the viral illness. As transplant centers worldwide receive referrals for COVID-19 related respiratory failure, information regarding evaluation, listing, and posttransplant care continues to be published, but further research will be needed to care for this complex population.

The first lung transplant for COVID-19 in the United States occurred at Northwestern Hospital on June 5th, 2020, and was publicized for its innovativeness. Information from their three lung transplants

completed thus far includes information regarding pathologic findings of the explanted lung tissue; pulmonary fibrosis was the dominant feature, suggesting COVID-19-induced acute respiratory distress syndrome with prolonged time supported by mechanical support may only be survivable with the use of lung transplant (Bharat, et al. *Sci Transl Med.* 2020;12(574):eabe4282).

Lung transplant in the setting of COVID-19 fibrosis increases surgical complexity as well, with case reports of dense adhesions and distortion of regular surgical planes (Bharat, et al. *Sci. Transl. Med.* 2020; Lang, et al. *Lancet Respir Med.* 2020;8:1057). Recognizing the difficulty with deciding to use transplantation after an infectious disease,





Dr. Louis

Dr. Turner

The International Society for Heart and Lung Transplant (ISHLT) has created guidelines regarding indications for transplantation (ISHLT. org). Continued research will be necessary to identify those at the highest likelihood for success from transplantation, preparation for the increased complexity, and long-term outcomes. Further information is available in a CHEST webinar titled "Lung Transplantation in the Era of COVID-19" (http://www. chestnet.org/Guidelines-and-Resources/Online-Series/Webinar/ Lung-Transplantation-in-the-Eraof-COVID-19).

Clauden Louis, MD Grant Turner, MD Fellows-in-Training NetWork Members

#### Women's lung health

#### Pregnancy in cystic fibrosis

The newest in the line of modulator therapy, Trikafta (elexacaftor/tezacaftor/ivacaftor and ivacaftor), is expected to improve life expectancy and quality of life for patients with cystic fibrosis (CF). This evolution in therapy will shape how providers care for their patients, particularly women of reproductive age. Conventionally, women with significantly impaired lung function due to CF have been advised to avoid pregnancy due to potential complications

for mother and baby. It is likely that now, with improved lung function while receiving Trikafta, more women will feel better equipped to attempt pregnancy.

There are several considerations in this setting, including the need for careful drug safety and monitoring, creating a plan of action for possible decline in lung function while off cer-

tain CF-related medications, and counseling on drug interactions during lactation. In our experience with women becoming pregnant while receiving Trikafta or contemplating

pregnancy, all



Dr. Banerjee

have opted to discontinue modulator therapy with declines in lung function. Trikafta does not report teratogenicity based on animal studies of the individual components of the drug; however, ivacaftor is known to cause impairment in fertility and reproductive indices, including nonviable embryos and implantation failure in a rat model at five times the maximum recommended human dose, dosed prior to and during early embryogenesis. Small mammal models have decreased birth weight at high doses of elexacaftor, tezacaftor and ivacaftor administered individually. There is evidence of placental transfer of ivacaftor and breast milk concentrations of tezacaftor and ivacaftor are higher than plasma concentrations in rats. There are no human data in parturient or lactating women or infants. Three women became pregnant during the phase 3 clinical study of Trikafta, one with elective termination, one pregnancy was carried to full term with normal birth outcome, and one ended in a spontaneous abortion, which was deemed not to be related to the study drug. Translating this information into recommendations for patients has important implications.

> Debasree Banerjee, MD, MS Steering Committee Member

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