NASHVILLE, TENN. – If a pulmonologist becomes involved early in the care of patients admitted to the hospital for an acute exacerbation of chronic obstructive pulmonary disease (AECOPD), the rate of readmission is reduced substantially relative to no pulmonologist involvement, according to a retrospective cohort review presented at the annual meeting of the American College of Chest Physicians (CHEST).

“When stratified by severity of COPD at the time of admission, the difference in the readmission rate was even greater,” reported Nakisa Hekmat-Joo, MD, a third-year resident at Staten Island University Hospital, New York.

Sleep duration is now considered “an essential component for ideal heart and brain health,” according to the AHA’s updated checklist, now called Life’s Essential 8. “Our study is the first to show that sleep metrics add independent predictive value for cardiovascular disease (CVD) events over and above the original seven CVH metrics, providing support for updating the guidelines from Life’s Simple 7 (LS7) to Life’s Essential 8,” lead author Nour Makarem, PhD, of the Mailman School of Public Health at Columbia University Irving Medical Center, New York, said in an interview.

For the study, her team compared four versions of LS7 checklists that included sleep in relation to CVD risk.

“CVH scores that included sleep duration alone as a measure of overall sleep health, as well as scores that included multiple dimensions of sleep duration, were associated with lower CVD risk,” she reported.
Sleep and CVH // continued from page 1

sleep health (that is, sleep duration, efficiency, and regularity; daytime sleepiness; and sleep disorders), were both predictive of future CVD,” she said.

Study participants scoring in the highest tertile of the CVH checklists that included sleep had up to a 47% lower CVD risk.

Sleeping 7 hours or more but less than 9 hours nightly was considered “ideal,” according to the study, published online in the Journal of the American Heart Association (2022. doi: 10.1161/JAHA.122.025252).

Lower the odds

Dr. Makarem and colleagues analyzed data from participants in the Multi-Ethnic Study of Atherosclerosis (MESA) sleep study using overnight polysomnography, 7-day wrist actigraphy, validated questionnaires, and outcomes. They used the data to evaluate the four iterations of an expanded LS7 score:

- Score 1 included sleep duration;
- Score 2 included sleep characteristics linked to CVD in the literature (sleep duration, insomnia, daytime sleepiness, and obstructive sleep apnea [OSA]);
- Score 3 included sleep characteristics associated with CVD in MESA (sleep duration and efficiency, daytime sleepiness, and OSA); and
- Score 4, also based on CVD in MESA, included sleep regularity.

Among 1,920 participants (mean age 69 years; 54% women; 40%, White individuals), the mean LS7 score was 7.3, and the means of the CVH score was 7.3, and the means of the CVH score 4, which included multidimensional sleep health, had 43% and 47% lower incident CVD risk (hazard ratios, 0.57 and 0.53), respectively. The LS7 score alone was not associated with CVD incidence (HR, 0.62).

Sleep ‘devalued’

The sleep field has been fighting to get more sleep education into medical education for decades,” t Michael A. Grandner, PhD, Director of the Sleep & Health Research Program and of the Behavioral Sleep Medicine Clinic at the University of Arizona College of Medicine, Tucson, said in an interview. “To my knowledge, there still is not a lot of attention given to it, partly because the culture in medical school and among residents is one of not sleeping,” said Dr. Grandner, who was not involved in the study. “The culture among physicians is ‘Who needs sleep?’

“Sleep made it to the checklist because it is a biological requirement for human life,” he noted. “We sleep for the same reason we breathe and drink. It’s imperative. Yet we live in a society that devalues sleep.”

Clinicians should ask all patients about how they’re sleeping at every visit, Dr. Grandner said. “It’s now part of the official definition of health. Just like you would be remiss if you didn’t ask about smoking or test blood pressure, you’d be missing something important by not asking about sleep – something that has similar billing to diet, exercise, blood pressure, and all the other ‘essentials.’”

No conflicts were declared.

Erratum

Mary Jo S. Farmer, MD, PhD, FCCP, should be listed as the first author in the Networks article “Pulmonary Vascular Disease Section – Key Messages from the 2022 ESC/ERS Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension” (page 19, November issue).
The primary outcome was length of stay (LOS). Although the slightly lower LOS in the pulmonologist-treated group did not approach significance (4.16 vs. 4.21 days; \( P = .88 \)), the readmission rate at 90 days, which was a secondary outcome, was reduced by almost half (30.1% vs. 57.6%; \( P < .0001 \)).

At admission, there was no significant difference between those receiving a pulmonologist consult and those who did not. The average \( O_2 \) saturation was lower in the group seen by a pulmonologist (93% vs. 95.4%; \( P < .0001 \)), but the most striking difference was the lower readmission rate, which remained significant after controlling for severity and for pulmonary function.

“When we stratified patients for baseline severity, the advantage of a pulmonologist consult was even greater for those with the most severe disease,” Dr. Hekmat-Joo said. Among those with the greatest severity, the 90-day readmission rate was nearly three times greater in the absence of a pulmonologist consult (72% vs. 28%).

Although the comparison of outcomes for those receiving a pulmonologist consult vs. those who did not was adjusted for COPD severity, the potential for pulmonologist consults to be ordered for those patients who looked the sickest was acknowledged that this has to be demonstrated, with every COPD admission, Dr. Hekmat-Joo said. “I strongly believe that a prospective study is feasible and will answer the question in an unbiased manner if done properly,” he said in an interview. If a multicenter, well-controlled study was positive, it could change practice.

In the event of a study showing major clinical benefits, particularly a reduction in mortality, “I believe it is feasible to have a pulmonary consult to see every COPD exacerbation patient admitted to the hospital,” Dr. Hanania said. Dr. Hekmat-Joo reports no relevant financial relationships. Dr. Hanania has financial relationships. Dr. Hanania has financial relationships with AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Mylan, Novartis, Regeneron, Sanofi, and Sunovion.

The potential for benefit as seen in this retrospective study is a rational expectation and might be related to more appropriate therapy upon discharge as well as to earlier and more rigorous follow-up, according to Dr. Hanania. Although he cautioned that there is a meaningful risk of selection bias in a retrospective study, he thinks this study “is certainly probing an important issue.”

“Mortality from a hospitalized COPD exacerbation exceeds that of a myocardial infarction,” Dr. Hanania pointed out. Noting that all patients with an MI are evaluated by a cardiologist, he sees the logic of a pulmonologist consult – although he acknowledged that evidence is needed.

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Toward a healthy and sustainable critical care workforce in the COVID-19 era: A call for action

BY KELLY C. VRANAS, MD, AND MEETA PRASAD KERLIN, MD

The COVID-19 pandemic has caused unprecedented and unpredictable strain on health care systems worldwide, forcing rapid organizational modifications and innovations to ensure availability of critical care resources during acute surge events. Yet, while much attention has been paid to the availability of ICU beds and ventilators, COVID-19 has insidiously and significantly harmed the most precious critical care resource of all: the human beings who are the lifeblood of critical care delivery. We are now at a crucial moment in history to better understand the pandemic’s impact on our human resources and enact changes to reverse the damage that it has inflicted on our workforce.

To understand the impact of the pandemic on critical care clinicians, we must first acknowledge the context in which they work. ICUs, where critical care delivery predominantly occurs, increasingly utilize interprofessional staffing models in which clinicians from multiple disciplines – physicians, nurses, clinical pharmacists, respiratory therapists, and dieticians, among others – bring their unique expertise to team-based clinical decisions and care delivery. Such a multidisciplinary approach helps enable the provision of more comprehensive, higher-quality critical care. In this way, the interprofessional ICU care team is an embodiment of the notion that the “whole” is more than just the sum of its parts. Therefore, we must consider the impact of the pandemic on interprofessional critical care clinicians as the team that they are.


Finally, it has contributed to a workforce crisis: nearly 300,000 health care workers have left the US health care sector since the beginning of the pandemic, and approximately two-thirds of acute and critical care nurses have considered doing so (Wong E. "Why Healthcare Workers Are Quitting in Droves“ https://tinyurl.com/yaj5sd65. The Atlantic. Accessed November 7, 2022). Such a "brain drain" of clinicians – whose expertise cannot be easily replicated or replaced – represents a staffing crisis that threatens our ability to provide high-quality, safe care for the foreseeable future.

To combat burnout, it is first necessary to identify the mechanisms by which the pandemic has induced harm. Early during the pandemic, critical care clinicians feared for their own safety with little information of how the virus was spread. At a time when the world was under lockdown, vaccines were not yet available, and hospitals were overwhelmed with surges of critically ill patients, clinicians struggled like the rest of the world to meet their own basic needs such as child care, grocery shopping, and time with family. They experienced distress from high volumes of patients with extreme mortality rates, helplessness due to lack of treatment options, and moral injury over restrictive visitation policies (Vranas KC, et al. Chest. 2022;162[2]:331-345; Vranas KC, et al. Chest. 2021;160[5]:1714-1728). Over time, critical care clinicians have no doubt experienced further exhaustion related to the duration of the pandemic, often without adequate time to recover and process the trauma they have experienced. More recently, a new source of distress for clinicians has emerged from variability in vaccine uptake among the public. Clinicians have experienced compassion fatigue and even moral outrage toward those who chose not to receive a vaccine that is highly effective at preventing severe illness. They also suffered from ethical conflicts over how to treat unvaccinated patients and whether they should be given equal priority and access to limited therapies (Shaw D. Bioethics. 2022;36[8]:883-890).

Furthermore, the pandemic has damaged the relationship between clinicians and their institutions. Early in the pandemic, the widespread shortages of personal protective equipment harmed trust among clinicians due to their perception that their safety was not prioritized. Hospitals have also struggled with having to make rapid decisions on how to equitably allocate fixed resources in response to unanticipated and unpredictable demands, while also maintaining financial solvency. In some cases, these challenging policy decisions (eg, whether to continue elective procedures during acute surge events) lacked transparency and input from the team at the frontlines of patient care. As a result, clinicians have felt undervalued and without a voice in decisions that directly impact both the care they can provide their patients and their own well-being.

It is incumbent upon us now to take steps to repair the damage inflicted on our critical care workforce by the pandemic. To this end, there have been calls for the urgent implementation of strategies to mitigate the psychological burden experienced by critical care clinicians. However, many of these focus on interventions to increase coping strategies and resilience among individual clinicians. While programs such as mindfulness apps and resilience training are valuable, they are not sufficient. The very nature of these solutions implies that the solution (and therefore, the problem) of burnout lies in the individual clinician. Yet, as described above, many of the mechanisms of harm to clinicians’ well-being are systems-level issues that will necessarily require systems-level solutions.

Therefore, we propose a comprehensive, layered approach to begin to reverse the damage inflicted by the pandemic on critical care clinicians’ well-being, with solutions organized by ecological levels of individual clinicians, departments, institutions, and society. With this approach, we hope to address specific aspects of our critical care delivery system that, taken together, will fortify the well-being of our critical care workforce as a whole. We offer suggestions below that are both informed by existing evidence, as well as our own opinions as intensivists and researchers.

At the level of the individual clinician:

- Proactively provide access to mental health resources. Clinicians have limited time or energy to navigate mental health and support services and find it helpful when others proactively reach out to them.
- Provide opportunities for clinicians to experience community and support among peers. Clinicians find benefit in town halls, debrief sessions, and peer support groups, particularly during times of acute strain.

At the level of the department:

- Allow more flexibility in work schedules. Even prior to the pandemic, the lack of scheduling flexibility and the number of consecutive days worked had been identified as key contributors to burnout; these have been exacerbated during times of caseload surges, when clinicians have been asked or even required to increase their hours and work extra shifts.
• Promote a culture of psychological safety in which clinicians feel empowered to say “I cannot work” for whatever reason. This will require the establishment of formalized backup systems that easily accommodate call-outs without relying on individual clinicians to find their own coverage.

At the level of the health care system:
• Prioritize transparency, and bring administrators and clinicians together for policy decisions. Break down silos between the frontline workers involved in direct patient care and hospital executives, both to inform those decisions and demonstrate the value of clinicians’ perspectives.

• Compensate clinicians for extra work. Consider hazard pay or ensure extra time off for extra time worked.

• Make it “easier” for clinicians to do their jobs by helping them meet their basic needs. Create schedules with designated breaks during shifts. Provide adequate office space and call rooms. Facilitate access to childcare. Provide parking.

• Minimize moral injury: Develop protocols for scarce resource allocation that exclude the treatment team from making decisions about allocation of scarce resources. Avoid visitor restrictions given the harm these policies inflict on patients, families, and members of the care team.

At the level of society:
• Study mechanisms to improve communication about public health with the public. Both science and communication are essential to promoting and protecting public health; more research is needed to improve the way scientific knowledge and evidence-based recommendations are communicated to the public.

In conclusion, the COVID-19 pandemic has forever changed our critical care workforce and the way we deliver care. The time is now to act on the lessons learned from the COVID-19 pandemic through implementation of systems-level solutions to combat burnout and ensure both the health and sustainability of our critical care workforce for the season ahead.

Dr. Vranas is with the Center to Improve Veteran Involvement in Care, VA Portland Health Care System, the Division of Pulmonary and Critical Care, Oregon Health & Science University; Portland, OR; and the Palliative and Advanced Illness Research (PAIR) Center, and Division of Pulmonary, Allergy and Critical Care, Perelman School of Medicine, University of Pennsylvania; Philadelphia, PA.

Dr. Kerlin is with the Palliative and Advanced Illness Research (PAIR) Center, University of Pennsylvania; Philadelphia, PA.

This month in the journal CHEST®

Editor’s picks

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


Inhaled Nitric Oxide vs Epoprostenol During Acute Respiratory Failure: An Observational Target Trial Emulation. By Nicholas A. Bosch, MD, et al.

Effectiveness of a Long-term Home-Based Exercise Training Program in Patients With COPD After Pulmonary Rehabilitation: A Multicenter Randomized Controlled Trial. By Anja Frei, PhD, et al.

A Regional Command Center for Pandemic Surge. By Youcef Azeili, MD, PhD, et al.


COVID-19: Lessons Learned, Lessons Unlearned, Lessons for the Future

By Steven M. Hollenberg, MD, et al.

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Drug-Drug Interactions in the Management of Patients With Pulmonary Arterial Hypertension

By Sheryl Wu, PharmD, et al.

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Dr. Kerlin is with the Palliative and Advanced Illness Research (PAIR) Center, University of Pennsylvania; Philadelphia, PA.
Scenes from CHEST 2022

After several long years of connecting via computer screens, the pulmonary, critical care, and sleep medicine community reunited in person Oct. 16-19 in Nashville for CHEST 2022. Attendees were welcomed back to a jam-packed schedule of more than 300 sessions full of the latest research and practice-changing updates, hands-on education mixed with entertainment, and opportunities to connect and collaborate.

CHEST 2022 brought back popular activities like the CHEST Challenge Championship and live gaming, and offered more than a few new options – including a rocking Opening Reception at the Wildhorse Saloon and opportunities for attendees to raise their voices on advocacy issues important to them. And that’s just to name a few of the exciting elements that made this year’s annual meeting a success.


Attendees at the Women & Pulmonary Luncheon hear career development advice from guest speaker Janet Bickel.

Annual meeting attendees show their CHEST pride with buttons and this year’s free souvenir T-shirt.

Keynote speaker Neil Pasricha offers advice for practicing “The Art of Happiness” at the Opening Session.

Opening Reception attendees brush up on their line-dancing skills at the Wildhorse Saloon.

Recipients of the prestigious Fellow of the American College of Chest Physicians designation are honored at the Opening Session.

Audience members at the CHEST Challenge Championship cheer on this year’s competitors.
Since its inception in 1996, the CHEST Foundation has served patients and clinicians alike by supporting initiatives to educate, empower, and improve, but this may have been one of its most exciting and impactful years yet. As 2022 draws to a close, look back at the progress made over the past 12 months and the initiatives that will help the Foundation continue to support clinicians and patients in 2023.

**Collaboration and communication key in 2022**

2022 saw the launch of two new initiatives that will be integral to improving patient care in the years to come: ‘The First 5 Minutes™’ and Bridging Specialties™: Timely Diagnosis for ILD Patients.

A collaborative partnership between CHEST and Three Lakes Foundation, Bridging Specialties Plus, a newly launched ILD Clinical Toolkit brings together pulmonologists and primary care physicians to define a clearer clinician-guided approach to diagnosis for ILDs like pulmonary fibrosis (PF).

A Steering Committee of multi-disciplinary clinicians – including pulmonologists, primary care physicians, and a nurse practitioner – have led the development of important resources including a white paper highlighting the most recent data into delays in diagnosis.

Plus, a newly launched ILD Clinical Toolkit offers the following and more:

- An early detection learning module offering information about reasons for delayed ILD diagnosis, symptoms to watch and listen for (like crackles on auscultation), suggested patient workups, and recommendations on proactive steps to take, including when to refer to a pulmonologist;
- A decision-making tool offering interactive simulated patient visits; and
- Radiologic imaging videos covering key patterns, common CT scan appearances and imaging features that can help in diagnosis of ILDs.

Clinicians can access the toolkit at bit.ly/Bridging-Specialties.

**The First 5 Minutes**

The First 5 Minutes initiative, developed in response to themes identified during the Foundation’s Listening Tour in 2020, kicked off in Bexar County, TX, in June with an in-person pilot training program at the University of Texas Health Science Center.

There, relationship-centered communication trainers from the Academy of Communication Healthcare led 18 clinicians through interactive activities on empathetic listening and trust-building communication skills.

Attendees at CHEST 2022 had the opportunity to participate in a similar interactive session on Monday, October 17, where they practiced empathetic listening skills with fellow attendees and learned how establishing trust with patients in the first 5 minutes of interactions can lead to more efficient communication and improve patient adherence. Learn more at bit.ly/First-5-Minutes.

CHEST gratefully acknowledges the following founding supporters of the First 5 Minutes™: Amgen, AstraZeneca, Bexar County, Novartis, Regeneron, Sanofi, and VIATRIS.

**Making medicine a more inclusive practice**

In February 2022, the American College of Chest Physicians (CHEST), the American Thoracic Society (ATS), and the American Lung Association announced a partnership with the prestigious Harold Amos Medical Faculty Development Program (AMFDP), a Robert Wood Johnson Foundation initiative, to sponsor a scholar in pulmonary and critical care medicine.

The recipient of that grant, George Alba, MD, Instructor of Medicine at Harvard Medical School and Bexar County, TX, in June with an in-person pilot training program at the University of Texas Health Science Center.

In February 2022, the American College of Chest Physicians (CHEST), the American Thoracic Society (ATS), and the American Lung Association announced a partnership with the prestigious Harold Amos Medical Faculty Development Program (AMFDP), a Robert Wood Johnson Foundation initiative, to sponsor a scholar in pulmonary and critical care medicine. The recipient of that grant, George Alba, MD, Instructor of Medicine at Harvard Medical School and Pulmonary and Critical Care Physician at Massachusetts General, was announced earlier this year. Through his AMFDP award project, “Pulmonary Endothelial NEDD9 and Acute Lung Injury,” Dr. Alba seeks to advance NEDD9 antagonism as a potential therapeutic target in acute respiratory distress syndrome (ARDS).

“Growing up, I saw through my father’s example how education unlocks opportunities. Our community came together to help him on this path. Now a retired doctor of osteopathy in neonatology, it inspired me to pursue a career in medicine,” said Dr. Alba. “This award comes at a critical time in my junior faculty career: it allows me to continue pursuing my research in a meaningful way while also gaining new skills that will be critical for my ongoing career development.”

Visit bit.ly/3X4VphB to learn more about the AMFDP initiative and Dr. Alba.

**Fun and fellowship – for a good cause**

In addition, to all of this, the CHEST Foundation continued to host engaging events throughout the year to encourage connection, raise awareness, and fundraise for important initiatives.

This included the annual Belmont Stakes Dinner and Auction on June 11 in New York City. The fun-filled

**Twenty-five years of life-changing grants**

In addition to all of this, the CHEST Foundation provides financial grants to advance medicine and support to those in need. More than 12 million dollars later, the CHEST Foundation is proud to bolster the field of medicine and enhance patient care through this support. Learn more about the impact of grants from recent recipients via the QR code here and in the September issue of CHEST Physician.
Race and spirometry

BY NICHOLAS E. GHIONNI, DO, AND CHRISTIAN J. WOODS, MD, FCCP

The European Respiratory Society (ERS) and American Thoracic Society (ATS) just published an update to their guidelines on lung function interpretation (Stanojevic S, et al. Eur Respir J. 2022; 60:2101499). As with any update, the document builds on past work and integrates new advances the field has seen since 2005.

The current iteration comes at a time when academics, clinicians, and epidemiologists are re-analyzing what we think we know about the complex ways race and ethnicity intersect with the practice of medicine. Several experts on lung function testing, many if not most of whom are authors on the ERS/ATS guideline, have written letters or published reviews commenting on the way accounting for race or ethnicity affects lung function interpretation.

Race/ethnicity and lung function was also the topic of an excellent session at the recent CHEST 2022 Annual Meeting in Nashville, Tennessee. Here, we’ll provide a brief review and direct the reader to relevant sources for a more detailed analysis.

Spirometry is an integral part of the diagnosis and management of a wide range of pulmonary conditions. Dr. Aaron Baugh from the University of California San Francisco (UCSF) lectured on the spirometer’s history at CHEST 2022 and detailed its interactions with race over the past 2 centuries. Other authors have chronicled this history, as well (Braun L, et al. Can J Respir Ther. 2015;51[4]:99-101). The short version is that since the British surgeon John Hutchinson created the first spirometer in 1846, race has been a part of the discussion of lung function interpretation.

In 2022, we know far more about the factors that determine lung function than we did in the 19th century. Age, height, and sex assigned at birth all explain a high percentage of the variability seen in FEV1 and FVC. When modeled, race also explains a portion of the variability, and the NHANES III investigators found its inclusion in regression equations, along with age, height, and sex, improved their precision. Case closed, right? Modern medicine is defined by phenotyping, precision, and individualized care, so why shouldn’t race be a part of lung function interpretation?

Well, it’s complicated. With the increasing recognition of health disparities across racial groups the way race is incorporated in medical practice is understandably being scrutinized. As clinicians and academics, we must analyze the root cause of differences in health outcomes between racial groups.

Publications on pulse oximetry (Gottlieb ER, et al. JAMA Intern Med. 2022; 182:849-858) and glomerular filtration rate (Williams WW, et al. N Engl J Med. 2021;385:1804-1806) have revealed some of the ways our use of instruments and equations may exacerbate or perpetuate current disparities. Even small differences in a measure like pulse oximetry could have a profound impact on clinical decisions at the individual and population levels.

The 2022 ERS/ATS lung function interpretation guidelines have abandoned the use of NHANES III as a reference set. They now recommend the equations developed by the Global Lung Initiative (GLI) for referencing to normal for spirometry, diffusion capacity, and lung volumes. For spirometry the GLI was able to integrate data from countries around the world. This allowed ethnicity to be included in their regression equations and, similar to NHANES III, they found ethnicity improved the precision of their equations. They also published an equation that did not account for country of origin that could be applied to individuals of any race/ethnicity (Quanjer PH, et al. Eur Respir J. 2014;43:505-512). This allowed for applying the GLI equations to external data sets with or without ethnicity included as a co-variante.

Given well-established discrepancies in spirometry, it should come as no surprise that applying the race/ethnicity-neutral GLI equations to non-White populations increases the percentage of patients with pulmonary defects (Moffett AT, et al. Am J Respir Crit Care Med. 2021; A1030). Other data suggest that elimination of race/ethnicity as a co-variante improves the association between percent predicted lung function and important outcomes like mortality (McCormack MC, et al. Am J Respir Crit Care Med. 2022;205:723-724). The first analysis implies that by adjusting for race/ethnicity we may be missing abnormalities, and the second suggests accuracy for outcomes is lost. So case closed, right? Let’s abandon race/ethnicity as a co-variante for our spirometry reference equations.

Perhaps, but a few caveats are in order. It’s important to note that doing so would result in a dramatic increase in abnormal findings in otherwise healthy and asymptomatic non-White individuals. This could negatively affect eligibility for employment and military service.

As clinicians and academics, we must analyze the root cause of differences in health outcomes between racial groups.

As pulmonary medicine academics and researchers, we need to continue to study the impact integrating race/ethnicity has on precision, accuracy, and clinical outcomes. As pulmonary medicine clinicians, we need to be aware of the reference equations being used in our lab, understand how inclusion of race/ethnicity affects findings, and act accordingly, depending on the clinical situation.

Dr. Ghionni is a Pulmonary/Critical Care Fellow, and Dr. Woods is Program Director – PCCM Fellowship and Associate Program Director – IM Residency, Medstar Washington Hospital Center; Dr. Woods is Associate Professor of Medicine, Georgetown University School of Medicine, Washington, DC.
**CARDIOLOGY**

*Best anticoagulant for minimizing bleeding risk?*

**BY ROB HICKS, MBBS**

A commonly prescribed direct oral anticoagulant (DOAC) has the lowest risk of bleeding, say researchers. Used to prevent strokes in those with atrial fibrillation (Afib), DOACs have recently become more common than warfarin, the previous standard treatment, as they do not require as much follow-up monitoring – which was “particularly valuable” during the COVID-19 pandemic – and have “less risk” of side effects, highlighted the authors of a new study, published in Annals of Internal Medicine (2022 Nov 1. doi: 10.7326/M22-0511).

However, the authors explained that, although current guidelines recommend using DOACs over warfarin in patients with Afib, “head-to-head trial data do not exist to guide the choice of DOAC.” So, they set out to try and fill this evidence gap by doing a large-scale comparison between all DOACs – apixaban, dabigatran, edoxaban, and rivaroxaban – in routine clinical practice.

Wallis Lau, PhD, University College London, and co–lead author, said: “Direct oral anticoagulants have been prescribed with increasing frequency worldwide in recent years, but evidence comparing them directly has been limited.”

**One drug stood out**

For the multinational population-based cohort study the researchers compared the efficacy and risk of side effects for the four most common DOACs. They reviewed data – from five standardized electronic health care databases that covered 221 million people in the United Kingdom, France, Germany, and the United States – of 527,226 patients who had been newly diagnosed with Afib between 2010 and 2019, and who had received a new DOAC prescription. The study included 281,320 apixaban users, 61,008 dabigatran users, 12,722 edoxaban users, and 172,176 rivaroxaban users.

Database-specific hazard ratios of ischemic stroke or systemic embolism, intracranial hemorrhage, gastrointestinal bleeding, “said the authors, with a 19%-28% lower risk when compared directly with each of the other three DOACs.

“Apixaban stood out as having lower risk of gastrointestinal bleeding,” said the authors, with a 19%-28% lower risk when compared directly with each of the other three DOACs. The researchers found that all four drugs were comparable on outcomes for ischemic stroke, intracranial hemorrhage, and all-cause mortality.

However, they identified a difference in the risk of gastrointestinal bleeding, which they highlighted “is one of the most common and concerning side effects of DOACs.” “Apixaban stood out as having lower risk of gastrointestinal bleeding,” said the authors, with a 19%-28% lower risk when compared directly with each of the other three DOACs. Specifically, apixaban use was associated with lower risk for gastrointestinal bleeding than use of dabigatran (HR, 0.81; 95% confidence interval, 0.70-0.94), edoxaban (HR, 0.77; 95% CI, 0.66-0.91), or rivaroxaban (HR, 0.72; 95% CI, 0.66-0.79).

The researchers highlighted that their findings held true when looking at data only from those older than 80, and those with chronic kidney disease, two groups that are “often underrepresented” in clinical trials.

**Apixaban may be preferable**

The researchers concluded that, among patients with Afib, apixaban use was associated with lower risk for GI bleeding and had similar rates of stroke or embolism, intracranial hemorrhage and all-cause mortality, compared with dabigatran, edoxaban, and rivaroxaban.

“Our results indicate that apixaban may be preferable to other blood thinners because of the lower rate of gastrointestinal bleeding and similar rates of stroke, a finding that we hope will be supported by randomized controlled trials,” said Dr. Lau. However, he emphasized that, “as with all medications, potential risks and benefits can differ between people, so considering the full spectrum of outcomes and side effects will still be necessary for each individual patient.”

The authors reported that they had no conflicts.

**CORONAVIRUS**

*A huge deal*: Millions have long COVID, more expected

**BY SOLARINA HO**

MedPage News

Roughly 7% of all adult Americans may currently have had long COVID, with symptoms that have lasted 3 months or longer, according to the latest U.S. government survey done in October. More than a quarter say their condition is severe enough to significantly limit their day-to-day activities – yet the problem is only barely starting to get the attention of employers, the health care system, and policymakers.

With no cure or treatment in sight, long COVID is already burdening not only the health care system, but also the economy – and that burden will grow. Many experts worry about possible long-term ripple effects, from increased spending on medical care costs to lost wages due to not being able to work, as well as the policy implications that come with addressing these issues.

“At this point, anyone who’s looking at this seriously would say this is a huge deal,” said senior Brookings Institution fellow Katie Bach, the author of a study that analyzed long COVID’s impact on the labor market.

“Long COVID continues on following page

Jonathan Ludmir, MD, FCCP, comments: In my clinical practice, apixaban has consistently been my first choice of DOAC for patients with atrial fibrillation given its strong safety profile compared with warfarin. This retrospective review of the four main DOACs demonstrates a lower GI bleeding risk profile associated with apixaban. While this study seems to strengthen apixaban as a primary choice, it, of course needs to be balanced with cost as well as the fact that it is a b.i.d. medication, often a challenge for patients.
LONG COVID continued from previous page

been peer reviewed.
More than 7% of all those who answered said they had long COVID at the time of the survey, which the researchers said corresponded to approximately 18.5 million U.S. adults. The same study found that a quarter of those, or an estimated 4.7 million adults, said their daily activities were impacted “a lot.”

This can translate into pain not only for the patients, but for governments and employers, too.

In high-income countries around the world, government surveys and other studies are shedding light on the extent to which post-COVID-19 symptoms – commonly known as long COVID – are affecting populations. While results vary, they generally fall within similar ranges.

The World Health Organization estimates that between 10%-20% of those with COVID-19 go on to have an array of medium- to long-term post-COVID-19 symptoms that range from mild to debilitating.

Women appear almost twice as likely as men to get long COVID. Many patients have other medical conditions and disabilities that make them more vulnerable.

U.S. Government Accountability Office puts that estimate at 10% to 30%; one of the latest studies published at the end of October in The Journal of the American Medical Association found that 15% of U.S. adults who had tested positive for COVID-19 reported current long-COVID symptoms. Elsewhere, a study from the Netherlands published in The Lancet in August found that one in eight COVID-19 cases, or 12.7%, were likely to become long COVID.

“It’s very clear that the condition is devastating people’s lives and livelihoods,” wrote WHO Director-General Tedros Adhanom Ghebreyesus in an article for The Guardian newspaper in October.

“The world has already lost a significant number of the workforce to illness, death, fatigue, unplanned retirement due to an increase in long-term disability, which not only impacts the health system, but is a hit to the overarching economy ... the impact of long COVID for all countries is very serious and needs immediate and sustained action equivalent to its scale.”

Global snapshot:
Patients describe a spectrum of persistent issues, with extreme fatigue, brain fog or cognitive problems, and shortness of breath among the most common complaints. Many also have manageable symptoms that worsen significantly after even mild physical or mental exertion.

While many are older, a large number are also in their prime working age. The Census Bureau data show that people ages 40-49 are more likely than any other group to get long COVID, which has broader implications for labor markets and the global economy. Already, experts have estimated that long COVID is likely to cost the U.S. trillions of dollars and affect multiple industries.

“Whether they’re in the financial world, the medical system, lawyers, they’re telling me they’re sitting at
Nearly a third of respondents in the Census Bureau's Household Pulse Survey who said they have had COVID-19 reported symptoms that lasted 3 months or longer. People between the ages of 30 and 59 were the most affected, with about 32% reporting symptoms. Across the entire adult U.S. population, the survey found that 1 in 7 adults have had long COVID at some point during the pandemic, with about 1 in 18 saying it limited their activity to some degree, and 1 in 50 saying they have faced "a lot" of limits on their activities. Any way these numbers are dissected, long COVID has impacted a large swath of the population. Yet research into the causes and possible treatments of long COVID is just getting underway.

"The amount of energy and time devoted to it is way, way less than it should be, given how many people are likely affected," said David Cutler, PhD, professor of economics at Harvard University, Cambridge, Mass. "We're way, way underdoing it".
LONG COVID continued from previous page

And I think that’s really a terrible thing.”

Population surveys and studies from around the world show that long COVID lives up to its name, with people reporting serious symptoms for months on end. “In October, Statistics Canada and the Public Health Agency of Canada published early results from a questionnaire done between spring and summer 2022 that found just under 15% of adults who had a confirmed or suspected case of COVID-19 went on to have new or continuing symptoms 3 or more months later. Nearly half, or 47.3%, dealt with symptoms that lasted a year or more. More than one in five said their symptoms “often or always” limited their day-to-day activities, which included tasks such as preparing meals, doing errands, chores, and basic functions such as personal care.

Nearly three-quarters of workers or students said they missed an average of 20 days of work/school.
average of 20 days of work/school. “We haven’t yet been able to determine exactly when symptoms resolve,” said Rainu Kaushal, MD, the senior associate dean for clinical research at Weill Cornell Medicine in New York. She is co-leading a national study on long COVID in adults and children, funded by the National Institutes of Health.

RECOVER Initiative. “But there does seem to be, for many of the milder symptoms, resolution at about 4-6 weeks. There seems to be a second point of resolution around 6 months for certain symptoms, and then some symptoms do seem to be permanent, and those tend to be patients who have underlying conditions,” she said.

Experts recommend urgent policy changes to help people with long COVID. “The population needs to be prepared, that understanding long COVID is going to be a very long and difficult process,” said Alexander Charney, MD, PhD, associate professor and the lead principal investigator of the RECOVER adult cohort at Icahn School of Medicine at Mount Sinai in New York. He said the government can do a great deal, including setting up a network of connected clinics treating long COVID, standardizing best practices, and sharing information.

But the only known way to prevent long COVID is to prevent COVID-19 infections, experts say.
Repeat COVID infection doubles mortality risk

BY LISA O’MARY

Getting COVID-19 a second time doubles a person’s chance of dying and triples the likelihood of being hospitalized in the next 6 months, a new study found. Vaccination and booster status did not improve survival or hospitalization rates among people infected more than once.

“Reinfection with COVID-19 increases the risk of both acute outcomes and long COVID,” author Ziyad Al-Aly, MD, told Reuters. “This was evident in unvaccinated, vaccinated, and boosted people.”

The study was published in the journal Nature Medicine (2022 Nov 10. doi: 10.1038/s41591-022-02051-3).

Researchers analyzed U.S. Department of Veterans Affairs data, including 443,588 people with a first
infection of SARS-CoV-2, 40,947 people who were infected two or more times, and 5.3 million people who had not been infected and whose data served as a control.

“During the past few months, there’s been an air of invincibility among people who have had COVID-19 or their vaccinations and boosters, and especially among people who have had an infection and also received vaccines; some people started to [refer] to these individuals as having a sort of superimmunity to the virus,” Dr. Al-Aly said in a press release from Washington University in St. Louis. “Without ambiguity, our research showed that getting an infection a second, third, or fourth time contributes to additional health risks in the acute phase, meaning the first 30 days after infection, and in the months beyond, meaning the long COVID phase.”

Being infected with COVID-19 more than once also dramatically increased the risk of developing lung problems, heart conditions, or brain conditions. The heightened risks persisted for 6 months.

The Veterans Affairs population does not reflect the general population and they are generally older with more than normal health complications, said John Moore, PhD, a professor of microbiology and immunology at Weill Cornell Medicine, New York. Dr. Moore was not involved in the study.
PULMONOLOGY

CDC warns of early uptick in respiratory disease

BY LUCY HICKS
MDedge News

The Centers for Disease Control and Prevention is warning of an early surge in respiratory disease caused by multiple viruses. As influenza viruses, respiratory syncytial virus (RSV), SARS-CoV-2, and rhinovirus/enterovirus simultaneously circulate, the CDC cautioned that this confluence of viral activity could strain the health care system, according to a Nov. 4 CDC Health Network Alert advisory. “This early increase in disease incidence highlights the importance of optimizing respiratory virus prevention and treatment measures, including prompt vaccination and antiviral treatment,” the alert stated.

The CDC reports that RSV activity is increasing nationally, but in some areas – such as the South and Mountain West – cases appear to be trending downward.

Influenza cases continue to climb, with the virus activity being the highest in the South, Mid-Atlantic, and the south-central West Coast, according to CDC data. “In fact, we’re seeing the highest influenza hospitalization rates going back a decade,” said José Romero, MD, director of the CDC’s National Center for Immunization and Respiratory Diseases, during a press briefing. The agency estimates that there have been 1.6 million illnesses, 13,000 hospitalizations, and 730 deaths from the flu so far this season. As of Nov. 4, there have been two pediatric deaths.

COVID-19 cases appear to have plateaued in the past 3 weeks, Dr. Romero said; however, the CDC expects that there will be “high-level circulation of SARS-CoV-2 this fall and winter,” the health alert stated.

The CDC advised that all eligible individuals aged 6 months or older should be vaccinated against COVID-19 and influenza. To protect against RSV hospitalization, high-risk children should receive the monoclonal antibody drug palivizumab (Synagis). High-risk children include infants born before 29 weeks, children younger than age 2 with chronic lung disease or hemodynamically significant congenital heart disease, and children with suppressed immune systems or neuromuscular disorders.

Any patient with confirmed or suspected flu who is hospitalized, at higher risk for influenza complications, or who has a severe or progressive illness should be treated as early as possible with antivirals, such as oral oseltamivir (Tamiflu).

Patients with confirmed SARS-CoV-2 infection with increased risk of complications should also be treated with antivirals, such as nirmatrelvir and ritonavir (Paxlovid) or remdesivir (Veklury).

“There’s no doubt that we will face some challenges this winter,” said Dawn O’Connell, HHS Assistant Secretary for Preparedness and Response. “But it’s important to remember that RSV and flu are not new, and we have safe and effective vaccines for COVID-19 and the flu.”
Race and gender: Tailoring treatment for sleep

BY WALTER ALEXANDER  
MDedge News

FROM CHEST 2022  •  While trials of various interventions for obstructive sleep apnea and insomnia were effective, there was a strong suggestion that tailoring them according to the race/gender of the target populations strengthens engagement and improvements, according to a presentation by Dayna A. Johnson, PhD, MPH, at the annual meeting of the American College of Chest Physicians (CHEST).

Dr. Johnson, assistant professor at Emory University in Atlanta, stated that determinants of sleep disparities are multifactorial across the lifespan, from in utero to aging, but it was also important to focus on social determinants of poor sleep.

The complexity of factors, she said, calls for multilevel interventions beyond screening and treatment. Racism and discrimination come into play, especially with regard to anxiety and stress. In addition, neighborhood factors including safety, noise and light pollution, ventilation, and thermal comfort come into play, affecting sleep.

Dr. Johnson cited the example of parents who work multiple jobs to provide for their families: “Minimum wage is not a livable wage, and parents may not be available to ensure that children have consistent bedtime.” Interventions, she added, may have to be at the neighborhood level, including placing sleep specialists in the local neighborhood “where the need is.” Cleaning up a neighborhood reduces crime and overall health, while light shielding in public housing can lower light pollution.

Observing that African Americans have higher rates of obstructive sleep apnea, Dr. Johnson and colleagues designed a screening tool specifically for African Americans with five prediction models with increasing levels of factor measurements (from 4 to 10). The prediction accuracy across the models ascended in lockstep with the number of measures from 74.0% to 76.1%, with the simplest model including only age, body mass index, male sex, and snoring. The latter model added witnessed apneas, high depressive symptoms, two measures of waist and neck size, and sleepiness. Dr. Johnson pointed out that accuracy for well-established predictive models is notably lower: STOP-Bang score ranges from 56% to 66%; NoSAS ranges from 58% to 66%, and the HCHS prediction model accuracy is 70%. Dr. Johnson said that a Latino model they developed was more accurate than the traditional models, but not as accurate as their model for African Americans.

Turning to specific interventions, and underscoring higher levels of stress and anxiety among African American and Hispanic populations, Dr. Johnson cited MINDS (Mindfulness Intervention to Improve Sleep and Reduce Diabetes Risk Among a Diverse Sample in Atlanta), her study at Emory University of mindfulness meditation. Although prior studies have confirmed sleep benefits of mindfulness meditation, studies tailored for African American or Hispanic populations have been lacking.

The MINDS pilot study investigators enrolled 17 individuals (mostly women, with a mixture of racial and ethnic groups comprising Black, White, Asian, and Hispanic patients) with poor sleep quality as measured by the Pittsburgh Sleep Quality Index (PSQI). Most patients, Dr. Johnson said, were overweight. Because of COVID restrictions on clinic visits, the diabetes portion of the study was dropped. All participants received at least 3 days of instruction on mindfulness meditation, on dealing with stress and anxiety, and on optimum sleep health practices. While PSQI scores higher than 5 are considered to indicate poor sleep quality, the mean PSQI score at study outset in MINDS was 9.2, she stated.

After 30 days of the intervention, stress (on a perceived stress scale) was improved, as were PSQI scores and actigraphy measures of sleep duration, efficiency and wakefulness after sleep onset, Dr. Johnson reported. “Participants found the mindfulness app to be acceptable and appropriate, and to reduce time to falling asleep,” Dr. Johnson said.

Qualitative data gathered post intervention from four focus groups (two to six participants in each; 1-1.5 hours in length), revealed general acceptability of the MINDS app. It showed also that, among those with 50% or more adherence to the intervention, time to falling asleep was reduced, as were sleep awakenings at night. The most striking finding, Dr. Johnson said, was that individuals from among racial/ethnic minorities expressed appreciation of the diversity of the meditation instructors, and said that they preferred instruction from a person of their own race and sex. Findings would be even more striking with a larger sample size, Dr. Johnson speculated.

Citing TASHIE (Tailored Approach to Sleep Health Education), a further observational study on obstructive sleep apnea knowledge conducted at New York University, Dr. Johnson addressed the fact that current messages are not tailored to racial and/ or ethnic minorities with low-to-moderate symptom knowledge. Also, a 3-arm randomized clinical trial of Internet-delivered treatment (Sleep Healthy or SHUTI) with a version revised for Black women (SHUTI-BWHS) showed findings similar to those of other studies cited and suggested: “Tailoring may be necessary to increase uptake and sustainability and to improve sleep among racial/ethnic minorities.”

Dr. Johnson noted, in closing, that Black/African American individuals have higher risk for obstructive sleep apnea than that of their White counterparts and lower rates of screening for treatment.

Dr. Johnson’s research was funded by the National Institutes of Health; National Heart, Lung, and Blood Institute; Woodruff Health Sciences Center; Synergy Award; Rollins School of Public Health Dean’s Pilot and Innovation Award; and Georgia Center for Diabetes Translation Research Pilot and Feasibility award program. She reported no relevant conflicts.

Achieving diversity, equity, and inclusion: Invite everyone

BY WALTER ALEXANDER  
MDedge News

FROM CHEST 2022  •  What you really don’t want to do, if you want to improve diversity, equity, and inclusion (DEI) at your academic institution, is to recruit diverse people to your program and then have them come and feel not included, said Vivian Asare, MD. “That can work against you,” she stated in an oral presentation at the annual meeting of the American College of Chest Physicians (CHEST). Dr. Asare is assistant professor and vice chief of DEI for Yale Pulmonary, Critical Care, and Sleep Medicine, and associate medical director of Yale Centers for Sleep Medicine, New Haven, Conn.

In offering a path to successful DEI, Dr. Asare said: “The first step is to build a team and discuss your mission. Invite everyone to participate and include your leadership because they’re the ones who set the stage, ensure sustainability, and can be a liaison with faculty.” Then a DEI leader should be elected, she added.

The next and very important step is to survey the current institutional climate. “You need to tap into how people feel about DEI in your program.” That entails speaking directly with the stakeholders (faculty, staff, trainees) and identifying their specific concerns and what they think is lacking. Retreat and serious group discussions, and self-reflecting (asking “what initiatives would be good for us?”), and meeting one-on-one with individuals for a truly personalized approach are among potentially productive strategies for identifying the priorities and

DIVERSITY continued on following page
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DEI-related topics specific to a particular academic sleep program.

Dr. Asare offered up a sample DEI survey (Am J Obstet Gynecol. 2020 Nov;223(5):715.e1-715.e7), that made direct statements inviting the respondent to check off one of the following responses: Yes, No, Somewhat, Do not know, and Not applicable. Among sample statements:

- Our department is actively committed to issues of diversity, equity, and inclusion.
- Faculty searches in the department regularly attract a diverse pool of highly qualified candidates and/or attract a pool that represents the availability of MDs in this field.
- Our outreach and recruitment processes employ targeted practices for attracting diverse populations.

Dr. Asare said that a survey can be a simple approach for garnering information that can be useful for prioritizing DEI topics of concern and igniting interest in them. Engagement requires regular DEI committee meetings with minutes or a newsletter and with updates and topics brought to faculty meetings.

Key DEI areas of focus

Dr. Asare listed several key DEI areas: recruitment/retention, mentorship, scholarship, and inclusion and community engagement.

Under scholarship, for example, she cited topics for potential inclusion in a DEI curriculum: unconscious bias and anti-racism training, racism, discrimination and micro-aggression education (bystander/deescalation training), cultural competency and awareness, workplace civility, and health disparities.

"We all know that implicit bias in providers is a reality, unfortunately," Dr. Asare said. Being aware of these implicit biases is a start, but instruction on how to actively overcome them has to be provided. Tools may include perspective-taking, exploring common identity, and self-reflection.

To create an inclusive environment for all faculty, trainees, and staff may involve establishing a "welcome committee" for new faculty, perhaps with designating a "peer buddy," creating social events and other opportunities for all opinions and ideas to be heard and valued. Particularly for underserved and disadvantaged patient populations, patient advocacy and community service need to be fostered through support groups and provision of resources.

"The first step is to build a team and discuss your mission. Invite everyone to participate and include your leadership because they’re the ones who set the stage, ensure sustainability, and can be a liaison with faculty."

Summarizing, Dr. Asare reiterated several key elements for a successful DEI program: Build a team and discuss the mission, survey the current climate allowing open communication and dialogue, plan and engage, organize, and set areas of DEI focus. Find out where you are and where you want to be with respect to DEI, she concluded.

Dr. Asare declared that she had no conflicts of interest.

When you support CHEST’s philanthropic efforts, you join forces with other individuals committed to expanding their impact on lung disease and chest medicine. You will fund programs that change how people live, receive treatment, and enjoy an improved quality of life. 
Iron deficiency may protect against bacterial pneumonia

BY HEIDI SPLETE
MDedge News

FROM CHEST 2022 • Patients with iron deficiency anemia who developed bacterial pneumonia showed improved outcomes compared to those without iron deficiency anemia, based on data from more than 450,000 individuals in the National Inpatient Sample.

Iron deficiency is the most common nutritional deficiency worldwide, and can lead to anemia, but iron also has been identified as essential to the survival and growth of pathogenic organisms, Mubarak Yusuf, MD, said in a presentation at the annual meeting of the American College of Chest Physicians (CHEST).

However, the specific impact of iron deficiency anemia (IDA) on outcomes in patients hospitalized with acute bacterial infections has not been explored, said Dr. Yusuf, a third-year internal medicine resident at Lincoln Medical Center in New York.

In the study, Dr. Yusuf and colleagues reviewed data from the Nationwide Inpatient Sample (NIS) Database for 2016-2019. They identified 452,040 adults aged 18 or older with a primary diagnosis of bacterial pneumonia based on ICD-10 codes. Patients with a principal diagnosis other than bacterial pneumonia were excluded.

Of these, 5.5% had a secondary diagnosis of IDA. The mean age of the study population was similar between the IDA and non-IDA groups (68 years) and racial distribution was similar, with a White majority of approximately 77%. Slightly more patients in the IDA group were women (58.5% vs. 51.6%) and this difference was statistically significant ($P < .00001$). Most of the patients (94.6%) in the IDA group had at least three comorbidities, as did 78.1% of the non-IDA group.

The primary outcome was mortality, and the overall mortality in the study population was 2.89%. Although the mortality percentage was higher in the IDA group compared to the non-IDA group (3.25% vs. 2.87%), "when we adjusted for confounders, we noticed a decreased odds of mortality in the IDA group" with an adjusted odds ratio of 0.74 ($P = .001$), Dr. Yusuf said.

In addition, secondary outcomes of septic shock, acute respiratory failure, and cardiac arrest were lower in the IDA group in a regression analysis, with adjusted odds ratios of 0.71, 0.78, and 0.57, respectively.

The mean length of stay was 0.3 days higher in the IDA group, and the researchers found a nonsignificant increase in total hospital costs of $402.5 for IDA patients compared to those without IDA, said Dr. Yusuf.

The take-home message from the study is actually a question to the clinician, Dr. Yusuf said. "Should you consider a delay in treatment [of iron deficiency anemia] if the patient is not symptomatic?" he asked.

More research is needed to investigate the improved outcomes in the iron deficient population, but the large sample size supports an association that is worth exploring, he concluded.

"The findings of this research may suggest a protective effect of iron deficiency in acute bacterial pneumonia," Dr. Yusuf said in a press release accompanying the meeting presentation. "More research is needed to elucidate the improved outcomes found in this population, but this research may lead clinicians to consider a delay in treatment of nonsymptomatic iron deficiency in acute bacterial infection," he added.

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

David L. Bowton, MD, FCCP comments: The study by Yusef and colleagues is a fascinating analysis of the National Inpatient Sample examining the link between iron deficiency anemia (IDA) and outcomes from sepsis. Their data suggest that patients with IDA had a lower mortality than those without IDA. Iron is an essential nutrient for both bacteria and humans. The mechanisms by which this might occur remain speculative. Many bacteria require iron for their pathogenicity, while excess iron has been linked to oxidative injury and can trigger cell death.

Humans have evolved an extraordinary system for both storing and sequestering iron to enable its availability for essential processes while minimizing the potential adverse consequences of unnecessary iron availability.

Importantly, as with all studies involving administrative data, the criteria for the diagnosis of either IDA or sepsis are not known. A recent meta-analysis found an increased risk of infection in patients receiving intravenous iron (for a variety of indications), but without an apparent increase in mortality (Shah AA, et al. JAMA Network Open. 2021;4(11):e2133935).

The acute treatment of IDA with intravenous iron prior to major abdominal surgery did not reduce transfusion requirements nor have an impact on mortality (Richards T, et al. Lancet. 2020;396(10259):1353-1361). Collectively, I believe the available evidence suggests we should be cautious in the administration of iron to acutely ill patients.

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