

already present at low levels of cumulative cigarette smoking (the mean exposure was just 4 pack-years).

To truly reduce the burden of COPD, we will need to understand the complexities of its natural history, profile of risk factors, and phenotypic manifestations across the entire lifespan. The study by Çolak and colleagues is an important starting point to characterize COPD in the first 50 years of life. Although the importance of smoking cessation cannot be overemphasized, we argue that understanding the interplay among smoking, early life risk factors, and developmental processes in age spans that have been traditionally left out of COPD research will be key to fully advance prevention strategies for stages when the natural history of the disease can still be substantially modified. ■

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References

1. Lange P, Celli B, Agustí A, Boje Jensen G, Divo M, Faner R, *et al*. Lung-function trajectories leading to chronic obstructive pulmonary disease. *N Engl J Med* 2015;373:111–122.
2. Çolak Y, Afzal S, Nordestgaard BG, Vestbo J, Lange P. Prevalence, characteristics, and prognosis of early chronic obstructive pulmonary disease: the Copenhagen general population study. *Am J Respir Crit Care Med* 2020;201:671–680.
3. Martinez FJ, Han MK, Allinson JP, Barr RG, Boucher RC, Calverley PMA, *et al*. At the root: defining and halting progression of early chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2018;197:1540–1551.
4. Guerra S, Sherrill DL, Venker C, Ceccato CM, Halonen M, Martinez FD. Chronic bronchitis before age 50 years predicts incident airflow limitation and mortality risk. *Thorax* 2009;64:894–900.
5. Woodruff PG, Barr RG, Bleecker E, Christenson SA, Couper D, Curtis JL, *et al*.; SPIROMICS Research Group. Clinical significance of symptoms in smokers with preserved pulmonary function. *N Engl J Med* 2016; 374:1811–1821.
6. Martinez FD. Early-life origins of chronic obstructive pulmonary disease. *N Engl J Med* 2016;375:871–878.
7. McGeachie MJ, Yates KP, Zhou X, Guo F, Sternberg AL, Van Natta ML, *et al*. Patterns of growth and decline in lung function in persistent childhood asthma. *N Engl J Med* 2016;374:1842–1852.
8. Tai A, Tran H, Roberts M, Clarke N, Wilson J, Robertson CF. The association between childhood asthma and adult chronic obstructive pulmonary disease. *Thorax* 2014;69:805–810.
9. Guerra S, Stern DA, Zhou M, Sherrill DL, Wright AL, Morgan WJ, *et al*. Combined effects of parental and active smoking on early lung function deficits: a prospective study from birth to age 26 years. *Thorax* 2013;68:1021–1028.

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Understanding Patient- and Hospital-Level Factors Leading to Differences, and Disparities, in Critical Care

Racial and ethnic differences in care delivery and outcomes have been well documented in health care (1). Even among critically ill patients with clearly defined indications for care, multidimensional differences in care exist. Minority patients in North America more often receive aggressive end-of-life care, are less likely to discontinue mechanical ventilation or opt for palliative care services, and are more likely to receive care at the end of life in a hospital (2–4).

Indeed, differences exist across the temporal and causal spectra of critical illness. African Americans have higher rates of acute lung injury and cardiac arrest and nearly double the rate of sepsis in comparison to nonminorities (5–7). Although racial/ethnic variations in critical care are well established, one of the fundamental challenges has been pinpointing where and what *differences* are *disparities* that contribute to differential outcomes of care. Disparities in healthcare can be described as differences

in health status, health outcomes, and access to care between population groups (8–10). These differences can be closely intertwined with health inequity, which are often rooted in social injustice and result from the unjust distribution of economic, social, or environmental disadvantage of specific population groups (8, 10).

We applaud the work of Danziger and colleagues (pp. 681–687) in this issue of the *Journal*, which examined temporal trends of improvement in critical care outcomes in 208 U.S. hospitals (11). This study used a large and diverse dataset with patient-level data on demographics, admission diagnoses, and illness severity to adjust mortality rates among patients presenting to an ICU. Among approximately 1.1 million critically ill patients, almost one-quarter of African American and one-half of Hispanic patients received critical care in just one of 14 (7%) predominantly minority hospitals. On average, patients in minority-serving hospitals had somewhat unique characteristics—they tended to be younger and had higher severity of illness upon ICU admission. However, even accounting for many patient-based differences, the authors found that over the past decade, minority-serving hospitals had significantly less improvement in ICU mortality than nonminority hospitals and that African American patients appeared worst off, especially so when treated in minority hospitals. These findings

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highlight the compounding effect of both patient-level and hospital-level factors on critical care outcomes.

This paper provides evidence that the differential socioeconomic health experience among minority patients extends even to those with acute critical illness. Many African Americans and Hispanics are more likely to live close to and come to hospitals, often urban, that may be disproportionately challenged by funding models and the ability to recruit and retain healthcare professionals, and therefore unsurprisingly be characterized by markers of lower-quality health care and outcomes (12, 13). Indeed, previous studies have shown that the majority of racial/ethnic differences in critical care delivery and outcomes can be attributed to between-hospital differences rather than between-patient differences (14).

However, it is difficult in observational research to have sufficiently granular data to fully adjust for known confounding factors that may contribute to healthcare disparities for minority patients and minority-serving hospitals. Prior conceptual frameworks on racial/ethnic disparities in critical care have alluded to a range of hospital-, community-, and patient-level factors that occur along the continuum of acute critical illness, such as genetic predisposition and chronic conditions; socioeconomic and insurance status; health literacy; primary and preventative care provision; individual, cultural, or spiritual-based preferences; and family support structures, among many others (7, 15–19).

Although implementation of the Affordable Care Act has allowed uninsured minorities to increasingly access and use health services (20), in the “pay for performance” healthcare context, applying punitive financial measures might have the unintended effect of further exacerbating racial/ethnic disparities by reducing or shifting resources and limiting access to preventive, primary, secondary, and tertiary care services for patients of some hospitals (21). A shift toward alternative systems such as some form of more universal health coverage might improve access to health services and reduce national healthcare disparities, without increasing costs (22).

The main message of this study is both plausible and deserving of attention. Whether these findings reflect socioeconomic barriers to achieving equitable healthcare access, a more medically disadvantaged population, and/or differences in hospital care and resource use, cannot be entirely untangled. However, the findings are likely a reflection of all such factors. Initiatives aimed not only at individuals, but also at hospitals that disproportionately serve minority and African American populations, are potential foci to address disparities in health quality, delivery, and outcomes. This is a promising area for implementation science. In addition to continued attention on individuals’ prevention and primary care and insurance coverage models, we targeted initiatives and funding might also be directed toward specific hospitals, organizations, or care systems at most need, in a staggered or step-wedge manner, allowing estimation of impact on specific practices, and outcomes over time, across all targeted hospitals. Minority-serving hospitals face unique challenges, and the high minority usage of a small number of hospitals underscores the need for additional support for both patients and the locations where they receive care. ■

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References

- Schneider EC, Zaslavsky AM, Epstein AM. Racial disparities in the quality of care for enrollees in medicare managed care. *JAMA* 2002; 287:1288–1294.
- Maciejewski PK, Phelps AC, Kacel EL, Balboni TA, Balboni M, Wright AA, et al. Religious coping and behavioral disengagement: opposing influences on advance care planning and receipt of intensive care near death. *Psychooncology* 2012; 21:714–723.
- True G, Phipps EJ, Braitman LE, Harralson T, Harris D, Tester W. Treatment preferences and advance care planning at end of life: the role of ethnicity and spiritual coping in cancer patients. *Ann Behav Med* 2005;30:174–179.
- Phelps AC, Maciejewski PK, Nilsson M, Balboni TA, Wright AA, Paulk ME, et al. Religious coping and use of intensive life-prolonging care near death in patients with advanced cancer. *JAMA* 2009;301: 1140–1147.
- Dombrovskiy VY, Martin AA, Sunderram J, Paz HL. Occurrence and outcomes of sepsis: influence of race. *Crit Care Med* 2007;35: 763–768.
- Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. *N Engl J Med* 2003;348: 1546–1554.
- Smedley BD, Stith AY, Nelson AR, editors. Unequal treatment: confronting racial and ethnic disparities in health care. Washington, DC: National Academies Press; 2003 [accessed 2020 Jan 10]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK220358/>.
- Braveman P. What are health disparities and health equity? We need to be clear. *Public Health Rep* 2014;129:5–8.
- Hebert PL, Sisk JE, Howell EA. When does a difference become a disparity? Conceptualizing racial and ethnic disparities in health. *Health Aff (Millwood)* 2008;27:374–382.
- Boston Public Health Commission. Health disparities vs. health inequities [accessed 2020 Jan 11]. Available from: <https://www.bphc.org/whatwedo/health-equity-social-justice/what-is-health-equity/Pages/Health-Disparities-vs.-Health-Inequities.aspx>.
- Danziger J, Ángel Armengol de la Hoz M, Li W, Komorowski M, Octávio Deliberato R, Rush BNM, et al. Temporal trends in critical care outcomes in U.S. minority-serving hospitals. *Am J Respir Crit Care Med* 2020;201:681–687.
- Barnato AE, Lucas FL, Staiger D, Wennberg DE, Chandra A. Hospital-level racial disparities in acute myocardial infarction treatment and outcomes. *Med Care* 2005;43:308–319.
- Skinner J, Chandra A, Staiger D, Lee J, McClellan M. Mortality after acute myocardial infarction in hospitals that disproportionately treat black patients. *Circulation* 2005;112: 2634–2641.
- Barnato AE, Berhane Z, Weissfeld LA, Chang C-CH, Linde-Zwirble WT, Angus DC; Robert Wood Johnson Foundation ICU End-of-Life Peer Group. Racial variation in end-of-life intensive care use: a race or hospital effect? *Health Serv Res* 2006;41:2219–2237.

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15. Chin MH, Walters AE, Cook SC, Huang ES. Interventions to reduce racial and ethnic disparities in health care. *Med Care Res Rev* 2007; 64(Suppl):7S–28S.
16. Epstein AM, Ayanian JZ. Racial disparities in medical care. *N Engl J Med* 2001;344:1471–1473.
17. Soto GJ, Martin GS, Gong MN. Healthcare disparities in critical illness. *Crit Care Med* 2013;41:2784–2793.
18. Commonwealth Fund. Diverse communities, common concerns: assessing health care quality for minority Americans. 2002 [accessed 2020 Jan 11]. Available from: <https://www.commonwealthfund.org/publications/fund-reports/2002/mar/diverse-communities-common-concerns-assessing-health-care>.
19. Lillie-Blanton M, Hoffman C. The role of health insurance coverage in reducing racial/ethnic disparities in health care. *Health Aff (Millwood)* 2005;24:398–408.
20. McMorrow S, Long SK, Kenney GM, Anderson N. Uninsurance disparities have narrowed for black and Hispanic adults under the Affordable Care Act. *Health Aff (Millwood)* 2015;34: 1774–1778.
21. Casalino LP, Elster A, Eisenberg A, Lewis E, Montgomery J, Ramos D. Will pay-for-performance and quality reporting affect health care disparities? *Health Aff (Millwood)* 2007;26: w405–w414. [Published erratum appears in *Health Aff (Millwood)* 26: 1794.]
22. Himmelstein DU, Campbell T, Woolhandler S. Health care administrative costs in the United States and Canada, 2017. *Ann Intern Med* 2020;172:134–142.

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Early Aspergillosis in Cystic Fibrosis and Air Trapping: Guilt by Association?

In this issue of the *Journal*, Breuer and colleagues (pp. 688–696) report their findings of *Aspergillus* species in BAL specimens collected longitudinally from young children with cystic fibrosis (CF), examining association with a range of radiologic and clinical markers of pulmonary disease (1). This work is part of the AREST-CF (Australian Respiratory Early Surveillance Team for Cystic Fibrosis) program, which serves as an informative example of integrating research with distinct regional clinical practice patterns. CF clinical providers and researchers continue to debate how best to surveil and monitor both lung disease and airway microbiology in children. Publications from the AREST-CF program, including this one, are relevant to these discussions, as surveillance bronchoscopy and computed tomography (CT) chest imaging have been included in the care of hundreds of children over several years.

The authors report relatively high prevalence of airway infection with *Aspergillus* species (mostly *Aspergillus fumigatus*) in children with CF younger than 5 years. Multiple cross-sectional studies have similarly reported that *Aspergillus* is present in many of our patients, often at earlier ages than previously recognized (2, 3). The term “infection” in this context is more challenging and perhaps controversial, but the investigators demonstrate, through longitudinal data collection, that children with *Aspergillus* in the airway have greater abnormalities on CT imaging at the time of infection and in the years following (specifically, more air trapping). Increased air trapping and bronchiectasis have been seen in older populations with *A. fumigatus* infection, as well as allergic bronchopulmonary aspergillosis (4–6). Others have shown that older individuals with CF infected with *A. fumigatus* often have lower pulmonary function and greater rate of decline in FEV₁% predicted (pp) (7). Another Australasian research group recently reported similar findings to Breuer and colleagues,

identifying increased air trapping, but not bronchiectasis, on CT in 5-year-olds with CF who grew *Aspergillus* from BAL specimens (3).

CT abnormalities associated with *Aspergillus* culture positivity suggest a host response to infection, despite the lack of abnormally elevated serum IgE typical of sensitization. CF care providers will know the challenges in diagnosing allergic bronchopulmonary aspergillosis, and it appears that validated biomarkers or diagnostic criteria for *Aspergillus* bronchitis may be even more limited. A phenotyping classification distinguishing allergic from infective aspergillosis in adults with CF based on blood and sputum biomarkers was proposed, but recent follow-up studies suggest further development is necessary (8, 9). The present study did not find significant differences in traditional inflammatory markers in BAL specimens between individuals with *Aspergillus*, *Staphylococcus aureus*, *Haemophilus influenzae*, or *Pseudomonas aeruginosa*. It is interesting that a majority of BAL fluid samples did not grow any of these four microbes, and coinfection rates between *Aspergillus* and the three keystone bacterial pathogens reported were remarkably low. When *Aspergillus* was identified, one of these three bacteria was also cultured only 29% of the time. This is somewhat surprising but may strengthen the premise that *Aspergillus* itself is contributing to pulmonary injury and signs of disease in these children. It is likely that more aggressive antibiotic strategies contribute to lower prevalence of traditional bacterial pathogens (10). It is also possible that antibacterial treatment or inhaled medications themselves increase risk for *Aspergillus* airway infection, although indication bias must be understood.

Similar to bronchoscopy, CT imaging has not been universally applied as a surveillance tool in young (or older) children with CF. Because of this, the clinical importance of changes in CT scores can be difficult to understand. The authors report the median CT scores for the entire population at the end of study (5–6 yr old), providing context for the changes associated with *Aspergillus* infection (see Table E2 in the online supplement of Reference 1). The study population median percentage of lung scored abnormal was 0.06% for bronchiectasis, 2.93% for air trapping, and 3.92% for total disease score. In the most conservative model (see Table E3 of Reference 1), *Aspergillus*

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