



A Message from the President's Task Force

By Randall A. Oyer, MD

Advancing age is the biggest risk factor for cancer. According to the [National Cancer Institute](#), the median age at which cancer is diagnosed in the United States is 66 years. One-quarter of new cancer cases are diagnosed in people aged 65 to 74. An aging population is expanding this demographic trend. By the year 2030, [70 percent of all cancers are expected to occur in adults age 65 and older](#). Understanding how emerging cancer treatments affect older adults is critical for the delivery of high-quality, patient-centered care.

Yet older adults are consistently precluded from participating in clinical trials for promising new treatments. A 2019 analysis of more than 300 oncology randomized clinical trials found trial participants to be significantly younger than patients in the general population with the same tumor types. Authors of the report published in [JAMA Oncology](#) characterize the age disparity they identified as “pervasive and worsening.” In the authors’ analysis of 262,354 participants enrolled in 302 oncology clinical trials between 1994 and 2015, the median age of participants was 6.49 years younger than the median age of other patients with the same cancers.

Calling that gap a “substantial difference,” the authors added that it seems to be widening. Their analysis revealed the difference between the median age of trial participants and the population-based disease-site-specific median age to be growing at a rate of -0.19 years annually.

Although there are no lack of oncology clinical trials in which patients of all ages can enroll, [less than 2 percent](#) of patients diagnosed with cancer participate in clinical trials in the U.S. In fact, lack of accrual to cancer clinical trials can end studies early. One study found that 1 in 4 cancer clinical trials are stopped early, and 1 in 10 are ended due to poor accrual. In this era of COVID-19, the challenge to equitably resource clinical trial participation among patients most affected by cancer is even more difficult. COVID-19 is posing a significant challenge to the continuation of ongoing oncology clinical trials; in many cases, accrual for new trials has been slowed, paused, or halted altogether. Add to this the fact that older adults are experiencing more complications and poorer outcomes in relation to COVID-19, and the challenge before us can appear daunting.

Still, this pandemic has not stopped medical research altogether. It continues today, albeit often in modified form. Investigational approaches to treatment are considered standard of care for some cancers, and many of those trials continue.

Once COVID-19 is no longer a barrier to clinical study, we will emerge from this pandemic with a renewed zeal for research. With that zeal should be a commitment to enroll in clinical trials patients of all ages, races, ethnicities, and other demographics that reflect those most affected by cancer.

ACCC has worked to identify and address the various barriers to quality cancer care that older adults can experience. Through the [Multidisciplinary Approaches to Caring for Geriatric Patients with Cancer](#) project, ACCC describes best practices for serving this growing patient population in the form of research publications, case studies, surveys, webinars, and geriatric assessment tools. Currently, ACCC is creating a how-to guide for lower-resourced programs to perform key functions of geriatric assessment and better care for older adults with cancer.

Featured Clinical Research: The Impact of COVID-19 on Minority Communities

In June, the *New England Journal of Medicine* published a study by Eboni G. Price-Haywood, MD, MPH, and colleagues, [Hospitalization and Mortality among Black Patients and White Patients with Covid-19](#), that examined EHR patient data from Ochsner Health, an integrated healthcare delivery system, between March 1 and April 11, 2020. Ochsner Health's self-identified patient demographics are 31% black non-Hispanic and 65% white non-Hispanic. For the study, researchers combed the large health system's EHR data to identify patients who tested positive for SARS-CoV-2 and to analyze the rates of hospitalization and in-hospital death among COVID-19-positive patients. Of the cohort of 3,481 COVID-19-positive patients eligible for the study, 39% were hospitalized. Three-fourths (76.9%) of patients hospitalized were black. Of the 326 in-patient hospital deaths, 230 (70.6%) occurred in black patients. Study results report that black race, increasing age, a higher score on the Charlson Comorbidity Index, public insurance, residence in a low-income area, and obesity were associated with increased odds of hospitalization. However, when adjusted for sociodemographic and clinical characteristics on admission, black race was not found to be independently associated with higher mortality.

The study authors note that at the time of their report: "Although many reports on COVID-19 have highlighted age- and sex-related differences in health outcomes, racial and ethnic differences in outcomes have yet to be described in depth."

Unequal Impact

On June 11, the *New England Journal of Medicine*, released an accompanying audio interview editorial titled, "[The Impact of Covid-19 on Minority Communities](#)," with Editorial Board Member Michele K. Evans, MD, Senior Investigator and Deputy Scientific Director at the *National Institute on Aging*. Conducting the interview was Stephen Morrissey, PhD, Executive Managing Editor of

the journal. Participating in audio editorial were Editor-in-Chief Eric Rubin, MD, PhD, and Deputy Editor Lindsey Baden, MD.

Commenting on the study results, Dr. Evans, noted that although the patients' hospital cohorts were fairly similar (about 40% of both the black and non-Hispanic white COVID-19-positive patients were hospitalized), there was greater morbidity among the black patient cohort. The study findings showed that the patient's health at the time of admission determined the outcome, not the patient's race.

The disparities in hospitalizations and in-hospital deaths are underpinned by "...long-standing and persistent health disparities among the poor, among minority populations, in general, and particularly for African Americans," Dr. Michele Evans said. These disparities exist for most chronic diseases (e.g., cardiovascular disease, diabetes), for many types of cancer where African Americans have a greater incidence of mortality, and from the very start of life. African American women experience higher rates of maternal morbidity and mortality—independent of education or income.

"So, once these disparities begin at birth, if we don't have the economic supports, the health system supports, to work against what happens at birth, we wind up with these serious, persistent health disparities," said Dr. Evans. "This certainly ties into what Dr. Price-Haywood and colleagues found. When you look at their COVID-positive patients who were hospitalized, African American [patients] were younger than white patients, 60 compared to 69. Although this may not be statistically significant, it perhaps is a subtle sign of the accelerated aging phenotype or the weathering that's associated with health disparities and premature mortality among African Americans."

Challenges at Every Level

Many minority communities are also experiencing greater incidence of less severe Covid-19. Dr. Evans emphasized four main drivers of this disparity:

- **Employment status.** Essential worker positions and gig economy non-traditional and part-time jobs do not allow for work from home options. Many African Americans and other minority populations are employed as "essential workers" with jobs in public transportation, healthcare, food service, and other industries. "For example, about 50% or so of essential workers in food and agriculture are people of color...these workers, could not distance themselves or substantially reduce their exposure," Dr. Evans said.
- **Economic inequality.** Pay gaps and lack of economic opportunity substantially impacts the development of health disparities and co-morbidities. Education does not eradicate the problem, noted Dr. Evans. "College-educated African American and Hispanic men earn maybe 80 percent of what college-educated white men [earn], and when you look at African American and Hispanic females, the pay gap is even worse." With SARS-CoV-2, these factors put these underserved patient populations at a disadvantage. A further concern is the lack of knowledge about the long-term health effects of surviving COVID-19 infection.

- ***Residential segregation.*** There are pockets of segregation within cities and as a result ZIP codes can be “predictors of health, of school quality, of job access, of housing quality, of population density, city services, as well as the availability of high-quality food...residential segregation has substantial effect on healthcare outcomes and, in this case, on infectious disease,” Dr. Evans said.
- ***Healthcare access and quality.*** As noted above the gig economy jobs, as well as “essential worker” jobs in many industries, do not provide health insurance, resulting in unequal access to healthcare.

In terms of health disparities and inequalities being revealed by the current pandemic, the conversation turned to how much is due to long-standing issues of racism in medicine and what may be new in the context of the SAR-CoV-2 pandemic?

Dr. Rubin shared his perspective that the problem is two-fold: there is long-standing racism in the medical field and in how patients are treated, and there are racism issues in public health, “in our communities outside of our institutions.”

Dr. Evans concurred, expanding on Dr. Rubin’s comment. “I will say in medicine we have recognized health disparities. We have recognized the influence of social determinants of health,” she said. “But we have not fully marshalled our intellectual resources to prioritize this as we did with the war on cancer that Nixon funded or the quest for us to unravel the human genome led by Francis Collins. Racial discrimination as a social determinant of health causes real harm and causes real disease. There are numerous studies that link racism and discrimination to accelerated aging, to poor brain health, to chronic kidney disease, and sub-clinical atherosclerotic disease in African Americans. It’s not a political agenda. We need to be approaching it as an etiological factor in disease more commonly.”

In conclusion, Dr. Evans was asked for suggestions on what can be done immediately. Dr. Evans urged that healthcare professionals:

- *Focus our efforts on attaining health equity. Healthcare is a right not a privilege.*
- *Protect our patients from environmental toxic racism by working to understand and trying to mitigate its wide-ranging effects on health.*
- *Recognize the vulnerability of African American and minority students and trainees already in the biomedicine pipeline at the undergraduate, medical school, and post graduate levels. Listen to them. Acknowledge their experience.*
- *Reject being a bystander by becoming an upstander so that you can advocate for your colleagues and these trainees through the education process.*
- *Address under-representation of African Americans not just as practicing physicians, as academics in medical institutions, and also as biomedical researchers.*
- *Fix the funding gap between African American and white scientists by understanding and examining how to equitably ameliorate the gap that occurs at each stage of the funding and grant review process. NIH is actively taking steps to do this, but all funding agencies need to do this.*

- *Expand the research resources that are allocated to understanding and ameliorating health disparities and conditions that disproportionately affect African American and minority populations.*

Read the study by Dr. Price-Haywood and colleagues [here](#) and listen to the *New England Journal of Medicine* editorial audio interview with Dr. Michele Evans [here](#).

Toward More Inclusive Clinical Trial Eligibility Criteria

Despite the growing number of older adult cancer patients (aged 65 and above), this population has remained under-represented in cancer clinical trials. One way the U.S. Food and Drug Administration (FDA) is working to change the status quo is through guidance documents for industry.

Last month the FDA issued a finalized non-binding guidance on broader clinical trial eligibility. In the guidance on [Patients with Organ Dysfunction or Prior or Concurrent Malignancies](#), the agency recognizes that the overall U.S. population is living longer, living with more comorbid conditions, and that the population of old, and very old, cancer survivors is growing. The guidance states: *Unnecessarily restrictive eligibility criteria may slow patient accrual, limit patients' access to clinical trials, and, lead to trial results that do not fully represent treatment effects in the patient population that will ultimately use the drug.*

This final guidance includes discussion of potential inclusion in clinical trials of individuals living with such comorbidities as renal, cardiovascular, or hepatic metabolic dysfunction, as well as, individuals with concurrent or previous cancers. With respect to the latter patient population, the guidance recommends that: *Patients with prior malignancies of the same or different tumor type and patients with concurrent malignancies of the same or different tumor type... whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational drug should generally be eligible for enrollment in clinical trials.*

Read the [final guidance](#).

Still to Come

In March 2020, the agency released [draft guidance](#) that emphasizes why clinical trials need to be more inclusive of older adults. The agency points to concerns regarding differences in how a younger adult vs. an older adult respond to a drug and potential for variations in the toxicity profile "due to age-related physiologic changes." Drug pharmacokinetics or the patient's pharmacodynamic response to the drug may vary in older age. Older adults with comorbidities may be taking medications that could affect cancer drug efficacy and/or the type and frequency of side effects experienced.

The draft guidance on [Inclusion of Older Adults in Cancer Clinical Trials](#) was developed by the FDA's Oncology Center of Excellence (OCE) along with the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER). Older adults are defined in the document as aged 65 and above. The guidance makes non-binding

recommendations for “adequate representation” of this patient population to improve assessment of the benefit-risk profile of oncology drugs in older adults. In particular, the guidance stresses the importance of including adults older than age 75 in trials. Estimates are that the population of “oldest” adults, age 85 and above, will almost triple by 2060, from 6.4 million in 2016 to 19 million.¹

Among the recommendations included in the FDA’s draft guidance:

- Clinical trials should include study populations that reflect the intended population that may receive the therapy being evaluated.
- Sponsors should develop a strategy to enroll diverse populations, including different age groups, that align with the population the drug is intended to treat.
- Older adults should be enrolled in all phases of clinical trials as long as it is safe and ethical to do so.
- Trial sponsors should consider the age demographics of their target population in early development.
- Strategy for inclusion of older adults should be informed by any known information for older adults.

[Read the full draft guidance](#) which includes recommendations for industry on early clinical development, trial design, and post-market considerations. The comment period for the draft guidance closed on May 5.

Reference

1. US Census Bureau. *2017 National Population Projections Tables. Main Series. Table 2: Projected Age and Sex Composition of the population: 2017–2060*. Washington, DC: US Census Bureau, Population Division; 2018.

A Focus on Adults with Cancer

Each month, we’ll be asking an ACCC member to share their expertise in a specific area of research concentration. In this issue, we asked Ashley Rosko, MD, associate professor in the Department of Internal Medicine at *The Ohio State University (OSU)*, medical director of the oncogeriatric program at the *OSU Comprehensive Cancer Center – James*, and co-director of the *Cancer and Aging Resiliency Clinic at the James* to highlight opportunities to augment enrollment of older adults with cancer in cancer clinical trials.

Pivotal to improving outcomes for older adults with cancer is advancing science through clinical trial enrollment. Investigational cancer therapeutics are expected to enroll patients across the entire age spectrum to allow for a broad application and understanding across demographics.¹ In general, eligibility criteria are implemented to ensure safety of trial participants. However, overly restrictive eligibility criteria result in barriers to patient enrollment, resulting in lower patient accrual and decreased generalizability of trial results.²

As previously referenced, the FDA recently published [guidance statements](#) for cancer clinical trial eligibility criteria to safely include patients who have historically been excluded. This guidance document considers the safe enrollment of patients with HIV, chronic HBV or chronic HCV with appropriate immune function; inclusion of patients with organ dysfunction; inclusion of patients with concurrent or secondary malignancies; inclusion of individuals with brain metastases; and eliminating minimum age requirements for pediatric studies. These statements are intended to provide broader eligibility for clinical trial enrollment and a more generalizable and informed therapeutic intent.

Another effort important for clinical trial outcomes is understanding the patient experience throughout the clinical trial period. The FDA Oncology Center of Excellence (OCE) announced an initiative to pilot [Project Patient Voice](#). Project Patient Voice is a web-based platform to provide information for patients and caregivers about patient-reported symptoms from data collected from cancer clinical trials. The goal is to report patient-reported symptom data that has been collected but not previously publicly reported. This information can be used by the cancer clinical team to provide additional information about the patient experience of specific cancer therapeutics and ultimately shape treatment decisions.

A multi-pronged approach is required to ensure that clinical trials are developed for the patients most in need. Careful attention to inclusion/exclusion criteria and clinically meaningful endpoints (i.e., patient-reported outcomes) are only two methods to enhance trial enrollment for older adults. Implementation of these guidelines and development of protocols specific for vulnerable older adults requires institutions and cancer cooperative groups to work in concert to develop best practices. Importantly, the ACCC focus on health equity is laying the groundwork for a concerted effort to close the gap in cancer research for the community.

Reference

1. Singh H, Hurria A, Klepin HD. Progress Through Collaboration: An ASCO and U.S. Food and Drug Administration Workshop to Improve the Evidence Base for Treating Older Adults with Cancer. *Am Soc Clin Oncol Educ Book*. May 23, 2018;38:392-399.
Available at https://ascopubs.org/doi/10.1200/EDBK_201133.

The **ACCC Research Review** newsletter is developed as part of the 2020-21 ACCC President's Theme. Its goal is to help bring research opportunities into community practices/programs to ensure that all Americans may benefit equally from cancer research. For additional resources and to learn how your cancer center can become involved, please visit acc-cancer.org/president-20-21.

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