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Disparities in PET Imaging of Prostate Cancer at a Tertiary Academic Medical Center

TO THE EDITOR: We read with interest the article by Bucknor et al. titled, "Disparities in PET Imaging for Prostate Cancer at a Tertiary Academic Medical Center" (*1*). The authors compare enrollment data between 2 cohorts: one having standard-of-care (SOC) ^{18}F-fluciclovine PET and a second undergoing ^{68}Ga-prostate-specific membrane antigen (PSMA)–11 PET. As SOC, ^{18}F-fluciclovine PET is generally eligible for reimbursement by insurance whereas ^{68}Ga-PSMA-11 PET was offered under a Food and Drug Administration–reviewed investigational new drug protocol with cost-recovery mechanism.

More participants were reported in the investigational arm (1,502, 85.5%) than in the SOC arm (254, 14.5%) over the same period. The authors indicate that the proportion of African Americans who had SOC PET was 6.7%, as opposed to a mere 1.4% in the investigational arm. The percentages for Asians were 8.7% and 5.8%, respectively, and for Whites, 71.6% and 80%, respectively. The 2010 San Francisco Bay Area Census indicates a population distribution of 6.7% African Americans, 23.3% Asians, and 52.5% Whites. Although the proportion who had SOC PET was aligned with the geographic racial mix, for the investigational arm the African American inclusion was more than 4 times lower. Finding that African American patients had increased odds of receiving imaging with ^{18}F-fluciclovine versus ^{68}Ga-PSMA-11, compared with non-Hispanic White patients, the authors conclude that access to ^{68}Ga-PSMA-11 for African American patients was limited, compared with White patients.

The authors acknowledge the limitations of a single-site study. As a point of reference, our institution is located in the same geographic area (Northern California). We started a second program for PSMA PET imaging in May 2018 using 2-(3-{1-carboxy-5-[(6-^{18}F-fluoro-pyridine-3-carbonyl)-amino]-pentyl}-ureido)-pentanedioic acid (^{18}F-DCFPyL) at biochemical recurrence of prostate cancer (NCT03501940) (*2*), after completing a phase II study of ^{68}Ga-PSMA-11 (NCT02673151). In total, 187 participants have been enrolled to date in the investigational cohort, whereas 436 patients have undergone SOC ^{18}F-fluciclovine PET over the same period. The proportion of African Americans who had SOC PET was 4.4%, versus 4.8% in the investigational arm. The respective percentages were 13.1% and 8.6% for Asians and 68% and 79.7% for Whites.

How can 2 institutions be so geographically close yet have such a different experience in equitable access to care through a research trial? Part of the answer may be related to the need to include a more complete set of predictor variables. For example, the amount of the health-care expenditure for which the patient is held responsible, rather than merely the classification of insurance as "commercial," "government," or "unknown," may be more telling of a patient's ability to pay in an era of significant copayments and high deductibles (*3*). In addition, the authors, as well as other contributors to the literature (*4*), point out several other patient-specific factors that could be considered as predictors in future studies. However, referral to a tertiary- or quaternary-care center for imaging may have more to do with the behavior of the referring provider or the number of physicians involved in the care of the patient than with characteristics of the patients themselves (*5*).

The different results between our geographically close institutions may also be a direct result of inadvertent effects of trial design. The authors state, "Remarkably, despite the requirement for study participation and the possibility of self-pay, nearly six times as many patients in this study were imaged with ^{68}Ga-PSMA-11 compared to ^{18}F-fluciclovine," and go on to highlight potential disparities in access to imaging research trials for African-American patients. The Food and Drug Administration–approved cost-recovery mechanism used to pay for ^{68}Ga-PSMA-11 in the study allows institutions to charge private insurance (not Medicare) and individuals the direct cost of manufacturing the radiopharmaceutical, audited by an external certified public accountant. However, the cost-recovery mechanism does not govern the charges for technical and professional fees for a PET/CT examination. Bucknor et al. indicate a charge associated with cost recovery at their institution ranging between $900 and $1,400, depending on the number of syntheses performed in a year; however, although mentioned briefly, they do not detail the technical and professional fees billed to participants or insurance in their protocols. We expect these fees to be at least as much as cost recovery for the radiopharmaceutical dose, based on known Medicare charges.

At our institution, we applied for a research access program through the Prostate Cancer Foundation in 2017. On approval, ^{18}F-DCFPyL was provided at no cost and we waived the technical and professional fees for all participants. Therefore, the participants who have PSMA PET at our institution do not receive bills related to the radiopharmaceutical, imaging acquisition, or report.

Although very important to bring novel radiopharmaceuticals to the United States, cost-recovery trials may create unequal access when there are no mechanisms to provide the same opportunities for disadvantaged patient groups. As the authors themselves point out, "Through this mechanism, patients often would be financially liable for the direct cost of the radiotracer and possibly the cost of the technical component of the PET imaging, which could pose a significant barrier to low income groups." Barriers to care access can result from bias (perceived or unperceived), shortcomings of research recruitment strategies, or geographic availability of services. However, barriers can also be created by the threat of

financial burden; when one arm of a trial compels the patient to agree to responsibility for a bill of any amount whereas the other arm is SOC and fully covered by insurance, decisions of patients and their families can vary greatly depending on their perceived level of financial security and ability to take financial risk. These barriers can be just as harmful but are completely avoidable.

When the charges are not waived for those who cannot pay, the result may be denial of patient access to the superior examination, in this case PSMA PET (*6*). All clinical trials should provide equal access to all races and ethnic groups. Our institution's research access program still needs to improve access to match the regional racial composition, but billing for participation is not a factor.

Every man with prostate cancer who meets eligibility criteria deserves equal access to trials of PSMA PET regardless of how much he can afford to pay.

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Reply: Disparities in PET Imaging of Prostate Cancer at a Tertiary Academic Medical Center

REPLY: Iagaru and Franc note the key finding of our paper (*1*): that in patients with biochemical recurrence of prostate cancer, Black or African American patients had nearly 4 times lower odds of receiving PET imaging with ^{68}Ga-PSMA-11, as opposed to ^{18}F-fluciclovine, than did their non-Hispanic White counterparts. This held true even though we controlled for age, preferred language, neighborhood socioeconomic status, and health insurance, among other demographic factors.

Iagaru and Franc describe a "different experience in equitable access to care through a research trial" at their neighboring institution in Northern California. They point out that, in contrast to our study, a very slightly higher percentage of Black patients had access to PSMA PET (^{18}F-DCFPyL) (4.8%) than to ^{18}F-fluciclovine (4.4%) at their institution, and they go on to note differences in how their trial was conducted with regard to patient financial liability. However, they do not clearly address the fact that the additional data they report demonstrate similar concerning trends in equitable access to advanced imaging technologies.

The other side of the coin to decreased access for any one demographic group is often relatively increased access for a different group. Similar to our own institution, Iagaru and Franc found at their institution an 11.7% absolute increase in the percentage of White patients who received PSMA PET imaging: 79.7% compared with 68%. We reported a similar absolute increase of 8.4% at the University of California San Francisco: 80% compared with 71.6%. Although Iagaru and Franc do not report the results of further statistical analysis, their stated data suggest similar preferential access for non-Hispanic White patients to a novel advanced imaging technology. The difference appears to be that, whereas at our institution better access for non-Hispanic White patients was disproportionately associated with decreased access for Black patients, at their institution the burden of reduced access was distributed across a wider spectrum of different racial and ethnic minorities. Indeed, they report a 33% lower rate of use of PSMA PET for Asian American patients. At both institutions, access for persons of color to a rapidly emerging gold standard for PET imaging in prostate cancer was likely reduced.

How can two sets of investigators look at the same data and reach such different conclusions? Part of the answer may be related to the traditional roles of imaging departments, which tend to more often focus on how to provide the highest-quality imaging experience for the patients who make it through the doors and less time thinking about how and why different patients reach the doorstep. Radiology is often thought of as an intermediary step in health-care delivery, unlikely to contribute directly to differential patient outcomes. But it is critical to recognize that many of the most frustratingly persistent health disparities we face may result from the accruement of differential patient experiences across multiple aspects of a health system.

A commitment to health equity means working intentionally and systematically to apply our research toolkits to investigations of health-care delivery across all domains. There has never been a moment with a greater mandate to proactively identify and root out biases that reduce patient access to the best possible care. Let's not waste this moment.

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