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Johannes Czernin, MD
Editor in Chief, Journal of Nuclear Medicine
Los Angeles, CA, United States

Dear Professor Czernin,

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 two cohorts: one having standard of care (SOC) ^{18}F-Fluciclovine PET and a second undergoing ^{68}Ga-PSMA11 PET. As SOC, ^{18}F-Fluciclovine PET is generally eligible for reimbursement by insurance whereas ^{68}Ga-PSMA11 PET was offered under an FDA-reviewed investigational new drug protocol (IND) with cost recovery mechanism.

It is of note that more participants are reported in the investigational arm (1502, 85.5%) than the standard of care arm (254, 14.5%) over the same period of time. 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; 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. While the proportion who had SOC PET was aligned with the geographical racial mix, for the investigational arm the African American inclusion was >4 times lower. Finding that African American patients had increased odds of receiving imaging with ^{18}F-Fluciclovine versus ^{68}Ga-PSMA-11 compared to non-Hispanic White patients, the authors conclude that access to ^{68}Ga-PSMA-11 for African American patients was limited, compared to 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 ^{18}F-DCFPyL at biochemical recurrence of prostate cancer (NCT NCT03501940) (*2*), after completing a phase II study of ^{68}Ga-PSMA11 (NCT02673151). A total of 187 participants were enrolled to date in the investigational cohort, while 436 patients underwent SOC ^{18}F-Fluciclovine PET over the same period of time. The proportion of African Americans who had SOC PET was 4.4% vs. 4.8% in the investigational arm. The percentages for Asians were 13.1% and 8.6%, respectively; for Whites they were 68% and 79.7%.

How can two 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 healthcare 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/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 characteristics of the patient him/herself (*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 FDA-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, it does not govern the charges for technical and professional fees of a PET/CT examination. Bucknor et al. indicate a charge associated with cost recovery at their institution ranging between $900 and $1400, 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. Upon 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.

While very important to bring novel radiopharmaceuticals to the US, 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 while 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 can't 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/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.

Sincerely,

Andrei Iagaru, MD
Benjamin Franc, MD, MBA

References

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