

Improving Diversity in Clinical Trials: How Early-Stage Investigators Are Reaching Underserved Populations

MATTHEW GAVIDIA



REID

Sonya Reid, MD, MPH, assistant professor, Division of Hematology/Oncology, Vanderbilt-Ingram Cancer Center, Nashville, Tennessee.

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Recently, the Bristol Myers Squibb Foundation (BMSF), in partnership with National Medical Fellowships and the American Association for Cancer Research, announced plans to address these issues by training early-stage investigators from the fields of oncology, hematology, cardiology, and immunology in essential community engagement research methods.

Five oncologists selected as part of the inaugural 52-physician cohort of BMSF's Diversity in Clinical Trials Career Development Program spoke with *Evidence-Based Oncology*[™] on what they seek to learn, on unmet needs that they see in patient populations of their respective studies, and how they would like to address the long-standing issue of diversity in clinical trials.

Being "Intentional" About Improving Patient Diversity in Clinical Trials

In caring for patients with breast cancer, which is the leading cause of cancer-associated mortality among Black females in the United States, Sonya Reid, MD, MPH, assistant professor, Division of Hematology/Oncology, Vanderbilt-Ingram Cancer Center, Nashville, Tennessee, seeks to address key disparities in outcomes among minority and underserved populations.

Currently, Black women with breast cancer have 5- and 10-year mortality rates that are double the rates of White women. Factors such as screening rates, stage at diagnosis, tumor biology, and social determinants of health have all been noted to influence patient outcomes.³

"We know social determinants of health are key factors that we need to address to get to the root of what is causing a lot of these disparities in breast cancer survival...less than 3% of patients who are accrued within breast cancer clinical trials are Black," said Reid.

"Without improved racially diverse representation in these trials, oncology standards based primarily on non-Hispanic White patient data are at risk of not being generalizable. We see an underrepresentation of minority patients in prospective clinical trials as well as in genomic databases."

In 2020, only 2% to 9% of participants included in clinical trials that led to FDA approval of 4 new breast cancer treatments were Black, with Hispanics accounting for 0% to 9% participation in those same trials.⁴ Moreover, significantly fewer studies of African, Latin American, and Asian ancestral populations have been identified within the genomic databases that are used for precision medicine research, in comparison with European populations.⁵

"This just speaks to the work that needs to be done," said Reid. "We must be intentional about recruiting a diverse population in clinical trials to further understand the underpinnings of what's causing these differences in cancer outcomes."

Reid has been actively involved in breast cancer research in this country and, previously, in Jamaica, where she was raised and received her medical school training before moving to the United States. She expressed her enthusiasm about learning, through the BMSF program, how to not only execute, but also develop, clinical trials that are more community engaged, community focused, and patient focused. She is also excited about the opportunity to mentor and train medical students in community-based clinical research in the second year of the program.

Building trust within underserved communities to help ameliorate diversity issues in clinical trials will require careful attention,

Reid said. "We know that 80% of cancer patients are treated not in academic centers, but in the community," she explained. "I'm really looking forward to trying to understand the best practices as we develop clinical trials with that in mind from the beginning."

Reid's research primarily focuses on health disparities in breast cancer, with a particular interest in young-onset breast cancer and hereditary breast cancer. Specifically, she is investigating genomic differences that may be contributing to the racial survival disparity in breast cancer.

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—Sonya Reid, MD, MPH, assistant professor, Division of Hematology-Oncology, Vanderbilt-Ingram Cancer Center



SILVERA

Richard Silvera, MD, MPH, assistant professor, Infectious Disease, Icahn School of Medicine at Mount Sinai, New York City.

A Quest of Improve Outcomes Among Black Men With HIV and Cancer

In caring for patients with HIV and those at risk for HIV infection, Richard Silvera, MD, MPH, assistant professor, Infectious Disease, at Icahn School of Medicine at Mount Sinai, aims to improve medical outcomes for the Black community—particularly older Black men—by encouraging them to get tested for HIV as well as for anal cancer, a disease that is often overlooked in screening.

In the process of researching the connection between anal cancer and HIV, Silvera hopes to observe cells in an efficient, accessible way while educating and reaching out to the Black community.

Although Black individuals represent only 13% of the US population, they account for a significantly larger share of HIV diagnoses (43%), of people estimated to be living with HIV disease (42%), and deaths among people with HIV (44%) than any other racial group in the nation.⁶

For populations with HIV, particularly men of color who have sex with men (MSM), Silvera noted the substantial risk posed by human papillomavirus (HPV), the most common sexually transmitted disease worldwide, in leading to the development of anal cancer.

Research has shown that HIV increases the risk of HPV infection and the development of abnormal cells that cause anal cancer, namely high-grade anal intraepithelial neoplasia or high-grade squamous intraepithelial lesions. These lesions are much more likely to occur in MSM populations, older individuals, and those with compromised immune systems.⁷

"All those problems kind of interact with each other in a somewhat complicated way. We know that people of color are overrepresented among people with HIV. We know that HIV



RODRIGUEZ

Analiz Rodrigues, MD, PhD, director, Neurosurgical Oncology, University of Arkansas for Medical Services, Little Rock.

is a medical problem that people of color have to face, and that's due to structural inequities, history, and all sorts of other things," said Silvera.

While studying English in college, Silvera's interest in HIV was piqued during a course that covered literature on HIV and AIDS. He learned that HIV's impact was not only biological, but had political, economic, and social implications as well.

"I wanted to have research be a big component of what I did going forward, because research is kind of a way of taking individual people's stories and putting them together to affect whole groups of people," Silvera recalled.

Because anal cancer incidence is markedly higher among people with HIV than in the general population,⁸ and even more so among MSM populations and older people, Silvera seeks to prioritize the representation of these at-risk groups in clinical trials.

Moreover, Silvera said, he is looking forward to learning more about the structure of clinical trials and how to be a successful researcher through the BMSF program—skills that may not be easily honed by those without access to social or mentoring networks, he noted.

"As a gay Black man myself, I want to try to bring that perspective and that experience into this research, because there will be insights that you just cannot learn in a book," Silvera said. "I think you need this diverse perspective to have it all—aspects of both those who are experiencing this disease, as well as those who are trying to cure it or treat it."

Taking on Health Care Disparities in the Rural South

An Afro-Latina and the first physician in her family, Analiz Rodriguez, MD, PhD, director, Neurosurgical Oncology, University of Arkansas for Medical Services in Little Rock, has known since the third grade that she wanted to be a neurosurgeon and help minority and marginalized communities.

These pursuits led her to the state of Arkansas, which ranks sixth-worst in the nation for cancer mortality rate.⁹ As a neurosurgeon-scientist specializing in brain tumors, Rodriguez strives to bring novel therapies and clinical trials to the rural South.

"I think that I chose to practice in the rural South for many reasons—one key reason is that I feel the health care disparities are just more apparent. I also very much enjoy working with rural patients," said Rodriguez.

"My goal in coming to Arkansas was to provide cutting-edge research and treatments for patients through clinical trials," she explained. "I fundamentally do not believe that it's fair that you should die from cancer earlier than other people based on your zip code, the color of your skin, or what language you speak."

Her academic center is the only one of its kind in Arkansas, so access to higher-level cancer care—such as immunotherapy—remains unavailable to many of the state's residents.¹⁰ In particular, high rates of poverty and lack of access to health care have been reported in the mostly rural Eastern part of the state, known as the Arkansas Delta, which includes 4 of the 5 Arkansas counties with the highest rate of cancer. One of these, Monroe County, has the highest rate of cancer deaths in the state, at 249.5 deaths per 100,000.¹⁰

Rodriguez said she plans to leverage the lessons gained from the BMSF program in building clinical trials to improve access for certain communities that have been underserved historically, particularly Black Americans; they make up a higher share of the population in Southern states than in many other locations in the country.¹¹

She's also interested in investigating how lifestyle may impact the immune microenvironment and patient response to certain therapies.

"Our country is very much segregated. We have a lot of places where there are food deserts. And if you live in a certain area, and you don't have access to certain types of food, because of

your environment, you may have a different outcome in regard to your cancer.

Rodriguez said studying the same types of people—those who are more affluent, while leaving out minorities and those from rural areas—will mean that some questions will go unstudied and unanswered.

"We have a lot of technology, a lot of resources. It just doesn't make sense that we're still having this conversation in 2022, but let's get rid of this problem and move forward."

In her clinical research, Rodriguez hopes to observe cancer models and learn how the disease affects a wide range of populations by both race and location.

A Pediatric Hematologist/Oncologist Hopes to Build Trust in Her Community

Raised by Mexican immigrant parents in East Los Angeles, Sonia Morales, MD, pediatric hematologist-oncologist, Children's Hospital of Orange County, California, learned early, from her own health experiences, about the physical and mental challenges pediatric patients face in managing lifelong diseases.

Diagnosed with optic glioma as a child, the trajectory of her patient journey fueled Morales' interest in medicine and led to a career in pediatrics specializing in hematology-oncology.

For the more than 500,000 pediatric cancer survivors in the United States today, Morales noted that the transition from a children's hospital to adult care can complicate adherence to many long-term follow-up needs. These include, to start, screening for secondary malignancies or osteopenia, mental health counseling for developmental concerns, and addressing posttraumatic stress disorder—and this is all especially true for underserved groups like Hispanic and other minority survivors.

"Minority populations are already at risk for poor health outcomes due to socioeconomic inequities and health disparities. A lot of our patients are not in affluent areas or areas where there are academic centers, so there's decreased availability of clinical trials," said Morales.

"The overall survival in Hispanic children for some reason—potentially due to genetics, and we've heard about zip codes affecting your health as well—[is not as good] as in their White counterparts."

Research results have indicated that, compared with White children, Black children are between 38% and 95% more likely to die of several types of cancer, and Hispanic children were between 31% and 65% more likely to die.¹² Socioeconomic status was shown to significantly mediate the racial/ethnic disparities in surviving childhood cancers, including acute lymphoblastic leukemia, acute myeloid leukemia, neuroblastoma, and non-Hodgkin lymphoma.

"In order to work toward equity, we need to start drawing more information from our disadvantaged communities, those that we're not normally representing in our research samples," emphasized Morales. She is excited that her penchant for career growth and development dovetail with the opportunity presented by the BMSF program to be paired with like-minded individuals of similar backgrounds who all share the same goals: improving health equity and eliminating existing disparities.

Ensuring representation of underserved Hispanic and minority populations in future clinical trials is key to reducing sample bias and providing data that better reflect the whole US population, said Morales. Adolescents and young adult populations in general are already understudied in research, making efforts to include younger members of minority communities even more crucial.¹³

"We need trust in the community. We also need our communities to feel like they're helping us with research and also that they're guiding the research....I think gone are the days where we go and tell the community what they need," Morales pointed out. "I think we should start striving to learn from our patients, »



MORALES
Sonia Morales, MD, pediatric hematologist-oncologist, Children's Hospital of Orange County, California.



WILLS-SANIN
Beatriz Wills-Sanin, MD, clinical fellow, Hematology and Oncology, Memorial Sloan-Kettering Cancer Center.

learn from the families, and try to gauge more of what their needs are, and then work together to develop interventions.”

Morales’ research seeks to help families fully understand their cancer diagnoses, treatment plans, and survivorship roadmaps.

Improving Clinical Trial Diversity Means Building a Willingness to Participate

Born in Bogota, Colombia, Beatriz Wills-Sanin, MD, clinical fellow, Hematology and Oncology, Memorial Sloan Kettering Cancer Center, New York, New York, first became passionate about increasing diversity in clinical trial research while working in underserved Colombian communities during medical school.

As she became exposed to different pathologies and patients of diverse race/ethnicity and background, Wills-Sanin found that the lack of access to centralized care in these communities, particularly in regard to cervical cancer screening and HPV vaccination, influenced her decision to pursue a career in medical oncology.

Then, through her subsequent residency at the Johns Hopkins School of Public Health, she learned that improving diversity in clinical trials concerns not only access, but the willingness among minority patients to participate.

“I learned about how many patients visualize health care and clinical trials in the community. For instance, even speaking about lung cancer screening was kind of a taboo for these patients, because many viewed clinical trials or participation in any screening or routine clinical practice as an experiment rather than standard of care,” said Wills-Sanin.

Prior events such as the Tuskegee syphilis study continue to arouse suspicion of clinical trials for Black Americans, and discrimination and language barriers can also exacerbate mistrust in the medical system for minorities.¹⁴

“Building community outreach to [people in underserved] areas who would not otherwise have access is very important. One of the things that we did in medical school other than screening is education—doing focus groups about lung cancer screening and Pap smears, as well as the importance of just taking care of yourself and having a primary care physician.”

In learning about clinical trial design through the BMSF program, Wills-Sanin noted that one of the biggest factors addressed so far is eligibility. Loosening stringent inclusion criteria could promote accrual of minority patients who would otherwise be deemed too complex or difficult to treat.

“Other ways to improve accrual and participation include understanding and acknowledging the [patients’] socioeconomic circumstances and transport barriers, as well as improving the exposure that these programs have in different areas,” she commented. “One of the biggest advantages of participating in this program is building a network of wonderful mentors and physicians who, like me, share the common interest in developing programs for underserved communities.”

Now in advanced clinical training for hematologic malignancies, with a special interest in lymphoma, Wills-Sanin seeks to investigate new opportunities for immunotherapy in cutaneous T-cell

How Each Investigator Would Address Diversity in Clinical Trials



“We have to be intentional in our clinical trial design, as well as give support—whether that be academic community partnerships or supporting those smaller centers that may not be as research heavy—to build up their clinical research infrastructure,” said **SONYA REID, MD, MPH.**



“I think an important thing for bringing diversity into the workforce is having clinical research be a concept introduced earlier in education. I think it will lead to more diverse groups of people coming into research, and I also think it will let people know that they can be a researcher,” said **RICHARD SILVERA, MD, MPH.**



“I feel that the workforce diversity among physicians needs to be increased in order to help address some common challenges that limit accrual of people who have been historically excluded in clinical trials. This includes language barriers, not having clinical trial consent forms in other languages, and not under-

standing how to revamp certain processes with the appropriate cultural context,” said **ANALIZ RODRIGUEZ, MD, PHD.**



“Increasing diversity in your workforce and getting community engagement, community participation, at the initiation of your trials—even when you’re designing trials. That will help in building trust within our communities that are not always so trusting of the health care system. The more they see individuals like yourself that are of similar backgrounds, the more willing they will be to participate in research and clinical trials,” said **SONIA MORALES, MD.**



“I think that opening sites in different hospitals and building up multi-institutional collaborations is essential to be able to improve diversity in clinical trial accrual. Primary care physicians should be available to all of the community, not only those patients who are near big cities and huge academic hospitals, but [those throughout] the whole country,” said **BEATRIZ WILLS-SANIN, MD.** ♦

lymphoma and improve understanding of racial disparity in lymphoma. ♦

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