

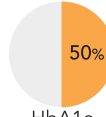
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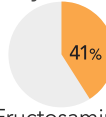
Clinical  
Laboratory  
News

### DETECTING PREDIABETES IN AFRICANS

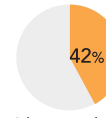
Sensitivity



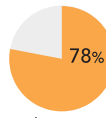
HbA1c



Fructosamine



Glycated  
Albumin



HbA1c +  
Glycated Albumin

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**Time for  
Universal  
BRCA  
Screening?**



**The  
Big Deal  
about Small  
Volumes**



**THE  
RIGHT TIME  
TO DO THE  
RIGHT THING**

Labs Take on  
Health Disparities





# BRIDGING THE HEALTH DISPARITIES GAP



How Laboratories Can Improve Care  
for Vulnerable Populations

BY JULIE KIRKWOOD



**H**ealth disparities persist in the U.S. for a variety of reasons, including lack of access to care, cost, and caregiver biases. Even beyond social factors, there are situations in which a person's race, ethnicity, disability, geography, or gender may influence his or her risk of disease and ability to recover. Health disparities also extract a financial cost, heaping a financial burden on families that can least afford it.

Clinical laboratories can and should play a role in reducing such health disparities, according to laboratory medicine experts.

"If we know that there are disease processes for which disparity exists, we would be selling our physician colleagues short by not trying to determine the appropriate clinical testing parameters available in the clinical lab, and how they may differ among populations," said Octavia Peck Palmer, PhD, an assistant professor of pathology at the University of Pittsburgh School of Medicine.

While researchers are well on their way to developing new diagnostics and therapies to tackle disparities, there are several steps laboratories can take right now to improve care.





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### BETTER REFERENCE RANGES

A reference range is defined for each clinical test as 95% of the normal population. Each laboratory must determine what the normal population is and make sure it reflects the patient population served, Peck Palmer said. Several tests warrant ethnic/race-specific reference ranges. “When laboratories establish or review reference ranges, it is imperative that the laboratory has appropriate representation of individuals from different ethnic groups,” she said.

Case in point, researchers at the University of Hawaii John A. Burns School of Medicine analyzed data from Americans of European, African, Asian, and Hispanic ancestry to evaluate the distributions of common clinical lab results of health subjects using the 2011–2012 National Health and Nutrition Examination Survey (NHANES). Of 38 common biochemical and hematological tests, normal ranges for 33, when stratified by sex and race/ethnicity, showed statistically significant differences from NHANES laboratory manual reference ranges (Hawaii J Med Public Health 2015;74:302–10).

“There are many racial/ethnic differences,” said co-author Eunjung Lim, PhD, an assistant professor in biostatistics. “That’s why we are proposing that in the future we should develop racial/ethnic-specific reference intervals that would be more accurate and help improve quality of patient care.” Inaccurate reference ranges can lead to misdiagnosis or delayed diagnosis. They can also render minorities ineligible for specific pharmacological interventions, organ transplants, and clinical trials, experts said.

Such issues arose in Africa with black participants in National Institutes of Health-funded AIDS drug trials, according to Timothy Kien Amukele, MD, PhD, an assistant professor of pathology at the Johns Hopkins University School of Medicine in Baltimore. “They kept having to do all these investigations on people who had neutropenia,”

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• Octavia Peck Palmer, PhD

Amukele said. “It was costing all this money. They would stop the drug, which meant the people weren’t getting the drugs they needed, and it would not resolve.”

Trouble was, the reference ranges didn’t reflect the fact that healthy people of African ancestry tend to have lower white blood cell (WBC) counts than Caucasians, he noted. This has appeared in the medical literature at least since the 1960s, when it was coined “benign neutropenia.”

Amukele, himself an African American, once had a low WBC count when he was a teen. Doctors thought maybe he had HIV. “My mom was completely freaked out,” Amukele recalled. “She was crying. It was a total mess. And then it turns out it was nothing. Nothing. It was normal. So these things have real impacts, and we haven’t fleshed them out completely.”

After his experience with the drug trials in Africa, Amukele searched the medical literature to identify common laboratory tests for which typical reference ranges would misclassify at least 10% of people of African ancestry. Twelve analytes made his list: immunoglobulin G, magnesium, neutrophils, total serum protein, total WBC, serum albumin, lactate dehydrogenase, blood urea nitrogen, alanine transferase, creatinine, CD8+, and total serum bilirubin.

“The response I got was, ‘Everybody knows that reference ranges vary based on biology, it’s just not that interesting,’” Amukele explained. “But the point I was making is, ‘No, the care providers don’t know about this difference.’”

### UPDATED REQUISITION FORMS AND REPORTS

Another step laboratories can take to reduce health disparities is to gather more information on laboratory requisition forms. For example, if a patient is undergoing transgender hormone therapy, that patient’s laboratory results may appear abnormal.

A study published in the *American Journal of Medicine* identified reference ranges that should be adjusted for patients transitioning from male to female (2014;127:159–62). Those differences cannot even be considered if the laboratory is not aware of the patient's transition status, Peck Palmer said. "We have begun this conversation at our institution and are working to ensure that all meaningful patient information can be recorded," she said.

Another opportunity to reduce disparities is to append interpretive clinical information to patient test results. Deborah Cragun, PhD, CGC, an assistant professor at the University of South Florida and Moffitt Cancer Center in Tampa, has been studying why black breast cancer patients are less likely than white patients to get tested for *BRCA* mutations and to receive genetic counseling (Breast Cancer Res Treat 2015;151:169–76).

One reason, she found, was simply that nobody told them to. Perhaps the doctors assumed black women wouldn't want testing or that they couldn't pay, she said. Regardless, reformatted lab reports could help close that gap. "Especially now, when individuals are often getting copies of their test results, if there's language on there—it doesn't need to say 'we recommend' because labs shouldn't recommend—but it can say that according to National Comprehensive Cancer Center Network [NCCN] guidelines, women with these certain risk factors outlined by NCCN should be referred for a genetic risk assessment," Cragun said.

Laboratories can also advocate for Lynch syndrome tumor screening at their institutions, according to Cragun. About 3% of colorectal cancers are caused by Lynch syndrome, which is hereditary, and detection can prevent future cancers.

Lynch syndrome tumor screening is being adopted at certain university and academic medical centers, but less so at community hospitals and places that have large minority patient populations. "My concern is that as this gets rolled out unevenly—it's just the hospital system's



**"If there are findings that come out of the molecular studies that show clear ways to intervene and to help a population of people—that would be a big deal."**

• Renā Robinson, PhD



decision—that we're going to increase disparities," Cragun said. She noted recent research that looked at Lynch syndrome screening in Louisiana (*Am J Gastroenterol* 2015;110:948–55). The researchers found low rates of public hospital screening and of screening in young, high-risk patients. They suggested as possible contributors inadequate provider education and disparities in patients' access to specialized services.

### NEW DIAGNOSTICS AND PERSONALIZED MEDICINE

In the future, laboratories may play a role in fighting health disparities by measuring ancestry-informative markers to determine a patient's racial admixture. Work by Melinda Aldrich, MD, PhD, an assistant professor at the Vanderbilt University Medical Center Genetics Institute in Nashville has shown, for example, that lung function reference equations—which already take race into account—are even more accurate when the clinician knows how much of the patient's ancestry is African and how much is European.

There are also many clinical areas in which researchers are discovering biological differences between racial and ethnic populations that could lead to personalized therapies, along with related new laboratory tests. For example, Peck Palmer's research has shown that severe sepsis occurs more frequently and leads to more deaths in blacks than in whites or Hispanics, even among patients with similar economic backgrounds and similar access to healthcare.

Her preliminary work in patients hospitalized with community-acquired pneumonia revealed that the *zinc finger protein 816* gene is downregulated in black patients compared to white patients. Furthermore, black patients with specific polymorphisms in the *ZNF816* gene had a higher risk for severe sepsis compared to white patients.

Renā Robinson, PhD, an assistant professor of chemistry at the University of Pittsburgh, is embarking on a study to identify what, if any, biological markers are involved in racial disparities in Alzheimer's disease, which is two to three times

more common in African Americans than Caucasians. "We may be able to identify some potential target for therapeutic intervention or maybe diagnosis," Robinson said. "That would be the hope."

Still, it is hard to separate the biological causes of health disparities from the social factors involved, according to Jesse Roman, MD, chairman of medicine at the University of Louisville School of Medicine who also chairs the health equality subcommittee of the American Thoracic Society. "To get to the genes and all that kind of thing, that's great, but I would advocate let's deal with the socioeconomics and discrimination first," Roman said.

While genetics and epigenetics certainly play a role in disparities, social conditions are often tightly intertwined, Roman said. For example, in his native Puerto Rico, the higher instance of asthma might be linked to stress—a social factor—but stress influences a gene related to responsiveness to bronchodilators.

In his opinion, the greatest impact laboratory medicine could have right now is in hiring a diverse workforce and pushing, as a profession, to lower the cost of laboratory tests. "Many of the health disparities today are still related to access to care," he said.

Robinson, too, is concerned about access. "I think there is a role and room for genetics and molecular studies to make a difference, but I am also a realist," she said. "You can come up with a diagnostic assay but if it isn't affordable to people or heavily subsidized by insurance companies, then it isn't helpful. And so that issue would need to be addressed as well."

Yet Robinson is hopeful that bioscience research like hers can make a difference. "I'm definitely optimistic in that regard," she said. "If there are findings that come out of the molecular studies that show clear ways to intervene and to help a population of people—that would be a big deal." ■

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