

**MEDICINE AND SOCIETY: PEER-REVIEWED ARTICLE**

**How Should Representation of Subjects With LEP Become More Equitable in Clinical Trials?**

Jonathan Alhalel, Nicolás Francone, Sharon Post, Catherine A. O'Brian, PhD, and Melissa A. Simon, MD, MPH

**Abstract**

Underrepresentation of individuals with limited English proficiency (LEP) who speak Spanish is ongoing in phase 3 biomedical clinical trials and exacerbates health inequity. This article suggests strategies for increasing representation of Spanish speakers in clinical trials by emphasizing the importance of early engagement with Spanish language communities, inclusive participant recruitment, and collaborative trial design and implementation. Although investigators and institutions administering government-funded research must meet federal requirements for language assistance, journal editors, peer reviewers, institutional review board members, academic health centers, and all beneficiaries of the biomedical and behavioral research enterprise in the United States must motivate linguistic inclusion.

**Underrepresentation Exacerbates Inequity**

Hispanics with limited English proficiency (LEP) are underrepresented in clinical trials for health care interventions that can improve health outcomes, which limits the generalizability of the findings.<sup>1,2,3,4,5</sup> Underrepresentation of Spanish speakers in research limits subgroup analyses to determine whether treatments are effective for this population, which exacerbates health inequity,<sup>6</sup> especially in type 2 diabetes care in the United States.<sup>7</sup> By *underrepresented*, we mean that participation of individuals from racial, ethnic, or linguistic groups is not proportional to their share of the population meant to benefit from trial findings. For instance, in adult vaccine trials reporting racial/ethnic participation data, Hispanics composed 11.6% of trial participants (as low as 3% in cancer clinical trials),<sup>6</sup> although they constituted 18.5% of the US adult population in 2019.<sup>3</sup> Notably, only 54% of cancer trials and 34% of vaccine trials reported ethnicity, limiting understanding of health disparities in those studies.<sup>3,8</sup>

For Spanish-speaking Hispanics in particular, limited access to culturally and linguistically appropriate services (CLAS) is a barrier to accessing health care and participating in clinical trials, despite federal law recognizing the legal right to CLAS for individuals with LEP.<sup>9,10</sup> Ideally, meaningful inclusion in clinical trials would go beyond numerical representation and include powering studies to detect differences between

racial, ethnic, and linguistic groups with respect to the effectiveness of new interventions and to identify health inequities and barriers to care that are unique to these groups. Failure to meet this standard of inclusivity for Spanish-speaking participants in clinical trials perpetuates health care inequities and limits physicians' ability to provide the most effective treatments for all patients. For example, a study of the accuracy of depression-screening instruments that were developed in trials that typically excluded non-English speakers found that ultrashort screening instruments might be inaccurate when used with Spanish-speaking populations.<sup>11</sup> Therefore, physicians, researchers, and funders must embrace a broader ethical obligation to expand language access and inclusive participation during clinical trial recruitment and throughout the research pipeline. Given that Hispanics are the largest—and a growing—minority group with LEP in the United States and are often language discordant with health care professionals, their unique situation needs to be explored and discussed.<sup>12,13,14</sup>

### **Excluding Non-English Speakers From Clinical Research**

Proposed explanations for low recruitment of Black, Indigenous, and people of color (BIPOC) in research include concerns about safety and exploitation based on past and present racism, discrimination and ill-treatment within the health care system, BIPOC's unfamiliarity with research, and the effect of socioeconomic factors on participants' ability to devote time to a clinical trial.<sup>15</sup> In the case of Spanish-speaking participants, commonly stated reasons for exclusion include researchers' inadequate preparation and the need to adapt study measurement tools for Spanish-speaking participants and to recruit bilingual staff.<sup>1</sup>

These reasons do not reflect immutable characteristics of Spanish speakers themselves, nor can they be explained merely by gaps in technical capacity to ensure language access in clinical research. Rather, underrepresentation of Spanish speakers in clinical trials reflects exclusionary practices (eg, English fluency requirements) that can be reversed by prioritizing inclusion in study design and engaging Spanish-speaking communities in the earliest stages of clinical research. Nevertheless, exclusion of individuals with LEP in clinical trials may be on the rise. The proportion of emergency medicine journal research articles excluding non-English speaking (NES) individuals increased from 6.4% in 2004 to 16.2% in 2014, and 42% of articles failed to mention whether NES individuals were included in or excluded from the research.<sup>16</sup> Without the expectation to report or explain the exclusion of non-English speakers from studies, there is no accountability for inclusivity, leading to research designs that exclude individuals with LEP from the onset. The exclusion and lack of reporting reflects a lack of will to shift research culture toward equity and inclusion.

### **Role of Language Discordance**

A 2013 Pew Research analysis showed that 32% of Hispanics ages 5 and older speak English less than “very well” or “not at all,”<sup>17</sup> yet there is little research on the use of Spanish in recruiting patients for clinical trials.<sup>18</sup> Adding a dedicated enrollment phone line in Spanish increased the representation of Hispanics in one study from 14% to 24%,<sup>19</sup> and the quality and quantity of physician-patient communication in the clinical setting has been shown to affect patients' decision making for clinical trial enrollment.<sup>20</sup> These findings suggest that having Spanish-speaking research staff can improve clinical trial enrollment of Hispanics with LEP.

Legal requirements for language assistance and mandates for proportional racial and ethnic representation in federally funded research have proven unsuccessful in changing **exclusionary research designs**.<sup>21</sup> Studies show that interpreters are underutilized in medical settings despite legal requirements but document improvements in patient outcomes when professional interpreter services are used with LEP populations.<sup>22,23</sup> There is little reason to believe that interpreters are widely available for clinical trials, for which less federal guidance on access to language assistance and less knowledge of the benefits of such access exists.<sup>24</sup> The underuse of **Spanish interpreters in health care**, together with the common practice of explicitly excluding non-English speakers from trial recruitment and inconsistent reporting of racial and ethnic representation in study populations, reflects structural racism that systematically neglects the basic requirement for Spanish-speaking individuals to share equitably in the benefits of clinical research.

The connection between underrepresentation in clinical trials and worse health outcomes among Hispanic persons with LEP is strongly suggested by the worse health outcomes Hispanic persons experience with respect to diabetes. Hispanic patients in the United States were twice as likely to be hospitalized for treatment of end-stage renal disease related to diabetes in 2017 compared to non-Hispanic White patients and 1.3 times more likely than non-Hispanic White patients to die from diabetes in 2018.<sup>25</sup> A systemic review of 14 367 clinical trials registered on ClinicalTrials.gov between 1 January 2019 and 1 December 2020 with English language proficiency as an inclusion criterion found that 19% required trial participants to be able to read, speak, and/or understand English.<sup>6</sup> Furthermore, examination of the subset of 85 diabetes trials showed that 29% required English language proficiency and hence excluded Hispanic persons with LEP, and only 9% specified Spanish language accommodation.<sup>6</sup> The principles of justice and respect demand equity in clinical trial participation with no exception for any discriminatory practices.

It is important to note a counterargument rooted in the principle of beneficence. Language assistance services in clinical trials add to costs that may reduce the number of potentially beneficial trials conducted, thereby depriving many of those potential benefits. However, given that language access in health care has been recognized by US law as a civil right<sup>10</sup> and that there is evidence of harm to individuals with LEP from underrepresentation in clinical trials, we posit that proper representation of such individuals in clinical trials has greater potential for maximizing benefits and minimizing harms than the alternative of exclusion.

### **A Language Justice Approach**

The idea of distributive justice—the fair distribution of scarce resources—begets an ethical and moral imperative to embed inclusive practices, such as language assistance, in clinical trials.<sup>26</sup> A language justice perspective takes linguistic diversity as its starting point, valuing the autonomy and self-respect of linguistically diverse individuals and identifying an ethical demand for health care and research institutions to create inclusive, multilingual spaces that facilitate participation and the equitable distribution of the benefits they produce.<sup>27</sup> While the focus of this paper is on the Hispanic population in the United States, we assert that there is likewise a need for inclusiveness across other language barriers, such as those encountered by Asian (eg, Chinese, Vietnamese) populations, to achieve equity in clinical trial access. We posit that cost and other barriers to inclusivity can be mitigated as artificial intelligence technologies

advance and make translation of forms, recruitment materials, and other resources more readily available.

### Recommendations

A restructuring of clinical trials is fundamental to create inclusive, multilingual spaces, and opportunities exist to make valuable, long-lasting changes. These opportunities include requiring every study protocol to include consideration of and goals for linguistic groups, investment and planning to ensure that adequate language resources are available to properly educate patients on their options, and clear protections for individuals with LEP during the informed consent process and continuously after study enrollment. Fulfilling the ethical demands for inclusive clinical trials also requires research funders to prioritize language access by including expenses for language assistance resources in all clinical trial budgets.

As gatekeepers to publication, journal editors and reviewers can set more stringent standards for inclusive clinical trials, thereby encouraging inclusive recruiting if researchers wish to share their findings with the scientific community. Strategies can include guidelines for authors and reviewers on inclusive submission requirements and sample language to explain the reasoning behind paper rejection if authors do not include or explain representation of specific populations in their studies.<sup>28</sup> Physicians can also play a role in inclusivity by actively prioritizing language access in clinical practice and creating the expectation for linguistic inclusiveness in research.

### Conclusion

Much work is needed to overcome the inequities Hispanics face in clinical trial enrollment. More specifically, Hispanics with LEP have worse health outcomes and are often excluded in clinical trials simply because of the language they speak, leaving them underrepresented. The current exclusion leaves a large window of opportunity for health equity and improved quality of life for individuals with LEP. To truly advance racial and ethnic representation in research and especially clinical trials, we should all strive to work together for linguistic inclusiveness as a goal.

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**Jonathan Alhalel** is a fourth-year medical student at the Northwestern University Feinberg School of Medicine in Chicago, Illinois, where he previously served as a research trainee at the Center for Health Equity Transformation. He plans to pursue residency training in ophthalmology.

**Nicolás Francone** is a fourth-year medical student the Northwestern University Feinberg School of Medicine in Chicago, Illinois, who intends to pursue residency training in obstetrics and gynecology. Previously, he was a National Institutes of Health research trainee. His research interests include implementing medical Spanish courses to curb health disparities due to patient-physician language discordance.

**Sharon Post** is a scientific editor at the Center for Health Equity Transformation in the Feinberg School of Medicine at Northwestern University in Chicago, Illinois. She was previously the director of the Center for Long-Term Care Reform at Health & Medicine Policy Research Group.

**Catherine A. O'Brian, PhD** is a scientific editor at the Center for Health Equity Transformation in the Feinberg School of Medicine at Northwestern University in Chicago, Illinois. She earned a doctorate in biochemistry from the University of Chicago and conducted postdoctoral studies in cancer research at Columbia University.

**Melissa A. Simon, MD, MPH** is the George H. Gardner, MD, Professor of Clinical Gynecology and vice chair of research in the Department of Obstetrics and Gynecology at the Northwestern University Feinberg School of Medicine in Chicago, Illinois. She is also the founder and director of the Center for Health Equity Transformation and the Chicago Cancer Health Equity Collaborative, as well as a co-leader of the Cancer Control and Survivorship Program of the Robert H. Lurie Comprehensive Cancer Center.

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