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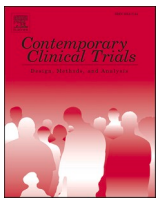

Short Communication

The association between non-English primary language and COVID-19 clinical trial eligibility and enrollment: A retrospective cohort study

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ABSTRACT

Background: Establishing equitable access to COVID-19 clinical trials is an important step in mitigating outcomes disparities. Historically, language has served as a barrier to equitable clinical trial participation.
Methods: A centralized research infrastructure was established at our institution to screen potential trial participants and to promote efficient and equitable access to COVID-19 clinical trials. Rates of eligibility and enrollment in COVID-19 clinical trials by primary language between April 9 and July 31, 2020 (during the first regional COVID-19 surge) were evaluated using logistic regression. Estimates were adjusted for potential confounders including age, sex, and time.
Results: A total of 1245 patients were admitted to the hospital with COVID-19 during the study period and screened for clinical trial eligibility. Among all screened patients, 487 (39%) had a non-English primary language. After adjustment, patients with a non-English primary language had 1.98 times higher odds (CI 1.51 to 2.59) of being eligible for 1 or more COVID-19 clinical trials. Among eligible patients, those with a non-English primary language had 1.83 times higher odds (CI 1.36 to 2.47) of enrolling in COVID-19 clinical trials than patients with English as the primary language.
Conclusion: These findings suggest that there are modifiable barriers that can be addressed to lessen the impact of language discordance on access to clinical trials and provide an opportunity to further investigate factors associated with clinical trial participation for patients whose primary language is not English.

1. Introduction

Socioeconomic disparities in COVID-19 outcomes in the United States (U.S.) are well-documented [1,2]. Multiple factors have been implicated, including language: people with a non-English primary language are at increased risk of contracting and dying from COVID-19 [3–5]. Language discordance between patients and clinicians has been identified as a barrier to equitable clinical trial enrollment, though systematic data describing the representation of patients with a non-English primary language in COVID-19 trials are lacking [6]. Equitable access to, and participation in, clinical trials is critical to mitigate outcomes disparities and ensure the generalizability of COVID-19 therapeutics [7]. To help promote efficient and equitable access to COVID-19 clinical trials, our institution developed a centralized research infrastructure that facilitated eligibility screening and enrollment for all actively enrolling trials for patients with COVID-19 admitted to our academic medical center [8]. We evaluated the association between primary language and both eligibility for and enrollment in COVID-19 clinical trials during the first regional COVID-19 surge.

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2. Materials and methods

Our institution created a centralized research screening infrastructure dedicated to COVID-19-related clinical trials in April 2020. As part of this process, a central team of research staff systematically screened every patient newly admitted to the hospital or newly diagnosed with COVID-19 daily for all currently enrolling clinical trials and communicated directly with all research teams regarding newly eligible inpatients [8]. This stands in contrast to traditional, de-centralized clinical trial recruitment strategies, in which creating a comprehensive approach to identifying, screening, and approaching potential study participants is deferred to each study team. Language-concordant informed consent for all enrolling trials was obtained using dedicated hospital translation services, including phone-based interpreters, video-based interpreters, and an expanded pool of in-person interpreters, depending on interpreter availability.

We collected COVID-19 trial screening and enrollment data for the first hospitalization of all adults who were admitted to our institution with COVID-19 after the implementation of this centralized infrastructure and between April 9 and July 31, 2020. We extracted demographic data for patients from the electronic health record, and defined patients as having non-English primary language if their primary language was a non-English language. We excluded patients whose primary language was recorded as 'Unknown.'

We used descriptive statistics to summarize the study cohort and logistic regression to estimate the association between primary language and eligibility and enrollment status, respectively, after adjustment for age, sex, and month of screening (to account for changes in the number of actively enrolling trials). We did not to adjust for race/ethnicity because of the well-known limitations of administratively-captured race/ethnicity data in electronic health records [9,10]. The threshold for significance was $p < 0.05$. All analyses were conducted in R version 4. This study was approved by the Mass General Brigham institutional review board.

3. Results

Among 1245 screened patients, two thirds (65%, $n = 812$) were eligible for at least one trial and 36% ($n = 292$) of those eligible were enrolled. Baseline characteristics are presented in Table 1. The mean age was 59 years (standard deviation 18), 56% ($n = 696$) of all screened patients were men, and 39% ($n = 487$) had a non-English primary language. Among all patients, approximately half (48%, $n = 595$) were Non-Hispanic White, 12% ($n = 155$) were Non-Hispanic Black, 9% ($n = 116$) were Hispanic, 4% ($n = 50$) were Asian/Pacific Islander, and 26% ($n = 329$) were Other/Unknown.

Patients with a non-English primary language represented 45% ($n = 367$) of all eligible patients and 55% ($n = 160$) of all enrolled patients, with variation in the proportion of eligible and enrolled patients over time (Fig. 1). Approximately 44% of all eligible patients with non-English primary language subsequently enrolled in a study. In adjusted analyses (Table 2), patients with a non-English primary language were both more likely to be eligible for (adjusted odds ratio [AOR] 1.98, 95% confidence interval (CI) 1.51 to 2.59, $p < 0.001$) and, among eligible patients, more likely to be enrolled in (AOR 1.83, 95% CI 1.36 to 2.47, $p < 0.001$) clinical trials than patients with English as their primary language.

Table 1
Baseline characteristics of patients with COVID-19 by eligibility and enrollment status, April–July 2020.

	All Patients	Eligible Patients	Enrolled Patients
	$N = 1245$	$N = 812$	$N = 292$
	Mean (SD) or N (%)	*Mean (SD) or N (%)*	*Mean (SD) or N (%)*
Age	59 (18)	59 (17)	56 (15)
Gender			
Men	696 (55.9%)	471 (58.0%)	172 (58.9%)
Women	549 (44.1%)	341 (42.0%)	120 (41.1%)
Primary Language			
English	758 (60.9%)	445 (54.8%)	132 (45.2%)
Non-English	487 (39.1%)	367 (45.2%)	160 (54.8%)
Race/Ethnicity			
Asian/Pacific Islander	50 (4.0%)	33 (4.0%)	10 (3.4%)
Hispanic	116 (9.3%)	85 (10.5%)	46 (15.8%)
Non-Hispanic Black	155 (12.4%)	107 (13.2%)	25 (8.6%)
Non-Hispanic White	595 (47.8%)	351 (43.2%)	104 (35.6%)
Other/Unknown	329 (26.4%)	236 (29.1%)	106 (36.3%)
Month Screened			
April	707 (56.8%)	549 (67.6%)	180 (61.6%)
May	356 (28.6%)	199 (24.5%)	84 (28.8%)
June	126 (10.1%)	48 (5.9%)	23 (7.9%)
July	54 (4.4%)	16 (2.0%)	5 (1.7%)

4. Discussion

In our analysis of COVID-19 clinical trial enrollment at an academic

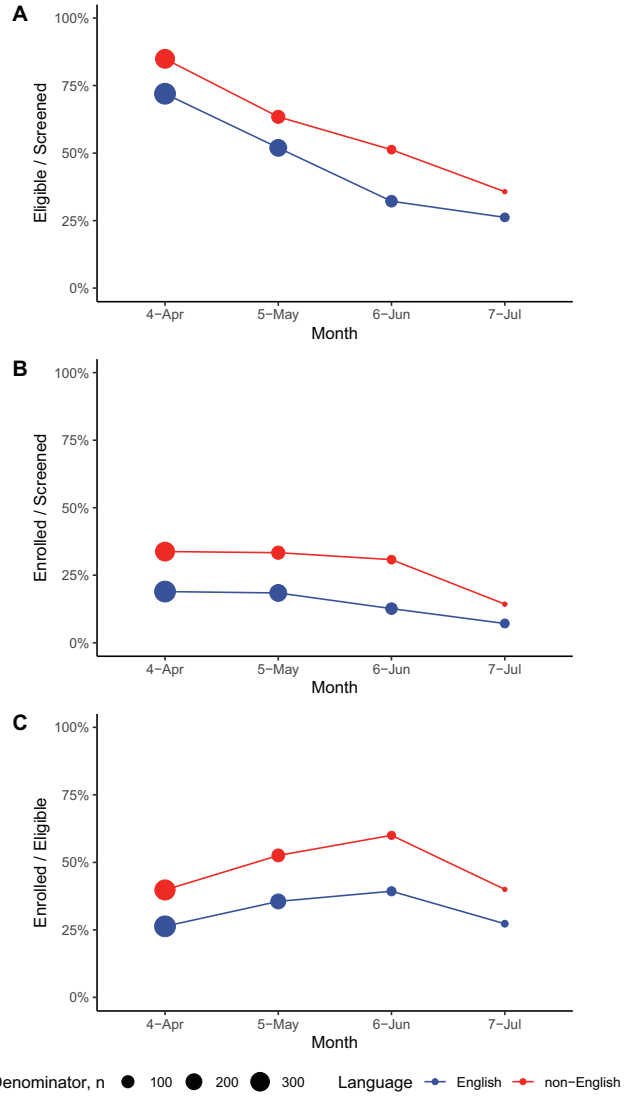

Fig. 1. Proportion of Eligible and Enrolled Patients by Month and Primary Language, April–July 2020.

Table 2
Factors Associated with Eligibility and Enrollment Status.

	Eligible	*P*-Value	Enrolled	P-Value
	Odds Ratio (95% CI)		*Odds Ratio (95% CI)*	
Age	1.01 (0.89–1.15)	0.864	0.80 (0.68–0.94)	0.007
Primary Language				
English	-REF-		-REF-	
Non-English	1.98 (1.51–2.59)	<0.001	1.83 (1.36–2.47)	<0.001
Gender				
Female	-REF-		-REF-	
Male	1.41 (1.09–1.81)	0.008	1.04 (0.77–1.40)	0.810
Month Screened				
April	-REF-		-REF-	
May	0.38 (0.29–0.50)	<0.001	1.63 (1.16–2.29)	0.005
June	0.18 (0.12–0.27)	<0.001	2.00 (1.09–3.68)	0.025
July	0.12 (0.06–0.22)	<0.001	1.02 (0.31–2.91)	0.971

medical center following the implementation of a centralized research infrastructure, we found that patients with a non-English primary language were significantly more likely to be eligible for and subsequently enroll in COVID-19 clinical trials than patients with English as their primary language, even after controlling for potentially confounding demographic factors such as age and sex. These data suggest that the well-documented disparities that are known to adversely affect patients with a non-English primary language in clinical research are not inevitable. Furthermore, this study provides an opportunity to investigate the multitude of factors that impact representation of patients with a non-English primary language in clinical research.

For all patients to benefit equally from advances in clinical medicine, clinical trial participants must reflect the larger patient population that the trial findings are meant to serve [11]. This is especially relevant for COVID-19 clinical trials, as the COVID-19 pandemic has had disproportionately negative impacts on sociodemographic minority patient populations [2,4]. Lack of representation of patients with a non-English primary language in clinical trials is a well-described challenge that predates the pandemic, and more recent work has highlighted the potential for systematic underrepresentation of patients with a non-English primary language in COVID-19 clinical trials [12–14].

We describe a high enrollment rate for patients with a non-English primary language in actively enrolling COVID-19 clinical trials at our institution, with over 44% of eligible patients with a non-English primary language subsequently enrolling in a study. Notably, our hospital supports dedicated language resources. Previous work has shown that lack of utilization of professional interpretation services and language-concordant recruitment materials can be barriers to adequate representation of non-English speakers in clinical research [6,15–18]. Our findings suggest that equity-focused trial recruitment strategies, including systematic patient screening and resources to facilitate trial enrollment in a patient's preferred language, may play an important role in mitigating the language discordance barrier. This is supported by prior studies that have reported similarly high levels of participation among minority patient populations following the incorporation of language-concordant enrollment strategies [19–21].

In addition to structural factors related to trial recruitment methodology, community influences may have also affected clinical trial participation for patients with a non-English primary language in our study. Previous work has found important differences in perceptions and behaviors related to the COVID-19 pandemic among patients with limited English proficiency as compared to patients who are English proficient [22]. While these differences have primarily been observed in behaviors related to lack of healthcare utilization, such as vaccine hesitancy, the disproportionate impact of COVID-19 on minority patient populations may also serve to activate healthcare engagement and increase trial participation [22]. For example, people with limited English proficiency were noted to have increased rates of COVID-19 testing as compared to native English speakers in Massachusetts early in the pandemic [23].

There are also limitations to this study. Potential confounders including location of residence and income were not included in the analysis and therefore our findings may overestimate the impact of primary language. However, Massachusetts residents who self-report limited English proficiency have been shown to have significantly lower earnings than English-proficient residents [24]. As low income is an independent risk factor for trial non-participation, income alone is unlikely to explain the higher levels of clinical trial participation observed among patients with non-English primary language in our study [25]. Additionally, this study includes patients treated at a single, quaternary care academic medical center in a large, metropolitan area and thus may not be broadly generalizable.

5. Conclusions

Ensuring equitable access to clinical trials is an important step in addressing the outcomes disparities that have been well-documented in the COVID-19 pandemic. Our study assessed the relationship between primary language and eligibility and enrollment rates in COVID-19 clinical trials at a single institution following the implementation of a centralized research infrastructure that included dedicated language resources. We found that patients with a non-English primary language were significantly more likely to be eligible for and enroll in COVID-19 clinical trials than patients with English as the primary language. This finding suggests that there are discrete and modifiable barriers that can be addressed to mitigate the impact of language discordance on clinical trial accrual. Future work is needed to understand individual drivers of trial participation for patients with a non-English primary language and how language discordance affects the consent and study enrollment process.

Declaration of Competing Interest

ACT reports receiving a financial honorarium from Elsevier, Inc. for his work as Co-Editor-in-Chief of the journal *SSM-Mental Health.* CMN receives consulting fees from Axle Informatics. THM reports receiving a financial honorarium from Springer Nature. MD has research funding from Novartis and Eli Lilly; he has received consulting fees from Tillotts Pharma, ORIC Pharmaceuticals, Partner Therapeutics, SQZ Biotech, AzurRx, Eli Lilly, Mallinckrodt Pharmaceuticals, Aditum, and Moderna; he has received honoraria from UpToDate, Sandoz Academy, Experts at Your Fingertips, and WebMD; and he is a member of the Scientific Advisory Board for Neoleukin Therapeutics.

Data availability

The data that has been used is confidential.

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