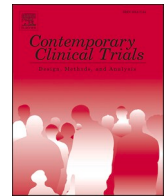




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## Short Communication

# Successful recruitment of monolingual Spanish speaking Latinos to university phase II and III outpatient COVID-19 clinical treatment trials in Northern California

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## ABSTRACT

Through a public County/University partnership, we employed a Spanish/English bilingual research coordinator to increase awareness of newly available treatments with FDA Emergency Use Authorization and clinical trial opportunities for Latino outpatients with mild to moderate COVID-19. Out of the 550 San Mateo County outpatients with COVID-19 referred to Stanford University between July 2020 and April 2022, 9.5% elected to receive monoclonal antibody EUA treatment. COVID-19 treatment trial enrollment of County patients, 5% of those recruited, was commensurate with non-County populations enrollment. Recruitment models such as ours have the potential to increase US Latino populations' recruitment in outpatient COVID-19 treatment trials and contribute to decreasing COVID-19 health disparities.

## 1. Background

Historically and currently, US Latino populations continue to be persistently underrepresented in clinical trials [1]. The US Federal Drug Administration (FDA) has ongoing efforts to increase diversity in clinical trials through education and outreach campaigns [2]. The FDA has released guidance for COVID-19 vaccine trials to strongly encourage the enrollment of populations most affected by COVID-19, specifically racial and ethnic minorities [3]. African American and Asian Americans were underrepresented relative to their population percentage in the clinical trials for the two initial COVID-19 vaccines granted Emergency Use Authorization in the US while Latinos were not [1]. These vaccine trials showed similar efficacy and safety for white and racial/ethnic minority participants. Highlighting inclusion of racially and ethnically diverse populations in these vaccine trials can inform education campaigns and prevent disparities in vaccination. Similar racial and ethnic minority participant data is needed for COVID-19 treatment trials to inform generalizability, education campaigns and prevent disparities in treatment access. A March 2021 review of participants in 5 COVID-19

outpatient treatment trials in high impact journals found Whites were overrepresented in trials compared to percent of US COVID-19 cases (74.1% in trials, 50% US COVID-19 cases), African Americans and Asian Americans were accurately represented in trials based on their percent US COVID-19 cases (African Americans 11.1% cases vs 13.3% in trials), Asians (3.2% cases, 3% in trials) and Latinos were greatly underrepresented in trials (5.7%) compared to 29.1% COVID-19 cases [4].

In a strong collaborative effort, we implemented the San Mateo Medical Center, public County Health System ("County") and Stanford University ("University") outpatient COVID-19 research collaboration to increase recruitment of historically underrepresented populations [5,6] specifically monolingual Spanish speaking Latinos in COVID-19 outpatient research. We aimed to increase access to and participation in COVID-19 outpatient treatment trials at a time in the California pandemic when Latinos were overrepresented in COVID-19 cases [7] and deaths [8]. Of note is that our patient population included both US born and foreign born Latinos in all of the COVID-19 treatment trials. Acculturation scales for US Latinos consistently include language as an important variable for health outcomes which often correlates with time

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living in the US [9]. We describe County recruitment efforts by preferred language for clinical trial recruitment, gender and age.

## 2. Methods

San Mateo County in northern California with a population of approximately 775,000 persons serves as the connecting hub between the urban centers of San Francisco and San Jose, California. San Mateo Medical Center (SMMC) serves the healthcare needs of approximately 68,000 county residents through 11 outpatient clinics, an acute care hospital and two skilled nursing facilities. Patient care is provided regardless of financial means or immigration status. SMMC payer mix is 59% Medi-Cal, 22% Medicare, 15% County Indigent Program, 2% self-pay and 4% other.

Through a Spanish/English bilingual County recruiter phone offer, County patients with mild or moderate COVID-19 who met study inclusion criteria were invited to participate in the following University Treatment trials: Lambda interferon, Favipravir, ACTIV-2, Acebilustat, and ACTIV-6 beginning July 2020, the NIH sponsored Long COVID-19 natural history study (RECOVER) beginning December 2021, monoclonal antibody emergency use authorization (EUA) Treatment beginning January 2021 and Paxlovid oral therapy (EUA) beginning February 2022. We prioritized eligible patients for EUA treatments (monoclonal antibodies or Paxlovid) and for efficiency a bilingual County recruiter offered patients treatment after timely consultation with an ordering physician. While initial recruitment was done by a bilingual County recruiter, enrollment and all other treatment trial study procedures occurred at Stanford University located 17 miles from the County hospital. EUA monoclonal antibody treatment was not available at the County site.

The bilingual recruiter received a daily list of County Health SARS CoV 2 infected patients. The recruiter accessed the County Health system patient portal and reviewed each patient's medical record for inclusion and exclusion criteria for University COVID-19 treatment trials and EUA treatments. All eligible patients were approached by phone by bilingual recruiter to offer them participation in research or EUA treatments. The first step in this interaction involved asking patient's their language of preference. An interpreter service was used by recruiter for non-English/Spanish patients. Once a patient agreed to learn more about treatment trial or EUA monoclonal antibody treatment, their personal information was shared with the Stanford Treat COVID team who evaluated patient for enrollment, further describing study procedures, study visit frequency and informed consent. We

regularly promoted study opportunities for County patients to County clinicians to increase clinician awareness and provided periodic updates on recruitment referrals at clinician attended meetings and via email communication. County primary care clinicians were notified through the County electronic medical record of their patient's interest in and referral to University for all outpatient COVID-19 treatment studies, the RECOVER study, monoclonal antibody EUA or Paxlovid EUA. For the first project year, recruitment phone calls were made by County physician with in kind University support. Beginning the second project year, University funded a part time bilingual recruiter at \$30,000 annual salary for a 20 h a week position. Prior to this intervention, no COVID-19 outpatient clinical treatment trials or natural history studies were available to patients seen at the County site.

## 3. Results

Between July 27, 2020 and April 26, 2022, 472 County newly diagnosed COVID-19 outpatients were recruited for University COVID-19 Phase II and Phase III treatment trial participation (Table 1): 53% were female, 84% Latino ethnicity, and 73% preferred to learn about study opportunities in Spanish. During the project period, Latinos comprised 73% of all non-hospitalized COVID-19 patients (outpatients;) 67% of COVID-19 outpatients preferred to have their healthcare communication in Spanish. This collaboration successfully connected 52 (1.5%) COVID-19 outpatients at high risk for severe COVID-19 to EUA monoclonal antibody treatments likely avoiding hospitalizations. County patients were also successfully recruited into the Long term COVID natural history study. No social or other adverse events were reported for County Health participants referred or enrolled in University outpatient COVID-19 trials.

## 4. Conclusion

Common barriers to historically underrepresented populations participation in clinical trials include distrust, provider perception and lack of access to routine health care [10]. Monolingual Spanish speaking US Latinos have the additional barrier of language access. A Spanish/English bilingual recruiter based at the County Health system was critical to study recruitment success. The bilingual recruiter served the dual functions of outpatient COVID-19 study recruitment and connecting County patients to EUA COVID-19 treatments. Timely availability of Spanish language COVID-19 treatment study recruitment materials, consents and interviews was also essential for our recruitment efforts.

**Table 1**

San Mateo Medical Center (County Health System) Patients Referred for Stanford University COVID-19 Outpatient Treatment Clinical Trials, Long COVID-19 Recover Natural History Study, Emergency Use Authorization (EUA) Monoclonal Antibody Intravenous and/or Paxlovid Oral Treatment July 26, 2020-April 26, 2022.

		Total SMMC COVID positive non-hospitalized patients n (%)	Treatment trials n (%)	Long term COVID n (%)	EUA TX Monoclonal Antibody n (%)	EUA TX Paxlovid n (%)
Gender	Male	1808 (54.1%)	220 (46.6%)	10 (38%)	22 (42%)	3 (50%)
	Female	1537 (45.9%)	251 (53.2%)	16 (62%)	30 (58%)	3 (50%)
	Total	3345 (100.0%)	471 (99.8%)***	26 (100%)	52 (100%)	6 (100%)
	Latino	2450 (73.2%)	398 (84.3%)	23 (88%)	37 (71%)	3 (50%)
Race	White, non-Latino	384 (11.5%)	36 (7.6%)	1 (4%)	6 (12%)	1 (17%)
	Black	62 (1.9%)	8 (1.7%)	0 (0%)	0 (0%)	0 (0%)
	Asian	129 (3.9%)	14 (3.0%)	1 (4%)	5 (10%)	2 (33%)
	Others*	320 (9.6%)	15 (3.2%)	1 (4%)	4 (8%)	0 (0%)
	Total	3345 (100.0%)	471 (99.8%)***	26 (100%)	52 (100%)	6 (100%)
	Spanish	2228 (66.6%)	343 (72.7%)	21 (81%)	35 (67%)	1 (17%)
	English	870 (26.0%)	105 (22.2%)	4 (15%)	12 (23%)	3 (50%)
Preferred Language	Portuguese	131 (3.9%)	18 (3.8%)	0 (0%)	2 (4%)	1 (17%)
	Others**	116 (3.5%)	6 (1.3%)	1 (4%)	3 (6%)	1 (17%)
	Total	3345 (100.0%)	472 (100.0%)	26 (100%)	52 (100%)	6 (100%)
	Total n	3345	472	26	52	6

\* Native American, Pacific Islander.

\*\* Arabic, Mandarin, Russian, Tagalog, Turkish, Tongan.

\*\*\* One missing data reported as NO DATA.

Approximately 5% of County patients eventually enrolled in University treatment studies which is commensurate with Stanford University outpatient COVID-19 study enrollment from other non-public County community recruitment venues.

Our public County Health University COVID-19 outpatient research collaboration indicates that Latinos are willing to participate in COVID-19 clinical trials at rates commensurate to other local populations when provided the opportunity by a trusted messenger within the County Health system. Future outpatient COVID-19 studies can be recruited through this collaborative model. Future COVID-19 clinical trial recruitment efforts for California Latinos should collect data and evaluate other access challenges, such as prohibitive distance to trial sites for persons with limited transportation options, limited flexibility in work and caregiving schedules, and lack of access to technology for monitoring that may be required as part of the trial. Incentives are likely needed to adequately reimburse participants for travel and other related study costs [11].

We present a model for under resourced public County Health systems where patients historically have had fewer clinical trial participation opportunities to increase access to University outpatient COVID-19 trials. Our County Health System/University partnership yielded timely recruitment into outpatient COVID-19 treatment trials during a public health emergency. Racial and ethnic minority participation in COVID-19 treatment trials is essential to evaluate possible different safety or efficacy responses to medical products due to intrinsic factors (e.g. genetics, metabolism elimination) extrinsic factors (e.g. diet, environmental exposures or sociocultural factors) or interaction between these factors [3]. Inclusion of diverse US populations in COVID-19 treatment studies promotes better treatment effectiveness generalizability by ensuring the study population is more representative of the population that will use the drug if approved. Recruitment models such as ours have the potential to increase US Latino populations' recruitment in outpatient COVID-19 treatment trials and contribute to decreasing COVID-19 health disparities.

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## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

No data was used for the research described in the article.

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