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Outreach to Diversify Clinical Trial Participation: A Randomized Recruitment Study

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Abstract

Background/Aims—Racial and ethnic minorities remain underrepresented in clinical research, yet few recruitment strategies have been rigorously evaluated.

Methods—We experimentally tested whether targeted recruitment letters acknowledging diabetes health disparities and health risks specific to recipients' racial/ethnic group improved two metrics of trial participation: willingness to be screened and enrollment. This experiment was efficiently nested within a randomized clinical trial examining a preventive lifestyle intervention among women at high risk for diabetes. Pregnant women with gestational diabetes or impaired glucose tolerance (N = 445) were randomized to receive a targeted recruitment letter with health risk information specific to their racial/ethnic group (n = 216), or a standard letter with risk information for the general population (n = 229). All letters were bilingual in English and Spanish.

Results—The targeted as compared to the standard letter did not improve screening or enrollment rates overall or within separate racial/ethnic groups. Among Latina women who preferred Spanish, the targeted letter showed trends for improved screening (66.7% vs. 33.3%, p = .06) and enrollment rates (38.9% vs. 13.3%, p = .13). In contrast, among Latina women who preferred English, the targeted letter significantly lowered screening (29.6% vs. 57.1%, p = .04) and showed trends for lowered enrollment rates (25.9% vs. 50.0%, p = .07).

Conclusions—Results from this randomized study appear to suggest that recruitment letters with diabetes health risk information targeted to recipients' race/ethnicity may improve one metric of clinical trial participation among Latina women who prefer Spanish, but not English. Larger experimental studies, incorporating input from diverse participant stakeholders, are needed to develop evidence-based minority recruitment strategies.

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This manuscript describes data derived from "A Pregnancy and Postpartum Lifestyle Evaluation Study" (APPLES), which was registered at ClinicalTrials.gov (NCT01489163).

Portions of this work were presented in 2014 at the Society of Behavioral Medicine Annual Meeting (earning an Early Stage Investigator Abstract Award from the Ethnic Minority and Multicultural Health Special Interest Group) and the African American Collaborative Obesity Research Network National Workshop.

Keywords

Randomized clinical trials; recruitment; participation; racial and ethnic minorities; health disparities; targeting; direct mail; communication; diabetes; disease risk

Inclusion of expanding racial/ethnic minority populations is essential to produce generalizable results from randomized clinical trials and eliminate health disparities. Yet the evidence base for recruitment strategies remains limited.[1, 2] The lack of experimental research hinders efforts to engage diverse samples.

Descriptive research suggests that direct mail can be a valuable tool for minority recruitment,[3, 4] providing wide reach with relatively little effort.[5] While few randomized studies have examined direct mail strategies for clinical trials,[6] initial evidence[7–9] suggests that small, no-cost modifications to mailed materials may improve minority participation.

Targeting, or developing messages for specific audiences based on group-level characteristics,[10] is used widely in health research and consumer marketing.[11–15] Targeting typically involves identical content designed to appeal to all recipients,[7–9] who are expected (but not necessarily known) to share a common characteristic such as minority group status. The implications of targeting based on known, individual-level characteristics remain unclear. Matching content to known characteristics could increase perceived personal relevance. Yet tensions related to discrimination and privacy call for careful testing and monitoring of unintended consequences. Tensions may be heightened in applied research settings where participants have an existing relationship with the research-sponsoring institution. While these settings offer greater recruitment efficiency through approved use of health records to identify eligible patients, researchers must engage diverse participants thoughtfully and respectfully.

This randomized recruitment study focused on pregnant women with gestational diabetes (GDM) or gestational impaired glucose tolerance. While racial/ethnic disparities exist in GDM prevalence[16] and progression to postpartum diabetes,[17] all women with GDM are at elevated risk for diabetes[18] and may benefit, individually or collectively, from participation in clinical trials.

We tested the hypothesis that clinical trial recruitment letters with diabetes health risk information individually targeted to recipients' race/ethnicity could improve two metrics of participation: willingness to be screened and enrollment into the trial. Given generally poor awareness about diabetes health disparities,[19] we speculated that increasing awareness about risks affecting a group with which women identify could promote participation.[6] We further speculated that acknowledging and valuing diversity, rather than ignoring it, may prove helpful given research suggesting that pro-diversity statements increase trust among minority adults.[20]

Methods

This randomized study was efficiently nested within a randomized clinical trial, "A Pregnancy and Postpartum Lifestyle Evaluation Study" (APPLES). APPLES examines the efficacy of a lifestyle intervention adapted from the Diabetes Prevention Program[21] for women with pregnancies complicated by GDM or impaired glucose tolerance. APPLES and the recruitment procedures described here were approved by an institutional review board; APPLES was also registered at ClinicalTrials.gov (NCT01489163).

Setting

Kaiser Permanente Northern California (KPNC) is a large integrated healthcare delivery system serving more than 3 million people broadly representative of the region's ethnic and socioeconomic diversity.[22] In this setting nearly all pregnant women receive glucose screening as part of standard obstetrical care.[23]

Procedure

A computer program scanned the electronic health record database (EHR) to identify women meeting initial eligibility criteria for APPLES, i.e., a single gestation pregnancy, glucose values diagnostic of GDM or impaired glucose tolerance,[24] age 20–45 years, absence of certain health conditions (e.g., cancer), receiving care in one of five geographically-based medical facilities, and physician approval to be contacted. Characteristics including women's preferred language, pre-pregnancy body mass index, age, gestational age at time of diagnosis, and race/ethnicity were assessed through the EHR. Race/ethnicity in the EHR is largely self-reported, e.g., through clinic or emergency room visits or health plan membership applications. In a separate sample of 1,676 pregnant women with GDM, we observed a 90% match between single racial/ethnic categories in the EHR and self-report on a subsequent research questionnaire, coded by Institute of Medicine standards;[25] of the mismatches, 71% resulted from a single category being listed in the EHR for women who identified as multiracial on the questionnaire (Brown and Ferrara, unpublished data).

Following identification in the EHR, women were randomly assigned to receive targeted or standard recruitment letters in a 1:1 allocation. Block randomization[26] was stratified on medical facility (five groups) and ethnicity (White vs. non-White). Randomly selected assignment sequences were generated in blocks of four for the two ethnic groupings within each facility, and applied as potentially eligible women were identified over time. Random assignments were automatically date- and time-stamped in a database. Both women and staff were blind to allocation. A week after sending recruitment letters, one of seven recruiters (three bilingual in English and Spanish) contacted women by telephone and invited them to complete the telephone-based screening. Eligible women were invited to complete a baseline clinic visit and randomization into the trial.

All letters were bilingual in English and Spanish (double sided) and personalized with the recipient's name and address in the salutation. All letters described the APPLES trial, its lifestyle intervention, and general diabetes risk information, e.g., "Having GDM raises a

woman's risk for getting type 2 diabetes later in life…" Standard letters contained non-ethnic-specific diabetes risk information for the general population. Targeted letters contained two additional sentences describing diabetes health disparities and risk information specific to recipients' race/ethnicity per individual-level EHR data (i.e., African American, Asian/Pacific Islander, Latina, or White; Table 1). Targeted letters also contained two pro-diversity statements: "We invite you to join a diverse group of women…" and "The results of this study may help improve care for all women with GDM, from diverse ethnic backgrounds." Racial/ethnic-specific diabetes risk information reflected findings from KPNC clinical databases (Ferrara, unpublished data), similar to those from Kaiser Permanente Southern California.[17]

Participants

A total of 445 women were included (Table 2), representing a subset of potential APPLES participants identified upon implementation of the current study. Both minority and White women were included given that many of the geographic areas sampled are highly diverse,[27] and residents may be responsive to pro-diversity messages.

Statistical analyses

The primary outcome was screening rate, i.e., the proportion of women who agreed to be screened by telephone for the APPLES trial. The secondary outcome was enrollment rate, i.e., the proportion that was deemed eligible, completed the baseline clinic visit, and agreed to be randomized into the trial. We tested the effect of letter type (targeted vs. standard) using chi-square and Fisher's exact tests, overall and within racial/ethnic and linguistic subgroups, at a significance level of $\alpha = .05$. We calculated effect sizes as odds ratios (ORs) with 95% confidence intervals (CIs).

Results

Telephone recruiter, ethnicity (White vs. non-White), and other patient characteristics were equivalent across letter types (p values ≥ .57; Table 2). The targeted as compared to standard letter did not improve screening or enrollment rates in the overall sample nor the four racial/ethnic groups (p values ≥ .48; Figure 1). However, among Latina women who preferred Spanish (n = 33), the targeted letter showed a trend for improved screening rate, 66.7% (n = 12/18) vs. 33.3% (n = 5/15), p = .06, OR (95% CI) = 4.0 (0.94, 17.11); and yielded a non-significantly higher enrollment rate, 38.9% (n = 7/18) vs. 13.3% (n = 2/15), p = .13, OR = 4.14 (0.71, 24.16). In contrast, among Latina women who preferred English (n = 55), the targeted letter significantly lowered the screening rate, 29.6% (n = 8/27) vs. 57.1% (n = 16/28), p = .04, OR = 0.32 (0.10, 0.96), and yielded a non-significantly lower enrollment rate, 25.9% (n = 7/27) vs. 50.0% (n = 14/28), p = .07, OR = 0.35 (0.11, 1.09).

Discussion

This randomized study addressed a key methodological issue: increasing minority participation in clinical trials. A recruitment letter acknowledging diabetes health disparities and risk information individually targeted to recipients' race/ethnicity did not improve

screening or enrollment rates in the overall sample nor within four racial/ethnic groups in an intervention trial among pregnant women at high risk for diabetes. However, the targeted letter showed a trend for an improved screening rate among Latina women who prefer Spanish. This trend was marginally statistically significant given the small sample. Still, Latina women who preferred Spanish appeared to show four times greater odds of being willing to be screened for the trial after receiving the targeted letter. Although speculative, this effect size could translate into improved screening rates in large clinical trials where hundreds more, if not thousands of letters are mailed.[7, 8, 28] The tentative finding in a growing and underserved segment of the population, which researchers may find difficult to reach, may warrant further examination.

In contrast the targeted letter significantly decreased the screening rate, and non-significantly decreased the enrollment rate, among Latina women who preferred English. Specifically, the targeted letter resulted in 68% decreased odds of being willing to be screened for the trial in this linguistic subgroup. That the same bilingual, targeted letter appeared to yield opposite results across linguistic subgroups suggests there may have been insufficient homogeneity among Latina women to make a common communication approach successful.[10] Here we can only speculate as to why. Latina women who preferred English may have perceived the targeted health risk information as irrelevant, e.g., if such women felt less connected to their ethnic group.[29, 30] The bilingual nature of the letter may have exacerbated this irrelevance for women who do not prefer, and indeed may not speak Spanish. At worst, women in this group may have found the targeted health information to be psychologically threatening,[31] by connecting personal characteristics to negative health outcomes[32]; or a disingenuous attempt at persuasion, similar to commonplace direct mail consumer marketing.[8] Methodologically, mismatches between EHR and self-described ethnicity may also have played a role, despite the strong concordance observed in a separate sample. Research to explicitly pre-test outreach messages and solicit qualitative patient input is needed to both clarify explanations of our negative results and inform new strategies.

Of note, the overall enrollment rate—with almost one-third of women agreeing to be randomized into the trial—was high in comparison to many community-based clinical trials outside of Kaiser in which 1–3% of direct mail recipients may generally respond, be eligible, and enroll.[5, 33, 34] In addition to careful pre-screening, enrollment may have benefitted from the pre-established relationship between recipients and the sender's institution as well as telephone follow-up to mailed letters.

Study limitations include, first, the limited sample size. Second, we were unable to determine whether women read the letters they received. However, the randomized design and fact that other letter characteristics (e.g., external envelope and letterhead) were identical across letter types provides some assurance that this did not affect outcomes. Third, the historically limited granularity of race/ethnicity data in the EHR meant we could not craft targeted messages or assess variations in outcomes within diverse Asian and Pacific Islander groups. Indeed, Pacific Islander women may not have identified at all with the targeted message as presented. Finally, lack of diabetes risk information for multiracial women meant we were unable to craft targeted messages for women who identify with more than one racial/ethnic group, despite growth of the multiracial population in the US.[35]

Limitations notwithstanding, this study significantly adds to the literature on clinical trial recruitment. Most important was the randomized design, given how few strategies have been experimentally tested. This study extends the recruitment literature from academia to an applied research setting, in which the known denominator of eligible women permitted a valuable evaluation of reach in specific subgroups.

Similar targeted outreach strategies could be tested in other applied research settings (e.g., community clinics), longitudinal studies, and efforts to re-engage prior participants in new trials. Such strategies could also be tested to improve patient engagement in clinical care, outside of randomized trials. As EHRs are adopted across health systems and rich patient data become increasingly accessible, individually-targeted patient engagement strategies present innovative opportunities to achieve meaningful use of electronic health data.[36, 37] In light the present results, systematic work is needed to determine whether targeted approaches are appropriate for specific subgroups. Qualitative input from diverse participant stakeholders, as well as larger experimental studies with sufficient power to address multiple ethnic and linguistic subgroups, would enhance the further development of culturally-congruent and evidence-based minority recruitment strategies.

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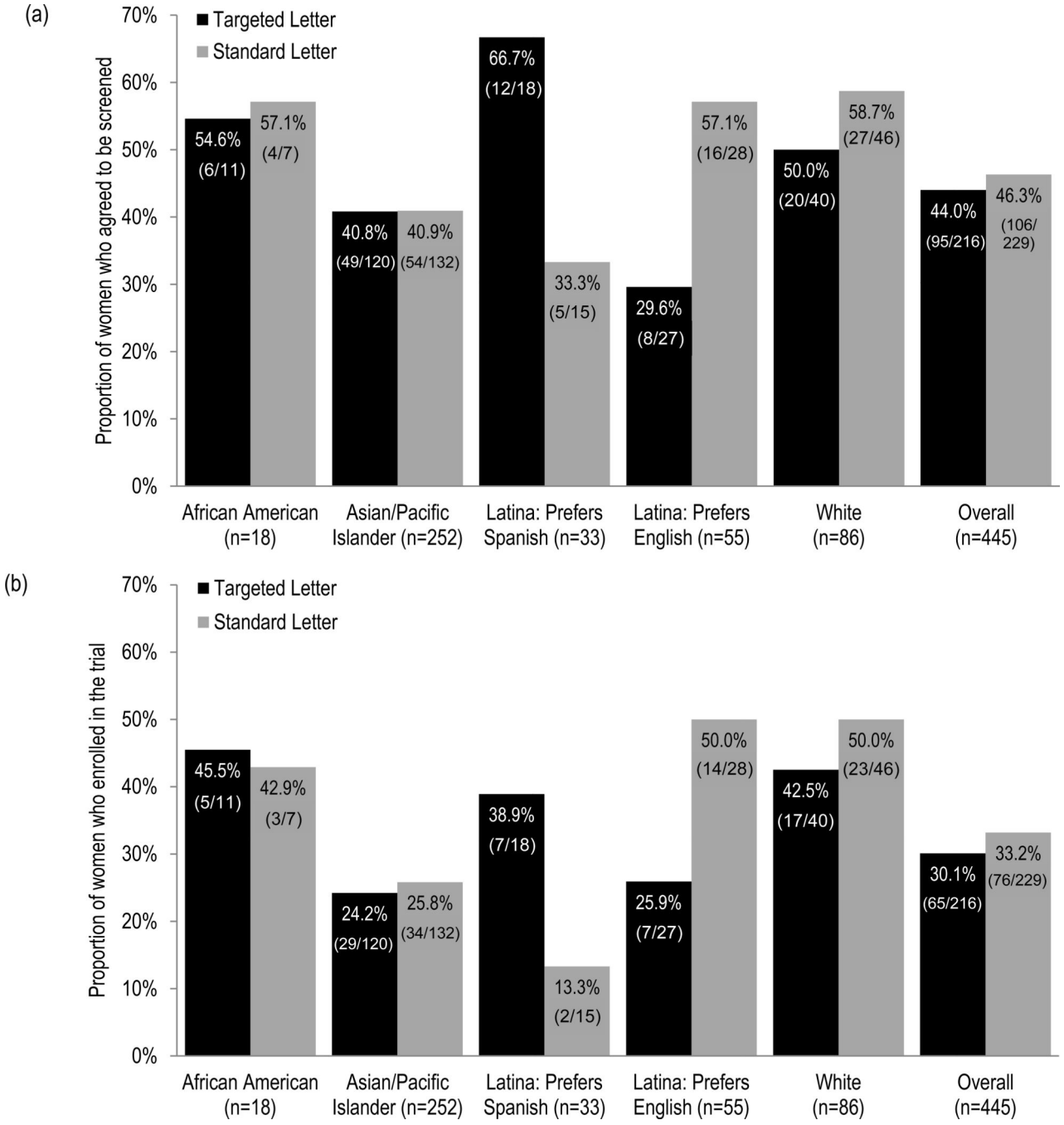

Figure 1.

(a) Screening rates by letter type and race/ethnicity. (b) Enrollment rates by letter type and race/ethnicity.

Note. One Latina participant with unknown language preference did not contribute to the linguistic subgroup analysis.

Table 1

Sample recruitment letter content for women with gestational diabetes

	Targeted	Standard
Content	Diabetes health disparities and risk information specific to recipients' racial/ethnic group	Diabetes risk information for the general population
Sample	"Having GDM raises a woman's risk for getting type 2 diabetes later in life…"	
	"…This risk is especially high for African American, Asian, Latina, Native American, and Pacific Islander women…"	"…Overall, 24% of women with GDM may get type 2 diabetes by the time their children are 10 years old."
	Asian or Pacific Islander "…For example, 23% of Asian women with GDM may get type 2 diabetes by the time their children are 10 years old."	
	African American "…For example, 31% of African American women with GDM may get type 2 diabetes by the time their children are 10 years old."	
	Latina "…For example, 28% of Latina women with GDM may get type 2 diabetes by the time their children are 10 years old."	
	White "…However, even 20% of White women with GDM may get type 2 diabetes by the time their children are 10 years old."	

Table 2

Sample characteristics by recruitment letter type

	Targeted	Standard
N	216	229
Race/ethnicity		
African American	11 (5.1%)	7 (3.1%)
Asian or Pacific Islander	120 (55.6%)	132 (57.6%)
Latina	45 (20.8%)	44 (19.2%)
White	40 (18.5%)	46 (20.1%)
Preferred language[†]		
English	172 (79.6%)	188 (82.1%)
Spanish	21 (9.7%)	17 (7.4%)
Other	22 (10.2%)	23 (10.0%)
Pre-pregnancy body mass index, kg/m^2[‡]		
< 25	79 (36.6%)	91 (39.7%)
25 to < 30	65 (30.1%)	64 (27.9%)
≥ 30	55 (25.5%)	60 (26.2%)
Age at diagnosis, years		
< 25	7 (3.2%)	9 (3.9%)
25 to 29	45 (20.8%)	50 (21.8%)
30 to 34	81 (37.5%)	96 (41.9%)
≥ 35	83 (38.4%)	74 (32.3%)
Gestational age at diagnosis, weeks		
< 14	36 (16.7%)	37 (16.2%)
14 to 27	109 (50.5%)	117 (51.1%)
≥ 28	71 (32.9%)	75 (32.8%)

[†]Preferred language: *n* = 2 missing.

[‡]Pre-pregnancy body mass index: *n* = 31 missing.