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Recruiting and retaining nulliparous individuals with a family history of hypertensive disorders of pregnancy to participate in scientific research prior to pregnancy: The Sisterhood Study

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Abstract

Introduction: Recruiting women with a family history (FH) of hypertensive disorders of pregnancy (HDP) to participate in research before pregnancy could offer insight into genetic and lifestyle factors that incur higher risk of cardiovascular disease during pregnancy and throughout the life course

Methods: The Sisterhood Study piloted low-touch, remote recruitment strategies that relied on women with a history of preeclampsia to share study information with family and friends. It aimed to enroll 150 women with a FH of HDP and 150 controls.

Results: The study recruited 328 women (104 with a FH of HDP, 131 without a FH, and 93 with unknown FH) prior to pregnancy. The majority identified as non-Hispanic White (74.7%) and had > high school education (91.8%).

Discussion: Although the population was enriched with nulliparous women with a FH of HDP, it was not sufficient to recruit a diverse cohort large enough to meet the study aim.

Keywords

Pre-pregnancy cardiovascular health; hypertensive disorders of pregnancy; preeclampsia; study recruitment

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Introduction

Hypertensive disorders of pregnancy (HDP) are associated with higher risk of maternal and infant morbidity and mortality, as well as a two-fold higher risk of long-term cardiovascular disease (CVD) in the birthing individual.[1,2] Little work has been done to engage birthing individuals prior to pregnancy to determine if cardiovascular risk precedes pregnancy or may be secondary to HDP. Conducting longitudinal investigations of individuals from preconception through postpartum could enhance our understanding of the mechanisms by which pre-pregnancy health, HDP, and subsequent risk of CVD are linked, and guide interventions to reduce lifetime risk of CVD. Studies including women with a family history of preeclampsia, a risk factor for HDP, could offer particular insight into the mechanisms by which intergenerational transmission of disease occur and clarify the shared genetic, lifestyle and environmental factors that may incur higher risk of CVD during pregnancy and throughout the life course.[3]

The Sisterhood Study was designed to recruit a pre-pregnancy cohort of nulliparous sisters and daughters of women with a history of HDP. The requirements for this strategy's success are the ability to recruit adequate numbers of women with a subsequent pregnancy and a HDP rate sufficient to perform studies with adequate power in a reasonable time period. In this report, we describe recruitment strategies utilized by the Sisterhood study, the feasibility of these strategies in recruiting the target population, and degree of participation throughout the study.

Methods

The Sisterhood Study aimed to recruit nulliparous, premenopausal women aged ≥ 18 years living in the United States with a target of 150 sisters and daughters of women with a history of a HDP (first-degree relatives), and 150 without a family history of a HDP. Given that recruitment materials utilized the term "women," we will use this term to describe participants. Recruitment occurred from 8/21/2018–4/1/2020. Two prespecified recruitment strategies were employed through existing partnerships with the Preeclampsia Foundation and BabyCenter. First, the study team communicated with individuals with a history of preeclampsia in the Preeclampsia Foundation via email and newsletter posts, and requested that they encourage their reproductive-aged sisters or daughters to participate in the study. This strategy was used to enrich the study population for individuals with a family history of HDP. Second, a marketing campaign was launched with BabyCenter, a digital parenting resource that reaches millions of users in the United States each year. This strategy aimed to enroll a diverse population of individuals with and without a family history of HDP. Planned, periodic assessments of enrollment were performed to allow for adjustment of recruitment strategies (i.e. geographic specific recruitment) in an attempt to recruit a diverse study population. This study was approved by the Institutional Review Board at Advarra. All participants provided online written consent.

The initial survey taken by the target population (nulliparous daughters, sisters, and friends of women with prior preeclampsia) consisted of 12 questions assessing study eligibility,

sociodemographic characteristics, reproductive history, medical history, family history and contraception use. Women who completed this initial online survey and met study eligibility were asked to record a self-measured blood pressure within 2 weeks and received a $10 gift card. They also could opt-in to receive text reminders regarding study participation and/or newsletters from the Preeclampsia Registry and the Preeclampsia Foundation. Finally, a follow-up survey was presented to the study cohort 6 months after enrollment to assess changes in medical history, subsequent pregnancy rates and pregnancy status.

We evaluated initial survey responses to determine the number of eligible nulliparous women by family history of HDP (1st degree relative, unknown or other family history, or none). We then calculated descriptive statistics by family history, race, ethnicity, educational status, relationship status, and medical history. Finally, to assess the degree of study retention, we calculated the percent of women who completed the blood pressure measurement and follow-up survey, overall and in each subgroup. In addition, we assessed the percent of participants who became pregnant by the time of the follow-up survey. We used analysis of variance (ANOVA) and student's t-tests to determine if overall follow-up differed within each subgroup. Analyses were performed on Stata V14.

Results

Among 328 participants who met eligibility criteria and completed the initial survey, 104 (31.7%) reported a first-degree relative with HDP. Mean (SD) age was 30.4 (6.3) years, 28.7% had a post-graduate degree, and 10.1% self-identified as Hispanic, 5.2% as non-Hispanic Black and 74.7% as non-Hispanic White (Table 1). A greater proportion of individuals who reported a first-degree relative with a family history of HDP were on medications for high blood pressure, however differences were not statistically significant ($p = 0.06$), and baseline blood pressures were similar between groups.

Blood pressure measurements were completed by 67.4% (221/328) of participants and the 6-month follow-up survey by 20.4% (67/328) of participants (Table 2). Study retention did not differ between women with and without a family history of HDP. Retention was higher among individuals who self-identified as non-Hispanic White, had a post-graduate degree, were married, had a personal history of heart disease, and who received text reminders regarding study participation. However, these differences were not statistically significant ($p > 0.05$). Of those who completed the follow-up survey, eight women reported pregnancy outcomes. Seven women reported miscarriages; one woman reported a live birth that was completed 15 months after enrollment. This woman reported having hypertension during pregnancy, but did not have an official diagnosis or family history of HDP.

Discussion

In this 18-month feasibility study, 328 women (104 with a first-degree relative with HDP, 131 without a family history, and 93 with unknown family history) were recruited via low-touch, remote recruitment strategies prior to their first pregnancy. This represents a critical time during which optimizing cardiovascular health could prevent both adverse maternal and fetal outcomes, but also at a time when women may not prioritize their

cardiovascular health.[4] However, the study only recruited 69.3% of its pre-determined goal of 150 individuals with a first-degree relative with HDP, a group at higher risk of preeclampsia who could benefit from early interventions to improve health prior to and during pregnancy.[5] Remote recruitment strategies that relied on women with a history of preeclampsia to share study information with family and friends enriched the study population with individuals who have a family history of preeclampsia, but was not sufficient to meet the study recruitment aims. In addition, there was only one live birth reported and no pregnancies complicated by preeclampsia during the follow-up period. A broader expanse of communication channels targeting those with a history of preeclampsia and women trying to conceive may have been needed to achieve an adequately powered study cohort.

The majority of women recruited using these remote strategies were also non-Hispanic White and reported at least a college degree. The demographic characteristics of this sample are similar to those of national cardiovascular trials which, on average, include less than 5% non-Hispanic Black adults.[6–8] These data reflect a need to equitably target recruitment to match the sociodemographic distribution of birthing individuals to participate in research at the national level. Although reasons for non-participation are unavailable in this study, potential explanations include mistrust rooted in historical unethical practices, time and economic barriers, and lack of awareness about current opportunities to participate in research.[8] Overcoming these barriers will require expansion of the remote, low-touch recruitment strategies employed by this feasibility study to actively engage communities, and build trust and interest in scientific research to ensure recruitment of a culturally diverse group. One potential strategy to achieve these goals is to utilize community-based participatory research strategies which are built on partnerships between community and research members. These strategies have shown promise in improving participation among historically underrepresented groups in research.[9]

Study retention was also low in the present study with approximately 67% of participants completing a blood pressure measurement within 2-weeks of the initial survey, and 20% completing the follow-up survey. Overall retention did not differ by family history of HDP, and ranged from approximately 5% among non-Hispanic Black individuals to 23% among non-Hispanic White individuals, and from 15% among those with a high school education or less to 29% among those with a graduate degree, although the study was underpowered to detect differences between groups. This again reflects a need to target diverse communication channels, and ensure tailored recruitment and retention strategies focused on underlying social determinants that may influence participation and retention in research. Potential reasons for poor follow-up include lack of participant compensation for completion of the follow-up survey, and a 6-month gap between the initial and follow-up surveys with no interim communications. Suggestions for improving study retention include providing incentives and reimbursements throughout the duration of the study sending follow-up reminders, and engaging community leaders to encourage continued participation.[10]

This study was strengthened by focused recruitment of individuals pre-pregnancy with a family history of HDP using low-touch and remote strategies sustainable during a global

pandemic. Limitations include convenience sampling across multiple online websites and small sample sizes, particularly among racial and ethnic subgroups. In addition, individual-level data regarding recruitment strategies (e.g., email, newsletters) were not available, so we were unable to determine which strategies were most efficacious.

Conclusion

This feasibility study demonstrates that low-touch and remote strategies enriched the study population with nulliparous women with a family history of HDP, but was not sufficient to recruit and retain a demographically diverse nulliparous cohort large enough to meet the study aim. Additional work is needed to engage communities that have historically been underrepresented in research to help equitably improve participation in maternal health research.

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Table 1.

Demographic characteristics of participants in The Sisterhood Study, overall and by family history of hypertensive disorders of pregnancy (HDP)

	Overall	Family History of HDP		
		No family history	First-degree relative with HDP	Other relative with HDP or unknown family history
N	**328**	**131**	**104**	**93**
Age (mean [sd])	30.4 (6.3)	29.6 (6.0)	30.9 (6.9)	31.0 (5.9)
Race/Ethnicity (%)				
Hispanic	10.1	13.7	6.7	8.6
Non-Hispanic Asian Pacific-Islander	2.1	2.3	1.9	2.2
Non-Hispanic American Indian	0.6	0.8	1.0	1.1
Non-Hispanic Black	5.2	3.8	2.9	9.7
Non-Hispanic White	74.7	74.1	84.6	64.5
Other	0.8	4.6	1.9	10.8
Missing	1.5	0.8	1.0	3.2
Education (%)				
High School or Less	8.2	8.4	5.8	10.8
Some College, College, Vocational School	61.9	61.8	64.4	59.1
Graduate Degree	28.7	28.2	28.9	29.0
Other	0.9	0.8	1.0	1.1
Missing	0.3	0.8	0.0	0.0
Relationship Status (%)				
Married	47.3	57.3	27.9	54.8
Unmarried but in relationship	30.8	26.7	36.5	30.1
Single	21.3	15.3	35.6	13.9
Other	0.3	0.8	0.0	1.1
Missing	0.3	0.0	0.0	0.0
Medical History (%) [2]				
Hypertension	6.7	4.6	11.5	4.3
Hyperlipidemia	0.0	0.0	0.0	0.0
Heart Disease	0.6	0.0	0.0	2.2 (1.5_
Baseline Systolic Blood Pressure (mean [sd]) [3]	121.5 (14.6)	122.3 (14.0)	121.4 (15.5)	120.5 (14.7)

	Overall	Family History of HDP		
		No family history	First-degree relative with HDP	Other relative with HDP or unknown family history
Baseline Diastolic Blood Pressure (mean [sd]) [3]	76.5 (10.1)	76.4 (9.9)	77.1 (10.2)	76.1 (10.7)

[1] Hypertensive disorders of pregnancy is abbreviated as HDP

[2] Self-reported use of medications for hypertension, hyperlipidemia or heart disease

[3] N = 221 overall; N = 96 for individuals without a family history of HDP; N = 67 for individuals with a first-degree relative (mother, sister or daughter) with a history of HDP; N = 58 for individuals with other and unknown family history of HDP

Table 2.

Number and percent of participants that completed each segment of the Sisterhood Study

	Number of participants completing each study segment			Percent of participants retained throughout study		
	Initial Survey	BP[1]	Follow-up Survey	Initial Survey to BP[1]	BP[1] to Follow-Up Survey	Overall (Initial Survey to Follow-Up Survey)
Overall	328	221	67	67.4	30.3	20.4
Family History of Hypertensive Disorder of Pregnancy						
None	131	96	31	73.3	32.3	23.7
First-degree	104	67	17	64.4	25.4	16.3
Other or unknown family history	93	58	19	62.4	32.8	20.4
Race/Ethnicity						
Hispanic	33	25	6	75.8	24.0	18.2
Non-Hispanic American Indian	2	2	0	100.0	0.0	0.0
Non-Hispanic Asian Pacific-Islander	7	4	0	57.1	0.0	0.0
Non-Hispanic Black	17	11	1	64.7	9.1	5.9
Non-Hispanic White	245	161	57	65.7	35.4	23.3
Other	21	15	3	71.4	20.0	14.3
Education						
High School or Less	27	20	4	74.1	20.0	14.8
Some College, College or Vocational	203	141	36	69.5	25.5	17.7
Graduate Degree	94	58	27	61.7	46.6	28.7
Relationship Status						
Married	155	96	36	61.9	37.5	23.2
Unmarried in relationship	101	80	18	79.2	22.5	17.8
Single	70	44	13	62.9	29.5	18.6
Other	1	0	0			
Medical History						
Hypertension	64	56	8	87.5	14.3	12.5
Heart Disease	5	3	1	60.0	33.3	20.0
Recruitment Effort						
None	126	87	22	69.0	25.3	17.5

	Number of participants completing each study segment			Percent of participants retained throughout study		
	Initial Survey	BP[1]	Follow-up Survey	Initial Survey to BP[1]	BP[1] to Follow-Up Survey	Overall (Initial Survey to Follow-Up Survey)
Text reminders only	107	68	26	63.6	38.2	24.3
Newsletter only	29	20	3	69.0	15.0	10.3
Text and newsletter	66	46	16	69.7	34.8	24.2

[1] - Blood pressure

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