

A prospective community engagement initiative to improve clinical research participation in patients with peripheral artery disease

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Abstract

Objective: Patients diagnosed with peripheral artery disease are difficult to recruit into clinical trials. However, there is currently no high-quality, patient-centered information explaining why peripheral artery disease patients choose to participate or not participate in clinical research studies.

Methods: The current study was a prospective community engagement initiative that specifically asked patients with and without peripheral artery disease: (1) what motivates them to participate in clinical research studies, (2) their willingness to participate in different research procedures, (3) the barriers to participation, (4) preferences about study design, and (5) demographic and disease-related factors influencing participation. Data were gathered through focus groups ($n=19$, participants aged 55–79 years) and mailed questionnaires ($n=438$, respondents aged 18–85 years).

Results: More than half of the respondents stated that they would be willing to participate in a study during evening or weekend time slots. Peripheral artery disease patients ($n=45$) were more willing than those without peripheral artery disease ($n=360$) to participate in drug infusion studies (48% versus 18%, $p<0.001$) and trials of investigational drugs (44% versus 21%, $p<0.001$). Motivating factors and barriers to participation were largely consistent with previous studies.

Conclusion: Adults in our geographic region are interested in participating in clinical research studies related to their health; they would like their doctor to tell them what studies they qualify for and they prefer to receive a one-page advertisement that has color pictures of the research procedures. Peripheral artery disease patients are more willing than those without peripheral artery disease to participate in drug infusion studies, trials of investigational drugs, microneurography, and spinal/epidural infusions.

Keywords

Advertising, aging, exercise therapy, lower extremity blood supply, atherosclerosis, barriers to clinical trial enrollment, cardiovascular health

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Introduction

Peripheral artery disease (PAD) affects nearly 8.5 million adults in the United States, costing 21 billion dollars annually.¹ PAD is characterized by the narrowing of peripheral arteries, most commonly due to atherosclerosis.² Many patients present with exertional discomfort in the lower extremities termed, “intermittent claudication.” This significantly decreases quality of life by limiting patients’ functional capacity and walking tolerance.^{3,4} PAD is also associated with an increased risk of myocardial infarction, stroke, and limb amputation.⁵ Medical therapies for PAD have not kept pace with the growing burden

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of disability from the disease, and non-invasive treatments remain largely unavailable or ineffective for most patients.⁶

The symptomatology of PAD creates a barrier to participation in clinical research studies. PAD patients tend to be older, have multiple comorbidities, and have diminished physical mobility, creating a population that is difficult to recruit and retain.^{6–8} Many previous clinical trials for patients with PAD have had to modify or stop their intervention due to difficulty in recruiting enough patients to obtain adequate statistical power.^{9,10} For example, a trial comparing the effects of exercise versus angioplasty on claudication screened 327 potential participants, but only 23 (6%) were willing to be randomized into the trial, causing the trial to be terminated early for slow enrollment.¹⁰ This result is not uncommon; a review retrospectively examining randomized controlled trials for cardiovascular disease found that 10.9% of all trials were terminated early due to low recruitment.¹¹ Furthermore, completed research tends to have small sample sizes, which hinders the generalizability of the work.¹² Therefore, achieving appropriate levels of patient participation in clinical research is a significant obstacle to evidence-based practice.

Previous studies have retrospectively examined how recruitment is impacted by methods of patient identification, communication/advertisement, and study design.^{13–16} In PAD patients specifically, several studies discussed pros and cons of different forms of communication¹⁷ and reasons for patient non-participation,^{12,18,19} but these cited studies did not engage with PAD patients before or during the research process. In recent years, researchers have partnered with PAD patients to improve home-based walking exercise trials; for instance, PAD patients were enthusiastic about a wearable activity monitor, so this was incorporated into the training program.²⁰ In another study, researchers provided coaching for individual PAD patients regarding which walking path would be best.²¹ Encouraged by these recent advancements, we believe a new approach to recruitment is warranted; namely, researchers should seek guidance from PAD patients themselves throughout the research process. To our knowledge, the following is currently unknown: (1) what motivates PAD patients to participate in clinical research studies, (2) their willingness to undergo research-related procedures, (3) the barriers to participation, (4) patient preferences about study design, and (5) demographic and disease-related factors influencing participation. Therefore, the purpose of this community engagement study was to quantify these factors and identify ways to improve recruitment in our ongoing clinical research studies. PAD recruitment and retention rates have been disappointingly low for decades and we believe our data will shed some light on this problem.

Materials and methods

Pilot phase to design questionnaire

Previously published studies in a variety of patient populations have evaluated willingness to participate in research,²²

motivating factors,^{13,23} barriers to participation,^{8,12,24–27} preferences about study design,²² desire for feedback after the study,^{28–30} and outcomes that are most important to the patient.³¹ To the extent possible, we used identical questions when designing our questionnaire. However, some questions related to the specific focus of our laboratory (i.e. exercise physiology and blood pressure studies) or the PAD patient population had to be written de novo and therefore have not been validated. To ensure that the questionnaire took less than 10 min for completion and addressed the factors that were most relevant to our research questions, we piloted each item among our laboratory members and received advice from social science faculty experts on campus.

Focus groups

Ethical approval for the focus groups was obtained from Penn State College of Medicine Institutional Review Board (STUDY00003626). All potential participants were informed about the focus group process through telephone and subsequently provided written informed consent. All patient information was de-identified, and the PI did not personally join the focus groups, so analyses were blinded. PAD patients and healthy subjects aged 50 years and above who had previously participated in cardiovascular research in our laboratory (and were willing to be contacted again) were recruited. We intended to have two focus groups with 8–10 people per focus group (one session in the early morning and one session in midmorning). This sample size is similar to a prior focus group study in PAD that enrolled 15 total patients (three separate sessions) and looked specifically at barriers and motivating factors for undergoing walking exercise.³² In total, we contacted 64 potential participants through telephone, and 23 initially agreed to participate, with ultimately 19 patients in the focus groups.

Participants (Table 1) were mailed the 44-question custom questionnaire prior to the focus group, which served as a template for group discussion. These questions were based on previous publications^{22,29,30,33} and our research group's specific interests. Focus groups were facilitated by two employees from the Penn State Survey Research Center and lasted ~2 h. The Survey Research Center is an on-campus purchased service that provides expert social science research methodology, including data collection, analysis, and interpretation. They advised to pay the participants US\$20 and also provide food and drinks so as to increase participation rates. Topics discussed at the focus group included willingness to join research studies, motivation, barriers to participation, and patient preference in study design. Feedback was also obtained from the participants to reduce the number of questionnaire questions from 44 to 24 (which were used in the mailed questionnaires, below). All focus group discussion was audio-recorded and subsequently transcribed and summarized by the Survey Research Center.

Table 1. Demographics of the focus group participants (left column) and questionnaire respondents (right column).

	Focus group participants	Mailed questionnaire respondents
Total participants	19	415
Male/female	12/7	152/255
Age 18–30 years	0	2
Age 31–54 years	0	100
Age 55–64 years	7	131
Age 65–84 years	9	125
Age 75–84 years	3	43
Age > 85 years	0	6
Prior research experience		
Completed surveys	–	236
Participated in physiology studies	19	82
Participated in sponsored drug trial	–	45
Never participated in any research	–	117
Diagnosed PAD	13/19	45
No diagnosis of PAD	6/19	360
Interested in participating in future research studies	15/19	377
Able to walk 300 ft easily	11	259
Able to walk 300 ft some difficulty	4	81
Able to walk 300 ft much difficulty	3	8
Not able to walk 300 ft	1	50
Able to walk 1500 ft easily	5	211
Able to walk 1500 ft some difficulty	9	78
Able to walk 1500 ft much difficulty	4	20
Not able to walk 1500 ft	1	88
Distance from research laboratory		
<30 miles	19	233
31–60 miles	0	104
>61 miles	0	68
Education		
High school diploma or less	6	94
Some college or associate degree	4	118
Bachelor's degree	4	89
Graduate/professional school	5	105
Hispanic/non-Hispanic	0/19	5/401
Black	2/19	10
White	16/19	389
Asian	1/19	2
Other	0/19	2
Current occupation		
Employed for wages	4	128
Employed for self	3	22
Military	0	1
Homemaker	0	13
Retired	10	191
Unable to work/out of work	2	52

Data are presented as frequencies. PAD: peripheral artery disease.

Mailed questionnaire

Potential subjects aged 21 years and above with and without PAD were identified through Penn State Hershey Cardiology Research database of subjects who have agreed to be contacted in future studies, the Clinical Research Centers database, the

vascular surgery clinic list, the vascular diagnostic ultrasound laboratory database, and the Penn State Institute for Personalized Medicine database. Identified subjects were mailed letters directly to their home address. All letters had the Penn State Health logo and addresses were handwritten. Within the envelope was the shortened questionnaire (24 opinion

questions, see Supplemental Appendix 1), a written explanation of the purpose of the research as mandated by Penn State College of Medicine Institutional Review Board STUDY00004606, a brochure containing images of common research procedures employed in our laboratory (such as ultrasound, treadmill walking, and biking), an “engagement response form” that allowed participants to select aspects of the research process that they would want to become involved in for future studies (Supplemental Appendix 3), and a business reply envelope to return the questionnaire and engagement response form. Based on prior publications and input from the Survey Research Center, we expected a 10% response rate and we wanted 250 completed questionnaires to perform analyses, so we chose to send 2500 envelopes. Over a 4-month period, 2543 surveys were mailed, and 415 responses were returned (16.3% response rate).

Statistical analysis

All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). The survey data were analyzed for response frequency. All study variables were summarized with frequencies and percentages or with means, medians, and standard deviations prior to any analysis to assess the distribution of the data and check for any errors. To simplify analysis, we considered both “strongly agree” and “agree” as indicating a respondent was favorable toward a given question. A chi-square test was used to test for association between the presence of PAD and various factors influencing participation in clinical research studies. An exact test was used when cell counts were too small to support the assumptions of the asymptotic chi-square test. Percentages were used to quantify differences in these factors between the PAD and non-PAD groups. Significance was set at $p < 0.05$.

Results

Patient-reported data are shown in Table 1 for both focus group participants (left panel) and the mailed questionnaire respondents (right panel).

Motivating factors to participate

The dialogue generated during focus group sessions revealed that patients’ largest motivation for joining a study was to help others through assisting scientific development. One patient stated “We’re all here for the same reason. Hoping to find a cure, and I feel, even if they can’t cure me, the research they do on me could help somebody else in the future. The pain I’ve dealt with having PAD I don’t wish that on anybody, and if there’s any way at all that can be alleviated that’d make me feel good to know I had some part in it.” The second largest motivating factor for patients was increased medical knowledge of their condition. Patients felt that testing through EKG, blood work, and other study associated

tests benefited their understanding of their disease state and helped them manage their condition. Patients stated that compensation was not their major motivation to participate in studies; however, compensation was described as helpful.

Responses from the mailed questionnaires ($n=415$ respondents) indicated that 85% ($n=347$) of survey participants were interested in participating in a study related to their medical conditions. Motivation to participate mirrored the results of the focus group discussion. In total, 260 participants felt that the largest motivation to join a study was for a chance to improve their own health (66%), followed by the opportunity to improve the lives of others ($n=127$; 32%). Motivation to join a study was not significantly different between PAD patients and non-PAD patients. The majority of patients ($n=273$; 66%) indicated that their decision to participate was not influenced by the amount of monetary compensation.

Willingness to participate in clinical research studies

The focus group participants, all of whom had participated in prior experiments in our laboratory, were willing to participate in non-invasive testing with short durations of exercise and non-painful procedures. Participants felt that they would be more receptive to invasive or uncomfortable studies, such as those with muscle biopsy, if they were given more information regarding the procedures used, preferably through pictures and video. One patient explained that he “wouldn’t want to participate in the spinal cord infusion because I don’t know anything about it.” Patients also stated that talking to previously enrolled patients through phone may be a successful mode of encouragement to participate in more in-depth studies because it would be helpful “to know what, previous people had experienced.” The majority of focus group subjects suggested that future studies should focus on investigational drugs (15/19), 14 want our laboratory to continue doing cardiovascular imaging studies, 10 want more dietary supplements to be tested, 14 want to see the effects of exercise training, and 12 want there to be more behavior change programs, such as dieting or smoking cessation.

Responses from the mailed questionnaires ($n=415$ respondents) indicated that the types of studies non-PAD patients were willing to participate in were different than the types of studies PAD patients were willing to be a part of (Figure 1). The proportion of PAD patients who would participate in studies with MRI and ultrasound was significantly greater than the proportion of willing non-PAD patients ($p=0.012$; $p=0.027$, respectively). The proportion of PAD patients willing to be a part of more invasive studies was significantly greater than the proportion of willing non-PAD patients, such as in studies including medications not yet approved by the FDA ($p < 0.001$), studies with medication infusions ($p < 0.001$), studies including microneurography ($p=0.013$), and studies including anesthetic infusion into the

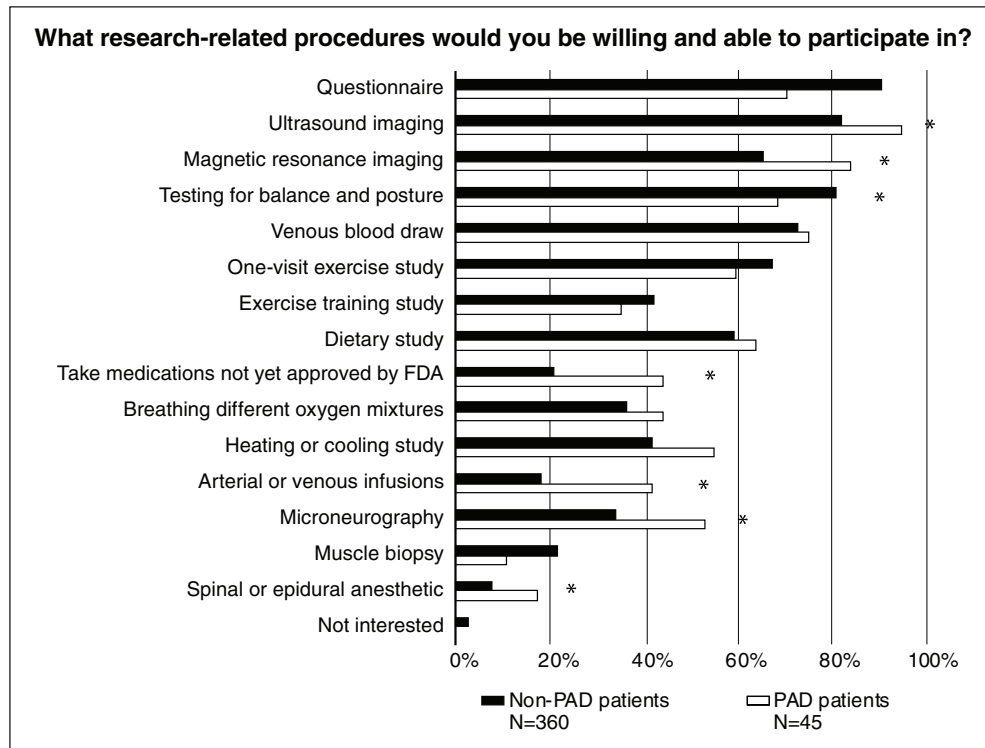


Figure 1. Percentage of patients (x-axis) with peripheral artery disease (PAD, white bars) and those without peripheral artery disease (non-PAD, black bars) self-reporting they would be willing and able to participate in clinical research studies with different procedures (y-axis). *denotes a significant difference between groups ($p < 0.05$) as measured by chi-square test.

spinal cord ($p=0.043$). The proportion of PAD patients willing to participate in procedures with balance was less than the proportion of non-PAD patients ($p=0.048$).

Barriers to participation

The focus group participants, all of whom had participated in prior experiments in our laboratory, discussed lack of close parking, the times and days that the studies are offered, and the amount of time required during the visit as barriers to participation. Patients also noted that fear of participation was a large reason to be discouraged from a study; one patient said he has been discouraged due to “fear of the unknown. What’s going to happen if I’m in a medical study? What are these medicines going to do to me?” Another patient explained that her reservation to participate stems from not knowing what the “side effects are after the procedure.”

Responses from the mailed questionnaires ($n=415$ respondents) indicated that barriers to participation were not significantly different between PAD patients and non-PAD patients. PAD patients were found to use the same modes of transportation as patients without a PAD diagnosis with the majority of patients personally driving ($n=316$; 81%) or having a friend or family member drive ($n=60$; 15%). However, patients who indicated difficulty in walking 1500 ft without stopping were significantly more likely to have a family or friend drive, and less likely to drive themselves

($p < 0.001$). As expected, people living closer to the study center were more likely to attend; 50% of patients within 30 miles of travel were willing to participate, 20% within 60 miles, 12% within 120 miles, and 4% of participants that traveled over 120 miles were willing to participate. The majority ($n=217$; 56%) of patients were willing to visit Hershey Medical center for three or more visits in 1 month, an additional 29% ($n=113$) were willing to attend two visits, and 10% ($n=39$) of participants were willing to have one study visit in a month. In response to the question, “What time(s) are you able to participate in an experiment at Hershey Medical Center? Please check all that apply.” the following responses were obtained: 253 participants (61%) stated weekdays from 7:00am to 11:00am, 195 participants (47%) stated weekdays from 12:00pm to 4:00pm, 236 participants (57%) stated weekdays from 4:00pm to 8:00pm, and 178 participants stated Saturday mornings from 7:00am to 11:00am. The ability to participate based on the scheduled time of the study was not significantly different between non-PAD and PAD ($p=0.623$).

Preferences about study design

The focus group participants, all of whom had participated in prior experiments in our laboratory, thought it was essential to have clear communication when being recruited for a clinical research study. The most common suggestion for

advertising the study was to use a one-sided fact sheet about the study with color photos and possibly have doctors give this to their patients (see Supplemental Appendix 2 for a brochure that resulted from this dialogue). The fact sheet should include what the clinical research entailed from prior participants, time requirements and procedures, side effects and expected pain levels associated with procedures and treatments to allay fear and build trust. Suggested additional communication modes included posters in physician offices with tear-off contact information, a letter or conversation before or after surgery, and advertisements in newspapers, health clubs, support groups, and a more prominent location on the website were also recommended by the groups. Focus group patients also felt that it was important to receive the results of the study and their individual results through mail or phone. However, participants emphasized that the results must be understandable for patients; one patient suggested to contextualize their results, so that patients can see “where (they) fall within the norms of your age and your group.”

The mailed questionnaire ($n=415$) indicated that 86% ($n=347$) would prefer to hear about studies they qualify for from their doctor. There was no significant difference in interest or desire to hear from physicians about studies when PAD patients specifically were compared to all participants ($p=0.88$). After the completion of the study, 87% ($n=352$) would like to receive a summary of their individual results, and 87% ($n=353$) of respondents would like to receive a summary of what the study found overall. When asked what outcomes are most important to individuals, 72% ($n=265$) of patients selected “staying healthy to avoid surgeries and other medical procedures” as most important, whereas 16% ($n=58$) ranked this statement as second most important to them. However, 22% ($n=75$) ranked “being able to walk long distances without discomfort” as most important, whereas 16% ($n=58$) ranked this statement as second most important. Furthermore, 22% ($n=72$) ranked “being able to walk short distances without discomfort” as most important, and 13% ranked this statement ($n=44$) as second most important. Finally, 22% ($n=78$) ranked “wanting to stay healthy to spend less on healthcare” as most important, and 36% ranked this as second most important.

Demographic factors influencing participation

Questions 19–24 in the mailed questionnaire quantified sex, age, race, ethnicity, education level, and current employment status (see Supplemental Appendix 1). Based on the literature,^{34–36} we had compelling reasons to believe that these demographic factors would influence patient motivation and willingness to participate in clinical research studies (especially Question 7, see Supplemental Appendix). However, these analyses were largely unremarkable. When considering all the respondents regardless of PAD status, women were more willing to complete a questionnaire ($p=0.037$), but men were more willing to take medications not yet

approved by the FDA ($p=0.031$), receive medication infusions into arteries or veins ($p < 0.001$), and undergo a muscle biopsy ($p=0.050$). Age did not affect the respondents’ willingness to participate in different research procedures (Question 7, see Supplemental Appendix). Unfortunately, we were not able to assess the influence of race and ethnicity due to low response rate (only 10 African Americans, 5 Hispanics, and 2 Asians completed the questionnaire). Education level was not associated with any meaningful differences in motivating factors or willingness. Employment status did not appear to influence motivating factors or preference in study design; however it did influence willingness to participate. Those working for wages were more willing than unemployed persons to participate in studies, including surveys ($p=0.014$), balance and posture testing ($p=0.012$), and one visit exercise ($p=0.004$). However, unemployed persons were more willing to participate in studies with venous blood draw ($p=0.018$), venous or arterial medication infusions ($p=0.008$), and anesthetic infusion into the spinal cord ($p=0.007$).

Discussion

Numerous prior investigators have reported that PAD patients are difficult to recruit and retain in clinical research studies.^{7,10,12,15,17,19} While some studies have quantified reasons for non-participation,^{12,15,19} these studies did not engage PAD patients before, during, or after the research study. As stated previously, PAD recruitment and retention have been dismal in recent years and we believe that a patient-centered approach is needed for the entirety of the clinical research process (i.e. study design, data collection, data analysis, and reporting). The purpose of this study was to quantify (1) what motivates PAD patients to participate in clinical research studies, (2) their willingness to undergo research-related procedures, (3) the barriers to participation, (4) patient preferences about study design, and (5) demographic and disease-related factors influencing participation. To our knowledge, we are the first to specifically ask PAD patients about these topics and engage them in the clinical research process. Indeed, we prospectively quantified patient preferences and opinions about clinical research studies to improve the way we conduct future studies. The current report has numerous novel findings which will be discussed along with previously published data.

Motivating factors to participate

In a prior survey study ($n=62$ people), 88% of respondents stated that they were motivated by the opportunity to help others and 95% of respondents expected some benefits to being in the study.³⁷ A study examining fire fighters’ willingness to participate in clinical trials for burns found that the largest motivating factor was altruism and the belief in science, followed by the belief that they would have better

clinical outcomes.³⁸ Our findings are congruent in that people were motivated by the chance to improve their own health ($n=274$; 66%), followed by the opportunity to improve the lives of others ($n=132$; 32%). Our study added to the literature by showing that motivation to join a study for PAD patients is not significantly different from the population of patients not diagnosed with PAD.

Willingness to participate in clinical research studies

Prior studies have shown that patients are more willing to participate if they feel that “patients are the main beneficiaries,” and less likely to participate if they believe that the “researchers are the main beneficiaries.”³⁹ Willingness is also impacted by the procedures involved in the trial. A study with 965 participants found that about one-third (36%, $n=345$) of patients decline to participate due to “issues with the protocol”, including not wanting to have an imaging scan, or worry that a drug not yet approved by the FDA would be dangerous.⁴⁰ Question 7 from our questionnaire (see Supplemental Appendix 1) asked which types of research procedures the respondents would be willing to participate in. To our knowledge, we are the first to quantify this information (in any patient population). It is remarkable that patients with PAD were actually more willing than non-PAD patients to take medications not yet approved by the FDA, receive medications infused into their arteries or veins, and undergo microneurography. Conversely, PAD patients were less interested in balance and posture testing as compared with non-PAD patients. It is worth noting that in the past 10 years, PAD patients have not been asked to participate in arterial drug infusion studies or microneurography in our laboratory. Neuropathy associated with PAD may mediate PAD patient reluctance to participate in studies with balance and posture testing. However, it is unclear why PAD patients were more willing to be involved in more invasive studies. Perhaps the symptomatology and comorbidities associated with PAD lead to more diagnostic and therapeutic invasive procedures (e.g. blood draws, angiography, and surgery) ultimately impacting their view of invasive study designs and the risk to benefit ratio.

Barriers to participation

Common barriers cited by patients are lack of motivation, poor physical health, work/time conflicts, domestic responsibilities, and transportation difficulties.^{12,16,18,19} Our study confirmed these findings and shows that those needing to travel farther to our testing center were less likely to participate. In addition, some trials show that a common barrier is fear of side effects,⁴¹ which was a finding reiterated in our focus group. In our study, it is not surprising that patients that indicated difficulty in walking 1500 ft without stopping were significantly more likely to have a family member or friend

drive and less likely to drive themselves. These are the “sicker” patients who are more likely to benefit from a therapy yet they are reliant on someone else to transport them to the laboratory. Thus, future studies should consider what days and times are most convenient for this subset of patients (e.g. the patient may be able to attend a research study on a weekday morning but their family member has to work so they are not able to come).

Preferences about study design

Study design preferences have been evaluated in the general population and retrospectively in PAD patients. A review of 45 trials using controlled interventions aimed at increasing recruitment in all patients determined that telephone calling to non-responders using opt-out rather than opt-in procedures in contacting potential participants increased patient recruitment.¹³ This review article also demonstrated that having surgeons as the main communicators as opposed to nurses did not impact recruitment.¹³ However, some studies do suggest that patients would like to hear about trials they qualify for from their family physicians.²² These results were reaffirmed in our focus group of PAD patients, who would like to hear from their doctor (see Supplemental Appendix 1, Question 3). Trials in PAD patients have determined that the best modes of communication to recruit African American PAD patients are mailings ($n=60$, 34.4%), followed by television advertisements ($n=42$, 24.1%), followed by community events ($n=24$, 13.8%).¹⁵ Similarly, a study in Chicago determined that over half of their recruited participants have come from newspaper advertisements and mailings, whereas community outreach yielded few participants.¹⁷ Recent studies have promoted walking training in a community (non-hospital) setting, but the effect of this training on clinical outcomes is not yet proven.^{21,42} Our focus groups specifically asked patients how they would like the studies to be advertised and we then implemented this advice in the creation of a brochure for a subsequent clinical research study (Supplemental Appendix 2). Consistent with previous publications,^{28–30} our focus group participants and questionnaire respondents were eager to learn the overall results of the trial as well as their personal results. Regarding what outcomes are most important to PAD patients, there is no clear consensus in the clinical or basic science literature. Walking studies often quantify claudication onset time and peak walking time⁴³ and other studies evaluate quality of life, the ankle-brachial index, or components of the walking impairment questionnaire.^{4,7} Despite our best efforts to clarify what patient-centered outcomes are most important to PAD patients (see Supplemental Appendix question 13), we did not obtain a clear consensus. It is possible our question was poorly worded (it has never been validated in any other studies) and it is also possible that the wide variability in patient’s leg symptoms is why we obtained such a wide variety of answers for this question.

Demographic factors influencing participation

A study looking at research participation in the state of Maryland ($n=5154$ respondents) found that those more likely to be recruited to a clinical trial were 65 years or above, had poor health status, had some college or higher level of education, and were more likely to be from the urban rather than rural setting.⁴⁴ Respondents were less likely to be recruited to a study if they were black or if they were classified as middle income.⁴⁴ Several other studies have also shown that patient age,⁴⁵ education level,⁴⁶ and ethnicity⁴⁷ influence likelihood of enrollment. Our study collected demographic data but was unable to look specifically at subgroups because of low response rates.

Limitations and lessons learned

This study is limited by the fact that all of the data are self-reported. It is possible that the participants misunderstood certain questions or misreported some information. This is particularly important regarding PAD symptom severity, as this patient-reported outcome has notoriously poor test-retest reliability since some days are less symptomatic than others.⁴⁸ The focus groups were limited by the population recruited, as all of these people had previously participated in studies in our laboratory and were therefore more familiar with clinical research than the general population. This group may also be more willing to participate in studies than the general population and have built a level of trust with the researchers affiliated with our laboratory. Therefore, the focus group answers may be confounded by a selection bias and likely do not fully represent the target population of all PAD patients. This is why our use of a mailed questionnaire was so vital to the overall study. Although our mailed questionnaire had over 400 participants and had a mixture of occupational statuses and education levels, the respondents were nearly all Caucasian. Moreover, we did not formally calculate the sample size prior to collecting the questionnaire data, so it is unclear how many respondents would be needed if we wanted to conduct additional hypothesis tests. Furthermore, this study is limited by non-response bias, as we are only analyzing data from those willing to fill out and return the survey, which may be different from the general population. Finally, this study could be limited by spectrum bias, as patients were considered a part of the PAD population if they were specifically diagnosed with PAD. However, other patients in the study could have claudication and PAD symptoms but not yet have the formal diagnosis.

Our research group learned several things during the process that will be beneficial for future clinical research studies. For instance, we have strengthened relationships between basic science researchers and vascular surgeons by hosting monthly journal clubs and having combined dinners with visiting scientists. Based on the feedback from PAD patients, we also updated our research flyer for our ongoing randomized

controlled trial (Supplemental Appendix 2) and now have a database of people who are willing to become more engaged in the entire research process (Supplemental Appendix 3).

Summary and conclusion

Based on the data collected from the focus groups and mailed questionnaire, we can make the following statements with a high degree of confidence: Caucasian adults in our geographic region are interested in participating in clinical research studies related to their health, they would like their doctor to tell them what studies they qualify for, they prefer to receive an advertisement that is one page and has color pictures of the research procedures, and they are motivated to learn about their health and improve their health. In addition, they are willing to participate in non-invasive cardiovascular imaging studies and short-duration exercise studies, they would like to receive their individual data when the study is complete, they want to know what the overall scientific findings of a study are, and more than half of the respondents are willing/able to participate in a study during the evening or weekend time slots (this was especially true for patients who are currently employed for wages). Also based on our data (Figure 1), PAD patients are more willing than those without PAD to participate in drug infusion studies, trials of investigational drugs, microneurography, and spinal/epidural infusions. Based on our experience and the previously published literature, it seems reasonable to claim that collaboration between researchers and clinicians will lead to better quality and quantity of recruitment. Finally, we speculate that engaging PAD patients in all aspects of the research process will lead to better recruitment and retention as compared to the “standard of care” (i.e. spending large amounts of money on radio and television advertising, printed brochures, searching electronic medical records, and direct mailing). However, this remains to be directly tested in future studies.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

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Informed consent

Written informed consent was obtained from all subjects before the study.

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Supplemental material

Supplemental material for this article is available online.

References

- Gerhard-Herman MD, Gornik HL, Barrett C, et al. 2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2017; 135(12): e686–e725.
- Muller MD, Reed AB, Leuenberger UA, et al. Physiology in medicine: peripheral arterial disease. *J Appl Physiol* 2013; 115(9): 1219–1226.
- Golomb BA, Dang TT and Criqui MH. Peripheral arterial disease: morbidity and mortality implications. *Circulation* 2006; 114(7): 688–699.
- Morris DR, Rodriguez AJ, Moxon JV, et al. Association of lower extremity performance with cardiovascular and all-cause mortality in patients with peripheral artery disease: a systematic review and meta-analysis. *J Am Heart Assoc* 2014; 3(4): e001105.
- Sigvant B, Hasvold P, Kragsterman B, et al. Cardiovascular outcomes in patients with peripheral arterial disease as an initial or subsequent manifestation of atherosclerotic disease: results from a Swedish nationwide study. *J Vasc Surg* 2017; 66(2): 507–514.
- McDermott MM. The importance and challenge of recruitment for peripheral artery disease randomized clinical trials. *Vasc Med* 2016; 21(4): 352–354.
- Abbott JD. Lessons learned from recent randomized clinical trials for intermittent claudication. *Circ Cardiovasc Interv* 2012; 5(2): 139–141.
- Cavalcante BR, Farah BQ, dos A, Barbosa JP, et al. Are the barriers for physical activity practice equal for all peripheral artery disease patients. *Arch Phys Med Rehabil* 2015; 96(2): 248–252.
- Murphy TP, Hirsch AT, Ricotta JJ, et al. The claudication: exercise vs. endoluminal revascularization (CLEVER) study: rationale and methods. *J Vasc Surg* 2008; 47(6): 1356–1363.
- Hobbs SD and Bradbury AW. The EXercise versus Angioplasty in Claudication Trial (EXACT): reasons for recruitment failure and the implications for research into and treatment of intermittent claudication. *J Vasc Surg* 2006; 44(2): 432–433.
- Bernardez-Pereira S, Lopes RD, Carrion MJ, et al. Prevalence, characteristics, and predictors of early termination of cardiovascular clinical trials due to low recruitment: insights from the ClinicalTrials.gov registry. *Am Heart J* 2014; 168(2): 213–219.
- Brostow DP, Hirsch AT and Kurzer MS. Recruiting older patients with peripheral arterial disease: evaluating challenges and strategies. *Patient Prefer Adherence* 2015; 9: 1121–1128.
- Bower P, Brueton V, Gamble C, et al. Interventions to improve recruitment and retention in clinical trials: a survey and workshop to assess current practice and future priorities. *Trials* 2014; 15: 399.
- Dowling NM, Olson N, Mish T, et al. A model for the design and implementation of a participant recruitment registry for clinical studies of older adults. *Clin Trials* 2012; 9(2): 204–214.
- Love B, Nwachokor D and Collins T. Recruiting African Americans with peripheral artery disease for a behavioral intervention trial. *Vasc Med* 2016; 21(4): 345–351.
- Caldieraro-Bentley AJ, Kelechi TJ, Treat-Jacobson D, et al. Challenges in recruitment of persons with peripheral artery disease for exercise studies. *J Vasc Nurs* 2018; 36(3): 111–120.
- McDermott MM, Domanchuk K, Dyer A, et al. Recruiting participants with peripheral arterial disease for clinical trials: experience from the Study to Improve Leg Circulation (SILC). *J Vasc Surg* 2009; 49(3): 653–659.
- Harwood AE, Smith GE, Cayton T, et al. A systematic review of the uptake and adherence rates to supervised exercise programs in patients with intermittent claudication. *Ann Vasc Surg* 2016; 34: 280–289.
- Guidon M and McGee H. Recruitment to clinical trials of exercise: challenges in the peripheral arterial disease population. *Physiotherapy* 2013; 99(4): 305–310.
- McDermott MM, Spring B, Berger JS, et al. Effect of a home-based exercise intervention of wearable technology and telephone coaching on walking performance in peripheral artery disease: the HONOR randomized clinical trial. *JAMA* 2018; 319(16): 1665–1676.
- Mays RJ, Hiatt WR, Casserly IP, et al. Community-based walking exercise for peripheral artery disease: an exploratory pilot study. *Vasc Med* 2015; 20(4): 339–347.
- Sood A, Prasad K, Chhatwani L, et al. Patients' attitudes and preferences about participation and recruitment strategies in clinical trials. *Mayo Clin Proc* 2009; 84(3): 243–247.
- Treweek S, Lockhart P, Pitkethly M, et al. Methods to improve recruitment to randomised controlled trials: cochrane systematic review and meta-analysis. *BMJ Open* 2013; 3(2): e002360.
- Ridda I, MacIntyre CR, Lindley RI, et al. Difficulties in recruiting older people in clinical trials: an examination of barriers and solutions. *Vaccine* 2010; 28(4): 901–906.
- Carter A, Humphreys L, Snowdon N, et al. Participant recruitment into a randomised controlled trial of exercise therapy for people with multiple sclerosis. *Trials* 2015; 16: 468.
- Nary DE, Froehlich-Grobe K and Aaronson L. Recruitment issues in a randomized controlled exercise trial targeting wheelchair users. *Contemp Clin Trials* 2011; 32(2): 188–195.
- Paskett ED, Cooper MR, Stark N, et al. Clinical trial enrollment of rural patients with cancer. *Cancer Pract* 2002; 10(1): 28–35.
- Fernandez CV, Kodish E and Weijer C. Informing study participants of research results: an ethical imperative. *IRB* 2003; 25(3): 12–19.
- Partridge AH, Wong JS, Knudsen K, et al. Offering participants results of a clinical trial: sharing results of a negative study. *Lancet* 2005; 365(9463): 963–964.
- Cox K, Moghaddam N, Bird L, et al. Feedback of trial results to participants: a survey of clinicians' and patients' attitudes and experiences. *Eur J Oncol Nurs* 2011; 15(2): 124–129.

31. Chalmers I. What do I want from health research and researchers when I am a patient? *BMJ* 1995; 310(6990): 1315–1318.
32. Galea MN, Bray SR and Ginis KA. Barriers and facilitators for walking in individuals with intermittent claudication. *J Aging Phys Act* 2008; 16(1): 69–83; quiz 84.
33. Nead KT, Zhou M, Diaz Caceres R, et al. Walking impairment questionnaire improves mortality risk prediction models in a high-risk cohort independent of peripheral arterial disease status. *Circ Cardiovasc Qual Outcomes* 2013; 6(3): 255–261.
34. Chang P, Nead KT, Olin JW, et al. Clinical and socioeconomic factors associated with unrecognized peripheral artery disease. *Vasc Med* 2014; 19(4): 289–296.
35. Murthy VH, Krumholz HM and Gross CP. Participation in cancer clinical trials: race-, sex-, and age-based disparities. *JAMA* 2004; 291(22): 2720–2726.
36. Johnson DA, Joosten YA, Wilkins CH, et al. Case study: community engagement and clinical trial success: outreach to African American women. *Clin Transl Sci* 2015; 8(4): 388–390.
37. Gaul C, Malcherczyk A, Schmidt T, et al. [Motivation of patients to participate in clinical trials: an explorative survey]. *Med Klin* 2010; 105(2): 73–79.
38. Horch JD, Carr EC, Harasym P, et al. Firefighter willingness to participate in a stem cell clinical trial for burns: a mixed methods study. *Burns* 2016; 42(8): 1740–1750.
39. Kaplan CP, Napoles AM, Narine S, et al. Knowledge and attitudes regarding clinical trials and willingness to participate among prostate cancer patients. *Contemp Clin Trials* 2015; 45(Pt. B): 443–448.
40. Brintnall-Karabelas J, Sung S, Cadman ME, et al. Improving recruitment in clinical trials: why eligible participants decline. *J Empir Res Hum Res Ethics* 2011; 6(1): 69–74.
41. Zammar G, Meister H, Shah J, et al. So different, yet so similar: meta-analysis and policy modeling of willingness to participate in clinical trials among Brazilians and Indians. *PLoS ONE* 2010; 5(12): e14368.
42. Mays RJ, Rogers RK, Hiatt WR, et al. Community walking programs for treatment of peripheral artery disease. *J Vasc Surg* 2013; 58(6): 1678–1687.
43. Gardner AW, Skinner JS, Cantwell BW, et al. Progressive vs single-stage treadmill tests for evaluation of claudication. *Med Sci Sports Exerc* 1991; 23(4): 402–408.
44. Baquet CR, Commiskey P, Daniel Mullins C, et al. Recruitment and participation in clinical trials: socio-demographic, rural/urban, and health care access predictors. *Cancer Detect Prev* 2006; 30(1): 24–33.
45. Nelson AM, Martin IG and Getz KA. Generational value differences affecting public perceptions of and willingness to participate in clinical trials. *Ther Innov Regul Sci* 2015; 49(6): 940–946.
46. Kurt A, Kincaid H, Semler L, et al. Impact of race versus education and race versus income on patients' motivation to participate in clinical trials. *J Racial Ethn Health Disparities* 2018; 5(5): 1042–1051.
47. Pariera KL, Murphy ST, Meng J, et al. Exploring willingness to participate in clinical trials by ethnicity. *J Racial Ethn Health Disparities* 2017; 4(4): 763–769.
48. Kumlien C, Nordanstig J, Lundstrom M, et al. Validity and test retest reliability of the vascular quality of life Questionnaire-6: a short form of a disease-specific health-related quality of life instrument for patients with peripheral arterial disease. *Health Qual Life Outcomes* 2017; 15(1): 187.