

Why Do Patients Decline Heart Failure Trials, and What Should We Do About It?

Supriya Shore (✉ supriyashore@Hotmail.com)

University of Michigan <https://orcid.org/0000-0002-5436-6097>

Candace Speight

Emory University

Anita Kelkar

Wake Forest Baptist Medical Center

Divya Kishore

Emory University School of Medicine

Neal Dickert

Emory University

Research article

Keywords: Trial Recruitment, randomized controlled trials, trial participation, patient engagement

Posted Date: June 25th, 2019

DOI: <https://doi.org/10.21203/rs.2.10610/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Abstract

Background: Low patient enrollment in randomized clinical trials (RCTs) escalates costs, leads to underrepresentation of real-world patient populations, and delays generation of knowledge. Limited data exists on why patients decline participation in RCTs and what factors may lead to increased participation rates. **Methods:** In-person and telephone interviews were conducted with 19 patients with congestive heart failure who declined participation in RCTs. Interviews were conducted using a structured interview guide. Interviews were transcribed verbatim, and qualitative descriptive analysis was performed. **Results:** Participants' median age was 63 years (IQR 51.5-69), 42% were female, and 53% were Black or African-American. Only 6 participants could accurately describe the intervention and clearly understood design of the trial in which they were asked to participate. Most participants made the decision not to participate quickly; only 1 participant took time to deliberate. The most common reasons for not participating were concern for adverse events from the intervention being studied (n=15) and perception of participation being too burdensome (n=10). The most common suggestion provided to increase participant recruitment was involving primary care physicians or cardiologists known to the patients. **Conclusion:** These findings suggest that patients often decide not to participate in clinical trials quickly, with relatively minimal understanding of the trial. Reasons for declining were heterogeneous, but the most common suggestions for improvement were engaging physicians known to them in the process of recruitment and making participation less burdensome. Addressing these issues may reduce barriers to participation and enhance respect for patients.

Introduction

Recruitment and retention of participants in clinical trials is challenging, and low recruitment threatens the ability to improve care in cardiovascular disease. It is widely recognized that many trials fail to meet recruitment targets, and an increasing number of study sites are necessary to meet those targets.^{1,2} The cost of conducting clinical trials has also continued to rise, promoting migration of trials away from the US.³ These challenges threaten our ability to reliably generate timely information on important therapies. In addition to delaying completion, variation in enrollment can reduce the power of clinical trials to answer questions. For example, the Warfarin versus Aspirin in reduced cardiac ejection fraction (WARCEF) trial took longer than 7 years to recruit with an average of 1 patient every 6.25 months. This resulted in enrollment of fewer patients than the targeted sample size and reduced the study's power.^{4,5}

There is a dearth of evidence regarding why challenges to trial enrollment exist and what interventions can help improve recruitment. Novel informatics-based strategies offer exciting potential for increasing enrollment, but it remains important to understand why patients who decline to participate make this decision.⁶ The fact that recruitment rates vary across sites, conditions, and studies suggests that there may be potentially modifiable factors that could increase efficiency.⁷ In order to develop tools targeting ethically modifiable barriers to enrollment, the first step is to understand *why* eligible patients decline. Unfortunately, most existing studies on research decisions have focused on patients who agree to

participate, have involved hypothetical decisions, or have been limited to analysis of more “surface-level” or demographic characteristics of patients who decline to enroll.⁸ These studies offer insufficient insight into what drives these decisions.

The objective of this study was to understand reasons for declining participation in heart failure trials in greater depth. We conducted an exploratory study using structured interviews with patients who had declined participation in clinical trials for heart failure. The primary aim was to understand at a more granular level why they declined to participate and to obtain their views regarding potential changes that might affect their interest in participating while respecting them as decision-makers.

Methods

Study Design

We conducted a qualitative, descriptive study using in-depth, structured interviews with patients with congestive heart failure who declined participation in a clinical trial. The study was conducted from 2013 to 2017. The study was explicitly designed as an exploratory study given the absence of data on this topic. Its goal was to provide rich description of the range of reasons why patients decline to participate and their views on potential changes to the recruitment process.

Study population

We approached patients with heart failure admitted to two hospitals in Atlanta, GA and one hospital in Philadelphia, PA who were approached for clinical trial participation but declined to participate. Eligible patients were 18 years of age or older, spoke English, and had no obvious cognitive impairment. Patients were referred to the study team by coordinators from the primary trials, and sampling was done by convenience. Recruitment continued until thematic saturation was reached. The study was deemed exempt from review by the Emory University IRB.

Interview guide

The interview guide was formulated after reviewing existing literature and with input from a multi-disciplinary group with expertise in cardiology, clinical trials, ethics, and qualitative research. The guide contained the following quantitative domains: demographic information, the 7-item Research Attitude Questionnaire (RAQ), and the 4-item Trust in Medical Researchers (TMR2) scale. The latter two instruments are validated tools assessing attitudes towards research and trust in researchers.^{9, 10} The interview guide included structured questions assessing the patient’s understanding of the trial for which they were approached, perceived risk and benefits of participating, impression of the recruiter, rationale for not participating, and experience with prior research participation. Interviewers were trained to ask

follow-up probes to further elucidate participants' reasons for their responses and to clarify the nature of those responses. After iterative refinement by the study team, the interview guide was piloted with 3 participants and revised after review of pilot interviews by the multidisciplinary research team. Supplemental Appendix A shows the final interview guide used in our study. Consent was obtained from all participants. Each participant was paid \$25.

Data collection and Analysis

All interviews were performed by a trained interviewer. Interviews were conducted in person or over the telephone. Interviews were audio recorded, transcribed verbatim, and redacted for errors.

Quantitative data were entered into Microsoft Excel. Qualitative analysis was performed using MAXQDA 12 (VERBI Software – Consult – Sozialforschung GmbH, Berlin, Germany). The analytic goal was to identify salient themes within and across key domains. Data were analyzed using the template analytic method.¹¹ A domain-based codebook was created *a priori* based on expected responses. Inductive codes were added as themes emerged. The codebook was refined iteratively, with review and recoding of all transcripts using the finalized codebook. Four authors (SS, CS, ND, DK) coded the data, with each interview coded by at least two authors. Coded segments for codes of primary analytic interest were reviewed by the group to ensure that those segments reflected a single, coherent theme. In cases of uncertainty or conflict, the codes were reviewed by three authors (SS, CS, ND) and resolved by consensus.

Results

A total of 43 consecutive patients were asked to participate in this interview study between 2013 and 2017, and 21 patients agreed to be interviewed (Figure 1). Two interviews were excluded from analysis; one subject stated that he was not eligible for trial enrollment due to a study drug allergy, and another stated that she was still considering participation in the trial. Of the interviews included in final analysis, 11 (57.9%) were conducted in-person, and 8 (42.1%) were conducted over the telephone. Fifteen participants were asked to enroll in the initial study during inpatient hospitalization, three in outpatient heart failure clinics, and one from the emergency department. They were referred from seven different trials.

Overall, the median age was 63 years (IQR 51.5 – 69 years), and 8 (42.1%) participants were female (Table 1). The majority of participants identified as Black or African-American (n=10, 52.6%) and had at least some college education (n=14, 73.7%). The RAQ (median 30, maximum possible 35) and TMR2 (median 13, maximum possible 20) scores were relatively high, suggesting a generally positive attitude toward research and trust in medical researchers.

Understanding of clinical trial about which the participant was approached

Participants were asked to describe the clinical trial in which they were asked to enroll. Only 6 participants could describe that trial participation involved both exposure to an intervention and randomization to an intervention or control arm. Eleven participants only described one of those features, and the remaining two participants did not spontaneously recall either of those study features. Five participants reported quickly terminating the initial enrollment conversation with the recruiter. As one participant recounted *"I didn't let her go too far, I didn't want to waste their time going through this entirely"*.

When asked about the potential benefit of participating in the clinical trial, 2 participants were unable to recall any benefits. The majority of the participants believed that there were no direct benefits from participation. *"Basically none. Except maybe during the study if the stuff worked it might help them but God knows when the FDA would approve it. So it basically boils down to not much of anything for me."* Of those who felt that there was a potential for benefit, benefits were most commonly described as the possibility of receiving better treatment or improvement in health status. *"I just assumed that it would help me recover and maintain a healthier heart"*.

When asked to recount the potential risks from participation, nearly one-half of the participants did not recall any risks. Other participants reported concern for potential adverse events from participation. *"It's something new that they're trying out and see, with me, I've only got 20% of my heart as it is, so to be honest, to me it was a little bit scary.... I didn't know what that medicine would do"*. Some reported financial concerns related to health impact of participation *"The hospital takes no responsibility if your participation with the trial drug screws you up, then you've got to pay for it, getting yourself fixed"*. Other risks perceived included: the potential to receive placebo which was perceived to be inadequate therapy *"They weren't going to tell me the dosage or sometimes they were going to put in a fake pull and not tell me.... If I'm not knowing what's going in my body, I'm not going to do it and I'm no lab rat;"* and the possibility of losing confidentiality *"There's so much going on. I have had identity taken and stuff"*.

Participants were asked to grade the risk of participating in the clinical trial they were approached for on a scale of 1 to 5, with 1 being no risk and 5 being very risky. Six participants graded study participation as no risk and only three participants felt it was very risky. All other participants graded the risk in between these extremes.

Process of decision-making

Most participation decisions were made quickly. Only one participant reported taking time after the recruiter spoke with them to carefully deliberate their decision about whether to participate in the clinical trial. The remaining 18 participants reported making a quick decision against participating during the initial explanation. As one participant said, *"I didn't need any time because even though I let her go*

through the whole thing, I knew kind of when she walked in, when she said it was about studying a medication, I kind of knew I wasn't going to be interested just because of – I'm just not that kind of person. I'm not a guinea pig."

Perception about the recruiter and nature of the conversation

Overall, the majority of participants had a positive perception of the person who had asked them to participate. As one participant stated, *"We had a nice pleasant conversation. She even helped me realize the benefits of trying it or not trying it. She was very informative."* A minority of participants described their conversation with the person who asked them to participate negatively. One described being uncomfortable by the presence of a trainee accompanying the recruiter who did not introduce herself to the participant. *"One was a little older, I don't know whether she was in training or what, but she didn't speak up very much, and that bothered me"*. One participant did not like the recruiter's communication style and felt information was being withheld. This participant also felt that the recruiter may have made assumptions about her based on her race: *"We need someone that really is going to sit down and discuss what it's all about with you. She was talking, but I'm the one that had to ask for information. I just felt that at some point that she might've thought that because I have the curly hair and my race, that I am ignorant"*. Another participant felt pressured into making a decision regarding participation. *"I had to make a decision that day, right then and there, and since I had to make a decision that day right then and there, I walked away from it"*. One participant described simply feeling overwhelmed with the situation:

"Well, it wasn't really a conversation. I was being pumped with all different kinds of medicine and diuretics. I was told I had congestive heart failure. It was a lot of things thrown at me at once. I was seeing all kinds of different doctors, trying to remember their names, who was who and what was what, and it was just so overwhelming. So when she came up to talk to me, like I said, she introduced herself and she started talking about a research study and – you know, and I was listening. It's just that when you go to the hospital, a lot of times you don't really understand what's happening to you, and you feel overwhelmed and everything, and different people are coming, asking you different things and everything, and a lot of the times, you have to make decisions right there on the spot."

Role of family and physicians in decision-making

In the process of decision-making, only 1 participant reported discussing enrollment in the study with their family after deciding to not participate. None of the participants involved family members while contemplating trial enrollment. Two participants felt that conversations with family members could have potentially influenced their decision about whether to participate in the clinical trial; most did not believe it would be helpful.

Similarly, only 1 of the participants discussed clinical trial enrollment with physicians known to them. Three participants stated that they did not participate specifically because their primary care provider or primary outpatient cardiologist was not involved. *"If [my doctor] says no, it's no. If she doesn't approve it, I don't care what specialist I go to"*. Half of the participants felt that involving physicians known to them in the process of trial recruitment would have been helpful. *"If my doctor had spoken to me, and led me to believe that [this institution] is involved on this, then yes, I would, because you see, I trust my doctor"*.

Rationale for not participating and suggestions to improve participation

Key themes for not participating in the clinical trial and suggestions to improve participation are listed in Table 2. The most common reason for not participating was concern about potential adverse events *"My health is very fragile and I didn't want to upset the apple cart anyway because I was finally doing better"*. The next most common reason was the feeling that participating in a trial would be too burdensome. For the majority of these participants, traveling for routine visits required as part clinical trial enrollment was a major inconvenience *"My finances were not right and my transportation was not running properly and it was kind of tough."* Others described personal hardships. *"I'm the sole caregiver for my mom who's too sick, so anything that may impact my ability to take care of her would be problematic"*, or inconvenience related to taking the study medications. *"They did a good job as far as explaining and I would have participated in it except when they got to the size of those four pills, that ended it for me right there."* Other participants reported not participating due to perceptions that the institution or researchers would take no responsibility for adverse effects. *"It's something in the written material. They make it very clear that if anything goes wrong it's your blow baby."* Others reported not participating due to the possibility of receiving inadequate treatment. *"Not knowing if I would be getting the drug or not or if I would just be getting a placebo"*.

When asked what would have made them more likely to participate in the trial, the most common suggestion was involving physicians known to them *"If my doctor says so, I'd consider it"*. Other suggestions included making participation easier by decreasing the number of follow-up visits or shortening the duration of the trial *"If it could be made convenient it would be different"*, and providing more information on safety of the intervention. A few felt that if the recruiters approaching them were better trained, they might have participated in the clinical trial. *"I wish that I had had more information or a person to talk to me, you know, with a good understanding, and then I might have changed my mind. I would've went with it and see, because I might be losing out on something now [for] myself"*.

Prior experience with clinical trial recruitment and participation

Overall, half of the participants reported having some prior experience with clinical trial participation either personally or with family members. Of these participants, half reported having a negative experience, which influenced future participation: *“Even though sometimes I would go in three times a month, that’s just another reason I don’t like to get in the study, because you want me once a month then ask me can I come in again next week, yeah sure, I can, but—And I feel obligated to come in because I am taking your medicine.”*

The remaining participants reported having a positive or neutral experience during previous clinical trial participation. Reasons for participating previously and not this time included: (i) participation being less cumbersome before *“The last time, I was hospitalized. I guess I was kind of held captive there, I was already there. I didn’t have to travel anywhere”*; (ii) previous participation was less likely to be harmful *“Previous participation did not involve any medications, it was just a matter of doing some walking and blood pressure checks”*; and (iii) physicians known to the participant were involved *“From speaking to my cardiologist, the research staff got permission and then talked to me about the study”*.

General attitudes toward research and patient characteristics

During the interviews, several themes emerged regarding participants’ general views on research, which broadly classified these decliners into two categories: The first group, representing the majority of participants in our study (n=16), had a positive attitude towards research in general. *“I have no qualms with research. I know that’s how you discover new medications and I know that’s how it helps people and all of that”*. This group typically had what might be considered modifiable reasons for not participating – mainly related to fear of adverse events from medications or concern about burden imposed by participation. These individuals often inflated risks from participation and stated that they would be less likely to decline participation if they had discussed participating in the trial with their own cardiologist or a physician known to them.

A minority of participants (n=3) had strong negative opinions about research, especially if drug companies were involved. One participant felt research was too intrusive *“I know you can’t tell, but I’m kind of shy and kind of a recluse, like inward, like I like to be in the house and you know, I don’t want people looking at me and studying me and all that stuff, either. That’s not my thing”*. The other two had deeply rooted mistrust in research *“Research is all about getting funding. You know, as long as you stretch it out, the more you get paid. Ain’t nobody really trying to help nobody. They just trying to get paid. But most of these scientists and doctors, they’re straight crooks. You know, it’s about money, point blank”*. These individuals did not feel modifications made to the process of enrollment or trial design would increase their likelihood of participation *“I just ain’t a participator”*.

Discussion

This is the first study to our knowledge involving in-depth interviews exploring the reasons why patients with congestive heart failure decline participation in clinical trials. We found that few participants understood details of the clinical trial for which they were approached, and the vast majority decided not to participate quickly after being approached. Participants reported multiple different reasons offered for not participating, many of which are ethically addressable and modifiable. The most common reasons for declining were concern for developing an adverse event and the perception that participation was too cumbersome. The most common suggestion provided to increase recruitment rates was to involve physicians known to them in the process of recruitment.

Our study highlights that the initial barrier in trial recruitment is patient engagement and education. Most participants in our interviews were unable to identify what participation in a randomized trial entailed, several stopped the recruiter from getting into details regarding participation, and all but one participant decided quickly to not participate during the initial conversation. The most common reason for not participating was a generic concern for a potential adverse event rather than concern regarding specific elements of the study for which they were initially approached. Only a minority in our study had a fundamentally negative view of research. These observations suggest a need for research into how to better establish rapport with potential participants, how best to engage with participants about clinical trials, and how to enhance communication about routine protections in place for research subjects. Efforts to address these barriers could take place at the level of individual coordinators or could be more community-based, involving disease awareness events, conversations with patient advocacy groups, and the use of mass media or social networking sites.

We also found that several participants declined to enroll in a clinical trial because they perceived enrollment as burdensome. This finding is not surprising but has real practical implications. First, it highlights that it may be valuable to seek input from patients regarding how to address burdens of participation. Second, it suggests a need to identify burdensome aspects of participation and, ideally, design studies in ways that minimize those burdens. One helpful way to gather data about what elements of studies are perceived as burdensome is to assemble a recruitment database in which reasons for not participating are captured. Such a database could be reviewed at regular intervals to make amendments to research protocols as feasible in order to facilitate enrollment, and to incorporate emerging knowledge into the design of future studies.

Notably, nearly half of the participants felt that involving physicians known to them in the process of recruitment and decision-making would have a positive impact. However, this was uncommonly experienced among this population. Involving clinicians in research decisions and communication may raise ethical concerns by blurring the line between clinical care and clinical research. Some may worry that patients will perceive pressure by their physician to enroll or have an inflated conception of the likelihood of benefit from trial participation (therapeutic misestimation). However, failure to engage treating physicians leaves patients to make unfamiliar decisions that have medical consequences without trusted guidance. In this way, it is critical to acknowledge that research enrollment decisions (especially clinical trials) both affect and are made in the context of clinical care. Appropriate processes

should be developed to promote effective interactions between patients and their doctors about research decisions. Of course, this may be challenging from a workload perspective on treating clinicians.¹²

The optimal model for interacting with treating physicians is not established and will likely differ for different kinds of trials. In some cases, it may be helpful to approach the treating physician prior to approaching an eligible patient; in other cases, it may be most productive to facilitate a conversation between the treating physician and an eligible patient after they have been approached for a clinical trial. Developing approaches to these issues is especially important given the move toward novel informatics-based strategies.¹³ These tools are making more interactions with patients about clinical trials electronic. While this is beneficial from a volume and efficiency perspective in terms of ability to approach patients, decisions made in the context of direct electronic solicitations further remove patients from their treating physicians and may exacerbate some of these problems.

Limitations

The findings of our study should be interpreted in the light of several limitations. First, this was designed as an exploratory study due to lack of data on this subject; as a result, the sample size is small. However, we conducted in-depth interviews, probing to clarify viewpoints of trial participation decliners to obtain much more in-depth information than has been elicited in prior work. Second, all participants were recruited from large academic centers. Third, despite declining participation in a trial, these patients are individuals who agreed to participate in our interviews. The extent to which these viewpoints are generalizable to other people who decline participation is unknown.

CONCLUSION

In this study, patients reported that the most common reasons for declining participation in a clinical trial were the fear of an adverse event and the burden imposed by participation. The majority of these individuals reported that involving physicians known to them in the process of recruitment would have a positive impact on trial enrollment. Furthermore, only a minority could clearly explain what participation in a randomized trial involved, and several prematurely terminated the conversation when approached by a research coordinator. Together, these findings highlight the need for greater patient education and engagement in research and for more studies focusing on development of evidence-based strategies for recruitment.

Declarations

Ethics Approval and Consent to Participate

Consent was obtained from all participants. The study was deemed exempt from review by the Emory University IRB.

Consent for Publication

Not applicable

Availability of Data and Materials

The data generated and analyzed during the current study are not publicly available but de-identified data are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Funding sources

The authors have no external funding sources to disclose.

Authors' Contributions

SS: Data analysis, interpretation of data, drafted initial manuscript and revised it

CDS: Data collection and analysis, interpretation of data, revision of the manuscript

AK: Data collection, revision of the manuscript

DK: Interpretation of data, revision of the manuscript

NWD: Data analysis, interpretation of data, drafted initial manuscript and revised it

Acknowledgement

The authors acknowledge Victoria Scicluna and Alex Fehr for their assistance with conducting interviews as part of this study.

References

1. *Institute of Medicine. A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program.* Washington DC: National Academies Press; 2010.
2. Samman Tahhan A, Vaduganathan M, Kelkar A, Georgiopoulou VV, Kalogeropoulos AP, Greene SJ, Fonarow GC, Gheorghiade M and Butler J. Trends in Heart Failure Clinical Trials From 2001-2012. *J Card Fail.* 2016;22:171-9.
3. Vaduganathan M, Samman Tahhan A, Greene SJ, Okafor M, Kumar S and Butler J. Globalization of heart failure clinical trials: a systematic review of 305 trials conducted over 16 years. *Eur J Heart Fail.* 2018;20:1068-1071.

4. Homma S, Thompson JL, Pullicino PM, Levin B, Freudenberger RS, Teerlink JR, Ammon SE, Graham S, Sacco RL, Mann DL, Mohr JP, Massie BM, Labovitz AJ, Anker SD, Lok DJ, Ponikowski P, Estol CJ, Lip GY, Di Tullio MR, Sanford AR, Mejia V, Gabriel AP, del Valle ML, Buchsbaum R and Investigators W. Warfarin and aspirin in patients with heart failure and sinus rhythm. *N Engl J Med*. 2012;366:1859-69.
5. Dickert NW, Halpern SD and Butler J. Incentivizing recruitment and retention to address enrollment challenges in clinical research. *Circ Cardiovasc Qual Outcomes*. 2013;6:367-70.
6. Weng C. Optimizing Clinical Research Participant Selection with Informatics. *Trends Pharmacol Sci*. 2015;36:706-709.
7. Gheorghiade M, Vaduganathan M, Greene SJ, Mentz RJ, Adams KF, Jr., Anker SD, Arnold M, Baschiera F, Cleland JG, Cotter G, Fonarow GC, Giordano C, Metra M, Misselwitz F, Muhlhofer E, Nodari S, Frank Peacock W, Pieske BM, Sabbah HN, Sato N, Shah MR, Stockbridge NL, Teerlink JR, van Veldhuisen DJ, Zalewski A, Zannad F and Butler J. Site selection in global clinical trials in patients hospitalized for heart failure: perceived problems and potential solutions. *Heart Fail Rev*. 2014;19:135-52.
8. Martin SS, Ou FS, Newby LK, Sutton V, Adams P, Felker GM and Wang TY. Patient- and trial-specific barriers to participation in cardiovascular randomized clinical trials. *J Am Coll Cardiol*. 2013;61:762-9.
9. Rubright JD, Cary MS, Karlawish JH and Kim SY. Measuring how people view biomedical research: Reliability and validity analysis of the Research Attitudes Questionnaire. *J Empir Res Hum Res Ethics*. 2011;6:63-8.
10. Hall MA, Camacho F, Lawlor JS, Depuy V, Sugarman J and Weinfurt K. Measuring trust in medical researchers. *Med Care*. 2006;44:1048-53.
11. Cassell C. Template Analysis *The SAGE Dictionary of Qualitative Management Research* UK: SAGE Publications Ltd; 2008.
12. Miller FG and Rosenstein DL. The therapeutic orientation to clinical trials. *N Engl J Med*. 2003;348:1383-6.
13. Embi PJ, Jain A, Clark J, Bizjack S, Hornung R and Harris CM. Effect of a clinical trial alert system on physician participation in trial recruitment. *Arch Intern Med*. 2005;165:2272-7.

Tables

Table 1: Baseline characteristics of participants

Characteristic	N = 19
Age (median, IQR), years	63 (51.5 – 69)
Female sex	8 (42.1%)
Race	
White	7 (36.8%)
Black or African-American	10 (52.6%)
Other	2 (10.6%)
Education level	
Less than high school	0
Some high school	2 (10.6%)
High school or GED	2 (10.6%)
Some college	7 (36.8%)
College graduate	3 (15.8%)
Some post-graduate	1 (5.2%)
Post-graduate or professional degree	3 (15.8%)
Other	1 (5.2%)
Employment Status	
Employed full-time	1 (5.2%)
Employed part-time	1 (5.2%)
Unemployed	2 (10.6%)
Retired	8 (42.2%)
Disabled	7 (36.8%)
Marital Status	
Single	4 (21.0%)
Married	8 (42.2%)
Divorced or separated	4 (21.0%)
Unmarried living with partner	1 (5.2%)
Widow or widower	2 (10.6%)
RAQ score (median, range)	30 (18 – 35)
TMR2 score (median, range)	13 (8-18)

Table 2: Key themes for not participating in the clinical trial approached for and suggestions to increase participation rates

Key themes for not participating in the clinical trial	
Concern for an adverse event No prior adverse events (n = 11) Prior experience with medication adverse events (n = 4)	"I'm kind of an old school. They come out with all this new stuff and talk about how great it is. Six months down the road, they said, boy, don't you ever touch that stuff, it'll kill you. And so I said, hey, I don't need it." "I am very hesitant about taking new medication. I'm very cautious because I'm real sensitive to them, and I -- you know, just the idea of going on to another medication, I just -- I resist that from every doctor, so -- but my declining participating in this study had to do with the fact that I had to take a new medication"
Receive inadequate treatment (n = 3)	"They weren't going to tell me the dosage. Or sometime they was going to put a fake pill in there and not tell me. So like I said, I want to know what's going in my body at all times. So that's why I declined it"
Participation too burdensome (n = 10)	"Yeah, I'm too old. Plus I've got other issues, and then time constraints that I would be putting more pressure on myself to be here and be there, and other stuff in my schedule now, this late in life, it's not a good thing but if it could be made convenient, it would be different."
Mistrust in research staff (n = 2)	"I felt that I wasn't given the facts in the first beginning, so it was more easy to say no. With that presentation I wouldn't have gotten into it, because like I said, it was omission. That's just like if I tell you to eat this apple butt I know that there's a worm in it. I already know there's a worm in it, but you don't, but I'm telling you to eat it."
Suggestions to improve participation	
Making participation	"I really don't want to go that distance for my checkup, I told her it would be better if I could go to xxx facility which is not far from me, but she said it was only there at the main facility."

easier (n = 3)	
Providing more information on drug safety (n=3)	"If I had seen any kind of preliminary work. They mentioned that there's been some animal studies and I would have liked to have seen the stats on that and that sort of thing."
Involvement of physicians known to the patient (n=6)	"Yeah, I would do it if my doctor had told me to do it. You know, but if it's just to help some drug company, I ain't about that."
Changes in how patients are approached by research staff (n =2)	"I think maybe the conversation should take place at a later date. When people first come into the hospital, they're bombarded with doctors and tests and everything, and so they're so concerned about their own health and what's going to happen to them next and all of that. There's so much going on and there's so much you're trying to process and so much you're trying to understand and then you're on all kind of medications and everything. I just think that's just the wrong time to approach somebody about research programs."

Figures

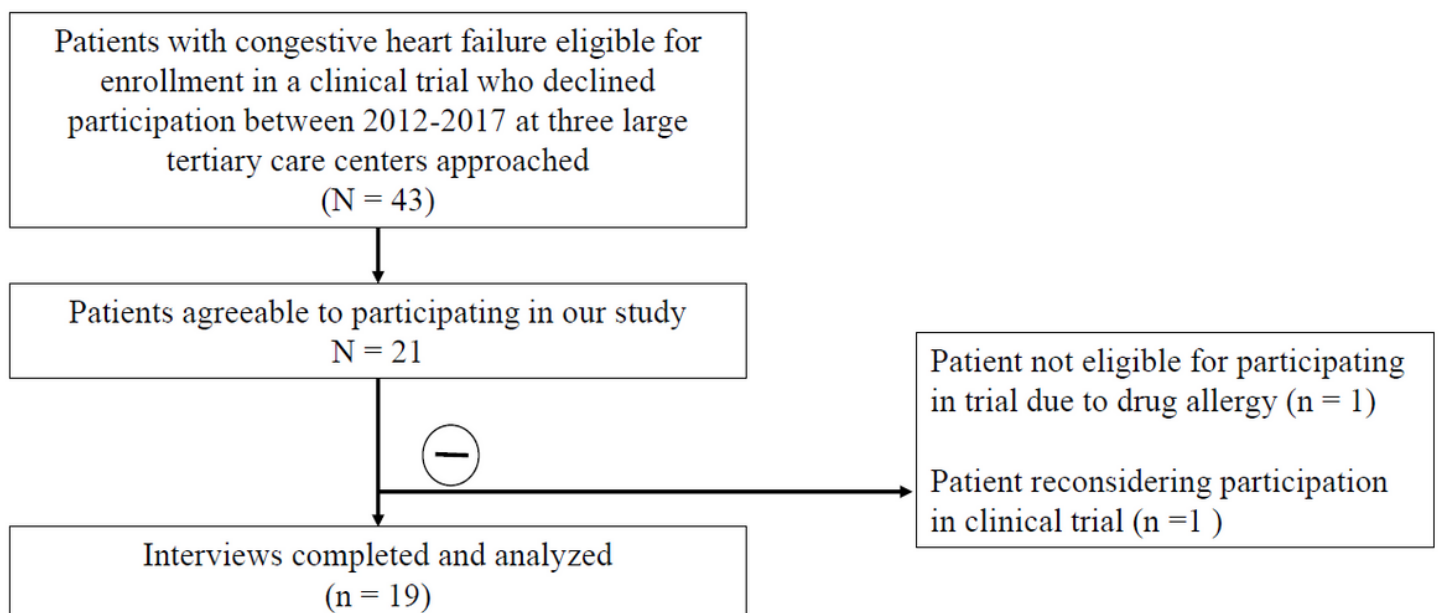


Figure 1

Patient flow

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SUPPLEMENTALMATERIAL.docx](#)