A Decentralized Clinical Trial of a Digital Intervention with Multiple Health Trackers for Heart Failure: Early Learnings and Practical Considerations

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Abstract. DT4HF (Digital Tools for Heart Failure) is carrying out, to the best of our knowledge, the only fully decentralized randomized clinical trial assessing an intervention for heart failure self-management. Participants in the study use a smart scale and activity tracker to monitor important self-management behaviors, and those in the Intervention Group also play a digital game to help further motivate adherence to these behaviors. All study activities take place remotely. In this paper, we describe our experiences recruiting and enrolling participants during the first six months of the study. We also discuss themes and challenges that are unique to decentralized trials and contribute to existing literature by describing how we have dealt with these issues and what considerations might be relevant to other researchers executing decentralized trials. While completing screening, enrollment, and installation entirely remotely presents challenges, we have already begun to see some of the benefits of the decentralized design and the positive impact the study is having on participants.

Keywords: Heart Failure · Self-Management · Remote Monitoring · Decentralized Trials · Digital Health

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1 Introduction

1.1 Background and Related Work

More than six million Americans live with heart failure (HF), a chronic condition which is the leading cause of hospitalization among older adults in the U.S. [5] HF is expected to increase in prevalence, incurring tens of billions of dollars in costs in the coming years [1]. Furthermore, there are widening geographical [2, 3] and racial [4] disparities in the HF patient population. For example, Mujib et al. [2] found evidence of a "heart failure belt" spanning the southeast United States, with age-adjusted mortality rates 69% higher than the national rate. Given the chronic nature of HF, diligent self-management is required to improve outcomes, involving adherence to a regimen of medication, regular physical activity, weight management, and monitoring of diet and fluid intake. Self-management may be aided by digital health technologies that allow for continuous monitoring and measurement, track important information, and provide feedback directly to users.

The increasing uptake of novel digital health tools for managing and monitoring many elements of one's health has coincided with a trend towards decentralized clinical trials (DCTs), or trials where activities "occur at locations other than traditional clinical trial sites," such as virtually or in participants' homes [8]. The Clinical Trials Transformation Initiative (CTTI), which was co-founded by the U.S. Food and Drug Administration (FDA) and Duke University, released recommendations for the conduct of DCTs in 2018, citing possible improved retention, greater control for participants, and increased participant diversity [6]. In 2020, the Decentralized Trials and Research Alliance was launched by the FDA and more than 50 other health-focused organizations, from pharmaceutical companies to patient advocacy groups [7]. In May 2023, the FDA released draft guidance on DCTs, stating that, "by enabling remote participation, DCTs may enhance convenience for trial participants, reduce the burden on caregivers, and facilitate research on… diseases affecting populations with limited mobility or access to traditional trial sites" [8].

Indeed, many clinical trials have incorporated elements of remote participation in their design, aided largely by digital health devices such as wearable sensors and mobile apps which can both collect data passively to be shared with research teams and can serve as elements of health interventions for patients managing chronic health conditions. Tools like Apple's ResearchKit [23] have made it possible for researchers to set up studies that can easily access and integrate the rich data collected through or synced with the devices people use every day. Trials focusing on HF or cardiovascular health more broadly have provided participants with step counters/activity trackers [9–13], weight scales [10], blood pressure monitors [10, 11], sleep trackers [11], and ECG sensors [13], among others. While embracing elements of remote trial participation, these studies are not completely decentralized. Nearly all of them are still tethered to some primary clinical site through which they recruit participants. A few notable exceptions are the MyHeart Counts study [22], which participants can join by downloading the app and going through an eConsent process, and Health eHeart [14], which recruits participants online. However, these studies are focused on heart health broadly, not just HF.

To the best of our knowledge, our study, DT4HF (Digital Tools for Heart Failure), is the first fully decentralized trial for HF patients. DT4HF assesses the efficacy of a sensor-controlled digital game (SCDG) for helping older adults with HF improve adherence to key self-management behaviors, i.e., daily physical activity and weight monitoring. We recruit participants entirely remotely, with a focus on the seven southern states that have higher rates of HF, in hopes that the decentralized approach may target a portion of the patient population that is of high need and are underserved [2, 3].

1.2 Research Aims

In this paper, we discuss major themes that have emerged six months after beginning enrollment. We build upon prior work by describing screening, enrollment, and installation processes as one of the first fully decentralized trials testing a digital intervention for HF self-management. We contribute to existing literature by providing detailed descriptions of the unique challenges and benefits of decentralized studies that we have seen firsthand in DT4HF, as well as strategies used to address these issues. We also discuss our early experiences with recruitment and compare our recruitment rate with those of similar centralized studies. As clinical studies increasingly move towards decentralization, we hope our findings and reflections may be useful to others planning or executing similar studies.

2 Methods

2.1 Study Procedure

DT4HF is a randomized clinical trial that aims to assess the efficacy of a SCDG for helping older adults with HF improve adherence to important self-management behaviors (weight management and physical activity). In total, the study will recruit two-hundred participants with HF, each randomized to either the Intervention (IG) or the Control Groups (CG). All participants are 45 years of age or older, have been hospitalized for HF within the past 12 months, and live in one of the seven southern U.S. states (Alabama, Arkansas, Georgia, Louisiana, Mississippi, Oklahoma, and Texas). Participants in both groups receive a Withings smart scale and activity tracker in the mail to regularly track their daily weight and steps. The IG also plays the SCDG, Heart Health Mountain, developed and tested by the study team [15], which collects data from the scale and tracker and provides personalized feedback to continually motivate participants to actively engage in important behaviors. In the game, participants progressively climb a mountain by adhering to their self-management behaviors and completing mini-games and challenges containing educational information related to HF. The game was designed using behavior change theoretical frameworks, specifically the Fogg Behavioral Model and self-determination theory, as described in detail elsewhere [21]. Our study protocol, which describes the methods in greater detail, is also available elsewhere [16].

The first participant was enrolled in the study in November 2022. As of May 2023, twenty participants have been enrolled across five of the seven eligible states.

Recruitment. For the first six months, our primary method of recruitment has been through TrialFacts, an online recruiting company [20]. TrialFacts distributes advertisements through social media to people who appear to meet our inclusion criteria. Potential participants then complete a survey demonstrating interest and indicating a time that works for them for a screening call with the study team.

Screening and Enrollment. Once a potential participant has demonstrated interest and been referred through TrialFacts, a member of our team conducts a screening call to confirm eligibility (i.e., age, ability to walk independently, willingness to install apps with remote support, WiFi status at home). During this call, our team informs potential participants that they need to provide a hospital discharge summary showing that they were hospitalized for HF within the past 12 months. If they are not able to do this, they may provide written confirmation of their HF diagnosis and recent hospitalization from their healthcare provider with a list of current medications. Potential participants also complete a brief mini-cognitive screening [17] to assess cognitive eligibility for the study. If a potential participant is confirmed as eligible and has shared their discharge summary, a study team member calls the participant and goes through the Informed Consent document, which the participant electronically signs.

Installation of Apps and Devices. After a participant has consented to participate, their devices (Withings Body scale and Pulse HR activity tracker) are sent by mail. All participants receive printed instructions for installing these devices, the accompanying Withings Health Mate app, and the digital game app (for participants in the IG). Participants in the CG receive printouts of standard evidence-based HF educational content [18] which IG participants receive through playing the game. All participants are instructed not to install their devices until a study team member calls to walk them through the installation, which can take place either on Zoom or over the phone (depending on the participant's preference). Installation calls have taken anywhere between twenty minutes and two hours.

2.2 Assessment of Early Learnings and Practical Considerations

To reflect upon the major themes and issues that have arisen during the initial months of enrollment, our team extracted data from the project management platform, Trello, to glean information related to participant recruitment, such as the amount of time between first contact and enrollment in the study and the average number of touchpoints with each potential participant. We reviewed all data in Trello[1] on the progress of participants from the time they initially expressed interest, continuously as they progressed through the 24 weeks of data collection. We also reviewed notes taken by the technical support team

[1] Trello is used systematically by the study team to log notes following any touchpoint with participants during the initial phases of the study (recruitment, enrollment, and installation) and to track their progress over the course of the study. If 3 days elapse where no data is synced from a participant's study apps or devices, the study team contacts them to address any issues (whether technical, such as installing a new WiFi router at home, or logistical, such as going on vacation). These incidents are then logged as official "protocol deviations" and are out of the scope of this paper.

from installation calls with newly enrolled participants. Additionally, we discuss four qualitative interviews which informed us directly about participants' experiences in the study. By reporting on the unique challenges and benefits that come with decentralized studies and sharing how our team has addressed these issues, this paper contributes to existing literature on conducting decentralized clinical trials that leverage digital tools.

3 Results

3.1 Overview

Six months after our first participant was enrolled (from November 2022 to May 2023), we enrolled twenty participants, including nine IG and eleven CG participants (see Table 1), which is 27.8% of the 72 patients who completed the pre-screening survey through TrialFacts. Of the twenty enrolled participants, five have dropped out (25% attrition was allowed in the study design [16]). The average age of participants is 58.5, and seventy percent of the currently enrolled participants are male. Eighty percent are White, fifteen percent are Black or African American, and five percent are American Indian or Alaskan Native. The participants live in five of the targeted seven states. Fourteen of the twenty live in Texas; two participants live in each of Georgia and Oklahoma; and one participant lives in each of Louisiana and Alabama. The average distance (in miles) of participants' zip codes from the UT Austin campus zip code is 310.4 (min: 8.4, max: 928). From the time of first contact until the date of installation of the participant's study apps and devices, the average elapsed time was 15.4 days. During this time, our study team had an average of 3.4 contacts with each participant (e.g., a follow-up on missed calls or a reminder to send discharge summaries).

Table 1. Recruitment data for enrolled participants

Participant number	Points of contact before enrollment	Days between first contact and equipment installation	Distance from UT Austin (miles)	State	Dropped since enrollment?
1	6	16	88.8	TX	Yes
2	3	23	149.5	TX	No
3	3	11	140.7	TX	No
4	2	11	307.4	TX	No
5	4	37	730.3	AL	No
6	3	17	913.1	GA	No
7	3	7	239.3	TX	Yes
8	4	27	211.1	TX	Yes

(*continued*)

Table 1. (*continued*)

Participant number	Points of contact before enrollment	Days between first contact and equipment installation	Distance from UT Austin (miles)	State	Dropped since enrollment?
9	6	12	149.2	TX	No
10	2	10	20.7	TX	No
11	3	13	397.9	OK	No
12	4	21	104.9	TX	No
13	1	9	126	TX	No
14	3	12	8.4	TX	No
15	2	14	511.4	LA	No
16	2	14	223.1	TX	No
17	6	N/A	928	GA	Yes
18	3	9	480	OK	No
19	5	14	373	TX	No
20	2	16	104.9	TX	Yes
Average	3.4 ($\sigma = 1.42$)	15.42 ($\sigma = 7.07$)	310.39 ($\sigma = 269.04$)		

3.2 Themes and Challenges

Screening. A potential participant's completion of an initial screening questionnaire is far from an automatic indicator that they will be willing and able to enroll in the study. Even though the screening questionnaire asks potential participants to commit to answering their phones at the time they designate, many do not. The screening call requires potential participants' full attention for ten to fifteen minutes, as it includes a brief cognitive screening, so the call cannot take place while they are doing something else, such as driving or shopping. Of the potential participants that can be reached for a screening call, some turn down participation in the study (see Table 2) upon realizing that some effort will be required of them (e.g., completing surveys, installing digital tools). Since participation in the study comes with a small financial incentive, some participants are enticed by this prospect without realizing what is necessary on their part. Nine of the seventy-two initially screened potential participants ultimately declined participation; an additional twenty-two were lost to follow-up. Finally, the biggest barrier to enrollment has been not meeting inclusion criteria. Even though it is a part of the initial screening questionnaire, potential participants often do not meet the criteria of having a hospitalization related to HF in the past 12 months. Twenty-one of the seventy-two initially screened potential participants were ultimately not eligible for the study—twelve of these had not had a hospitalization in the past 12 months, eight did not have a HF diagnosis or related hospitalization. This discrepancy between the information the patient provides

through their initial screening questionnaire and the facts of their medical diagnoses and hospitalizations is a challenge for decentralized trials, as traditional clinical trial sites would be able to verify and screen for this information internally.

Table 2. Outcomes for all potential participants screened in first 6 months

Not eligible: No HF diagnosis or related hospitalization	8 (11.1%)
Not eligible: Hospitalization was not in previous 12 months	12 (16.7%)
Not eligible: Age	1 (1.4%)
Turned down participation	9 (12.5%)
Lost to follow-up	22 (30.6%)
Enrolled in study	20 (27.8%)
Total	**72**

Enrollment. Once a potential participant is deemed eligible from the screening call, a big hurdle is receiving a copy of their discharge summary from their recent hospitalization and validating the diagnosis of HF. Participants can either scan or photograph a hard copy of their discharge summary or download it electronically through their patient portal, and then upload the file to the study's secure platform. Given an older study population, uploading and transferring files can be intimidating or discouraging to some participants. It is common for the study team to follow up several times to assist participants with locating and/or uploading the correct file.

Additionally, some potential participants have had a recent hospitalization but not a HF diagnosis; they might have had, for example, a heart arrhythmia or a cardiac arrest. Health literacy can be a relevant factor, as potential participants might think they are eligible for a HF study given some kind of cardiac-related hospitalization. This is also a challenge traditional trials would not face, as they are generally connected to a hospital or clinic that can automatically access discharge summaries and verify diagnoses; patients are not usually in the position of vouching for their own diagnoses.

While the process of obtaining and validating potential participants' discharge summaries is the most time-consuming part of the enrollment process and requires the most effort on the part of the patient, the study team believes it is the best way to rigorously assess an important inclusion criterion, especially given that the study is not tied to any clinical site.

Installation of Apps and Devices. Once a participant has been enrolled in the study after completing Informed Consent, they receive their study devices (Withings Body scale and Pulse HR activity tracker) by mail. A member of the study team conducts a telephone or Zoom call to walk them through the installation of the devices, as well as the Withings app and, for game group participants, the Heart Health Mountain app. While installation calls with Control Group participants are typically shorter given that there is one less thing to install and explain, the length of all installation calls vary considerably

depending on the participant's familiarity with apps and sensor-connected devices, WiFi or syncing issues, or communication challenges due to being remote.

Technical issues while syncing the scale or activity tracker to the Withings app on the participant's phone happen fairly frequently and are generally not due to user error or communication issues. The scale had consistently more issues syncing to the Withings app on participants' phones than the watch. Troubleshooting steps available through the Withings website often helped, such as taking out batteries and restarting the scale, holding the phone near to the scale, making the phone "forget" the device, or attempting the installation on a different device such as a tablet. Slow WiFi was also occasionally the cause of syncing issues. When troubleshooting efforts still did not resolve syncing or other technical issues, the issues usually resolved themselves over the course of a few days or through a troubleshooting call at a later time. We were able to progressively foresee and address certain technical issues; for example, activity trackers could not be successfully installed with a low battery, so as the study progressed and our stock of activity trackers began to lose battery charge, the team began plugging the trackers in to charge prior to mailing them to participants.

Outside of technical issues, installation calls varied in that participants themselves ranged significantly in their familiarity with digital health devices, technological literacy, and confidence in navigating the installation. Typically, the study team member completing the installation began by asking participants whether they had ever used similar devices before; some regularly used Fitbits or Apple Watches, others had never used any kind of health tracker before. Some participants came into the call having already prepped and charged devices and downloaded the required apps, while others required step-by-step instruction and were more unsure and tentative during the installation. For participants who were less experienced with health trackers and more easily discouraged, consistent encouragement was vital. When roadblocks arose with these participants (such as having clicked the wrong button and being unable to return to the right screen), the remote design of the study proved difficult as the study team was not able to intervene except through verbal guidance, and while some sort of remote administration tool may have helped address this issue, this was not something we considered for privacy reasons. Instead, strategies such as having the participant send a screenshot or verbally describe every option visible on the screen was helpful. All participants were ultimately able to install their devices and apps with the remote support provided by the study team.

4 Discussion

As previously mentioned, one of the elements of the study that presents added challenges given the decentralized design is the recruitment of participants, as DT4HF has no primary study site tied to a clinical database and large group of patients. After the first six months of the study, however, our recruitment rate stands at 27.8% (twenty participants enrolled out of seventy-two who completed our initial screening questionnaire). Despite being a fully decentralized study, our recruitment rate may be comparable to and, in some cases, higher than, similar studies with traditional trial sites. A comprehensive review of recruitment, consent, and retention rates of hundreds of trials found that the

median recruitment rate (participants per trial site, per month) was 0.95 [19]. Having recruited twenty patients in six months, our recruitment rate is 3.33, which would put us just below the 80th percentile (3.70) of studies in the review. Of course, this review encompasses a wide range of study types and focus areas; it serves as just one reference point for trial recruitment rates. As for studies focused on HF specifically, while we did not complete a comprehensive review, we found recruitment rates to range significantly, from less than 1% [13] to about 40% [10]. While there is no single reliable metric to serve as a reference point for clinical trial recruitment rates, this study's rate certainly does not seem to be significantly lower than traditional clinical studies (in some cases it may even be higher), despite the additional challenges in screening and enrolling patients that have arisen from the study's decentralized design. Thus, while it may be a good idea to plan for the possibility of lower recruitment rates and make sample sizes estimates accordingly, the prospect of lower recruitment rates in decentralized trials should not dissuade researchers from this study design. Regardless of the circumstances, it is important for researchers to analyze recruitment rates early on in trials to inform their strategies. As such, our team is currently pursuing additional avenues for recruitment in an effort to raise our recruitment rates over the course of the 24 months of recruitment that remain. For example, the strategies we are currently pursuing include (1) expanding from working with only social media marketing-based recruitment partners to Internet-search based recruitment partners (allowing us to advertise our study to people who are actively searching for information, resources, or research opportunities related to HF), (2) utilizing word-of-mouth and networking at local clinical settings to solicit interest, (3) radio advertising in areas that correspond to the zip codes with the highest concentration of HF cases in the U.S.

A final strategy that we used to boost our recruitment rate was reexamining the inclusion criteria with a focus on what was causing the most interested participants to be ineligible. For example, initially, our inclusion criteria required having been hospitalized for HF within the past 6 months, but this was causing a large number of interested participants to be ineligible. To address this, we discussed the topic with clinical experts and submitted an IRB update proposing to adapt our inclusion criteria to include those hospitalized within the past 12 months, which allows us to maintain our focus on HF patients with recent hospitalizations while being inclusive of more potential participants. We advise other researchers who may be assessing their recruitment rates and strategies to ask themselves where it might be possible to expand either their inclusion criteria or the places they are looking to recruit.

While our study is in its early stages, initial assessments of participants' experiences have begun to shed light on the potential benefits of the study's decentralized design. To date, four qualitative interviews have been completed with participants.[2] Two of the four interviewees had used health self-tracking devices prior to the study, and they both reported positive experiences in the study; they felt that regular use of their devices helped them keep tabs on their HF and feel confident that they were on the right path. The other two interviewees had never used such devices previously, but they also reported extremely positive experiences. One of these interviewees shared that prior to the study,

[2] One out of every five participants will be interviewed when they reach the 12-week mark (the halfway point in the study).

he thought "that stuff was for treehuggers." This participant has had a life-changing experience in the study, claiming that using health trackers for the first time has helped him care about his health again; his devices have become "integral and paramount" to his daily routine, leading to him having more energy, motivation, and even better relationships with those around him. The second interviewee who also had never used any digital trackers before stated that he "just never thought about it," but now says that he "will not be without some sort of monitor, even after the study is over." This participant lives in a remote area more than one hundred and fifty miles from the nearest large city (more than a quarter of participants in the study live more than fifty miles from the nearest large city). The study's decentralized design may thus allow participants like these to be more engaged and derive more value from the study, as they are not required to make regular visits to a central clinic, which are usually found in larger cities. Given that two of the four interviewees did not use or were not interested in using digital tools prior to the study, their motivation to participate in a study on digital tools for self-management may not have been sufficient to travel long distances multiple times to a central research site. However, with a small sample size given the study is still in its early stages, it remains to be seen whether we will continue to see this trend.

On a final, related note: an important aspect of our study is the personalization of both our approach to working with participants and the digital tools themselves. Participants come into the study with very different backgrounds, self-management preferences, and experiences with technology. Participants' motivations for joining the study (as reported in their initial screening questionnaires) range from looking for knowledge and educational resources, to looking for accountability, to just wanting to participate in research. Some were newly diagnosed and looking to learn the ropes of self-management, while others have lived with HF for years, even decades. With the variation in participants' levels of familiarity with technology and comfort using new digital tools, the study team can quickly adapt over the course of the installation (i.e., by simplifying explanations, taking things more slowly, etc.) What really shapes participants' experiences in the study, however, is the digital tools themselves, and this is even more true in a decentralized study where the in-person element is removed, and the focus is fully on the digital tools. As such, it is critical for decentralized studies testing digital tools to ensure that they can be adaptable, encompassing a range of participants' potential contexts and preferences. Future research should seek to explore additional ways that patients' unique circumstances, goals, and/or health management preferences could be incorporated into health interventions.

5 Conclusion

The first six months of DT4HF have demonstrated both the challenges and the potential advantages of a decentralized design for a clinical trial. Screening and enrollment in particular come with the challenge of potential participants having to vouch for their own diagnosis, which they may not be aware is not a fit for the study's eligibility criteria. For patients who are indeed eligible, the study faces the challenge of not being able to verify a potential participant's diagnosis without a hospital discharge summary, which can be difficult for participants to locate and transmit virtually. Remote installations of

digital tools often come with technical issues, but remote support from the study team has been sufficient to ensure that all study participants are able to get their equipment set up properly. While the study is still in its early stages, we have seen some advantages of the decentralized design in that we have successfully enrolled multiple participants who live in remote areas who may not have been able to participate in a centralized trial as easily. Our early assessments of participants' experiences have indicated that some participants have come to view the digital tools as crucial in their self-management routines, despite having never used anything similar before the study. As our study progresses and as other studies testing digital health interventions evolve, it is vital to ensure that interventions can adapt to variations in patients' health-related preferences and circumstances in order to create meaningful, positive change in their lives.

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