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Baseline Characteristics and Barriers to Recruitment in Cardiac and Pulmonary Rehabilitation NIH Funded Trials

Crystal Grimshaw, MS[1], **Steven J. Keteyian, PhD**[1], **Roberto Benzo, MD, MS**[2], **Joseph Finkelstein, MD, PhD**[3], **Daniel E. Forman, MD**[4], **Diann E. Gaalema, PhD**[5], **Pamela N. Peterson, MD, MSPH**[6], **Paula T. Einhorn, MD**[7], **Antonello Punturieri, MD, PhD**[7], **Susan Shero, RN, MS**[7], **Jerome L. Fleg, MD**[7]

[1]Henry Ford Health, Detroit, MI

[2]Mayo Clinic, Rochester MN

[3]Icahn School of Medicine at Mount Sinai, NY

[4]Department of Medicine (Cardiology and Geriatrics), University of Pittsburgh, and the Geriatrics, Research, Education, and Clinical Center (GRECC), VA Pittsburgh Healthcare System, Pittsburgh, PA.

[5]University of Vermont, Burlington VT

[6]Denver Health Medical Center and University of Colorado Anschutz Medical Center, Denver and Aurora CO

[7]National Heart, Lung, and Blood Institute, Bethesda MD

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In the United States, approximately 30% of patients who qualify for cardiac rehabilitation (CR) enroll[1] and only about 3–4% of patients eligible for pulmonary rehabilitation (PR) enroll,[2] despite both programs representing a class I guideline-recommended treatment strategy. In 2018, the National Heart, Lung, and Blood Institute and the National Institute of Aging funded four CR and two PR phase two clinical trials to address the following issues: (a) test strategies that will lead to increased use of CR and PR in the United States population who are eligible based on clinical guidelines, (b) reduce disparities in the use of CR and PR based on age, sex, race/ethnicity, and socioeconomic status (SES); and (c) test whether increased use of CR and PR, whether by traditional center-based or new models, is accompanied by improvements in relevant clinical and patient-centered outcomes, including exercise capacity, cardiovascular and pulmonary risk factors, and quality of life.[3]

Corresponding author: Crystal Grimshaw, MS, 6525 Second Avenue, Detroit, MI 48202, cgrimsh1@hfhs.org.

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Study-specific challenges due to the novel coronavirus disease 19 (COVID-19) were previously reported.[4] For all six clinical trials, this paper provides an update of study-specific demographics, as well as a summary of recruitment challenges and how they were addressed.

PROJECT UPDATES

The six funded trials represent a wide variety of patients with an average age of ~64 yr, ~35% women, and ~24% Black race. The main barriers across all six trials were (a) an interruption in trial conduct and subsequent operational adjustments due to COVID-19, (b) a modest lack of access to technology for remote delivery models, and (c) a low interest in participating in CR or PR. Listed below is a summary of relevant issues for each trial.

Project Title: Improving ATTENDance to Cardiac Rehabilitation (iATTEND). Principal Investigator: Steven J. Keteyian, PhD, Henry Ford Hospital, Detroit, MI (HL 143099).

Trial eligible patients were enrolled into iATTEND between March 2019 and December 2022. As shown in the table, 32% of subjects were women, 53% identified as Black (66% women), and 34% had an annual income ≤ $50,000. The mean age was younger than planned (59 ɑ 12 yr); however, 34% (n=95) were ≥ 65 yr (71 ɑ 5 yr).

Like most other clinical trials that were underway when COVID-19 started in the United States, iATTEND suspended operations between mid-March and August 2020. At that time, 26 patients were actively participating in either the experimental (hybrid CR involving telehealth and center-based CR) or usual care (center-based CR only) arms of the trial. The target sample (n) originally planned for iATTEND was 270. However, to partially compensate for the varying loss of data from the 26 subjects who had their trial participation stopped, we enrolled 282 subjects; average enrollment rate was ~7 subjects/mo.

The reasons patients do not regularly attend CR are many (e.g., co-morbidities, lack of transportation, dependent care duties), yet central to iATTEND is the premise that hybrid CR (i.e., virtual, synchronized telehealth) could help mitigate several of the known barriers and improve attendance. Implementing a hybrid CR model requires that patients have access to a smart device and exercise equipment. Among patients eligible and contacted to participate in iATTEND, 96% had a smart device and 19% stated no access to proper exercise equipment, either at home, work, or in their community.

Project Title: Improving Participation in Cardiac Rehabilitation Among Lower-Socioeconomic Status Patients: Efficacy of Early Case Management and Financial Incentives. The Healthy Lifestyle Program (HeLP) Study. Principal Investigator: Diann E. Gaalema, PhD, University of Vermont, Burlington, VT (HL 143305).

The Healthy Lifestyle Program (HeLP) study seeks to test the efficacy of case management or incentives for completing CR sessions, alone, and in combination, on improving CR participation among patients with lower SES. Details of the trial can be found elsewhere.[5] We began recruitment in December of 2018. The only major recruitment challenge during the trial was restrictions put in place during the COVID-19 epidemic. Due to COVID-19 restrictions, recruitment was shut down completely for 14 wk (March 16 2020-May 22

2020) and severely reduced for another 4 wk (May 22 2020-June 16 2020) as research staff were unable to access hospitalized patients.

Following resumption of research activities, recruitment was bolstered by adding an additional clinical site. Drawing from those eligible for CR at any one of the three clinical sites, we completed recruitment in November 2022. As can be seen in the Table, the sample recruited was reflective of the clinical population and geographic area recruited from. All participants, by entry criteria, were lower SES. We recruited women representative to the rates they are present with eligible diagnoses (35%), and we recruited a sample that was three times as diverse (16% minorities) as the geographic area (95% non-Hispanic White). Approximately a quarter of our sample was from rural counties and participants were relatively young (57.7+11.4 yr), with high rates of smoking at the time of their qualifying event (44%). Educational attainment was also limited, with only 26% having any type of college degree (2-yr, 4-yr, or advanced).

Project Title: Enhancing Cardiac Rehabilitation Adherence Through Home-Based Rehabilitation and Behavioral Nudges (ERA Nudge). Principal Investigator: Pamela Peterson, MD, Denver Health Medical Center, Denver, CO (HL 143324).

The overarching goal of the project, Enhancing Cardiac Rehabilitation Adherence through Home-based Rehabilitation and Behavioral Nudges: ERA Nudge, is to increase adherence and completion of CR in an urban, low SES, and diverse population. This single site trial was performed at Denver Health Medical Center, a large urban integrated safety net health system. The project utilized a multi-pronged approach to increase enrollment, adherence, and completion. We are testing the *choice* of home versus hospital-based rehabilitation and behavioral "nudge" messages. The acceptability and uptake of a home-based program among a safety net population is unknown. Behavioral nudges utilize principles from the fields of behavioral economics and cognitive psychology and have the potential to augment the impact of messaging interventions to modify behavior and enhance adherence.[6–9] Recruitment was suspended for approximately 6 wk when COVID-19 related lock-downs occurred. Despite COVID-19, we were able to exceed our recruitment goals, randomizing 435 patients (goal 400). Enrollment is complete with 315 patients having completed the program and follow-up is ongoing. Our study population (Table) is representative of our health care system in that it is racially and ethnically diverse and of low SES (17.9% Black, 49.9% high school education or less).

Project Title: Modified Application of Cardiac Rehabilitation for Older Adults (MACRO). Principal Investigator: Daniel E. Forman, MD, University of Pittsburgh, Pittsburgh, PA (AG 060499).

The Modified Application of Cardiac Rehabilitation for Older Adults (MACRO) is a National Institute of Aging-funded trial at University of Pittsburgh and Washington University. MACRO tests the utility of a coaching intervention to improve functional enhancement attributable to enrollment and participation in existing clinical CR programs (all which offered options for site-, remote-, and hybrid-formats) for adults eligible for CR aged ≥70 yr. Innovations of MACRO include holistic risk assessments, flexible conceptualization of the CR format, motivational prompts, and facilitated deprescription

of sedating medications. MACRO was profoundly affected by COVID-19 as the original protocol entailed frequent face-to-face encounters, which were elemental for engagement, fidelity, and safety. While MACRO was originally launched in October 2019, operations were entirely discontinued by the DSMB in March 2020. All of its 42 then randomized, active enrollees were mandated to be released. The study team was told to revise the protocol to be safe and feasible for a post-COVID world. A methods report[10] describes an extensively redesigned MACRO protocol that is achievable remotely, but which preserved the essential premise and aims of the trial. Key points include shift of the primary endpoint the Short Physical Performance Battery[11] to the Activity Measure for Post-Acute Care Computer Adaptive Test[12]. MACRO relaunched with zero enrollment in Pittsburgh and St. Louis in December 2020. The revised methods enable enrollment from a wider catchment area. Enrollment is now >300 (28.6% women, 11.2% Black) and on target for completion by July 2023 (Table).

Project Title: Increasing Adherence to Pulmonary Rehabilitation After COPD-Related Hospitalizations. Principal Investigator: Roberto Benzo MD, MS, Mayo Clinic, Rochester, MN (HL 142933).

Despite proven benefits, the proportion of people with chronic obstructive pulmonary disease (COPD) who receive PR after a COPD-related hospitalization is outstandingly small. The current model of a center-based PR program fails to address the needs of many patients with COPD. After the COVID-19 epidemic, telehealth has become a viable option for patients referred to center-based rehabilitation.

After a COPD-related hospitalization (exacerbation or pneumonia), patients were randomized to either home-based PR or Choice (referral to conventional center-based PR or telehealth-based PR) after hospital discharge. Starting PR after hospitalization is challenging. Of 1137 patients contacted, 947 (83%) declined the PR. Reasons given included: being overwhelmed after the hospital admission, 246 (22%); not interested, 133 (12%); not willing to participate in research, 57 (5%); already in a research study, 133 (12%); already having an active lifestyle and not perceiving the need of PR, 132 (12%); already enrolled in center-based PR or a post-hospitalization monitoring program, 189 (17%); and 57 (5%) claimed to have other priorities. Of 225 patients (45% women, 95% white) randomized to PR or Choice of home or center-based PR, 30% did not start PR. Ninety-nine percent of the participants in the choice arm opted for home-based PR. Participants strongly preferred home-based PR over the center-based option when they could choose. The interim adherence (completion) to home-based PR in this study is 10%, a 3-fold increase compared to the reported completion having only a center-based option[13]. Increasing the options for PR after a COPD-related hospitalization may represent a valid alternative to improve the current reported dismal uptake of PR (3%) after hospital admission

Project Title: Comprehensive Health Informatics Engagement Framework for Pulmonary Rehabilitation (CHIEF-PR). Principal Investigator: Joseph Finkelstein, MD, PhD, Icahn School of Medicine at Mount Sinai, New York, NY (HL 143317).

The Comprehensive Health Informatics Engagement Framework for Pulmonary Rehabilitation (CHIEF-PR) was introduced to facilitate PR referrals, initial assessments, completion rates, and PR maintenance in patients with COPD after an acute exacerbation. The CHIEF-PR supports a multilevel approach that addresses current barriers to PR uptake and completion. On the healthcare level, it uses data from electronic health records for clinical decision support to identify COPD patients eligible for PR;[14] on the provider level, it helps heighten provider awareness about PR;[15] and on the patient level, it supports home-based telerehabilitation[16] that empowers patients with interactive information about benefits of PR[17] and engages them on a daily basis in following their individualized pulmonary PR program.[18] The objective of this study is to demonstrate in a randomized controlled trial that CHIEF-PR is effective in increasing the use of PR in patients after an acute exacerbation and improving clinical and patient-reported outcomes.

Overall, all 120 patients of the planned sample size were enrolled in the study. Participants age was 70±12 yr, 56% were females, and 36% were Black, 50% spent 12 yr or less in school. Due to the COVID-19 pandemic, the study was suspended during the stay-at-home order in New York City from March to May 2020. To enhance patient safety in the post-lockdown period and to continue with patient enrollment, a protocol for remote assessment of exercise capacity[18] was implemented, allowing patient assessment to be successfully conducted at their homes. Preliminary analysis of the study results suggests increased participation and higher PR completion rates in the intervention group as compared to the control as well as improvement in patient-reported outcomes.[19 20]

DISCUSSION

Despite both the interruption from the COVID-19 pandemic causing several of the trials to revamp protocols and other identified barriers to recruitment, all studies are tracking toward completion. A total of 1,548 patients were recruited, allowing the investigators to study at-risk populations that are often under-represented and understudied in CR and PR. Emphasis on diverse trial participation resulted in a high representation of women, Blacks, and persons of lower SES, often significantly underrepresented in rehabilitation clinically and in trials. Additionally, five of the funded studies incorporate a non-traditional model for CR and PR delivery, providing insight on alternate ways of conducting these programs to improve enrollment and participation. The sixth trial led by Dr. Gaalema assessed the impact of financial incentives on CR attendance among patients with a lower SES. All six trials align with the objectives set forth in the funding opportunities advanced by both National Heart, Lung, and Blood Institute and the National Institute of Aging in 2017.

The biggest recruitment hurdle for all the studies was COVID-19, requiring one study (MACRO) to completely stop recruitment, revise the existing protocol, and restart the trial. Two studies had to add additional CR locations to improve recruitment after COVID-19. Although access to exercise equipment and a smart device were anticipated as potential obstacles for the home-based programs, this issue did not represent a major barrier to subject

enrollment across all trials. One study reported that 83% of those who qualified for PR declined participation.

The research reported here addresses the underutilization of CR and PR and promotes use of non-traditional delivery models. The outcome data collected from the six funded trials will help programs implement novel strategies such as the remote delivery of rehabilitation services and the use of incentives and behavioral “nudges” to improve patient adherence. The five studies that incorporated a home-based model will also provide much needed safety data. Overall, this research will contribute information needed to shape the future delivery of CR and PR to patients accessing these services.

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Table.

Demographic and clinical characteristics of patients participating in the National Institutes of Health funded cardiac and pulmonary rehabilitation clinical trials

Trial Name	**iATTEND**	**HeLP**	**ERA Nudge**	**MACRO**	**Increasing Adherence to Pulmonary Rehabilitation After COPD-Related Hospitalizations**	**CHIEF-PR**
Primary Outcome	Effect of remote/ home-based CR on attendance	Effect of financial incentives and/or case management on CR attendance	Effect of home vs hospital-based CR and nudge messages on adherence	Effect of CR on Short Physical Performance Battery	Adherence and effectiveness of home-based PR	Percentage of eligible COPD patients completing 3-mo PR
Sample Size, n	282	192	435	294	225	120
Age, yr (mean ± SD)	59.1 ± 11.9	57.7+11.4	56.5 ± 11	76.0 ± 5.4	71 ± 9	70±12
Race						
White	42	84	69	87.8	95	30
Black	53	5	17.9	11.2	ND	36
Asian	3	2	1.2	0.3	ND	2
Native American/American Indian/Alaska Native	2	3	0.9	0	ND	2
Pacific Islander/Native Hawaiian	1	ND	0.5	0	ND	1
More than one race	ND	5	0.5	0	ND	ND
Unknown or not reported	ND	ND	10.1	0.7	ND	29
Sex						
Men	68	65	71	71.4	55	44
Women	32	35	28.7	28.6	45	56
Unknown or not reported	ND	ND	0.2	ND	ND	ND
Residence						
Rural	1	24	0	ND	34	0
Urban	99	75	100	ND	66	100
Indication for Rehabilitation						
Myocardial infarction/Acute coronary syndrome	35	46	40	6.1	ND	ND
Heart Failure	22	14	24.8	19	ND	ND

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Trial Name	iATTEND	HeLP	ERA Nudge	MACRO	Increasing Adherence to Pulmonary Rehabilitation After COPD-Related Hospitalizations	CHIEF-PR
Coronary artery bypass graft	12	15	6.4	15.6	ND	ND
Valve replacement/repair	10	11	10.3	24.8	ND	ND
Heart transplant	3	ND	ND	ND	ND	ND
Percutaneous coronary intervention	13	12	41.4	29.9	ND	ND
Coronary artery disease only	6	2	ND	ND	ND	ND
Stable angina	ND	ND	1.6	ND	ND	ND
Cardiac device placement with diagnosis of heart failure and/or ischemic heart disease	ND	ND	ND	2	ND	ND
Ischemic heart disease	ND	ND	ND	1	ND	ND
Peripheral Arterial Disease	ND	ND	ND	1	ND	ND
Other	ND	ND	ND	0.3	ND	ND
Post COPD-related Hospitalization	ND	ND	ND	ND	100	100
Education level						
<High school	4	17	20.9	1.7	37	27
High school	10	31	19.3	27.9	37	23
GED	4	8	9.7	27.9	ND	ND
Some college	29	18	23	34.7	63	30
2- yr degree	12	9	7.6	12	63	30
4- yr degree	22	12	12	16.7	ND	20
Advanced degree	19	5	7.1	18.4		20
Unknown or not reported	ND	ND	0.5	ND		ND
Employment Status						
Full time	50	ND	30.1	3.4	ND	7
Part time	8	ND	12	6.8	ND	1
Homemaker	1	ND	ND	ND	ND	ND
Unemployed	8	ND	27.6	1	ND	92
Retired	21	ND	11.7	86.1	ND	92
Disabled	12	ND	14.3	ND	ND	ND

Trial Name	iATTEND	HeLP	ERA Nudge	MACRO	Increasing Adherence to Pulmonary Rehabilitation After COPD-Related Hospitalizations	CHIEF-PR
Veteran Disability	ND	ND	ND	2	ND	
Prefer not to answer	ND	ND	2.1	ND	ND	ND
Unknown or not reported	ND	ND	2.3	ND	ND	ND
Other	ND	ND	ND	0.7	ND	ND

Data are presented as %, unless otherwise noted.

Abbreviations: iATTEND, The Improving ATTENDance to Cardiac Rehabilitation Trial; CHIEF-PR, Comprehensive Health Informatics Engagement Framework for Pulmonary Rehabilitation; COPD, chronic obstructive pulmonary disease; CR, cardiac rehabilitation; ERA Nudge, Enhancing Cardiac Rehabilitation Adherence Through Home-Based Rehabilitation and Behavioral Nudges; GED, general educational development; HeLP, Improving Participation in Cardiac Rehabilitation Among Lower-Socioeconomic Status Patients: Efficacy of Early Case Management and Financial Incentives. The Healthy Lifestyle Program Study; MACRO, Modified Application of Cardiac Rehabilitation for Older Adults; ND, no data; PR, pulmonary rehabilitation.