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Design and Participant Characteristics for a Randomized Effectiveness Trial of an Intensive Lifestyle Intervention to Reduce Cardiovascular Risk in Adults with Type 2 Diabetes: The I-D-HEALTH Study

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Abstract

Intervening in Diabetes with Healthy Eating, Activity and Linkages To Healthcare (I-D-HEALTH) is a community-based randomized trial evaluating the effectiveness of a group-based adaption of the Look AHEAD intensive lifestyle intervention. Most potentially eligible patients were identified through electronic medical record queries or referral to a diabetes resource hub. Trial enrollees had a usual source of primary care, elevated body mass index (BMI) and type 2 diabetes.

I-D-HEALTH participants were randomized to either standard care alone or standard care plus free-of-charge access to a group-based lifestyle intervention (GLI) offered by the YMCA. GLI participation was encouraged, but not required, for the latter group. The primary outcome is percent weight change over 6, 12 and 24 months. Secondary outcomes include direct intervention costs and direct medical and non-medical expenditures, as well as changes in systolic blood pressure, hemoglobin A1c and cholesterol.

Among 331 I-D-HEALTH participants, 167 were randomized to standard care and 164 to GLI. The mean age (± standard deviation) in each group was 57.1 years (±12.2) and 57.6 years (±10.5), respectively. Mean BMI was 34.9 kg/m^2 (±7.3) among standard care participants and 36.2 kg/m^2 (±7.8) among GLI participants. In both groups, approximately one third of participants were non-Hispanic Whites. We detected no significant differences between groups in mean systolic blood pressure, hemoglobin A1c or total cholesterol (P>0.05 for all characteristics above).

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Conflicts of interest: None

The I-D-HEALTH study enrolled a diverse sample of adults with diabetes and offers a unique opportunity to evaluate the effectiveness of offering a community-based intensive lifestyle intervention.

Keywords

type 2 diabetes mellitus; overweight/obesity; lifestyle intervention; community research

1. INTRODUCTION

Obesity-related complications impose a tremendous burden on the health of Americans [1]. Over two-thirds of American adults are overweight or obese, and obesity prevalance has remained stable or increased over time [2]. Obese persons have an increased risk of bodily pain, depression, immobility, disability, cardiovascular disease and mortality [3–8].

Obesity is also a dominant risk factor for several common chronic diseases, including type 2 diabetes [9, 10]. Among US adults with type 2 diabetes, the mean body mass index (BMI) is 33 kg/m^2, and only 10% have a BMI below 25 kg/m^2 [11]. Over 29 million Americans have diabetes today [12], and the nation's high rates of obesity are expected to drive increases in diabetes prevalence that could reach 25–28% of the population by 2050 [13].

The Look AHEAD (Action for Health in Diabetes) study was a large clinical trial designed to evaluate the efficacy and safety of an intensive lifestyle intervention to prevent cardiovascular events in adults with type 2 diabetes [14]. Over four years, patients randomized to the Look AHEAD intervention reduced weight, improved fitness and improved control of hemoglobin A1c, systolic blood pressure and high-density lipoprotein cholesterol (HDL-C) [15]. Over ten years, differences remained statistically significant for weight loss, improved fitness and hemoglobin A1c control, but there were no significant differences in cardiovascular events [16]. However, patients in the intervention group were less likely to be treated with insulin and experienced reductions in urinary incontinence, sleep apnea, depression and improvements in quality of life, physical functioning and mobility. These findings demonstrate that intensive lifestyle interventions offer patients an approach to obesity and cardiovascular risk management that can lower medication needs and improve patient-centered outcomes. Unfortunately, because the Look AHEAD intervention was heavily resource-intensive, it may, without thoughtful modifications and additional evaluation, prove challenging to translate into real-world settings [17].

Primary care settings are equipped to identify diabetes, activate individuals to improve self-management behaviors, and provide follow-up testing and pharmacologic management of diabetes [18]. However, evidence-based intensive lifestyle interventions typically involve multiple hours of ongoing, structured contact over extended periods, which may prove challenging or impractical for many primary care settings [19, 20]. Community-based organizations are better suited to offer intensive behavioral interventions to diverse populations by incorporating culturally sensitive programs that address social and environmental barriers to behavioral change and maintenance [21, 22]. In this context, we are conducting a randomized comparative effectiveness trial named the Intervening in

Diabetes with Healthy Eating, Activity, and Linkages To Healthcare (I-D-HEALTH) study in adults who have a usual source of primary care, elevated BMI and type 2 diabetes. We will evaluate levels of participation, health outcomes and costs associated with offering free-of-charge access to a community-based intensive lifestyle intervention, versus offering standard lifestyle counseling alone. This important translational research will advance the evidence base by evaluating a potentially scalable implementation approach that integrates core components of Look AHEAD's intensive lifestyle intervention into an existing framework for community-based intervention delivery in partnership with local YMCA organizations.

2. RESEARCH DESIGN AND METHODS

2.1. Study Design and Inclusion Criteria

I-D-HEALTH is a two-arm, individually randomized encouragement trial comparing standard care alone versus standard care plus free-of-charge access to a group-based lifestyle intervention (GLI) that is an adaptation of the Look AHEAD intervention. At the time of enrollment, study participants have type 2 diabetes that has been confirmed by a primary care provider, are age 18 years and older and have a BMI of at least 24 kg/m^2. Individuals were excluded from study participation if they had a hemoglobin A1c (A1c) of 11.0% or higher, systolic blood pressure ≥180 mmHg, diastolic blood pressure ≥105 mmHg, significant cardiovascular disease, severe chronic obstructive pulmonary disease asthma that required supplemental oxygen, were pregnant, or had any other known contraindication to regular physical activity. Individuals were also excluded if they used a medication known to produce hyperglycemia, had a disease other than diabetes mellitus that leads to abnormal glucose metabolism, or were unable to read written English or Spanish.

The study protocol was registered in the National Clinical Trials Registry (NCT01435603) and approved by the Northwestern University Institutional Review Board (IRB).

2.2. Recruitment Flow

The GLI is being delivered at two YMCA ("Y") sites in metropolitan Chicago. Trial recruitment occurred in the communities surrounding each site. Before recruiting individual patients for potential trial inclusion, we engaged primary care practices in the communities surrounding the two Y-based GLI delivery sites. These primary care delivery sites included a broad mix of federally qualified health center (FQHC) practices, independent solo practices and academically affiliated practices.

We used two main channels for trial recruitment, both of which involved linking overweight patients with diabetes to a community resource coordination center (i.e., hub) at Northwestern University. The diabetes resource hub includes a secure fax line, telephone call center and relational resource database, and is staffed by lay health promoters who were trained to offer brief education about lifestyle intervention resources for patients with diabetes.

In one recruitment channel, primary care providers (PCPs) recommended the resource hub to individual patients during in-person clinic visits. The PCP then completed, signed and

faxed a referral form to the resource hub, which acknowledged that the patient had diabetes and had been advised to achieve 5–10% weight loss through changes in diet and increased physical activity. Following receipt of a referral form, a health promoter called the patient at home within two days, asked about his or her preferences for making healthy lifestyle changes and provided detailed information about diet, physical activity and lifestyle modification resources available in the community. The health promoter then informed the patient about the opportunity to participate in a research study that provided additional health information, ongoing support and an opportunity to have more frequent risk factor testing to track progress and determine if subsequent lifestyle changes were leading to meaningful health improvements. Patients interested in learning more were then pre-screened for study eligibility.

In the other main recruitment channel, patients were identified through their PCPs' electronic medical record databases and contacted directly by the study team via an outreach call. After approval by the healthcare provider, each potential participant was mailed a lead letter explaining the study and containing a phone number s/he could call to opt out of study recruitment. Patients who did not opt out of recruitment were called by an I-D-HEALTH research assistant (RA), who described the study and confirmed the patient met major enrollment criteria. After discussing the study, these patients were also offered the hub resource information in the same manner described above.

A small number of individuals self-referred themselves for trial participation after receiving a study recruitment flyer (flyers were distributed at the two Y study sites) or discussing the study with previously enrolled participants. Like other study participants, self-referring patients were required to have their PCP complete a referral form. If a patient did not have a PCP, the research team provided information about local safety net providers and encouraged the patient to complete enrollment after obtaining PCP verification.

Individuals who were interested, provider-approved and eligible were scheduled for an in-person screening verification and enrollment visit at one of the two Y intervention sites. At this screening/enrollment visit, an RA obtained informed consent and written HIPAA authorization to collect protected health information (PHI) for the trial. The RA then verified final study eligibility after taking measurements of height, weight, blood pressure and A1c,

2.3. Randomization and Blinding

Individuals who completed study enrollment and met final inclusion criteria were randomized to standard counseling (control) or the GLI arm. However, participants were not informed that the study involved randomization. Instead, RAs told all participants that they would receive information about community resources that could help them lose weight and make changes in their diet and physical activity. They were also told that they *might* be contacted by an employee of the Y, who could provide additional information about diet and physical activity programs to help prevent diabetes or its complications. This procedure was used because: 1) all study participants received one of two different approaches for supporting healthy lifestyle changes that were both considered acceptable in current practice; 2) the knowledge of a random treatment comparison might lead study subjects to

participate more (or less) with intervention offerings as well as research follow-up visits; and 3) randomization itself did not impose more than minimal risk to require full disclosure.

Prior to the study enrollment phase, randomization lists were generated by a senior statistician using SAS, version 9.2 (Cary, NC). Lists were created using 1-to-1 allocation, with blocks of 4, stratified by Y study site and race (non-Hispanic White; African-American; Other). Randomization blocks were implemented by the study programmer (AC) and pre-loaded into a back-end field of a Microsoft Access (Redmond, WA) database table that was not available to study RAs. After the study RA collected data required for randomization at each participant's screening/enrollment visit, she clicked a button in Access to execute the randomization. The program verified all necessary variables had been collected, identified the appropriate randomization block and selected the next randomization assignment within the block. The program then notified the RA that the participant's randomization had been completed and displayed the participant's numeric study ID, but the RA remained blinded to the randomization assignment.

Within 3 business days of study enrollment, the research manager (EAF) queried the database containing randomization assignments. As detailed in section 2.5 below, she then shared the name and contact information of each new participant randomized to the GLI arm with a Y-based intervention coordinator.

2.4. Data Collection and Outcome Assessment

At the screening/enrollment visit, all participants complete a limited battery of baseline biometric, metabolic and survey procedures. Follow-up data for each participant is collected during an in-person visit with an RA at 6, 12 and 24 months after enrollment. RAs conducting follow-up data collection are blinded to each participant's randomization status.

The primary study outcome is the percent change in weight between baseline and follow-up measurements at 6, 12 and 24 months. Body weight was measured using a calibrated digital or balance beam scale, and height was measured using a wall-mounted stadiometer. Secondary outcomes include changes in systolic blood pressure, A1c, total cholesterol, HDL-C. Blood pressures were assessed as the average of two values measured with an aneroid sphygmomanometer with participants seated and relaxed for at least 5 minutes. If the two readings differed by more than 10 mmHg, a third measure was taken and blood pressure was analyzed as the mean of the closest two values. Non-fasting total cholesterol and HDL-C were measured from capillary blood using a Cholestech LDX lipid analyzer [23]. A1c was assessed from a fingerstick capillary blood sample using a DCA Vantage portable bench-top analyzer [24, 25].

We are also collecting secondary outcome data for other health and cost measures. Impact of the intervention on participants' quality of life will be evaluated using the Physical Component Summary (PCS), Mental Component Summary (MCS) and SF-6D preference-based health utility index, each derived from the self-administered Medical Outcomes Study 12-item Short Form (SF-12) health survey [26, 27]. Direct medical and direct non-medical costs will be collected using methods identical to those used by the Look AHEAD Economic Evaluation Workgroup [28]. Ten-year total ischemic heart disease risk will be

estimated using the UKPDS Outcomes Model [29]. Intervention delivery costs will be estimated by accounting of per-participant supply costs and annual reporting of work hours spent by staff on the intervention.

2.5. Intervention Goals and Components

While continuing to receive clinical diabetes care from their own PCP, all study participants receive brief dietary and lifestyle information—such as a community resource guide and publicly available materials about healthy lifestyle changes [30–32]—from a study RA at baseline, 6, 12 and 24 months.

In addition to brief RA advice and usual clinical care, participants randomized to the GLI arm also receive free-of-charge access to a group-based adaption of the Look AHEAD lifestyle intervention. Within 3 business days of study enrollment, the research manager provides a Y-based intervention coordinator the name and contact information for each new participant randomized to the GLI arm. The Y coordinator then telephones potential participants at least 3 times and offers each participant the opportunity to take part in the GLI free-of-charge. Thus, active participation in the GLI is encouraged but not required. Interested study participants are then assembled by the Y coordinator into groups of 5–12 persons who can meet at a mutually agreeable time at the Y locations.

The GLI was adapted from the Look AHEAD lifestyle intervention, introducing modifications that included delivery by trained wellness instructors employed by Y's, transitioning to a completely group-based delivery format, and eliminating the use of meal-replacements as a strategy to amplify weight loss. Similar to Look AHEAD, the intervention involves face-to-face delivery and uses a cognitive-behavioral skill-based training approach applying principles such as brief motivational interviewing, self-efficacy building, accountability and peer and instructor support. At each session, participants receive printed handouts that guide them through the sessions key learning goals and assign "homework" between sessions, in addition to tools for supporting actions such as goal setting, calorie-counting, self-monitoring of physical activity and diet, and problem solving. During GLI adaption, we also worked with a team of consultants and local clinicians to adapt and incorporate protocols from Look AHEAD that were designed to ensure participant safety through additional education about minimizing the frequency and severity of hypoglycemic episodes, cardiovascular harms and foot injuries among previously sedentary adult participants with type 2 diabetes who were planning to increase physical activity and lose weight.

The goals of the GLI are analogous to those of the Look AHEAD lifestyle intervention[14]: (1) an initial weight loss targeting a goal of 10% of baseline body weight, and; (2) at least 175 minutes per week of moderate physical activity, with maintenance of these lifestyle changes for at least two years. The intervention emphasizes self-esteem, empowerment and social support and follows the premise that lasting lifestyle changes require training in diet, exercise and behavior modification skills. The intervention is comprised of a structured protocol that allows for tailoring to meet the needs of individual participants, and diet and physical activity components that are flexible and acceptable within the unique communities in which they are implemented. The GLI involves three phases that are analogous to the

Look AHEAD study intervention [33]: a 24-session core curriculum over six months; a 12-session transition phase over six months, and; a 24-session maintenance phase over one year.

a. GLI Core Curriculum—The core curriculum of the GLI uses content from Look AHEAD's 24-session core curriculum, with 60-to-90-minute intervention sessions offered weekly in intact groups of five or more participants each over 26 weeks. Topics covered include healthy lifestyle changes, self-monitoring of diet and physical activity, reduction of total calorie and saturated fat intake and strategies for improving diet and increasing physical activity, including utilization of "training partners." Participants who miss a session receive a written tutorial summarizing that week's content and have the choice of: (1) attending the missed session at the same or another facility if a second group is receiving the core curriculum concomitantly, or; (2) meeting with the instructor individually to make up the visit prior to the next scheduled session.

b. Transition Phase—After completing the core curriculum, participants enter a six-month transition phase involving two group sessions each month (12 total sessions). These sessions encourage more independent routines for maintaining healthier eating and physical activity goals and develop greater self-efficacy for individual problem solving skills to prevent weigh regain. This second phase, prior to entering a less-intensive maintenance period, is consistent with Look AHEAD's successful lifestyle intervention approach for adults with type 2 diabetes [33].

c. Maintenance Phase—During the second year of the GLI, participants are invited to participate in monthly group visits, plus two six-week "refresher" sets of weekly group classes (24 total group sessions during this year). Maintenance sessions include a combination of troubleshooting to address individual barriers for maintaining program goals, and "short courses" that focus on specific topics. For example, a short course on exercise might teach participants a new exercise modality (e.g. "Tai chi"). Nutritional topics might include recipe makeover, eating healthy during holidays, or using measuring cups and scale to portion foods. Behavioral topics include "Preventing lapses from becoming relapses," "Emotions and eating," or "Getting my family involved."

The study also includes a "feedback loop" between study staff and referring primary care practices. After completion of follow-up visits at 6, 12 and 24 months, an RA mails weight and clinical outcome results to each participant's primary care practice. Among patients randomized to GLI encouragement, the Y coordinator also mails providers additional information about the number of GLI sessions attended and weight lost. If a GLI participant reports severe hypoglycemia, chest pain, or shortness of breath with exertion to study staff at the Y, the staff member informs the patient to report this to his/her PCP immediately and to stop any further GLI participation until the PCP advises that s/he can continue. In this situation, the Y staff member also notifies the study team immediately and an additional letter is sent to the participant's PCP.

2.6. YMCA Instructor Training

All GLI instructors are at least 18 years of age and have: (1) a high school diploma or equivalent; (2) at least one year of prior experience teaching wellness-related classes with some basic knowledge of health, nutrition and fitness; (3) interpersonal skills needed to effectively moderate a group of adults (as judged by interview with a Y supervisor); and (4) current certifications in CPR, First Aid, Safety and Risk Management, and Y New Employee Orientation. Our research team selected these criteria in partnership with the Y to balance the need to assure fidelity to the intervention with the importance of being held accountable to high standards of professionalism for the Y organization. The use of these somewhat modest instructor eligibility criteria required that each individual complete a structured training program (described below). Approaches to training and methods for monitoring ongoing fidelity of program delivery were developed and refined in three prior studies involving translation of the Diabetes Prevention Program lifestyle intervention [34–36].

GLI instructor training and certification consists of a 2.5-day course run by the Northwestern University training core. The training course was based on the Look AHEAD Lifestyle Intervention but was adapted from our prior training course for a community-based adaption of the Diabetes Prevention Program that has been offered to over 100 “lay” instructors affiliated with a variety of community organizations (including the Y) in several states [21, 37, 38]. During training, all GLI instructors receive a GLI operations manual, the Participant Handouts and toolkits of supportive educational materials (e.g. measuring cups, spoons and food labels). GLI instructors also agree not to alter program content without permission of the Northwestern University training core.

GLI instructors receive ongoing support and supervision while delivering the intervention to study participants. Based on direct observation of their first “live” GLI group session, all instructors are required to demonstrate adequate skill in intervention delivery (as judged by a leader of the Northwestern University training core). One year later, instructors attend a one-day retraining seminar, including maintenance lessons, delivered by the Northwestern University training core; recertification is contingent on demonstration of ongoing skills and knowledge.

Throughout intervention delivery, instructors have daily access to the YMCA coordinator and the Northwestern University training core to discuss program content or participant issues. The study project coordinator, YMCA director and YMCA coordinator also meet regularly to discuss operations, including instructor concerns and program quality assurance.

2.7. Statistical Power

I-D-HEALTH targeted a sample size accrual of 328 participants, which provides more than 80% power at the α=0.05 significance level to detect an absolute between-group mean difference in percent weight loss at 12 months as low as 4.75% (SD 6.5%) among GLI participants. We targeted a difference of this magnitude (i.e. 4.75%) based on the difference between 5% weight loss (a commonly accepted standard for clinically meaningful weight

loss [39, 40]) and weight loss results from prior studies of minimal counseling interventions that were comparable to the proposed standard care arm [41–43].

Based on participation rates previously observed in exercise programs in demographically similar samples [44, 45], we assumed that as few as 30% of participants randomized to the GLI study arm will actually take part in the intervention. We also assumed an intra-cluster correlation of 5% or less for changes in weight within each of 8 GLI treatment groups and attrition not exceeding 20% at 12 months. Under these same assumptions, the sample size of 328 also provides 80% power to detect a between group difference in hemoglobin A1c as small 0.64% (SD 0.993), systolic blood pressure as small as 3.55 mmHg (SD 19.98), and total cholesterol/HDL ratio as small as −3.80% (SD 11.30%).

2.8. Statistical Analysis

a. Recruitment Channels and Baseline Characteristics—In this manuscript, we present descriptive statistics summarizing trial recruitment and the baseline characteristics of the randomized study cohort. When examining potential differences across study groups, we compared means of continuous variables using unpaired t-tests or, in the presence of non-normal data distributions, Wilcoxon rank-sum tests. We used chi-square tests to compare group-level proportions for categorical variables.

b. Intention-to-Treat Analysis—Primary study analyses will be based on the intention-to-treat principle. We will compare the adjusted effect of study group assignment on changes in body weight, CVD risk factor levels (i.e. A1c, SBP, total and HDL cholesterol) and health status indicators (i.e. PCS-12, MCS-12, SF-6D). All statistical tests will be performed using two-sided tests with α=0.05.

Percent change in body weight will be examined both as a continuous outcome and a binary measure of whether the study participant lost at least 5% of body weight, which is a commonly accepted standard for clinically meaningful weight loss [39] that is associated with significant improvements in CVD risk factors in individuals with type 2 diabetes [40]. When selecting covariates, we will compare baseline characteristics (sex, race, age, income, education, health status indicators and primary language) longitudinally one-at-a-time with each outcome; characteristics found to have a significant association with each outcome at a 0.15 level will be considered for inclusion in the respective overall maximal model. A backward stepwise model building procedure will be used to determine the overall parsimonious models for the continuous and binary outcomes such that remaining covariates are significant at the 0.05 level. To assess effects of GLI assignment, we will first test if there is a significant difference in treatment effect between study time points. If there is no significant difference, we will evaluate the overall treatment effect.

We will select an appropriate approach to control for relevant correlated data structures, based on model diagnostics. We will initially assume that longitudinal mixed-effect regression models, including fixed treatment and covariate effects and random intercept and time effects, will provide optimal modeling of variance components. If the intraclass correlation of patient-level data nested within primary care physician is high enough that the design effect is greater than 2.0, we will also cluster by primary care physician. For any

outcome where a clear covariance structure is not apparent after a thorough review of model diagnostics, we will use marginal modeling approaches such as generalized estimating equations with robust variance estimates to ensure models are robust to misspecification of within-cluster correlation [46].

Since GLI instructors deliver intervention sessions to small groups of patients, it is possible that final data will exhibit clustering at the levels of the individual patient and the GLI small group. Among patients who attend the GLI, we will collect data on intervention group and explore potential heteroskedasticity across groups. If we observe group-level clustering, we will also explore more complex models that appropriately model empirical variance structures [47].

Although we will engage in substantial efforts to minimize sample attrition, we expect some study participants will be lost to follow-up and some outcome data will be missing. We will use chi-square tests to compare proportions of missingness between intervention arms at each time point during follow-up. We plan to impute missing data when estimating intention-to-treat regression models; an appropriate imputation approach will be selected based upon a review of the patterns of missingness.

c. Instrumental Variable Analysis—Although our primary analysis will follow the intention-to-treat principle, our study may have low generalizability if a significant proportion of participants randomized to GLI encouragement choose not to attend the intervention at the Y. Based on results from a prior encouragement trial conducted by our research team [48], we expect several participants who are offered the GLI will not attend the program or will only attend a small number of GLI sessions. Thus, we will also estimate separately the probability of attendance when offered the GLI, and the effect of the GLI among attenders. Although such comparisons of self-selected subgroups can introduce various forms of selection bias, we will use random treatment assignment as an instrumental variable (IV) [49, 50], where GLI attendance is incorporated in a two-stage generalized least squares IV approach [51]. Thus, the first stage of the IV regression will use random treatment assignment to predict the probability of GLI attendance. The second stage will use predicted values from the first stage to estimate the effect of the GLI.

d. Subgroup Analyses—Although the study is not designed to test subgroup treatment effects, we will explore potential heterogeneity in treatment effects by summarizing primary and secondary outcomes by important population subgroups, such as sex, age group (18–44; 45–64; ≥65), race/ethnicity (non-Hispanic White; African-American; Hispanic) and primary language (Spanish; English).

e. Cost Analysis—We will calculate and report descriptive data for each randomized treatment arm regarding their direct intervention costs, as well as direct medical and non-medical expenditures.

3. RESULTS

3.1. Recruitment Channels

Trial recruitment began in January 2013 and concluded in July 2014. Over the study's 19-month recruitment period, 2,957 patients were identified as potentially eligible for the study through provider referral to the diabetes resource hub, electronic medical record databases or self-referral (Figure 1). Among the 2,860 individuals whose PCP provided implicit or explicit approval to approach, 915 (32.0%) were unreachable by phone and 900 (31.5%) declined study participation.

Among the 982 patients who completed telephone pre-screening, a total of 543 (55.3%) were deemed ineligible for study participation. Among those who were ineligible, 320 (58.9%) did not have type 2 diabetes; most of these patients were recruited for the study after referral to the diabetes resource hub due to prediabetes.

Three hundred seventy nine individuals who completed the telephone pre-screen attended an in-person screening/enrollment visit. Eight (2.1%) declined study participation, while 40 (10.6%) were deemed ineligible due to exclusion criteria. Ultimately, 331 participants were enrolled and randomized into the final study sample, representing 11.2% of 2,957 referred patients. If we assume that the rate of eligibility was similar among unreachable or declining patients at each step of recruitment, then approximately 1,026 of the 2,860 patients approached were likely eligible and approximately 32% (331/1,026) of the eligible patient population enrolled in the trial. All 331 enrolled participants were randomized; 167 were randomized to the Standard Care group and 164 were randomized to GLI encouragement.

3.2. Baseline Characteristics of the Randomized Cohort

The characteristics of randomized participants are shown in Table 1. The mean age at randomization was 57.4 years (standard deviation [SD] 11.4). There were roughly equal numbers of males and females, and there was good representation of White non-Hispanic (34.4%), African-American (30.5%) and Hispanic (27.5%) race/ethnicity. Forty-two of the 91 Hispanic participants were Spanish speakers, representing 12.7% of the full study sample. Of the 301 participants who reported household income, 15.0% reported household income below $10,000 and 15.0% reported income of at least $100,000.

Cardiometabolic risk factors were modestly elevated, reflecting the underlying risk of the diabetic study sample as well as their access to primary care. The mean weight was 220.0 pounds (SD 53.3), and mean BMI was 35.6 kg/m^2 (SD 7.6). Mean systolic blood pressure was 126.5 mmHg (SD 16.8), and mean A1c was 7.2% (SD 1.3). Mean total cholesterol was 172.0 mg/dL (SD 44.9), while mean HDL-C was 44.1 mg/dL (SD 13.1) and mean non-HDL cholesterol was 127.8 mg/dL (SD 46.0). The mean ratio of total cholesterol to HDL-C was 4.2 (SD 1.8).

Study participants were also likely to receive medication-based treatment for diabetes-related risk factors at baseline. More than three-fourths were prescribed antiglycemic medications (87.9%) or antihypertensive medications (76.4%), while more than half were prescribed antilipidemic medications (58.6%). Participants randomized to GLI

encouragement were less likely than the Standard Care group to be on antiglycemic medications, both overall (83.2% versus 92.7%, P=0.008) and for non-insulin antiglycemics (73.1% versus 86.0%, P=0.004). In all other measured baseline characteristics, we detected no statistically significant differences between the two trial arms.

4. DISCUSSION

I-D-HEALTH successfully enrolled a large and diverse sample of adults with diabetes receiving primary care services from more than 44 clinical practice locations in metropolitan Chicago. This trial now offers a unique opportunity to evaluate the incremental effectiveness of offering a community-based intensive lifestyle intervention for reducing the burden of obesity and other cardiovascular-related risk factors.

Despite reaching our accrual goal, we faced several notable challenges during the recruitment phase. For example, just prior to the launch of I-D-HEALTH, the study's location was shifted to Chicago. This change required the engagement of a much larger number of primary care providers across a larger array of primary care practices, as well as the need to revisit our original sample size assumptions, which had been based on clustering of treatment effects within just nine primary care clinic locations. When recalculating the new sample size target, we were also forced to consider how the change in location had introduced a more racially and economically diverse patient population. Anticipating that such a study population might be more difficult to engage electively in a healthy lifestyle intervention program, the new sample size was also inflated using conservative assumptions about lower uptake into the intervention program.

The study team was ultimately able to enroll 331 diabetic primary care patients by adopting a variety of adaptive recruitment strategies, such as outreach visits to PCP office settings near the implementing Y sites and the development of strong relationships with three large clinical delivery organizations that were willing to collaborate to engage potentially eligible patients identified through electronic health record queries. Each recruitment approach had tradeoffs in terms of resource intensity and the resulting yield of study participants. For example, we successfully attracted 573 referrals to the resource hub from clinical providers following intensive outreach visits to provider practices, but this outreach channel only yielded 30 study participants, at an estimated cost of $505 per study enrollee (Table 2). Conversely, it took over one year to establish agreements with clinical delivery organizations for outreach protocols pertaining to electronic health record queries, but this strategy ultimately yielded 300 study participants at an estimated cost of only $15 per study enrollee.

Other noteworthy recruitment challenges include patient apprehension toward traveling to a community-based research office that was located in an unfamiliar neighborhood; transportation barriers for many persons who relied on the public transit system; disinterest in making healthy lifestyle changes to improve a chronic condition (diabetes) that many patients had been managing with medications for many years; and rejection of a diabetes diagnosis by some patients who had been identified by electronic medical record queries as taking antiglycemic medications or having diabetes listed on their clinical problem list.

Having completed its accrual goal, the I-D-HEALTH study is now positioned to contribute important new evidence about both the uptake and effectiveness of delivering an intensive lifestyle intervention program to urban-dwelling adults with type 2 diabetes who are largely of minority race or ethnicity and face economic challenges to healthy lifestyle changes. Compared with the Look AHEAD efficacy trial, I-D-HEALTH is a lower-cost intervention design that no longer includes a meal replacement component and offers group-based lifestyle coach visits. Furthermore, I-D-HEALTH intervention instructors are not academically trained nutritionists or healthcare educators but are instead employees of local Ys. Having previously demonstrated that Ys can successfully implement multi-component, longitudinal intensive lifestyle interventions for diabetes prevention [34, 38], the I-D-HEALTH study can now advance our understanding of the participation, weight loss effectiveness and costs of this potentially scalable intervention design for adults who already have type 2 diabetes. The study will also provide important information about participants' ability to participate in such an intervention, and their ability to make subsequent lifestyle changes of sufficient magnitude to translate into lower body mass, improved cardiovascular risk factor control, or the reduced need for medications to manage those risk factors.

5. CONCLUSIONS

The I-D-HEALTH study successfully enrolled a large and diverse sample of overweight or obese adult primary care patients with diabetes and increased cardiometabolic risk. Over the next 24 months, this study is positioned to provide important new evidence about the levels of participation in an evidence-based group lifestyle intervention that is offered free-of-charge in a community-based YMCA location; the Y's costs to offer this intervention; and the effects of participating on changes in body weight, cardiovascular-related risk factors and health-related quality of life.

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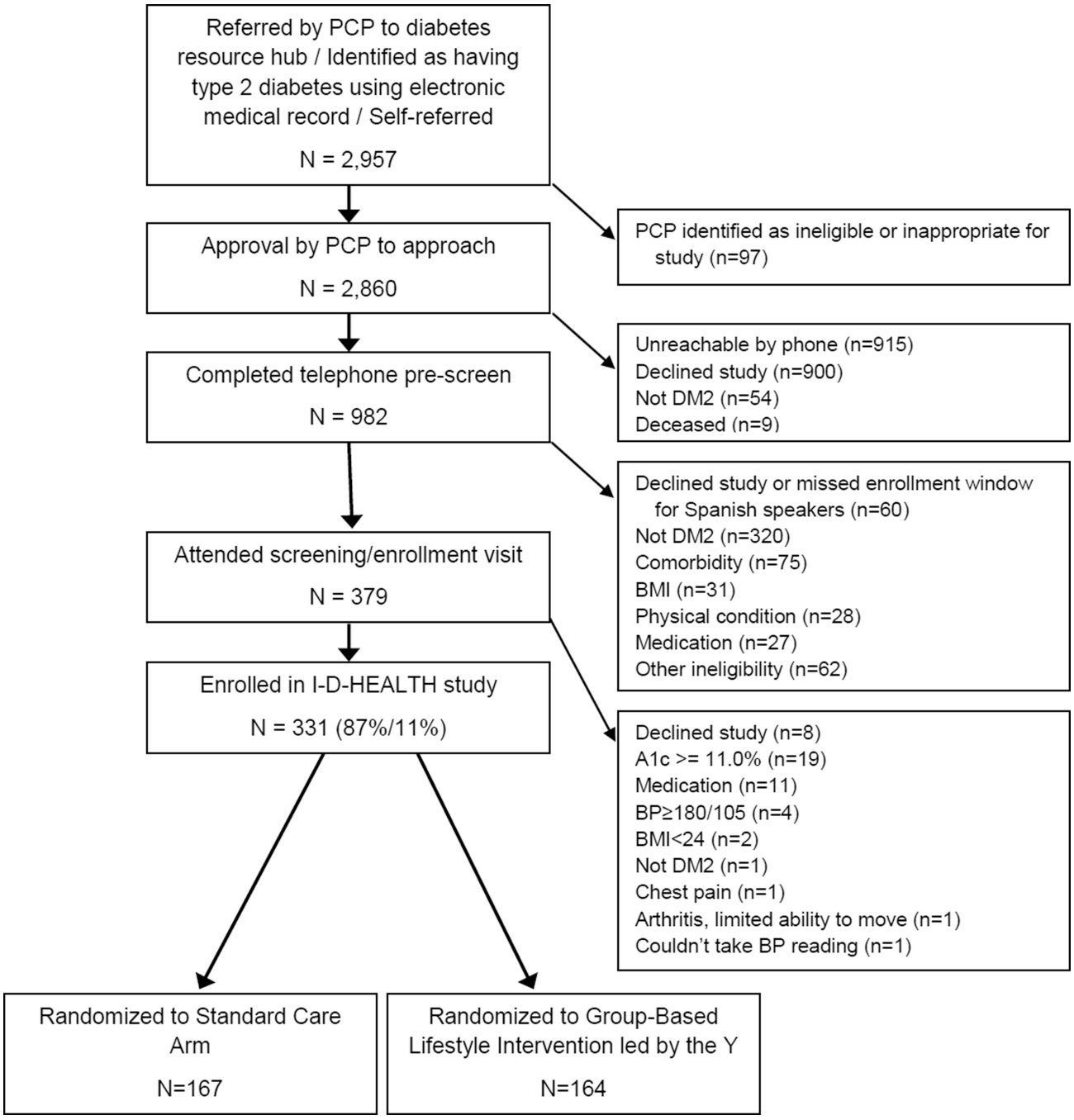

Figure 1. CONSORT Diagram

Boxes and arrows indicate the flow of potentially eligible patients as deemed approachable, eligible, enrolled and randomized; side arrows provide reasons for non-approach, ineligibility and non-enrollment

Abbreviations: PCP, primary care provider; DM2, type 2 diabetes; BMI, body mass index; BP, blood pressure

Table 1

Baseline Characteristics of the Randomized Cohort

Characteristic	Total		Standard Care		GLI	
	N=331		n=167		n=164	
Age, mean (SD)	57.4	(11.4)	57.1	(12.2)	57.6	(10.5)
Age, n (%)						
<45	54	(16.3)	30	(18.0)	24	(14.6)
45–54	77	(23.3)	43	(25.7)	34	(20.7)
55–64	118	(35.6)	51	(30.4)	67	(40.9)
≥65	82	(24.8)	43	(25.7)	39	(23.8)
Sex, n (%)						
Male	165	(49.8)	86	(51.5)	79	(48.2)
Female	166	(50.2)	81	(48.5)	85	(51.8)
Race/Ethnicity, n (%)						
White non-Hispanic	114	(34.4)	58	(34.7)	56	(34.1)
African-American	101	(30.5)	51	(30.5)	50	(30.5)
Hispanic	91	(27.5)	43	(25.8)	48	(29.3)
Other/Mixed	25	(7.6)	15	(9.0)	10	(6.1)
Language, n (%)						
English	289	(87.3)	148	(88.6)	141	(86.0)
Spanish	42	(12.7)	19	(11.4)	23	(14.0)
Household Income, n (%)[a]						
<$10,000	45	(15.0)	22	(14.1)	23	(15.9)
$10,000 – $24,999	72	(23.9)	35	(22.4)	37	(25.5)
$25,000 – $49,999	66	(21.9)	34	(21.8)	32	(22.1)
$50,000 – $99,999	73	(24.3)	36	(23.1)	37	(25.5)
≥$100,000	45	(15.0)	29	(18.6)	16	(11.0)
Weight (lbs), mean (SD)	220.0	(53.3)	217.0	(52.6)	223.0	(54.0)

Characteristic	Total		Standard Care		GLI	
	N=331		n=167		n=164	
BMI (kg/m^2), mean (SD)	35.6	(7.6)	34.9	(7.3)	36.2	(7.8)
Systolic blood pressure (mmHg), mean (SD)	126.5	(16.8)	127.0	(17.6)	126.0	(16.0)
Hemoglobin A1c, mean (SD)	7.2	(1.3)	7.1	(1.3)	7.3	(1.2)
Total cholesterol (mg/dL), mean (SD)	172.0	(44.9)	170.0	(44.2)	174.0	(45.7)
HDL-C (mg/dL), mean (SD)	44.1	(13.1)	43.2	(13.4)	45.0	(12.8)
Non-HDL cholesterol (mg/dL), mean (SD)	127.8	(46.0)	126.4	(46.0)	129.2	(46.1)
Total cholesterol/HDL ratio, mean (SD)	4.2	(1.8)	4.3	(1.8)	4.2	(1.7)
Antiglycemic medications, n (%)	291	(87.9)	152	(92.7)	139	(83.2)[b]
Insulin	79	(23.9)	45	(27.4)	34	(20.4)
Other	263	(79.5)	141	(86.0)	122	(73.1)[b]
Antilipidemic medications, n (%)	194	(58.6)	101	(61.6)	93	(55.7)
Statins	184	(55.6)	97	(59.2)	87	(52.1)
Other	26	(7.9)	12	(7.3)	14	(8.4)
Antihypertensive medications, n (%)	253	(76.4)	129	(78.6)	124	(74.3)

Abbreviations: GLI, group-based lifestyle intervention; SD, standard deviation; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol, LDL-C, low-density lipoprotein cholesterol

[a] 301 of 331 participants reported household income data (156 standard care, 145 GLI)

[b] P<0.01 for chi-square test investigating differences across study groups

Table 2

Yield of Different Outreach Channels for Accrual of Participants into I-D-HEALTH

Outreach Channel	Required Resources	Cost ($)	Patients Referred (No.)	Enrolled in Trial (No.)	Cost Per Enrollee ($)
Outreach visits to primary care practices	Staff visits to practices (182 hours)	$4,186	573	30	$505
	Staff travel (670 miles)	$375			
	Provider detailing materials, patient fliers/marketing	$1,695			
	Salary for health navigator who conducted patient referrals	$8,889			
	Total cost:	**$15,145**			
EHR database queries	Data management	$3,081	2374	300	$15
	Lead letters sent to patients	$1,543			
	Total cost:	**$4,624**			
Website	Programmer time to post downloadable referral form, cost of web domains	**$250**	10	1	$250

Abbreviations: EHR, electronic health record