Research Protocol - 2020-0438

Complete Health Improvement Program to Improve Glycemic Control and Reduce Cost of Care for Geisinger Health Plan Members with Type 2 Diabetes

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1 ABBREVIATIONS USED IN THE PROTOCOL

Abbreviation	Term
AE	Adverse event
CHIP	Complete Health Improvement Program
EHR	Electronic Health Record
GAD-7	General Anxiety Disorder 7
GIRB	Geisinger IRB
HbA1c	Hemoglobin A1c
HIPAA	Health Insurance Portability and Accountability Act
IRB	Institutional Review Board
ITLC	Intensive Therapeutic Lifestyle Change
PHQ-9	Patient Health Questionnaire 9
PHI	Protected Health Information

2 ABSTRACT

Type 2 diabetes mellitus (T2DM) is a driver of poor health outcomes and high healthcare costs. Comprehensive lifestyle change can improve glycemic control, reduce complications, and reduce cost of care among patients with T2DM. Unfortunately, many patients fail to achieve adequate lifestyle change and thus experience adverse health events and/or become dependent upon expensive medical care. The Complete Health Improvement Program (CHIP) is an Intensive Therapeutic Lifestyle Change program administered in the outpatient setting. This is a pilot randomized-controlled trial comparing the clinical, utilization, and financial outcomes of adult health plan members with T2DM offered CHIP versus those only offered standard health plan coverage.

Sixty GHP members will be randomized 1:1 (stratified by most recent HbA1c value) into either the CHIP intervention group or the control group. The intervention group will attend 18 classes covering topics such as diet, sleep, exercise instruction, stress management, and toxic substance avoidance. Biometrics (weight, BMI, waist circumference, systolic/diastolic blood pressure), biomarkers (HbA1c, LDL-C) and psychometrics (Wellbeing360 survey) will be collected on all participants at baseline, 3-months and 6-months.

We hypothesize that GHP members with type 2 diabetes offered CHIP in addition to standard insurance coverage will have improvement in HbA1c and as well as in other biometrics, biomarkers, psychometrics and utilization/financial outcomes. The primary aim is to compare change in HbA1c, LDL-C, systolic blood pressure, body mass index, and waist circumference for GHP members offered CHIP versus members offered standard insurance coverage at 3- and 6-months. Since this is a pilot study, the focus of the analysis will be estimating the mean and standard deviation of the change at 3- and 6-month for each primary and secondary outcome. We will also estimate the difference of the changes between groups and the variability.

We seek to validate a scalable and replicable intervention which could be offered by a health plan alongside standard medical coverage to improve key health and financial outcomes for members with T2DM.

3 BACKGROUND AND SIGNIFICANCE

Type 2 diabetes mellitus (T2DM) is a key driver of poor health outcomes and high cost of healthcare in the United States. T2DM affects approximately 10% of adults in the United States and is associated with complications including cardiovascular events, loss of vision, diabetic kidney disease, and premature death (Center for Disease Control and Prevention, 2020). Healthcare costs are 2.3 times higher for patients with T2DM, and total direct costs of type 2 diabetes care exceed $230 billion annually (American Diabetes Association, 2018).

Lifestyle intervention can dramatically influence the course of T2DM. For example, in the DiRECT trial, 46% of patients undergoing intensive calorie reduction (825-853 calories per day) followed by gradual dietary advancement achieved clinical remission of T2DM, defined as HbA1c below 6.5% while off all diabetes medications (Lean, Leslie, Barnes, & Brosnahan, 2018). Similarly, 30% of patients in a cohort drawn from the ADDITION-Cambridge trial achieved remission of T2DM through lifestyle change alone (Dambha-Miller, Day, Streiltz, & Griffin, 2019). Unfortunately, in the real world most patients with T2DM fail to achieve clinical remission, and only about half of patients achieve an HbA1c below 7% even with medications (Edelman & Polonsky, 2017).

Several shortcomings of the most common lifestyle approaches in T2DM limit their population health impact. First, protocols based on dramatic calorie reduction may be challenging to sustain on a long-term basis. Admittedly, 24-month follow-up of the DiRECT trial cohort found 36% of intervention arm subjects remained in diabetes remission (Lean, Leslie, Barnes, & Brosnahan, 2018). However, follow-up of calorie restriction programs has been inconsistent beyond 24 months (Dombrowski et al. 2014). Second, achieving a consistent approach to lifestyle change in a real-world health system is challenging due to competing demands on providers and a lack of standardization. For example, 2019 guidelines from the American Diabetes Association (ADA) suggest that each patient develop a personalized diabetes self-management education and support (DSMES) plan, allowing some variety in lifestyle strategies (American Diabetes Association, 2019). Unfortunately, as evidenced by high rates of medication prescription and poor clinical outcomes, adequate DSMES plans are not consistently implemented. Lastly, interventions focused narrowly on parameters specific to diabetes, such as glycemic control and body mass

index, may not be optimized to achieve other important health outcomes such as cardiovascular prevention, dementia prevention, and cancer prevention.

An alternative approach to lifestyle intervention in T2DM would be to apply a lifestyle program designed to optimize overall health rather than one specifically targeting T2DM. In theory, such an approach could improve diabetes-related outcomes and might additionally help prevent adverse health events which are less directly linked to T2DM. Such an approach would offer the potential to achieve overall wellness and reduce overall healthcare costs. From the perspective of a healthcare payer, a standardized and scalable program offering general health benefits would be an appealing population health tool for improving members' health while also controlling healthcare costs.

Intensive Therapeutic Lifestyle Change (ITLC) describes comprehensive lifestyle programs aiming to improve outcomes for multiple common chronic conditions simultaneously. ITLC programs are designed to target the root causes common to the pathophysiology of multiple interrelated chronic conditions, including cardiovascular disease, cerebrovascular disease, fatty liver disease, certain cancers, T2DM, hypertension and dementia. Proposed mechanisms by which ITLC may confer health benefits include targeting inflammation, stress response, malnutrition, impaired metabolism, DNA damage, and microbial dysbiosis (Bodai, et al., 2018). In general, ITLC programs address all Six Pillars of lifestyle medicine as defined by the American College of Lifestyle Medicine with the aim of simultaneously impacting a range of disease drivers. These Six Pillars include physical activity, nutrition, sleep, social relationships, stress management, and avoidance of risky substances (American College of Lifestyle Medicine, 2020). Although ITLC overlaps significantly with the standard approach to diabetes management (e.g. DSMES emphasizing dietary improvement and increased exercise), ITLC is comparatively more comprehensive and more transformative.

A major factor limiting widespread adoption of ITLC is the investment of time and money required by many ITLC programs. Early ITLC programs required a residential experience, making large-scale implementation for community dwelling adults impractical. The Complete Health Improvement Program (CHIP) is a version of ITLC which was developed and validated for the ambulatory setting. CHIP is generally administered through a series of classes over a 1- to

3-month period. CHIP has been shown in an RCT to improve key biometrics and biomarkers relevant to type 2 diabetes, including glucose, systolic blood pressure, and LDL-C (Aldana et al. 2005, 371-381). This RCT included healthy adults and individuals with pre-existing diagnoses, such as hyperlipidemia, T2DM, and obesity. CHIP has been validated in multiple settings in the United States and internationally and has demonstrated sustained biomarker/biometric improvements at 36 months (Morton, et al., 2014; Kent, et al., 2013; Kotekal, et al., 2019). Of particular interest, when offered to Vanderbilt University and Vanderbilt Health System employees in a pilot scale study, CHIP was shown to improve key biomarkers and biometrics, to decrease diabetes medication use, and to decrease total cost of care on participants' employer-sponsored health plans by >$1,000 per participant within 6-months (Shurney, et al., 2013). Another pilot study of individuals covered by Ohio University health insurance demonstrated improvement in biomarkers (Remy et al. 2017, 293-300) in an employed Appalachian population. The authors of the Ohio University study currently have a trial in progress assessing the effectiveness of CHIP for clinical outcomes, cost of care on the university health plan, and absenteeism which has enrolled university employees with various components of metabolic syndrome, including diabetes, prediabetes, obesity, overweight, hypertension, prehypertension, cardiovascular disease and dyslipidemia. Their study will compare outcomes including healthcare costs in the interventional group to those of an observational control group (Drozek 2020).

Despite promising evidence on the effectiveness of CHIP to achieve key outcomes, further study is needed to determine whether CHIP would be a viable population health tool from the perspective of a health insurance plan. It is important to note that many studies demonstrating various benefits of CHIP were conducted by potentially biased study teams linked to the Lifestyle Medicine Institute, which licenses CHIP (Aldana et al. 2005, 371-381; Kent et al.). In addition, aside from the Rockford, Illinois CHIP RCT publications (Merrill, Taylor, and Aldana 2008, 314-321; Aldana et al. 2005, 371-381), most CHIP studies have utilized pre-post designs without randomized control groups (Leibold et al. 2016, 84-91) and/or samples which may have been biased due to recruitment methodology (Kent et al. 2015; Shurney et al 2013; Drozek 2020). An RCT by a research team unaffiliated with the Lifestyle Medicine Institute is needed to confirm the generalizability of the clinical effectiveness of CHIP and to assess CHIP's ROI. Despite favorable pilot studies, to our knowledge there has never been a rigorous evaluation of a

population scale implementation of CHIP intended to improve the overall health and total cost of care of high-risk individuals such as patients with T2DM. Specifically, both the Vanderbilt and Ohio University studies addressing ROI are pilot scale and appear to lack rigorous randomized control groups, thus making them subject to selection bias. Both of these studies rely upon combinations of pre-post comparisons and comparisons between presumably motivated intervention groups that were actively enrolled in CHIP versus non-randomized, observational health plan member controls, which likely represents a less motivated population (Remy et al. 2017, 293-300; Anonymous; Drozek 2020). The lack of true randomization casts doubt upon the scale of ROI reported by Vanderbilt and ROI which may ultimately be reported by Ohio University. Unfortunately, implementing CHIP requires various licensing fees and per participant charges paid to the Lifestyle Medicine Institute, in addition to the local costs of administering the program. Even at large scale, CHIP can be expected to cost at least $300-$500 per participant. Due to this significant cost, it is imperative to rigorously evaluate the clinical and financial ROI of CHIP before implementing it at a population scale. Finally, to our knowledge there has never been a flexible online/in person application of CHIP. This could be an effective tool to bring CHIP to rural populations and might prove of general use in this era of uncertainty related to pandemics, climate events and other disruptions.

In the current study, we will implement a pilot-scale randomized controlled trial assessing the effectiveness of an adaptation of CHIP which utilizes a flexible hybrid online/in-person protocol. We hope to assess whether this protocol, offered to Geisinger Health Plan (GHP) members, enables CHIP to be administered effectively to a rural population while respecting current social distancing limitations necessitated by the pandemic. This pilot study at the Lewisburg YMCA at the Miller Center, a comprehensive health and wellness center owned jointly by Geisinger and Evangelical Community Hospital and administered by the YMCA. Through this pilot study, we hope to gain insight into whether and how such an application of CHIP could be a cost-effective tool for health plans such as GHP to achieve clinical and financial goals for adult members with T2DM. Through this pilot study, we hope to gain experience implementing CHIP at the Miller Center and to gain preliminary data to support efforts to obtain external funding in order to complete a full-scale clinical trial.

The Miller Center for Recreation and Wellness is a 501(c)3 not-for profit entity owned by a joint venture of Evangelical Community Hospital (ECH) and Geisinger. ECH possesses 51% interest in the joint venture, with Geisinger possessing 49%. As the slight majority member, ECH is responsible for day-to-day operations and operational/administrative oversight of the Center. The Miller Center does not have employees, rather, the Center is staffed with ECH and YMCA employees, and various other contractors for specific programs and services. ECH employees at the Miller Center are responsible for administrative oversight, accounting, facilities and maintenance, supply procurement, new business development, marketing and communications, and oversight of the Greater Susquehanna Valley YMCA operations to ensure that they are fulfilling their Management Services Agreement (MSA) with the Miller Center. The YMCA at the Miller Center is responsible for oversight of membership, the fitness center, sports and recreation, and childcare operations. The Miller Center is ultimately governed by a Board of Directors that is comprised of appointed representatives from ECH, Geisinger, the Greater Susquehanna Valley YMCA, and the community. The Miller Center is a Collaborating Institution under Evangelical Hospital's Federalwide Assurance.

4 HYPOTHESIS AND SPECIFIC AIMS

4.1 Hypothesis

Geisinger Health Plan members with T2DM offered CHIP in addition to standard insurance coverage will have improvement in HbA1c and improvements in other biometrics, biomarkers, psychometrics and utilization/financial outcomes, including LDL-C, systolic blood pressure, body mass index, waist circumference, number of diabetes medications prescribed, Wellbeing360 survey, and total cost of healthcare.

4.2 Specific Aim 1

To compare change in HbA1c, LDL-C, systolic blood pressure, body mass index, and waist circumference for GHP members offered CHIP versus members offered standard insurance coverage at 3- and 6-months.

4.3 Specific Aim 2

To compare number of diabetes drugs prescribed and total health care costs of GHP members offered CHIP versus GHP members offered standard insurance coverage at 3- and 6-months.

4.4 Specific Aim 3

To compare change in responses on the Wellbeing360 survey of GHP member offered CHIP versus employees offered standard employee wellness options

5 STUDY DESIGN

5.1 Description

This is a pilot randomized-controlled trial comparing the clinical, utilization, and financial outcomes of adult health plan members with T2DM offered CHIP versus those only offered standard health plan coverage.

5.2 Study Population

5.2.1 Approximate Number of Subjects

Approximately 60 adults who are Geisinger Health Plan members with Type 2 Diabetes Mellitus will participate in this study.

5.2.2 Inclusion Criteria

1. Geisinger Health Plan member for a full year prior to enrollment in the study, with plans to remain covered for a full year after the first study visit
2. HbA1c resulted within a year of enrollment in the study
3. ≥ 18 years
4. Current type 2 diabetes diagnosis
5. Living in the five-county region served by the Miller Center (Lycoming, Montour, Northumberland, Snyder and Union) with the ability to arrange their own transportation to the Miller Center in Lewisburg at least 10 times in a 3-month period
6. Access to computer, phone, or tablet with sufficient internet to complete program activities.

5.2.3 Exclusion Criteria

1. Presence of medical condition requiring specific diet other than gluten-free diet, a weight loss diet or diet directed at cardiovascular disease and/or metabolic syndrome (e.g. phenylketonuria)
2. Presence of medical condition contraindicating participation in CHIP, as determined by the Principal Investigator
    a. Cancer on active treatment
    b. Very advanced organ failure meeting one or more of the following criteria:
        i. Heart
            1. On milrinone or dobutamine drip
            2. Presence of ventricular assist device (VAD)
            3. Listed for or received a heart transplant
        ii. Lungs
            1. On home oxygen for COPD, interstitial lung disease, or any lung disease besides sleep apnea
            2. Listed for or received a lung transplant
        iii. Liver
            1. Cirrhosis with MELD score ≥ 9
            2. Listed for or received a liver transplant
        iv. Kidney
            1. On dialysis
            2. eGRF <15
            3. Listed for or received a kidney transplant
        v. Dementia
        vi. Severe difficulty swallowing
        vii. Presence of any form of feeding tube
        viii. Eating disorders (e.g. anorexia nervosa or bulimia)
        ix. Malabsorption (does not include mild malabsorption such as in celiac disease)
        x. Underweight status (BMI < 18.5 kg/m^2)
        xi. Stem cell transplant recipient

3. Diabetes in remission or already very tightly controlled with lifestyle alone, defined as HbA1c less than 6.5% on two separate occasions separated by at least 3 months while not on any diabetes medications. These must include the two most recent HbA1c values (i.e. if either of the last two HbA1c values was 6.5% or greater, the patient has had only one HbA1c value, *or* the patient was on a diabetes medication at the time of the HbA1c test, the patient is not excluded)
4. Pregnancy or plan to become pregnant within one year
5. Inability to give informed consent due to mental or psychiatric impairment
6. Any advanced neurological condition that would prevent a patient from altering their diet and/or participating in daily exercise?
7. Participation in the Fresh Food Farmacy program
8. Bariatric surgery within the past 2 years
9. Patient on warfarin
10. Hospice status
11. Cannot read and speak English fluently
12. Patient is currently enrolled in another clinical trial or plans to be within the next 12 months
13. Patient is not motivated (<7 out of 10) to improve their health through intensive lifestyle change
14. Patient has participated in intensive therapeutic lifestyle change through one of the following programs within the past 5 years:
    a. Previous CHIP program
    b. Ornish program
    c. Pritikin program.

5.3 Additional Guidance regarding specific diets

Patients can be enrolled in CHIP even if a physician has suggested that they eat one of the following diets. These patients will be encouraged to replace their current diet with CHIP:

- Mediterranean
- DASH
- MIND
- Atkins
- South Beach

- Keto
- Low carb
- High protein (unless for malnutrition or a specific health condition relating to nutritional deficiencies)
- Other diets targeting diabetes, obesity, or metabolic syndrome.

Diets we are able to accommodate (i.e. they can be on both a CHIP diet and this diet at once):

- Gluten free (celiac)
- Kosher (patient can decline to eat our pre-prepared food but would be able to make kosher food at home consistent with CHIP)
- Halal (patient can decline to eat our pre-prepared food but would be able to make halal food at home consistent with CHIP)
- Vegetarian
- Vegan
- Taking communion (alcohol is not encouraged on CHIP, but we will not discourage wine with communion)
- Coffee and tea drinkers
- Low sodium
- Low oxalate (e.g. for kidney stones)
- Food allergies.

Diets that we are not able to accommodate (patients will be excluded):

- Phenylketonuria (PKU)
- Any malabsorption or malnutrition diet except for a gluten-free diet for celiac
- Feeding tube of any sort
- Low vitamin K due to warfarin therapy
- Low potassium.

Any diets not covered in the above guidance will be assessed at the discretion of the study medical director, with any necessary input from the Lifestyle Medicine Institute team, according to the following criteria:

- Is the CHIP diet safe for this patient?
- Could this patient participate meaningfully in the CHIP dietary intervention?

5.4 Recruitment

Members meeting the above criteria will be invited via direct mail, MyGeisinger messages or phone to participate in this study. Potential participants will be asked complete the pre-screening questionnaire to confirm that they meet the study's inclusion and exclusion criteria. Potential

participants meeting the study criteria will be asked to review an electronic consent form. A link to the electronic consent form may be sent to those that are interested by email with permission from the potential participant. Study staff will be available by phone to answer any questions that participants may have while reviewing the electronic consent form. After consent is obtained, participants will be randomized 1:1 to either the control or intervention arm based on their most recent HbA1c on file with GHP. The reasons for any potential subjects' exclusion from the study will be tracked by the study team.

5.5 Study Duration

5.5.1 Approximate Duration of Subject Participation

Subjects will participate in the study for approximately 6 months. This includes the enrollment followed by 12 weeks of active intervention, as well as follow-up for 14 weeks post-intervention completion to include biometric, biomarker, and psychometric assessments.

5.5.2 Approximate Duration of Study

This pilot study will be completed in approximately 15 months. The end of the study will be the collection and completion of data analysis for all study data. The fifteen-month duration accounts for recruitment and start-up, 12-week intervention period, an additional 14-week biometric/biomarker measurement period, a 3-month lag in claims data processing, and a 3-month electronic data retrieval and analysis period.

5.6 Procedures

The CHIP intervention arm will be modeled after Vanderbilt's version of CHIP with adjustments made to fit the needs of GHP members and current logistical limitations related to COVID-19 (Shurney, et al., 2013). The CHIP curriculum will be administered during twice weekly 1-hour classes over a 6-week period, followed by weekly 1-hour classes for an additional 6 weeks. The protocol will begin with a 1-month in-person period, with participants subsequently offered the choice between in-person and online attendance for the remaining sessions. The protocol will be flexible with contingencies for inclement weather and any necessary social distancing related to the COVID-19 pandemic. Online classes will be conducted by the facilitators from the Miller Center over a HIPAA-compliant Microsoft Teams application.

Facilitators

Facilitators will be existing employees of Evangelical Community Hospital Health and Wellness. They will undergo CHIP facilitator training through the Lifestyle Medicine Institute's online program.

Intervention

GHP members randomized to the intervention arm will participate in the following:

- Attend 2 group meetings per week over 6 weeks, followed by one group meeting per week for 6 weeks (12 weeks total); meetings will be held in the evening and last approximately one to two hours. Meetings include:
    - Educational materials presented through a small group interactive lecture format based on the standard CHIP curriculum, including topics such as diet, sleep, exercise instruction, stress management, and toxic substance avoidance. The educational portion lasts approximately one hour.
    - Ten meetings will include a cooking demonstration and partaking in a meal prepared in the Cornerstone Kitchen according to The Optimal Diet, The Official CHIP Cookbook. Online participants will be encouraged to prepare the recipes at home. The group meal will last approximately one hour.
- Receive a copy of The Optimal Diet, The Official CHIP Cookbook.
- Receive access to online resources through CHIPHub.
- Participate in virtual meetings should in-person meetings be restricted.
    - Participants will be sent the menu for meals associated with all sessions at the start of the class. When participants cannot attend due to pandemic restrictions, or if they choose to attend a meeting virtually, they will be encouraged to buy their own ingredients and prepare the same meal they would have been served on site at the Miller Center. Participants will be encouraged to prepare the meal before the class, post photographs and communicate via discussion board and/or video chat. The meeting can include discussion of participants' experience cooking.
    - The same interactive lectures used for in-person meetings will be used for virtual meetings.

Additional procedures for the hybrid online/in-person approach will be as follows:

- Participants will be asked to enroll only if they can make a good faith effort to attend at least 80% of classes live (in-person or online) and to watch classes they miss within one week of the live event
- Participants will be expected to attend in person at the Miller Center twice weekly for the first month, practicing appropriate social distancing measures as may be necessary at the time of this event. After the first month, they will have the option of attending either in-person at the Miller Center or over Microsoft Teams for all subsequent classes except for the final class.
- All classes can be moved to a mandatory online format in case of inclement weather and/or if current public health recommendations preclude in-person classes from being held. The facilitators will lead all classes from meeting spaces at the Miller Center. This decision to alter format due to weather or pandemic concerns will be made at the discretion of the Miller Center director
- Participants will be disenrolled from the program if they request to be removed from the study (e.g. if they withdraw consent, if they move out of the area). The study doctor could decide to disenroll participants from this research study if they believe it is in the participant's best interest, if a participant had two consecutive HbA1c results less than 6.5% while off all diabetes medications, if a participant does not follow the study direction, if a participant is not able attend the required classes, or for any other reason
- Part way through the program, the facilitators will send an email to all participants encouraging them to complete as much of the program as possible. It is expected that many, if not most, of the participants will miss at least some classes. The facilitators will choose a time around the mid-point of the class to send an email reminding participants that materials are available online to review and to encourage those who have missed classes to attend the remaining classes if they are available. Participants will also be encouraged to eat CHIP meals from the *Eat Well* cookbook even if they are not able to attend classes
    - If a participant reaches out indicating they do not have time to complete the entire curriculum, the facilitators will help the participant determine what is feasible and encourage partial completion of key material

- If a participant reaches out requesting individualized help of any sort (e.g. troubleshooting diet), the facilitator will refer the participant to the course materials that are mot relevant to the participant's questions

- Results will be analyzed using an intention-to-treat framework, meaning that participants whose participation is suboptimal will not be asked to disenroll unless they request to do so, and we will attempt to complete all biometrics, biomarkers, and surveys for these participants. All relevant available data will be used for all analyses except for cases where participants withdraw consent.

Control group

GHP members assigned to the control arm will receive the routine standard of care for GHP members. Members will receive a summary of diabetes-related benefits available to members with type 2 diabetes. Because there are slight variations in coverage between various GHP plans, we will provide control group members with a telephone number to inquire about their diabetes-related benefits. We will track retention of the control group to inform design of a future fully powered study.

Participant Compensation

Participants will be compensated for their participation in the study as follows:

- Participants in the control group will be compensated up to $75. Participants will receive a $25 check after each completed blood draw at weeks 1, 12 and 26.
- Participants in the intervention group will be compensated up to $150. Participants will receive a $25 check for each completed blood draw at weeks 1, 12 and 26. They will also receive a $25 check for each month that they complete at least 75% of the required CHIP classes.

We feel this is adequate reimbursement for participants' time and travel at these timepoints. Participants will receive their checks in the mail up to 8 weeks after they are issued. In order for checks to be issued, participants will be asked to complete a W-9 form. This form will include participants name, address, and Social Security Number.

Data Collection

A study team member will attend the first CHIP session at the Miller Center and the last session to collect biometrics, biomarkers and psychometrics. Study samples (biomarkers) may also be collected at a Geisinger lab. All participants will also be scheduled for 6-month appointments with the research phlebotomist or at a Geisinger lab. The following data will be collected:

- Biometrics: Weight, BMI, Waist circumference, Systolic and diastolic blood pressure
- Biomarkers (blood tests): HbA1c, LDL-C
- Psychometrics: Wellbeing360 survey
- Current medication list

Data collection protocols will be as follows:

- Biometric, biomarker, and medication data will be collected by the study team at the Miller Center or biomarkers may be collected at a Geisinger lab. Baseline appointments will be offered before and after the first scheduled class and 3-month data collection will occur the week of the final class. Data collection at 6-months will occur at appointments scheduled individually with participants. Participants will complete the Wellbeing360 survey through CHIPHub. They will be given as much time as they need to complete the survey. Study staff will make up to three reminder calls to participants around the time they are due for each survey to encourage them to complete the surveys and assist with any technical difficulties. Data will be uploaded to the Lifestyle Medicine Institute's HIPAA-compliant servers, with the raw data transferred to secure Geisinger servers within one week. Medication lists will be determined based upon a medication reconciliation process which will begin by asking each participant what medication he or she takes. If a participant is not confident of his or her medication list, a study team member will obtain the medication list from the patient's primary care office and/or review the patient's chart in Epic to confirm medication list accuracy. The study team will obtain permission to access medication information for patients who are not seen within the Geisinger system. For participant with complex medication lists, or those which for any reason cannot be reconciled/entered into the database within the span of a standard biometric/biomarker appointment, the study team will prioritize collection of biomarkers and biometrics during the in-person encounter, as these need to be collected in-person and are especially time sensitive. For medication reconciliation and data entry

which requires more time with the participant, or guidance from the study physician, a study team member will follow up over the phone.

- Control arm subjects will have the same measures collected with the same protocols at the Miller Center at private appointments at baseline, 3-months and 6-months and the biomarkers for the control group may also be collected at a Geisinger lab.

5.6.1 Study Time and Events Table

Intervention Arm

		CHIP Program: 2 classes per week												CHIP Program: 1 class per week							
Week	0	1		2		3		4		5		6		7	8	9	10	11	12	26	52
Consent	X																				
Randomization	X																				
CHIP Program		P	P	P	P	P	P	P	P	H	H	H	H	H	H	H	H	H	P		
Height		X																			
Weight		X																	X	X	
Waist circumference		X																	X	X	
Blood Pressure		X																	X	X	
HbA1c		X																	X	X	
Cholesterol		X																	X	X	
Wellbeing360 Survey		X																	X	X	
Satisfaction Survey																			X		X

P = in person **H** = Hybrid (in-person/online)

Control Arm

Week	0	1	12	26
Consent	X			
Randomization	X			
Height		X		
Weight		X	X	X
Waist circumference		X	X	X
Blood Pressure		X	X	X
HbA1c		X	X	X
Cholesterol		X	X	X
Wellbeing360 Survey		X	X	X

5.7 Primary Endpoints

Clinical endpoint: Change in HbA1c at 6 months compared to baseline.

Feasibility endpoint: What proportion of individuals contacted agree to participate; what proportion of participants complete the intervention; what proportion of individuals contacted are excluded from the study based on lack of access to transportation or internet.

5.8 Secondary Endpoints

- HbA1c control at 3 months
- LDL-C at 3 and 6 months
- Biometrics at 3 and 6 months: weight, body mass index, blood pressure
- Psychosocial/behavioral: Wellbeing360 at 3 and 6 months
- Health behaviors, as measured by CHIP participation: overall program completion, attendance stratified by in-person versus online, proportion of required in-person visits attended
- Number of diabetes medications prescribed at 3 and 6 months
- Total cost of care over 6 months and comparison of total cost of care over the same 6 months the year prior and the 6 months immediately leading up to the study start date.

5.9 Statistics

Analysis will be performed by a member of the Geisinger Biostatistics Core.

5.9.1 Statistical Analysis Plan

Randomization scheme: The randomization scheme will be stratified on the potential study participant's most recent HbA1c value ($< 6.5\%$ vs $\geq 6.5\%$).

Analysis methods: Descriptive statistics and plots for each variable will be inspected to identify influential points and to assess normality. Non-normally distributed variables will be transformed (e.g., logarithmic) as appropriate for parametric analysis, otherwise non-parametric methods will be used. Means, standard deviations, medians, ranges (maximum/interquartile) and 95%

confidence levels will be calculated for baseline outcome variables (HbA1c, LDL-C, systolic blood pressure) for the entire group, and stratified by CHIP vs. control group. The difference in outcomes will be calculated and treated as dependent variables. Since this is a pilot study the focus of the analysis will be estimating the mean and standard deviation of the change at 3- and 6-month for each primary and secondary outcome. We will also estimate the difference of the changes between groups and the variability. These estimates will then be used to design a larger scale study that will seek external funding. All estimates will be calculated under the 'intent-to-treat' principle. We will also collect and report on the proportion of individuals contacted and consent to participate, and compliance on attending the CHIP session. For those individuals contacted and do not agree to participate, we will collect the reason (e.g., not interested, lack of access to transportation, lack of internet, not able to reach).

5.9.2 Statistical Power and Sample Size Considerations

Using published data from Vanderbilt our study would require almost 300 participants per group. However, since this will be a new endeavor at The Miller Center and with the adaptations to the CHIP protocol, we have decided our best initial step is to conduct a pilot study to work out the process of offering this program and recruiting subjects. Therefore, for the pilot study we are interested in the variability of the estimates needed to design a larger scale study. With 30 participants per group the study is able to estimate the 95% confidence interval of mean change in HbA1c (or any of the other change variables) with a half-width of 0.37 of the standard deviation of the change. Also, with 30 participants per group, the study is able to estimate the 95% confidence interval of the difference in change in HbA1c with a half-width of 0.52 of the standard deviation of the change. This will provide us with a range of possible values for future sample size calculations.

5.10 Data Management

5.10.1 Data Collection and Storage

Potential participants will be identified by a GHP data broker from an institutional data warehouse. The list of GHP members, including data relevant to recruitment contact (name, address, phone number, etc.) and most recent HgA1c will be provided to the study team.

A PACDC broker will create and maintain a database for project tracking in a secure Research Electronic Data Capture system (REDCap). This electronic data will be stored on Geisinger's secure network and will house recruitment and study data. The database will contain Protected Health Information (PHI) elements, such as name, date of birth, medical record number, and date of consent. Only IRB-approved study team members authorized by the PI will have access to this database and data collected for this research. These records will be kept indefinitely as communicated to patients and described in the informed consent form. Any data transmitted externally will be consistent with data sharing language included in applicable agreements.

- The research team may perform manual chart reviews to access any required data elements that are not available through the initial data pull and to verify data from the initial data pull.
- Biometric data will be obtained and recorded by a designated member of the study team and transcribed into the secure study database.
- CHIP metrics (e.g., attendance, engagement, etc.) will be tracked by the Miller Center staff and housed in a secure database.
- Surveys may be administered online or by paper. CHIP Lifestyle Medicine, proprietors of the CHIP program, will collect the Wellbeing360 data. This survey information will be entered and housed in the secure REDCap database.

The following data, including relevant dates, will be collected:

- Name
- Medical record number (if a participant does not have a Geisinger medical record number, we will create one to allow for lab testing)
- Address
- Phone number
- Email address
- Primary Provider Affiliation
- Lab values

- Baseline demographic variables of patients (age, sex, ethnicity, tobacco use, comorbidities)
- Biometrics (including height, weight, BMI, waist circumference, and blood pressure)
- Psychometrics: Wellbeing360 data
- Current medications
- GHP claims data (including number of claims and total cost of inpatient, emergency department, outpatient encounters, etc)

5.10.2 Records Retention

Records of data generated in the course of the study and maintained by the study team shall be retained for at least 6 years and could be used for future research studies submitted and approved by the IRB.

6 SAFETY MONITORING

6.1 Adverse Event Reporting

Not applicable for this minimum risk study.

7 SAFETY MONITORING

7.1 Sample Collection

For the purpose of this study, the following blood samples are being collected:

- HbA1c
- LDL (Direct Measure)

Blood samples will be obtained through venipuncture by qualified personnel following all applicable Geisinger guidelines. Blood for the HbA1c test will be drawn in a 4 mL lavender-top (K2 EDTA) tube. Blood for the LDL test will be drawn in a 3.5mL gold-top (serum separator tube) tube.

Blood samples will be collected at the baseline visit, and at weeks 12 and 26. These blood draws will occur at the Miller Center to coincide with the CHIP Program or at a Geisinger lab. Study control patients will be able to schedule an appointment at the Miller Center with a trained research phlebotomist for their lab draws or at a Geisinger lab. Tubes will be labeled with patient name, MRN and date and time of collection.

If samples are collected at the Miller Center blood will then be transferred to the Geisinger Medical Center lab by a designated member of the study team or a Geisinger courier for processing and testing. All labs will be processed according to standard procedures at Geisinger, whether the sample is collected at the Miller Center or at a Geisinger lab. No study specific storage, processing, or testing requirements are requested. A study lab manual will be provided to study staff and laboratory staff that outlines the specimens collected, specimen labeling and transportation guidelines.

7.1.1 Total Volume of Blood Collected

The total volume of blood collected from each subject will be approximately 22.5mL. Patients will have 7.5mL of blood drawn at three different timepoints throughout the study (week 1, week 12, and week 26).

7.2 Retention

Records of data generated in the course of the study shall be retained for at least 6 years and could be used for future research studies submitted to and approved by the IRB.

No specimen will be maintained for research purposes after testing is complete.

8 PROTECTION OF HUMAN SUBJECTS

8.1 Informed Consent and HIPAA Authorization

The investigator will provide for the protection of the subjects by following all applicable regulations. The informed consent/authorization form will be submitted to the IRB for review and approval.

Before any procedures specified in this protocol are performed, a subject must:

- Be informed of all pertinent aspects of the study and all elements of informed consent.
- Be given time to ask questions and time to consider the decision to participate.
- Voluntarily agree to participate in the study.
- Sign and date an IRB-approved informed consent form.

8.2 Protection of Human Subjects Against Risks

Risk of Loss of Confidentiality

There is a risk of loss of confidentiality. In order to minimize that risk, all electronic study data will be kept in password-protected computer files, and hard copy data will be stored in a locked environment that is only accessible only to the study team members. Data will be coded by assigning a unique study identification number to each participant. Analysis will be performed using the coded data. Only aggregate data without personal identifiers will be included when presenting results or submitting manuscripts for publication.

Blood Draw Risk

Providing blood samples via venipuncture can pose a minimal risk to participants. Individuals may feel faint, experience mild pain, bruising, irritation or redness at the site of puncture. In rare cases, an infection could develop.

Risk of Low Blood Sugars or Low Blood Pressures

Patients in this study will have type 2 diabetes (which is associated with hypertension), and they may be on medications for diabetes and/or blood pressure which have the potential to overshoot and cause low blood sugars and/or low blood pressures. Intensive therapeutic lifestyle change through CHIP may help to control blood sugars and blood pressures. This may increase patients' risk of medication-associated low blood sugars and/or low blood pressures, especially if patients do not adjust their medications to account for the effects of CHIP. Patients will be advised to discuss their CHIP participation with their primary care providers and to assess with those providers whether medication changes or more intensive monitoring is indicated to reduce the risk of low blood sugars and/or low blood pressures. The PI is a general internal medicine physician and will be available to answer patients' questions and/or address urgent issues, the management of all non-urgent issues will be directed to patients' existing healthcare teams.

9 PUBLICATION PLAN

We plan to submit a scientific abstract to upcoming meetings and to publish the data as a manuscript in a peer-reviewed journal.

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