CLINICAL PROTOCOL

The Effects of a Digital Customized Healthy Habit Software (Pro2col Health) on Health-Related Habits, Healthspan, and Biological Age

Investigational Product (if applicable):	Pro2col
CRO Protocol Number:	P083124
IRB Protocol Number:	Pro00081923
Sponsor:	None; Internal Investigation
Version and Date:	Version 1 9/6/2024

TABLE OF CONTENTS

List of Abbreviations and Definitions of Terms.

Abbreviation/ Term	Definition
AE	Adverse Event
AHA	American Heart Association
BMI	Body Mass Index
CIB/PI	Clinical Investigator Brochure/Package Insert
CRF	Case Report Form
CRO	Contract Research Organization
EOS	End of study
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICF/ICD	Informed consent form/Informed consent document
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
INP	Investigational Nutritional Product
IRB	Institutional Review Board
PHQ-9	Patient Health Questionnaire 9
PI	Principal Investigator
PPP	Per Protocol Population
QA	Quality Assurance
QC	Quality Control
®	Registered Trademark
SAE	Serious Adverse Event
SF-36	Short Form 36
SOPs	Standard Operating Procedures
USDA	United States Department of Agriculture

1. ETHICS

1.1. Institutional Review Board (IRB)/Independent Ethics Committee (IEC)

It is the responsibility of the investigator to have prospective approval of the study protocol, protocol amendments, informed consent forms, and other relevant documents, e.g., recruitment materials, if applicable, from the IRB/IEC. All correspondence with the IRB/IEC should be retained in the Investigator File (Site Master File). Copies of IRB/IEC approvals should be forwarded to the Sponsor.

The only circumstance in which a protocol amendment may be initiated prior to IRB/IEC approval is where the change is necessary to eliminate apparent immediate hazards to the subjects. In that event, the investigator must notify the IRB/IEC and the Sponsor in writing within 5 working days after the implementation.

1.2. Ethical Conduct of the Study

The study will be performed in accordance with the protocol, International Conference on Harmonization Good Clinical Practice guidelines (ICH E6-R2) and applicable local regulatory requirements and laws.

1.3. Subject Information and Consent

All parties will ensure protection of subject personal data and will not include subject names on any forms, reports, publications, or in any other disclosures. In case of data transfer, Sponsor will maintain high standards of confidentiality and protection of subject personal data.

The informed consent form must be agreed to by the Sponsor and the IRB/IEC and must be in compliance with ICH GCP, local regulatory requirements, and legal requirements.

The investigator must ensure that each study subject, or his/her legally acceptable representative, is fully informed about the nature and objectives of the study and possible risks associated with participation. The investigator, or a person designated by the investigator, will obtain written informed consent from each subject or the subject's legally acceptable representative before any study-specific activity is performed. The informed consent form used in this study, and any changes made during the course of the study, must be prospectively approved by both the IRB/IEC and the Sponsor before use. The investigator will retain the original of each subject's signed consent form.

2. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

Details on the administrative structure of the study (e.g., investigator, coordinating, steering committee, administration, monitoring and evaluation committees, institutions, statistician, central laboratory facilities, external service provider (ESP or CRO), or clinical study supply management) will be maintained in the Sponsor's Study Master File throughout the study for inclusion in the clinical study report.

3. STUDY OBJECTIVES

3.1. Primary Objective

- The primary objective is to explore the effects of a 4-6-week (28-42 days depending on subject availability for last testing day) intervention utilizing a novel health application (Pro2col Health) on daily activity, nutritional awareness, and numerous health outcomes in overweight but otherwise healthy subjects.

3.2. Secondary Objectives

- To assess subjective indications of depression using the PHQ-9 Scale.
- To assess subjective indications of quality of life, using the SF-36 Health Survey.

3.3. Exploratory Objectives

- Record any adverse event (AE) experienced by study subjects after enrollment in the digital application.

4. OUTCOMES MEASURE

4.1. Primary Outcomes – these measures will be taken at week 0 (pre) and week 7 (post)

- **Healthspan**, as assessed via a digital score within the application software.
- **Biological Age**, as assessed via an algorithm sourced within the application.
- **Lifestyle Risk Factors**, as assessed via questionnaires within the application.
- **Energy and Vitality**, as assessed via questionnaires within the application.
- **Strength and Endurance**, as assessed by performance measures including a timed mile walk/run, push-ups to exhaustion, and chair get-ups to exhaustion.
- **Body Composition**, as assessed via a previously validated digital scale.
- **Blood Pressure**, as assessed via an electronic blood pressure cuff.
- **Lifestyle Habits**, as assessed by specific interfaces within the application and guided by an AI "coach."
- **Daily Steps**, as collected via the Apple Health or Google Fit application on the subject's pre-existing personal device.

4.2. Secondary Outcomes – these measures will be taken at week 0 (pre) and week 7 (post)

- **Depression,** as assessed by the previously validated PHQ-9 subjective questionnaire.
- **Quality of Life,** as assessed by the previously validated SF-36 subjective questionnaire.

5. INVESTIGATIONAL PLAN

5.1. Overall Study Design and Plan

This is a non-blinded randomized controlled pilot trial conducted over up to 8 weeks. Week 0 will involve baseline measurements and enrollment, Weeks 1-6 constitute the intervention, and Week 7 to 8 is reserved for post-testing. The study will enroll up to 200 participants, with a minimum of 50 participants who meet the inclusion criteria, and a minimum target of 20 participants completing the study in each group (experimental and control).

Participants will be recruited from across the United States using a decentralized electronic database. The study will include individuals aged 21-60 with a BMI $\geq$ 25 (overweight) and $\leq$ 35. Additionally, qualified subjects must have current daily activity records that show an average daily step count under 5,000. Participants must also be free of disease and must own either a personal smartphone device with the Apple Health or Google Fit application. Finally, participants must be willing to keep their device with them at all times to ensure accurate activity tracking.

Following baseline testing and enrollment in the study, participants will be randomly assigned to either the control (CON) or experimental (PRO) group. The control group will receive subject-facing materials depicting current general activity recommendations as published by the American Heart Association (AHA) and current dietary guidelines provided by the United States Department of Agriculture (USDA). The experimental group will be enrolled in the Prime Health Technologies software (Pro2col), which provides a digital diagnostic score to calculate healthspan and biological age, along with AI and group community-based coaching dynamics. Subjects will be assigned a 6 week progressive protocol targeting improvements in daily activity levels, nutritional awareness, and overall lifestyle risk factors. Both groups will then be monitored by study staff throughout the duration of the intervention period with post-testing taking place following the last week of the experiment.

Due to the remote nature of subject recruitment, no in-person facility visits are required for participants.

5.2. Selection of Study Population

The following eligibility criteria are designed to select subjects for whom protocol requirements are considered appropriate. All relevant medical and non-medical conditions should be taken into consideration when deciding whether this protocol is suitable for a particular subject.

5.2.1 Inclusion Criteria

- Male or female, aged 21-60 years.
- A BMI categorized as overweight ($\geq$ 25) but not stage II obesity ($\leq$ 35)
- Daily steps < 5,000.

- Ownership of a smartphone device with either the Apple Health or Google Fit application.
- Willingness to carry their phone in their pocket or on their person at all times to track steps during study.
- Willing to download the Pro2col application and connect it with either the Apple Health or Google Fit application.
- Willingness to complete physical tasks including a timed one-mile walk/run, regular or modified push-ups to exhaustion, and chair get-ups to exhaustion.
- For the experimental group, subjects must be willing to follow the application protocol which is laid out later in this document.
- Able to read, understand, sign and date the informed consent document (English only)
- Able and willing to comply with the scheduled visit(s) and study requirements.

5.2.2 Exclusion Criteria

Subjects presenting any of the following will not be included in the study:

- Currently taking (within the past 30 days) ergogenic dietary supplements including, creatine, protein, amino acids, or stimulants other than caffeine (yohimbe, ephedrine, etc.)
- Currently taking performance enhancing drugs (testosterone or other anabolic-androgenic steroids), human growth hormone, insulin, etc.
- History or current malignancy
- Receiving chemotherapy agents or radiation treatments
- Musculoskeletal disease (muscular dystrophy, arthritis, etc.)
- Recent (<3-months) musculoskeletal injuries
- BMI < 25 or > 35 kg/m^2
- Diagnosis of a terminal illness
- Use of prescription medications that influence body composition (i.e., prescription hormone therapies, etc.)
- History of alcohol abuse
- History or current drug abuse
- History or current diagnosis of depression.
- History or current diagnosis of suicidal thoughts/ideation.
- A score of ≥ 10 arbitrary units on the PHQ-9 during baseline testing.
- History or current cigarette smoke (including vaping) within the past 14 days from the screening visit
- Insulin-dependent diabetes and/or metformin use
- Chronic kidney or liver disease
- Has significant concurrent illnesses (controlled or uncontrolled), such as diabetes, lupus, epilepsy, or cardiac disorders, hepatitis B/C, HIV, serious mental health illness such as dementia or schizophrenia; psychiatric hospitalization in the past two years,

or other, which in the opinion of the investigator, such conditions might be aggravated as a result of treatment

- The investigator feels that for any reason the subject is not eligible to participate in the study
- History of uncontrolled cardiovascular disease (i.e., myocardial infarction, hypertension, hypercholesterolemia, peripheral vascular disease, other)
- Developmental disability or cognitive impairment that would preclude adequate comprehension of the informed consent form and/or ability to follow study subject requirement and/or record the necessary study measurements
- A family member of the investigator or an employee of the investigator
- Participation in any other investigational study within 30 days prior to consent.

6. CONDITIONS

6.1. Study Administration

All study activities will be performed under the supervision of the investigator in accordance with the protocol requirements, and with adherence to Good Clinical Practices (GCP) and International Conference on Harmonization (ICH E6 R2).

Only study subjects who signed the informed consent form and meet all entry criteria will be enrolled and randomly assigned to a study group.

6.2. Identity of Experimental Condition

The Experimental Condition involves the use of a novel smartphone application. This application provides a digital diagnostic score to calculate healthspan and biological age, along with AI and group community-based coaching dynamics. Subjects will be assigned a 4-6-week (28-42 days depending on subject availability for last testing day) progressive protocol designed to implement lifestyle changes and solidify adherable practices including the following:

- Daily practice of intermittent fasting, eating within a time restricted eating window ranging from 8 to 12 hours.
- Increased daily steps.
- Increased awareness of hydration practices.
- Journaling
- Adherence to a lower carbohydrate, higher-protein diet.
- Improved exercise habits.
- Stress management
- Sleep habits
- Improved lifestyle risk factors, like smoking and alcohol intake

The above factors are individualized based on subject responses to questionnaires within the application. An AI-based coach and application algorithms will then send users push notifications to improve adherence to their new lifestyle factors as well as provide feedback for their logged data entries. Specifically, the application users will be required to connect the Pro2col application with either the Apple Health or Google Fit application so that necessary data can be transmitted between these applications without user input. The application creates a personalized protocol by using responses from the embedded health questionnaire to establish baseline figures that the user will improve upon. For example, if a user reports walking between 4,001-5,000 steps daily, their program will start them at 4,000 steps in week 1, gradually increasing each week until they reach the program's goal (e.g., 10,000 steps). Below are the key elements used to generate an individualized protocol, with specific goals for this user:

Steps Goal: 10,000 Steps

Incremental Approach: Starting from the user's baseline, steps will gradually increase each week to reach the target of 10,000 steps over a 4-6-week period (28-42 days depending on subject availability for the last testing day).

Example:

Week 1: Starting at the baseline (e.g., 4,000 steps)

Week 2: 5,200 steps

Week 3: 6,400 steps

Week 4: 7,600 steps

Week 5: 8,800 steps

Week 6: 10,000 steps

Calorie Goal: Moderate Fat Loss

Caloric intake will be reduced on average by 250 calories from basal calorie needs.

Hydration Goal: Subjects will have a target water consumption goal of 10 Cups of Water

Incremental Approach: Starting from the user's baseline (e.g., 5 cups), water intake will increase each week until reaching 10 cups over 6 weeks.

Example:

Week 1: 5 cups

Week 2: 6 cups

Week 3: 7 cups

Week 4: 8 cups

Week 5: 9 cups

Week 6: 10 cups

Eating Window: 8 Hours

Incremental Approach: The eating window will decrease each week until it reaches an 8-hour window over 6 weeks. For example if they are currently eating 16 hours per day (for example 6 am to 10 pm), we would modify as such:

Example:

Week 1: 16-hour eating window

Week 2: 14-hour eating window

Week 3: 12-hour eating window

Week 4: 10-hour eating window

Week 5: 9-hour eating window

Week 6: 8-hour eating window

Subjects will also be awarded with points within the application for hitting their goal.

6.3. Identity of Control Condition

Subjects randomly enrolled in the control group will be given materials published by the American Heart Association (AHA) and United States Department of Agriculture (USDA). The AHA flyer is linked **here** and the USDA booklet is linked **here**.

6.4. Blinding

Study officials nor participants will be blinded to study conditions.

6.5. Expected / Unexpected Risk

Risks or side effects associated with physical fitness programs:

- Musculoskeletal injury
- Fatigue
- Shortness of Breath
- Light-headedness or Dizziness
- Fainting

Risks or side effects associated with intermittent fasting:

- Fainting
- Dizziness
- Hunger

Risks or side effects associated with low carbohydrate diets:

- Fainting
- Dizziness
- Hunger
- Fatigue

General Statement:

Although no immediate risks or side effects are anticipated for this study, all aspects of this clinical investigation will be conducted under the direct supervision and oversight of the investigator and designated study staff. Adverse events whether spontaneous, or self-reported, will be collected and analyzed.

6.6. Prior and Concomitant Medications and Therapies

Subjects must abstain from exclusionary procedures/medications/therapies as listed under the Exclusion Criteria for the duration of the study, and prior to the study relative to certain Exclusion Criteria.

7. STUDY PROCEDURES

Study procedures as described in this section are depicted in the schedule of study visits of Appendix 1. Methodologies for study outcomes are described in Appendix 1.

7.1. SCREENING

Subjects who signed the informed consent form will have the following assessments performed:

- Inclusion and exclusion criteria
- Medical and medication history
- Demographic and baseline characteristics

Subjects who meet all required entry criteria will be enrolled in the study and will be assigned a **subject No./ID** in the 100 series starting with **"101"** and continuing in sequential order until enrollment is met.

Enrolled subjects will be scheduled for a remote consultation with a member of the study staff to go over the details of the study, their condition assignment, and all related materials and procedures for the study.

7.2. BASELINE TESTING

Subjects who continue to be eligible for this study will then complete baseline testing. Subjective questionnaires will be provided to assess items such as current activity levels, nutrition habits, and lifestyle factors related to health and wellness. Enrolled and randomized subjects will also receive a blood pressure cuff and digital scale to record blood pressure and bodyweight/body composition, respectively. Moreover, subjects will complete electronic calculations to estimate their healthspan and biological age. Finally, subjects will perform three physical fitness tests, including:

- Timed one mile walk/run
- Push-ups (or modified push-ups for women) to exhaustion
- Chair get-ups to exhaustion

7.3. INTERVENTION

Subjects will follow their assigned condition for 6 weeks. Subjects in the control group will be monitored by study staff but otherwise uninstructed in regard to activity and nutrition. Their adherence to the provided educational materials is entirely up to them. The experimental group will be initiated into a 4-6-week (28-42 days depending on subject availability for the last testing day) progressive protocol on the Pro2col app. They will receive daily updates, notification, and education regarding healthy habits such as exercise, hydration, and improved nutrition practices. An AI coach will be responsible for providing instructions and feedback to all application users.

7.4. POST-TESTING

Subjects who complete the 4-6-week (28-42 days depending on subject availability for last testing day) intervention and continue to be eligible for this study will then complete post testing. Subjective questionnaires will be provided to assess items such as current activity levels, nutrition habits, and lifestyle factors related to health and wellness. Enrolled and randomized subjects will also receive a blood pressure cuff and digital scale to record blood pressure and bodyweight/body composition, respectively. Moreover, subjects will complete electronic calculations to estimate their healthspan and biological age. Finally, subjects will perform three physical fitness tests, including:

- Timed one mile walk/run
- Push-ups (or modified push-ups for women) to exhaustion
- Chair get-ups to exhaustion

Finally, upon completion of the study (or early withdrawal), subjects will be directed to delete the investigational application from their smart device, and no further data will be collected.

7.5. Subject Withdrawal and Early Termination

Subjects may withdraw from the study at any time at their own request, or they may be withdrawn at any time at the discretion of the investigator or Sponsor for safety, behavioral, or administrative reasons. Every effort should be made to document the subject outcome, if possible. The investigator should inquire about the reason for withdrawal, request the subject return for a final visit, and if applicable, follow-up with the subject regarding any unresolved adverse events.

If the subject withdraws from the study and also withdraws consent for disclosure of future information, no further evaluations will be performed, and no additional data will be collected. The Sponsor may retain and continue to use any data collected before such withdrawal of consent.

7.6.1. Protocol Deviations

Protocol deviations will be tracked and managed during the conduct of the study. A protocol deviation is defined as a non-conformance from the protocol which occurs at any time during the conduct of the study. Exceptions will not be granted by the Sponsor for any planned or unplanned deviation. All protocol deviations will be tracked.

7.6.2 Status Classification

Classification	Criteria
Screen Failure	Signs the ICD but does not meet entry criteria or withdraws prior to Baseline Testing
Enrolled	Signs the ICD and met all inclusion/exclusion criteria
Initiated	Signs the ICD and successfully completes Baseline Testing

Discontinued/Withdrawal	Signed the ICD but does not successfully complete the Intervention
Completed	Signs the ICD and successfully completes the Intervention and Post-Testing

8. ASSESSMENTS

8.1. Clinical Evaluations

The following clinical evaluations will be conducted during the study review:

- **Medical and Medication History** – An assessment of the subject's health status prior to enrollment to ascertain appropriateness for study participation based on inclusion/exclusion criteria.

- **Adverse Event Reporting –** Investigator examination of the subject and notation of any observations made by the study investigator of a potential adverse event.

8.2. Assessment of Safety

Self-reported and observed adverse events.

9. ADVERSE EVENT REPORTING

9.1. Introduction

All observed or volunteered adverse events regardless of treatment group or suspected causal relationship to the INP(s) will be reported as described in the following sections.

For all adverse events, the investigator must pursue and obtain information adequate both to determine the outcome of the adverse event and to assess whether it meets the criteria for classification as a serious adverse event requiring immediate notification to the Sponsor or its designated representative. For all adverse events, sufficient information should be obtained by the investigator to try to determine the causality of the event. For adverse events with a suspected causal relationship to the experimental product, follow-up by the investigator is required until the event or its sequel resolve or stabilize at a level acceptable to the investigator, and Sponsor concurs with that assessment.

9.2. Reporting Period

Serious adverse events require immediate notification within **24 hours** to the IRB and its designated project manager. When reporting a serious adverse event, the investigator or designee completes the SAE form with as much information as possible however, at a minimum the Subject ID, Name of INP, SAE, and Name of person reporting the event.

All adverse events (serious and non-serious) must be collected on the subject's case report form (CRF) from the time the subject signed informed consent through the last subject visit.

9.3. Definition of an Adverse Event

An adverse event is any untoward medical occurrence in a clinical investigation associated with the use of an investigational product in human subjects. The event need not necessarily have a suspected causal relationship with the treatment or usage.

Examples of adverse events include but are not limited to:

- Clinically significant symptoms and signs
- Changes in physical examination findings

- Hypersensitivity

Additionally, they may include the signs or symptoms resulting from:

- Product misuse
- Product dependency
- Extravasation
- Study related procedure (e.g., resistance training protocol)

9.4. Serious Adverse Events

A medical device adverse event is serious when both of the following criteria are fulfilled:

- The event involves patient/subject/consumer contact
- The event results in:
  - Death
  - Serious deterioration in state of health. This includes:
    - Life-threatening illness or injury
    - Permanent impairment of a body function
    - Permanent damage to a body structure
  - Requires medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure
  - Requires inpatient hospitalization or prolongation of existing hospitalization

9.5. Severity Assessment

If required on the adverse event case report forms, the investigator will use the adjectives MILD, MODERATE, or SEVERE to describe the maximum intensity of the adverse event. For purposes of consistency, these intensity grades are defined as follows:	
MILD	Does not interfere with the subject's usual function.
MODERATE	Interferes to some extent with the subject's usual function.
SEVERE	Interferes significantly with the subject's usual function.

Note the distinction between the severity and the seriousness of an adverse event. A severe event is not necessarily a serious event. For example, a headache may be severe (interferes significantly with the subject's usual function) but would not be classified

serious unless it met one of the criteria for serious adverse events, listed above.

9.6. Causality Assessment

The investigator's assessment of causality must be provided for all adverse events (serious and non-serious). An investigator's causality assessment is the determination of whether there exists a reasonable possibility that the INP caused or contributed to an adverse event. If the investigator's final determination of causality is unknown and the investigator does not know whether or not INP caused the event, then the event will be handled as "related to INP" for reporting purposes. If the investigator's causality assessment is "unknown but not related to INP", this should be clearly documented on study records.

In addition, if the investigator determines a serious adverse event is associated with study procedures, the investigator must record this suspected causal relationship in the source documents and CRF, as appropriate, and report such an assessment in accordance with the serious adverse event reporting requirements, if applicable.

10. STATISTICAL METHODS

10.1. Sample Size Determination

The targeted sample size of 50 participants was determined by the Sponsor based on a meta-analysis involving 206,873 participants (Staiano et al., 2024). This analysis demonstrated that digital health interventions led to improvements in physical activity (+1,329 steps/day), reduced sedentary behavior (−7 hours/week), and increased vigorous exercise (+1 hour/week). Using these values, we conducted a power analysis, which identified an effect size difference of 0.8 between the control and experimental groups for average changes in habits like daily steps. This analysis confirmed that a sample size of 50 subjects would be sufficient.

https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-015-0950-4

10.2. Demographics and Baseline Characteristics

Demographic information will include age, gender, height, weight, BMI, race, and ethnicity. Baseline characteristics, including health data, subjective questionnaires, and anthropometrics will be summarized by treatment.

10.3. Analyses

10.3.1 Primary Analysis

Descriptive statistics will be reported including mean, median, minimum and maximum values, standard deviation, and 95% confidence intervals of the mean. All outcome measure data will be reported as mean ± standard deviation (SD). Relative and absolute changes between groups for all outcomes will be reported and analyzed for statistical significance using paired *t* tests. Additionally, effect sizes will be calculated as Cohen's d_g

for between-subjects analyses as the difference between group means divided by the pooled standard deviation times a correction factor [1]. Statistical significance will be set at $p < 0.05$ and all analyses will be performed using SPSS Version 28.0.

Cohen's $d_g = \frac{\left(X_{Group\ A} - X_{Group\ B}\right)}{SD_{pooled}} \times \left(1 - \frac{3}{4 \times (N1+N2) - 9}\right)$

10.3.2 Interim Analysis

There will be no interim analysis.

10.3.3 Safety Analysis

All safety analyses and summaries will be based on the Safety population. The number and percentage of subjects reporting AEs during the study will be tabulated and summarized. Subjects experiencing serious adverse events, treatment-related adverse events, and discontinuation from the study due to adverse events will also be summarized. Treatment-related adverse events will include events marked as being at least possibly or probably related to the study dose. Adverse events will be presented by severity and by relation to treatment. Enrollment status with respect to number of subjects enrolled, completed, lost-to-follow and discontinuation regardless of reason will be presented. All adverse events and concomitant medications will be presented in listings.

11. QUALITY CONTROL AND QUALITY ASSURANCE

During study conduct, the Sponsor or its agent will conduct periodic monitoring reviews (in person or remote) to oversee the progress of the clinical trial and to ensure that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs) as applicable, Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

The Sponsor representative may review source documents to confirm that the data recorded on CRFs/eCRF is accurate. The investigator and institution will allow Sponsor's representative or its agents, and appropriate regulatory authorities, direct access to source documents to perform this verification.

The study site may be subject to review by the institutional review board (IRB)/independent ethics committee (IEC), and/or to quality assurance audits performed by Sponsor, and/or to inspection by appropriate regulatory authorities.

It is important that the investigator(s) and their relevant personnel are available during any in-person monitoring visits and possible audits or inspections, and that sufficient time is devoted to the process.

12. ADMINISTRATIVE REQUIREMENTS

12.1. Protocol Amendments and Administrative Changes

Amendments and administrative changes are not to be made to this protocol without consultation with and the agreement of the Sponsor. The investigator and Sponsor should discuss amendment or administrative change. If agreement is reached, such amendment or administrative change will be developed in writing by the Sponsor and submitted to the investigator.

The investigator will be responsible for ensuring that all protocol amendments are approved in writing by the appropriate IRB or IEC before the institution of the changes specified in the amendment (except when necessary to eliminate an immediate hazard to the subjects). The investigator will also ensure that the Sponsor receives a copy of the written IRB or IEC approval of these changes.

The investigator will be responsible for ensuring that the IRB or IEC receives written notification of all administrative changes to the protocol prior to institution of the specified changes. The investigator will ensure that the Sponsor receives a copy of these written notifications.

12.2. Data Handling and Record Keeping

The investigator will document all study related procedures directly on the source record or medical chart as the primary source of data collection. Study related information/data points required by the sponsor for analysis will be transcribed by the investigator or designee from the source record, onto the CRF/eCRF (data collection tool) for this study using good documentation practices.

In some instances, the sponsor will provide a CRF template for use as the primary source of data collection.

The investigator is encouraged, however, not required to maintain additional source records on matters respective to the subject's safety and wellbeing not already captured on the CRFs/eCRF or source template.

Black or blue ink must be used on all data collection requirements. All errors and omissions must be crossed out by means of a single line, and the date and initials of the correction or addition of correct information must be provided. Use of white-out or write-overs will not be permitted. All study related records will be kept in a secure and locked location and shall only be accessible to the assigned study personnel during the conduct of the study, and to the regulatory authorities in the event of an inspection.

All raw and analyzed data files will be stored electronically on a private Google Drive folder that is accessible only to study staff. This folder is password protected and requires permission for outside entities to access its files.

12.3. Case Report Forms / Electronic Data Record

As used in this protocol, the term case report form (CRF) should be understood to refer to either a paper form or an electronic data record or both, depending on the data collection

method used in this study.

A CRF is required and should be completed for each enrolled subject. The completed original CRFs are the sole property of the sponsor and should not be made available in

any form to third parties, except for authorized representatives of the sponsor or appropriate regulatory authorities, without written permission from the sponsor.

It is the investigator's responsibility to ensure completion, review and approve all CRFs. CRFs must be signed by the investigator or by an authorized staff member. These signatures serve to attest that the information contained on the CRFs is true and accurate.

At all times, the investigator has final personal responsibility for the accuracy and authenticity of all clinical and laboratory data entered on the CRFs. In cases where the source documents are the hospital or the physician's chart, the information collected on the CRFs must match those charts.

12.4. Record Retention

To enable evaluations and/or audits from regulatory authorities or the Sponsor, the investigator agrees to keep records including the identity of all participating subjects (sufficient information to link records, e.g., CRFs and hospital records), all original signed informed consent forms, copies of all CRFs, serious adverse event forms, source documents, and detailed records of treatment disposition. The records should be retained by the investigator according to ICH guidelines, local regulations, or as specified in the Clinical Study Agreement, whichever is longer.

If the investigator relocates, retires, or for any reason withdraws from the study, the Sponsor should be prospectively notified of the event, and the location of study records.

The study records must be transferred to an acceptable designee, such as another investigator, another institution, or to the Sponsor.

13. PUBLICATION OF STUDY RESULTS

Publication of study results by the investigator is discussed in the Clinical Study Agreement, as appropriate. Results from this study may be published in the form of oral or written presentations at scientific meetings or as one or more peer-reviewed journal articles, with Sponsor’s prior approval, otherwise shall be kept strictly confidential. In these cases, no information on individual subjects will be revealed.

14. REFERENCES

M., Staiano, A.E. et al. A systematic umbrella review and meta-meta-analysis of eHealth and mHealth interventions for improving lifestyle behaviors. npj Digit. Med. 7, 179 (2024).

APPENDIX 1. METHODOLOGIES FOR STUDY OUTCOMES.

Healthspan
A subject's healthspan will be calculated using a proprietary algorithm housed within the prime health application. Briefly, subjects will answer a number of questions regarding their daily health habits, activities, and attitudes. These data will then be placed into a mathematical equation that uses data and statistics from numerous published studies regarding longevity and mortality risk. The outcome number is a subject's estimated "Healthspan," which describes their remaining healthy and active years of life. Importantly, this number can increase or decrease based on a subject's reported lifestyle changes at the end of the intervention period.

Biological Age
The subject's biological age will be estimated using the same proprietary formula used to estimate Healthspan. Briefly, biological age is different from chronological age, which simply reflects the number of years an individual has spent on Earth. Biological age, on the other hand, takes healthy lifestyle factors into account that may prematurely age individuals past their chronological age. Conversely, active and healthy users may find that their biological age is lower than their chronological age. Importantly, this number can increase or decrease based on a subject's reported lifestyle changes at the end of the intervention period.

Lifestyle Risk Factors
These risk factors are assessed by a number of questions pertaining to lifestyle habits that the subject must answer when enrolling in the application. As also extracted from the questionnaire.

Energy and Vitality
These outcome measures are subjective reports based on subject responses to specific questions within the application's questionnaires.

Strength and Endurance
Application users will be required to perform three objective performance tests to get accurate estimates of their healthspan and biological age. These performance tests include:
Upper Body Strength: Upper body strength will be assessed using the push-ups to failure protocol. Users will be instructed via the application on correct form and technique for push-ups specific to their gender. They will then perform as many push-ups as possible before reaching concentric muscle failure. This number will be reported to assess their upper body strength.
Endurance: Endurance will be assessed using a one mile walk time. Subjects will perform this assessment at their own determined pace, which is obviously restricted by their physical ability. Running is allowed, but not all subjects will be able to run the full mile. Thus, walking is allowed in this assessment.
Lower Body Strength: Lower body strength will be assessed by chair get-ups to concentric muscle failure. Briefly, subjects must use a chair or a related sturdy surface that reaches the height of their patella. They must fully sit and return to start for each repetition. They will

continue to perform get-ups to concentric muscle failure. This number will be reported to assess their lower body strength.

Body Composition
Body composition will be measured using a previously validated digital scale (RENPHO Smart Scale) that will be delivered to participants upon enrollment in the study. The scale uses bioelectrical impedance to estimate body composition. This involves a low level electrical current being sent through the body; the user cannot feel, hear, or otherwise sense this electrical current. The rate at which the current passes through the body is then input into an algorithm to estimate body composition based on known electrical current rates in human body tissue.

Body composition will also be estimated by questions embedded within the application and a corresponding algorithm.

Blood Pressure
Blood pressure will be measured using a previously validated electronic blood pressure cuff (Oklar Cuff Model C02) that will be delivered to participants upon enrollment in the study. The blood pressure cuff is capable of executing blood pressure measurements with minimal input from the user. Blood pressure is reported as systolic over diastolic, and the user will input these numbers into the application questionnaire.

Daily Steps
Daily steps will be assessed using communication between the Pro2col application and the user's Apple Health or Google Fit application. Apple Health and Google Fit both collect daily step counts by way of accelerometry, gyroscopy, and global positioning systems (GPS) and these data will be transferred to and housed within the Pro2col application.

Depression
Symptoms of depression will be assessed using the Patient Health Questionnaire-9 (PHQ-9). This questionnaire is a previously validated tool that collects information about depression symptoms in users. The user answers nine questions relating to depression symptoms on a scale of 0-3, with 0 representing no issues at all, and 3 representing experiencing the symptom nearly every day. The user's total score is a summation of their responses, and is scored as follows:

1-4 Minimal depression
5-9 Mild depression
10-14 Moderate depression
15-19 Moderately severe depression
20-27 Severe depression

Importantly, users who score $\geq$ 10 arbitrary units on the PHQ-9 during baseline testing will fail to continue being eligible for the study. In this instance, a study staff member will contact the individual, explain the reasoning, and thank the subject for their time. Due to the remote nature of this study, it is impossible to partner with a mental health clinic for subject referrals. Subjects will be encouraged to speak with their primary care physician if they are

concerned about their score. An email script will be crafted to provide further information for this instance.

Quality of Life

Quality of life will be assessed by the previously validated 36-item Short Form survey (SF-36). The SF-36 houses a number of questions pertaining to various factors of quality of life. Subjects will answer questions in a variety of manners, from simple "yes" or "no" responses to Likert-adjacent scaled responses that allow the subject to select the answer that best corresponds to their attitudes and beliefs. The scoring instructions for the SF-36 can be accessed in the .pdf linked **here**.