STUDY PROTOCOL

A Retrospective Study to Evaluate the Effectiveness of FuturHealth Program in Combination with GLP-1 Treatment in Weight Management in Participants ≥ 18-Year-Old

Protocol Number FH-100-001

Study Product:	FuturHealth Program (FHP) alone or in combination with GLP-1 medications.
Indication:	Weight management
Name and Affiliation of Principal Investigator:	Luis A. Rojas, PhD. InCSD CEO and President
Name and Address of Sponsor:	FuturHealth Inc. 325 W Washington St Ste 2 - 944 San Diego, CA 92103

Good Clinical Practice (GCP) Statement

This study will be performed in compliance with the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) GCP and applicable regulatory requirements, including the archiving of essential documents. Information contained in this protocol is confidential in nature, and may not be used, divulged, published, or otherwise disclosed to others except to the extent necessary to obtain approval as required by law.

People to whom this information is disclosed should be informed that it is confidential and may not be further disclosed without the express permission of FuturHealth, Inc.

DOCUMENT APPROVAL

This study will be conducted in compliance with the protocol, GCP, and applicable regulatory requirements.

SPONSOR REPRESENTATIVE

02/04/2025

Signature **Date**

Print Name: Sabrina Burgi

PRINCIPAL INVESTIGATOR

02/03/2025

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LIST OF ABBREVIATIONS

Abbreviation or Specialist Term	Definition
AE	Adverse event
BMI	Body Mass Index
CRF	Case report form
EHR	Electronic Health Record
EMR	Electronic Medical Records
FH	FuturHealth
FHP	FuturHealth Program
GCP	Good Clinical Practice
GDRP	General Data Protection Regulation
GIP	Gastric Inhibitory Polypeptide
GLP-1 RA	Glucagon-Like Peptide 1 Receptor Agonist
H0	Null Hypothesis
Ha	Alternative Hypothesis
HIPAA	Health Insurance Portability and Accountability Act
IA	Interim Analyses
ICF	Informed Consent Form
IRB	Institutional Review Board
ONC	Office of the National Coordinator for Health Information Technology
PCI	Payment Card Industry
PIPEDA	Personal Information Protection and Electronic Documents Act
RCT	Randomized Clinical Trials
SAE	Serious Adverse Event
SD	Standard Deviation
T2D	Type 2 Diabetes
VLCD	Very Low-Calorie Diet

1. PROTOCOL SUMMARY

1.1 SYNOPSIS

PROTOCOL TITLE: A Retrospective Study to Evaluate the Effectiveness of FuturHealth Program Alone or in Combination with GLP-1 Treatment in Weight Management in Participants ≥ 18 Years Old.

RATIONALE:

As described by Castro, R. (2025), Rodriguez P., et al. (2024), among others, glucagon-like peptide 1 receptor agonist (GLP-1 RA) Semaglutide and the dual GLP-1 RA/gastric inhibitory polypeptide (GIP) agonist Tirzepatide, have demonstrated the ability to aid in substantial weight reduction in patients with obesity, with and without type 2 diabetes (T2D). GLP-1 RA medications will henceforth be referred in this document as GLP-1 treatments.

Several randomized clinical trials (RCTs) have been completed to study how GLP-1 treatments can be beneficial to weight loss; however, the way weight loss has been analyzed has not been defined completely. For example, in the study conducted by Wilding JPH, Batterham RL, Calanna S, et al. (2021) obese subjects without diabetes, were treated for 68 weeks with 2.4 mg of Semaglutide dosed once weekly. This study, however, missed describing critical elements associated with the estimand's attributes for the evaluation of their primary endpoint. The authors concluded that the intervention in addition to "lifestyle intervention" lead to an average change from baseline body weight of -14.9% vs -2.4% for subjects on placebo. Similarly, subjects on treatment saw higher probability of 5%, 10%, or 15% weight reduction compared to placebo, 86.4% vs 31.5%, 69.1% vs 12%, and 50.5% vs 4.9%, respectively.

In their publication, Garvey WT, Frias JP, Jastreboff AM, et al. (2023) did not specify the use of a particular diet or any additional exercise during their study, the study mentioned several attributes related to the attributes of the estimand for the evaluation of the primary endpoint (i.e. as the primary estimand) are missing. This study included obese subjects with T2D that were dosed with 10 mg or 15 mg of Tirzepatide once weekly for 72 weeks. This study found that 79% - 83% of active subjects, dosed at 10mg or 15mg respectively, lost 5% bodyweight vs 32% in placebo; their trial also demonstrated that the higher of the two doses showed greater weight loss from baseline.

Rodriguez P., et al. (2024), conducted a head-to-head comparison of the two medications in overweight or obese adults, providing new data. Their findings aligned with previous RCT results, showing that both medications resulted in significantly greater weight loss than placebo. Specifically, 82% and 96% of individuals, with and without T2D respectively, treated with Tirzepatide at 10 mg per week achieved ≥5% weight loss by 72 weeks, with or without T2D. Similarly, 73% and 92% of individuals, with and without T2D respectively, treated with Semaglutide at 2.4 mg per week achieved ≥5% weight loss by 68 weeks. These results suggest that, for individuals with T2D, Tirzepatide may have a more significant impact on weight loss when compared to Semaglutide. This study did not specify if any additional specialized diet or exercise was used in adjunct for weight loss, focusing primarily on comparing Tirzepatide with Semaglutide. For subjects with T2D, Tirzepatide was found to be significantly more beneficial to weight loss than Semaglutide.

In summary, there is strong evidence derived from clinical trials about the effectiveness of GLP-1 treatments, even when the comparisons between different interventions did not describe, with details, some of the attributes of the primary estimand. As mentioned above, they did not provide details about the overall characteristics of the population of interest (e.g., diabetes status, proportion of subjects by BMI group, distribution of subjects by gender, age group, etc.), the treatment conditions (i.e., in terms of duration of the interventions, dose, dose regiment, etc.), and other intercurrent events (e.g.,

comorbidities, diet, exercise, concomitant medications). Additionally, social status (i.e., in terms of capabilities to access weight loss programs), among other factors known to impact weight management and overall health are not described in those studies. It is critical to define how the population level summaries will be carried out, including statistical methods/models, missing data strategies, etc. to properly evaluate the effectiveness of GLP-1 treatments for weight loss. Weight management does not rely only on pharmacotherapies, but in many other strategies including, but not limited to, nutritional programs designed to meet caloric and macro goals necessary to support healthy weight loss.

With these limitations considered, and with the goal of understanding the impact of a nutritional program in weight management, this study will analyze data from more than 40 thousand participants that have joined the FuturHealth Program (FHP) since 01-16-2024. Most of the participants who are a part of the FHP are using GLP-1 treatment, as recommended by their treating physician. This study will assume that all other factors (i.e., intercurrent events as previously described) are randomly distributed across participants in the FHP, in other words, the data will be used "as is" and only observable data (e.g., gender, age, age group, etc.), will be used for analysis purposes. The aim of this study is to describe the effectiveness of the FHP primarily between participants using Semaglutide and Tirzepatide, and also to compare the FHP vs the results published by Rodriguez P., et al. (2024). This data will be used to derive the null hypothesis for percent mean weight loss after 3 and 6 months of treatment to perform a one-sample t-test to evaluate the difference between the published data and the retrospective data collected by FuturHealth Inc.

INDICATION: Weight loss

PHASE OF DEVELOPMENT: NA

INVESTIGATIONAL SITES/LOCATIONS: Data was collected mainly in the USA using the FuturHealth App, also referred to in this document as the APP.

OBJECTIVES/ENDPOINTS

Objectives	**Endpoints**
Primary	
To evaluate the effectiveness of the FHP when used in combination with GLP-1 treatments (Semaglutide or Tirzepatide) for the management of weight loss after 3- and 6-months in participants registered in the FHP.	The difference in the mean percent change from baseline in weight between the FHP + Semaglutide vs FHP + Tirzepatide at 3- and 6-months in participants registered in the FHP.
Secondary	
To evaluate the effectiveness of the FHP when used in combination with GLP-1 treatments (Semaglutide or Tirzepatide) for the management of weight loss after 3- and 6-months when compared to GLP-1 treatment alone using the data published by Rodriguez P., et al. (2024)	The mean percent change from baseline in the weight difference between the FHP + Semaglutide and FHP + Tirzepatide vs GLP-1 reported data by Rodriguez P., et al. (2024) in terms of percent change in weight at 3- and 6-months. Note: according to Rodriguez P., et al. (2024), the mean percent change in the weight at 3 and 6 months for Semaglutide was -3.5% and -5.8 %, and - 5.9% and -10.1% for Tirzepatide.
Exploratory	

To describe changes in Body Mass Index (BMI) in participants registered in the FHP.	The change from baseline in BMI in participants in the FHP + Semaglutide vs FHP + Tirzepatide at each timepoint (<1 Month, 1, 2, 3, 3 to 6 months, and > 6 Months)
	The proportion of participants in each BMI Category at each timepoint (<1 Month, 1, 2, 3, 3 to 6 months, and > 6 Months).
To describe the changes in weight loss between the FHP + Semaglutide vs FHP + Tirzepatide.	The change from baseline in weight in participants in the FHP + Semaglutide vs FHP + Tirzepatide at each timepoint (< 1 Month, 1, 2, 3, 3 to 6, and > 6 Months).
To describe changes in HbA1C at each post-baseline time point by FHP group.	The proportion of participants at < 1 Month, 1, 2, 3, 3 to 6, and > 6 Months in the following HbA1C range categories: < 5.7%; ≥ 5.7% to < 6.4%; and ≥ 6.4% in the FHP + Semaglutide group vs FHP + Tirzepatide group.
To describe changes in Fasting Glucose at each post-baseline time point by FHP group.	The proportion of participants at < 1 Month, 1, 2, 3, 3 to 6, and > 6 Months in the following fasting glucose categories: <100 mg/dL; ≥ 100 to <120 mg/dL; and ≥ 120 mg/dL in the FHP + Semaglutide group vs FHP + Tirzepatide group.

Note: The Semaglutide group includes the brand names Ozempic and Wegovy. The Tirzepatide group includes the brand name Zepbound.

SUMMARY OF STUDY DESIGN:

This is a non-experimental retrospective study, on participants ≥18 years old registered in the FHP. Data will be summarized and analyzed, as deemed appropriate, on subjects with more than 1 post-baseline record.

Data analysis will be performed on an ongoing basis and evaluated to compare changes from baseline within and between participants enrolled in different programs (FHP alone, FHP in combination with Semaglutide, FHP in combination with Tirzepatide, and FHP in combination with other GLP-1 treatments). Analysis will include any observed variable or factor that may impact the response variable (e.g., weight loss) and with the understanding that other non-observed factors may also impact (e.g., physical activity, social status, comorbidities, etc.). Since non-observed data is not available, no inferential or descriptive statistics presented to summarize or visualize the data using plots, will not account for those factors.

This study also aims to perform a non-equivalent test in the form of a one-sample t-test, using the data collected from the FHP participants, comparing the mean and the percent of weight loss at 3, 6, and more than 6 months to a known or hypothesized population mean, in this case the Rodriguez P., et al. (2024) study. In their study 41,222 overweight or obese adults, that had regular care and no GLP-1 RA use in the year prior to initiation, an available baseline weight, and were receiving Semaglutide or Tirzepatide treatment between May 2022 and September 2023 were identified using electronic health record (EHR) data linked to dispensing information from a collective of US health care systems. The on-treatment weight outcomes, as reported by the investigators, through November 3, 2023, were assessed with the analysis completed on April 3, 2024.

The results from this study as described by Rodriguez P., et al. (2024) were as follows: “Patients receiving Tirzepatide were significantly more likely to achieve weight loss (≥ 5%; hazard ratio [HR], 1.76, 95%CI, 1.68, 1.84; ≥ 10%; HR, 2.54; 95%CI, 2.37, 2.73; and ≥ 15%; HR, 3.24; 95% CI, 2.91, 3.61). On-treatment changes in weight were larger for patients receiving Tirzepatide at 3 months (difference, −2.4%; 95% CI

−2.5% to −2.2%), 6 months (difference, −4.3%; 95%CI, −4.7%to −4.0%), and 12 months (difference, −6.9%; 95% CI, −7.9% to −5.8%)." These estimates will be used to perform t-test analysis as described in the Objectives and Endpoint section described above.

STUDY INTERVENTIONS

As described above, this is a non-interventional, non-experimental study, and all participants are on the FHP using a GLP-1 treatment as prescribed by their treating physician (in most cases).

STUDY DURATION: This is an ongoing study using data (primarily from the USA) collected from the FuturHealth App since 01-16-2024.

NUMBER OF PARTICIPANTS: For the first Interim Analysis (IA) approximately 41,679 records related to participants in the FHP will be used. Additional data will be collected and analyzed as deemed necessary by FuturHealth Inc.

INCLUSION CRITERIA:

Male or female ≥ 18 years of age at the time of signing the informed consent form (ICF).

EXCLUSION CRITERIA:
All participants' data in the FuturHealth database will be used for analysis.

STATISTICAL METHODS:

GENERAL STATISTICAL CONSIDERATIONS

The Sponsor representative, InCSD LLC. will be responsible for the statistical analysis of this study. All statistical analysis will be performed using SAS® Version 9.4 or higher (SAS Institute, Cary, NC, USA).

Descriptive statistics will be displayed to provide an overview of the study results. For continuous variables, descriptive statistics will include number of participants with available measurements (n), mean, standard deviation (SD), median, minimum, and maximum.

For categorical variables, the number and percentage of participants in each category will be presented. Unless otherwise noted, the denominator for percentages will be based on the number of participants included in the respective analysis set. Participants with missing data can generally be accounted for using the following approaches:

- For summaries of Demographics and Baseline Characteristics: summarize percentages based on all participants in the analysis set and include a "Missing" category (corresponding to participants with missing data for the variable being summarized) as the last row in the list of categories being summarized.
- For summaries of Effectiveness, unless otherwise specified: summarize percentages based only on those participants with observed data for the variable being summarized. As the denominator may be different from the number of participants in the analysis set being considered, the denominator should be displayed in the table.

Unless otherwise noted, all percentages will be displayed to one decimal place. No percentage will be displayed for zero counts, and no decimal will be presented when the percentage is 100%.

For the tabulations, the lower and upper confidence limits for the percentages will be truncated at 0 and 100% respectively.

Decimal places for descriptive statistics will always apply the following rules:

- "n" will be an integer.

- n (%) will include the number and proportion of participants who had evaluable records at the post-baseline time point.
- n, sub (%) will include the number and proportion of participants within each HbA1C category at each post-baseline time point.
- Mean, SD, and median will use one additional decimal place compared to the original data.
- Minimum and maximum will have the same number of decimal places as the original value.

If no participants have data at a given time point, for example, then only n=0 will be presented. However, if n<3, only n, minimum, and maximum will be presented. If n=3, only n, mean, median, minimum, and maximum will be presented. The other descriptive statistics will be left blank.

Derived variables, in general, will display the mean, SD, and median to 1 more decimal place than the variables used in the derivation. If the number of decimal places reported in the raw data is varied, then either the maximum raw number of reported decimal places or 3, whichever is the lowest, will be used as a guide for the descriptive statistics.

Timepoints will be reported by month as follows: < 1, 1, 2, 3, 3 to 6, and > 6 Months.

Analysis will be performed using participants enrolled in the FHP taking either "Semaglutide", "Tirzepatide", "Other", or "No Treatment Listed", and with at least 1 record greater than 25 days post-baseline.

SAMPLE SIZE CALCULATION

As a retrospective study, the sample size used for analysis purposes was not computed pursuing a particular power or under any pre-specified effect size and alpha level for the control of the type I error. All evaluable data, (participants with at least one post-baseline record and enrolled in the FHP for at least 25 days) will be included in all reports/analyses.

ANALYSIS METHODS

(1) The following data will be tabulated using descriptive statistics:

- Demographics and Baseline characteristics [e.g., gender, age, age group (18 to ≤ 35 years old), country, weight by gender, target weight, BMI by gender, etc.]
- Overview of the FHP (content) and Target Populations
- FuturHealth Program Overall Nutritional Values: calories per meal, calories per day, protein (grams/meals and grams/day) and macros (grams/meals) – carbs and fats.
- HbA1C: < 5.7%; ≥ 5.7% and < 6.4%; and ≥ 6.4%
- Fasting Glucose (mg/dL): < 100; ≥ 100 and < 120; and ≥ 120
- Change from Baseline in Weight by time point
- Change from Baseline in BMI by time point
- Proportion of participants by BMI categories: Overweight and below < 30; Obesity class 1 (30 to < 35), Obesity class 2 (35 to <40) and Obesity class 3/ severe obesity (≥ 40).
- Shift in BMI categories over time.

The primary endpoint will be analyzed using an ANCOVA Generalized Linear Model which will include treatment arm, baseline body weight (lbs.), and gender as predictors.

The secondary endpoints will be analyzed using a One-Sample T-Test.

Additional summaries and figures may be created. Details will be included in the Statistical Analysis Plan (SAP).

1.2 Schedule of Activities (SoA)

Not applicable since this is a non-experimental retrospective study, on participants ≥18 years old registered in the FHP.

2. INTRODUCTION

According to the World Health Organization (2020), more than 650 million adults worldwide suffer from obesity, and the prevalence of this condition has increased rapidly over the past 50 years.

The study performed by Walker et al., (2018) revealed that the increasing prevalence of overweight and obesity in the United States, is upwards of 68% nationally, and that the burden of overweight and obesity among men has ranged from 72.3% to 73.9% to 71.3% in in 2007–2008, 2009–2010, and 2011–2012, respectively. The authors also mention that for women, the prevalence of overweight and obesity has varied from 64.1% to 65.8% to 63.7% in the same time periods, respectively.

In 2021, Kim, JY (2021), also described that obesity has become one of the most important public health problems globally and is strongly associated with T2D, cardiovascular diseases including myocardial infarction and stroke, osteoarthritis, obstructive sleep apnea, depression, and some types of cancer, such as breast, ovarian, prostate, liver, kidney, and colon cancer [Dixon, E. (2014) and Smith CJ, et al. (2020) cited by Kim, JY (2021)].

In 2025, the trend around obesity remains the same and could be confirmed by the National Institute of Diabetes and Digestive and Kidney Disease (2025), who considers obesity as a chronic disease affecting more than 1 in 3 adults and about 17% of children and adolescents in the United States.

Obesity has undoubtedly been one of the most important public health problems worldwide in recent history, which suggests the need for evidence-based dietary strategies for weight maintenance. With many perceived barriers to managing weight and preventing obesity such as a lack of time, food choices, health education, patient-physician relationship, motivation, stress, and sleeping habits, among others, many people struggle to achieve and maintain weight loss Walker et al, (2018).

Lifestyle interventions, particularly in the form of diet and exercise, are the first lines of treatment for obesity and overweight. Reducing daily calorie intake is an important factor for weight loss, and low-calorie diets, especially low-fat or low-carbohydrate diets, have been suggested as the first dietary strategy to achieve this; in some cases, a short term very low-calorie diet (VLCD) is recommended, Kim, JY (2021). However, many people struggle to maintain a healthy diet for the long term.

Surgical interventions offer an effective alternative for some people with severe obesity but carries a greater risk in connection with the procedure and is not without complications. Additionally, surgical intervention requires close follow-up of the individual which can interfere with daily life and carries a higher cost compared to other treatments.

Pharmacotherapy may therefore serve as a valuable adjunct to lifestyle intervention for individuals with obesity and overweight in order to achieve and sustain clinically relevant weight loss, to improve comorbid conditions, and to facilitate a healthier lifestyle. Weight management medications are not for everyone with a high BMI, the National Institute of Diabetes and Digestive and Kidney Disease (2024), encompasses a wide range of tools to support individuals in their journey to optimal health.

Understanding that there is no single best strategy for healthy weight management, FuturHealth's weight loss programs offer reliable options to assist participants in their journey for weight management. Weight loss can help to improve many conditions associated with obesity such as mood/depression, sleep apnea, reflux, joint pain, fatty liver, diabetes/prediabetes, hypertension, and dyslipidemia. FuturHealth's goal is not just to improve the number on the scale but to contribute to the improvement on the quality of life and overall health for participants on the programs.

2.1 Study Rationale

To achieve this goal, this study will analyze data from more than 40 thousand participants that have joined the FHP since 01-16-2024, in where most of the participants are using GLP-1 treatment, as recommended by their treating physician. The evaluation of the program's performance using all data available and data from clinical trials as comparators, is an efficient strategy to generate evidence and data to describe the effectiveness of the FHP, when combined with Semaglutide, Tirzepatide, or other GLP-1 treatments (i.e., Combination of any of the available treatments).

As previously described, it is important to measure FHP performance in relationship with clinical trials where patients were treated with Semaglutide or Tirzepatide alone. The effect size, the magnitude and the average treatment effect when using the FHP in combination with those GLP-1 treatments can be computed after 3, 6, and more than 6 months of exposure.

2.2 Background

GLP-1 is a naturally occurring hormone secreted by intestinal L-cells shortly after food ingestion, playing a key role in the metabolism of ingested nutrients. In addition to this, GLP-1 has other notable effects, including the slowing of gastric emptying, inhibition of glucagon secretion, and promotion of satiety. Both preclinical and clinical studies have suggested that sustained activation of GLP-1 receptors is associated with weight loss (Baggio LL, et al., 2007).

GLP-1 RAs are synthetic analogs that mimic the natural effects of GLP-1, these agonists bind to GLP-1 receptors in the brain and other organs (Andreasen CR, et al., 2021; Cleveland Clinic, 2025). Research has shown that GLP-1 RAs can reduce perceived appetite and hunger, decrease cravings for energy-dense fatty foods, and improve eating control (Blundell J, et al., 2017; Friedrichsen M, et al., 2020).

Diet-induced weight loss is often difficult to sustain due to the compensatory changes in weight-regulating hormones, such as leptin, ghrelin, and GIP. As individuals lose weight, these hormone responses intensify, making further weight loss more challenging (Sumithran P, et al., 2011; Hall KD, Kahan S, 2018). The mechanism of GLP-1 RA treatment can counteract some of these effects, making it easier for overweight or obese individuals to achieve and maintain a weight loss of 5% or more of their body weight.

A systematic review and meta-analysis by Vosoughi K. et al. (2022), which included over 17,000 subjects from 22 trials with a median duration of 39 weeks, found that GLP-1 RA treatment led to significantly greater weight loss compared to a placebo. Among those treated with GLP-1 RA, 50.2% achieved a ≥5% weight loss, compared to only 17.1% in the placebo group. Furthermore, 17.5% of GLP-1 RA subjects experienced ≥10% weight loss, compared to 3.1% in the placebo group.

In the Phase III clinical trial NCT03611582 (Novo Nordisk A/S, 2025), once-weekly subcutaneous Semaglutide was compared with placebo over 68 weeks, used in conjunction with intensive behavioral therapy and an initial low-calorie diet. The study demonstrated that Semaglutide-treated subjects lost on average, 10.3% more body weight than those on placebo. A similar Phase III trial NCT04184622 by Eli Lilly and Company (2025), investigated Tirzepatide, another GLP-1 RA, over 72 weeks. Subjects receiving 5, 10, or 15 mg of Tirzepatide showed substantial and sustained weight loss, with 50% and 57% of subjects in the 10 mg and 15 mg groups, respectively, achieving a ≥20% reduction in body weight, compared to only 3% in the placebo group.

Both Semaglutide and Tirzepatide have shown to be highly effective for weight loss when combined with diet and exercise, as demonstrated in several clinical trials. Rodriguez P. et al. (2024) conducted a head-to-head comparison of the two medications in overweight or obese adults, providing new data. Their findings aligned with previous RCT results, showing that both medications resulted in significantly greater weight loss than placebo. Specifically, 82% and 96% of individuals with or without T2D treated with Tirzepatide at 10 mg per week achieved ≥5% weight loss by 72 weeks. Similarly, 73% and 92% of individuals with or without T2D treated with Semaglutide at 2.4 mg per week achieved ≥5% weight loss by 68 weeks. These results suggest that, for individuals with T2D, Tirzepatide may have a more significant impact on weight loss compared to Semaglutide.

GLP-1 treatments are effective in losing up to 20% of body weight before reaching a plateau and lose effectiveness immediately once discontinued. Despite their significant benefits for weight loss and diabetes control, GLP-1 providers often do not equip consumers with the tools needed to eventually get off the treatment and adopt lasting lifestyle changes. Addressing this gap, FuturHealth programs provide tailored Custom Meal Plans and recipes designed to support long-term health and wellness. Providing comprehensive nutritional support that meets the needs of GLP-1 users helps alleviate the uncertainty surrounding dietary changes. This approach empowers GLP-1 users, so they do not rely solely on medication, promoting a healthier lifestyle during and after use of GLP-1 treatments. The goal of FuturHealth is to assist and empower anyone looking to make a sustainable, positive, healthy change.

2.3 Benefit/Risk Assessment

There are no risks associated with this study, due to the retrospective nature of the study design. This study will represent a significant benefit to all stakeholders, primarily to the FHP participants who will have additional evidence of the effectiveness of this weight management strategy when combined with GLP-1 treatments. Additional specific details, regarding which group would see the most benefit (e.g., age group, BMI group, gender, etc.) as well as how soon and how much weight reduction, in general, could be observed once in the program will be generated. In general, data generated for this study will serve as reliable guidance for all decision makers. The Sponsor can not only revisit marketing campaigns but also manufacturing strategies to maximize the program's effectiveness and ensure that it is approachable to different segments in this critical population. The impact on health outcomes in general is exponential as it will help free up some of the financial and operational burden induced by the nearly 260 million Americans who are expected to be overweight or obese by 2050. This influx of overweight or obese Americans is expected to strain the health-care system and increase medical costs, according to a study published by Ng, Marie et al., (2024). The authors suggest that if

"past trends and patterns continue, an additional 3.33 million children and young adolescents (aged 5–14 years), 3.41 million older adolescents (aged 15–24 years), and 41.4 million adults (aged ≥25 years) will have overweight or obesity by 2050. By 2050, the total number of children and adolescents with overweight and obesity will reach 43.1 million (37·2–47·4) and the total number of adults with overweight and obesity will reach 213 million (202–221). In 2050, in most states, a projected one in three adolescents (aged 15–24 years) and two in three adults (≥25 years) will have obesity. Although southern states, such as Oklahoma, Mississippi, Alabama, Arkansas, West Virginia, and Kentucky, are forecast to continue to have a high prevalence of obesity, the highest percentage changes from 2021 are projected in states such as Utah for adolescents and Colorado for adults".

So, in conclusion, the benefits of this study will serve as a valuable source to assist this population, healthcare professionals, and organizations like FuturHealth to continue investing in this type of programs as additional alternatives for weight management and overall improvement of health and quality of life.

3. STUDY OBJECTIVES / ENDPOINTS

Objectives	Endpoints
Primary	
To evaluate the effectiveness of the FHP when used in combination with GLP-1 treatments (Semaglutide or Tirzepatide) for the management of weight loss after 3- and 6-Months in participants registered in the FHP.	The difference in the mean percent change from baseline in weight between the FHP + Semaglutide vs FHP + Tirzepatide at 3- and 6-Months in participants registered in the FHP.
Secondary	
To evaluate the effectiveness of the FHP when used in combination with GLP-1 treatments (Semaglutide or Tirzepatide) for the management of weight loss after 3- and 6-Months when compared to GLP-1 treatment alone using the data published by Rodriguez P., et al. (2024)	The mean percent change from baseline in the weight difference between the FHP + Semaglutide and FHP + Tirzepatide vs GLP-1 reported data by Rodriguez P., et al. (2024) in terms of percent change in weight at 3- and 6-Months. Note: according to Rodriguez P., et al. (2024), the mean percent change in the weight at 3 and 6 months for Semaglutide was -3.5% and -5.8 % and - 5.9% and -10.1% for Tirzepatide.
Exploratory	
To describe changes in Body Mass Index (BMI) in participants registered in the FHP.	The change from baseline in BMI in participants in the FHP + Semaglutide vs FHP + Tirzepatide at each timepoint (<1 Month, 1, 2, 3, 3 to 6 months, and > 6 Months)
	The proportion of participants in each BMI Category at each timepoint (<1 Month, 1, 2, 3, 3 to 6 months, and > 6 Months).

To describe the changes in weight loss between the FHP + Semaglutide vs FHP + Tirzepatide.	The change from baseline in weight in participants in the FHP + Semaglutide vs FHP + Tirzepatide at each timepoint (<1 Month, 1, 2, 3, 3 to 6 months, and > 6 Months)
To describe changes in HbA1C at each post-baseline timepoint by FHP group.	The proportion of participants at <1, 1, 2, 3, 6, and > 6 Months Post-Baseline in the following HbA1C categories: < 5.7%; ≥ 5.7% to < 6.4%; and ≥ 6.4% in the FHP + Semaglutide group vs FHP + Tirzepatide group.
To describe changes in Fasting Glucose at each post-baseline timepoint by FHP group.	The proportion of participants at <1, 1, 2, 3, 6, and > 6 Months Post-Baseline in the following fasting glucose categories: <100 mg/dL; ≥100 to <120 mg/dL; and ≥ 120 mg/dL in the FHP + Semaglutide group vs FHP + Tirzepatide group.

Note: The Semaglutide group includes the brand names Ozempic and Wegovy. The Tirzepatide group includes the brand name Zepbound.

4. STUDY DESIGN

4.1 Overall Study Design

This is a non-experimental retrospective study, on participants ≥18 years old registered in the FHP. Data will be summarized and analyzed as deemed appropriate on subjects with more than 1 post-baseline record.

Data analysis will be performed on an ongoing basis and evaluated to compare changes from baseline within and between participants enrolled in different programs (FHP alone, FHP in combination with Semaglutide, FHP in combination with Tirzepatide, and FHP in combination with other GLP-1 treatments). Analysis will include any observed variable or factor that may impact the response variable (for example weight loss) and understanding that other non-observed factors may also impacted (example physical activity, social status, comorbidities, etc.) but since this non-observed data is not available, then any inferential or descriptive statistics presented to summarize or visualize the data using plots, does not count for those factors.

This study also aims to perform a non-equivalent test in the form of a one-sample t-test, using the data collected from the FHP participants, comparing the mean and the percent of weight loss at 3- and 6-Months to a known or hypothesized population mean, in this case the Rodriguez P., et al. (2024) in where 41,222 overweight or obesity adults receiving Semaglutide or Tirzepatide between May 2022 and September 2023 were identified using electronic health record (EHR) data linked to dispensing information from a collective of US health care systems. As reported by the investigators, on-treatment weight outcomes through November 3, 2023, were assessed. Adults who were overweight or obese, had regular care in the year prior to initiation, no prior glucagon-like peptide 1 receptor agonist use, a prescription within 60 days prior to initiation, and an available baseline weight were identified. The analysis was completed on April 3, 2024.

The results from this study as described by Rodriguez P., et al. (2024) were as follows: "Patients receiving Tirzepatide were significantly more likely to achieve weight loss (5%; hazard ratio [HR], 1.76, 95% CI, 1.68, 1.84; 10%; HR, 2.54; 95% CI, 2.37, 2.73; and 15%; HR, 3.24; 95% CI, 2.91, 3.61). On-treatment changes in weight were larger for patients receiving Tirzepatide at 3 months (difference, −2.4%; 95% CI −2.5% to −2.2%), 6 months (difference, −4.3%; 95%CI, −4.7% to −4.0%), and 12 months (difference, −6.9%; 95%CI, −7.9%to −5.8%)." These estimates will be used to perform t-test analysis as described in the Section 3 above.

4.2 Scientific Rationale for Study Design

A retrospective study design allows us to compare data collected through the FH app in order to determine how participants exposed to different GLP-1 treatments in combination with FHP affects weight loss and other biomarkers such as BMI and HbA1C.

In addition, in this study a one-sample t-test will be used to compare the mean weight loss in different GLP-1 treatments in combination with FHP vs the mean weight loss observed and published in the studies published by Rodriguez P., et al. (2024), which will be used as the hypothesized population mean for each respective case.

4.3 End of Study Definition

There is no planned end to the study, data collection will be continued to progressively monitor the effectiveness and safety of the FHP.

5. POPULATION OF INTEREST

5.1 Inclusion Criteria

Male or female ≥ 18 years of age at the time of signing the informed consent form (ICF)

5.2 Exclusion Criteria

All participants in the FuturHealth database will be used for analysis. It is important to note that all FuturHealth participants under any GLP-1 treatment follow the Inclusion/Exclusion criteria described in the Mohit Joshipura, MD and OpenLoop Clinical Operations, Medical Weight Loss Client Master Clinical Protocol (2024).

5.3 Lifestyle Considerations

As described above, since this is a retrospective study, no lifestyle considerations will be used to determine the eligibility of the data to be considered for analysis purposes.

6. STUDY INTERVENTION

During this non-interventional, retrospective study, the participants' prescribed GLP-1 RA treatments, synthetic analogs as described in Section 2.2, in combination with the FHP are the main focus for the evaluation of the primary and secondary endpoints.

6.1 GLP-1 RA Treatments

The table below provides a general description of the GLP-1 treatments used by participants enrolled in the FHP.

Table 1: GLP-1 RA treatments used by FHP participants enrolled in the FuturHealth Program

GLP-1 RA	Route of administration	Dose and Administration	Indication
WEGOVY (Semaglutide) Initial U.S. Approval: 2017[1]	Injection/ subcutaneous in the abdomen, thigh or upper arm	- Once weekly as an adjunct to diet and increased physical activity, on the same day each week, at any time of day, with or without meals - Initiate at 0.25 mg once weekly for 4 weeks. Then follow the dosage escalation schedule, titrating every 4 weeks to achieve the maintenance dosage - The maintenance dosage of WEGOVY in adults is either 2.4 mg (recommended) or 1.7 mg once weekly - The maintenance dosage of WEGOVY in pediatric patients aged 12 years and older is 2.4 mg once weekly	- Indicated in combination with a reduced calorie diet and increased physical activity. - To reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established cardiovascular disease and either obesity or overweight. - To reduce excess body weight and maintain weight reduction long term in: • Adults and pediatric patients aged 12 years and older with obesity • Adults with overweight in the presence of at least one weight-related comorbid condition.
OZEMPIC (Semaglutide) Initial U.S. Approval: 2017[3]	Injection/ subcutaneous in the abdomen, thigh or upper arm	- Once weekly at any time of day, with or without meals (2.1). - Start at 0.25 mg once weekly. After 4 weeks, increase the dosage to 0.5 mg once weekly	- Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. - To reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus and established cardiovascular disease
ZEPBOUND (Tirzepatide) Initial U.S. Approval: 2022[2]	Injection/ subcutaneous in the abdomen, thigh or upper arm	- The recommended starting dosage is 2.5 mg once weekly. - After 4 weeks, increase to 5 mg injected subcutaneously once weekly. - Increase the dosage in 2.5 mg increments after at least 4 weeks on the current dose. - The recommended maintenance dosages are 5 mg, 10 mg, or 15 mg.	- Adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of: • 30 kg/m2 or greater (obesity) or • 27 kg/m2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes mellitus, obstructive sleep apnea or cardiovascular disease).

For additional details please see package insert for each medication at:
[1] https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/215256s011lbl.pdf
[2] https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/217806s003lbl.pdf
[3] https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/209637s032lbl.pdf
Note: Ozempic and Wegovy are different brand names for the same injectable drug, Semaglutide. The difference is that Wegovy was approved to manage weight in adults and kids 12 and up who have obesity and Ozempic was approved to lower blood sugar for subjects with type 2 diabetes.

6.2 FuturHealth's Weight Loss Program

FuturHealth's weight loss programs encompass a wide range of tools to support participants in their journey to optimal health. The FHP is individualized to each participant, once they have met with their clinician, discussed their goals, treatment options to reach those goals, and decide on medication together. During the consultation the clinician will decide if the patient will require labs prior to being prescribed medication.

The participant is encouraged to address nutritional needs via the meal planning portion of the FHP or via the pre-made meal offerings. There are no set programs with set meals/calorie counts for prepared meals. The pre-set nutrition programs are designed to meet calories and macro goals that support healthy weight loss.

FuturHealth's clinical partners require a monthly refill application (using the OpenLoop Intake Form), to address weight loss as well as ensure there are no significant side effects.

Participants' concerns are handled by FuturHealth customer support at 831-900-4723 or via chat using chat.fh.co

The OpenLoop Clinical Operations, (2024), Compounded GLP-1 Severe or Unexpected Adverse Event Reporting Process is used to monitor and address any safety concerns. In the event of any allergic reaction participants should seek emergency medical attention or call the **Poison Control Helpline at 1-800-222-1222**.

6.2.1 FHP Program Description

FuturHealth offers tailored custom nutritional plans to meet the dietary needs of all participants. Details about the FHP, target populations and overall nutritional values are described in Table 2 and Table 3 below:

Table 2: Overview of FuturHealth Program and Target Populations

Content (General Overview)	Target Population
Fat Protein Efficient and Dual Efficient meals	Meals targeting patients who want to lose weight and are taking GLP-1s.
Carbohydrate efficient meals: no meat, animal proteins, or dairy products Vegetarian and carbohydrate efficient meals: no meat or animal proteins. Meals that contain no beans, grains, dairy, or added sugar. Substitutions are offered based on diet preferences.	Meals targeting patients who want to lose weight, are taking GLP-1s, and are following a vegetarian diet.
Meals that are primarily vegetarian with the addition of fish as a protein source.	Meals targeting patients who want to lose weight, are taking GLP-1s, and are following a pescatarian diet.
Carbohydrate efficient meals: typically limits refined carbohydrates and have portion controlled carbohydrates. General guidelines	Meals targeting patients who want to lose weight, are taking GLP-1s, and are following a diet to address diabetes.

are 35-45 grams of carbohydrates for a female and 45 to 60 grams per meal for males.

Table 3: Overall Nutritional Values

		Protein		Macros (grams / meals) [1]	
Calories a meal	Calories a day	grams / meals	grams a day	Carbs	Fats
350 to 500	1200 to 1500	20-30	60-90	30 to 60	< 20

[1] Macros vary by plan and for different weight classes.

7. STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

Not applicable.

8. STUDY ASSESSMENTS AND PROCEDURES

Not applicable.

9. STATISTICAL CONSIDERATIONS

9.1 General Considerations

InCSD LLC. will be responsible for the statistical analysis of this study. All statistical analysis will be performed using SAS® Version 9.4 or higher (SAS Institute, Cary, NC, USA).

Descriptive statistics will be displayed to provide an overview of the study results. For continuous variables, descriptive statistics will include number of participants with available measurements (n), mean, standard deviation (SD), median, minimum, and maximum.

For categorical variables, the number and percentage of participants in each category will be presented. Unless otherwise noted, the denominator for percentages will be based on the number of participants included in the respective analysis set. Participants with missing data can generally be accounted for using the following approaches:

- For summaries of Demographics and Baseline Characteristics: summarize percentages based on all participants in the analysis set and include a “Missing” category (corresponding to participants with missing data for the variable being summarized) as the last row in the list of categories being summarized.
- For summaries of Effectiveness, unless otherwise specified: summarize percentages based only on those participants with observed data for the variable being summarized. As the denominator may be different from the number of participants in the analysis set being considered, the denominator should be displayed in the table.

Unless otherwise noted, all percentages will be displayed to one decimal place. No percentage will be displayed for zero counts, and no decimal will be presented when the percentage is 100%.

For the tabulations, the lower and upper confidence limits for the percentages will be truncated at 0 and 100% respectively.

Decimal places for descriptive statistics will always apply the following rules:

- "n" will be an integer.
- n (%) will include the number and proportion of participants who had evaluable records at the post-baseline time point.
- n, sub (%) will include the number and proportion of participants within each HbA1C category at each post-baseline time point.
- Mean, SD, and median will use one additional decimal place compared to the original data.
- Minimum and maximum will have the same number of decimal places as the original value.

If no participants have data at a given time point, for example, then only n=0 will be presented. However, if n<3, only n, minimum, and maximum will be presented. If n=3, only n, mean, median, minimum, and maximum will be presented. The other descriptive statistics will be left blank.

Derived variables, in general, will display the mean, standard deviation (SD), and median to 1 more decimal place than the variables used in the derivation. If the number of decimal places reported in the raw data is varied, then either the maximum raw number of reported decimal places or 3, whichever is the lowest, will be used as a guide for the descriptive statistics.

Time points will be reported by month as follows: < 1, 1, 2, 3, 3 to 6, and > 6 months.

Analysis will be performed using participants enrolled in the FuturHealth Weight Loss Program and taking either "Semaglutide", "Tirzepatide", "Other", or "No Treatment Listed", and with at least 1 record greater than 25 days post-baseline.

9.2 Statistical Hypotheses

The following null hypotheses will be tested:

Null Hypothesis 1:

The mean percent change in body weight (lbs.) from baseline at 3 months in the participants in the FHP on Semaglutide is the same as in the participants in the FHP on Tirzepatide.

Null Hypothesis 2:

The mean percent change in body weight (lbs.) from baseline at 6 months in the participants in the FHP on Semaglutide is the same as in the participants in the FHP on Tirzepatide.

Null Hypothesis 3:

The mean percent change in body weight (lbs.) from baseline at 3 months is equal between Semaglutide + FHP and Semaglutide alone.

A -3.6% (95% CI of -3.7% to -3.4%) change from baseline to Month 3, obtained from Rodriguez P. et. al., (2024) publication will be used as the comparator using a one-sample left sided test.

Null Hypothesis 4:

The mean percent change in body weight (lbs.) from baseline to 6 months is the same between Semaglutide + FHP and Semaglutide alone.

A -5.8% (95% CI of -6.0% to -5.5%), change from baseline to Month 6, obtained from Rodriguez P. et. al., (2024) publication will be used as the comparator using a one-sample left sided test.

Null Hypothesis 5:

The mean percent change in body weight (lbs.) from baseline at 3 months is equal between Tirzepatide + FHP and Tirzepatide alone.

A -5.9% (95% CI of -6.0% to -5.8%) change from baseline to Month 3, obtained from Rodriguez P. et. al., (2024) publication will be used as the comparator using a one-sample left sided test.

Null Hypothesis 6:

The mean percent change in body weight (lbs.) from baseline to 6 months is the same between Tirzepatide + FHP and Tirzepatide alone.

A -10.10% (95% CI of -10.4% to -9.9%), change from baseline to Month 6, obtained from Rodriguez P. et. al., (2024) publication will be used as the comparator using a one-sample left sided test.

Note: additional inferential analysis may be carried out. Details will be provided in the SAP.

9.2.1 Testing Strategy

All inferential analysis will be performed without adjustment for multiplicity and nominal p-values will be displayed.

9.3 Determination of Sample Size

As previously described, this is a retrospective study, and the sample size used for analysis purposes was not computed pursuing a particular Power and under any pre-specified effect size and alpha level for the control of the type I error. All evaluable data, (participants with at least one post-baseline record and enrolled in the FHP for at least 25 days) will be included in all reports/analyses.

9.4 Missing data strategies

Missing data will not be imputed.

9.5 Planned Analysis

This is an ongoing study, and several analyses are planned to evaluate the effectiveness of the FHP in combination with GLP-1 treatment. The first interim analysis (IA) will be executed with

approximately 41,679 records from participants in the FHP. Additional data will be collected and analyzed as deemed necessary by the FuturHealth Inc.

9.6 Subgroup Analysis

The following factors will be used for subgroup analysis:

- Gender
    - Male
    - Female
    - Unreported
- Age group (18 to ≤ 35 vs >35 to 50 years old)
- Country: USA vs non-USA
- Body Mass Index
    - Overweight and below (< 30)
    - Obesity class 1 (30 to < 35)
    - Obesity class 2 (35 to <40)
    - Obesity class 3 or severe obesity (≥ 40).
- HbA1C
    - < 5.7%
    - ≥ 5.7% to <6.4%
    - ≥ 6.4%
- Fasting Glucose (mg/dL)
    - < 100
    - ≥ 100 and < 120
    - ≥ 120

9.7 Analysis Sets

- All Participants (ALP): The ALP will consist of all Participants who have given informed consent/registered in the FHP.
- All Evaluable Participants (AEP): A subset of the ALP limited to participants at least 18 years old, who logged in and signed up with the FHP and have at least 1 record greater than 25 days post-baseline (first entry).
- FHP Alone (FPA): A subset of the AEP including only participants who didn't report using GLP-1 treatment.
- FHP and Semaglutide (FHS): A subset of the AEP including only participants who reported using "Semaglutide", "Ozempic" or "Wegovy" in combination with FHP.

- FHP and Tirzepatide (FHT): A subset of the AEP including only participants who reported using "Zepbound" or "Tirzepatide" in combination with FHP.
- FHP and Other (FHO): A subset of the ARP including only participants who reported using "Other" in combination with FHP.

9.8 Participant Disposition, Demographics, and Baseline Characteristics

A summary of all participants' disposition will be created using the ALP dataset to describe the number and percentage of participants by analysis sets and their demographics and baseline characteristics, including age, age group, country group, weight, weight by gender, and BMI group.

9.9 Medical History

Participant's medical history was not collected in this retrospective study.

9.10 Prior/Concomitant Medication

Participant's medication history was not collected in this retrospective study.

9.11 Efficacy Analysis

9.11.1 Analysis of the Primary Efficacy Endpoint

Inferential Analysis using the AEP:

- The difference in the mean percent change from baseline in body weight between FHP + Semaglutide vs FHP + Tirzepatide at 3 months and 6 months will be analyzed using an ANCOVA which will include treatment arm, baseline body weight (lbs.), and gender as predictors.

9.11.2 Analysis of the Secondary Efficacy Endpoints

- The difference in the mean percent change from baseline in body weight at 3- and 6-months between the FHP + Semaglutide vs Semaglutide alone will be performed using a One-Sample T-Test.

  Note:

  The mean percent change from baseline in body weight at 3- and 6-months and the 95% CI, for the null hypothesis (H0) - Semaglutide alone, will be obtained from Rodriguez P. et al., (2024) publication.

- The difference in the mean percent change from baseline in body weight at 3- and 6-months between the FHP + Tirzepatide in participants vs Tirzepatide alone will be performed using a One-Sample T-Test.

  Note:

  The mean percent change from baseline in body weight at 3- and 6-months and the 95% CI, for the null hypothesis (H0) - Tirzepatide alone, will be obtained from Rodriguez P. et al., (2024) publication.

In addition, the following figures will be created using the AEP.

- Mean and Median Change from Baseline in Weight (lbs.) at each timepoint by Treatment
- Mean and Median Change from Baseline in Weight (lbs.) at each timepoint by Treatment and BMI Category at Baseline
- Mean and Median Change from Baseline in Weight (lbs.) at each timepoint (≥ 3 Months) by Treatment and BMI Category at Baseline.
- Mean and Median Percent Change from Baseline in Weight (lbs.) at each timepoint by Treatment
- Mean and Median Percent Change from Baseline in Weight (lbs.) at each timepoint by Treatment and BMI Category at Baseline
- Mean and Median Percent Change from Baseline in Weight (lbs.) at each timepoint (≥ 3 Months) by Treatment and BMI Category at Baseline
- Mean and Median Change from Baseline in BMI at each timepoint by Treatment
- Mean and Median Change from Baseline in BMI at each timepoint by Treatment and BMI Category at Baseline
- Mean and Median Change from Baseline in BMI at each timepoint (≥ 3 Months) by Treatment and BMI Category at Baseline
- Mean and Median Percent Change from Baseline in BMI at each timepoint by Treatment
- Mean and Median Percent Change from Baseline in BMI at each time point by Treatment and BMI Category at Baseline
- Mean and Median Percent Change from Baseline in BMI at each timepoint (≥ 3 Months) by Treatment and BMI Category at Baseline

Additional summaries and figures may be created. Details will be included in the Statistical Analysis Plan (SAP).

9.12 Safety Analysis

Any safety concern reported by the FHP participants will be summarized using the AEP.

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

No text is to be entered into in this section; rather it should be included under the relevant subheadings below.

10.1 Regulatory, Ethical, and Study Oversight Considerations

10.1.1 Good Clinical Practice (GCP) Documents

The GCP documents are listed below.

- Signed original protocol (i.e., Investigator's Agreement).

- *Curricula vitae* of all investigators and sub-investigators.
- Any other relevant GCP documents

The GCP documents must be received from the Principal Investigator and reviewed and approved by FuturHealth, Inc. or its designee before the study site can initiate the study and before will authorize shipment of IP to the study site. Copies of the Investigator's GCP documents must be retained at the study site in a secure location. Additional documents, including a copy of the protocol and applicable amendment(s) and copies of regulatory references. It is the Investigator's responsibility to ensure that copies of all required GCP documents are organized, current, and available for inspection.

Since the study does not use any identifiable participant's information then an Institutional Review Board is not required.

10.1.2 Declaration of Helsinki and Good Clinical Practice

This study will be conducted in compliance with the April 1996 ICH Guidance for Industry GCP E6 (including archiving of essential study documents), the Integrated Addendum to ICH E6 (R2) of November 2016, the Declaration of Helsinki, the applicable regulations of the country(ies) in which the study is conducted, and with the Commission Directives 2001/20/EC and 2005/28/EC.

10.1.3 Regulations

Refer to the following United States Code of Federal Regulations (CFR):

- FDA Regulations 21 CFR, Parts 50.20 – 50.27 Subpart B – Informed Consent of Human Participants.
- FDA Regulations 21 CFR, Parts 312.50 – 312.70 Subpart D – Responsibilities of Sponsor and Investigator.

10.2 Committees

Not applicable.

10.2.1 Informed Consent Process

FuturHealth Inc. de identifies all participants' information such that it is no longer considered protected health information or personally identifiable information.

When FuturHealth participants join the FHP, they consent to use the deidentified data voluntarily provided by them to be used by third parties for analytics, research, or any other purpose permitted by applicable law.

10.2.2 Study Discontinuation and Closure

Not applicable

10.2.3 Confidentiality and Privacy

The PI will ensure that the confidentiality of the participants' data will be preserved. In the case any other documents submitted to the Sponsor, the participants will not be identified by their

names, but by an identification system, which consists of a number in the study. The Investigator will maintain documents not meant for submission to the Sponsor (e.g., the confidential subject identification code and the signed ICFs) in strict confidence.

10.2.4 Key Roles and Study Governance

Principal Investigator	**Medical Director**
Luis Rojas, PhD. Senior Research Scientist Statistician	Morgan Harris, MD. Medical Director
InCSD	InCSD
16160 Kenneth Dr, Stilwell, KS, 66085	16160 Kenneth Dr, Stilwell, KS 66085
(305) 510-4820	(414) 935-8782
Luis.rojas@incsd.com	Morgan.harris@incsd.com

10.2.5 Safety Oversight

Not applicable. As described before, participants in the FHP follow the OpenLoop Clinical Operations, (2024).

10.2.6 Quality Assurance and Quality Control

This study will be governed by the InCSD Quality Manual.

10.2.7 Data Handling and Record Keeping

All data will be transferred to the Sponsor no later than 60 days after the study is completed unless otherwise specified by the Sponsor.

10.2.7.1 Data Collection and Management Responsibilities

The data is collected by OpenLoop using Healthie electronic medical record (EMR) platform and the FuturHealth APP. The data is reconciled it in the FuturHealth-data repository.

Healthie's is compliant with US Health Insurance Portability and Accountability Act (HIPAA) regulations. That includes the Privacy, Security, & Breach Notification Rules and the Administrative & Physical Safeguards. In addition, Healthie has the following certifications:

(1) SOC 2 Certified: Security standard relevant to the trust services criteria categories covering security, availability, processing integrity, confidentiality and privacy.

(2) PIPEDA-Compliant: Healthie’s infrastructure protects data in compliance with the Canadian Personal Information Protection and Electronic Documents Act (PIPEDA).

(3) PCI-Certified: Healthie’s payment processor is certified as Payment Card Industry (PCI) Service Provider Level 1, the highest possible level.

(4) GDPR-Compliant: The General Data Protection Regulation (GDPR) is a regulation that requires businesses to protect the personal data and privacy of EU citizens for transactions.

(5) ONC Certified: This Health IT Module is compliant with the Office of the National Coordinator for Health Information Technology (ONC) Certification Criteria for Health

IT and has been certified by an ONC-Authorized Certification Body (ONC-ACB) in accordance with the applicable certification criteria adopted by the Secretary of Health and Human Services. This certification does not represent an endorsement by the U.S. Department of Health and Human Services.

(6) HITRUST-Certified: Healthie is HITRUST Certified (Type R2) certified, utilizing the HITRUST CSF® framework, which integrates over 50 security and privacy standards, including HIPAA, NIST, and GDPR. This ensures comprehensive, scalable protection and compliance, allowing us to meet the highest data security standards in an evolving regulatory landscape.

10.2.7.2 Study Records Retention

The sponsor will use their current repository and internal records retention policies.

10.2.8 Protocol Deviations

Not applicable.

10.2.9 Publication and Data Sharing Policy

All information concerning FuturHealth, Inc. operations, patent applications, formula, manufacturing processes, basic scientific data, and formulation information supplied by FuturHealth, Inc., or its designee to the Investigator, and not previously published, is considered confidential and remains the sole property of FuturHealth, Inc. The Investigator agrees to use this information for purposes of study execution through finalization and will not use it for other purposes without the written consent of the Sponsor.

The information generated by this study is the property of FuturHealth, Inc. Publication or other public presentation of data resulting from this study requires prior review and written approval of FuturHealth, Inc. Abstracts, manuscripts, and presentation materials should be provided to FuturHealth, Inc. for review and approval at least 30 days prior to the relevant submission deadline.

It is agreed that the results of the study will not be submitted for presentation, abstract, poster exhibition, or publication by the Investigator until FuturHealth, Inc. has reviewed and commented on such a presentation or manuscript for publication.

10.3 Protocol Amendment History

Version	Date	Description of Change	Brief Rationale
1	03FEB2025	First Version	

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