Cover Page

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A Real-World Registry Study on Integrated Traditional Chinese and Western Medicine Interventions for Obesity

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Principal Investigator: Gang Chen, MD, PhD

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This document is submitted for public posting on ClinicalTrials.gov in accordance with PRS requirements.

It does not include names or other directly identifiable information of research participants.

Obesity, as a significant risk factor for major chronic diseases such as cardiovascular and cerebrovascular diseases, cancer, and diabetes, can be effectively prevented and managed to improve the health environment, promote rational dietary habits, disseminate health knowledge, and enhance health literacy. Integrated traditional Chinese and Western medicine interventions demonstrate remarkable advantages in treating chronic diseases characterized by multifactorial etiology, overlapping symptoms, and coexisting conditions.

1. Research Objectives

This study summarizes the integrated traditional Chinese and Western medicine intervention methods for obesity through real-world research, elucidates the disease progression trajectory, and validates the etiology.

2. Main Research Content

Conduct health information and physical fitness surveys for urban and rural residents, and register at least 10,000 obese individuals for real-world case registration studies. Collect multimodal diagnostic and therapeutic data, including electronic medical records (EMRs), imaging reports, laboratory test results, and comprehensive lifestyle monitoring. Summarize the efficacy of integrated traditional Chinese and Western medicine interventions applied to obese populations across different age groups, disease stages, and physical constitutions. Map the disease progression pathways of obesity and identify key nodes for disease advancement and prevention. Perform health economics evaluations of various obesity prevention and treatment strategies from perspectives such as treatment costs and cost-effectiveness, providing real-world research evidence for optimizing public health policies and integrated traditional Chinese and Western medicine prevention and treatment strategies.

3. Study Subjects

This is an observational, non-interventional real-world registry study.All interventions are administered as part of routine clinical care, with no randomization or experimental assignment.

3.1 Case Data

Obese patients in the study population were prospectively recruited during the study period, provided informed consent, and signed the informed consent form.

3.2 Diagnostic Criteria

（1）According to the "Diagnosis and Treatment Guidelines for Obesity (2024 Edition)" issued by the National Health Commission, obesity is defined as: BMI ≥28 kg/m^2;

（2）Referring to the "Expert Consensus and Group Standards for Weight Management in Overweight or Obese Populations," overweight or obesity is classified into four stages based on BMI and the

presence of comorbidities. Stage 0: overweight, without preexisting conditions related to overweight or obesity or associated diseases; Stage 1: overweight, with one or more preexisting conditions related to overweight or obesity; or obesity, with no or one or more preexisting conditions related to overweight or obesity; Stage 2: overweight or obesity, with one or more conditions related to overweight or obesity; Stage 3: overweight or obesity, with one or more severe complications related to overweight or obesity.

Diseases associated with overweight or obesity can be classified into the following categories:

① Prediabetes or pre-obesity-related conditions: elevated blood pressure at normal levels, borderline hyperlipidemia, prediabetes, hyperuricemia, etc.;

② Overweight or obesity-related diseases: type 2 diabetes mellitus, dyslipidemia, hypertension, coronary atherosclerotic heart disease, nonalcoholic fatty liver disease, polycystic ovary syndrome (PCOS), female infertility, sleep apnea syndrome, osteoarthritis, gout, etc.

③ Severe complications associated with overweight or obesity-related diseases: myocardial infarction (MI), heart failure, stroke, chronic complications of diabetes (retinopathy, renal insufficiency: glomerular filtration rate <60 ml/1.73 m2), cirrhosis, obesity-related cancers, etc.

3.3 Inclusion Criteria

(1) Age 18 years or above, gender unrestricted;

(2) Weight fluctuation ≤5% over the past 3 months with BMI ≥28.0 kg/m²;

(3) Good compliance, willing to adhere to the follow-up principles;

(4) Consent to sign the informed consent form.

3.4 Exclusion Criteria

(1) Concomitant severe diseases of the heart, liver, lungs, kidneys, brain, hematologic system, and neuropsychiatric system;

(2) Secondary obesity (referring to obesity caused by other clearly diagnosed diseases, such as hypothalamic or pituitary inflammation, tumors and trauma, Cushing's syndrome, hypothyroidism, hypogonadism, polycystic ovary syndrome, etc.);

(3) Iatrogenic obesity (referring to obesity induced by medications and therapeutic interventions during the treatment of other diseases);

(4) Pregnant or lactating women;

(5) The investigator is deemed unsuitable for participation in this study.

3.5 Criteria for Withdrawal or Shedding

Participants have the right to withdraw from the study at any time for any reason. Investigators should contact participants via telephone or follow-up, or obtain as comprehensive information as possible

about the withdrawal reasons through their relatives.

Due to disease recurrence, adverse events, treatment protocol violations, or other reasons, investigators also have the authority to discontinue participation in the study. Excessive subject withdrawals may compromise the reliability of the study results, and thus unnecessary withdrawals should be avoided. If a subject withdraws due to adverse events or abnormal laboratory findings, such events should be documented in the case report form.

The subject will be terminated early for any of the following reasons:

(1) Violation of protocol: The main content of the protocol violation, particularly when it involves the safety of the subjects;

(2) Loss of contact or withdrawal of informed consent;

(3) Pregnancy during the study period;

(4) Intolerable adverse events: The subject's health condition does not permit participation in this trial;

All cases of discontinuation should be documented in detail with the reasons, and end-point specimens should be retained, with the CRF forms kept for future reference.

3.6 Exposure Factors

Exposure factors: Traditional Chinese Medicine (TCM) interventions, including herbal compound formulations, acupoint thread embedding, fine-needle/electroacupuncture, and appropriate techniques such as auricular acupressure.

Non-exposure factors: Western weight-loss medications, bariatric surgery, and comprehensive lifestyle interventions.

Each follow-up period records all concomitant medications and treatment modalities from the last follow-up to the current one, accurately documenting drug dosages, administration times, non-pharmacological therapies, and their application durations.

4. Subject Enrollment and Follow-up

4.1 Screening Period

Confirm that the subject meets all enrollment criteria and satisfies none of the exclusion criteria, and the subject signs the informed consent form.

4.2 Patient Screening and Enrollment Method

This study adopted an "offline unified Excel template + rigorous multi-level quality control" approach to ensure that the screening and enrollment process was complete, traceable, and free from selective bias, fully complying with the Real-World Evidence (RWE) Guidelines for Drug Development and Review (2021) and the STROBE-RWS statement requirements.

The measures are as follows:

Each center used the uniformly distributed "Screening Log Template V2025.xlsx" (including data validity validation and automatic enrollment rate calculation formulas) to conduct 100% individual registration of all potentially eligible patients during the study period.

Each center designates one full-time Research Coordinator (CRC) responsible for completing the screening log daily (for outpatient services) or weekly (for inpatient services).

By 18:00 every Sunday, each center shall submit the updated monthly 'Screening Log.xlsx' and the Case Report Forms (CRFs) of enrolled patients to the research team via hospital email.

The research team conducts a 100% source data verification of all center screening logs weekly and calculates the enrollment rate (number of enrolled individuals ÷ total number of individuals meeting the inclusion/exclusion criteria).

Each month, an independent clinical investigator (CRA) randomly selects ≥10% of the centers for on-site audits to verify the consistency between Excel logs and hospital HIS/EMR/paper medical records, and conducts random checks on at least 10 original medical records of unenrolled patients.

Enrollment rate requirements: Prospective registration ≥90%. A consecutive 2-month enrollment rate <80% triggers on-site monitoring, and data from centers with <70% enrollment rate are only included in sensitivity analysis or excluded.

All original screening log Excel files shall be archived by the lead institution for at least 10 years and subject to unannounced inspections by drug regulatory authorities. Upon completion of the study, all center screening logs and enrollment rates will be publicly released in supplementary tables.

4.3 Evaluation Items

4.3.1 Basic Items

（1）Basic information: demographic information collected at study sites (e.g., age, sex, education level, occupation, marital status).Personally identifiable information (such as names, ID numbers, or contact details) is collected locally but is not included in publicly posted documents.;

（2）Allergic history ；

（3）Medical history: history of diseases, surgeries, trauma, and blood transfusions;

（4）Family history: Collect the medical history of direct relatives including father, mother, siblings, children, grandparents, and maternal grandparents.

（5）Personal history: smoking history, alcohol consumption history, weight history, and menstrual

history (for females);

（6）Signs: blood pressure, pulse, heart rate, respiration;

（7）Specialized examination: Body characteristics: height, weight, BMI, waist circumference, hip circumference; food intake speed, appetite, satiety;

（8）Auxiliary tests: Blood analysis, urine chemical analysis + sediment quantification, stool routine examination, electrocardiogram (ECG), glycated hemoglobin (HbA1c), fasting blood glucose, 2-hour blood glucose, fasting insulin, 2-hour insulin, liver function (AST, ALT, GGT), renal function (UREA, CR, UA), lipid profile (CHOL, TG, HDL-C, LDL-C);

（9）Symptom information;

（10）TCM constitution identification;

（11）The Psychiatric Health Questionnaire-9 (PHQ-9);

（12）Generalized Anxiety Disorder Scale (GAD-7).

4.3.2 Diagnostic and Therapeutic Information:

(1) Diagnosis: Traditional Chinese Medicine (TCM) Diagnosis and Western Medicine Diagnosis

(2) Staging: Obesity Staging

(3) Intervention Measures: ① Diet: Energy-restricted diet, very low-calorie diet, high-protein diet, low-carbohydrate diet, low-fat diet, intermittent fasting (number of fasting days per week, number of fasting sessions per day); ② Exercise: Strength resistance training (number of exercise days per week, duration per session); aerobic endurance exercise (number of exercise days per week; duration per session); ③ Oral administration of traditional Chinese medicine (composition of herbal ingredients); ④ Appropriate traditional Chinese medicine techniques: Acupoint embedding (principal and auxiliary points), fine needle/electroacupuncture (principal and auxiliary points), auricular acupressure and moxibustion; ⑤ Western medicine treatment; ⑥ Other therapeutic measures.

4.3.3 Biobank Collection

Blood, stool, and tongue coating samples

(1) Blood sample:

(1) Blood sample collection

Collect two blood samples (1 tube of 2mL anticoagulant and 1 tube of 5mL procoagulant), select the samples from participants in the study, and store them separately from those of other examinees for subsequent aliquoting. Arrange the samples according to their sample numbers whenever possible.

After blood sample collection, avoid vigorous shaking and promptly transfer it to the laboratory department via cold chain transportation, and complete the Blood Sample Registration Form.

(2) Blood sample aliquoting tube box numbering

Each participant receives 4 × 0.5mL EP tubes, with labels printed and affixed (or pre-printed with numbers on the tube walls).

General Principle for EP Tube Numbering: Hubei Provincial Hospital of Traditional Chinese Medicine adds "SZ", and the following numbers are adjusted according to the center's corresponding changes: For serum sample tubes, the number is "S" added after the sub-packaging serial number (2 tubes); for plasma tubes, the number is "P" added after the sub-packaging serial number (1 tube); for blood cell tubes, the number is "B" added after the sub-packaging serial number (1 tube).

Principle for numbering individual packaging tubes:

①Serum tube numbers: SX000001S, SX000002S,...

② Plasma tube numbers: SX000001P, SX000002P,...

③ Blood cell tube numbers: SX000001B, SX000002B,...

EP tube box numbering principle (white box):

① The first box contains serum EP tubes with the following box numbers: SX000001S-SX000100S (2 parallel boxes)

② The second box contains serum EP tubes with the following box numbers: SX000001S-SX000100S

③Number of the fully loaded plasma EP tube box: SX000001P-SX000100P

④Number of blood cell EP tube boxes in full packaging: SX000001B-SX000100B

(3) Specific steps for blood sample aliquoting

① Prepare consumables: EP tubes, EP tube boxes, Pasteurization habit, yellow garbage bags, latex gloves, centrifuge tube racks, disinfectant, tissues, and markers.

② Print the daily Blood Sample Registration Form and store it properly, ensuring each page has a header.

③ After completing the laboratory tests, collect blood samples and aliquot them into separate tubes:

Coagulation: Leave at room temperature for 30 minutes, then centrifuge at 1000 rpm for 10 minutes. Use a pipette to transfer the serum into two 0.5mL EP tubes (Note: Ensure the centrifuge is balanced before pressing the start button), and verify the sample number on the EP tubes.

Anticoagulation: Perform centrifugation as soon as possible. Centrifuge at 1000 rpm for 10 minutes. Use a new Pasteur pipette to transfer plasma into one 0.5mL EP tube, and transfer the remaining dried blood into another 0.5mL EP tube. Verify the sample number on the EP tube.

Note: Due to significant interindividual variations in the quantities of blood components, it is essential to ensure even distribution among all tubes during aliquoting. Each tube should not be overfilled to prevent the cap from springing open during freezing.

After completion of sub-packaging, each sub-packaging tube shall be placed into its respective EP tube box, with the storage order of sub-packaging tubes within each box starting from the upper left side in parallel. Simultaneously, mark the sample start and end numbers (e.g., SX000001S-SX000100S...) on the sub-packaging box using a marker pen.

Complete the 'Blood Sample Registration Form' on the day of the physical examination, recording detailed information such as the examinee's examination number, item number, examinee's name, and whether any abnormalities (e.g., hemolysis) occurred during sample aliquoting (fill in one page per day, but ensure continuous numbering of sample numbers).

(4) Blood Sample Preservation Procedures

①EP tube box numbering: Mark the starting and ending numbers of stored EP tubes on the top and two vertical sides of the box using an oil-based marker pen.

② Ensure the sample tube caps are securely closed. Samples prepared on the same day should be promptly and systematically transferred to the-80°C freezer after being placed in the EP tube box to avoid repeated freeze-thaw cycles (Note: If necessary, use a rubber band to secure the sample box).

③ Fill out the Blood Sample Registration Form and Blood EP Tube Box Registration Form on the computer daily.

④ Regularly monitor the refrigerator temperature. After full loading, samples shall be uniformly transported via cold chain logistics to the Tongji Medical College Sample Bank for storage.

（2）stool specimen

(1) Collection steps:

① Collection: Empty the bladder before defecation and collect fresh feces using a sterile toilet bowl;

② Sampling: Collect the central portion of feces (avoid contact with urine/toner), using a fecal collection and preservation tube, and perform sampling according to the instructions and procedures. Ensure the sample is promptly placed in a frozen environment to prevent microbial DNA degradation.

③ Targeted metabolic samples can be immediately frozen to-20°C.

(2) Instructions for Use of Fecal Collection and Storage Tubes:

① Open the fecal collection kit and remove the fecal sampling tube, disposable gloves, sampling paper, and sample transport bag.

②Select one of the following methods for stool collection:

A. Squat toilet: Defecate in a clean squat toilet and collect a stool sample within 10 minutes of defecation. Do not allow urine to contaminate the sample. (This method does not require the use of toilet paper)

B.Toilet:

a. Lift the toilet seat, then apply the double-sided tape on both sides of the sampling paper to the left and right sides of the toilet, causing the center of the paper to dip in order to collect fecal samples.

b. Cover the toilet seat and defecate onto the sampling paper. Do not allow urine to contaminate the sampling paper or sample.

③ Put on disposable gloves and unscrew the lower cap of the fecal sampling tube.

④Take a full scoop of fecal sample with the sampling spoon provided with the sampling tube.

⑤ Transfer the collected fecal sample into the sampling tube, ensuring the sample is immersed in the liquid inside the tube. Adjust the liquid level to be between the upper and lower limit markings on the tube body, then tighten the lower tube cap in a clockwise direction.

⑥ Place the sampling tube into the sample transport bag for storage or mailing.

⑦ Discard the sampling paper into the trash bin.

(3) Precautions:

① Avoid exposing feces to air for more than 5 minutes to prevent changes in microbial communities;

②If immediate cryopreservation is not feasible after sampling, the sample should be placed on ice and frozen as soon as possible.

(3) Oral Sample Collection

(1) Collection time: Before brushing teeth in the morning, avoid rinsing the mouth, eating, or smoking prior to sampling.

① Use a broken cotton swab to repeatedly scrape the middle of the tongue coating 20-30 times, avoiding the wound site;

② Place the cotton swab into a 2ml cryovial and store immediately at-80°C, avoiding repeated freeze-thaw cycles, and transport with dry ice;

③If the sample volume is large or cannot be frozen immediately, the sample may be placed on ice, and frozen storage should be completed within 2 hours at the latest.

4.4 Follow-up

Follow-up visits were scheduled at weeks 4, 8, 12,16,20, and 24 after the contracted patients received treatment. A phase efficacy evaluation was conducted after week 12. If the weight loss was ≥ 5% from baseline, the current treatment regimen was continued until week 24. For patients with weight loss <5% or progressive weight gain, the treatment plan was adjusted to enhance weight management. If the weight loss remained <5% by week 24, referral to a higher-level hospital or involvement of a weight loss clinic as the primary provider was recommended, with multidisciplinary teams invited to participate in the diagnosis and treatment based on the patient's condition.

5. Evaluation Indicator Standards

5.1 Evaluation of Major Therapeutic Outcomes

The difference in percentage weight loss from baseline was at least 5%, and the difference was statistically significant.

5.2 Evaluation Methods for Secondary Outcomes [1]

(1) Improvement rates of waist circumference and hip circumference

(2) Incidence of obesity-related complications, including metabolic syndrome, prediabetes, type 2 diabetes mellitus, dyslipidemia, hypertension, nonalcoholic fatty liver disease (or metabolic-related fatty liver disease), polycystic ovary syndrome (PCOS), female infertility, male hypogonadism, obstructive sleep apnea syndrome (OSAS), asthma and/or reactive respiratory diseases, osteoarthritis, stress urinary incontinence, gastroesophageal reflux syndrome (GERD), gout, cardiovascular and cerebrovascular diseases, tumors, etc.

5.3 Evaluation Methods for Other Observation Indicators

(1) Improvement rate of morphological indicators

(2) Changes in combined clinical symptoms

(3) Changes in microbial diversity of the gut and tongue coating;

(4) Changes in dietary preferences and exercise habits

(5) Neuropsychiatric safety indicators (depression, anxiety disorders, etc.)

6. Safety Monitoring

6.1 Definition of Adverse Events

The term encompasses any symptoms, syndromes, or diseases that occur or worsen during clinical research and may affect the health of the subjects. It also includes clinically relevant conditions identified through laboratory or other diagnostic procedures, such as those requiring unplanned medical interventions or leading to withdrawal from the study. Adverse events may involve the onset of new diseases, deterioration of treatment-related symptoms or signs, or progression of comorbid conditions, which are unrelated to the trial participation and may result from a combination of one or more factors. Therefore, the term "adverse event" does not imply a causal relationship with the administered medication.

Regardless of whether the subject consents, any adverse events identified through investigator consultation, physical examination, laboratory tests, or other methods shall be recorded in the Case Report Form (CRF) and diligently tracked for treatment and documentation until recovery. Isolated abnormal laboratory findings are generally not considered adverse events unless accompanied by clinical symptoms, signs, or requiring treatment. When completing the CRF, the severity of each adverse event should be appropriately assessed:

Duration: Start and end dates;

Severity: Classified according to the following criteria based on the most severe degree of adverse reaction:

Mild: Easily tolerable, causing only mild discomfort and not affecting daily activities.

Moderate: causes significant discomfort and affects daily activities.

Severe: unable to perform daily activities.

In this study, only disease progression-related and drug-related adverse events were required to be recorded, with specific content determined through expert discussion to reach consensus.

6.2 Serious Adverse Events

6.2.1 Definition of Serious Adverse Events

During the observation period, any of the following adverse events occurred: fatal, immediately life-threatening, requiring hospitalization or prolonged hospital stay, resulting in permanent or severe disability, causing cancer, leading to congenital malformations, or having significant medical implications (referring to events that do not immediately endanger life or cause death or require hospitalization, but may harm the subject or necessitate measures to prevent the aforementioned outcomes), or requiring medical intervention to prevent permanent injury or damage.

Once a serious adverse event is identified, the investigator must report it to the ethics committee and the lead institution within 24 hours of occurrence. The case report form for serious adverse events should document all relevant information as comprehensively and meticulously as possible. The investigator must include the following evaluations and records in the case report form: a detailed description of the serious adverse event, its relationship to the antiviral medication, the measures taken, and the current outcome.

6.2.2 Serious Adverse Event Recording and Reporting Procedures

For any serious adverse event occurring during the study, regardless of whether it is related to the study medication, and whether it is expected or unexpected, the following steps should be followed in the study:

(1) Provide timely and appropriate medical care as needed, with the primary priority being the safety of the subject.

(2) Complete the serious adverse event report form provided in the investigator document as thoroughly as possible.

(3) The investigator must notify the lead institution of the event via telephone or fax within 24 hours for record-keeping.

(4) Monitor and document the entire course of events until resolution or clinical stabilization is achieved.

(5) Notify the study monitor of the final outcome of the adverse event, and issue a revised or updated serious adverse event report if necessary.

(6) Immediately report to the ethics committee and relevant authorities in accordance with the regulations on serious adverse event reporting. The investigator shall provide proof of notification to the ethics committee to the sponsor or its representative.

7. Ethical Requirements and Informed Consent

7.1 Ethics Review

This study must comply with the Helsinki Declaration and the regulations of China on clinical research. The clinical research protocol must be reviewed and approved by the ethics committee of the research unit hospital—Hubei Provincial Hospital of Traditional Chinese Medicine before the trial begins.

7.2 Informed Consent of Subjects

Prior to enrollment, the study physician is obligated to provide the subject or their designated representative with a written, comprehensive disclosure of the study's purpose, nature, procedures, and

potential benefits and risks. Subjects must be informed of their right to withdraw from the study at any time. A written informed consent form must be provided to each subject prior to enrollment, and their consent must be obtained through their understanding. Only after voluntary signing of the informed consent form can the subject be enrolled in the clinical study. The informed consent form shall be retained as part of the original clinical trial records for future reference. To protect subject privacy, the case report form shall not contain the subject's name. Investigators must identify and record subjects using their assigned codes.

8. Quality Control

8.1 Establishment of a Special Task Force for Cohort Studies

Prior to the initiation of the cohort study, a dedicated cohort study task force was established to provide professional training for team members, ensuring that all investigators master cohort study methodologies and strictly adhere to the study protocol.

8.2 Unified Recording Standards

Members of the cohort study task force thoroughly discussed the clinical research protocol and CRF prior to the initiation of the clinical study, standardizing the recording methods and assessment criteria.

8.3 Use the original medical records or original examination reports of the subjects as the original records

If the investigator makes any corrections to the original medical records, only additional narrative explanations may be provided, signed by the physician participating in the clinical study and dated, without altering the original records.

8.4 Accurately document medication and examination records

Researchers must accurately document the medication and examination records of subjects during follow-up and include them in the original medical records.

8.5 Investigators shall complete the CRF in a timely, truthful, detailed, and diligent manner.

8.6 Ensure the reliability and originality of the data.

In clinical research, monitors should promptly verify the consistency between the data in the original record form and the original medical records to ensure data reliability and confirm that all conclusions in the clinical study are derived from the original data.

8.7 The accuracy, reliability, and criteria for abnormality judgment of laboratory tests should be as consistent as possible across multiple visits.

8.8 Data Verification

Researchers must verify laboratory data that are significantly elevated or outside the clinically

acceptable range, with necessary explanations provided by physicians participating in the clinical study.

8.9 Improving Compliance

To ensure subject compliance, participants should be fully informed of the study's significance.

Researchers should take active measures (e.g., phone reminders for follow-up visits) to keep the case dropout rate below 20%.

9. Data Management and Statistical Analysis

9.1 Data Management

9.1.1 Data Management Model

This trial adopted an electronic data management system, and participants were trained before the trial initiation.

9.1.2 Medical Record Construction and Review

In the cohort task force, members serving as data administrators construct the Epidata repository based on the "Clinical Research Protocol". Upon completion, the repository is submitted for review by the principal investigator of the cohort study and task force members. Following unanimous approval, the data administrator creates accounts using the information provided by the investigators.

9.1.3 System Testing

Perform pre-test validation on the constructed Epidata to ensure accuracy and document the results.

9.1.4 Data Entry

Clinical investigators shall designate data entry personnel to promptly and accurately input the data from the study medical records into Epidata after subject visits. Monitors shall verify the completeness of all electronic case report forms and ensure consistency with the original materials, promptly correcting any errors and electronically signing them.

9.1.5 Data Questions and Answers

Regarding questions in Epidata. The monitor may submit inquiries online at any time. The investigator should provide online responses promptly, correct erroneous data, and the monitor may reissue inquiries if necessary. All exchanges of questions and answers between them should be conducted via a question form, which must be retained for reference.

9.1.6 Data Lock and Export

After each participant completes the trial and is reviewed by the monitor without errors, the data administrator locks the data until the last participant's data is locked. Once all data is locked, the data administrator exports the dataset suitable for statistical analysis and submits it to the statisticians for statistical analysis.

9.1.7 The principal investigator prepares the clinical study summary report based on the

statistical report.

9.2 Statistical Analysis

9.2.1 Statistical Inference Methods

It is determined through discussions among statisticians, principal investigators, and sponsors.

Data were tested for normal distribution using the Shapiro-Wilk test. Measurement data that followed a normal distribution were described as mean ± standard deviation ($x \pm (s)$), and analyzed using t-tests or analysis of variance (ANOVA). For data that did not follow a normal distribution, median (IQR) was used for description, and the Mann-Whitney U test was performed. Categorical data were described as frequency and percentage (%), and the chi-square test (χ^2) was used for analysis. When the chi-square test was not feasible, the Fisher exact probability method was employed. The cumulative incidence of weight regain in obese patients, progression to diabetes in prediabetic patients, and reversal of prediabetes were analyzed using Kaplan-Meier survival analysis, with statistical significance assessed by the Log-rank test. A Cox proportional hazards regression model was constructed to analyze the association between integrated traditional Chinese and Western medicine interventions and disease progression or treatment efficacy, after adjusting for potential confounding factors such as age, sex, family history, alcohol consumption, and dietary and exercise habits. A two-sided P-value <0.05 was considered statistically significant.

(1) Primary efficacy evaluation indicators: percentage of relative change; response rate;

(2) Secondary efficacy evaluation indicators: visceral fat content (measured by Inbody, CT, or MRI), incidence of MAFLD (including the incidence of steatohepatitis, hepatic fibrosis, cirrhosis, and hepatocellular carcinoma), incidence of type 2 diabetes mellitus, improvement rate of HOMA-IR, improvement rate of hepatic fat content, changes in microbial community diversity, incidence of obesity-related end-point events (including the incidence of metabolic-related diseases such as diabetes, hypertension, cardiovascular and cerebrovascular diseases, and tumors), and neuropsychiatric safety indicators (depression, anxiety disorders, etc.).

(3) Safety Analysis: First, according to the requirements of adverse reaction correlation, list and describe the adverse events and adverse reactions in both groups (including the number of cases for various adverse events, the number of cases where laboratory test indicators changed from "normal to abnormal" or "abnormal to more severe" before and after the trial, and the conversion rate), along with their causes and explanations. Statistical analysis of adverse reactions was performed using the chi-square test.

(4) Missing values: This study may result in missing data for a specified study visit due to the

following reasons: absence of data due to unrecorded or illegible data; no visit occurred; or subject withdrawal from the study prior to the visit.

This study employed the Last Observation Carried Forward (LOCF) method for handling missing values: the final observed value of the endpoint was assigned to subsequent missing evaluation points, treating the last observed response as the study endpoint.

9.2.2 Statistical Expression

(1) Statistical Tables: The report shall present the characteristics, internal composition, and quantitative relationships among research project groups using statistical tables. These tables must be visually prominent, hierarchically organized, and self-explanatory. The table content shall include titles, headings, numerical data (with consistent decimal places for identical indicators; zeros should be filled in, and gaps or missing values marked with a hyphen), and notes (using an asterisk (*) to indicate specific items, with notes placed below the table's baseline).

(2) Statistical Charts: The report will utilize statistical charts to visually and intuitively present quantitative relationships. Potential chart types include: bar charts, histograms, pie charts, percentage bars, line graphs, scatter plots, stem-and-leaf diagrams, and box plots. The chart title should be positioned centrally beneath the chart body. Coordinate axes must specify the origin, scale, and units. When comparing different entities within the same chart, distinct colors or line styles should be employed for differentiation, accompanied by a legend.

9.3 Statistical Software

SPSS 26.0 was used for data cleaning and analysis, with some graphical representations produced using R language, Prism 6.0, and R software 3.3.1.

10. Data preservation

Researchers shall retain all study materials, including confirmation of all subjects (to effectively cross-check different records such as CRFs and hospital original records), all original signed informed consent forms, all CRFs, and detailed records of drug distribution. The retention period is 5 years after the conclusion of the study.

All data from this clinical trial are owned by the research team. Without the written consent of the research team, investigators are not permitted to provide any information to third parties in any manner.

11. Modification of the Plan

After approval by the ethics committee, if significant modifications are required during implementation, the principal investigator of the responsible unit shall prepare a "Protocol Modification Statement" and sign it, which must be submitted to the ethics committee for approval before implementation.

12. Publication of Results

The data from this trial study are shared internally within our institution, and may be shared under an agreement after submission.