# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

09 Jun 2026

## The Effect of Sustainable Diet Combined with Time-Restricted Eating and Probiotic Supplementation on Cardiovascular Function among Patients with Chronic Heart Failure with reduced Ejection Fraction (HFrEF): A Randomized Clinical Trial Study

## Protocol summary

**Study aim**
Preparation of LP299v Probiotic Supplements Investigating of a sustainable diet in combination with TRE and probiotic supplements on cardiovascular function among patients with HFrEF

**Design**
A controlled clinical trial, parallel-group, single-blind, randomized, phase 3, among 90 HFrEF patients

**Settings and conduct**
This study is conducted in two phases, the probiotic capsule preparation phase and the clinical phase. The place of the study will be the cohort center of MUMS. After confirming the diagnosis of HFrEF by cardiologists, participants will be referred to the specialist for more detailed explanations if they participate in the project. After controlling inclusion criteria, the participants are assigned to one of the 3 study groups using stratified blocked randomization method and researcher and participants will be blinded. Also, unique codes generating by online website will be assigned on the medicinal container. As each person enters to study regarding to randomized consequences, medicinal container is assigned to person and no one (researcher and participants) know which participants will be in which intervention group. Medicine containers will also be opaque with closed lids and capsules will be the same in appearance, color, taste and smell.

**Participants/Inclusion and exclusion criteria**
Inclusion criteria: Clinical diagnosis of HFrEF Men and women with age range of 30-75 years, Complete the informed consent form Exclusion criteria: Using nutritional supplements, Not consuming more than 20% of the capsules, Unwillingness to continue cooperation in research

**Intervention groups**
Participants will be randomly divided into 3 groups: Dietary Advices + Probiotic Placebo: A Sustainable Diet with Time Restricted Eating + Probiotic Placebo: B Sustainable Diet with Time Restricted Eating + Probiotic Capsule: C

**Main outcome variables**
Echocardiography, biochemical and anthropometric indices

## General information

**Reason for update**
We kindly request an update to the trial record due to modifications in the title and certain aspects of the methods used.

**Acronym**

**IRCT registration information**
IRCT registration number: **IRCT20231225060520N1**
Registration date: **2024-01-23, 1402/11/03**
Registration timing: **prospective**

Last update: **2025-10-16, 1404/07/24**
Update count: **2**

**Registration date**
2024-01-23, 1402/11/03

**Registrant information**

**Name**
Pegah Rahbarinejad

**Name of organization / entity**

**Country**
Iran (Islamic Republic of)

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**Recruitment status**
**Recruitment complete**

**Funding source**

**Expected recruitment start date**
2025-04-04, 1404/01/15
**Expected recruitment end date**
2026-02-04, 1404/11/15
**Actual recruitment start date**
empty
**Actual recruitment end date**
empty
**Trial completion date**
empty

**Scientific title**
The Effect of Sustainable Diet Combined with Time-Restricted Eating and Probiotic Supplementation on Cardiovascular Function among Patients with Chronic Heart Failure with reduced Ejection Fraction (HFrEF): A Randomized Clinical Trial Study

**Public title**
The Effect of Diet with probiotic on Cardiovascular Function
**Purpose**
Supportive
**Inclusion/Exclusion criteria**
**Inclusion criteria:**
Clinical diagnosis of heart failure with echocardiogram showing systolic dysfunction with ejection fraction ≤ 40% based on New York Heart Association (NYHA) class II-IIID heart failure symptoms with ischemic or non-ischemic etiology Under standard treatment with drugs Men and women with age range of 30-75 years Willingness to participate in the study and complete the informed consent form
**Exclusion criteria:**
Use of nutritional supplements (oral or injectable, such as vitamins D, C, E, calcium, magnesium, potassium, multivitamin- mineral, omega 3) and herbal products with antioxidant and anti-inflammatory properties, probiotic or synbiotic supplements or products containing them during the study Not consuming more than 20% of the capsules Unwillingness to continue cooperation in research
**Age**
From **30 years** old to **75 years** old
**Gender**
Both

**Phase**
3
**Groups that have been masked**

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser

**Sample size**
Target sample size: **75**
**Randomization (investigator's opinion)**
Randomized
**Randomization description**
In this study, we will use stratified blocked randomization for random allocation. Body mass index (BMI) is considered as a classifier variable. By using the site www.sealdenvelope.com and the classifier variable (BMI) and selecting blocks of 6 on the site, a random sequence will be generated. The mentioned sequences are placed in opaque, numbered and sealed envelopes or SNOSE by the research associate. Upon entering each patient, after obtaining informed consent and checking the inclusion and non-inclusion and exclusion criteria, the first envelope is opened and the patient is assigned to one of the 3 relevant groups. In the same way, the randomization process will continue until the last patient. In order to apply concealment allocation in the random allocation process, unique codes will be used on medicine containers. So that the desired code is also generated by the online website. As each person enters the study based on the generated sequence, the medicine container in which the desired code is recorded is assigned to the person and therefore, before choosing the person, no one is aware of the type of treatment he/she will receive. Medicine containers are also non-transparent closed lids and capsules will be the same in terms of quantity, color, taste and smell.
**Blinding (investigator's opinion)**
Single blinded
**Blinding description**
This study is not blinded in terms of diet but will be blinded in terms of supplements. The probiotic supplement and its placebo will be produced by PARSILACT Company. All probiotic and its placebo supplements will provided by PARSILACT Company in prepacked pharmaceutical polyethylene bottle numbered for each patient according to the randomization sequence. The probiotic supplement and its placebo will be in the same form package. The researcher and patients will not be aware of the pharmaceutical polyethylene bottle's content until the end of the trial.
**Placebo**
Used
**Assignment**
Parallel
**Other design features**

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**
**Name of ethics committee**
Ethics committee of Mashhad University of Medical Sciences
**Street address**
Department of Nutrition, Faculty of Medicine, Ferdowsi University Campus, Azadi Square, Razavi Khorasan
**City**
Mashhad

**Province**
Razavi Khorasan
**Postal code**
9177948564
**Approval date**
2024-01-03, 1402/10/13
**Ethics committee reference number**
IR.MUMS.REC.1402.259

## Health conditions studied

### 1

**Description of health condition studied**
Patients with Chronic Heart Failure with reduced Ejection Fraction (HFrEF)
**ICD-10 code**
I50.9
**ICD-10 code description**
Heart failure, unspecified

## Primary outcomes

### 1

**Description**
N Terminal pro Natriuretic Peptide type B (NT-proBNP)
**Timepoint**
In the beginning of the study (before the start of the intervention) and 60 days after the intervention
**Method of measurement**
Kit for measuring N-terminal pro-natriuretic peptide type B in venous blood sample

## Secondary outcomes

empty

## Intervention groups

### 1

**Description**
First Intervention group: Dietary advices + Probiotic placebo (without Lactobacillus plantarum 299v, twice daily for 60 days)
**Category**
Placebo

### 2

**Description**
Second Intervention group: Sustainable diet combined with time-restricted eating + Probiotic placebo (without Lactobacillus plantarum 299v, twice daily for 60 days)
**Category**
Treatment - Other

### 3

**Description**
Third Intervention group: Sustainable diet combined with time-restricted eating + Probiotic Capsule (Lactobacillus plantarum 299v with a dose of 14 billion CFU, twice daily for 60 days)
**Category**
Treatment - Other

## Recruitment centers

### 1

**Recruitment center**
**Name of recruitment center**
Mashhad University of Medical Sciences
**Full name of responsible person**
Pegah Rahbarinejad
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## Sponsors / Funding sources

### 1

**Sponsor**
**Name of organization / entity**
Mashhad University of Medical Sciences
**Full name of responsible person**
Mohsen Tafaghodi Piadeh Gheibi
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Research and Technology Vice Chancellor, Qurashi Building, next to Hoize Cinema, University St., Mashhad, Razavi Khorasan
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Tafaghodim@mums.ac.ir
**Grant name**
**Grant code / Reference number**
**Is the source of funding the same sponsor organization/entity?**
Yes
**Title of funding source**
Mashhad University of Medical Sciences
**Proportion provided by this source**

100

**Public or private sector**
Public

**Domestic or foreign origin**
Domestic

**Category of foreign source of funding**
*empty*

**Country of origin**

**Type of organization providing the funding**
Academic

## Person responsible for general inquiries

**Contact**

**Name of organization / entity**
Mashhad University of Medical Sciences

**Full name of responsible person**
Pegah Rahbarinejad

**Position**
Ph.D. Student

**Latest degree**
Ph.D.

**Other areas of specialty/work**
Nutrition

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## Person responsible for scientific inquiries

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## Person responsible for updating data

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## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**
Undecided - It is not yet known if there will be a plan to make this available

**Study Protocol**
Undecided - It is not yet known if there will be a plan to make this available

**Statistical Analysis Plan**
Undecided - It is not yet known if there will be a plan to make this available

**Informed Consent Form**
Undecided - It is not yet known if there will be a plan to make this available

**Clinical Study Report**
Undecided - It is not yet known if there will be a plan to make this available

**Analytic Code**
Undecided - It is not yet known if there will be a plan to make this available

**Data Dictionary**
Undecided - It is not yet known if there will be a plan to make this available