Clinical Trial Protocol
Iranian Registry of Clinical Trials

07 Nov 2026

Comparison of two-month consumption of multi-strain probiotics with placebo for general health and patients with multiple sclerosis

Protocol summary

Study aim

The aim of this study was to compare the effects of two months of taking a multi-strain probiotic with a placebo on the general health and depression of patients with multiple sclerosis. The practical aim of this study is to improve the quality of life of patients with MS by reducing depressive symptoms and increasing their psychological well-being.

Design

A controlled, double-blind, randomized, phase 3 clinical trial with parallel groups on 50 patients. Block Randomization method was used for randomization.

Settings and conduct

This clinical trial is being conducted at Kashani Hospital. After screening and obtaining informed consent, 50 eligible patients will be enrolled in the study and will be allocated to two groups of 25 (probiotic and placebo) by an independent person using Block Randomization. The study is double-blind; participants, healthcare providers, and data analysts are unaware of the type of intervention. Probiotic and placebo capsules are identical in appearance and packaging and are coded.

Participants/Inclusion and exclusion criteria

inclusion ; Patients with relapsing-remitting multiple sclerosis (RRMS) with a definitive diagnosis by a specialist Patients aged 18 to 65 years. Patients willing and able to participate in the study Patients who report anxiety, depression, and other general health problems as a complication of the underlying multiple sclerosis exclusion; Patients taking probiotics or similar supplements in the past 3 months Patients with depression and anxiety as their chief clinical complaint History of allergy to any component of probiotics or similar drugs

Intervention groups

Comparison of two-month consumption of multi-strain probiotics with placebo for general health and patients with multiple sclerosis

Main outcome variables

General health based on the GHQ-28 questionnaire ;Depression severity based on the BDI-II questionnaire

General information

Reason for update

Acronym

IRCT registration information

IRCT registration number: **IRCT20230126057237N2**
Registration date: **2026-06-10, 1405/03/20**
Registration timing: **registered_while_recruiting**

Last update: **2026-06-10, 1405/03/20**
Update count: **0**

Registration date

2026-06-10, 1405/03/20

Registrant information

Name

Sasan Zandi esfahan

Name of organization / entity

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2026-06-10, 1405/03/20

Expected recruitment end date

2026-07-06, 1405/04/15

Actual recruitment start date

empty

Actual recruitment end date

empty

Trial completion date
empty

Scientific title
Comparison of two-month consumption of multi-strain probiotics with placebo for general health and patients with multiple sclerosis

Public title
The effect of probiotics on multiple sclerosis

Purpose
Supportive

Inclusion/Exclusion criteria

Inclusion criteria:
Patients with relapsing-remitting multiple sclerosis (RRMS) with a definitive diagnosis from a specialist physician Patients aged 18 to 65 Patients are willing and able to participate in the study Patients who report anxiety, depression, and other general health problems as a complication of their primary multiple sclerosis disease

Exclusion criteria:
Patient's use of probiotic medications or similar supplements in the past 3 months Patients whose chief clinical complaint is depression and anxiety History of allergy to any component of probiotics or similar medications

Age
From **18 years** old to **65 years** old

Gender
Both

Phase
3

Groups that have been masked

- Participant
- Care provider
- Outcome assessor
- Data analyser

Sample size
Target sample size: **50**

Randomization (investigator's opinion)
Randomized

Randomization description
After screening patients based on inclusion and exclusion criteria and obtaining informed consent, eligible participants are enrolled in the study. The recruitment process continues until a minimum of 50 patients are reached. To allocate participants to the two intervention (multi-drug probiotic) and control (placebo) groups, a block randomization method with four blocks is used to maintain a balance in the number of subjects in the two groups during the recruitment process. The basic idea of block randomization is to divide patients into M blocks of size 2N, such that in each block N patients are assigned to A and N patients to B. The block is then randomly selected. This method ensures equal treatment allocation in each block provided that the block is fully used. . The block size depends on the number of treatments, it should be short enough to avoid imbalance, and large enough to avoid guessing the treatment assignment in each group during the study. The block size should be at least 2 times the number of treatment nodes. The block size was not stated in the study so that the investigators were blinded to it. If the blocks were stated, the treatment series in each block could be guessed. For example, in a 2N=4 block, A A B should be B and in A A it can be inferred as B B. This can lead to selection bias. The solution to avoid this error is to: 1) not disclose the blocking mechanism 2) use random block sizes. The randomization sequence is generated by an independent person who is not involved in the recruitment and evaluation of patients, using reliable randomization software (such as Random Allocation Software or the website randomization.com). The final sequence is stored in the form of a coded list. Allocation Concealment: To prevent bias, the randomization sequence is placed in opaque, light-tight, numbered, and sealed envelopes. Each envelope is opened only at the time of each patient's entry into the study and in numerical order. The person responsible for opening the envelope is a person who is not involved in the outcome assessment. Allocation method: After opening the envelope, the patient is allocated to one of two groups based on the code inside the envelope: - Intervention group: at least 25 people receiving multi-faceted probiotics - Control group: at least 25 people receiving placebo Intervention standardization: The probiotic and placebo are completely similar in shape, color, size, and packaging and are coded to maintain blinding of participants and clinical caregivers.

Blinding (investigator's opinion)
Double blinded

Blinding description
This study will be double-blind. Participants, clinical caregivers, outcome assessors, and data analysts will be unaware of the type of intervention (probiotic or placebo). In the intervention group, patients will be treated with FamiLact capsules, and in the control group, patients will be treated with placebo capsules. The probiotic and placebo capsules are completely similar and indistinguishable in appearance, size, color, odor, packaging, and method of administration. The probiotic capsule is marketed by Zist Takhim Pharmaceutical Company [Iran] under the brand name FamiLact Capsule®, which was also used in this study. FamiLact® is a synbiotic formula (probiotic + prebiotic). This product contains high levels of safe and beneficial bacterial strains (Lactobacillus rhamnosus, Bifidobacterium lactis, Lactobacillus casei, Bifidobacterium bruchid, Lactobacillus acidophilus, Bifidobacterium longum, Lactobacillus plantarum, Bifidobacterium bifidum, Streptococcus thermophilus) along with fructooligosaccharide (FOS) as a prebiotic. In the intervention group, probiotic capsules were administered at a rate of one daily. In the control group, placebo capsules were used instead of Femi Lact capsules, which were completely identical in appearance to the original capsules and were in the form of a hard, two-part, white capsule. The ingredients in the Femi Lact capsules used are as follows: probiotic + prebiotic, and an inactive ingredient that included glycerin, distilled water, and titanium dioxide. Only similar inactive ingredients were used in the placebo capsules. The

packaging and dosage form of the probiotic and placebo capsules were identical and indistinguishable, thus maintaining blinding. Both products are packaged with identical codes, the only difference being the specific code used for blinding. The codes for each package (A and B) are assigned by an independent individual who is not involved in the data collection, evaluation, and analysis process and are stored in sealed envelopes. Researchers and patients will have no idea which code is for the probiotic and which is for the placebo.In the data analysis phase, the analysis is performed by a statistical consultant who is aware of the contents of the drug packages; therefore, the study was double-blind and the contents of the two drug groups are not known from the patient's entry into the study to the study and data collection. Maintaining blinding throughout the study: - The intervention and placebo packages are identical in appearance. - The person responsible for distributing the packages is not involved in the outcome assessment. - Participants will not be informed of their intervention type until the end of the study. - Data analysis is also performed based on A and B codes and decoding is done only after the statistical analysis is completed. In the event of a severe complication or a situation where treatment decision-making requires information about the type of intervention, the principal investigator may open the envelope related to that participant in coordination with the ethics committee. These cases will be recorded and reported.

Placebo
Used

Assignment
Parallel

Other design features
Focusing on the Gut-Brain Axis in MS Management Innovation in Using the Mechanism of Gut Microbiome Modulation as a Non-Drug Approach to Improve Neurological Symptoms. A Trial Design with a Short-Term Intervention Period (2 Months)Presenting Initial Evidence of Rapid Effects of Probiotics on the Central Nervous System

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee
کمیته اخلاق دانشگاه آزاد اسلامی نجف آباد

Street address
Islamic Azad University, Najafabad Branch, Daneshgah Blvd, Najafabad, Isfahan, Iran

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Province
Isfehan

Postal code
8514143131

Approval date
2025-10-09, 1404/07/17

Ethics committee reference number
IR.IAU.NAJAFABAD.REC.1404.229

Health conditions studied

1

Description of health condition studied
Multiple sclerosis

ICD-10 code
G35

ICD-10 code description
G35

Primary outcomes

1

Description
Depression based on the Beck Depression Inventory

Timepoint
Depression was measured using the Beck Depression Inventory at the beginning of the study (before the intervention) and at the end of the study (after 2 months from the start of the intervention)

Method of measurement
Beck Depression Inventory

2

Description
General health through the General Health Questionnaire28

Timepoint
General health was measured using the General Health Questionnaire 28 at the beginning of the study (before the intervention) and at the end of the study (after 2 months from the start of the intervention)

Method of measurement
General Health Questionnaire 28

Secondary outcomes

empty

Intervention groups

1

Description
In the intervention group, patients will be treated with FamiLact capsules, and in the control group, patients will be treated with placebo capsules. The probiotic capsule is available on the market by ZistTehmir Pharmaceutical Company [Iran] under the trade name FamiLact Capsule®, which was also used in this study. FamiLact® is a synbiotic formula (probiotic + prebiotic). This product contains high amounts of safe and beneficial bacterial strains (Lactobacillus rhamnosus, Bifidobacterium lactis, Lactobacillus casei,

Bifidobacterium bruh, Lactobacillus acidophilus, Bifidobacterium longum, Lactobacillus plantarum, Bifidobacterium bifidum, Streptococcus thermophilus) along with fructooligosaccharide (FOS) as a prebiotic. In the intervention group, the probiotic capsule is prescribed at a rate of one daily. Given that the drug is biofermented, patients are taught how to store it. Biofermentation probiotic supplements can be stored for 2 weeks at a temperature below 25°C, but the best storage conditions for this product are at 2 to 8°C (in the refrigerator), which increases the shelf life of probiotic bacteria and improves effectiveness. The best time to consume this type of probiotic is after eating. This product should be kept away from moisture, sunlight, and out of reach of children. The ingredients in the Femi Lact capsules used are as follows: probiotic + prebiotic, and an inactive ingredient that includes glycerin, distilled water, and titanium dioxide. The duration of the intervention is two months, and during this period, patients are visited by a neurologist monthly, and while neurological examinations and clinical status are reviewed, medications are distributed to them, and drug side effects are recorded. Also, patients are called every two weeks to monitor medication use and remind them of their monthly visits.

Category

Treatment - Drugs

2

Description

Control group: In the control group, placebo capsules were used instead of Femi Lact capsules, which were completely similar in appearance to the original drug capsules and were in the form of two-part hard white capsules.The ingredients in the Femi Lact capsules used are as follows: probiotic + prebiotic, and an inactive ingredient that included glycerin, distilled water, and titanium dioxide. Only similar inactive ingredients were used in the placebo capsules. The packaging and dosage form of the probiotic and placebo capsules were similar and could not be distinguished from each other, so that the blinding of the study was maintained.The duration of the intervention is two months and one capsule is used daily. During this period, patients are visited by a neurologist monthly and, in addition to neurological examinations and clinical status evaluation, medications are distributed to them. Also, telephone calls are made to patients every 2 weeks to monitor the course of medication use and to remind them of monthly visits.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Ayatollah Kashani Hospital

Full name of responsible person

Sasan Zandi Esfahan

Street address

اصفهان،الیادران،خیابان آیت‌الله کاشانی بین دهقانی و معصوم میرزا، بیمارستان آیت الله کاشانی

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

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Full name of responsible person

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Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?

Yes

Title of funding source

Islamic Azad University

Proportion provided by this source

5

Public or private sector

Private

Domestic or foreign origin

Domestic

Category of foreign source of funding

empty

Country of origin

Type of organization providing the funding

Persons

Person responsible for general inquiries

Contact

Name of organization / entity

Islamic Azad University

Full name of responsible person

Sasan Zandi Esfahan

Position
استادیار
Latest degree
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Person responsible for scientific inquiries

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Yes - There is 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
Title and more details about the data/document
Description of Shared Documents and Data Files In this trial, only de-identified datasets will be eligible for sharing. Individual Participant Data (IPD), including baseline characteristics, primary outcome scores (GHQ-28 and BDI-II), and variables required to reproduce the main analyses, will be shared after complete removal of all personal identifiers. If full de-identification of the entire dataset is feasible, the complete de-identified dataset may be shared; otherwise, only the subset of data related to primary outcomes and essential analytical variables will be made available. The following documents may be shared: - De-identified Individual Participant Data (IPD) - Final study protocol - Statistical Analysis Plan (SAP) - Generic version of the Informed Consent Form (ICF) - Statistical analysis code - Data Dictionary (variable definitions and coding structure) All documents will be shared only upon reasonable written request from qualified researchers, subject to Ethics Committee approval and a signed Data Use Agreement ensuring confidentiality and appropriate use of the data.
When the data will become available and for how long
Timing of Data and Document Release The release of

study documents and datasets will follow a predefined schedule. The access period will begin 6 months after publication of the main trial results and will remain open for at least 3 years after the final manuscript is published. Detailed timeline: - De-identified Individual Participant Data (IPD): Available 6 months after publication of the primary results. - Final study protocol: Released upon completion of trial registration (IRCT) or at the time of protocol paper publication. - Statistical Analysis Plan (SAP): Available at the time of publication of the main results, typically as a supplementary file. - Generic Informed Consent Form (ICF): Accessible upon publication of the protocol or main article. - Statistical analysis code: Available 6 months after publication of the main results. - Data Dictionary: Released concurrently with the IPD dataset.

To whom data/document is available

Eligibility for Requesting Study Data and Documents Access to the study data and documents will be limited to qualified researchers with a legitimate scientific purpose. Applicants must have an established institutional affiliation and provide a clear research rationale. Eligible groups include: - University faculty members and academic researchers - Researchers affiliated with recognized research institutes - Graduate students, with supervision and approval from their academic advisor - Industry researchers, only if the intended use is non-commercial, scientific, and accompanied by a signed confidentiality agreement Access will not be granted to individuals without research affiliation, to requests lacking a valid analysis plan, or to purposes unrelated to scientific inquiry. All requests require approval from the Ethics Committee and the principal investigators, and data will be shared only after signing a Data Use Agreement (DUA).

Under which criteria data/document could be used

Additional Conditions for Using Shared Data and Documents In addition to eligibility criteria for requesting access, the use of de-identified data and study documents is subject to several scientific and ethical requirements. The following conditions must be met for submitting a request and for using the shared materials: Requirements for submitting a data access request - Submission of a formal written request specifying the research purpose, analysis plan, and required data elements - Demonstration of a valid institutional affiliation (academic, research institute, or non-commercial industry research) - Provision of a clear and methodologically sound secondary analysis plan - Description of data confidentiality and security measures - Signing a Data Use Agreement (DUA) - Approval by the Ethics Committee and the principal investigators Requirements for using the data and documents - Data may only be used for scientific, academic, and non-commercial purposes - Analyses must strictly follow the approved analysis plan submitted with the request - Any new or modified analysis requires a new request and ethical approval - Attempts to re-identify participants are strictly prohibited - Secondary publications must include proper citation of the original trial - Data may not be shared with third parties without explicit written permission - Data must be stored in secure, encrypted environments - Use of documents (protocol, SAP, ICF, analysis code) is limited to reproducing analyses or conducting scientifically valid secondary analyses

From where data/document is obtainable

Applicant Guide to Requesting Data and Documentation Applicants seeking data or documentation for a study should submit their formal request through the following channels. These channels are listed in order of priority for response: 1. Primary and Priority Channel – Corresponding Investigator Email Name: Dr. Sasan Zandi, Isfahan Email: sasanzandiesfahan@yahoo.vom Description: All requests should be submitted first via email. The request should include the researcher's introduction, institutional affiliation, scientific objective, and proposed analysis plan. 2. Secondary Channel – Faculty of Medicine Research Office Postal Address: Faculty of Medicine, Islamic Azad University, Najafabad Branch, Daneshgah Boulevard, Najafabad, Iran Email: . 299752@iau.ir Telephone: 00983142292929 Description: Requests that require administrative review or institutional approval will be processed through this channel. 3. Third Path – Research Ethics Committee Postal Address: Research Ethics Committee, Islamic Azad University, Najafabad Branch, Iran Description: Requests that involve access to more sensitive data or require ethical approval are referred to the Ethics Committee after initial review. Important Notes for Applicants - The request must be in writing and include a clear scientific objective. - Submission of a secondary analysis plan is mandatory. - Access is only possible after signing a Data Use Agreement. - Initial response is usually sent within 2-4 weeks.

What processes are involved for a request to access data/document

English Version – Detailed Process for Requesting and Receiving Study Data/Documents Applicants must follow a clear, multi-step process to obtain access to de-identified datasets or study documents. The steps below ensure scientific integrity and protection of participant confidentiality. Steps in the Data Access Process 1. Submission of a formal request (1–2 weeks) The applicant must submit a written request including: - Scientific purpose and justification - Proposed secondary analysis plan - Specific data elements required - Institutional affiliation Initial screening typically takes 1–2 weeks. 2. Scientific and ethical review (2–4 weeks) The request will be reviewed by: - The principal investigators - The Research Ethics Committee (if required) This review phase usually requires 2–4 weeks. 3. Signing the Data Use Agreement (1 week) If approved, the applicant must sign a Data Use Agreement (DUA) outlining: - Scientific and non-commercial use only - Prohibition of re-identification - Prohibition of sharing data with third parties - Requirements for secure data storage This step typically takes about 1 week. 4. Preparation and release of data (1–2 weeks) After the DUA is signed: - Data are fully de-identified - Only approved variables are extracted - Files are encrypted and transferred securely This step requires 1–2 weeks. Estimated total time for the full process Approximately 4 to 9 weeks (depending on request complexity, dataset size, and ethical review requirements)

Comments