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Effects of nutrition in diabetic/non-diabetic participants who have increased fat in the liver

Submission date	**Recruitment status**	[_] Prospectively registered
25/01/2022	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
18/04/2022	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
09/07/2024	Digestive System	[_] Record updated in last year

Plain English summary of protocol

Background and study aims

The Twin Health platform uses a Whole-Body Digital Twin unique to the patient, powered by artificial intelligence and Internet of Things technology, to precisely understand the metabolic impairment in a patient's body. This strategy is successfully being used in patients with diabetes. Current ongoing studies in diabetic patients have shown a significant improvement in parameters that are involved in non-alcoholic fatty liver disease (NAFLD) such as body weight, fat content and insulin resistance. NAFLD is a group of conditions caused by high levels of fat in the liver. The aim of this study is to find out whether a precision-based approach of lifestyle modifications using the Twin Health platform can help to reduce disease progression in patients with NAFLD or nonalcoholic steatohepatitis (NASH). NASH is liver inflammation and damage caused by a build up of fat in the liver.

Who can participate?

Patients aged 18 years and over with NAFLD or NASH, BMI 19 kg/m² and above, who are not diabetic or diabetic and on a stable dose of antidiabetic medication for the last 3 months

What does the study involve?

Participants are randomly assigned to one of two groups: either the Twin Precision Treatment (TPT) along with standard care group or the standard care only group. The TPT group will get the usual care along with a few personalized lifestyle modifications. These include providing an optimal combination of macronutrients, micronutrients, and microbiome, while simultaneously guiding individual patients to avoid foods that cause blood glucose spikes and to replace them with foods that do not produce glucose spikes. Nutritional counselling will be provided by trained coaches through the app and via telephone. Participants will be asked to do 10,000 steps per day (measured using a Fitbit sensor) and do resistance and breathing exercises. Sleep will be monitored (using a Fitbit sensor) and participants will be counselled to get at least 7 hours of sleep. The sensors and the app will be used to provide a personalized diet, and the researchers will collect information on the blood sugar response to different foods (collected using a continuous glucose monitoring patch), changes in blood pressure, heart rate, and body composition via Fitbit sensors connected to the mobile app via Bluetooth and by participants entering their food intake into the app every day.

What are the possible benefits and risks of participating?
The study may or may not benefit the patients directly. Based on ongoing diabetes studies the researchers have found improvements in blood sugar, reductions in blood pressure and weight loss in patients on Twin Precision treatment. If the intervention works in this group of patients, there can be a reduction in disease progression and its associated complications. This includes progression to cirrhosis, need for liver transplant and risk of hepatocellular cancer.
Since the intervention is in the form of lifestyle modifications and dietary interventions based on micro and macronutrients, during the first 15 days there can be fatigue and headache which will subside with adequate hydration. The researchers do not foresee any serious adverse events. Occasionally there can be a drop in blood sugar levels in diabetic patients due to improvement in blood sugar control. However, all these patients will be continuously monitored for any change in blood sugar level and drug doses will be changed accordingly.

Where is the study run from?
TWIN Health (India)

When is the study starting and how long is it expected to run for?
December 2021 to October 2025

Who is funding the study?
TWIN Health (India)

Who is the main contact?
Dr Paramesh Shamanna
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Contact information

Type(s)
Principal investigator

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Additional identifiers

Protocol serial number
TPT-03/2021

Study information

Scientific Title
Efficacy of Twin Precision treatment in patients with non-alcoholic fatty liver disease - a multicenter, open-label, parallel-arm, randomized controlled trial

Acronym
TPT-NAFLD

Study objectives
Though several studies have been conducted, currently there is no approved pharmacological therapy for non-alcoholic fatty liver disease (NAFLD). Treatment strategies are largely focused on lifestyle modifications such as change in dietary habits and improvement in physical activity. However, the same dietary approach may not be effective and acceptable by all individuals. Twin

Precision Treatment is a personalized form of dietary intervention based on data collected from individuals using sensors and analyzed using computer technology.

The Twin Health platform uses a Whole-Body Digital Twin, powered by artificial intelligence and Internet of Things technology, to precisely understand the metabolic impairment in the patient's body, which is unique to the patient. This strategy is successfully being implemented in patients with diabetes. Current ongoing studies in diabetic patients (unpublished data) have shown significant improvement in parameters that are implicated in NAFLD such as body weight, fat content and insulin resistance.
Thus it is hypothesized that a precision-based approach using Twin Health platform on lifestyle modifications can help in reducing disease progression in patients with NAFLD or nonalcoholic steatohepatitis (NASH).

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 29/10/2021, Medisys Clinisearch Ethical Review Board (No 426, 4th Cross, 2nd Block, Kalyan Nagar, Bangalore 560043 Karnataka, India; +91 (0)8025421333, 25902546; mcerbblr@gmail.com), ref: MCERB/197
2. Approved 29/10/2021, Medisys Clinisearch Ethical Review Board (No 426, 4th cross, 2nd block, Kalyan Nagar, Bangalore 560043, Karnataka, India; +91 (0)8025421333, 25902546; mcerbblr@gmail.com), ref: MCERB/198
3. Approved 29/10/2021, Medisys Clinisearch Ethical Review Board (No 426, 4th cross, 2nd block, Kalyan Nagar, Bangalore 560043, Karnataka, India; +91 (0)8025421333, 25902546; mcerbblr@gmail.com), ref: MCERB/199
4. Approved 18/02/2022, Medisys Clinisearch Ethical Review Board (No 426, 4th cross, 2nd block, Kalyan Nagar, Bangalore 560043, Karnataka, India; +91 (0)8025421333, 25902546; mcerbblr@gmail.com), ref: MCERB/208
5. Approved 25/05/2022, Medisys Clinisearch Ethical Review Board (No 426, 4th cross, 2nd block, Kalyan Nagar, Bangalore 560043, Karnataka, India; +91 (0)8025421333, 25902546; mcerbblr@gmail.com), ref: MCERB/215
6. Approved 19/03/2022, Universal Ethics Committee (6/2RR Villa, 180/109, Rangarajapuram main road, kodambakkam, chennai-600024, Chennai, 600024, India; 044-23720600/ 32472446; universalethicscommittee@gmail.com), ref: UEC/APP/017/21-22
7. Approved 05/03/2022, Universal Ethics Committee (6/2RR Villa, 180/109, Rangarajapuram main road, kodambakkam, chennai-600024, Chennai, 600024, India; 044-23720600/32472446; universalethicscommitte@gmail.com), ref: UEC/APP/016/21-22
8. Approved 28/06/2022, Intersystem Biomedica Ethics Committee (C/O Kasturba health society, Sthanakwasi jain aradhna dham, 14 khandubhai desai road, vile parle, Mumbai-400056, Mumbai, 400056, India; 022-6736128, 9819181950, 9820050852; isbec.india@gmail.com), ref: ISBEC/NR-16 /KM-KM/2022

Primary study design
Interventional

Study design
Multicenter open-label parallel-arm randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Non-alcoholic fatty liver disease (NAFLD)

Interventions
Patients will be stratified based on the presence or absence of diabetes. Randomisation code will be generated using online software using block randomisation. Specific treatment will be assigned using Interactive Web Response Systems (IWRS). Participants are randomly assigned in a 1:1 ratio using central randomisation to one of two groups: either the Twin Precision Treatment (TPT) along with standard care group or the standard care only group. The TPT group will get the usual care along with a few personalized lifestyle modifications. These include providing an optimal combination of macronutrients, micronutrients, and microbiome, while simultaneously guiding individual patients to avoid foods that cause blood glucose spikes and to replace them with foods that do not produce glucose spikes. Nutritional counselling will be provided by trained coaches through the app and via telephone. Participants will be asked to do 10,000 steps per day (measured using a Fitbit sensor) and do resistance and breathing exercises. Sleep will be monitored (using a Fitbit sensor) and participants will be counselled to get at least 7 hours of sleep. The sensors and the app will be used to provide a personalized diet, and the researchers will collect information on the blood sugar response to different foods (collected using a continuous glucose monitoring patch), changes in blood pressure, heart rate, and body composition via Fitbit sensors connected to the mobile app via Bluetooth and by participants entering their food intake into the app every day. The duration of the intervention is 2 years and follow-up is 6 months.

Intervention Type
Other

Primary outcome(s)
1. Fibrosis score and hepatic fat content measured by magnetic resonance elastography (MRE) at 1 year
2. Liver fibrosis assessed using enhanced liver fibrosis (ELF) scores measured from baseline to the end of 1 year

Key secondary outcome(s)
1. Fibrosis score and hepatic fat content measured using transient elastography at baseline, day 180, day 360, day 540, day 720 and day 900
2. Liver fibrosis assessed using enhanced liver fibrosis (ELF) scores at 2 years
3. Metabolic changes measured using:
3.1. Fasting plasma glucose at baseline, day 30, day 60, day 90, day 180, day 270, day 360, day 450, day 540, day 630, day 720, and day 900
3.2. Insulin, lipid profile, hemoglobin A1c at baseline, day 90, day 180, day 270, day 360, day 450, day 540, day 630, day 720, and day 900
3.3. Adiponectin at baseline, day 180, day 360, day 540, day 720, and day 900
4. Non-invasive markers for fat and fibrosis:
4.1. Fat assessed using the Framingham Steatosis Index (FSI), Fatty Liver Index (FLI), NAFLD liver fat score
4.2. Fibrosis assessed using the AST to platelet ratio index (APRI), Fibrosis-4 score, NAFLD fibrosis score
Measured at baseline and every 3 months until 2 years
5. Quality of life measured using chronic liver disease questionnaire for nonalcoholic

steatohepatitis (CLDQ-NASH), EQ 5D at baseline and every 3 months until 2 years
6. Microbiome status measured using whole genome metagenomic sequencing at day 1, day 30, day 90, day 360, day 720, and day 900

Completion date
14/10/2025

Eligibility

Key inclusion criteria
1. Patients with NAFLD (either ELF score > 7.7 or MRE with kPa 2.5 to 5) or with a histological diagnosis of NASH (biopsy < 6 months old)
2. Age ≥18 years of age of either gender
3. BMI 19 kg/m² and above
4. Non-diabetic or diabetic (HbA1c <9%) on a stable dose of antidiabetic medications for the last 3 months
5. Willing to provide written informed consent and comply with the study protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
79

Key exclusion criteria
1. Those with a history of significant alcohol consumption. Significant alcohol intake is considered when alcohol consumption >7 standard drinks/week (70 g ethanol) in women and >14 standard drinks/week (140 g ethanol) in men (according to Asia-Pacific Guidelines)
2. AUDIT score >8 indicating harmful alcohol consumption
3. Patients with a diagnosis liver disease due to other etiologies such as alcohol or drug abuse, medication, chronic hepatitis B or C, autoimmune, hemochromatosis, Wilson’s disease, α1-antitrypsin deficiency
4. Those with clinical evidence of hepatic decompensation such as a history of ascites, esophageal bleeding varices, or spontaneous encephalopathy
5. Those with evidence of portal hypertension such as low platelet counts (< 1.5 lakhs per microlitres), esophageal varices, ascites, history of hepatic encephalopathy, splenomegaly (moderate, severe)
6. Child-Pugh class B/C

7. ALT and AST elevation greater than five times the upper limit of normal (ULN)
8. Alkaline phosphatase more than 2 ULN (less than 250–300 271 U/L)
9. Severe hypertension either treated or untreated. (defined as systolic blood pressure (SBP) >180 mmHg or diastolic blood pressure (DBP) >100 mmHg)
10. Patients with a history of clinically significant heart disease (New York Heart Association (NYHA) Class greater than grade II), peripheral vascular disease (history of claudication), or diagnosed pulmonary disease
11. History of bariatric surgery or intestinal bypass surgery within the 5 years prior to randomization or planned during the conduct of the study
12. Change in body weight more than 5% in the last 3 months
13. History of malignancy in the last 5 years
14. Active, serious medical disease with a likely life expectancy <2 years
15. Participation in an investigational new drug trial in the 60 days or 5 half-lives, whichever is longer, prior to randomization
16. Patients on supplements for weight loss, pioglitazone, vitamin E
17. Pregnant and lactating women and postpartum up to 2 years
18. Those with contraindications for MR elastography
19. Any other condition that, in the opinion of the Investigator, would impede compliance, hinder completion of the study, compromise the well-being of the patient, or interfere with the study outcomes

Date of first enrolment
31/12/2021

Date of final enrolment
11/10/2022

Locations

Countries of recruitment
India

Study participating centre
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Study participating centre
Chandana clinic
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Study participating centre
Trinity Gastroenterology & Liver Clinic
410, 5th Main Rd, HRBR Layout 2nd Block, HRBR Layout, Kalyan Nagar, Bengaluru, Karnataka
Bangalore
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560043

Study participating centre
Lilavati Hospital And Research Centre
A-791, Bandra Reclamation Rd, General Arunkumar Vaidya Nagar, Bandra West
Mumbai
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Study participating centre
Institute of Gastroenterology Sciences & Organ Transplant (IGOT)
Victoria Hospital Campus, Bengaluru, Karnataka
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Study participating centre
RPS Hospital
NO.65/2, Water canal road, Korattur North
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Study participating centre
DiabEndoindia
NO.26, Bishops Garden, Off Greenways Road, Raja Annamalai Puram
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Study participating centre
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Sponsor information

Organisation
TWINS Digital Services India pvt ltd

Funder(s)

Funder type
Industry

Funder Name
TWIN Health

Results and Publications

Individual participant data (IPD) sharing plan
All of the individual participant data collected during the trial will be shared on request from Dr Paramesh Shamanna (paramesh@twinhealth.com). The data will be accessible in a digital format after the consent is obtained from participants and participant identity will be anonymised. The data will be the shared individual participant data that underlie the results after de-identification. The files are able to be viewed by researchers whose proposed use of the data has been approved by an independent review committee identified for this purpose. The data will be available immediately following publication with no end date.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1	29/09/2021	21/02/2022	No	Yes
Protocol file	version 1	29/09/2021	21/02/2022	No	No