Digital, blended lifestyle intervention program for remission and improved management of type 2 diabetes

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Primary Objective: 1. To determine the effectiveness of a personalised, holistic 24-week digital lifestyle programme in achieving diabetes type 2 (T2DM) remission independence from blood glucose-lowering medications, in a Dutch population, in...

Ethical review	Approved WMO
Status	Pending
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON51256

Source
ToetsingOnline

Brief title
IBIDEM

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Ancora Health BV
Source(s) of monetary or material Support: Ancora Health BV

Intervention

Keyword: Diabetes, Digital, Lifestyle, Remission

Outcome measures

Primary outcome

Primary outcomes include diabetes status as measured by indicators of blood glucose control and insulin production, medication use, and study feasibility, including digital consumer engagement and study compliance:

HbA1c

Medication use

Secondary outcome

Secondary outcomes include biochemistry parameters (blood lipids), body composition, physical activity, and diet intake, as well lifestyle questionnaires and sleep activity.

Hs-CRP

Hypertension

Continuous glucose monitoring

Total cholesterol

HDL cholesterol

LDL cholesterol

Triglycerides

Leukocytes

Alcohol intake

Dietary intake

Physical activity

Sleep quality

Lifestyle questionnaire

Sleep

Diabetes

Stress

Depression

Anxiety

Compliance

App literacy

Feasibility

Trial compliance

Digital engagement

OGTT

C-peptide

Fasting blood glucose

Study description

Background summary

Prevalence T2DM
The world is facing multiple pandemics, from zoonoses to chronic diseases. Some can be prevented by encouraging social distancing, limited contact, isolation, and ultimately vaccines. While others, like diabetes, thrive under these circumstances due to poor adherence to healthy diets and reduced physical activity. It is estimated that one in eleven individuals suffer from diabetes

(T2DM), according to the International Diabetes Federation. Unfortunately, it is also estimated that by the year 2030, there will be an estimated 552 million cases of T2D.

Economic burden T2DM
There is a substantial intangible cost to diabetes, the pain and suffering of these patients is, unfortunately, difficult to quantify. In the Netherlands, the estimated cost of diabetes per patient per year is ¤9500 when indirect costs are also considered. These extra consists include the costs directly associated with diabetes, such as the diagnosis, disease management as well as T2DM triggered complications. While indirect costs include management of common commodities such as hypertension, elevated body mass index (BMI), cardiovascular disease, etc., loss of productivity such as sick days, inefficiency, etc. as well as other costs like welfare payments to patients suffering from diabetes related disability5. However, the overall total economic burden of T2DM in the Netherland was an estimated ¤5.9 billion as of 2016. This figure is expected to continue to rise due to the general ageing of the population as well as inactive and poor dietary behaviours.

This cost rose 26% between 2012 and 2017, and may increase more substantially due to current circumstances, as well as the ageing population In addition to the financial costs.
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Reversibility of T2DM
However, there is ever-increasing awareness that the tied can be turned, that impaired blood glucose tolerance and fasting glucose tolerance can be effectively treated with lifestyle interventions, thus preventing progression to T2DM. Studies have shown that early T2DM can be reversed using a number of different dietary strategies, so long as they achieve substantial weight loss. The reversibility of diabetes was first observed in bariatric patients undergoing gastric bypass surgery; patients* blood glucose levels completely normalised, have been observed to remain so for up to 10 years in 90% of patients. More recent studies have suggested that lifestyle interventions can achieve similar results. In one of the premier studies on the topic, Lim et. al. 2011 showed that diabetes could be reversed. Individuals following a 600kcal diet reduced their liver fat content by 30% and to have their blood glucose levels normalise within the first seven days of the study, while weight loss was on average 13 kilograms and insulin became supranormal (1.37*±*0.27 vs controls 1.15*±*0.18 nmol min*1 m*2) within 8 weeks. However, such a study is difficult to perform in larger settings and or real-world conditions due to the severe restrictions placed on the participants, making less strict and virtual interventions interesting alternatives.

The Look AHEAD study considered this and examined the influence of a diet and exercise intervention on individuals aged 45 years and older with T2DM. Individuals reduced caloric (1200 - 1800kcal; <30% calories from fat, and >15%

protein) intake and increased physical activity (< 175 minutes per week) in order to achieve an approximate 7% weight loss. It observed significant improvement of T2DM status, as much as 11.5% of patients achieved (partial) T2DM remission within the first year. On the other hand, recent improvements in technology have led to the rise in digital-based interventions. Patients participating in the Virta programme, an intensive digital diabetes, ketogenic diet programme, significantly improved body weight and HBA1c. Specifically, 94% of patients on insulin were able to reduce or eliminate their dosages. Sulfonylureas were entirely eliminated, patients lost on average 12% of their body weight, and HBA1c values reduced from 7.6 ± 0.09% to 6.3 ± 0.07% within one year. Similarly, other studies such TeLiPro, Low Carb Program, and Better Therapeutics observed improvements in TDM2 related outcomes (reduction in HbA1c > .5%, weight loss > 5%, and/or diabetes medication cessation) between three months to one year after program initiation, while other programmes like u-Healthcare, Our Path, GlycoLeap, Noom Coach were able to consistently show improvements in HBA1c and weight loss in participants between three and six months, while reports of harm were sparse. Taken together, this suggests a well-designed digital intensive lifestyle intervention has to potential to significantly improve healthcare outcomes in T2DM.

Study objective

Primary Objective:
1. To determine the effectiveness of a personalised, holistic 24-week digital lifestyle programme in achieving diabetes type 2 (T2DM) remission independence from blood glucose-lowering medications, in a Dutch population, in comparison with usual care.

Secondary Objective(s):
1. To determine if the 24-week digital lifestyle programme leads to improved glycaemic control in terms of reduced dependence on medications, in terms of reduced dosage or number of antihypertensive or antidiabetic medications, and/ or improved HbA1c in diabetes type 2 (T2DM) in a Dutch population, in comparison with usual care.
2. To determine if a digitally administered trial leads to other medical benefits in Dutch diabetes type two patients, including changes in blood chemistry and body composition.
3. To evaluate if a digital diabetes remission programme can be effectively delivered in conjunction with routine primary or secondary care, including the consideration feasibility of the programme, in terms of patient acceptability and compliance to the programme (app engagement).
4. To analyse the association between the different diabetyping methods developed by TNO and Ahlqvist and Udler with respect to genetic and phenotypic methods.
5. To determine if there is an association between diabetype and remission and or glycaemic control.
6. To determine the cost-effectiveness of running a digital lifestyle-based

intervention, in comparison to usual care over a 12- and 24-month period.

Study design

Open-label, randomised, controlled trial.

Intervention

Patients will partake in a 24-week intervention followed by a two-year follow-up period. The intervention will consist of diabetic phenotyping (diabetyping), and a personalised app-based lifestyle intervention, done in conjunction with usual care, the so-called blended care model. Individuals will be allocated to either a high (unsaturated) fat, low-carbohydrate Mediterranean (50 g) or a Mediterranean wiht limited carbohydrates (120 g) diet based on their diabetype, insulin use, and personal preference. This will be given in conjunction with physical activity programme, which will focus more on aerobic activity or resistance training depending on diabetype. All participants will be provided with additional coaching, which will include aspects of diet, physical activity but also aspects of mindfulness, and emotion regulation. The participants will be assessed at screening, before the start of the Maintenance phase, and at follow-ups one, two, and three. Control patients will follow the usual care and will also be followed up, following the same schedule. The treatment is further clarified below:

Prior to commencing the study, participants in the active intervention group will receive a home kit, approximately one to two weeks before. This will contain all the necessary products, information, and instructions (where applicable) for participating in the study. Moreover, they will be carefully informed about the types of personalisation*s available to them. The participants will have either a whole food type diet or a low carbohydrate diet recommended to them based on their metabolic profiles. In addition, they will also have specific types of exercise recommended to them, however, they will be able to choose which of these, and which combination of exercise and diets they follow. Participants* treating physicians and coaches will be informed about their choices, and will receive supporting medication adjustment documents, based on those made in previous studies. It will remain the responsibility of the treating physicians to adjust any medications the participants are receiving.

The control group is required to meet the same criteria as the intervention group. The control group only receives health assessments (with the exception of the diabetyping, glucose tolerance test, and genetic testing), they will not receive any health intervention. They will continue to receive standard diabetes care.

Study burden and risks

This study will lead to insight as to how a digital health intervention can be (successfully) carried out within the Netherlands in a type two diabetes population. Insights here will be used to improve the intervention, such that treatment efficacy can be further increased. This should translate into improved quality of life for patients with respect to improved blood glucose control and or complete diabetes remission. which will likely reduce the risk of or time to the development of complications associated with type two diabetes. Improvement of blood glucose control could look like reduced and or removal from hyperglycaemic medications, reduced frequency of blood glucose measurements. There is some risk associated with the commencement of this study. In rare circumstances, a participant could develop a serious condition, called ketoacidosis, and the complications associated with it.

This risk will be mitigated as much as possible through the careful introduction of a controlled diet, and gradual, medically supervised reduction of medication and blood glucose levels. Additionally, hyper or hypoglycaemia may also be experienced if participants do not carefully follow their prescribed diets.

Burdens the participants will experience include four clinic visits, 24 weeks of a digital diet and lifestyle intervention, venepunctures, questionnaires, and physical tests, as well as two years of follow-up. Additionally, participants may feel some discomforts or potential injuries from increased levels of activity and or diet or bruising/discomfort at the site of venepunctures or fingerpricks. During the active intervention phase of the study, this will take seven to ten hours per week. This includes (additional) exercise, meal planning, and interactions with the digital platform Ifood logging, participation in group sessions, etc). During the follow-up period, no additional requirements are made on the participants.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Diabetes: Diagnosis of T2DM without end-organ failure
Diagnosis of T2DM
BMI: 25-45 kg/m²
Age: 18 to 75 years
Most recent HbA1c value should be greater than 6.0% (>43 mmol/mol) and, if less than 6.5% (<48 mmol/mol), individuals should still be receiving anti-diabetic medication
Display interest and motivation to enroll in a digital, lifestyle intervention for diabetes
Tech-savvy - able to fully use a smartphone/ tablet and app

Exclusion criteria

- Serious co-morbidities, for example, a severe form of chronic obstructive pulmonary disease (Gold III or IV), heart failure (classes 2-4) kidney failure (eGFR / MDRD) <45 units, or other medically determined end-stage organ failure, on active donor list
- Myocardial infarction, stroke, angina, or coronary insufficiency within the previous six months
- Requirement of a prescribed medical diet
- Weight loss of more than five kg or greater than 10% within the past six months
- Participation in diabetes therapy within the preceding three years; participation in concurrent weight management or interventional research protocol,
- Untreated thyroid disease,
- Excessive alcohol intake (acute or chronic) defined as the average

consumption of three or more alcohol-containing beverages daily or consumption of more than 14 alcoholic beverages per week
- Incapacitated patients, and thus unable to fully participate in the trial.
- Uncontrolled blood pressure (SBP > 170 mmHg and/or DBP > 100 mmHg)
- Use of an insulin pump
- Type 1 diabetes
- Substance abuse
- Non-English or Non-Dutch speaking
- Cancer requiring treatment in the past five years, with the exception of non-melanoma skin cancer
- Chronic infectious disease requiring ongoing treatment
- Diabetic retinopathy requiring treatment
Pregnancy, consideration of pregnancy within the study period, lactation, or having given birth within the previous nine months
- History of keto-acidosis
- Current treatment with anti-obesity drugs
- Eating disorder or purging behaviour
- Currently uncontrolled major psychiatric disorder (e.g., schizophrenia, bipolar disorder) or use of antipsychotic drugs.
-- Hospital admission for depression
- Learning difficulties limiting the participation in a digital health intervention and or limiting the comprehension of trial goals or coaching curriculum.
- Other chronic diseases or conditions likely to limit lifespan to less than six years
- Severe visual impairment or other impairment preventing interaction with digital content
- Cholelithiasis or biliary dysfunction
- Creatinine > 2.0 mg·dL-1 or > 152.5 µmol·L-1
- Urinary albumin > 1 g·dL-1 or > 10 g·L-1
- Having undergone bariatric surgery
- A recent on-record estimated glomerular filtration rate of less than 30 mL/min per 1.732 m^2
- For nutritional ketosis specifically: impaired hepatic function (Bilirubin >2 mg·dL-1 or >34.2 µmol·L-1, Albumin < 3.5 g·dL-1 or <35 g·L-1)

Study design

Design

Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	03-03-2022
Enrollment:	410
Type:	Anticipated

Ethics review

Approved WMO Date:	12-01-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL77688.056.21