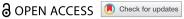


#### ORIGINAL RESEARCH ARTICLE



# Feasibility of a 12 weeks supervised exercise training intervention among people with Maturity Onset Diabetes of the Young (MODY) or type 2 diabetes in Greenland

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#### **ABSTRACT**

Preventing and managing Type 2 diabetes (T2D) involves adopting healthy lifestyle habits such as balanced nutrition and regular exercise. Maturity Onset Diabetes of The Young (MODY) shares diagnostic characteristics with T2D, but exercise responses in MODY remain unclear. In Greenland, MODY is 4-5 times more common than in other countries. No established exercise regimen exists for either T2D or MODY in Greenland. This study assessed the feasibility of a 12week supervised exercise programme for MODY and T2D in Greenland, focusing on attendance, satisfaction, and effects on cardiovascular disease (CVD) risk factors and quality of life (QoL). Conducted as an experimental, two-armed, controlled trial, nine participants (4 with MODY) engaged in prescribed training sessions twice weekly for 45-60 minutes, while another nine (4 with MODY) formed the control group. Key outcomes included adherence rates, satisfaction levels, changes in HbA1c, body composition, aerobic fitness, blood pressure, CVD risk factors, and SF-12 scores. Although training adherence was modest at 56%, participant satisfaction remained high. Notable findings included a slight decrease of -0.3 mmol/l in HDL-cholesterol and a 5.7-point increase in the mental component (MCS) of SF-12 within the intervention group. However, the study underscores the need to refine the study design before supervised exercise programmes can be widely implemented in clinical settings in Greenland.

#### **ARTICLE HISTORY**

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#### **KEYWORDS**

Type 2 diabetes; Maturity Onset Diabetes of the Young; MODY; exercise training; intervention; Greenland

#### Introduction

Globally, type 2 diabetes (T2D) is one of the most common diseases [1], and its occurrence is a rapidly growing challenge in Greenland as well [2,3]. It is estimated that 10-15% of patients diagnosed with T2D in Greenland have Maturity-Onset Diabetes of the Young (MODY). Additionally, 7% of the patients with T2D are estimated to have the Inuit-specific HNF1a variant of MODY. This hereditary monogenetic phenotype is rare in other regions of the world [4].

Lifestyle modification, including exercise, is a cornerstone in the prevention and treatment of T2D [5-7]. For many diabetic complications, there is an inverse doseresponse relationship with increased physical activity (PA) levels [8], and structured exercise also improves risk factors for diabetic complications among persons with

T2D [5,9–11]. In contrast, this has not been investigated among persons with MODY. MODY has several phenotypes, all characterised by impaired beta-cell function [12], whereas T2D is predominantly characterised by insulin resistance. Thus, it is unclear to what extent exercise recommendations developed for T2D may provide similar health benefits for persons living with MODY. Also, as many MODY phenotypes are treated with sulfonylureas and insulin, which increases the risk of hypoglycaemia [13-15], the safety of exercise recommendations should be considered before application.

Although guidelines recommend training for individuals with T2D [5], no structured training programme for managing T2D or MODY has been established in Greenland. To improve the management of diabetes in Greenland this will be imperative to improve. Typically a training programme

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for diabetes are developed in culturally dissimilar cultures and will include both standardised fitness activities such as aerobic interval and resistance training activities [16]. As the physical activity patterns in Greenland also differs from other countries like Denmark or USA [17], the fidelity and feasibility of exercise programmes including the typical fitness activities developed in these countries than Greenland is unknown. However, Danish guidelines recommend a minimum training period of 12 weeks for combined training in T2D [18]. Additionally, studies have shown that combined aerobic and resistance exercise interventions lasting 12 weeks or longer lead to significant improvements in cardiovascular risk factors, physical fitness, and body composition [11,19].

Therefore the primary aim of the study is to investigate the fidelity and feasibility, as expressed by attendance and satisfaction, of 12 weeks of supervised exercise training among persons with MODY or T2D in a clinical context in Greenland. Secondarily, we will describe the changes in cardiometabolic risk factors, quality of life (QoL) and safety among the participants across the intervention period for the entire sample and stratified according to diabetes type (MODY or T2D).

#### Materials and methods

### The research team

The research team is a part of clinical practice in the Greenlandic healthcare system, where the first, third, fourth, fifth, and last author were based during the study period. The third author are physiotherapist, employed in the department of physiotherapy at Queen Ingrid's Hospital (QIH) in Nuuk and was also a part of the intervention. The first author is Inuit and Greenlandic, while the rest of the research team is Caucasian and from Denmark. The first author attended several training sessions to ensure the training proceeded as planned.

## Study design

This study was an open-label two-armed controlled feasibility- and pilot study, retrospectively registered in clinicaltrials.gov (NCT05747118). Participants were allocated to either an 1) exercise (EX) or a 2) standard care (StC) group.

### Study setting, eligibility and recruitment

The healthcare system in Greenland is divided into five healthcare regions. One regional hospital is located in the largest town in each health care region. The remaining cities have healthcare centres and smaller healthcare units, while smaller settlements have nursing stations or settlement consultations. Medication, hospital treatment and health care services in general, are free of charge for all permanent residents in Greenland [20]. Steno Diabetes Center Greenland is responsible for treating diabetes and other lifestyle-related diseases. Basic treatment and followup for diabetes patients are managed by local healthcare clinics. Typically, there is a lifestyle section with health care professionals who may also have various other tasks than lifestyle. Patients with diabetes receive advice from lifestyle professionals during consultation. While pharmacological treatment, patient education and dietary councelling are employed, no supervised training is currently offered or implemented.

Potential participants were identified using an extraction from the electronic medical record (EMR). They were recruited from August to September 2022 in the capital of Greenland Nuuk through phone calls, posters at Steno Diabetes Center Greenland, and on social media to enable patients to sign up themselves. Furthermore, patients with T2D were informed about the project at consultations at Steno Diabetes Center Greenland during enrolment.

Participants were eligible if they were aged 18 years or above, diagnosed with T2D or MODY, resided in Nuuk, or were untrained (limited to of being physically active without a structured training programme). The last was excluded for two of the participants in the lack of finding the total number of participants, where one had a running programme and the other a fitness schedule. Exclusion criteria were patients who exercised in advance, heart problems, significant sequelae, pregnancy, participating in another intervention study simultaneously, not participating in tests and re-tests, or if assessed as not suitable by their health practitioner; for example, if they had severe mental health problems or already had difficulty showing up to controls, etc.

#### **Allocation**

Following the initial screening, five participants with T2D agreed to participate in the exercise intervention. The control group constituted participants matched by T2D duration and age (±3 years) as well as by HbA1c level (±5 mmol/ mol), who were only willing to participate in the StC. Due to the low number of patients with MODY living in Nuuk, we contacted all patients with MODY aged 18 years or above. Once enough agreed to participate in the training, we asked the remaining individuals to join the control group.

## Intervention

The exercise intervention consisted of 12 weeks of training at the physiotherapy department at QIH. The intervention was developed by the first author in close collaboration with several physiotherapists from the department and the research team. The first author was Inuit. The physiotherapist team included one Inuit physiotherapist from Greenland and three Caucasian physiotherapists (two from Denmark and one from Spain). No individuals with MODY or T2D were involved in the study design. The training programme was designed to meet the World Health Organization recommendations on PA for health for at least 150 minutes/week with moderate-intensity aerobic PA or 75 minutes/week with vigorous-intensity aerobic PA or an equivalent combination of both [21]. The intervention was initiated on 26 September 2022 and was completed after 12 weeks on 14 December 2022. Intervention patients received a prescribed and supervised mixed (aerobic and resistance) exercise training programme, whereas the control group received standard care. Aerobic exercise training improves insulin sensitivity, paralleling improved mitochondrial function. Resistance exercise training increases lean mass through improved strength, bone mineral density, blood pressure, lipid profiles, and skeletal muscle mass and benefits overall glucose management [21]. However, combined aerobic and resistance exercise training has been noted for a greater reduction in HbA1C compared with either type alone [22-24].

## Exercise training programme details

The training was divided into three phases, with four weeks for each phase. All sessions were facilitated by one or two physiotherapists from the physiotherapy department at QIH. The training programme consisted of twice-a-week supervised sessions of 60 min duration for 12 weeks.

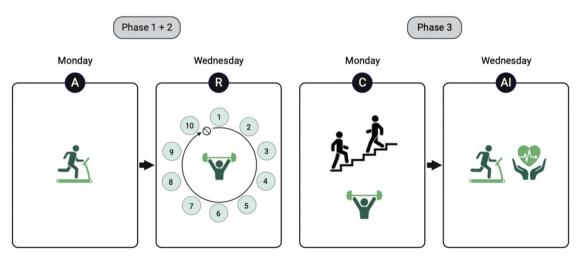
Each training session consisted of a 10 minutes warm-ups in a self-selected fitness machine on either a bicycle, treadmill, cross trainer or rowing machine. Afterwards, 40 minutes of training and 5–10 minutes of stretching exercises were completed. Both the aerobic and strength training intensities are designed to progressively challenge participants as they improve their fitness. For more details, see the description of the phases. A graphic overview of the exercise training programme is illustrated in Figure 1.

#### Phase 1 & 2

The training alternated during the week in the first and second phases, focused on aerobic and strength training.

Aerobic training took place on Mondays, on a bicycle, treadmill, cross trainer, or rowing machine with intensity according to the Borg Scale, at 13–14 in the first and 15–16 in the second phases.

Strength training took place on Wednesdays. Strength training consisted of circuit training with local recovery with ten stations over two rounds and 2 minute breaks between rounds. Strength exercises went through the whole body, focusing on large muscle groups in the upper and lower body. The core exercises included squats, pelvic lifts, knee flexion and extension, chest press, seated rows, arm exercises, and



Phase 1: 13-14 bs, 40/20 w/p Phase 2: 15-16 bs, 60/20 w/p Phase 3: 15-16 bs, 60/20 w/p

Figure 1. Graphic overview of the exercise training programme. Phase 1 are week 1- 4, phase 2 week 5-8, and phase 3 week 9-12. (A) indicates aerobe training, (R) resistance training, (C) combined training, and (AI) aerobic interval training. Mean exercise intensity (borg-scale [bs] for (A) and work/pause ratio [w/p] for (R)).

sit-ups. In the first phase, the intensity of the circuit training was 40/20 sec. work/break ratio for each exercise which increased to 60/20 sec. in the second phase. The intensity of the resistance training was assessed using the rate of perceived exertion (RPE) with a target RPE of 5 during the initial phase and 6 throughout the remaining part of the intervention.

#### Phase 3

In the third phase, every training session was combined with aerobic and strength training, with the same intensity as phase 2. On Mondays, the training took place at QIH's patient hotel, which is part of the QIH building. Participants walked or ran up and down the patient hotel's six-floor stairs. Occasionally, the participants underwent bodyweight strength exercises on the top floor. On Wednesdays, training took place in the training room. The participants underwent interval training on a self-selected fitness machine, followed by bodyweight strength exercises on the floor. Training in the training room was accompanied by music to facilitate group dynamics and create a good atmosphere [25].

#### **Outcomes**

Primary outcomes included the feasibility of training by adherence and satisfaction of participants. Secondary outcomes included changes in HbA1c, body weight and composition, fitness, cardiovascular risk factors, and self-assessed health from baseline to 12 weeks of follow-up.

## **Measurements**

To evaluate the effectiveness of the intervention, the participants were measured at baseline (before the start of the intervention) and at the end of the intervention (12 weeks after initiation). Sex, age, training background, smoking status, comorbidities, injuries, and other relevant background characteristics were collected via survey, while medication information was obtained from the EMR. Information about adverse events (AE) or serious adverse events (SAE) [26] associated with training was registered in the EMR if they were addressed.

## Satisfaction

Satisfaction was investigated in two ways. First, participants completed a physical questionnaire to measure overall patient satisfaction at the exact time. The questionnaire consisted of 22 questions divided into four domains: 1) physical facilities of the intervention, 2) training course, 3) training sessions, and 4) exercise instructors on the training course. The participants responded the questions to the extent to which they agree or disagree on Likert scale, with a list of statements within abovementioned domains. The Likert scale consisted of: to a large extent, to some extent, to a lesser extent, not at all. The scales were then converted to satisfied answers if answered on either of the two first scales and to dissatisfied answers if answered on either of the last two scales. The second part consisted of individual interviews to nuance findings from the questionnaire domains through different participants' perspectives.

## Attendance and adherence

For adherence to the prescribed training, participants' attendance was registered in the EMR for each training session. The conventional exercise-related adherence variable was the rate of attendance (ratio of total attended scheduled exercises). Exploratory adherence was defined as the permanent discontinuation of participation. Missed sessions could not be rescheduled within the intervention period due to a lack of time for health professionals. All compliance variables were counted together as one unit for the same patient.

## Health related quality of life (HRQoL)

HRQoL was assessed using the 12-item Short-Form Health Survey (SF-12), version 1 [27]. This 12-item generic questionnaire consists of eight subscales (physical functioning, physical role, bodily pain, general health, vitality, social functioning, emotional role, and mental health), which can be further aggregated into a physical component score (PCS) and mental component score (MCS). The scores have a mean of 50 and an SD of 10 in the US general population, with higher scores indicating better health. The SF-12 has been used in many studies with individuals with diabetes and has shown good reliability, known group validity, predictive validity, and responsiveness to change [28,29]. The questionnaire has been used in Greenlandic in previous population surveys in Greenland [30] but has to our knowledge not been validated. In our study, the questionnaire was eligible in Greenlandic and Danish.

#### Cardiovascular disease risk factors

Before and following the intervention, the participants underwent a screen consisting of an assessment of body weight and composition using a Tanita scale [31], office blood pressure, where participants rested for a couple of minutes before, and the measurements done over two times for precision and to ensure a valid measurement consisting of the average value of the two measurements. Finally, there was a submaximal

fitness test (Aastrands one-point-test on a bicycle ergometer with heart rate assessed (Garmin forerunner 245, Danish) [32]. Then, the participants donated a blood sample for analyses of HbA1c, cholesterols, and triglycerides. Blood samples were analysed using standard procedures at the QIH laboratory.

### **Interviews** and analyses

To support the satisfaction questionnaire, we performed three individual, semi-structured interviews. The three interview persons consisted of: participant 1 with MODY (intervention group), participant 2 with T2D (intervention group), and participant 3 with MODY (control group). The interviewer selected the informants on pairwise match, with a vision to include and compare the diabetes types. All interviews were conducted to hear the informants' arguments, attitudes, opinions, and assessments of the intervention.

All interviews were audio recorded and transcribed verbatim.

Since the interview questions for participants were all the same, data from the interviews were combined and analysed. Data was analysed by systematic text condensation [33], which is suitable for cross-sectional analysis to be carried out, where meaning-bearing units from several informants must be summarised [33]. Following the method, the analysis consisted of four steps. First, based on the interview transcriptions, themes were produced for further analysis, and second, meaning-bearing units concerning the themes were identified by reviewing the texts once more. The themes became codes and subgroups, and a matrix was constructed from the concluding codes and subgroups. A code and subgroup were generated in the third step to construct "artificial" quotations from the meaning-bearing units. Lastly, from the "artificial" citations, the final presentation of the results was produced. Individual quotes were found in transcription to be seen in a larger context, in order of selection of those assessed were the most telling to be used as results. The analysis was performed in the qualitative software program NVivo (release 1.7).

## Sample size estimation and statistical analyses

No formal sample size calculation was applied and the sample size was determined by what was feasible in the local context. Descriptive data are reported using means with standard deviations (SD), median and interquartile range (IQR) or number and proportion when appropriate. As this study is a feasibility study, not inferential analyses are applied and p-values is not reported. However, for the purpose of interpreting signs of associations, the 95% confidence interval (95% CI)) derived from a 2-tailed independent students t-test is provided. An unpaired t-test was used to assess the difference in follow-up values and the difference between changes between the groups. Analyses were conducted using Stata 17 and R version 4.1.2.

## Mixed methods integration

To illustrate how quantitative and qualitative data relate to and complement each other, we used joint displays. This method was selected to visually present our data and clarify the connections between the survey results and qualitative interview findings. Joint displays allow for an integrated presentation of the data, enabling a clear comparison and combination of results from both approaches [34]. After analysing both quantitative and qualitative data, we identified similarities between them. We then integrated the data by determining key areas of intersection. A joint display was designed and constructed to visually represent the integration of both data types [35].

#### Results

From August 8th to September 9th, a total of 604 patients diagnosed with T2D and residing in Nuuk, the capital of Greenland, were assessed for eligibility through the EMR. The primary reasons for refusal to participate included unwillingness to join or partial absence from Nuuk during the training period. Eighteen participants were allocated to the intervention (56%/n = 8 MODY), and 18 participants were included in the analyses (Figure 2). Of the 586 persons with T2D, only 8 (1%) were allocated, whereas 8 of 24 eligible persons with MODY (53%) were allocated. The reasons for not being allocated differed between MODY and T2D. For those with MODY, the primary reason was failure to meet eligibility criteria, notably due to age (<18 years) in four cases. For those with T2D, a few contacted us expressing interest in participating, while we reached out to the remaining individuals to match them with the MODY patients. Those who did not participate were simply not interested.

Table 1 illustrates the characteristics of the study population, comprising ten females and eight males with a mean age of 51.4 (SD = 17.3) years diagnosed with either T2D or MODY. The intervention group was slightly different from the control group with a higher mean age (55.1 (18.7) vs. 49.7 (16.5) years) along with lower BMI (27.9 (6.0) vs. 29.5 (7.9) kg/m2), and reduced aerobic fitness (30.2 (12.1) vs. 34.1 (5.3) ml/kg/min). The



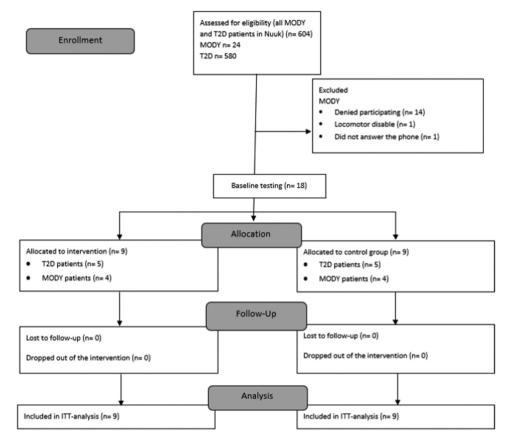


Figure 2. CONSORT flowchart. We filled the intervention group with T2D patients for the remaining five spots and selected five others to match with the control group (requirements: same sex, ±3 years of age, ±5 mmol/mol in HbA1c level). There is no record of how many T2D patients were contacted by phone or in the clinic.

intervention group had lower weight, fat mass, and muscle mass compared to the control group.

## **Feasibility**

#### Attendance and intensity

All participants in the intervention group completed the training intervention (100%) (Figure 3). Out of the 216 scheduled training sessions, a total of 121 sessions were completed, resulting in an average adherence rate of 56% per participant, with individual adherence ranging from 5% to 92%. Stratifying by diabetes types, participants with MODY completed 74 sessions (77%), while those with T2D completed 46 sessions (38%). The main reasons for cancellation of training included illness or non-illness-related factors such as work or travel commitments. Adherence rates varied over the course of the study, with the highest adherence observed in the third month, where an average of five participants cancelled per session (29% adherence), compared to 2.4 participants (66% adherence) in the first month and 4.6 participants (34% adherence) in the second month.

The average RPE for the sessions was reported as 8 (Borg Scale 18), with a range of 7 to 8 (Borg Scale 17 to 18). Individuals with T2D reported a slightly higher RPE of 8.5 (Borg Scale 18.5) (with a range of 8 to 9) (Borg Scale 18 to 19) compared to individuals with MODY, who reported an RPE of 7 (Borg Scale 17)(with a range of 7 to 8) (Borg Scale 17 to 18) (Figure 4).

### Satisfaction

Figure 5 shows satisfaction as expressed through the questionnaire divided into four domains. Seven out of the nine participants were satisfied with the physical framework of the course (78%). Eight out of nine were satisfied with the training intervention (89%). And seven out of nine with the training sessions (78%). All participants were satisfied with the coaches based on their exercise instruction and their ability to motivate. Generally no appreciable differences between the participants with MODY and T2D were observed.

Table 2 shows the relationship between the four domains and the questions from the questionnaire and the qualitative interviews.

**Table 1.** Baseline characteristics of participants.

	INT (n = 9)	CON (n = 9)
Sex (% female)	55.6	55.6
Age (years)	55.1 (18.7)	49.7 (16.5)
Aerobic fitness (kg/min/O <sub>2</sub> )	30.2 (12.1)	34.1 (5.3)
Ethnicity		
Inuit	9 (100)	7 (77.7)
Caucasian	0 (0)	2 (22.3)
Anthropometrics		
Height (cm)	163.7 (7.9)	171.5 (9.3)
Weight (kg)	74.4 (15.4)	86.9 (24.4)
BMI (kg/h²)	27.9 [6]	29.5 (7.9)
Fat percent (%)	31.5 (10.3)	31.5 (12.2)
Fat mass (kg)	24.4 (12.9)	29.2 (18.5)
Muscle mass (kg)	47.5 (6.6)	55.2 (14.2)
Bone m. d. (kg)	2.5 (0.3)	2.9 (0.7)
Blood pressure		
Systolic (mmHg)	129.5 (23)	129.7 (10.9)
Diastolic (mmHg)	77.2 (10.6)	80.2 (9.4)
Glycemic control		
HbA <sub>1c</sub> (mmol/mol)	51.7 (10.9)	52.1 (7.5)
Cardiovascular factors		
HDL-ch (mmol/l)	1.5 (0.4)	1.2 (0.3)
LDL-ch (mmol/l)	2.3 (0.7)	2.1 (0.7)
Total-ch (mmol/l)	4.1 (1)	3.6 (0.9)
Triglycerides (IQR, mmol/l)	1.3 (0.5)	2.0 (1.1)
Self-rated QoL		
PCS (SF-12)	42.3 (-7.7)	46.7 (-3)
MCS (SF-12)	49.9 (-0.1)	51.1 (1.1)
Medicaments		
Glucose lowering	5 (55)	7 (78)
Blood pressure lowering	5 (55)	1 [11]
Lipid lowering	4 (36)	4 (36)
Anticoagulants	1 (11)	0
Metformin	3 (33)	3 (33)
Glimepiride	1 (11)	2 (22)
Jardiance	3 (33)	1 (11)
Ozempic	3 (33)	4 (36)

Data is average (SD) or numbers and percent (%). Medicaments are based on number of people (Metformin).

Data from the interview generally cooperated the pattern from the questionnaires and the participants were satisfied with the training intervention (see Table 2). Regarding physical facilities, the participants requested more space for training, changing rooms, and baths. Being together with peers was essential for participating and showing up for training. The training influenced everyday life by affecting mood and thereby mental well-being. The participants liked the coaches and felt it was important that they could differentiate and target the training to each individual in the group (Table 2). Based on the interviews, no differences were identified between T2D and MODY. However, while all persons with MODY appreciated the timing of exercise (all persons found the time a day for exercise appropriate), this was only the case for 2 of 5 persons with T2D.

The average score for motivation to exercise was 4.33 (range 1 to 5), but where all persons with MODY were highly motivated, only three persons with T2D reported high motivation (score of 5). There remaining persons with T2D where indifferent (score of 3, N = 2) or not motivated for exercise at all (score of 1 and 2, N = 0).

## Change in cardiovascular (CVD) risk factors

Baseline, follow-up and change in CVD risk factors and HRQoL are described in Table 3. In comparison, there were no appreciable changes in any CVD risk factors. A small increase in LDC cholesterol was observed. Nevertheless, when stratified to the diabetes types,

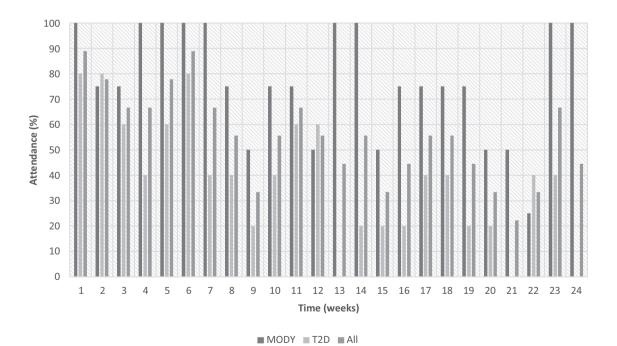
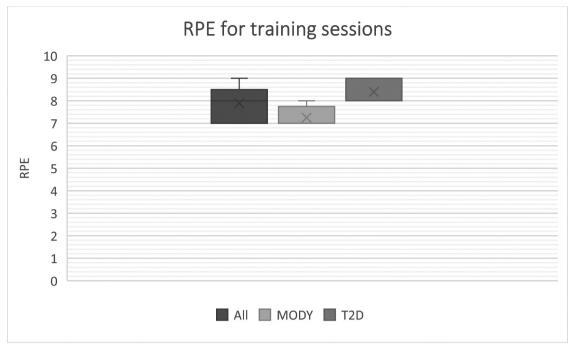
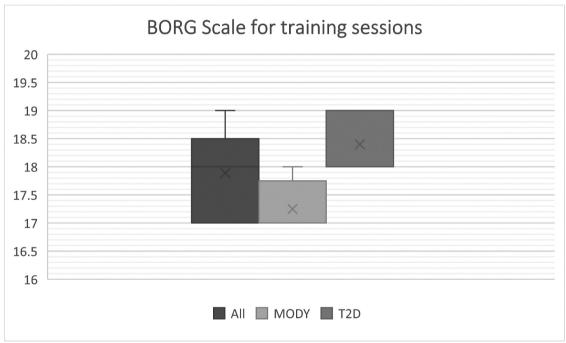


Figure 3. Attendance (%) on the y-axis and time (weeks) on the x-axis.





**Figure 4.** The overall RPE and Borg scale for training sessions. (RPE) rate of perceived exertion, (all) RPE/Borg scale for all participants, (MODY) RPE/Borg scale for MODY, (T2D) RPE/Borg scale for T2D. The box whisker plots: (X) the X indicate the mean RPE/Borg scale. Error bars represent participants perceived maximum RPE/Borg scale. The box whisker plots are based on a very small data set; therefore, there are no error bars in some of the figures as the minimum and highest value is the same.

the unchanged HbA1c level seen in the intervention group, was driven by an increase in MODY (2 mmol/mol (1; 4.9)) compared to T2D (1.6 mmol/mol (9.9; 6.7)). More information can be found in Appendix 1.

## Quality of life

The results are consistent with the benefit, where the change in PCS was similar between the groups, while MCS was consistent with an improvement (post-pre

# Satisfaction



Figure 5. Bar-chart with domains from the questionnaire on the x-axis, and numbers of satisfied participants (N) on the y-axis.

difference (95% CI): 5.7 (–11; 0.4)) in the intervention group while appeared unchanged in the control group (pre-post difference (95% CI): 0.4 (–7.4; 8.3)). PCS increased with (95% CI): 1.2 (–15.0; 12.6) for T2D, while MODY increased by mean (95% CI): 2.9 (–16.2; 10.5). MCS increased (95% CI): 4.9 (–13.4; 3.6) for T2D, whereas it increased (95% CI): 6.8 (–17.6; 4.1) for MODY.

### Safety

No AE's or SAE's were reported.

## **Discussion**

This study is the first structured exercise intervention involving individuals with T2D and MODY in a clinical setting in Greenland. We observed overall satisfaction with the training programme and observed positive changes in mental health. However, attendance and adherence to training sessions were generally low, with no clear indications of improvement in cardiometabolic risk factors. Furthermore, while attendance dropped considerably, particularly among individuals with T2D, those with MODY exhibited higher average attendance, which remained relatively stable throughout the intervention period.

## **Attendance**

Despite the low frequency of prescribed exercise training, typically two sessions per week, there was an overall low adherence to exercise (56%). This declining

adherence throughout the intervention period appears to be a common trend in other countries [36]. Such patterns could stem from shared factors observed in other studies. For instance, a systematic review by MacDonald et al. [36] explored adherence to physical activity (PA) interventions among individuals with T2D, assessing participants' compliance with intervention goals across various exercise or PA levels. The study included adults aged 18 years or above and interventions from seven other high-income countries, spanning intervention durations from three weeks to three years. Adherence to the PA intervention varied from 32% to 100%, with a median adherence of 58% [36]. Considering these findings, the attendance rate in our study was notably low but aligns closely with global trends. Attendance could be enhanced by technologyassistance for social support from peers or health professionals to create a community based support on meaningful PA engagement, and by strengthening the link between individuals' everyday lives and PA with initiating face-to-face conversations, whereby individuals no longer have to rely solely on their own resources and motivation to engage in PA [37].

Given the attendance gap between MODY and T2D participants, one could consider whether individuals with T2D perceive physical training as less relevant compared to those with MODY, potentially influenced by the absence of a specific motivational theory in our study [38]. It is noteworthy that behavioural interventions typically yield significant increases in objectively measured PA and training [39]. Hence, it is prudent to

Table 2. Joint display illustrating the relationship between quantitative and qualitative data.

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Domains from questionnaire	Quantitative questions	Quantitative results (%)	Quotes from qualitative interviews
Physical facilities	How do you assess access	Really good (22)	More space compared to rooms. It is a little cross-
	conditions and the physical	Good (78)	border to leave the training room, where you can
	environment – e.g. access	Bad (0)	meet all kinds of patients in the hallway. I've been
	conditions, waiting room and	Really bad (0)	a little reluctant to train among patients in the
	changing facilities?		beginning. (P1)
			Changing rooms and baths would be better. (P1)
Training intervention	Are you satisfied with the training	Yes, to a great extent (78)	But I feel energetic, in high spirits, happy, and smiling
	you received?	Yes, to some extent (11)	when I go to work after the workout in the
	To what extent would you	No, to a lesser extent (11)	morning. (P1)
	recommend the training to	No, not at all (0)	There is also that community with other diabetes
	others with diabetes?	To a great extent (100)	patients. (P1)
	Can you feel the difference in your	To some extent (0)	Although our ages are very different, it does not
	health after attending the	To a lesser extent (0)	matter to me. We can achieve with the training
	training?	Not at all (0)	according to our individual needs. (P1)
	Did the training meet your	Yes, to a great extent (22)	I hope to be called again soon and asked if I would
	expectations?	Yes, to some extend (56)	like to participate in another course. (P2)
	Would you like to participate in a	No, to a lesser extent (11)	I want to continue. I could easily make this part of my
	training course another time?	No, not at all (0)	week. I could go on. It's so nice. (P1)
	Describe in your own words what	Yes, to a great extent (56)	I would like to see diet counselling involved so that
	could have been better about	Yes, to some extend (33)	one could be targeted on a goal in the time frame
	the training (e.g. language	No, to a lesser extent (11)	one participates in the course. (P2)
	barrier, training site, training	No, not at all (0)	
	equipment, etc.)	Yes (100)	
	What has it been like to	No (0)	
	participate in body	It was exciting to try (100)	
	measurements?	It took too long (0)	
	What has it been like to take part	I didn't think it was relevant to me (0)	
	in a fitness test?	I found it uncomfortable (0)	
		It was exciting to try (100)	
		It took too long (0)	
		l didn't think it was relevant to me (0)	
		l found it uncomfortable (0)	

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Table 2. (Continued).			
Domains from questionnaire	Quantitative questions	Quantitative results (%)	Quotes from qualitative interviews
Training sessions	Was it appropriate to exercise twice a week? Was it nice that the training lasted 12 weeks? How does the training time (7.30 am 8.30 am) fit into your everyday life? If you could choose your own time for training, what would you choose? How hard do you think the training was on a scale of 1-10? Would you like the training to have been harder? How satisfied have you been with training with the others on the team? What was the atmosphere like during the training? Have you been looking forward to working out? How motivated have you been to go to the gym? What could be different for the training to be more motivating?	It was fine (78)  I would have only exercised once a week (0)  I would have exercised three times a week (22)  12 weeks was fine (67)  I would have exercised less than 12 weeks (11)  I would have exercised more than 12 weeks (11)  I would have exercised more than 12 weeks (11)  I would have exercised more than 12 weeks (12)  If's a good time (67)  Another time would be a better time (33)  If the same time as the course (56)  In the morning (33)  At lunch (0)  In the afternoon (11)  In the evening (0)  Scale 9 (22)  Yes (0)  No (78)  I don't know (22)  Very satisfied (3)  Neither satisfied (0)  Dissatisfied (11)  Very good (28)  Good (22)  Really bad (0)  Yes, to some extent (20)  No, to a lesser extent (0)  No, to a lesser extent (0)  No, or at all (0)  Highly motivated (56)  Motivated (22)  Not motivated (22)  Not motivated (22)  Not motivated (0)  Not motivated (0)	The training was sufficiently challenging. Because everyone could take it at their own pace, whether you ran upstairs or did circuit training. So it was very comfortable. (P1)  For example, 1 have learned many different forms of training, (P2)  Doing the stair exercise at the patient's hotel was hard at first. But in general, the training was appropriate in terms of intensity. I don't feel it was too hard. (P2)
			(Continued)

lable 2. (continued).			
Domains from questionnaire	Quantitative questions	Quantitative results (%)	Quotes from qualitative interviews
Exercise trainers	How satisfied are you with the coach's ability to motivate you? How satisfied are you with the coach's instruction of exercises?	Very satisfied (33) Satisfied (67) Neither satisfied nor dissatisfied (0) Dissatisfied (0) Very dissatisfied (0) Very satisfied (36) Satisfied (56) Neither satisfied nor dissatisfied (0) Dissatisfied (0) Very dissatisfied (0)	It is nice to be instructed and pressured when you are challenged to complete an exercise. I find this very motivating, and it gives me courage. (P1)  I experience a difference in each physiotherapist. They give something different separately; some are good at instructing, and some are good at motivating/ pushing to complete the exercises. It just makes it more fun. And we know what it will be like when we know which physiotherapist is the day's coach. (P1)  It's nice to have a coach present. They encouraged and pushed me a little when I felt hard during the training. Then, I could move on when it got hard instead of giving up if I was alone. (P2)

explore offering tailored training approaches for each diabetes subtype. Another crucial aspect is tailoring the intervention to fit participants' everyday life such as daily routines. While the timing worked well for MODY participants, it was not as optimal for those with T2D, potentially contributing to the attendance discrepancy. It appears that MODY may indeed have a more important impact on HRQoL. This could be linked to the perception of improvement resulting from active intervention, potentially reinforcing participation.

We observed a lower RPE among MODY participants compared to those with T2D, potentially attributable to factors such as younger age, lower obesity rates, or higher functional capacity [40]. Consequently, it may be beneficial to consider alternative exercises and potentially increase resistance for individuals with MODY.

In our study a standard intervention with a conventional training design was used. We would have expected that qualitative findings in our study would highlight the necessity for cultural adaptation, such as a preference for outdoor settings like nature. However, none of the qualitative interview results indicated that cultural adaptation of the training intervention would have influenced adherence. When discussing interventions in a country inhabited by Indigenous people, cultural adaptation is crucial to consider [41].

As an example, Hopkins et al. [42] culturally adapted an evidence-based intervention to promote a healthy diet and lifestyle for Yup'ik Alaska Native communities.

The Greenlandic population maintains close ties with nature, relying on it for lifestyle and recreational activities, making it an integral part of daily life. Research indicates that nature plays a fundamental role in the Greenlandic perception of a fulfilling life, and lack of regular contact with nature can have adverse effects [43]. The limited number of interviews in our study, with only two participants, raises concerns about the depth and comprehensiveness of our qualitative data, suggesting that data saturation may not have been achieved. As a feasibility study utilising both qualitative and quantitative methods, our findings might have been more robust had we focused solely on qualitative interviews, potentially providing clearer insights into the need for cultural adaptation. Hence, future studies might delve more deeply into the qualitative aspects of interventions similar to the one in our study. Another consideration is the study's location in the capital, Nuuk. Different responses might have been anticipated had the study been conducted in a small village in Northern or Eastern Greenland.

Another unique aspect of Greenland is the scattered population, with many living in isolation and lacking

Table 3. Secondary outcomes on cardiovascular disease risk factors and self-reported.

		(0 = 0) INI			(6 = u) NOO		
	Baseline	Follow-up	Within group dif.	Baseline	Follow-up	Within group dif.	Between group dif.
Aerobe fitness (kg/min/O <sub>2</sub> )	30.2 (12.1)	32.1 (13.5)	1.9 (-4.8; 8.5)	34.1 (5.3)	35.1 (5.1)	1.0 (0.1; 1.9)	6:0
Anthropometrics	1						•
Weight (kg)	74.4 (15.4)	75.1 (14.4)	0.7 (-1.3; 2.7)	86.9 (24.4)	86.0 (25.4)	-0.9 (-3.4; 0.8)	2.0
BMI (kg/m²)	27.9 (6.0)	28 (5.5)	0.1 (-0.6; 0.7)	29.5 (7.9)	29.6 (8.0)	0.5 (-1.2; 0.2)	9.0
Fat percent (%)	31.5 (10.3)	32.2 (10.5)	0.7 (-1.2; 1.7)	31.5 (12.2)	32 (12.1)	0.6 (-1.3; 2.4)	-0.3
Fat mass (kg)	24.4 (12.9)	25.1 (13.1)	0.1 (-1.1; 1.4)	29.2 (18.5)	29.3 (17.6)	0.1 (-2; 2.3)	0.0
Muscle mass (kg)	47.5 (6.6)	47.5 (6.9)	0.0 (-1.5; 1.6)	55.2 (14.2)	53.8 (13.3)	-1.4 (-2.6; -0.2)	1.4
Bone mineral density (kg)	2.5 (0.3)	2.6 (0.3)	0.1 (0.0; 0.1)	2.9 (0.7)	2.8 (0.6)	-0.1 (-0.1; 0.0)	0.1
Blood pressure							
Systolic (mmHg)	134.8 (23.0)	133.3 (13.2)	-1.5 (-13.1; 10.2)	129.7 (10.9)	130.9 (11.1)	1.2 (-6.5; 9.0)	-2.7
Diastolic (mmHg)	77.2 (10.6)	74.1 (6.7)	-3.0 (-11.6; 5.6)	80.2 (9.4)	77.2 (7.3)	-3.0 (-10.1; 4.1)	0.0
Glycemic control							
HbA <sub>1c</sub> (mmol/mol)	51.7 (10.9)	51.7 (7.3)	0.0 (-4.0; 4.0)	59.9 (24.3)	56.5 (20.9)	-3.4 (-10.5; -0.5)	5.5
Lipid control							
HDL cholesterol (mmol/l)	1.5 (0.4)	1.3 (0.4)	-0.2 (-0.2; 0.0)	1.1 (0.3)	1.3 (0.3)	0.2 (-0.3; 0.0)	-0.3
LDL cholesterol (mmol/l)	2.3 (0.7)	2.6 (0.8)	0.3 (-0.1; 0.8)	2.1 (0.7)	2.4 (0.9)	0.3 (-0.1; 1.0)	-0.1
Total cholesterol (mmol/I)	4.1 (0.97)	3.7 (0.7)	-0.4 (-0.6; 0.2)	3.6 (0.9)	3.9 (0.8)	0.3 (-0.1; 0.6)	-0.5
Triglycerides (mmol/I)	1.3 (0.5)	1.3 (0.4)	0.0 (-0.4; 0.4)	2.0 (1.1)	1.5 (0.9)	-0.5 (-1; 0.1)	0.5
Self-rated QoL (SF-12)							
PCS	42.3 (-7.7)	44.2 (-5.9)	1.9 (-9.8; 5.9)	46.7 (-3.0)	48.7 (-1.3)	1.7 (-7.1; 3.7)	-0.2
MCS	49.9 (-0.1)	55.6 (5.6)	5.7 (-11; 0.4)	51.1 (1.1)	50.7 (0.7)	-0.4 (-7.4; 8.3)	6.2

Data is mean (SD).
BMI: body mass index, HbA1c: haemoglobin A1c, HDL: high density lipoprotein, LDL: low density lipoprotein, PCS: physical score, MCS: mental score, QoL: quality of life.



access to physiotherapy services. Hence, providing a training intervention similar to the one in our study to the entire Greenlandic population will pose challenges. Thus, exploring the incorporation of online platforms and telemedicine into the intervention, either in whole or part, must be considered.

In a 2023 RCT, Blioumpa et al. evaluated the effects of a six-week telerehabilitation programme that included a supervised, individualised exercise regimen combining aerobic and resistance exercises, conducted online three times per week. Their structured and supervised approach, particularly via telehealth, appears effective in improving glycaemic control (HbA1c), functional capacity (6MWT), muscle strength, and quality of life in T2D patients compared to the control group [45]. Despite a lower frequency of exercise sessions, using telerehabilitation or online conferencing in our study may have improved outcomes by enhancing adherence and providing more comprehensive support. These factors might have made the twiceweekly sessions as effective, or even more effective, than the thrice-weekly sessions.

#### CVD risk factors

Overall, there was no improvement in CVD risk factors following the intervention. With a 56% attendance rate, participants averaged only one weekly appearance, possibly too low to affect CVD factors. Additionally, volume and intensity might have been too low in our study. The perceived intensity in our study might have been less effective for individuals new to exercise. If they find the intensity harder than it actually is, the intervention's impact will be limited. As increased exercise intensity might reduce compliance with supervised exercise programmes [44], it is necessary to consider whether objective measures such as pulse could help align RPE with the actual intensity.

A systematic review [9] found that supervised aerobic, resistance, and combined training significantly improved glycaemic control in individuals with T2D. The study emphasises the importance of exercise volume, especially frequency in aerobic training and volume of resistance exercises in combined training, in managing blood glucose levels. Additionally, adding resistance exercises to aerobic training further improves HbA1c levels.

Supporting this idea, findings from an RCT that compared aerobic, resistance, and combined training highlight the significance of exercise volume in reducing HbA1c levels following combined training programmes, indicating that the volume of training is crucial for a dose-response relationship [46]. Comparing our results reinforces the importance of recommending more frequent exercise sessions for individuals with T2D [47]. Another aspect to consider is whether participants, who might already be on high doses of medication, experience a ceiling effect, whereby additional exercise yields no further benefits [48]. Nonetheless, the results indicate that MODY exhibits poorer regulation of blood glucose levels compared to T2D. It raises questions about whether exercise should be tailored to each type, given the differences in diabetes complications.

We observed an increase in LDL cholesterol, which leaves some doubt as to whether irregularities in the laboratory are responsible for some of the findings.

## Mental health

Mental health, as measured by MCS, notably was associated with a 6.2 between-group difference in favour of the intervention group, representing a novel finding. Previous studies on physical exercise and self-assessed health among individuals with T2D typically show a reverse pattern on MCS and PCS. For instance, Myers et al.. (2013) explored the impact of self-assessed health following a nine-month intervention involving aerobic, strength, and combined exercise groups. They discovered that the combined exercise group exhibited stronger association in MCS compared to the aerobic exercise group [49]. Additionally, they found that aerobic exercise influenced MCS, while strength training impacted PCS. Considering the weight between training modalities in combined training relies on the effect on Health-Related Quality of Life (HRQoL), and given that our intervention lacked additional intensity calculated for strength training - instead opting for timebased rather than sets and repetitions - it is plausible that aerobic training had a more pronounced effect. This effect was likely predetermined by intensity using the Borg Scale. Furthermore, the results suggest a correlation with attendance, as higher attendance correlated with greater improvement.

## **Strengths and limitations**

This study has several strengths. Firstly, it demonstrates strong transferability as both men and women across a wide age range participated, ensuring broad representation. In addition, the transferability of exercise was seen against the similarities in responses in the diabetes types included, which is why both can be adapted to the same training modality. Secondly, the study exhibited excellent retention rates with no dropouts recorded. No participants were excluded due to low

attendance, which could have lowered the dropout rate. Thirdly, having enough participants with MODY to complete a training study is a significant strength.

The study also has important limitations. Firstly, recruitment occurred during August, a time of heightened travel activity and favourable weather conditions in Greenland, potentially leading to a lower recruitment rate. Additionally, pending MODY genetic test results during the recruitment phase posed a challenge in securing more participants, prompting the decision to match with T2D patients instead. Secondly, the lack of blinding and randomisation among participants meant that prior to the trial, participants were aware of which group they would be assigned to, potentially influencing their expectations of the training's efficacy.

The participants' expectations are uncertain, potentially introducing bias that could have impacted the results [50]. Confounding variables may have played a role. For example, unmet expectations might have led to demotivation, potentially contributing to the observed low adherence. Conversely, participants might have been overly enthusiastic about training, resulting in them exceeding the prescribed regimen.

Thirdly, the study's small sample size resulted in low statistical power. Participant representation varied considerably across gender, age, training status, and medical profiles within both groups, leading to wide confidence intervals around group differences (see Table 2). Fourthly, individualisation in training sessions was not documented, potentially resulting in exercise under- or over-dosing for some participants due to the absence of intensity dosing based on estimated individual HRmax. Fifthly, the study relied on a non-validated questionnaire, introducing the possibility of bias. To mitigate this, accompanying interviews were conducted to support the questionnaire results. Finally, due to the lack of a Greenlandic algorithm for SF-12 score estimation, a calculation method based on US population data was employed, as recommended for countries lacking country-specific scoring methods [51]. Additionally, participants in our study exhibited high baseline HRQoL, which could have limited our ability to detect improvements in mental health [49,52].

## **Conclusion and perspectives**

In conclusion, this study has shown that a standard training intervention as part of diabetes treatment within the clinical setting in Greenland is not presently feasible. We observed general challenges related to participant recruitment, adherence, and exercise training design, all of which must be addressed before supervised training can be considered viable in clinical practice. Prior to implementation in a clinical context, the next crucial step entails its transferability across various cities in Greenland and measuring the interventions' effectiveness.

## Implications for clinical practice

We discovered a difference in attendance rates between MODY and T2D patients, suggesting a need for tailored offerings for each group. However, given the small population size, organising such offerings poses challenges.

Findings from this study will guide the development and creation of future training interventions for people with lifestyle diseases within Greenland's healthcare system.

Implications for research

Future research should focus on several key areas to build on the findings of this study. First, detailed investigations into how individuals with MODY respond to different types of exercise are needed to develop tailored exercise recommendations for this group. Second, larger and more diverse participant samples, including individuals from various regions of Greenland, should be included to enhance the generalisability of the results and assess potential geographic influences. Finally, extending the duration of exercise programmes beyond 12 weeks could provide a better understanding of the long-term effects on CVD risk factors and quality of life in both MODY and T2D populations.

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## Disclosure statement

No potential conflict of interest was reported by the author(s).

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### **Authors' contributions**

LM conceived the study idea in collaboration with MHN and MEJ. LM cleaned and analysed the data. LM and MRL drafted the first version of the manuscript. All authors reviewed and approved the final draft of the manuscript.

## Availability of data and materials

The data used in this research is not available to the public in order to protect the anonymity of all participants. Data may be made available upon reasonable request from the corresponding author.



## **Ethical considerations**

The study was initiated after approval from the Scientific Ethics Committee (notification number: KVUG 2022–21 date: 11 August 2022) and approval from the Health Management of SHV (date: 9 September 2022). All participants provided written informed consent to participate in the study and for the results to be used for the research. All patients were informed of the risks and management of hypoglycaemia. All data were handled anonymously. In addition, the study was conducted in accordance with the Helsinki Declaration II [53] and followed the Data Protection Authority's guidelines for compliance to Greenlandic data legislation [54].

## **Consent for publication**

Written informed consent for publication of the personal data was obtained from all the participants.

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Appendix 1. Secondary outcomes on cardiovascular disease risk factors and self-reported stratified by diabetes types

		T2D Intervention $(n=5)$	: 5)		MODY	MODY Intervention $(n = 4)$	
	Baseline	Follow-up	Within group dif.	Baseline	Follow-up	Within group dif.	Between group dif.
Kondital (kg/min/O <sub>2</sub> )	26.8 (5.5)	33.4 (13.5)	6.6 (–5.8; 19)	34.5 (17.5)	32.3 (15.5)	-2.2 (-9.3; 4.8)	8.9
Anthropometrics							
Weight (kg)	77.4 (18.8)	77.5 (17.5)	0.1 (-3.5; 3.8)	70.8 (11.1)	72.1 (11.2)	1.3 (-2.4; 5.1)	1.2
BMI (kg/m²)	29.5 (6.6)	29.4 [6]	-0.1 (-1.2; 1.1)	25.9 (5.2)	26.1 (4.9)	0.2 (-1; 1.4)	0.3
Fat percent (%)	34.4 [11]	35.3 (9.5)	0.9 (-2.5; 4.3)	27.9 (9.5)	28.3 [10]	0.3 (-1.1; 1.8)	0.1
Fat mass (kg)	27.6 (15.3)	28.9 (13.8)	1.3 (-3.6; 6.2)	20.4 (9.5)	20.9 (9.8)	0.5 (-1; 1.9)	0.8
Muscle mass (kg)	47.3 (8.5)	48.1 (8.3)	0.9 (-3.8; 5.5)	47.8 (4.5)	48.6 (6.2)	0.8 (-2.6; 4.2)	0.1
Bone mineral density (kg)	2.5 (0.4)	2.6 (0.4)	0.1 (-0.1; 0.2)	2.5 (0.2)	2.6 (0.3)	0.1 (-0.1; 0.2)	0
Blood pressure							
Systolic (mmHg)	132.6 (18.6)	132.8 [10]	0.2 (-22.9; 23.3)	137.5 (16.4)	134 (18.1)	-3.5 (-22.3; 15.3)	3.7
Diastolic (mmHg)	79.2 (14.6)	77.2 (7.1)	-2 (-20.5; 16.5)	74.5 (6.0)	70.3 (3.9)	-4.3 (-13.6; 5)	-2.3
Glycemic control							
HbA <sub>1c</sub> (mmol/mol)	55.2 (13.6)	53.6 (8.2)	-1.6 (-9.9; 6.7)	47.3 (4.8)	49.3 (6.1)	2 (-1; 4.9)	3.6
Lipid control							
HDL cholesterol (mmol/l)	1.4 (0.5)	1.4 (0.5)	0 (0; 0)	1.5 (0.3)	1.3 (0.3)	-0.2 (-0.5; 0)	0.2
LDL cholesterol (mmol/l)	2.4 (0.6)	2.6 (0.5)	0.2 (-0.6; 1)	1.9 (0.9)	2.5 (1.1)	0.6 (-0.2; 1.3)	0.3
Total cholesterol (mmol/l)	4.1 (1.2)	3.8 (0.6)	-0.2 (-1; 0.5)	3.8 [1]	3.6 (0.9)	-0.2 (-1.1; 0.7)	0
Triglycerides (mmol/I) Self-rated QoL (SF-12)	1.4 (0.5)	1.5 (0.2)	0 (-0.6; 0.7)	1.1 (0.4)	1.0 (0.5)	-0.1 (-1; 0.8)	0.1
PCS	38.8 (-11.2)	40 (-10)	1.2 (-15.0; 12.6)	46.7 (-3.3)	49.5 (-0.7)	2.9 (-16.2; 10.5)	1.7
MCS	50.9 (0.9)	55.8 (5.8)	4.9 (-13.4; 3.6)	48.6 (-1.4)	55.3 (5.3)	6.8 (-17.6; 4.1)	1.9

Data is average (SD). BMI: body mass index, HbA1c: haemoglobin A1c, HDL: high density lipoprotein, LDL: low density lipoprotein, PCS: physical score, MCS: mental score, QoL: quality of life.