METABOLISM CLINICAL AND EXPERIMENTAL 66 (2017) 1–13

Available online at www.sciencedirect.com

Metabolism

www.metabolismjournal.com

Clinical Science

Effects of a culturally adapted lifestyle intervention on cardio-metabolic outcomes: a randomized controlled trial in Iraqi immigrants to Sweden at high risk for Type 2 diabetes☆

Faiza Siddiqui[a], *Azra Kurbasic*[b], *Ulf Lindblad*[c], *Peter M. Nilsson*[a], *Louise Bennet*[a,d,*]

[a] *Department of Clinical Sciences, Lund University, Malmö, Sweden*
[b] *Genetic and molecular epidemiology unit, Lund University, Malmö, Sweden*
[c] *Department of Community Medicine/Primary Health Care, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden*
[d] *Center for Primary Health Care Research, Region Skåne and Lund University, Malmö, Sweden*

ARTICLE INFO

Article history:
Received 5 April 2016
Accepted 2 October 2016

Keywords:
Body weight
Immigrants
Insulin sensitivity
Lifestyle
Randomized controlled trial

ABSTRACT

Background and Aims. Middle-Eastern immigrants constitute a growing proportion of the Swedish population and are at high risk for Type 2 diabetes. This calls for a more proactive preventive approach for dealing with diabetes risk in this target group. The aim was to test the effect of a culturally adapted lifestyle intervention programme on changes in lifestyle habits and cardio-metabolic outcomes comparing an intervention group with a control group receiving usual care.

Methods. Citizens of Malmö, Sweden born in Iraq and at high risk for Type 2 diabetes ($n = 636$) were invited. Participation rate was 15.1%. In all, 96 participants were randomized to the intervention group ($n = 50$) or to the control group ($n = 46$). The intervention group was offered seven group sessions addressing healthy diet and physical activity including one cooking class. Changes in body weight, physical activity levels and cardio-metabolic outcomes were evaluated using linear mixed-effects models.

Results. The mean follow-up time was 3.9 and 3.5 months in the intervention and control groups, respectively. The drop-out rate from baseline to the last visit was 30.0% in the intervention group ($n = 15$) and 30.4% in the control group ($n = 14$).
The mean insulin sensitivity index increased significantly at follow-up in the intervention group compared to the control group (10.9% per month, $p = 0.005$). The intervention group also reached a significant reduction in body weight (0.4% per month, $p = 0.004$), body mass index (0.4% per month, $p = 0.004$) and LDL-cholesterol (2.1% per month, $p = 0.036$) compared to the control group. In total, 14.3% in the intervention group reached the goal to lose ≥5% of body weight versus none in the control group.

Abbreviations: BMI, body mass index; DI, disposition index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; ISI, insulin sensitivity index; IPAQ, international physical activity questionnaire; MEDIM, impact of migration and ethnicity on diabetes in Malmö; MET, metabolic equivalent of task; OGTT, oral glucose tolerance test; PA, physical activity; PHC, primary health care; RCT, randomized control trial; SBP, systolic blood pressure; US, United States.

☆ Trial registration number: NCT01420198.

* *Corresponding author at:* Department of Clinical Sciences, Family Medicine, building 28, floor 11, Jan Waldenströms gata 35, Skåne University Hospital, 205 02 Malmö, Sweden.
E-mail address: Louise.bennet@med.lu.se (L. Bennet).

http://dx.doi.org/10.1016/j.metabol.2016.10.001

Conclusions. This culturally adapted lifestyle intervention programme shows a beneficial effect on insulin action, body weight reduction, as well as LDL-cholesterol reduction, in Middle-Eastern immigrants. The programme adapted to resources in primary health care provides tools for improved primary prevention and reduced cardio-metabolic risk in this high-risk group for Type 2 diabetes.

1. Introduction

Middle-Eastern immigrants constitute a growing proportion of the Swedish population, with Iraqi immigrants representing the largest non-European group [1]. Malmö, the third largest city in Sweden, has a growing immigrant population with at present approximately 11,000 Iraqi immigrants [1]. The MEDIM study ("impact of Migration and Ethnicity on Diabetes In Malmö"), conducted 2010 to 2012 among Iraqi immigrants, has shown that their prevalence of Type 2 diabetes is twice as high as compared to the native Swedish population (11.6% vs. 5.8%, $p < 0.001$), matched for age and sex [2].

Large randomized clinical trials based on lifestyle intervention such as the Diabetes Prevention Program in the United States (US) and the Finnish Diabetes Prevention Study have shown the efficacy of dietary modification and physical activity (PA) in delaying or preventing the onset of Type 2 diabetes [3,4]. However it is unlikely that these interventions will yield equivalent results in populations of different cultures in terms of dietary and PA habits, perception and experience of barriers, behavioral change and supporting factors [5–7]. Earlier studies have indicated that in order to be effective, lifestyle interventions in non-Western groups should focus on behavioral change through increased self-efficacy and self-empowerment [8]. In addition, a gender-specific approach should be applied and differences in PA preferences should be considered [8,9].

The high prevalence of diabetes and its risk factors in Middle-Eastern immigrants [10], calls for an even more proactive approach for dealing with diabetes risk in this high-risk group, than is currently the case in Swedish primary health care (PHC) or the community at large. However there is a scarcity of information on culturally adapted lifestyle interventions, particularly from randomized control trials (RCT) addressing non-western immigrants in the developed world [7,11].

The *aim* of this project, based on a RCT design, was to test the efficacy of a culturally adapted lifestyle intervention programme developed to address healthy diet and PA habits in Iraqi immigrants living in Sweden. Specific aims were to examine changes in body weight and PA levels as well as cardio-metabolic outcomes in the intervention group participating in the programme, and to compare these with changes in the control group receiving usual care.

2. Material and Methods

2.1. *Study Population*

Citizens of Malmö born in Iraq, aged 30–75 years and at high-risk of Type 2 diabetes were invited by post between October and December 2014 followed by a telephone contact, to participate in the MEDIM intervention study. The eligible study population was identified from the MEDIM population-based study, a cross-sectional study conducted between 2010 and 2012 including 1398 Iraqi-born and 757 Swedish born residents of Malmo matched for age and sex and residing in the same neighborhood [2]. 'At high-risk' was defined as having a body mass index (BMI) ≥28 kg/m^2 and/or waist circumference (≥80 cm in women and ≥94 cm in men) [12] and/or pre-diabetes i.e. impaired fasting plasma glucose ((FPG): 6.1–6.9 mmol/l and 2-h glucose <7.8 mmol/l), impaired glucose tolerance (FPG <6.1 mmol/l and 2-h glucose: 7.8–11 mmol/l) or impaired glucose regulation (FPG: 6.1–6.9 mmol/l and 2-h glucose: 7.8–11 mmol/l) [10], individuals with overt diabetes (FPG: ≥7 mmol/l or 2-h glucose: ≥11.1 mmol/l), mental incapacity to engage in the study, physical impairments limiting PA, or those who were pregnant were not eligible for participation in the intervention study. Of 636 individuals invited, 104 accepted to participate and attended the first visit and of these, 96 were eligible for participation in the study (corresponding to a participation rate of 15.1%). Fig. 1 shows a flow chart of study participants.

2.2. *Data Collection*

The study took place between mid-January and mid-June 2015 and was designed to include three health examinations. Each health examination comprised a physical examination, collection of fasting blood samples and oral glucose tolerance tests (OGTT; 75 g glucose) by trained study nurses speaking the participants' native language [10]. The study was conducted at a facility located close to the PHC centre and easily accessible to the participants.

Body weight was measured using an electronic scale while participants were requested to remove shoes and wear light clothing. A wall-mounted stadio-meter was used to measure height. Blood pressure was calculated as a mean of two readings taken 1 minute apart with the participant lying in supine position. The participants rested for 5 minutes before the readings were taken [10]. Radioimmunoassay (Access© Ultrasensitive Insulin, Beckman Coulter, USA) and high pressure liquid chromatography (Bio-Rad) were used to estimate serum insulin levels and HbA_{1C} respectively [13]. A HemoCue photometer (HemoCue AB, Ängelholm, Sweden) was used to measure plasma glucose levels [10,13]. Enzymatic methods were used to estimate plasma HDL-cholesterol (Boehringer Mannheim GmbH, Germany) and triglyceride levels (Bayer Diagnostics) [14] whereas Friedewald's equation was used to estimate plasma LDL-cholesterol levels [15].

The participants were also requested to fill in a four-day food diary in connection with the three health examinations. In the food diaries, participants indicated the type, frequency and quantity as well as cooking method and preparation of

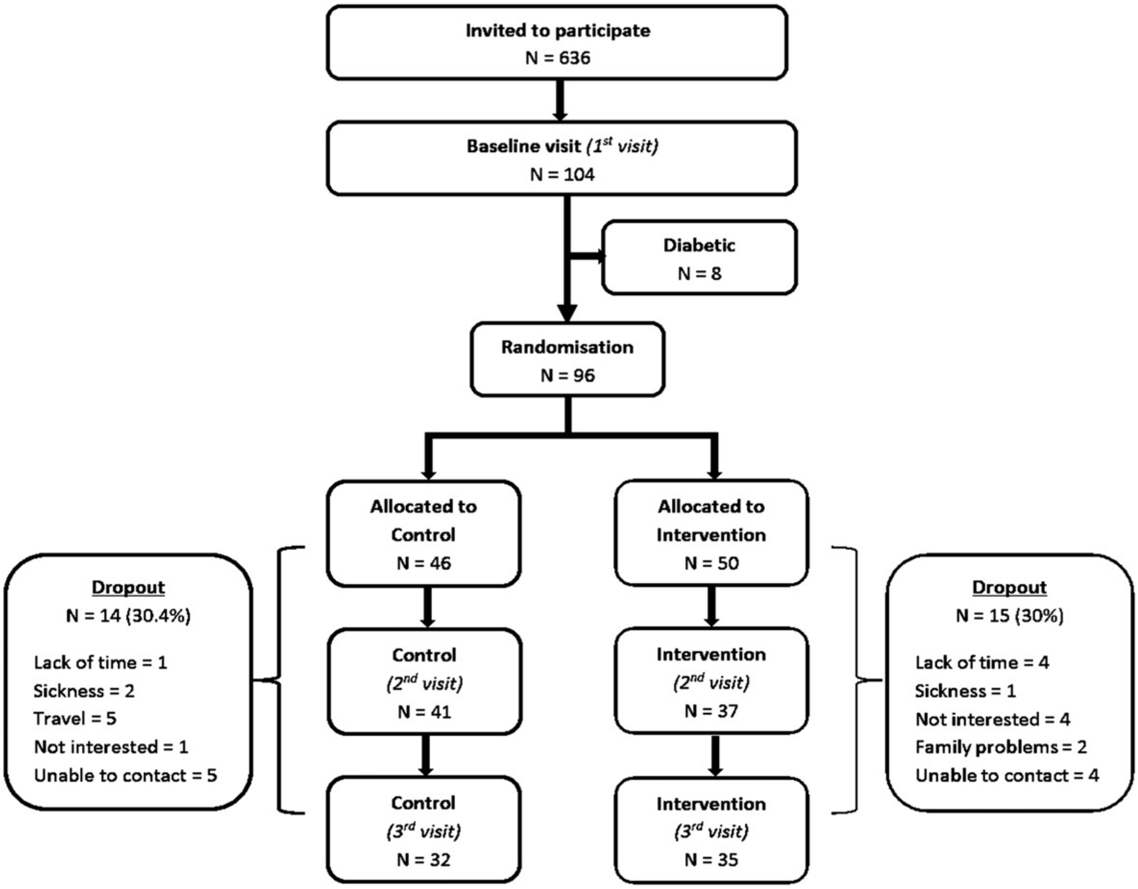

Fig. 1 – Flow chart of study participants.

foods and drinks consumed during those four days. The dietary data was then processed using the Dietist XP software version 3.2 [16] to obtain mean caloric intake at the start, mid and end of the study.

2.3. Randomisation

Following the first health examination, participants were randomized either to the control or to the intervention group with a 1:1 allocation ratio using a random number generator in the statistical software SPSS. Men and women were randomized separately however couples were randomized into the same group (intervention or control) to avoid information overflow between the groups. Randomisation was not stratified by age, pre-diabetes or FINDRISC score as mentioned in the study protocol [10], because of a lower than expected participation rate (15.1% vs. expected 60%). The expected participation rate was derived from an earlier study in Middle-Eastern immigrants [9]. Nurses performing the health examinations were not informed or aware of the participants' assignment to the control or the intervention group.

2.4. Outcomes

Our study goals were modified from those in the Finish Diabetes Prevention Study and Diabetes Prevention Program with lifestyle change as primary outcome and improvement in cardio-metabolic biomarkers as secondary outcome. The primary outcomes were defined as reduction in body weight by at least 5%, achieving moderate-intensity PA of at least 30 min per day five days a week and reduction in mean caloric intake. Secondary outcomes, were reduction in cardio-metabolic biomarkers such as FPG, 2-h glucose, HbA_{1C}, systolic blood pressure (SBP), diastolic blood pressure (DBP), plasma triglycerides and LDL-cholesterol. Further secondary outcomes included increase in insulin sensitivity index (ISI), disposition index (DI) and/or HDL-cholesterol.

2.5. Intervention

This intervention was culturally modified from the Diabetes Prevention Program intervention in that it included components such as gender-specific groups led by Arabic speaking health coaches with experience and knowledge of the Middle-Eastern lifestyle, culture and food habits and with experience in patient education and counseling. Further the cultural adaptation included identification of social and cultural barriers to lifestyle change, cooking classes and economic support for training clothes and admittance to the local PA centers.

The intervention group was invited to participate in seven group sessions including one cooking class, with intervals of 1–4 weeks, over the duration of 4 months. The group sessions addressed self-empowerment with special emphasis on cultural and social barriers and negative perceptions of lifestyle change. During the group sessions participants were encouraged to be more physically active in their daily life and to develop goals to overcome the barriers to performing routine PA. In addition, the focus was to increase knowledge of Type 2 diabetes and cardiovascular diseases and to educate participants regarding the effect of healthy lifestyle habits on diabetes and cardiovascular disease risk. The group sessions' content as outlined in Table 1 was based on the evidence-based guidelines for the prevention of Type 2 diabetes [17], but further developed by addressing culture and socioeconomic barriers as described above. A professional Arabic translator was present on all occasions. Prior to the intervention, a step-counter with written advice on achieving 10,000 steps per day was sent out to the participants in the intervention group along with the invitation. However, the step-counters were not used as a measure of PA in the study but only used as an indicator that the daily PA goal was reached or not and thus as a motivator for PA.

The control group was provided with 'treatment as usual', i.e. they were informed that increasing their PA levels and adopting healthy eating habits by cutting down on intake of sweets and fats will reduce their risk of diabetes and cardiovascular diseases. The written advice was sent out three times; at the start, mid and end of the study along with the health examination results.

Follow-up: After the health investigations the participants were informed of their health examination results. Participants with abnormal values for blood pressure (SBP ≥140 mmHg and/or DBP ≥90 mmHg) and/or two blood glucose values in the diabetic range (FPG ≥7 mmol/l and/or 2-h glucose ≥11.1 mmol/l) were referred to their PHC centre for follow-up.

2.6. Definitions

Age was calculated as the difference between the date of first examination and the birth date.

BMI was calculated as the ratio of body weight (kg) to squared height (m^2).

PA was self-reported by the participants using the 'International Physical Activity short form Questionnaire' (IPAQ) [18]. The total PA was reported as 'metabolic equivalent of task' (MET) hours/week where MET referred to the energy expenditure of vigorous and moderate-intensity PA as well as walking. MET-hours/week were calculated by multiplying the

Table 1 – Outline of the group sessions in the intervention group.

Sessions and their Aim(s)	Sessions' description (duration of each session: 1.5 h)
Session 1: Awareness	• Healthy and unhealthy life style habits and diabetes and cardiovascular disease risk. • Dietary and physical activity guidelines. • Introduction to the keyhole products. • Introduction to the plate model by the Swedish National food agency.
Session 2: Motivation/Getting started	• Discussion of the participants' lifestyle habits. • Introduction to the action plan. • Goal setting using the action plan (SMART goals). How to incorporate SMART goals into daily life.
Session 3: Maintaining the change/reduce the risk of relapse	• Discussion on the barriers to lifestyle change. • How to handle negative thoughts. • Discussion on common cooking methods for Iraqi food and how to make them less fatty. • Cultural barriers to the physical activity in women. • Information on locally available physical activity facilities such as women only swimming halls and gyms as well as facilities for the men.
Session 4: Social support and lifestyle change	• Discussion on social support. • Review the progress of lifestyle change. • How to overcome the barriers to physical activity. • Healthy eating at social events. • Drinks and their sugar content. • Sugar content in common snacks such as French fries and crisps.
Session 5: Maintaining the change	• How to maintain behavioral change. • Discussion on time management to incorporate physical activity in daily life. • Eating in the month of Ramadan with discussion on nutritional content of dates and honey.
Session 6: Review and feedback	• The importance of maintaining lifestyle change. • Revision of the earlier sessions. • Feedback from the participants.
Cooking Class	• Participants brought their favorite recipes and a chef with experience in preparing a diabetes friendly diet cooked Iraqi foods in a healthier way along with the participants.
Cultural Adaptations	• Separate sessions for men and women. • Groups led by a health coach and nurse with experience of Middle Eastern culture and lifestyle. • Discussion of cultural barriers to physical activity in the women e.g. Hesitancy to share physical activity facilities with men and fear of exclusion from the neighborhood if they perform outdoor physical activity. • Addressing the knowledge gaps and barriers e.g. Does being overweight increase my risk of diabetes? Fear of "heart beating fast" during physical activity. • Economic support to get admittance to physical activity centers and buy clothes and shoes for physical activity.

time spent in performing the activities during the week with MET values of the activities i.e. vigorous-PA (8.0 METs), moderate-PA (4.0 METs) and walking (3.3 METs) [19].

Family history of diabetes was self-reported by the participants as presence of diabetes in biological parents, siblings and/or children.

Education was categorized as less than high school (<12 years), or high school and above.

ISI and *DI* were calculated from the OGTT results using the following formulas [20].

$$\mathrm{ISI} = 10,000/\surd[(\mathrm{FPG}\ (\mathrm{mmol/l}) * \mathrm{fasting\ insulin}\ (\mathrm{mIE/l})\ ) \\ *(\mathrm{mean\ OGTT\ glucose\ conc}\ (\mathrm{mmol/l}) \\ *\mathrm{mean\ OGTT\ insulin\ conc}\ (\mathrm{mIE/l}))]$$

Corrected Insulin response (CIR) was calculated using the formula mentioned below with the pre-requisite that glucose levels at 30 min should be more than 4.44 mmol/l and higher than the fasting glucose level.

$$CIR = (100 * insulin\ at\ 30\ min(\frac{mIE}{l}))/(glucose\ at\ 30\ min\left(\frac{mmol}{l}\right) \\ *(glucose\ at\ 30\ min\left(\frac{mmol}{l}\right) - 3.89)).$$

DI which refers to an estimation of insulin secretion adjusted for insulin resistance was calculated as a product of CIR and ISI.

2.7. Statistical Analysis

Statistical analyses were performed using IBM SPSS version 21.0 and SAS version 9.3 (SAS Institute Inc., NC, USA). Firstly, differences at baseline between the two groups were compared using an independent sample t-test for normally distributed or Mann–Whitney *U* test for non-normally distributed continuous variables, and chi-square test or Fisher's-exact test for categorical variables (Table 2). Secondly, descriptive changes over time in the outcomes were reported (Table 3).

Thirdly, the effect of the intervention was studied using linear mixed-effects model analysis [21] (Table 4, Crude model). Only individuals with data available for at least two time points (i.e. health examinations) were included in the analysis. The outcome variables were natural log-transformed ($\log_e$), since some variables showed skewed distribution. In the crude model, "group-status", "time since baseline visit in months" and the interaction term "group-status" × "time since baseline visit" were included. The interaction term indicated if there was a difference in the trajectory of change over time between two groups i.e. estimates from the model (β-coefficients) indicated percentage change in outcome variables for a unit increase in time, when all other variables were kept constant. The percentage change was calculated using the formula 100*(expβ -1). Finally, the model was extended and adjusted for the covariates age, sex, BMI, family history of diabetes, PA and education. Levels of SBP and DBP were adjusted for anti-hypertensive drug use. No individuals included in the analysis were using lipid-lowering drugs (Table 4, Extended model).

Crude and extended models (Table 4) allowing for random-effects were fitted for the outcomes with enough variation in the data. Linear fixed-effects models were fitted to all phenotypes and a simple compound symmetry covariance structure was used which assumes a constant correlation between observations of the same participant. Since the results from the models with random-effects and fixed-effects were essentially the same, the results from the models with fixed-effects only, are presented. The significance level was set at $p \leq 0.05$ and no adjustment for the multiple testing was done.

Because of the low participation rate, drop-out and missing data, in this study we used the linear mixed-model approach, thus the initial power calculation presented in the study protocol [10] that was based on a previous study in Middle Eastern immigrants [9] was no longer relevant. Although the sample size may be underpowered, *post-hoc* power calculations are not informative with regard to the conclusions of the present study [22].

2.8. Ethics

All participants gave written informed consent before participation in the study. The Ethical Review Board of Lund University, Sweden approved the study (approval no. 2011/88).

3. Results

Out of the initial 104 participants, 8 (7.7%) were diagnosed with diabetes on the first visit and were excluded from the study. The remaining 96 participants were randomized to the intervention (N = 50) or to the control group (N = 46). The two groups were similar in terms of age and sex distribution. At baseline, the intervention group appeared to have slightly higher body weight, BMI and waist circumference as well as lower ISI compared to the control group; however these differences were not statistically significant (Table 2). Except for a significantly higher educational level, lower triglyceride levels, and a lower proportion of moderately active individuals (accumulating 10 MET-hours/week) in the intervention group, no statistically significant differences were observed between the two groups (Table 2). The mean follow-up time was 3.9 and 3.5 months in the intervention and control groups respectively.

The descriptive changes over time in cardio-metabolic outcomes in the two groups are presented in Table 3. In the intervention group, the mean body weight decreased from 85.5 kg at baseline to 83.0 kg at the last visit and BMI decreased from 31.0 kg/m^2 to 30.4 kg/m^2. Similarly, the mean LDL-cholesterol levels decreased from 3.4 mmol/l to 3.1 mmol/l and the median ISI increased from a baseline value of 62.4 (mmol/L mIE/L)$^{-1}$ to 90.3 (mmol/L mIE/L)$^{-1}$ by the end of the intervention.

The predicted values of outcomes (based on estimates from the analysis) for individuals were plotted against the corresponding time passed since the baseline visit, with the last individual observed at 4.9 and 4.4 months for the control and the intervention groups, respectively. Fig. 2 represents predicted lines for changes in body weight in the intervention and the control groups over time. Fig. 3 shows the increase over time in predicted values for log-transformed ISI in the intervention group whereas a decrease over time is seen for the control group. The change over time in predicted values for log-transformed LDL-cholesterol levels in the two groups

Table 2 – Baseline characteristics of the participants in the intervention and the control groups.

Variables	Intervention n = 50	Control n = 46	p-value
Age (years)	47.9 (10.4)	48.9 (9.05)	0.63
Male sex, n (%)	23 (46)	22 (47.8)	1.00
Family history of diabetes in first degree relatives, n (%)	34 (68)	24 (52.2)	0.14
Education <HS[+], n (%)	7 (14)	16 (34.8)	0.03
Unemployment, n (%)	26 (52)	24 (52.2)	1.00
Smoking, n (%)	8 (16)	8 (17.4)	0.86
Physical activity(MET[++]-hours/week), median(IQR[+++])	8.5 (0–47.6)	12.4 (0–66.3)	0.32[*]
Moderately active[**], n (%)	18 (36)	26 (56.5)	0.05
Mean caloric intake (kcal)	1886.3 (619)	2052.3 (616)	0.21
Body weight (kg)	85.5 (15.2)	80.0 (13.1)	0.06
Body mass index (kg/m^2)	31.0 (4.4)	29.6 (3.6)	0.09
Waist circumference men (cm)	108.2 (9.6)	106.1 (8.9)	0.45
Waist circumference women (cm)	100.7 (8.1)	97.2 (8.1)	0.13
Abdominal height (cm)	22.7 (3)	22.5 (2.3)	0.75
Systolic blood pressure (mmHg)	121.6 (13.3)	126.9 (16.1)	0.08
Diastolic blood pressure (mm Hg)	77.6 (8.4)	79.7 (11.2)	0.30
Anti-hypertensives, n (%)	8 (16)	6 (13)	0.68
Fasting glucose (mmol/L)	5.6 (0.5)	5.4 (0.7)	0.25
2-h glucose (mmol/L)	6.6 (1.8)	6.5 (1.8)	0.87
HbA1$_C$ (mmol/mol)	34 (4.7)	35(4.4)	0.33
HbA1$_C$ in %	5.3% (0.4)	5.4% (0.4)	
0-h insulin (mIE/L)	11.6 (6.4)	9.9 (5.7)	0.20
2-h insulin (mIE/L)	77.6 (54.8)	70.7 (52.1)	0.55
Insulin sensitivity index[*] (mmol/L mIE/L)$^{-1}$, median (IQR)	62.4 (44.1–102.3)	73.3 (55.8–121.5)	0.13[*]
Disposition index (mmol/L mmol/L mmol/L), median (IQR)	11,128.0 (6248.3–19,080.9)	11,113.0 (7000.0–19,263.5)	0.90[*]
Triglycerides (mmol/L)	1.3 (0.5)	1.7 (0.8)	0.01
Lipid-lowering drugs, n (%)	1 (2)	0 (0)	1.00[∞]
LDL-cholesterol (mmol/L)	3.4 (0.7)	3.3 (0.9)	0.51
HDL-cholesterol (mmol/L)	1.3 (0.3)	1.3 (0.4)	0.97
Follow-up time (months)[***]	3.9 (0.3)	3.5 (0.4)	<0.001

Data presented as mean (standard deviation), numbers (percentages) or median (interquartile range). Differences between groups were compared using independent sample t-test for continuous variables and chi-square test for categorical variables.

[+] High school.

[++] Metabolic Equivalent of Task.

[+++] Interquartile range.

[*] Mann–Whitney U-test.

[∞] Fisher's exact test.

[**] Individuals accumulating 10 MET-hours/week.

[***] n = 32 for control, n = 35 for intervention.

is presented in Fig. 4. Fig. 5 represents the increase over time in predicted values for log-transformed PA in the two groups.

Statistical changes over time are presented in Table 4. A modest but statistically significant decrease of 0.4% per month in body weight (kg) as well as for BMI (kg/m^2) (β −0.004, 95% CI: −0.007 to −0.001) were recorded for the intervention group compared to the control group after adjustment for the covariates presented in Table 4. Five participants in the intervention group (14.3%) but none in the control group lost 5% or more of their body weight by the end of the intervention (p = 0.054).

Change over time in ISI was significantly higher in the intervention compared to the control group (Table 4, Crude model) and remained significantly higher even after adjusting for the confounding effect of other variables (Table 4, Extended Model) revealing a 10.9% increase in the mean ISI per month in the intervention group compared to the control group. In addition, BMI (β −0.032, 95% CI: −0.061 to −0.005), waist circumference (β −0.012, 95% CI: −0.023 to −0.0004), and PA (β 0.002, 95% CI: 0.001–0.002) were also significantly associated with the mean ISI. A slight decrease in ISI over time was observed in the control group, however the change was statistically non-significant. Among participants who lost 0.5 kg (representing 50th percentile for body weight changes) or more during the intervention, 44% exhibited no improvement in insulin sensitivity.

LDL-cholesterol decreased by 2.1% per month in the intervention compared to the control group. However, no difference in change over time in HDL-cholesterol and triglycerides were observed between two groups.

The proportion of individuals accumulating 10 MET-hours/week (equivalent to achieving 30 min of moderate-intensity PA on at least 5 days of the week) on the last visit was higher in the intervention group compared to the control group (85.7% vs 64.5%, p = 0.045). However, when change over time in PA (MET-hours/week) was analyzed, no statistically significant difference was seen between the intervention and the control groups (Table 4).

In terms of dietary changes, no significant change over time in mean caloric intake was observed in the intervention group compared to the control group.

Table 3 – Descriptive changes over time in outcomes in the intervention and the control groups.

Variables	Intervention			Control		
	Visit 1 (n = 50)	Visit 2 (n = 37)	Visit 3 (n = 35)	Visit 1 (n = 46)	Visit 2 (n = 41)	Visit 3 (n = 32)
Physical activity (MET[+]-hours/week), median (IQR[++])	8.5 (0–47.6)	65.8 (20.6–101.2)	62.6 (23.1–151.1)	12.4 (0–66.3)	27.1 (1.9–126)	24.0 (6.3–129)
Mean caloric intake (kcal)	1886.3 (619)	1740.4 (557.6)	1692.6 (553.8)	2052.3 (616)	2055.9 (568)	1941.3 (511.4)
Body weight (kg)	85.5 (15.2)	85.2 (15.6)	83.0 (15.0)	80.0 (13.1)	80.8 (12.8)	80.8 (13.8)
Body mass index (kg/m^2)	31.0 (4.4)	30.8 (4.5)	30.4 (4.3)	29.6 (3.6)	29.6 (3.6)	29.6 (3.7)
Waist circumference men (cm)	108.2 (9.6)	107.3 (10.0)	107.8 (7.6)	106.1 (8.8)	105.6 (8.3)	106.4 (9.9)
Waist circumference women (cm)	100.7 (8.1)	103.0 (10.6)	100.4 (10.3)	97.2 (8.1)	98.4 (9.3)	95.2 (7.3)
Abdominal height (cm)	22.7 (3.0)	23 (3.0)	22.3 (3.0)	22.5 (2.3)	22.5 (2.7)	22.2 (2.9)
Systolic blood pressure (mmHg)	121.6 (13.3)	118.8 (16.1)	117.3 (14.1)	126.9 (16.1)	120.1 (14.0)	119.6 (12.9)
Diastolic blood pressure (mm Hg)	77.6 (8.4)	76.3 (10.5)	75.8 (9.1)	79.7 (11.2)	77.2 (12.0)	76.5 (10.7)
Fasting glucose (mmol/L)	5.6 (0.5)	5.7 (0.5)	5.7 (0.4)	5.4 (0.7)	5.5 (0.6)	5.6 (0.6)
2-h glucose (mmol/L)	6.6 (1.8)	6.3 (1.5)	6.1 (1.7)	6.5 (1.8)	6.5 (2.3)	6.3 (1.8)
$HbA1_C$ (mmol/mol)	34.3(4.7)	34.1(4.7)	34.2 (4.3)	35.2 (4.4)	35.4 (4.9)	34.7 (5.1)
$HbA1_C$ in %	5.3%	5.3%	5.3%	5.4%	5.4%	5.3%
0-h insulin (mIE/L)	11.6 (6.4)	11 (6.2)	11.8 (6.0)	9.9 (5.7)	12.1 (7.2)	12.3 (5.6)
2-h insulin (mIE/L)	77.6 (54.8)	65.9 (55.1)	56.6 (67.2)	70.7 (52.0)	86.1 (66.5)	70.8 (53.0)
Insulin sensitivity index• (mmol/L mIE/L)$^{-1}$, median (IQR[++])	62.4 (44.1–102.3)	76.1 (49.6–116.4)	90.3 (60.4–126.6)	73.3 (55.8–121.5)	75.8 (42.9–121.1)	62.1 (43.4–116.8)
Disposition index (mmol/L mmol/L mmol/L), median (IQR[++])	11,128.0 (6248.3–19,080.9)	12,310.6 (6237.9–19,623.5)	12,882.7 (7639.0–15,797.5)	11,113.0 (7000.0–19,263.5)	11,732.4 (5148.5–18,523.8)	10,275.5 (6294.6–13,900.1)
Triglycerides (mmol/L)	1.3 (0.5)	1.2 (0.5)	1.1 (0.6)	1.7 (0.8)	1.5 (0.7)	1.5 (0.6)
LDL-cholesterol (mmol/L)	3.4 (0.7)	3.3 (0.7)	3.1 (0.7)	3.3 (0.9)	3.4 (0.8)	3.4 (0.8)
HDL-cholesterol (mmol/L)	1.3 (0.3)	1.3 (0.3)	1.3 (0.3)	1.3 (0.4)	1.2 (0.3)	1.3 (0.4)

Data presented as mean (standard deviation).
[+] Metabolic Equivalent of Task.
[++] Interquartile range.

Table 4 – Change over time in outcome variables ($\log_e$-transformed) in the intervention group compared to the control group. The β is a parameter estimate for the interaction term "group-status" × "time since baseline visit (months)". The analysis included all individuals with data available for at least two time points.

Outcomes	*Crude Model*			*Extended Model* [+]		
	β	*p*-value	Confidence interval	β	*p*-value	Confidence interval
Weight (kg) $n_c^* = 42$, $n_i^* = 40$	−0.004	0.006	−0.007 to −0.001	−0.004	0.004 [++]	−0.007 to−0.001
Body mass index (kg/m$^{2)}$ $n_c^* = 42$, $n_i^* = 40$	−0.004	0.006	−0.007 to−0.001	−0.004	0.004 [++]	−0.007 to−0.001
Abdominal height (cm) $n_c^* = 42$, $n_i^* = 40$	−0.004	0.68	−0.021 to 0.014	0.002	0.87	−0.017 to 0.020
Waist circumference (cm) $n_c^* = 42$, $n_i^* = 40$	0.001	0.77	−0.004 to 0.006	0.003	0.19	−0.002 to 0.008
Fasting glucose (mmol/L) $n_c^* = 42$, $n_i^* = 40$	−0.008	0.22	−0.021 to 0.005	−0.006	0.37	−0.020 to 0.008
2-h glucose (mmol/L) $n_c^* = 36$, $n_i^* = 36$	−0.017	0.41	−0.057 to 0.023	−0.023	0.27	−0.063 to 0.018
HbA_{1C} (mmol/mol) $n_c^* = 40$, $n_i^* = 37$	−0.001	0.70	−0.008 to 0.006	−0.001	0.83	−0.008 to 0.006
Insulin sensitivity index (mmol/L mIE/L)$^{-1}$ $n_c^* = 42$, $n_i^* = 40$	0.096	0.008	0.025 to 0.167	0.104	0.005	0.032 to 0.175
Disposition index(mmol/L mmol/L mmol/L) $n_c^* = 36$, $n_i^* = 36$	0.030	0.56	−0.072 to 0.133	0.025	0.64	−0.080 to 0.129
Systolic blood pressure (mm of Hg) $n_c^* = 42$, $n_i^* = 40$	0.005	0.44	−0.007 to 0.017	0.006	0.37 [+++]	−0.007 to 0.018
Diastolic blood pressure(mm of Hg) $n_c^* = 42$, $n_i^* = 40$	0.004	0.54	−0.009 to 0.017	0.007	0.33 [+++]	−0.007 to 0.020
Triglycerides (mmol/L) $n_c^* = 41$, $n_i^* = 40$	−0.039	0.06	−0.082 to 0.002	−0.038	0.10 [**]	−0.083 to 0.008
LDL cholesterol (mmol/L) $n_c^* = 41$, $n_i^* = 40$	−0.023	0.020	−0.025 to − 0.005	−0.021	0.036 [**]	−0.042 to − 0.001
HDL cholesterol (mmol/L) $n_c^* = 41$, $n_i^* = 40$	0.004	0.63	−0.011 to 0.019	0.002	0.82 [**]	−0.014 to 0.018
Physical activity (MET [***] hours/week) $n_c^* = 40$, $n_i^* = 39$	0.163	0.23	−0.107 to 0.432	0.092	0.50	−0.178 to 0.362
Caloric Intake (kcal) $n_c^* = 34$, $n_i^* = 37$	−0.024	0.24	−0.065 to 0.016	−0.033	0.12	−0.076 to 0.009

The β-coefficient indicates percentage change (calculated as 100*(expβ −1) in the outcomes per month in the intervention group compared to the control group.

[+] Adjusted for age, sex, body mass index, family history of diabetes, physical activity and education.

[++] Adjusted for waist circumference instead of body mass index in addition to the variables described in (+).

[+++] Adjusted for antihypertensive medication in addition to the variables described in (+).

[*] n_c = n for control group, n_i = n for intervention group, n for extended models can vary slightly because of missing values.

[**] No individuals were using lipid-lowering medication.

[***] Metabolic Equivalent of Task.

3.1. *Drop-Outs*

A total of 29 participants in the intervention and control groups dropped out from the study on the last visit. The drop-out rate from baseline to the last visit was 30.0% in the intervention group and 30.4% in the control group respectively. In our study, we recruited a total of 16 couples out of which six couples (both spouses) and two individual dropped-out leading to a higher drop-out rate of 43.7% among couples than the overall drop-out rate.

3.2. *Representativeness of the Study Population*

Participants were older than non-participants (49 vs. 46.6 years, $p = 0.02$), they had slightly lower BMI (30.3 vs. 31.3, $p = 0.04$) and a smaller proportion (52.0 vs 76.0%, $p < 0.001$) were physically inactive (achieving less than 150 min/week of PA) as compared to non-participants. There were no significant differences in sex distribution, education level or employment level between participants and non- participants (data not shown).

4. Discussion

4.1. *Key Findings*

The key finding of this unique culturally adapted, randomized lifestyle intervention programme is that it is efficient in reducing cardio-metabolic risk by improving insulin sensitivity, reducing body weight as well as LDL-cholesterol in the fastest growing sub-population in Europe – immigrants from the Middle-East– who are a high-risk population for Type 2 diabetes.

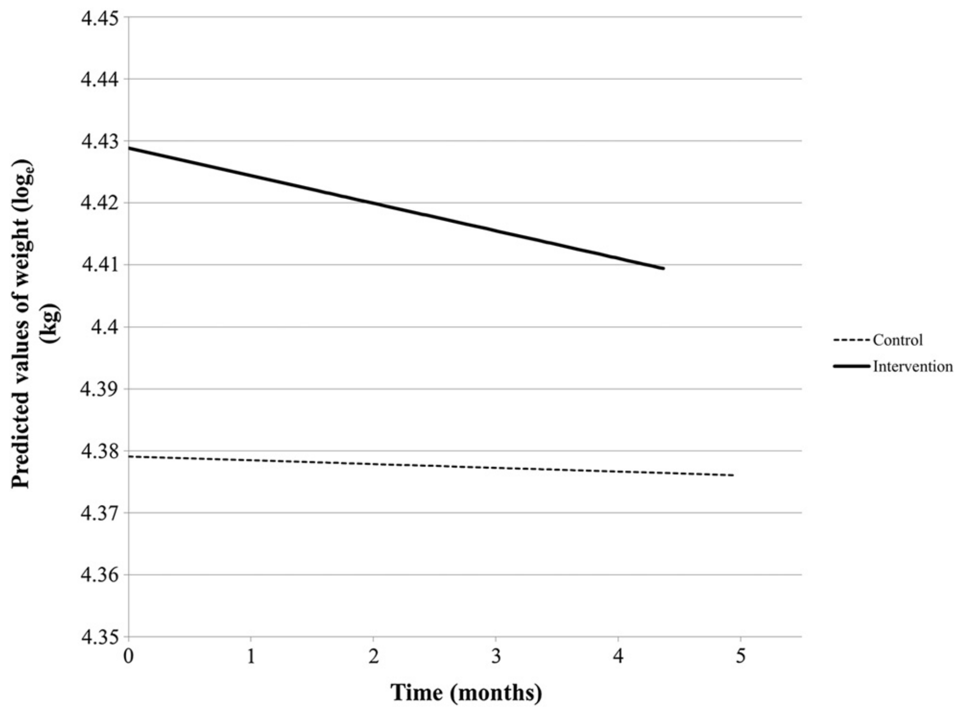

Fig. 2 – Predicted lines from the simple linear model for changes in body weight (log$_e$-transformed) over time in the individuals in the control and the intervention groups. The lines are based on predicted values for individuals and do not represent the mean follow-up time for the groups.

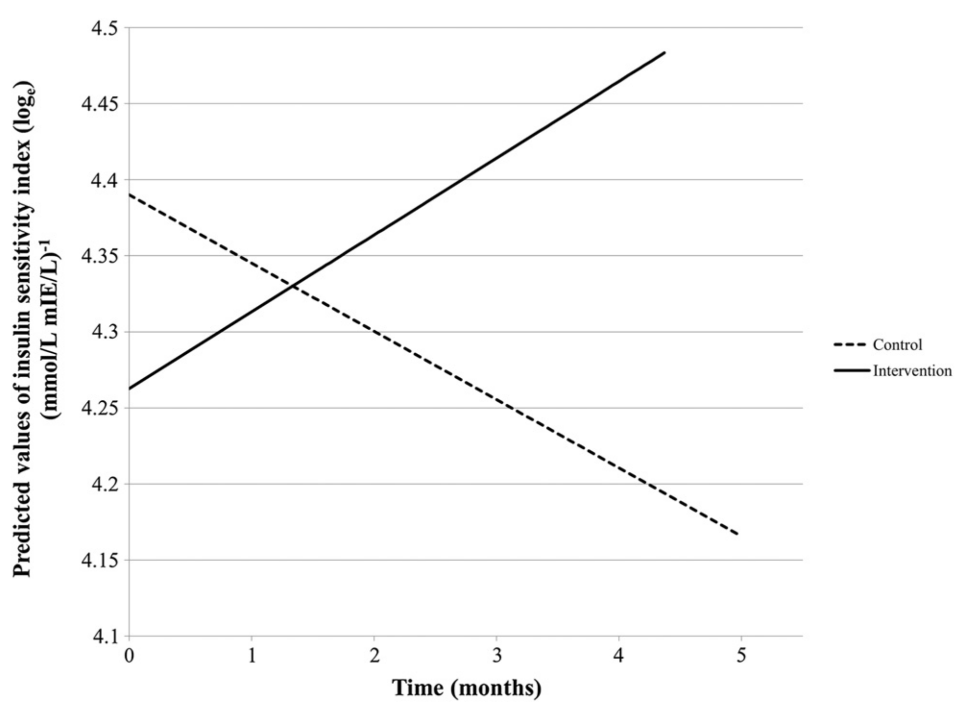

Fig. 3 – Predicted lines from the simple linear model for changes in the insulin sensitivity index (log$_e$-transformed) over time in the individuals in the control and the intervention groups. The lines are based on predicted values for individuals and do not represent the mean follow-up time for the groups.

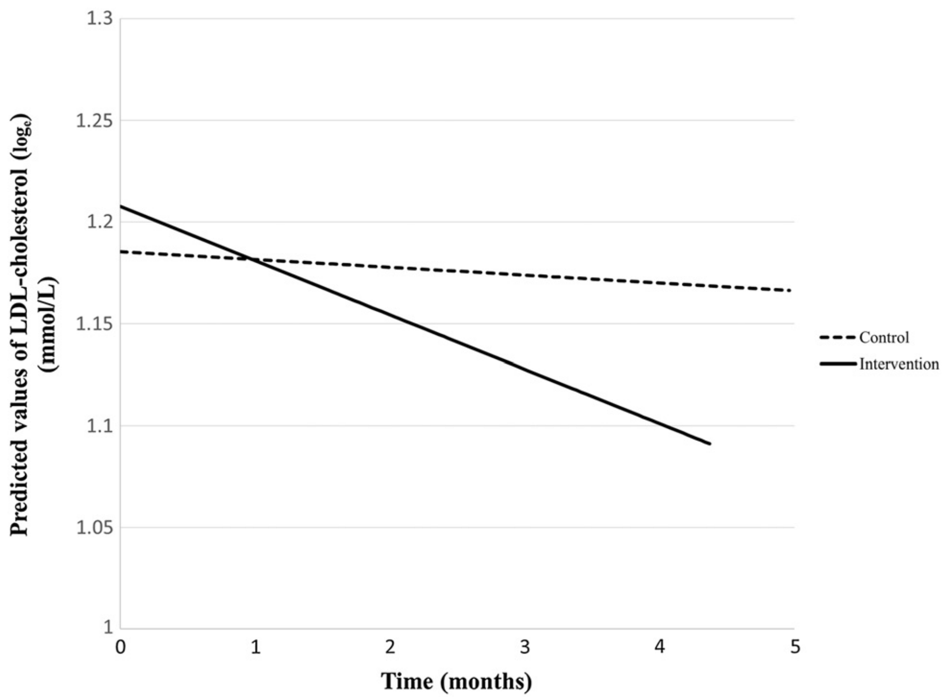

Fig. 4 – Predicted lines from the simple linear model for changes in the LDL-cholesterol levels (log$_e$-transformed) over time in the individuals in the control and the intervention groups. The lines are based on predicted values for individuals and do not represent the mean follow-up time for the groups.

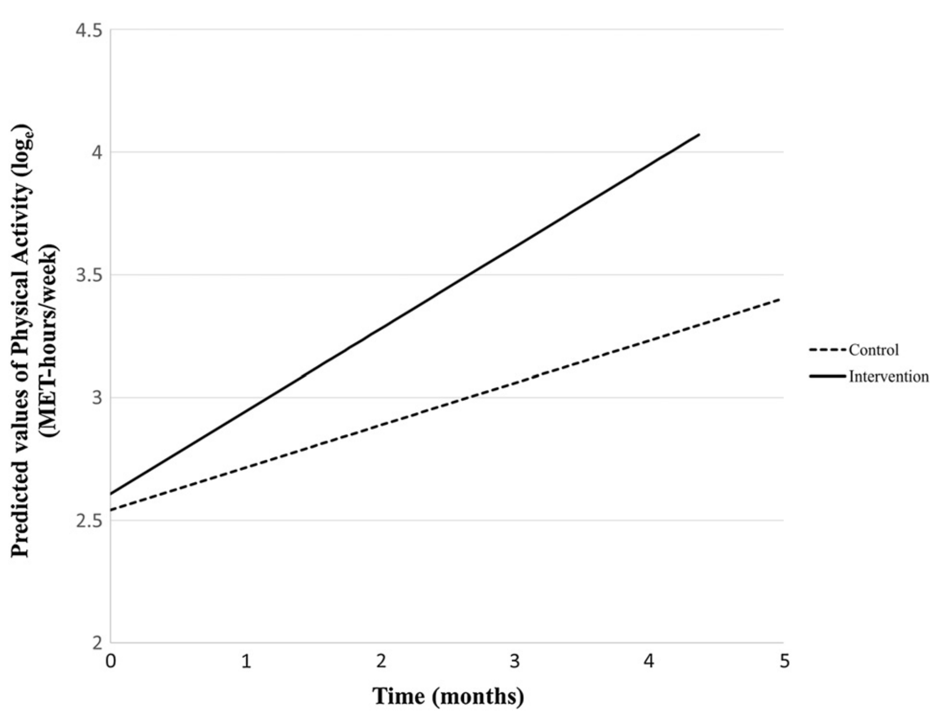

Fig. 5 – Predicted lines from the simple linear model for changes in the physical activity levels (log$_e$-transformed) over time in the individuals in the control and the intervention groups. The lines are based on predicted values for individuals and do not represent the mean follow-up time for the groups.

4.2. *Comparison with Other Studies*

To the best of our knowledge this study is the first randomized controlled intervention study on Middle-Eastern immigrants conducted in Europe addressing the impaired insulin sensitivity that is a major risk factor for Type 2 diabetes in this population [23]. Insulin sensitivity has been evaluated as an outcome in only a few culturally adapted lifestyle interventions, mainly in South-Asian [7,24,25], but not in Middle-Eastern immigrants. Only one previous intervention study, however non-randomized and not including a control group, has addressed Middle-Eastern immigrants [9]. That study, conducted in the US, reported beneficial changes in anthropometric measurements, PA and dietary habits [9]. Compared to that study the reduction in body weight (2.5 kg vs. 5.2 kg in the US study) and the proportion of individuals achieving ≥5% weight loss in the intervention group (14.3% vs. 59% in the US study), was modest in our study. However, the US study had a longer follow up (24-weeks) and participants higher BMI at baseline which may contribute to the more prominent body weight changes as participants in intervention studies generally exhibit greatest weight loss at six months [26]. However, the study design makes it difficult to draw conclusions and attribute changes fully to the US lifestyle intervention.

Culturally-tailored lifestyle interventions of 1–3 years duration in pre-diabetic non-Western immigrants, have also shown modest but significant changes in body weight in the intervention groups [27,28]. One non-randomized intervention study with a follow-up of 3.6 years conducted in a Middle-Eastern community addressing the general population irrespective of risk-profile, reported weight gain in both intervention and control groups [29].

4.3. *Interpretation and Implications of Findings*

Impaired insulin sensitivity leads to hyperglycaemia, compensatory hyperinsulinemia and dyslipidaemia which are important pathogenic factors underlying the development of Type 2 diabetes and metabolic syndrome [30] [31]. Both Type 2 diabetes and the metabolic syndrome are associated with increased risk of cardiovascular disease [30], especially in Iraqi immigrants [32]- as this group not only exhibits profound insulin resistance [23] but also a stronger association between Type 2 diabetes and cardiovascular disease compared to the native Swedes [32]. In addition, high LDL-cholesterol levels increase the risk of cardiovascular disease through vascular inflammation and atherosclerosis [33].

Even modest reduction in body weight is associated with improvement in insulin sensitivity [34] through mechanisms connected to reduced fatty acid mobilization, suppression of pro-inflammatory pathways [35] and increase in enzymatic activity of insulin receptors in skeletal muscles [36]. Improvement in insulin sensitivity as observed in our study together with the reduction in body weight and LDL- cholesterol represents an improved metabolic profile which will potentially reduce the risk of progression to diabetes and lower the risk of cardiovascular disease [30,37] in this high risk population.

Our findings also confirm beneficial effects of weight loss, reduction in waist circumference and increased PA on insulin sensitivity which is consistent with previous findings [39,40]. The strongest association was seen with BMI as estimates from the model indicated 3.2% improvement in ISI for one-unit decrease in BMI. However, in spite of body weight loss 44% of participants had no improvement at all in insulin sensitivity potentially representing non-responders. This could be because of certain phenotypic characteristics of these individuals [41] but was not investigated further since such an analysis would be beyond the scope of this paper.

In our preliminary analysis no significant change in mean caloric intake, was noticed in the intervention group compared to the control group; thus we could not show that the dietary intake effected the outcomes.

4.4. *Changes in Secondary Outcomes*

This study could not show improvement in FPG, 2-h glucose, HbA_{1C} level, DI, HDL cholesterol or triglyceride levels. This could be due to the short duration of our study since glycaemic changes are usually reported by lifestyle interventions of up to twelve months duration [42,43]. Also the mean FPG and 2-h glucose levels at baseline were within normal ranges, thus with a lower potential for improvement. There was no significant change in DI, calculated as a product of insulin secretion and insulin sensitivity. This may be an indication of reciprocal changes in insulin secretion in response to improved insulin sensitivity as reported previously by others [44].

4.5. *Strengths and Limitations of the Study*

Strengths are the thorough health investigations, including fasting samples, repeated OGTT's at baseline and follow-up visits enabling the assessment of ISI in the Middle-Eastern population. The study design, recruitment and randomisation process reduced selection bias. Other strengths were the adaptation of a culturally adapted group-based approach including gender specific groups, cooking class and economic support for admittance to PA centers. Further the resources applied in this study were designed to fit into resources available in the PHC of today including access to nutritionists, diabetes nurses, physiotherapists and health coaches; components that make this intervention feasible in PHC settings.

A limitation was the drop-out rate that in our study was twice as high as the drop-out rate of 14% seen in a previous intervention study on Middle-Eastern immigrants in the US [9] but on the contrary lower than the drop-out rate of 42% seen in an intervention study in an Iranian community [29]. The study in US had a greater focus on family involvement and support which might have contributed to a lower drop-out rate [9]. Our finding of a higher drop-out rate in couples indicates that couples tend to drop-out together. Therefore, a focus on couple retention can improve overall retention rates. Also the concordance of changes in ISI in five out of the eight couples who remained in the study indicates that couples tend to have similar outcomes owing probably to the adoption of similar lifestyle choices.

Another limitation was the relatively short time frame. The study was designed to finish before the start of the month of Ramadan since it affects dietary and PA habits. Therefore, the long-term effects of the intervention on the outcomes could not be evaluated. Feedback from the participants after the study was conducted indicated that retention rates could have been better if the duration was longer and health examinations and group sessions were more spaced out in time.

The low participation rate and the fact that participants had lower BMI and higher PA levels than non-participants could indicate difficulties in motivating high-risk individuals from the Middle East for lifestyle change. Non-participants also reported difficulties in taking time off from work, or childcare, as prominent causes of non-participation. There is scarcity of published literature addressing recruitment of ethnic populations into controlled trials in Europe [45]. Better participation rates might be achievable by increasing motivation for lifestyle change by addressing knowledge barriers prior to the intervention through an educational intervention as used in the US study [9]. In addition, incentives such as compensation for time off work and possibility of childcare can increase participation rates, however such strategies are often restricted by limited resources.

Another potential short-coming of the study was the use of the IPAQ instrument to measure PA level. Although the IPAQ is a valid and reliable measure of PA [18], this could have resulted in information bias due to over-reporting of PA by the intervention group [46].

4.6. *Conclusions*

To the best of our knowledge, this study is the first RCT of a culturally adapted lifestyle intervention among individuals of Middle-Eastern ancestry representing the largest immigrant group in Sweden today. The study provides insight into the effects and the challenges of implementing a lifestyle intervention for diabetes prevention in this immigrant group at high risk for Type 2 diabetes, We conclude that adopting a similar culturally-sensitive approach in PHC settings may improve the metabolic profile and reduce future cardio-metabolic risk in this diabetes-prone target group.

Author Contributions

FS contributed to the conduction of the study, compiled the data and wrote the manuscript. AK did the statistical analysis. PN and UL provided input on conduction of the trial as well as to the discussion and reviewed the manuscript. LB designed the trial, led the conduction of the trial, data acquisition, the analysis of the data and participated in writing the manuscript. All authors reviewed and edited the manuscript and approved the final version.

Funding

This study was funded by grants from Lund University (ALF grant Skåne 20,101,641, 20101837and 162,641), Region Skåne (226,661 and 121,811), Malmö Stad, The Swedish Society of Medicine (SLS97081 and 176,831), the Crafoord Foundation (20110719) and donation from Novo Nordisk Scandinavia AB. The funders had no role in study design, data collection or manuscript preparation.

Conflict of Interest

None.

Acknowledgements

We are grateful to the late Professor Carl-David Agardh Lund University, Sweden, Professor Marilyn Winkleby Stanford University, US, health coaches Katarina Balcker, Muna Mohammed and ImanYousif, study nurses Saranda Muhaxheri, Josefin Goode Khan, and Asma Saleh and study co-ordinator Sonja Ruhnke all Lund University Sweden.

REFERENCES

[1] Sweden S. Statistics Sweden. [Available from:] http://www.scb.se/.
[2] Bennet L, Groop L, Lindblad U, Agardh CD, Franks PW. Ethnicity is an independent risk indicator when estimating diabetes risk with FINDRISC scores: a cross sectional study comparing immigrants from the Middle East and native swedes. Prim Care Diabetes 2014;8(3):231–8.
[3] Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, et al. Prevention of Type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001;344(18):1343–50.
[4] Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of Type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346(6):393–403.
[5] Modesti PA, Galanti G, Cala P, Calabrese M. Lifestyle interventions in preventing new Type 2 diabetes in Asian populations. Intern Emerg Med 2015;11(3):375–84.
[6] Rechel B, Mladovsky P, Ingleby D, Mackenbach J, McKee M. Migration and health in an increasingly diverse Europe. Lancet 2013;381(9873):1235–45.
[7] Telle-Hjellset V, Raberg Kjollesdal MK, Bjorge B, Holmboe-Ottesen G, Wandel M, Birkeland KI, et al. The InnvaDiab-DE-PLAN study: a randomised controlled trial with a culturally adapted education programme improved the risk profile for Type 2 diabetes in Pakistani immigrant women. Br J Nutr 2013;109(3):529–38.
[8] Lirussi F. The global challenge of Type 2 diabetes and the strategies for response in ethnic minority groups. Diabetes Metab Res Rev 2010;26(6):421–32.
[9] Jaber LA, Pinelli NR, Brown MB, Funnell MM, Anderson R, Hammad A, et al. Feasibility of group lifestyle intervention for diabetes prevention in Arab Americans. Diabetes Res Clin Pract 2011;91(3):307–15.
[10] Saha S, Leijon M, Gerdtham U, Sundquist K, Sundquist J, Arvidsson D, et al. A culturally adapted lifestyle intervention addressing a middle eastern immigrant population at risk of diabetes, the MEDIM (impact of migration and ethnicity on diabetes in Malmö): study protocol for a randomized controlled trial. Trials 2013;14:279. http://dx.doi.org/10.1186/1745-6215-14-279.
[11] Renzaho AM, Boulton K, Swinburn B. Effectiveness of prevention programmes for obesity and chronic diseases among immigrants to developed countries - a systematic review. Public Health Nutr 2010;13(3):438–50.
[12] Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes

federation task force on epidemiology and prevention; National Heart, Lung, and Blood Institute; American Heart Association; world heart federation; international atherosclerosis society; and International Association for the Study of obesity. Circulation 2009;120(16):1640–5.

[13] von Schenck H, Falkensson M, Lundberg B. Evaluation of "HemoCue," a new device for determining hemoglobin. Clin Chem 1986;32(3):526–9.

[14] Allain CC, Poon LS, Chan CS, Richmond W, Fu PC. Enzymatic determination of total serum cholesterol. Clin Chem 1974; 20(4):470–5.

[15] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18(6):499–502.

[16] Diet and nutrition data computer programs for nutrition calculation [cited 2015]. [Available from:] http://www.kostdata.se/en.

[17] Paulweber B, Valensi P, Lindström J, Lalic N, Greaves C, McKee M, et al. A European evidence-based guideline for the prevention of Type 2 diabetes. Horm Metab Res 2010; 42(Suppl. 1):S3–36.

[18] Craig C, Marshall A, Sjöström M, Bauman A, Booth M, Ainsworth B, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003;35(8):1381–95.

[19] Guidelines for data processing and analysis of the international physical activity questionnaire (IPAQ)—short and long forms. [updated November 5, 2005; cited 2015 November 30. Available from:] https://docs.google.com/viewer?a=v&pid=sites&srcid=ZGVmYXVsdGRvbWFpbnx0aGVpcGFxfGd4OjE0NDgxMDk3NDU1YWRlZTM.

[20] Matsuda M, DeFronzo R. Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. Diabetes Care 1999;22(9):1462–70.

[21] Geert M, Geert V. Linear mixed models for longitudinal data; 2000[554 pp.].

[22] Hoenig J, Heiseya D. The abuse of power the pervasive fallacy of power calculations for data analysis. Am Stat 2001;55(1): 19–24.

[23] Bennet L, Groop L, Franks PW. Ethnic differences in the contribution of insulin action and secretion to Type 2 diabetes in immigrants from the Middle East compared to native swedes. Diabetes Res Clin Pract 2014;105(1):79–87.

[24] Andersen E, Hostmark AT, Holme I, Anderssen SA. Intervention effects on physical activity and insulin levels in men of Pakistani origin living in Oslo: a randomised controlled trial. J Immigr Minor Health 2013;15(1):101–10.

[25] Admiraal WM, Vlaar EM, Nierkens V, Holleman F, Middelkoop BJC, Stronks K, et al. Intensive lifestyle intervention in general practice to prevent Type 2 diabetes among 18 to 60-year-old south Asians: 1-year effects on the weight status and metabolic profile of participants in a randomized controlled trial. PLoS One 2013;8(7):e68605. http://dx.doi.org/10.1371/journal.pone.0068605.

[26] Jeffery RW, Drewnowski A, Epstein LH, Stunkard AJ, Wilson GT, Wing RR, et al. Long-term Maintainance of weight loss: current status. Health Psychol 2000;19(1(Suppl.)):5–16.

[27] Bhopal RS, Douglas A, Wallia S, Forbes JF, Lean ME, Gill JM, et al. Effect of a lifestyle intervention on weight change in south Asian individuals in the UK at high risk of Type 2 diabetes: a family-cluster randomised controlled trial. Lancet Diabetes Endocrinol 2014;2(3):218–27.

[28] Yeh MC, Heo M, Suchday S, Wong A, Poon E, Liu G, et al. Translation of the diabetes prevention program for diabetes risk reduction in Chinese immigrants in New York City. Diabet Med 2015;33(4):547–51.

[29] Harati H, Hadaegh F, Momenan AA, Ghanei L, Bozorgmanesh MR, Ghanbarian A, et al. Reduction in incidence of Type 2 diabetes by lifestyle intervention in a middle eastern community. Am J Prev Med 2010;38(6):628–636.e1.

[30] Kendall DM, Harmel AP. The metabolic syndrome, Type 2 diabetes, and cardiovascular disease: understanding the role of insulin resistance. Am J Manag Care 2002;8(20 Suppl): S635–53 [quiz S54–7].

[31] Reaven GM. Role of insulin resistance in human disease (syndrome X): an expanded definition. Annu Rev Med 1993; 44:121–31.

[32] Bennet L, Agardh CD, Lindblad U. Cardiovascular disease in relation to diabetes status in immigrants from the Middle East compared to native swedes: a cross-sectional study. BMC Public Health 2013;13:1133. http://dx.doi.org/10.1186/1471-2458-13-1133.

[33] Brunzell JD, Davidson M, Furberg CD, Goldberg RB, Howard BV, Stein JH, et al. Lipoprotein management in patients with cardiometabolic risk: consensus statement from the American Diabetes Association and the American College of Cardiology Foundation. Diabetes Care 2008;31(4):811–22.

[34] Ockene IS, Tellez TL, Rosal MC, Reed GW, Mordes J, Merriam PA, et al. Outcomes of a Latino community-based intervention for the prevention of diabetes: the Lawrence Latino diabetes prevention project. Am J Public Health 2012;102(2): 336–42.

[35] Schenk S, Harber MP, Shrivastava CR, Burant CF, Horowitz JF. Improved insulin sensitivity after weight loss and exercise training is mediated by a reduction in plasma fatty acid mobilization, not enhanced oxidative capacity. J Physiol 2009; 587(Pt 20):4949–61.

[36] Caro JF, Sinha MK, Raju SM, Ittoop O, Pories WJ, Flickinger EG, et al. Insulin receptor kinase in human skeletal muscle from obese subjects with and without noninsulin dependent diabetes. J Clin Invest 1987;79(5):1330–7.

[37] Howard BV, Robbins DC, Sievers ML, Lee ET, Rhoades D, Devereux RB, et al. LDL cholesterol as a strong predictor of coronary heart disease in diabetic individuals with insulin resistance and low LDL the strong heart study. Arterioscler Thromb Vasc Biol 2000;20:830–5.

[39] Ryan AS. Insulin resistance with aging: effects of diet and exercise. Sports Med 2000;30(5):327–46.

[40] Friedman JE, Dohm GL, Leggett-Frazier N, Elton CW, Tapscott EB, Pories WP, et al. Restoration of insulin responsiveness in skeletal muscle of morbidly obese patients after weight loss. Effect on muscle glucose transport and glucose transporter GLUT4. J Clin Invest 1992;89(2):701–5.

[41] Stefan N, Staiger H, Wagner R, Machann J, Schick F, Haring HU, et al. A high-risk phenotype associates with reduced improvement in glycaemia during a lifestyle intervention in prediabetes. Diabetologia 2015;58(12):2877–84.

[42] Gong QH, Kang JF, Ying YY, Li H, Zhang XH. Lifestyle interventions for adults with impaired glucose tolerance: a systematic review and meta-analysis of the effects on glycemic control. Intern Med 2015;54(3):303–10.

[43] Yamaoka K, Tango T. Efficacy of lifestyle education to prevent Type 2 diabetes: a meta-analysis of randomized controlled trials. Diabetes Care 2005;28(11):2780–6.

[44] Retnakaran R, Shen S, Hanley AJ, Vuksan V, Hamilton JK, Zinman B. Hyperbolic relationship between insulin secretion and sensitivity on oral glucose tolerance test. Obesity 2008;16(8):1901–7.

[45] Douglas A, Bhopal RS, Bhopal R, Forbes JF, Gill JM, Lawton J, et al. Recruiting south Asians to a lifestyle intervention trial: experiences and lessons from PODOSA (prevention of Diabetes & Obesity in south Asians). Trials 2011;12:220. http://dx.doi.org/10.1186/1745-6215-12-220.

[46] Arvidsson D, Leijon M, Sundquist J, Sundquist K, Lindblad U, Bennet L. Cross-cultural validation of a simple self-report instrument of physical activity in immigrants from the Middle East and native swedes. Scand J Public Health 2014; 42(3):255–62.