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Randomised controlled trial evaluating the effectiveness of behavioural interventions to modify cardiovascular risk factors in men and women with impaired glucose tolerance: outcomes at 6 months☆

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Abstract

Aims: To evaluate the efficacy of interventions to promote a healthy diet and physical activity in people with impaired glucose tolerance (IGT). *Methods:* A randomised controlled trial in Newcastle upon Tyne, UK, 1995–98. Participants included 67 adults (38 men; 29 women) aged 24–75 years with IGT. The intervention consisted of regular diet and physical activity counselling based on the stages of change model. Main outcome measures were changes between baseline and 6 months in nutrient intake; physical activity; anthropometric and physiological measurements including serum lipids; glucose tolerance; insulin sensitivity. *Results:* The difference in change in total fat consumption was significant between intervention and control groups (difference −21.8 (95% confidence interval (CI) −37.8 to −5.8) g/day, $P = 0.008$). A significantly larger proportion of intervention participants reported taking up vigorous activity than controls (difference 30.1, (95% CI 4.3–52.7)%, $P = 0.021$). The change in body mass index was significantly different between groups (difference −0.95 (95% CI −1.5 to −0.4) kg/m^2, $P = 0.001$). There was no significant difference in change in mean 2-h plasma glucose between groups (difference −0.19 (95% CI −1.1 to 0.71) mmol/l, NS) or in serum cholesterol (difference 0.02 (95% CI −0.26 to 0.31) mmol/l, NS). The difference in change in fasting serum insulin between groups was significant (difference −3.4 (95% CI −5.8 to −1.1) mU/l, $P = 0.005$). *Conclusions:* After 6 months of intensive lifestyle intervention in participants with IGT, there were changes in diet and physical activity, some cardiovascular risk factors and insulin sensitivity, but not glucose tolerance.

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Further follow-up is in progress to investigate whether these changes are sustained or augmented over 2 years.

Keywords: Impaired glucose tolerance; Diet; Physical activity; Type 2 diabetes; Coronary heart disease

1. Introduction

Impaired glucose tolerance is associated with a ten-fold higher risk of developing Type 2 diabetes mellitus (Type 2 DM) and a two-fold higher risk of developing ischaemic heart disease (IHD) compared with people who have normal glucose tolerance (NGT) [1]. Earlier studies have shown that behavioural interventions in people with IGT result in improvements in cardiovascular risk factors [2] [3] [4] but have tended to be over short periods of time (e.g. 3–12 weeks) and have used highly intensive interventions [3] [4]. Two recent landmark studies, the Da Qing study in China and the Diabetes Prevention Study (DPS) in Finland, have provided evidence from more long term, pragmatic interventions, [25,26] although in the Da Qing study only changes in glucose control, not insulin values, were published. Evidence is needed of the efficacy of sustainable interventions that are widely applicable in primary care in the UK. In this paper, we report the study design and main outcomes after 6 months follow-up of a 2-year randomised controlled trial of diet and physical activity counselling for participants with IGT. The study tested the null hypotheses that counselling from a dietician and physiotherapist would result in, (i) no improvements in diet or aerobic physical activity; (ii) no improvements in glucose tolerance and insulin sensitivity; and (iii) no improvements in cardiovascular risk factors after 6 months.

2. Materials and methods

2.1. Study design

The study was a randomised-controlled trial with one intervention and one control arm.

2.2. Setting

The study was conducted at the Royal Victoria Infirmary, Newcastle upon Tyne, UK.

2.3. Participants-inclusion and exclusion criteria

Men and women of European origin, aged 24–75 years, who had IGT identified on two consecutive oral glucose tolerance tests (OGTTs), the second within 2–12 weeks of the first, were eligible to participate. Individuals who were pregnant, on therapeutic diets or whose medical condition prevented them from undertaking moderate physical activity were excluded. Medications likely to interfere with glucose metabolism were noted. IGT, NGT and diabetes were defined using WHO 1985 criteria [5]. IGT was defined as a 2-h post glucose load plasma glucose ≥ 7.8 and < 11.1 mmol/l [5]. Diabetes and NGT were defined as 2-h plasma glucose ≥ 11.1 and < 7.8 mmol/l, respectively [5].

2.4. Recruitment

Individuals with IGT were recruited to the study from the following three sources

1. Research studies conducted in the Department of Medicine at the University of Newcastle between 1993 and 1994 [6,7];
2. Local hospital biochemistry laboratory databases;
3. General Practitioner (GP) surgeries.

2.5. Recruitment procedure

Potential participants were sent a letter inviting them to take part with a pre-paid reply slip. Respondents were subsequently contacted to arrange baseline appointments.

2.6. Allocation to intervention or control groups

Eligible participants who agreed to take part were randomly allocated using a random number table to the intervention or control group at the first baseline appointment. Researchers performing the randomisation were blinded to the group allocation.

2.7. Data collection

All intervention and control participants had three separate appointments at baseline and at 6 months during which the following measurements were made.

2.7.1. First appointment

Participants attended the Clinical Research Centre after an overnight fast. All participants provided informed consent.

2.7.2. Biochemical measurements

A WHO standard OGTT was performed [5] and fasting, 1 and 2-h venous blood samples taken to measure plasma glucose and serum insulin and C-peptide concentrations. Plasma glucose was measured by an automated glucose oxidase method on a YSI glucose analyser (Yellow Springs, Ohio, USA) [8]. Serum insulin and C-peptide concentrations were analysed by enzyme linked immunosorbent assay (ELISA) (DAKO Diagnostics, Ely, UK). Lipid concentrations were measured on fasting blood samples on a DAX analyser (Bayer, Basingstoke, UK). Cholesterol was estimated using a cholesterol oxidase/peroxidase and calibrants traceable to the Centres for Disease Control definitive method. Triglycerides were estimated using a lipase/glycerol kinase method and high density lipoprotein (HDL) cholesterol was estimated by measuring the supernatant cholesterol concentration following precipitation of apolipoprotein B containing lipoproteins with heparin and manganese. Low density lipoprotein (LDL) cholesterol was estimated from the Friedewald formula [9]. Apolipoprotein A-1 and B were estimated by an immunoturbidometric method (DPA analyser, Bayer). Non-esterified fatty acids (NEFA) were measured by an enzymatic colorimetric method on an automated Cobas Bio analyser, using a Wako kit (Alpha laboratories, Eastleigh, UK). Glycosylated haemoglobin (HbA_{1c}) was run on Biorad (Hemel Hempstead, UK) variant ion exchange method HPLC, calibrated to the National Glycohaemoglobin Standardisation Programme in the USA. Fibrinogen concentrations were measured by an Instrumentation Laboratory Automated Coagulation Analyser 3000 (Warrington, UK).

2.7.3. Clinical measurements

Weight was measured to the nearest 0.1 kg with the participants lightly clothed on SECA scales (Alpha Model 770 digital, SECA, Birmingham, UK) and height, without shoes, to the nearest 0.5 cm on a SECA stadiometer. Body mass index was calculated as weight in kg divided by height in metres squared (m^2). Waist and hip circumferences were measured to the nearest cm with the participants standing, using a spring loaded tape measure to ensure that a consistent tension was applied in all readings. Waist was measured at the midpoint between the lower costal margin and the iliac crest. Hip circumference was measured over the greater trochanters. Waist:hip ratio (WHR) was calculated from the mean of two waist and two hip measurements. Blood pressure was measured in duplicate with participants seated using a mercury sphygmomanometer at least 20 min after venopuncture following the guidelines of the British Hypertension Society [10].

2.7.4. Dietary measurements

Participants were given detailed instructions to complete a 4 day food diary comprising 2 weekdays and 2 weekend days [11]. The amounts consumed were subsequently quantified using a food atlas during an interview with a dietician [12,13].

2.7.5. Questionnaire

Participants were given a self-completion questionnaire on health related behaviours including physical activity. An episode of vigorous physical activity was defined as aerobic exercise, lasting longer than 20 min, sufficient to get out of breath.

2.8. Second appointment

2.8.1. Insulin sensitivity measurements

Insulin sensitivity was assessed using the short insulin tolerance test (ITT) [14]. Two cannulae were introduced under local anaesthetic — one retrogradely in a dorsal hand vein to obtain arterialised venous blood sampling [15] at 1 min intervals for 15 min and a second in the antecubital vein of the contra-lateral arm for the administration of insulin (Actrapid, Novo Nordisk, Crawley, UK) 0.05 U/kg). Whole blood glucose values were $\log_e$ transformed and plotted against time. The slope of the curve (K_{ITT}), which is an estimate of insulin sensitivity, was calculated by linear regression.

2.9. Third appointment

2.9.1. Physical activity measurements

The Shuttle test [16] [17] was used to assess physical activity. This is a reproducible, progressive walking test that minimises participant anxiety and can be used independent of functional limitations [18]. Participants walked up and down a 10-m course at a pace dictated by a pre-recorded audio signal played on a cassette recorder. The end of the test was determined when the participant failed to complete a shuttle within the required time. Resting pulse was recorded and the number of completed shuttles was counted. The pulse rate 2 min after completing the shuttle test was subtracted from the pulse immediately after the test to calculate the *recovery pulse*.

2.10. Intervention group

2.10.1. Interventions

The intervention consisted of regular counselling from a dietician and physiotherapist using the stages of change model of behaviour change [19] [20] [21]. The intervention group received the following interventions:

2.10.1.1. Dietary. The dietician performed a dietary assessment in a one to one interview using the baseline food diary and assessed the position of the participant on the stages of change cycle [21]. The dietician used stage-specific motivational interviewing to develop, with the participant, individual targets for behaviour change. Participants were encouraged to eat more fruits and vegetables, reduce the fat content of foods and reduce their sugar intake. The dietary goal was to reduce BMI to < 25 kg/m^2 in those participants who were overweight. In addition, dietary advice as recommended by the Nutrition Subcommittee of the British Diabetic Association was provided, aiming to achieve a dietary fat intake of 30% of total energy intake, a polyunsaturated to saturated fat ratio of 1.0, 50–55% of energy from carbohydrate and a dietary fibre intake of 20 g per 1000 kcal (4.2 MJ) [22].

2.10.1.2. Physical activity. The physiotherapist assessed participants' level of physical activity at baseline and provided a graded physical activity plan, tailored to the participant's lifestyle, designed to enable them to achieve 20–30 min of aerobic activity, two to three times per week. Information leaflets about exercise facilities available in Newcastle were provided as appropriate. A City Card (a card scheme offering upto 80% discount on use of all public leisure facilities in the city) was offered to all the participants.

2.10.1.3. Review appointments. Intervention participants had six reviews, each lasting 15–20 min, with the dietician and physiotherapist — three at two weekly intervals and then three at monthly intervals to provide ongoing support.

2.11. Control group

Participants in the control group were asked to live their normal, day to day life for the duration of the study.

2.12. Sample size

We calculated that a sample size of 100 participants (50 participants in each arm) was neces-

sary to detect, with 90% power at the 5% significance level, a 0.6 mmol/l difference in mean fasting plasma glucose; a 6 mm Hg difference in mean systolic blood pressure; and a 20% difference in the proportion with glucose intolerance.

2.13. Statistical analysis

The Statistical Package for Social Scientists (SPSS version 8.0, Chicago, IL, USA) was used for all analyses, which were performed on an intention-to-treat basis. Nutritional analysis of the food diaries was conducted using Microdiet computer software [23]. The independent sample *t*-test was used to compare differences in change between the control and intervention groups. Non-normally distributed variables were log-transformed before analysis, and the results are presented as geometric means. The difference between groups in the proportion of participants who reported undertaking vigorous activity was calculated from a method based on score intervals for the single proportion with continuity correction [24].

2.14. Study ethics

Ethical approval was obtained from the Joint Ethics Committee of Newcastle and North Tyne side Health Authority.

3. Results

3.1. Recruitment of participants

Fig. 1 shows the recruitment outcomes. A total of 498 individuals with IGT were identified from the three sources of recruitment (121 (24%) from concurrent research studies, 304 (61%) from local biochemistry laboratories and 53 (11%) from GPs). Of these, 208/498 (42%) agreed to attend for a repeat OGTT. On re-testing 82/208 (39%) were eligible to take part. Of those eligible, 78/82 (95%) were recruited into the study. Then 39 participants were randomised to the intervention group and 39 to the control group. Seven participants (two intervention, five control) dropped out within the first 6 months because of time, family difficulties, travel or other health problems. One participant (intervention) developed severe ischaemic heart disease before all baseline measurements were completed. Three participants (one intervention, two control) failed to attend their 6 month follow-up appointments. Results are presented on the remaining 67 participants (35 intervention, 32 control). The 11 participants for

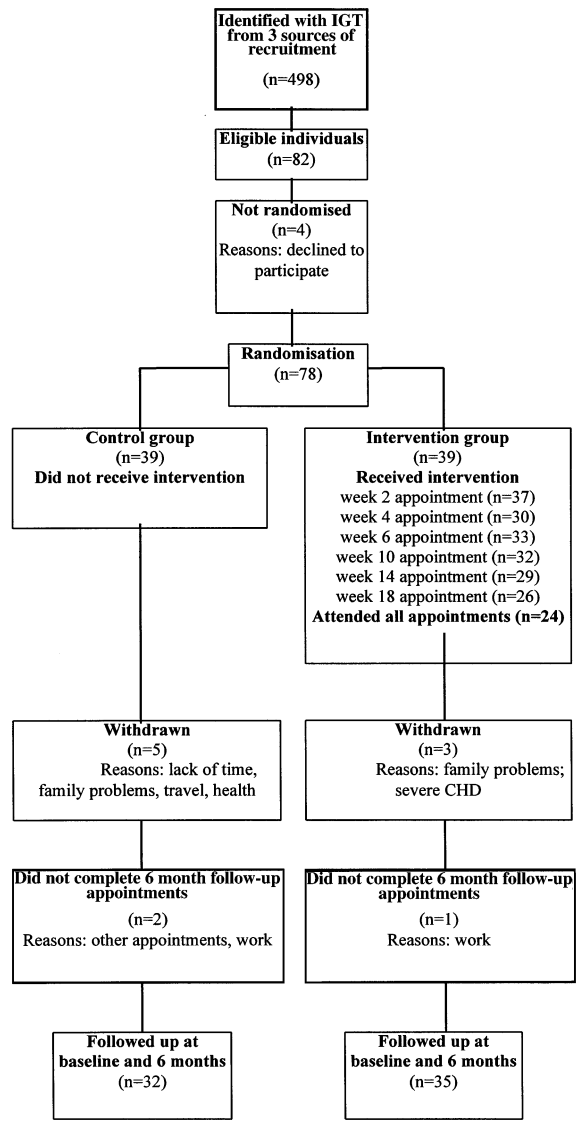

Fig. 1. IGT study: trial profile and recruitment outcomes.

whom results are not presented were not significantly different at baseline from the remaining 67 participants with respect to mean age (mean 58.5 years vs. 57.9 years) or sex (7/11 (64%) men, 4/11 (36%) women vs. 38/67 (57%) men, 29/67 (42%) women).

At baseline there was no significant difference between intervention and control participants with respect to age (58.2 (41–75) years vs. 57.5 (41–73) years). There were fewer women (10/32 (32%)) than men (22/32 (69%)) in the control group compared with the intervention group (19/35 (54%)) vs. (16/35 (46%)). There were no significant differences between groups at baseline in the main outcome measures.

Fig. 1 illustrates the uptake of the intervention. In total, 62% (24/39) of participants attended all six review appointments.

3.2. Nutrient intake

Table 1 shows that the difference in change in total fat consumption from baseline to 6 months between intervention and control groups was −21.8 (95% (CI) −37.8 to −5.8) g/day, $P = 0.008$). The change in monounsaturated fatty acids (MUFA) intake was significantly different between groups (−6.8 (−12.6 to −1.01) g/day, $P = 0.022$). The difference in change in polyunsaturated fat (PUFA) consumption between groups was also significant (−5.0 (−9.8 to −0.19) g/day, $P = 0.042$).

3.3. Resting pulse, shuttle walking test and reported physical activity

Table 2 shows that mean resting pulse decreased in the intervention group but increased in the control group (difference −3.6 (−7.1 to −0.2) beats/min, $P = 0.038$). The distance walked in the shuttle test increased for both groups with no treatment effect detectable (difference 10 (−29 to 49) m, NS). The proportion of participants who reported undertaking vigorous physical activity > three times/week increased significantly in the intervention group (+26.9%) but decreased in controls (−3.2%) (difference 30.1, (4.3–52.7)%, $P = 0.021$).

3.4. Anthropometry and mean blood pressure

Table 3 shows that weight decreased by −1.5 kg in the intervention group but increased in control participants by 0.54 kg (difference −2.0 (−3.2 to −0.8) kg, $P = 0.001$). Body mass index decreased by −0.56 kg/m^2 in the intervention group and increased in controls (0.39 kg/m^2) (difference −0.95, (−1.5 to −0.4) kg/m^2, $P = 0.001$). Mean systolic blood pressure decreased significantly in the intervention group (−7.9 mmHg) compared with the control group (−0.27 mmHg) (difference −7.6 (−15.2 to −0.006) mmHg, $P = 0.050$).

3.5. Glucose tolerance, plasma insulin, and C-peptide concentrations

Table 4 shows that there was no significant difference in change between groups in fasting or 2-h plasma glucose. There was no difference between the proportion of participants who had reverted to NGT (37% (13/35) intervention vs. 41% (13/32) control). The difference in change between groups in K_{ITT} was not statistically significant. Insulin resistance, measured by homeostasis model assessment (HOMA), decreased significantly in intervention (−0.7) but increased in control (0.3) subjects (difference −1.0, (−1.7 to −0.3), $P = 0.01$). Fasting serum insulin concentration decreased significantly in the intervention group (−2.5 mU/l) but increased slightly in the control group (+0.9 mU/l) (difference −3.4 (−5.8 to −1.1) mU/l, $P = 0.005$). The 2-h serum insulin concentration decreased much more in the intervention (−34.8 mU/l) than in the control group (−0.7 mU/l) (difference −34.1 (−66.2 to −2.1) mU/l, $P = 0.037$). Also 2-h, but not fasting, serum C-peptide concentration decreased significantly in the intervention group (difference −0.07 (−1.4 to −0.02) nmol/l, $P = 0.044$).

3.6. Blood lipid concentrations

Table 5 shows that the intervention resulted in no significant changes for any plasma lipid component, except for fasting NEFA in which the

Table 1
Mean (S.D.) and mean differences in daily energy and nutrient intakes between baseline and 6 months in the control and intervention groups[a]

	Control ($n = 32$)			Intervention ($n = 35$)			$d^2 - d^1$	95% CI for $d^2 - d^1$	P
	Baseline	6 months	d^1	Baseline	6 months[b]	d^2			
Energy (kJ)	8942 (2298)	8972 (2977)	30 (1994)	8317 (2464)	7485 (2390)	−832 (2563)	−862	−2002 to 279	NS
Total fat (g)	84.7 (23.4)	89.8 (34.3)	5.1 (29.8)	85.4 (29.0)	68.7 (30.0)	−16.8 (34.6)	−21.8	−37.8 to −5.8	0.008
Monounsaturated fat (g)	27.1 (8.5)	28.8 (11.6)	1.6 (10.9)	26.4 (10.1)	21.2 (10.1)	−5.2 (12.4)	−6.8	−12.6 to −1.01	0.022
Polyunsaturated fat (g)	13.5 (6.1)	15.6 (9.3)	2.1 (10.1)	15.6 (6.8)	12.7 (7.2)	−2.9 (9.2)	−5.0	−9.8 to −0.19	0.042
Saturated fat (g)	32.2 (11.8)	31.1 (15.1)	−0.8 (12.7)	27.9 (10.3)	23.9 (13.1)	−4.0 (13.5)	−3.1	−9.6 to 3.4	NS
Polyunsaturated/saturated fat ratio	0.47 (0.25)	0.57 (0.28)	0.09 (0.29)	0.59 (0.27)	0.59 (0.32)	−0.002 (0.35)	−0.10	−0.26 to 0.06	NS
Sucrose (g)	0.91 (1.9)	2.5 (4.3)	1.5 (4.8)	1.3 (2.5)	2.2 (5.4)	0.94 (6.1)	−0.6	−3.3 to 2.1	NS
Fibre (Southgate) (g)	19.8 (8.2)	19.0 (7.3)	−0.81 (5.7)	20.0 (6.6)	20.2 (7.5)	0.2 (6.0)	1.0	−1.9 to 3.9	NS
Starch (g)	133.7 (40.4)	129.5 (44.1)	−4.3 (38.9)	127.3 (33.1)	124.4 (36.6)	−2.9 (44.4)	1.37	−19.3 to 22.0	NS

[a] d^1 and d^2 = difference between baseline and 6 months in the control and intervention group, respectively; P values and 95% CI are for $d^2 - d^1$.
[b] $n = 33$.

Table 2
Mean (S.D.) and mean differences (unless indicated) in resting pulse, 'shuttle test' and lifestyle activity between baseline and 6 months in the control and intervention groups[a]

	Control ($n = 32$)			Intervention ($n = 35$)			$d^2 - d^1$	95% CI for $d^2 - d^1$	P
	Baseline	6 months	d^1	Baseline	6 months	d^2			
Resting pulse (beats/min)	71.9 (9.4)	73.7 (9.7)[b]	1.8 (5.7)	77.9 (10.5)	76.1 (11.0)	−1.8 (8.1)	−3.6	−7.1 to −0.22	0.038
Distance walked (m)	389 (206)	436 (230)[b]	47 (69)	405 (219)	463 (220)	57 (89)	10	−29 to 49	NS
Recovery pulse (beats/min)	21.7 (13.3)	22.7 (13.4)[b]	1.1 (12.3)	24.5 (11.8)	32.5 (18.0)	7.2 (17.1)	6.1	−1.6 to 13.9	NS
Vigorous activity (%(n))	18.8 (6)	15.6 (5)	−3.2	14.3 (5)[c]	41.2 (14)[c]	26.9	30.1	4.3 to 52.7	0.021

[a] d^1 and d^2 = difference between baseline and 6 months in the control and intervention group, respectively; P values and 95% CI are for $d^2 - d^1$.
[b] $n = 31$.
[c] $n = 34$.

Table 3
Mean (S.D.) and mean differences in anthropometry and mean blood pressure between baseline and 6 months in the control and intervention groups[a]

	Control ($n = 32$)			Intervention ($n = 35$)			$d^2 - d^1$	95% CI for $d^2 - d^1$	P
	Baseline	6 months	d^1	Baseline	6 months	d^2			
Weight (kg)	85.5 (14.2)	86.1 (13.8)	0.54 (2.2)	83.3 (16.1)	81.9 (16.6)	−1.5 (2.6)	−2.0	−3.2 to −0.8	0.001
BMI (kg/m^2)	29.9 (4.9)	30.3 (5.1)	0.39 (0.98)	30.4 (5.6)	29.9 (5.8)	−0.56 (1.2)	−0.95	−1.5 to −0.4	0.001
Waist circumference (cm)	99.6 (11.3)	99.7 (10.6)	0.06 (4.2)	97.9 (11.1)	97.1 (11.6)[b]	−0.79 (5.3)	−0.86	−3.2 to 1.5	NS
Hip circumference (cm)	104.0 (9.0)	104.8 (8.0)	0.72 (4.4)	106.2 (11.8)	105.4 (11.9)[b]	−0.85 (4.6)	−1.57	−3.8 to 0.64	NS
WHR	0.96 (0.08)	0.95 (0.08)	−0.006 (0.06)	0.93 (0.09)	0.92 (0.07)[b]	−0.004 (0.06)	0.002	−0.03 to 0.03	NS
Systolic blood pressure (mmHg)	132.8 (16.4)	132.6 (14.4)	−0.27 (14.3)	137.2 (19.9)	129.3 (19.5)	−7.9 (16.7)	−7.6	−15.2 to −0.006	0.050
Diastolic blood pressure (mmHg)	75.5 (9.8)	77.4 (9.2)	1.9 (10.0)	77.0 (12.6)	74.1 (10.0)	−2.9 (9.9)	−4.9	−9.7 to 0.04	0.052

[a] d^1 and d^2 = difference between baseline and 6 months in the control and intervention group, respectively; P values and 95% CI are for $d^2 - d^1$.
[b] $n = 34$.

Table 4
Mean and mean differences in glucose tolerance, insulin and C-peptide between baseline and 6 months in the control and intervention groups[a]

	Control ($n = 32$)			Intervention ($n = 35$)			$d^2 - d^1$	95%CI for $d^2 - d^1$	P
	Baseline	6 months	d^1	Baseline	6 months	d^2			
Fasting plasma glucose (mmol/l)	6.2 (0.9)	6.3 (0.9)	0.2 (1.1)	6.0 (0.9)	6.1 (0.9)	0.02 (0.6)	−0.12	−0.56 to 0.32	NS
2-h plasma glucose (mmol/l)	9.2 (0.9)	8.8 (2.1)	−0.5 (1.8)	9.1 (0.9)	8.5 (2.0)	−0.7 (1.9)	−0.19	−1.1 to 0.71	NS
HbA1c (%)	5.9 (0.5)	6.0 (0.5)[b]	0.18 (0.3)	5.8 (0.7)[c]	6.0 (0.7)	0.2 (0.4)	0.001	−0.17 to 0.17	NS
K_{ITT}	2.0 (0.7)[c]	1.9 (0.8)[c]	−0.86 (0.6)	1.9 (0.7)	2.0 (0.8)[c]	0.05 (0.8)	0.91	−0.22 to 0.49	NS
HOMA	3.8 (2.3)[d]	4.1 (2.4)[d]	0.3 (1.4)	3.6 (1.9)[e]	2.8 (1.4)[e]	−0.7 (1.3)	−0.99	−1.7 to −0.25	0.01
Fasting insulin (mU/l)†	11.9 (9.5–14.8)[e]	12.4 (9.7–15.7)[f]	0.9 (4.4)	11.4 (9.6–13.7)[c]	9.4 (8.0–11.0)[g]	−2.5 (4.2)	−3.4	−5.8 to 1.1	0.005
2-h insulin (mU/l)†	77.6 (56.0–107.5)[e]	75.0 (53.3–105.6)[f]	−0.7 (44.5)	79.5 (61.8–102.2)[c]	51.3 (38.9–67.7)[g]	−34.8 (72.5)	−34.1	−66.2 to −2.1	0.037
Fasting C-peptide† (nmol/l)	0.73 (0.6–0.9)[e]	0.79 (0.7–0.9)[f]	0.04 (0.2)	0.72 (0.6–0.9)[g]	0.68 (0.6–0.8)[c]	−0.1 (0.3)	−0.14	−0.3 to 0.002	0.053
2-h C-peptide† (nmol/l)	3.1 (2.6–3.9)[e]	3.4 (2.8–4.1)[f]	0.2 (1.0)	3.2 (2.6–3.8)[c]	2.9 (2.5–3.3)[g]	−0.5 (1.5)	−0.07	−1.4 to −0.02	0.044

[a] Values are mean (S.D.) except those marked †, which are geometric mean (95% CI); d^1 and d^2 = difference between baseline and 6 months in the control and intervention groups, respectively; P values and 95% CI are for $d^2 - d^1$.
[b] $n = 31$.
[c] $n = 30$.
[d] $n = 25$.
[e] $n = 28$.
[f] $n = 29$.
[g] $n = 34$.

Table 5
Mean and mean differences in lipids between baseline and 6 months in the control and intervention groups[a]

	Control ($n = 32$)			Intervention ($n = 35$)			$d^2 - d^1$	95% CI for $d^1 - d^2$	P
	Baseline	6 months	d^1	Baseline	6 months	d^2			
Total cholesterol (mmol/l)	5.7 (1.0)[b]	5.5 (1.0)	−0.18 (0.59)	5.7 (1.2)[c]	5.5 (1.2)	−0.16 (0.55)	0.02	−0.26 to 0.31	NS
HDL cholesterol (mmol/l)	1.1 (0.36)[b]	1.2 (0.34)[b]	0.06 (0.21)	1.2 (0.42)[d]	1.2 (0.43)[c]	0.04 (0.19)	−0.02	−0.12 to 0.08	NS
LDL cholesterol (mmol/l)	3.5 (1.0)[b]	3.3 (1.0)[b]	−0.21 (0.61)	3.6 (1.1)[e]	3.5 (1.1)[c]	−0.10 (0.54)	0.1	−0.18 to 0.41	NS
Triglycerides (mmol/l)†	2.2 (1.9–2.5)[b]	2.1 (1.8–2.5)	−0.01 (0.67)	1.9 (1.6–2.2)[c]	1.7 (1.4–2.0)	−0.22 (0.78)	−0.23	−0.59 to 0.13	NS
Fasting NEFA (mmol/l)	0.64 (0.18)[f]	0.70 (0.17)[g]	0.06 (0.19)	0.75 (0.21)[h]	0.62 (0.17)[i]	−0.13 (0.15)	−0.19	−0.29 to −0.08	0.001
Apolipoprotein A-1 (g/l)	1.5 (0.26)[b]	1.5 (0.26)	0.03 (0.15)	1.5 (0.36)[c]	1.6 (0.37)	0.05 (0.19)	0.01	−0.07 to 0.10	NS
Apolipoprotein B (g/l)	1.1 (0.27)[b]	1.1 (0.27)	−0.05 (0.16)	1.1 (0.27)[c]	1.1 (0.30)	−0.03 (0.23)	0.02	−0.08 to 0.12	NS
Fibrinogen (g/l)	3.5 (0.87)	3.5 (0.83)	0.03 (0.70)	3.6 (0.77)[c]	3.7 (0.93)[c]	0.14 (0.92)	0.11	−0.29 to 0.52	NS

[a] Values are mean (S.D.) except those marked †, which are geometric mean (95% CI); d^1 and d^2 = difference between baseline and 6 months in the control and intervention groups, respectively; P values and 95% CI are for $d^2 - d^1$.
[b] $n = 31$.
[c] $n = 34$.
[d] $n = 32$.
[e] $n = 33$.
[f] $n = 26$.
[g] $n = 27$.
[h] $n = 30$.
[i] $n = 29$.

difference in change between groups was significant (difference −0.19 (−0.29 to −0.08) mmol/l, $P = 0.001$).

4. Discussion

4.1. Interpretation

This is the largest trial investigating the effectiveness of dietary and physical activity counselling in individuals with IGT (present on two consecutive OGTTs) in the UK. The null hypothesis was rejected for the effect of dietary and exercise counselling on nutrient intake, physical activity uptake, cardiovascular risk factors and insulin sensitivity, but accepted for the effect on glucose tolerance. We have found improvements in dietary fat intake, physical activity uptake, body mass, systolic blood pressure and insulin sensitivity as a result of the intervention. We did not observe a significant change in fasting and 2-h plasma glucose levels or differences in the incidence of diabetes between groups.

The Da Qing study showed a clear difference in the incidence of diabetes between treatment and control groups irrespective of whether diabetes was defined using fasting or 2-h plasma glucose level [25]. It may be that with longer term follow-up, differences in change in plasma glucose and lipoprotein concentrations between the intervention and the control groups will be found. At present our findings at least partly support the evidence from the Da Qing [25] and DPS in Finland [26], which suggest that diet and physical activity interventions can modify risk factors for CHD in subjects with IGT.

The 78 participants recruited to our study had age and sex characteristics very similar to European participants with IGT recruited to a recent population based study [27]. Although our recruitment was from different sources, this suggests that our results may be generalisable to other populations of European origin with IGT.

We observed a significant decrease in total dietary fat intake in intervention participants (−19.6%), greater than in earlier studies in which decreases of 6–8% have been found [2] [28]. Reducing dietary fat, in particular saturated fat, was an important dietary education message for intervention participants [22,29]. Interestingly, intakes of MUFA and PUFA decreased significantly in intervention participants, in contrast to saturated fatty acids for which a non-significant reduction was achieved in the intervention group. Dietary measurement error, particularly in the overweight, is a potential problem in studies of this kind [30]. In total, 23/67 (34%) participants at baseline and 29/67 (43%) participants after 6 months reported a ratio of dietary energy intake relative to predicted basal metabolic rate of less than 1.1, suggestive of underreporting [31]. Excluding these participants strengthened the change in favour of the intervention, although due to small numbers these participants were maintained in our analyses. Further analysis is in progress to validate the 4-day food diary measurements using urinary biomarkers of nutrient intake [32,33].

There was no improvement in fitness assessed by the shuttle walking test; however, we observed a significant increase in self-reported vigorous physical activity assessed by questionnaire in the intervention but not the control group (+26.5 vs. −3.2%), which is comparable with other studies [28]. Although an externally validated method of measuring change in physical activity, such as heart rate monitoring, may have provided more reliable data, the difference in self reported activity between the intervention and control groups is consistent with the significant difference in change in resting pulse between these groups.

We found a small but significant decrease in weight in intervention participants compared with controls (−1.5 vs. −0.5 kg).This is less than the results of the Finnish DPS after 1 year of follow-up (−4.9 vs. −0.9 kg) [26]. Moderate weight loss in obese individuals is associated with improvements in a number of cardiovascular risk factors including blood pressure [34,35]. Consistent with this, we found a significant drop in systolic blood pressure in intervention compared with control participants (−7.9 vs. −0.27 mmHg). Interestingly, there were no differences in these findings when results were analysed separately in obese compared with non-obese participants. The Finnish DPS found similar changes in systolic

blood pressure after 1 year of follow-up (− 7.0 vs. 2.0 mmHg) [26]. We cannot exclude the possibility that greater familiarisation of intervention participants with the intervention team, which occurred during review appointments, compared with controls contributed to the decrease we observed in blood pressure.

Fasting serum insulin concentration is highly negatively correlated with insulin sensitivity in non-diabetic individuals [36]. We observed a significant difference in change between groups in fasting serum insulin concentrations and in HOMA, suggesting the intervention improved insulin sensitivity. There is conflicting evidence as to whether stimulated insulin sensitivity improved, however. The short ITT results showed no improvement but the reduced post-glucose load 2-h serum insulin and C-peptide concentrations suggest an increase in sensitivity as a result of the intervention. A possible explanation is that after 6 months there is a shift in the insulin sensitivity curve with a significant improvement in basal sensitivity but no significant change in maximal capacity. Further follow-up is necessary to investigate whether maximal insulin sensitivity improves in the longer term.

Earlier studies have reported that elevated NEFA concentrations are frequently found in insulin resistant individuals [37]. Consistent with the improvements we observed in basal insulin sensitivity, we found fasting plasma NEFA concentrations decreased significantly in intervention but not control participants. Further analysis is needed to determine whether the improvements in insulin sensitivity are the cause of, or result from, improvements in fatty acid metabolism as indicated by the decrease in NEFA concentrations.

4.2. Limitations

The main limitation of our study is the lack of power to examine health outcomes rather than risk factors for CHD. Larger studies, with sufficient power to test the hypothesis that lifestyle interventions for people with IGT can prevent Type 2 DM, are now underway in Europe and the USA [26,38].

Our speed of recruitment was slower than expected, which meant that we were only able to recruit 78 participants instead of the 100 originally intended. This was due to the difficulty of identifying individuals with IGT on two consecutive OGTTs (necessary because of the low reproducibility of 2-h plasma glucose [39,40]). Despite this, we were able to detect statistically significant changes in cardiovascular risk factors and the study adds to the previous research in this field.

4.3. Implications

The results of this study indicate that interventions, which use the stages of change model and are potentially applicable in primary care, can result in reduced risk factors for CHD and Type 2 DM in individuals with IGT after 6 months. The feasibility of screening for IGT in primary health care needs to be studied although there is some evidence that this could be done cost effectively [41,42]. Further investigations of the manpower and financial resources needed to motivate high risk individuals are needed to demonstrate that the interventions are transferable to Primary Health Care for the treatment of people with IGT.

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