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

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Summary

Background **The susceptibility to type 2 diabetes of people of south Asian descent is established, but there is little trial-based evidence for interventions to tackle this problem. We assessed a weight control and physical activity intervention in south Asian individuals in the UK.**

Methods **We did this non-blinded trial in two National Health Service (NHS) regions in Scotland (UK). Between July 1, 2007, and Oct 31, 2009, we recruited men and women of Indian and Pakistani origin, aged 35 years or older, with waist circumference 90 cm or greater in men or 80 cm or greater in women, and with impaired glucose tolerance or impaired fasting glucose determined by oral glucose tolerance test. Families were randomised (using a random number generator program, with permuted blocks of random size, stratified by location [Edinburgh or Glasgow], ethnic group [Indian or Pakistani], and number of participants in the family [one *vs* more than one]) to intervention or control. Participants in the same family were not randomised separately. The intervention group received 15 visits from a dietitian over 3 years and the control group received four visits in the same period. The primary outcome was weight change at 3 years. Analysis was by modified intention to treat, excluding participants who died or were lost to follow-up. We used linear regression models to provide mean differences in baseline-adjusted weight at 3 years. This trial is registered, number ISRCTN25729565.**

Findings **Of 1319 people who were screened with an oral glucose tolerance test, 196 (15%) had impaired glucose tolerance or impaired fasting glucose and 171 entered the trial. Participants were in 156 family clusters that were randomised (78 families with 85 participants were allocated to intervention; 78 families with 86 participants were allocated to control). 167 (98%) participants in 152 families completed the trial. Mean weight loss in the intervention group was 1·13 kg (SD 4·12), compared with a mean weight gain of 0·51 kg (3·65) in the control group, an adjusted mean difference of –1·64 kg (95% CI –2·83 to –0·44).**

Interpretation **Modest, medium-term changes in weight are achievable as a component of lifestyle-change strategies, which might control or prevent adiposity-related diseases.**

Funding **National Prevention Research Initiative, NHS Research and Development; NHS National Services Scotland; NHS Health Scotland.**

Introduction

The susceptibility to type 2 diabetes of people of south Asian descent was established in the UK in 1985.[1] There is little trial-based evidence for interventions to tackle this problem[2–4] although existing consensus guidelines emphasise weight management through dietary change and physical activity.[3,5,6] This approach has been shown to be effective in 3-year intervention trials of diabetes prevention programmes in other ethnic groups in several countries including China,[7] Finland,[8] the USA,[9] and India,[2] and is, arguably, cost effective.[10] Systematic reviews show that achieving sustained weight management (with or without increased physical activity) is difficult.[11,12] Intensive lifestyle interventions, however, can reduce progression from prediabetes (impaired glucose tolerance or impaired fasting glucose, or both) to diabetes by up to 60% over 3 years.[10,13,14]

Two lifestyle intervention trials are particularly relevant to people from south Asia. In the US Diabetes Prevention Programme,[9] effects were shown across all ethnic groups, including Asians (a mix of ethnic groups, including some south Asian individuals). Participants in the Indian Diabetes Prevention Programme showed slight weight gain overall but had a 28·5% reduced risk of progression to diabetes.[2] A systematic review of four pragmatic interventions suggested some promise and called for culturally tailored trials.[4]

The Prevention of Diabetes and Obesity in South Asians (PODOSA) study aimed to test the effectiveness of a family-based 3-year programme promoting weight loss and increased physical activity in individuals of south Asian descent living in the UK.

Methods

Study design and participants

We did this non-blinded, family-cluster randomised controlled trial in the National Health Service (NHS)

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For the **study protocol** see http://www.podosa.org/Resources.html

Lothian and NHS Greater Glasgow and Clyde Health Board regions (Scotland, UK). We identified participants at high risk of developing diabetes through screening using an oral glucose tolerance test. Recruitment into screening used a multipronged approach and took place between July 1, 2007, and Oct 31, 2009.[15] Recruitment via the NHS included direct referrals from health-care professionals and written invitations to potential recruits via general practices. Recruitment within the community was done by the research team and through partnerships (including small payment) with local south Asian organisations and individuals. Participants were encouraged to refer friends and family throughout the recruitment period. Self-identified men and women of Indian or Pakistani origin aged 35 years or older were eligible for screening if: their waists measured 90 cm or greater in men and 80 cm or greater in women; there was no diagnosis of diabetes (other than gestational diabetes); and the family cook was cooperative. The age and waist size cutoffs were to target screening at those at higher risk of impaired glucose tolerance or impaired fasting glucose. Participants receiving long-term oral corticosteroids, or weight loss medication, or with health disorders making adherence contraindicated or improbable, or pregnant, or who were unlikely to remain in the UK for 3 years, were excluded.

Screening participants were enrolled into the full trial if they had impaired glucose tolerance or impaired fasting glucose according to WHO criteria.[16] We invited adult relatives (known as family volunteers) to support participants in behaviour change. Eligible family volunteers were aged 18 years or older and reported interacting with participants at least weekly.

Individuals gave written, informed consent before undertaking screening and participants and family volunteers gave written, informed consent to trial dietitians before randomisation. Ethics approval was granted by the Scotland A Research Ethics Committee (07-MRE10-2). Outcomes were reviewed annually by a Data Monitoring and Ethics Committee.

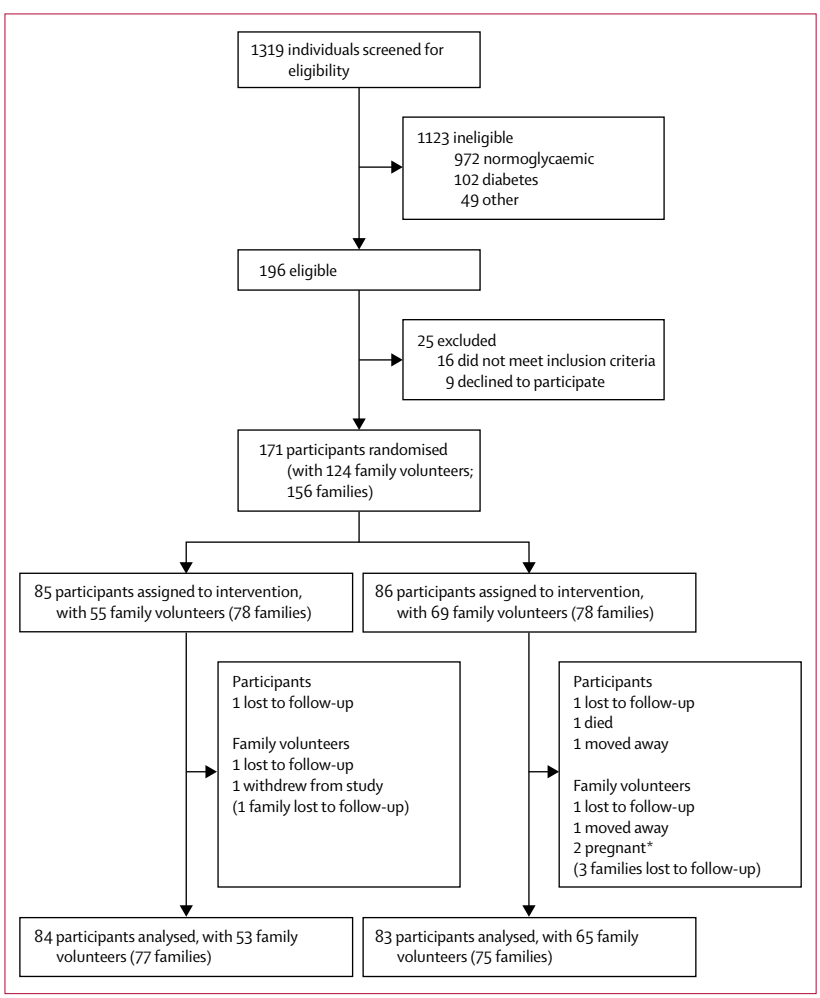

Figure 1: **Trial profile**
*Two family volunteers did not have their weight measured at 3 years because of pregnancy.

Randomisation and masking

We mapped each extended family unit. First degree relatives (parents, siblings, children) living in the same city were not randomised separately. The randomised family consisted of the participant (or participants) plus any family volunteers. Families were randomised in a 1:1 ratio to intervention or control. Randomisation lists were produced by the trial statistician (GDM) using a random number generator program. Permuted blocks were used and block size varied randomly. Stratification was by location (Edinburgh or Glasgow), ethnic group (Indian or Pakistani), and number of participants in the family (one *vs* more than one). When an eligible participant was recruited, the study manager sent an e-mail to the trial statistician, who replied giving the randomised group allocation. There was no masking of group status except for the 3-year measure of weight, waist size, and hip size by independent research nurses.

Procedures

The intervention was consultation with a dietitian; both participants and family volunteers were part of this intervention (appendix pp 5–10 summarise the contents of the intervention). Dietitians were trained in venepuncture, anthropometric and blood pressure measurement, delivery of information, behaviour change using the stages of change model,[17] and promotion of physical activity. Each family was mostly seen by the same dietitian throughout the study.

Families in the intervention group had 15 visits from a dietitian over 3 years (baseline, monthly for the first 3 months, then every 3 months (which is comparable with previous similar trials[2,7,8]). The dietitians advised participants and family volunteers on achieving weight loss through a calorie-deficit diet and physical activity of at least 30 min daily brisk walking, using culturally

adapted and translated resources, including the Counterweight Programme.[18] Details of cultural adaptation are reported elsewhere.[19] Other advice included information on shopping and cooking (with demonstrations). 3-day food diaries and a dietary patterns questionnaire were used to collect data to inform dietitians' advice. Participants were invited to attend annual group sessions, including a food shopping tour and brisk walking. Pedometers were given to the participants to provide step counts for motivation through self-monitoring and for the dietitians to assess progress. Bodyweight and waist circumference data, and the Chester step test,[20] were used as motivational devices by dietitians.

The control group was given standardised written and verbal advice on healthy eating, diabetes prevention, promotion of physical activity, and on accessing other weight control and physical activity services over four visits (baseline, then annually) with a dietitian. This advice aimed to halt increasing weight.[21]

In both the intervention and control groups family volunteers were asked to follow the advice given and to help the participants to follow it.

For all participants, at the 1-year, 2-year, and 3-year visits dietitians collected anthropomorphic data (weight [to the nearest 100 g] and height, and hip and waist circumferences [to the nearest cm]), and blood samples following standard operating procedures. At the 3-year visit, dietitians administered a 75 g oral glucose tolerance test and research nurses masked to study group repeated the anthropometric measurements. The nurses' measurements were used for the primary outcome analysis. Dietitians' measurements were used for all secondary outcomes. The oral glucose tolerance test followed standardised procedures, with venous blood taken after an overnight fast of 10–16 h and 2 h after glucose load, and was analysed in accredited laboratories. Weight, height, and waist and hip circumferences were measured at baseline and annually in family volunteers.

Physical activity was assessed in participants only by the short form of the International Physical Activity Questionnaire (IPAQ).[22] Data were also collected for prescribed medications and for adverse outcomes perceived by participants to be related to the intervention. We sought consent from participants to access information about diagnosis and diabetes from their general practitioners.

We did a cost analysis from a societal perspective, including health-service costs and the opportunity cost of time for trial participants. We excluded initial screening and trial recruitment costs. Health-service costs were the number and length of visits reported by dietitians and health-service use reported by participants. We valued dietitians' time using NHS salary and overheads and general practitioner visits and hospital clinic attendances using NHS unit costs.[23]

	Intervention group	Control group
Family-level summary		
Number of families	78 (100%)	78 (100%)
One recruit with IGT or IFG	71 (91%)	72 (92%)
Two recruits with IGT or IFG	7 (9%)	5 (6%)
Four recruits with IGT or IFG	0	1 (1%)
Number of families with family volunteers	41 (53%)	44 (56%)
Individual-level summary, trial participants		
Number of individuals with IGT or IFG	85 (100%)	86 (100%)
Sex		
Men	39 (46%)	39 (45%)
Women	46 (44%)	47 (45%)
Age (years)		
Mean (SD)	52·8 (10·2)	52·2 (10·3)
Range	37–80	35–78
Location		
Glasgow	66 (78%)	66 (77%)
Edinburgh	19 (22%)	20 (23%)
Ethnic group		
Indian	29 (34%)	28 (33%)
Pakistani	56 (66%)	58 (67%)
Religion		
Muslim	55 (65%)	59 (69%)
Hindu	6 (7%)	9 (10%)
Sikh	23 (27%)	16 (19%)
Other	1 (1%)	2 (2%)
Family cook was a participant	43 (51%)	42 (49%)
Family history of diabetes	60 (71%)	60 (70%)
Years lived in UK	32·0 (12·7)	30·8 (13·5)
Education		
No qualifications	32 (38%)	24 (28%)
School level	23 (27%)	26 (30%)
Further or higher	30 (35%)	36 (42%)
Currently smokes or chews tobacco	6 (7%)	5 (6%)
Currently drinks alcohol	8 (10%)	10 (12%)
Vegetarian	12 (15%)	12 (14%)
Min physical activity per day (median [IQR])		
MET.min*	446 (66–1095)	281 (120–660)
Total (moderate, vigorous, walking)	125 (20–300)	75 (30–180)
Moderate and vigorous only	0 (0–60)	0 (0– 60)
Walking only	60 (0–210)	50 (0–100)
Sitting time (h per day)	6 (4–8)	6 (4–9)
Number achieving 30 min total activity per day	32 (38%)	17 (20%)
Number achieving 150 min total activity per week	39 (46%)	24 (28%)
IPAQ activity category		
Low	51 (60%)	69 (80%)
Moderate	32 (38%)	14 (16%)
High	2 (2%)	3 (3%)
Height (cm)	161·3 (10·5)	162·5 (7·8)
Weight (kg)	79·8 (16·2)	80·7 (15·0)
BMI (kg/m²)	30·6 (5·0)	30·5 (4·6)
Waist circumference (cm)	102·7 (11·2)	103·3 (11·0)

(Continues on next page)

	Intervention group	Control group
(Continued from previous page)		
Hip circumference (cm)	106·9 (9·4)	107·3 (9·6)
Waist to hip ratio	0·96 (0·06)	0·96 (0·07)
BMI category (kg/m^2)		
<25	9 (11%)	11 (13%)
≤25 to <30	38 (45%)	29 (34%)
≥30	38 (45%)	46 (53%)
Systolic blood pressure (mm Hg)	136·9 (21·8)	137·0 (19·7)
Diastolic blood pressure (mm Hg)	82·7 (12·5)	83·5 (10·7)
Fasting plasma glucose (mmol/L)	5·8 (0·6)	5·8 (0·6)
2-h plasma glucose (mmol/L)	8·2 (1·6)	8·3 (1·5)
Present medications		
Cholesterol lowering	14 (16%)	25 (29%)
Antihypertensive	21 (25%)	27 (31%)

Data are n (%) or mean (SD) unless otherwise specified. IGT=impaired glucose tolerance. IFG=impaired fasting glucose. IPAQ=International Physical Activity Questionnaire. *MET.min is metabolic equivalents calculated as vigorous activity × 8, moderate activity × 4, and walking × 3·3.

Table 1: **Baseline characteristics of families and participants**

Participants' time included the dietitians' visits, time for moderate physical activity (from IPAQ), and the household's time for food shopping and meal preparation as reported by participants to dietitians. We used median hourly wages by sex and ethnicity reported by the National Equality Panel–Labour Force Survey.[24] Cost was calculated using a 3·5% annual rate of discount and reported using 2011 pay and price levels.

Outcomes

When the trial was designed, we intended that the primary outcome would be incidence of type 2 diabetes. However, after recruitment to the trial started in 2007, we noted that recruitment to screening was slower than expected and the prevalence of impaired glucose tolerance and impaired fasting glucose was lower than predicted, making it difficult to obtain the necessary sample size. The primary outcome of the trial was, therefore, altered on June 29, 2009, to change in weight at 3 years to ensure sufficient statistical power, in agreement with the Trial Steering Committee, Data Monitoring and Ethics Committee, and funders. Weight change at 3 years was included in the original protocol as a secondary outcome. Despite the amendment, the trial name, PODOSA, was retained.[25]

In the revised protocol, the secondary outcomes in participants were: changes in oral glucose tolerance test, progression to type 2 diabetes, BMI, waist circumference, and hip circumference, all at 3 years. HbA_{1c} was not measured because its use for diagnosis of diabetes was introduced in the UK after the trial had commenced. Secondary outcomes in family volunteers were change in weight, BMI, and waist and hip circumference at 3 years. Cost effectiveness of the intervention was included as a secondary outcome; however, as a full analysis was not possible with the trial data, we report here only within-trial costs.

Statistical analysis

When the protocol was amended in 2009, we knew that the number of families with more than one person recruited with impaired fasting glucose or impaired glucose tolerance was small, so the new power calculation did not take clustering into account. A sample of 150 people assessed at 3 years gave 86% power to detect a mean difference in weight of 2·5 kg between the two groups, assuming an SD of 5 kg with a two-sided 5% significance level.

Analyses were by modified intention to treat, excluding participants who died or were lost to follow-up, following a written analysis plan. In estimating the intraclass correlation coefficient the relevant variance component was negative, so by convention, the estimated intraclass correlation was taken to be zero. The primary outcome was analysed using a random effects, linear regression model with maximum likelihood estimation. The model was adjusted for the stratification variables of ethnicity and location. Change over time was incorporated by adjusting for baseline values in the model. The analysis did not include time as a fixed effect. Since the primary outcome measure was weight loss at 3 years, only the baseline weights and 3-year weights were included in the main analysis. Intervention or control group was a fixed effect. Results for continuous variables include an adjusted (for ethnicity and location) mean difference between baseline and 3 years, with a 95% CI and corresponding p value. For proportions, we fitted a generalised linear mixed model with terms for stratification variables and intervention or control group as described.

The time and costs related to dietitians, costs related to general practitioner and hospital outpatients, and participants' opportunity costs were described (without inferential statistics) by year and for the 3 years combined as appropriate. The conditional mean cost comparison between groups was modelled using linear regression and generalised linear parametric methods. We generated a bias-corrected bootstrap estimate of the difference in costs using standard methods.

We used SAS (version 9.3) for the analyses. This trial is registered, number ISRCTN25729565.

Role of the funding source

The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. A representative of the funders, National Prevention Research Initiative (Medical Research Council), was a member of the Trial Steering Group. Raw data were accessed by the trial manager (AD) and a statistician who was independent of the conduct of the trial (IB). The corresponding author had full access to all the data in the study and the final responsibility for the decision to submit for publication.

	Baseline	Year 1	Year 2	Year 3	Adjusted mean difference (95% CI)	p value
Anthropometry						
Weight (kg)						
Intervention	79·77 (16·23)	78·82 (16·11)	79·09 (15·94)	78·76 (16·57)	−1·64 (−2·83 to −0·44)	0·0076
Control	80·68 (14·98)	80·36 (14·80)	80·96 (15·10)	80·99 (15·34)	..	..
BMI (kg/m²)						
Intervention	30·59 (5·02)	30·18 (5·04)	30·31 (5·15)	30·18 (5·50)	−0·60 (−1·06 to −0·14)	0·0112
Control	30·49 (4·60)	30·39 (4·56)	30·57 (4·84)	30·65 (4·83)	..	..
Waist circumference (cm)						
Intervention	102·69 (11·16)	101·55 (11·34)	102·04 (11·22)	100·51 (11·51)	−1·89 (−3·27 to −0·52)	0·0072
Control	103·26 (11·01)	103·45 (11·66)	103·43 (11·19)	102·85 (11·14)	..	..
Hip circumference (cm)						
Intervention	106·85 (9·43)	105·68 (9·53)	105·95 (9·64)	104·48 (9·77)	−1·54 (−2·71 to −0·37)	0·0101
Control	107·34 (9·55)	106·90 (9·23)	107·26 (9·91)	106·67 (9·16)	..	..
Waist to hip ratio						
Intervention	0·96 (0·06)	0·96 (0·07)	0·96 (0·07)	0·96 (0·07)	−0·00 (−0·01 to 0·01)	0·6756
Control	0·96 (0·07)	0·97 (0·07)	0·97 (0·07)	0·96 (0·06)	..	..
Glycaemia						
Fasting plasma glucose (mmol/L)						
Intervention	5·77 (0·61)	..	..	5·84 (0·77)	−0·13 (−0·39 to 0·13)	0·3361
Control	5·82 (0·61)	..	..	5·98 (1·04)	..	..
2-h plasma glucose (mmol/L)						
Intervention	8·21 (1·63)	..	..	7·38 (2·49)	−0·56 (−1·32 to 0·19)	0·1428
Control	8·33 (1·51)	..	..	8·05 (2·56)	..	..
Blood pressure						
Systolic (mm Hg)						
Intervention	136·9 (21·78)	135·7 (16·64)	135·6 (18·40)	137·2 (18·73)	−1·19 (−5·50 to 3·12)	0·5856
Control	137·0 (19·66)	137·0 (19·55)	135·7 (16·21)	138·8 (17·95)	..	..
Diastolic (mm Hg)						
Intervention	82·7 (12·51)	81·6 (10·09)	80·8 (10·66)	81·3 (10·72)	−0·45 (−3·26 to 2·36)	0·7541
Control	83·5 (10·69)	82·6 (12·18)	81·6 (10·34)	82·7 (11·23)	..	..

N=84 for intervention group; N=83 for control group. Data are mean (SD) unless otherwise specified. Mean differences are adjusted for stratification variables at randomisation (ethnic group, city) and for corresponding baseline value.

Table 2: **Comparison between anthropometric, glycaemic, and blood pressure measures**

Results

2089 people were referred for screening, 1319 of whom were eligible, available, and agreed to be screened. The community-orientated, personal approaches to recruitment were the most successful yielding 1728 referrals (83%) to the screening stage. The response to written invitations via general practitioners was comparatively low at 265 of 5071 (5%). Of 1319 people who were screened (including an oral glucose tolerance test), 196 (15%) had impaired glucose tolerance or impaired fasting glucose and 171 entered the trial as participants (figure 1). The participants and 124 family volunteers were in 156 family clusters that were randomised (78 families with 85 participants and 55 family volunteers were allocated to intervention; 78 families with 86 participants and 69 family volunteers were allocated to control). 167 (98%) participants in 152 families and 118 (95%) family volunteers completed the trial.

Table 1 shows that at baseline the groups were much the same in terms of number of recruits per family and proportion with family volunteers. Details of recruitment and baseline characteristics have been reported previously.[15,25] The groups were much the same in terms of individual level variables, except for physical activity (more in intervention group) and cholesterol-lowering medication (less in intervention group). The characteristics of family volunteers were much the same in the two groups (appendix pp 5–6).

See Online for appendix

Data completeness for key variables was almost 100% (appendix p 7) and the dietitian visits were mostly completed as planned for participants (appendix p 8): the mean number of visits for the intervention group was 13·7 (SD 2·1) and for the control group was 3·9 (SD 0·3). The main reason for missed visits was being away from home. Family volunteers were usually present at annual visits but not at other visits (appendix

p 8). One participant and two family volunteers in the intervention group, and three participants and four family volunteers in the control group died or were lost to follow-up and were excluded from the analyses (figure 1).

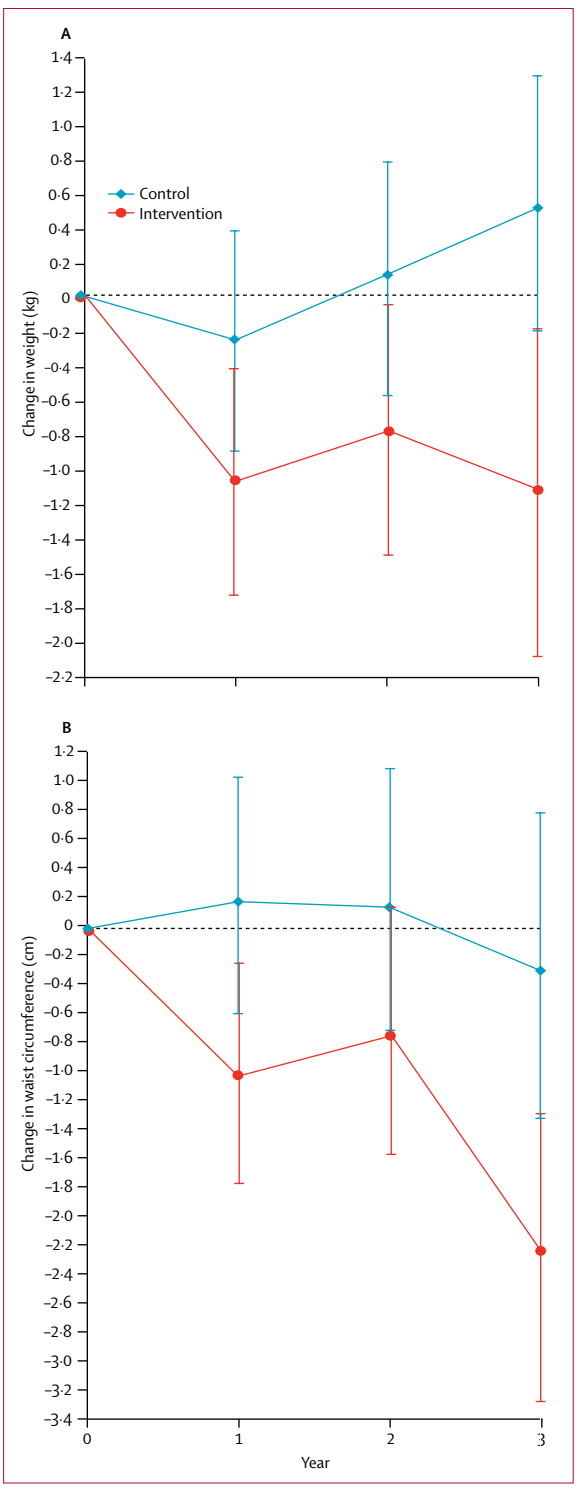

Figure 2: **Mean change in (A) weight and (B) waist circumference from baseline over 3 years**
Error bars are 95% CI.

Table 2 and figure 2A show that participants in the intervention group lost more weight than those in the control group by year 1 and sustained this advantage at year 3. The control group lost weight in year 1 but gained weight overall (mean weight loss in the intervention group was 1·13 kg [SD 4·12], compared with mean weight gain of 0·51 kg [3·65] in the control group). The adjusted mean difference at 3 years was –1·64 kg (95% CI –2·83 to –0·44) for the intervention group compared with the control group (p=0·0076). Secondary analysis including adjustment for baseline IPAQ activity category (low, moderate, or high) gave an adjusted mean difference of –1·64 kg (95% CI –2·89 to –0·40). Secondary analysis using dietitians' measures of 3-year weight gave an adjusted mean difference of –1·64 kg (–2·84 to –0·44). The pattern was much the same for BMI (table 2), waist circumference (table 2, figure 2B), and hip circumference (table 2). Fasting glucose increased slightly in both

	Number (%)	Adjusted odds ratio (95% CI)	p value
Diabetes*			
Progression to type 2 diabetes			
Intervention	12 (15%)	0·68 (0·27–1·67)	0·3705
Control	17 (21%)	..	..
Doctor diagnosed			
Intervention	10 (12%)	..	..
Control	10 (12%)	..	..
Based on 3 year OGTT			
Intervention	2 (2%)	..	..
Control	7 (9%)	..	..
Reverting to NGT			
Intervention	36 (44%)	1·23 (0·62–2·47)	0·5294
Control	32 (39%)	..	..
Weight change†			
Losing ≥2·5 kg			
Intervention	33 (39%)	3·92 (1·68–9·13)	0·0036
Control	12 (14%)	..	..
Losing ≥5% of bodyweight			
Intervention	21 (25%)	6·57 (1·92–22·44)	0·0052
Control	4 (5%)	..	..
Gaining ≥2·5 kg			
Intervention	19 (23%)	1·23 (0·55–2·79)	0·5895
Control	16 (19%)	..	..
Gaining ≥5% of bodyweight			
Intervention	8 (10%)	0·86 (0·29–2·57)	0·7706
Control	9 (11%)	..	..

Odds ratios are adjusted for stratification variables at randomisation (ethnic group, city). OGTT=oral glucose tolerance test. NGT=normal glucose tolerance. *N=81 for intervention group; N=82 for control group. †N=84 for intervention group; N=83 for control group.

Table 3: **Comparison between secondary outcomes relating to diabetes and weight change**

	Baseline	Year 1	Year 2	Year 3	Adjusted odds ratio (95% CI)	Difference in medians† (95% CI)	p value
MET.min*							
Intervention	446 (66–1095)	594 (231–1154)	528 (165–1200)	596 (198–1512)	..	156·0 (0·0 to 343·0)	0·0676
Control	281 (120–660)	398 (120–743)	273 (73–578)	396 (99–1026)	..	..	..
Total physical activity (min per day)							
Intervention	125·0 (20–300)	180·0 (70–315)	150·0 (50–315)	175·0 (60–420)	..	40·0 (0.0 to 95·0)	0·0751
Control	75·0 (30–180)	118 (30–195)	80·0 (20–160)	120·0 (30–280)	..	..	..
Sitting time (h per day)							
Intervention	6·0 (4–8)	6·0 (5–8)	6·0 (5–8)	6·0 (4–7)	..	−1·0 (−2·0 to 0·0)	0·0523
Control	6·0 (4–9)	6·0 (4–9)	7·0 (5–9)	7·0 (5–8)	..	..	..
Number achieving ≥30 min activity per day							
Intervention	32/84 (38%)	38/81 (47%)	32/83 (39%)	36/84 (43%)	1·14 (0·53 to 2·47)	..	0·7201
Control	17/83 (20%)	20/82 (24%)	13/83 (16%)	29/83 (35%)	..	..	..
Number achieving ≥150 min activity per week							
Intervention	39/85 (46%)	48/81 (59%)	42/83 (51%)	46/84 (55%)	1·19 (0·55 to 2·55)	..	0·6382
Control	24/86 (28%)	30/82 (37%)	26/83 (31%)	37/83 (45%)	..	..	..

Data are median (IQR) or n (%). *MET.min is metabolic equivalents calculated as vigorous activity×8, moderate activity×4, and walking×3·3. †Difference in median activity between groups at the final timepoint only, using a Mann Whitney test to for account the skewed nature of the values.

Table 4: **Comparison between groups of physical activity outcomes**

groups whereas 2 h glucose decreased slightly in both groups but neither difference was statistically significant (table 2). Blood pressure remained stable in both groups (table 2).

For family volunteers, weight and other measures of adiposity were mostly stable with no significant differences between the two groups (appendix p 9).

At 3 years, the proportion of participants who had lost 2·5 kg was higher in the intervention group than the control group (table 3) as was the proportion who had lost 5% of their bodyweight (table 3). Weight gain was common in both groups, with 23% of participants in the intervention group and 19% in the control group gaining 2·5 kg or more (table 3). Table 4 shows that there was little difference between groups at 3 years in participants reporting physical activity at the recommended level, with increases between baseline and year 1 in the intervention group and between year 2 and year 3 in the control group.

Progression to diabetes (either doctor diagnosed or by oral glucose tolerance test at 3 years) was observed less frequently in the intervention group than the control group (OR 0·68) but the difference was not statistically significant (95% CI 0·27–1·67; p=0·3705; table 3).

Table 5 shows that 3-year dietitian costs were £1190 for the intervention group and £575 for the control group; annual times and costs are in appendix p 10. The total extra 3-year mean cost for the intervention group was £1126 (95% CI −2414 to 4666), with £615 of that difference being dietitian costs, £324 being NHS general practice and hospital outpatient costs, and £207 being indirect opportunity costs to participants (table 5). Indirect costs were attributable to additional physical activity time, not food preparation or shopping time (appendix pp 10–11). The intervention group had 12·4 h of dietitian contact per family, which required 17·8 h of preparation and travel time—totalling 30·2 h, about double that in the control group (appendix p 10). Primary-care visits and costs did not differ between groups, but there were more outpatient visits in the intervention group than in the control group (costing £327 more; appendix p 10).

	Intervention	Control	Mean difference (95% CI)	p value
Dietitians	£1190	£575	£615 (561 to 668)	<0·0001
NHS general practice	£1045	£1068	£−23 (−235 to 189)	0·9999
NHS hospital outpatient	£1235	£908	£327 (−107 to 762)	0·1405
Dietitian and NHS costs combined	£3470	£2551	£919 (360 to 1478)	0·0013
Costs to participants	£14 643	£14 437	£207 (−3267 to 3681)	0·9145
Total	£18 113	£16 988	£1126 (−2414 to 4666)	0·5441

Mean 3-year costs per participant to the health service (dietitian visits, NHS general practice and outpatient services), and cost to participants relating to physical activity and food shopping and preparation by group. N=84 for intervention group; N=83 for control group. NHS=National Health Service.

Table 5: **Cost analysis**

Seven adverse events were perceived by participants to be attributable to the intervention (three in the intervention group, four in the control group). Five were mild and two were moderate. The moderate events, defined as interfering with routine activity, were: arthritis in the knee causing pain on walking and worries about changing habits—both occurred in the intervention group.

Discussion

In this study of 171 individuals of south Asian descent living in the UK, a culturally adapted, family-based lifestyle intervention consisting of about 15 visits from a dietitian over 3 years resulted in significantly greater weight loss than did annual contact and simple lifestyle

advice from a dietitian (control). Reductions in BMI and waist and hip circumferences were also significantly greater in the intervention group. The proportion of individuals who lost 2·5 kg over 3 years was higher in the intervention group than in the control group, as was the proportion who lost 5% of their bodyweight. However, about 20% of participants in both groups gained 2·5 kg during the course of the study. Progression to diabetes was observed less frequently in the intervention group than the control group, but the difference was not statistically significant. A cost analysis showed that the additional 3-year cost of the intervention in terms of health-service costs and indirect costs to participants was £1126 per participant.

Individuals tend to gain weight as they age,[12,26] especially after immigration from developing to developed countries. Our trial shows that provision of simple information about diet and lifestyle (as in the control group and family volunteers) did not stop this tendency whereas a tailored, moderate-intensity intervention targeted at those at high risk of developing diabetes counteracted it. The intervention led to modest but sustained weight loss, substantially increased the likelihood of losing at least 2·5 kg, and decreased waist and hip circumferences. These benefits need to be offset against the direct (health care) costs and opportunity costs for participants. Weight loss of 0·5–2·5 kg, especially centrally as shown by a decrease in waist circumference, when combined with some increase in physical activity,[26–29] has beneficial effects on metabolic variables, including potentially enhancing the uptake of glucose by adipose tissue.[9,26,29,30] Our results showing little difference between intervention and control groups in outcomes such as fasting glucose, 2-h postprandial-glucose, and blood pressure, are in line with findings at 3 years from other studies, especially those with similar weight loss.[8,10,29,31–33] In view of the sensitivity of individuals from south Asia from childhood onwards to metabolic disturbances associated with adiposity, weight loss might have equivalent or greater benefits than in populations of European ancestry, although the opposite view has also been postulated.[34] Weight loss had similar benefits in a range of ethnic groups in the US Diabetes Prevention Programme.[9] Sakane and colleagues[30] showed a 54% decrease in diabetes incidence, even though weight loss was small, and postulated that their Japanese population was especially sensitive to adiposity, perhaps through loss of liver fat.

Our trial differed from others in several ways.[8] For example, the intervention was home-based and delivered by dietitians and not by clinic-based staff, families not individuals were randomised, and the support of the family cook was mandatory for enrolment.[19] Dietitians also played a central part in most similar trials (eg, the US Diabetes Prevention Programme[9] and Finnish Diabetes Prevention Study[8]). A family focus is widely recommended (eg, by National Institute for Health and Care Excellence[6]) but trials adopting this recommendation are rare. Family involvement was judged especially important in south Asian individuals in view of the strong cultural emphasis on family life, eating together, and obligations in hospitality, points emphasised in national guidelines.[35] However, we were not able to recruit family volunteers for many families. The added value of family involvement remains to be explored in future studies.

The number of contacts with a dietitian in the intervention group in the present trial emulated the Finnish diabetes prevention study[8] but the content was less intensive and more focused on food and walking. The intensity of the intervention was much less than in the US Diabetes Prevention Programme[9] but was about the same as that in the Indian Diabetes Prevention Programme.[2] Our intervention led to smaller changes in weight, physical activity, and progression to diabetes than in the US[9] and Finnish[8] programmes. Our results are, however, not outliers but are much the same as those for a culturally adapted diabetes prevention programme for Latinos in the USA at 1 year[36] and in the SLIM trial at 3 years.[31] In the Indian Diabetes Prevention Programme[2] in which participants did not lose weight overall, participants had lower BMIs at baseline than those in the present study (average 25·7 kg/m² in the lifestyle intervention group, compared with 30·6 kg/m²

***Panel:* Research in context**

Systematic review

We searched Google Scholar and PubMed/Medline for reports published between Jan 1, 2009, and June 11, 2013, using combinations of the key words "Indian", "Pakistani", "south Asian", "diabetes", "prediabetes prevention", "weight loss", "physical activity", "impaired glucose tolerance", and "impaired fasting glucose". We contacted chief investigators of the DHIANN[37] and Bangladip studies and examined the abstracts of the World Congress of Diabetes Prevention, 2012.

We identified both systematic and narrative reviews of lifestyle interventions for prevention of progression from impaired glucose tolerance and impaired fasting glucose to diabetes;[6,10,14] nutrition interventions;[39] weight management;[12,39–41] promotion of physical activity;[4] and on diabetes in south Asian individuals, including evidence for lifestyle interventions in people from south Asia.[3] One trial, the India Diabetes Prevention Programme,[2] included people with impaired fasting glucose and impaired glucose tolerance and reported 3-year outcomes.

Interpretation

Intensive interventions to prevent progression to diabetes in those with impaired glucose tolerance or impaired fasting glucose through lifestyle change are generally effective and probably cost effective. The scientific literature shows the difficulty of intervening to reduce weight (not achieved in the Indian Diabetes Prevention Programme[2]), prevent weight gain, and increase physical activity in south Asian individuals.[3,4,41] The present study shows that a medium-intensity lifestyle intervention leads to modest but sustained weight loss at 3-year follow-up in south Asian individuals in the UK. A meta-analysis of studies of south Asian populations might be possible after D-CLIP[42] and DHIANN[37] report final-year results. Pending further research, policy makers and practitioners should note that the materials and approaches used in the present study might help to combat adiposity-related disorders but, alone, are an insufficient strategy.

in the present trial). A primary care based trial in south Asian individuals in the Netherlands had an intervention of similar intensity to the present trial, with 0·2 kg weight loss in the intervention group, and no changes in metabolic profiles at 1 year, with no significant differences compared with controls.[37] In a non-randomised assessment of 140 south Asian participants in Khush Dil, a community clinic service intervention in Edinburgh, weight loss at 6-months was about 0·61 kg compared with baseline.[38] More than 20% of participants in the present trial, including in the intervention group, gained more than 2·5 kg over 3 years. We have not found similar data for weight gain from other studies.

The estimate of the effect size on progression to diabetes (OR 0·68, 95% CI 0·27–1·67) was in line with that in the Indian Diabetes Prevention Programme (28% lower risk) and with predictions of reductions in type 2 diabetes on the basis of the effect of small amounts of weight loss in the Finnish US diabetes prevention programmes.[26] However, the difference we observed between groups was not statistically significant.

As far as we are aware, the present trial was the first culturally adapted, community-based, randomised trial of its kind outside India but it aligns with much existing guidance on interventions.[3,6] The strengths of the trial include cross-cultural adaptation,[19] the quality of data, involvement of the family, and high attendance and retention. Weaknesses include alteration to the primary outcome, the modest sample size, and absence of objective measures of physical activity, although the IPAQ has been validated against accelerometry.[22] Other limitations include that the trial only measured glucose at two timepoints, and there was no measure of insulin or HbA_{1c}. Our attempts to engage several members in each family met with little success, with little clustering within families of people with impaired fasting glucose or impaired glucose tolerance and an inability to recruit family volunteers in many families. Future work should investigate why some people lose weight and others gain weight, even in an intervention group; long-term outcomes (through data linkage); cost-effectiveness of interventions in south Asian individuals through meta-analyses (panel); the added value of family-based and home-based interventions compared with individual, clinic-based interventions; and how interventions can be improved. Our trial will contribute to future debates on these matters.

Contributors

RSB, SW, GDM, JFF, ML, JAM, NS, JT, SHW, and AShe designed the trial. IB did the statistical analysis. JBES codesigned and analysed health economics data. JMRG led on physical activity issues. SW, RB, and ASha were the research dietitians who were primarily responsible for study recruitment, screening, and delivery of interventions. RSB and AD (methods section) drafted the report and all authors provided critical commentary and input. Authorship order, with the exception of the last author, reflects overall contribution to the work presented. The last author position reflects the significant contributions of the trial statistician.

Conflicts of interest

JT received research grants, served as a consultant to or a member of advisory boards for, or gave lectures organised by AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly, ImpetoMedical, Merck, MSD, Sanofi-Aventis, Novartis, Novo Nordisk, and Servier. The remaining authors declare that they have no conflicts of interest.

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Stemming the tide of type 2 diabetes and its consequences in south Asian individuals

Globally, individuals of south Asian descent have increased susceptibility to type 2 diabetes.[1] By age 80 years, 50% of south Asian migrants to the UK have diabetes,[2] with a younger age of onset and greater effect on cardiovascular outcomes than European comparators.[3]

What can be done to stem this tide? The Indian Diabetes Prevention Programme,[4] which studied more than 500 people with impaired glucose tolerance, showed a reduction of more than 25% in diabetes incidence over 2·5 years in those randomised to a lifestyle intervention or metformin, alone or in combination, compared with control. In the lifestyle intervention group, no weight loss was noted and increased physical activity seemed to account for the beneficial effects.[4]

In *The Lancet Diabetes & Endocrinology*, Raj Bhopal and colleagues[5] report outcomes of a family-based intervention (PODOSA) in south Asian individuals with impaired glucose tolerance or impaired fasting glucose, living in the UK. This family-cluster randomised controlled trial was initially designed with incidence of diabetes at 3 years as its primary endpoint. Participants were randomised to an intensive lifestyle intervention (15 dietitian visits focussed on diet and physical activity) or control group (four dietitian visits with standardised advice on diet and physical activity). The intervention was culturally adapted and its acceptability to participants is borne out by impressive retention over 3 years. However, in view of unforeseen difficulties in recruitment of the planned 540 participants (because the frequency of impaired glucose tolerance and impaired fasting glucose was lower than expected), after 2 years of recruitment the primary endpoint was changed to weight loss, and only 171 participants were enrolled. At 3 years, there was a small reduction in weight in the intervention group compared with the control group (adjusted mean difference −1·64 kg [95% CI −2·83 to −0·44]). Although more participants in the intervention group lost weight, about 20% of participants in both groups gained more than 2·5 kg in weight. The number of participants achieving the recommended level of physical activity (≥30 min per day) did not differ significantly between groups (odds ratio [OR] 1·14 [95% CI 0·53–2·47]). While underpowered for this outcome, there was a suggestion of reduced incidence of diabetes in the intervention group compared with the control group (OR 0·68 [95% CI 0·27–1·67]).

Having engaged a south Asian population in PODOSA, it would have been informative to include an objective assessment of physical activity using monitors. Additionally, further useful information could have been gained with the inclusion of outcomes such as insulin concentration and bioimpedance measures of body fat and lean mass, which are simple and cost little to implement.

PODOSA showed that in a high-risk group of south Asian individuals, a lifestyle intervention resulted in weight loss. Could the modest weight loss achieved in PODOSA result in reduced progression to diabetes? Both the Finnish[6] and US[7] diabetes prevention trials (the former wholly, the latter largely consisting of participants of European origin), reported substantial reductions in progression to diabetes in response to lifestyle intervention. In both these trials, participants in the intervention groups achieved significant weight loss compared with those in the control groups (3·5 kg and 5·5 kg respectively), and major increases in physical activity. By contrast, in the Indian Diabetes Prevention Programme,[6] although participants in the lifestyle intervention group had substantially reduced progression to diabetes, they had no difference in weight change compared with participants in the control group. However, adherence to an exercise regimen requiring 30 min or more of daily brisk walking increased from 42% to 59%. It is surprising that PODOSA, with little change in physical activity, also hints at reduced progression to diabetes in response to lifestyle intervention (OR 0·68). But confidence limits around this estimate are wide (95% CI 0·27–1·67), and consistent with both a beneficial and harmful effect of the intervention, reflecting the too small sample size for this outcome, so that no definitive conclusions can be drawn. Alternatively, if the hint towards a reduction in diabetes is real, people from south Asia might be more responsive, in terms of diabetes progression, to weight loss than people of European origin. This

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intriguing hypothesis requires testing, and the planned longer term follow up of PODOSA could begin to address this question.

What are the next steps for diabetes prevention research? In view of the fact that half of south Asian migrants will develop diabetes, many in early adulthood, an approach that targets high-risk individuals in late adulthood might be unrewarding. Additionally, there is evidence for transgenerational transmission of diabetes risk.[8] Future trials could adopt the family-based approach tested successfully in PODOSA, but recruit from the entire south Asian population and provide lifestyle advice to all, coupled with a more intense intervention, including medication, for those at highest risk (eg, overweight, family history).

Substantial lifestyle changes are difficult to maintain long term. Crucial periods of development have been identified that strongly contribute to adult disease, including pregnancy, infancy, and adolescence.[9] Animal and limited human data suggest that short-term interventions, including drugs, during these periods might greatly reduce or even eliminate the risk of disease.[10,11] Exploration of the effect of brief interventions during key periods of development offers a methodologically challenging, but potentially rewarding, alternative strategy to reduce the effect of diabetes in south Asian individuals.

Ultimately, the goal of any diabetes prevention strategy is to reduce the burden of complications and especially cardiovascular disease, which causes the most morbidity and mortality, and to which south Asian individuals are particularly susceptible. Endpoints should include cardiovascular risk factors and subclinical cardiovascular disease. Consideration of multiple risk factors should be as embedded in prevention trials as it now is in clinical practice.

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