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**Did the weight loss in the Prevention of Diabetes and Obesity in South Asians (PODOSA) trial differ
by sex? An exploratory analysis.**

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Introduction

Little is known on whether weight loss interventions in pre-diabetic people affect males and females differently as the trials were not designed to test sex differences in adherence or response to intervention. The US Diabetes Prevention Programme (DPP) found greater weight loss in men than women but the difference was not stated (1). A systematic review and meta-analysis on sex-specific differences in diabetes prevention found no evidence of sex differences in weight loss in people with prediabetes although weight loss at 3-years follow-up was greater in men than women (confidence intervals overlapped) (2). In a further systematic review of weight loss interventions, weight loss was found to be greater in men than in women in 80% of studies where a direct comparison was possible. However in these reports, there was a lack of data on whether sex differences with weight loss interventions were evident in individuals of South Asian ethnicity (3). This is of importance given the high risk of diabetes in South Asians and evidence that weight loss interventions may be somewhat less effective in South Asians than other ethnic groups (4-6).

A secondary analysis of the BEACHeS feasibility study in Pakistani and Bangladeshi-origin children suggested sex differences in response to the intervention in South Asian population and emphasizes the need of examining sex differences in future; it showed the intervention reduced adiposity in girls but not boys, with girls in the intervention group gaining less weight, body mass index (BMI), waist circumference central and thigh skinfold than their respective controls ($p < 0.05$) (7). In Scotland, the Prevention of Diabetes and Obesity in South Asian (PODOSA) trial aimed at reducing the risk of developing type 2 diabetes in people from South Asian descent by encouraging weight loss through culturally adapted diet intervention and increase of physical activity (4;8).

There is a need to study sex differences in the effect of weight loss interventions specifically in pre-diabetic South Asian populations. Consequently, as an exploratory post hoc analysis, we aimed to assess whether men or women were more likely to lose weight in the PODOSA trial.

Methods

The PODOSA trial: study design, participants, randomisation and intervention.

The details of the PODOSA trial have been published (4;8). The trial recruited individuals at high risk of developing type 2 diabetes through screening using an oral glucose tolerance test (OGTT). Eligibility for recruitment was being of Indian- or Pakistani-origin, aged 35 years and over, a waist circumference of 90 cm and over for men and 80 cm and over for women, no diagnosis of diabetes and a cooperative family cook. Randomisation was done at the family level, stratified by location (Edinburgh or Glasgow), ethnic group (Indian or Pakistani) and number of participants in the household (one or more than one).

According to the (revised) primary research question approved by ethics committee, the trial steering committee and data monitoring committee in 2009, the trial aim and hence outcome was a clinically meaningful weight loss in the intervention group compared to the control group. The intervention group had 15 visits from a dietitian over 3 years. Dietitians advised on achieving weight loss through a culturally adapted calorie-deficit diet and through moderate physical activity of at least 30 minutes per day. The control group received standardised written and verbal advice on healthy eating, diabetes prevention and promotion of physical activity, over four visits.

Statistical Methods

This analysis focuses on change in weight between baseline and 3-years. Of 171 PODOSA participants, 4 were lost to follow-up, leaving 167. Histogram and Kolmogorov-Smirnov test for normality ($p\text{-value} > 0.15$) indicated change in weight was normally distributed. Mean changes in weight and standard deviations (SD) were calculated and reported by sex and randomisation group. Multivariate linear regression was used to calculate weight change by sex. To assess the effect of the intervention on change in weight by sex, we included the randomisation groups and the interaction term of sex and randomisation group into the model. Analysis was both unadjusted and adjusted for body mass index (BMI) at baseline to account for the initial BMI status of each participant. We report the regression estimates, their 95 % confidence interval (CI) and associated p-values.

Results

The table part A shows that for men, the mean change in weight in the intervention and control groups combined was -1.17 kg (SD 3.69). On average, we observed a moderate weight loss in the intervention group (mean -2.23 kg; SD 3.79) and a trivial weight loss in the control group (mean -0.06 kg; SD 3.27). For women, the mean change in weight in both groups combined was 0.40 kg (SD 4.07) with a slight weight loss in the intervention group (mean -0.18 kg; SD 4.20) but a weight gain in the control group (mean 0.96 kg; SD 3.91). There was, therefore, about an average of 2kg change in weight difference between intervention and control in male and 1 kg in female resulting in about an unadjusted 1kg differential effect of the intervention between male and female.

The table part B shows a statistically significant difference in change in weight between male and female with men losing 1.53 kg (95% CI: [0.32; 2.75]) more on average than women (model 1). The model including sex, randomisation group and their interaction (model 2) showed again a sex effect and a randomisation group effect with on average a greater weight loss in the intervention group. The interaction between sex and randomisation group was 1.04 kg although this was not statistically significant.

Discussion

This additional exploratory analysis on the South Asian participants of the PODOSA trial showed evidence of sex differences with men losing more weight on average than women. We found an effect of the intervention on change in weight as previously reported in the main analysis (4). However, looking at interaction between sex and randomisation group, the differential effect of the intervention between men and women compared to control was not statistically significant though this could be a type 2 error arising from small sample size.

Our finding of greater weight loss in Pakistani and Indian men than women in Scotland aligns with a lifestyle intervention on older Asian Indians in New Zealand which resulted in weight loss in men and women but greater in men (9). Lifestyle intervention leading to more weight loss in men than in women is consistent with previous findings (3) but we found no other lifestyle intervention on

prevention of diabetes specifically in South Asians reporting sex effect or interaction between intervention and sex.

As South Asians experience more insulin resistance than White Europeans at the same level of physical activity level (10), further trials will need to focus on more intensive intervention in South Asian compared to other ethnic group to achieve beneficial health outcomes in both men and women (6;10). The literature and present analysis suggest sex differences in weight loss in pre-diabetic South Asian so further trials should measure the differential impact of the intervention in men and women increasing sample size to allow the detection of an interaction effect. The possibility that interventions might impact differently on men and women needs further study.

Ethical approval

Ethical approval was obtained from the Scotland A Research Ethics Committee (07-MRE10-2) and participants gave written, informed consent prior to screening. This trial is registered, number ISRCTN25729565.

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Competing interest

None declared.

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Table: Mean (SD) change in weight by sex, by randomisation group and both groups combined (part A), and their effect and interaction adjusted for BMI at baseline (part B)

Part A

Sex	Intervention group		Control group		Both groups	
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Men	39	-2.23 (3.79)	37	-0.06 (3.27)	76	-1.17 (3.69)
Women	45	-0.18 (4.20)	46	0.96 (3.91)	91	0.40 (4.07)

Part B

Model	Change in weight (kg) estimate	95% CI	p-value
<i>Model 1: sex effect, adjusted for BMI at baseline</i>			
Sex (Women vs. Men)	1.53	[0.32;2.75]	0.0134
<i>Model 2: sex effect, randomisation group effect and their interaction adjusted for BMI at baseline</i>			
Sex (Women vs. Men)	0.98	[-0.70;2.67]	0.0140
Randomisation group (Intervention vs. Control)	-2.18	[-3.92;-0.43]	0.0060
Interaction between sex and randomisation group	1.03	[-1.33;3.38]	0.3919