

Prevention of diabetes and obesity in South Asians (PODOSA) Trial: key results, lessons and implications

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For the PODOSA Investigators Group



A community-based trial

The advertisement features three individuals against a background of vertical color stripes. On the left is a woman in a yellow and pink sari. In the center is a man with a grey beard and a white cap. On the right is a smiling man in a blue shirt holding a folder. Three speech bubbles contain testimonials. The top right corner has the 'podosa' logo with the tagline 'Prevention of Diabetes & Obesity in South Asians'. A grey banner at the bottom left contains the text '...Get Tested Help Prevent Diabetes!'.

Me and my family received expert advice from a registered dietitian.

The knowledge gained will hopefully benefit millions of people in the UK and South Asians worldwide.

The research team is very keen to work with the South Asian community so that together we can tackle the challenge of preventing diabetes.

**...Get Tested
Help Prevent Diabetes!**

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- * NKS
 - * REACH
 - * MEHIP
 - * MCS
 - * Al Meezan
 - * Our community recruiters
 - * Faith organisations
 - * Community groups in Edinburgh and Glasgow
 - * Trial steering committee
 - * Data monitoring and ethics committee

My first principles thinking in 1984

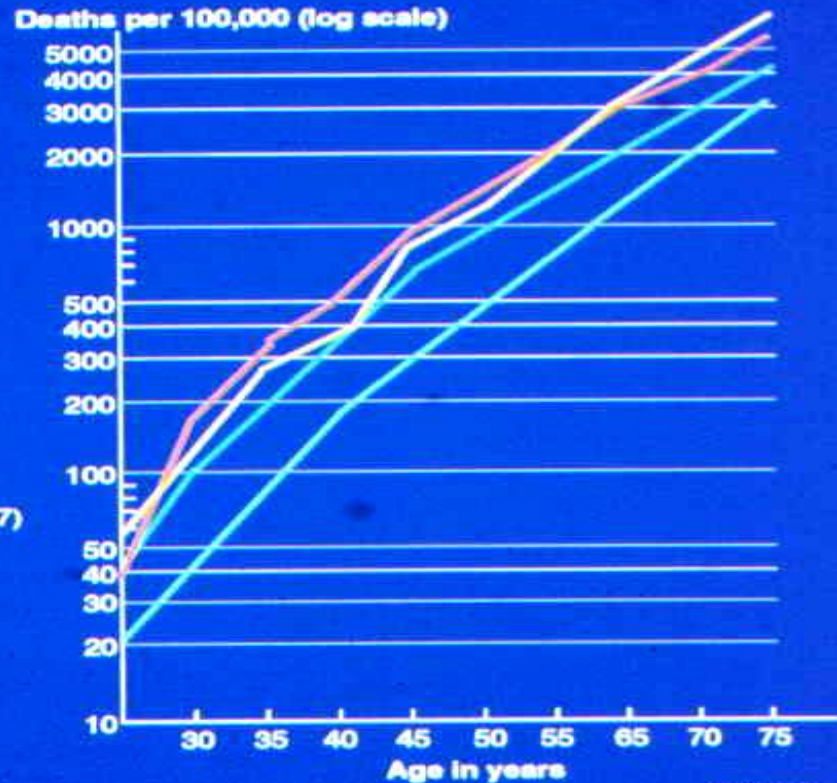
- * South Asians (Indians, Pakistanis, Sri Lankans, Nepalese) *should and probably do* have low rates of coronary heart disease
- * Reason: low smoking prevalence (especially women), much vegetarianism etc
- * I had no reason to believe diabetes was particularly common in South Asians
- * I was wrong!

The paper that made me think again

Deaths from all cardiovascular diseases (B.22, B.24–29) per 100,000, by age and sex in South African White and Asian groups

— Asian females
— Asian males
— White females
— White males

(Whites: Mean 1854–58). Asians: Mean 1955–57)



Adelstein, 1963

Major conceptual question: why might such variations exist?

- * South Asian populations are *either*:

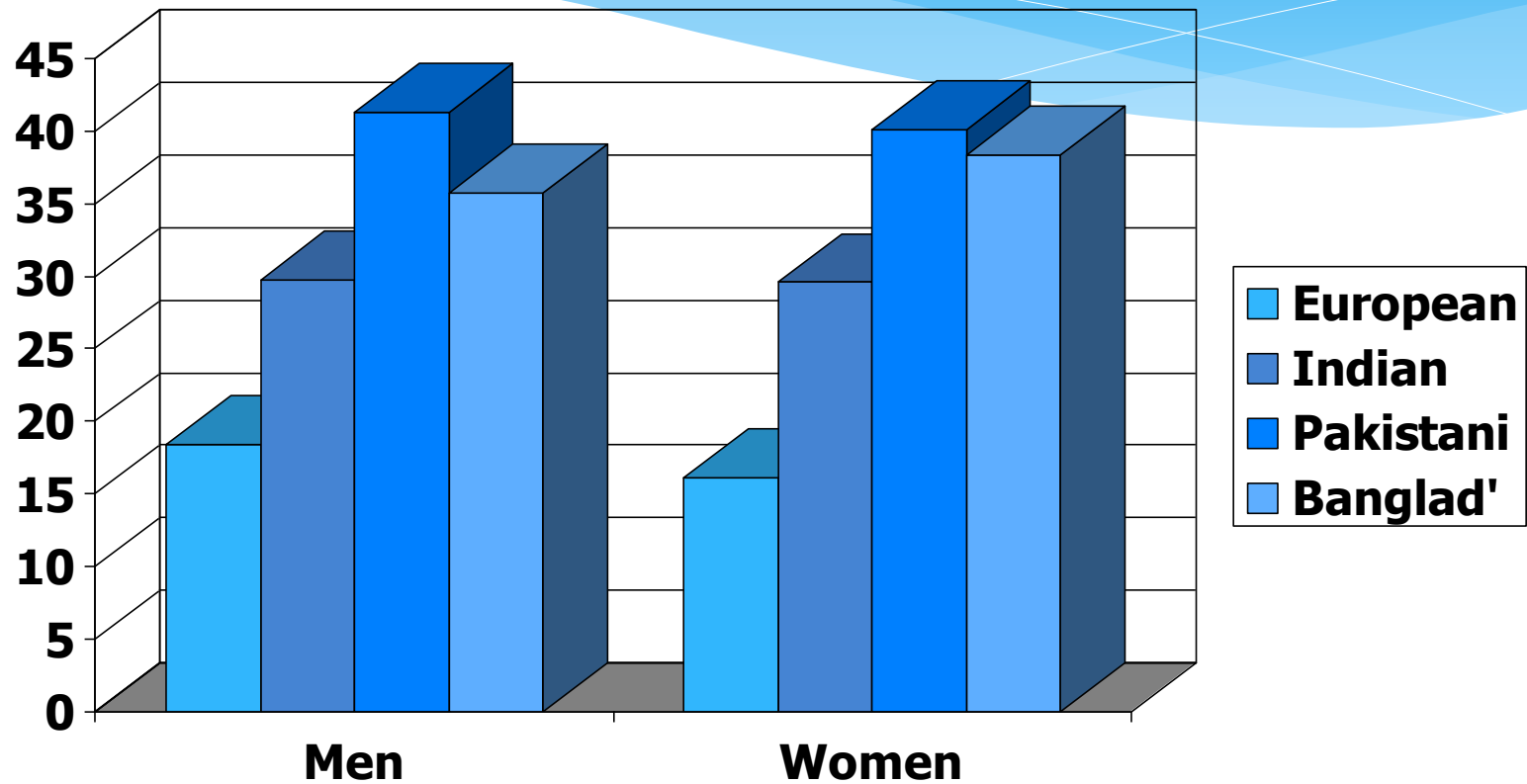
- * More exposed to the causes

or

- * More susceptible to the causes

Newcastle Heart Project (Bhopal et al, BMJ 1999;319:215-220)

Diabetes & IGT(%) (25-74 years)



Explanations are multiple

- * Artefacts of data or diagnostic criteria e.g. variable validity of OGTT & HbA1c
- * Biological factors e.g. premature ageing
- * Genetic/evolutionary
 - * thrifty genotype
 - * thrifty phenotype
 - * soldier to diplomat hypotheses
 - * mitochondrial efficiency
 - * adiposity distribution
 - * variable disease selection hypothesis
- * Social and economic deprivation, possibly interacting with nutritional change
- * Lifestyle factors e.g. physical inactivity and eating patterns

One explanation is prominent, the causes are complex



An explanatory causal model of a complex phenomenon- diabetes in South Asians-of the kind I want (Diabetes Medicine 2013; 30:35-42)

Birth

Small, relatively fatty baby, with low lean mass and fewer beta cells (a phenotype that tracks through life). This phenotype needs less energy than average.

Childhood/early adulthood

Excess energy intake resulting from low need and low physical activity readily stored in highly active, upper body, deep subcutaneous intra-abdominal and ectopic fat.

Insulin resistance with high insulin, glucose and triglycerides. The fatty-liver vicious cycle is activated.

Middle/old-age

Beta cell failure (fewer cells, exposed to apoptotic triggers and to high demands) leads to diabetes

Stemming the epidemic of diabetes in South Asians

- * Tackle the underlying causes
- * **Tackle intermediate states e.g. impaired glucose tolerance - PODOSA does this through tackling causes**
- * Tackle the disease

Some Prevention studies

- * **Da Qing study of 520 people with IGT in China - 42 percent reduction in the incidence of diabetes over six years**
- * **Finnish Diabetes Prevention Study of 522 people in Finland - reduced the incidence of diabetes by 58 percent**
- * **Diabetes Prevention Programme Research Group study of 3234 people in the USA- 58% reduction in the incidence of diabetes**
- * **Chennai, India trial in people aged 35-55 with persistent IGT - reduced diabetes by 30 percent (no decrease in weight)**

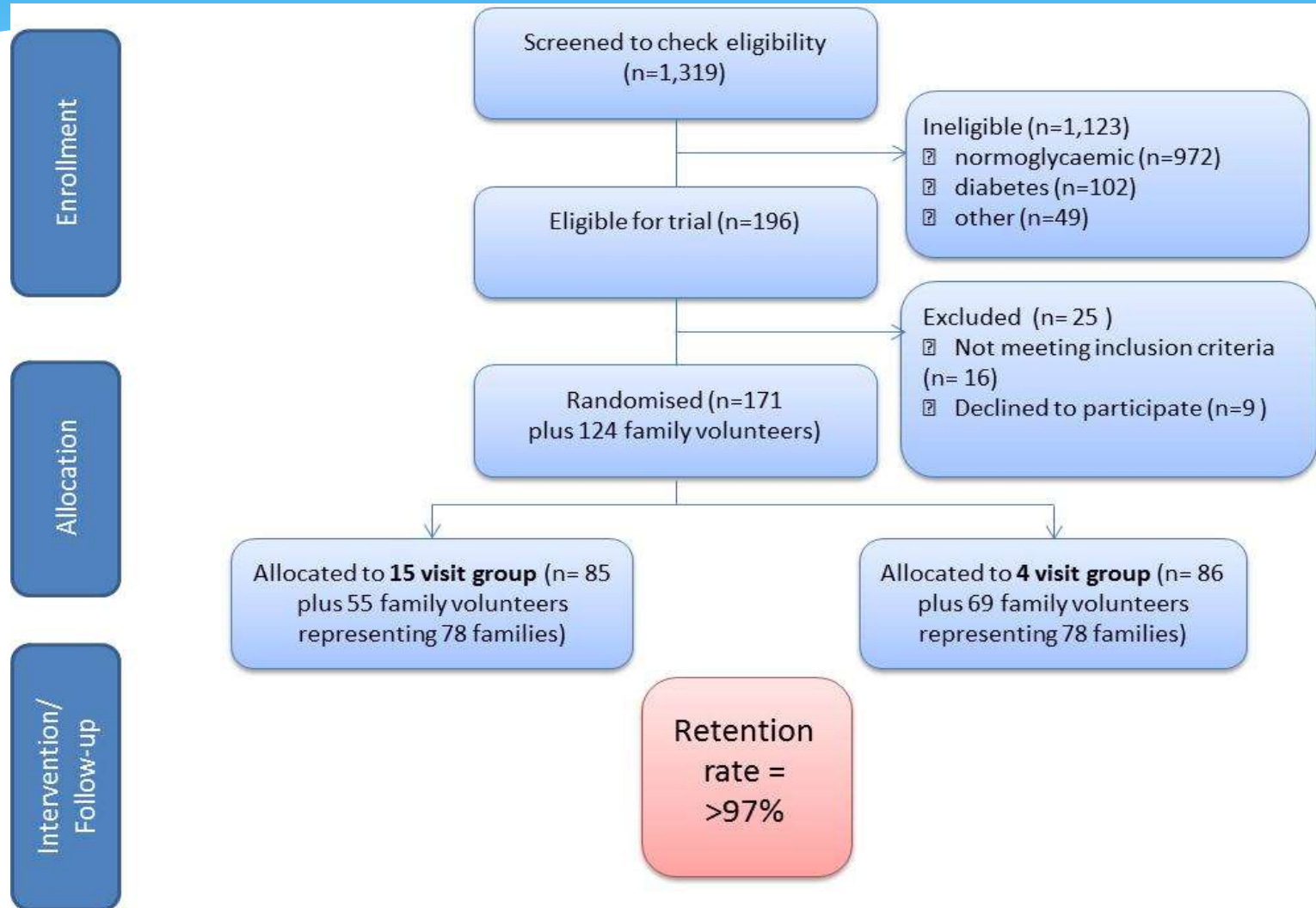
PODOSA: principal questions

- * We failed to recruit 600 participants so the primary question was changed from one on diabetes to weight loss
- * **(Revised) primary question:** does a family-based weight loss and physical activity programme result in a clinically meaningful weight loss in the intervention group compared to the control group? (previously outcome was type 2 diabetes)
- * What is the cost-effectiveness of this programme? (only cost data available)
- * What factors lead to trial recruitment, participation, concordance with advice and retention?

Outcomes

- * **Primary outcome (revised):** Weight change at 3 years
- * **Secondary outcomes:** changes in waist/hip, BMI, blood glucose, physical activity and progression to diabetes (longer term, now via data linkage)
- * **Health economics:** in-trial costs
- * **Qualitative study:** participation, adherence and retention

Trial Summary Consort Flowchart



Eligibility Criteria

- * Pakistani/Indian origin
- * Age \geq 35 years
- * Waist \geq 90 cm men / 80cm women
- * IGT/IFG on OGTT
- * Family cook will support main participant

Intervention

- * Bilingual, research dietitians
- * Tailored, motivational messages and materials targeted at diet & exercise
- * Pedometers and step counts, diet and physical activity diaries
- * Practical sessions – walking groups, cookery demos etc

Intervention Goals

Ideal:

- * weight loss of ≥ 3.5 kg;
- * increase in moderate physical activity to ≥ 30 minutes daily
- * BMI to less \leq to 25
- * reduce waist size to < 90 cm for men, and < 80 cm for women

In practice:

- * induce 5-10 percent weight loss
- * sample size based on 2.5 kg more weight loss in the intervention than control group

Cultural adaptation of trial

- * Inspiration: Finnish DPS but...
- * Delivery in the home, not the clinic
- * Involvement of the cook and family helpers
- * Multilingual panel to help prepare materials
- * Development of dietitian's toolkit, with translations in Urdu and Gurmukhi
- * Non-staff costs of adapting materials: £8000

Recruitment to screening

	Referrals or responses (% of total)	Initial target (%)	% of total screened
NHS			
Direct referrals	55 (3)	25	1
Written invitations via GPs	265 (13)	25	11
Community			
Snowball/contacts	630 (30)		47
Community groups etc	618 (29)	50	26
Research team recruitment	480 (23)		14

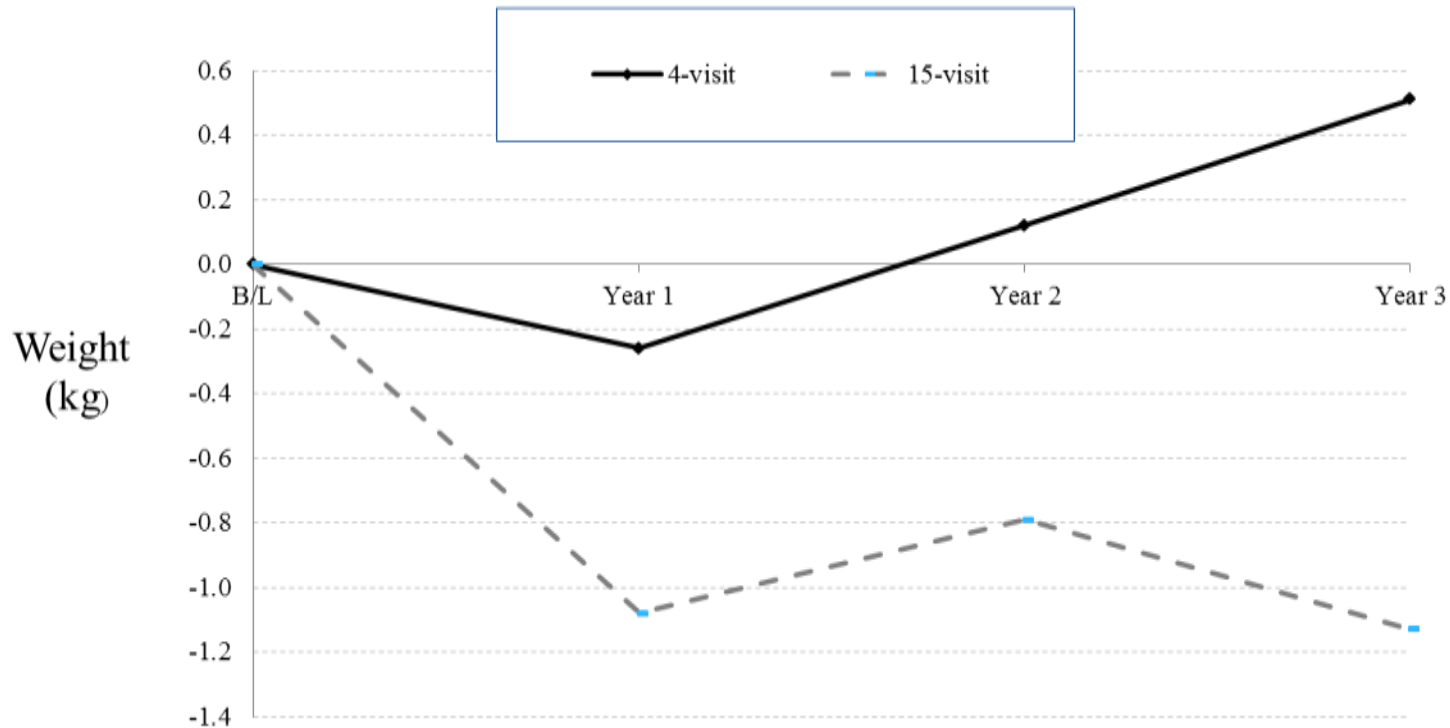
Baseline characteristics (167/171-97%- completed trial)

	Intervention	Control
Indian/Pakistani (%)	34/66	33/67
Family volunteers (%)	53	56
Family history DM (%)	71	70
Mean years in UK	32	31
Age (mean)	53	52
Waist (mean & SD)	102.7 (11.2)	103.3 (11.0)
BMI (mean & SD)	30.6 (5.0)	30.5 (4.6)
2-hour plasma glucose (mmoles/l & SD)	8.2 (1.6)	8.3 (1.5)

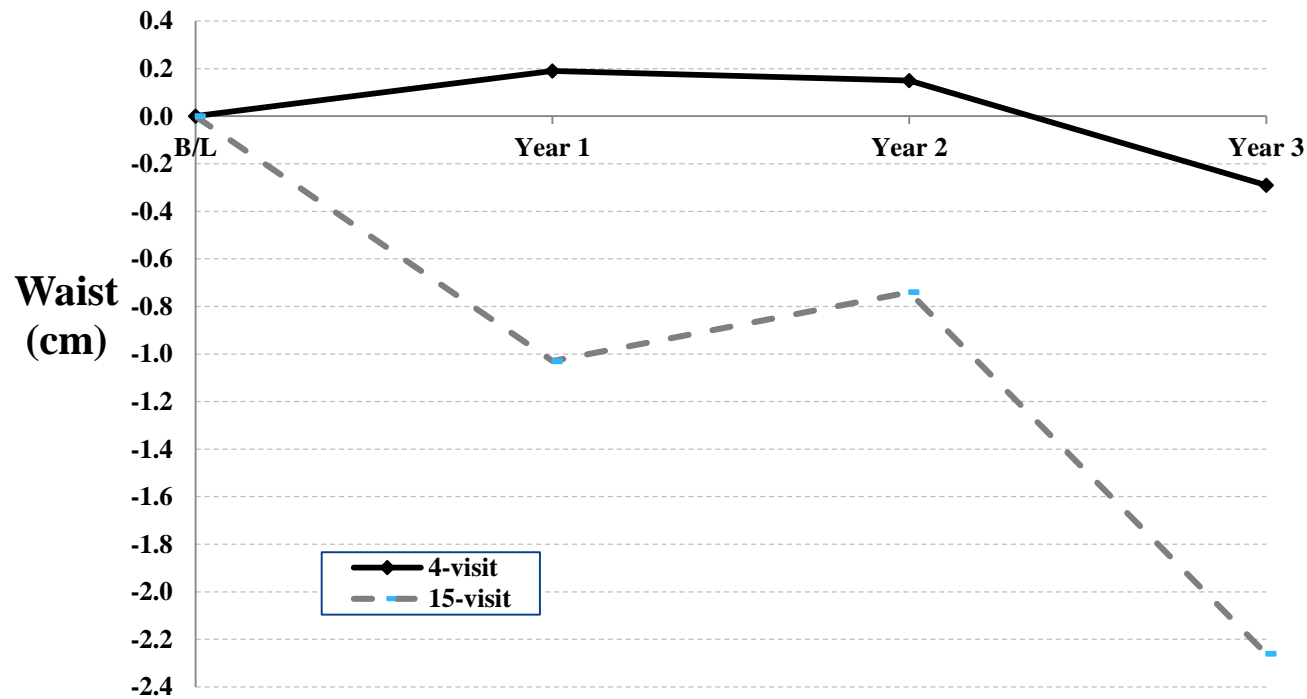
Adjusted mean difference between intervention and control group at three years

Weight (kg)	-1.64	(-2.83, -0.44)
BMI (kg/m²)	-0.60	(-1.06, -0.14)
Waist (centimetre)	-1.89	(-3.27, -0.52)
Hip (centimetre)	-1.54	(-2.71, -0.37)
Fasting glucose:	-0.13	(-0.39, 0.13)
2-hour post OGTT(mmole/l)	-0.56	(-1.32, 0.19)
Systolic BP (mm Hg)	-1.19	(-5.50 3.12)

Mean change in weight from baseline over three years



Mean change in waist from baseline over three years.



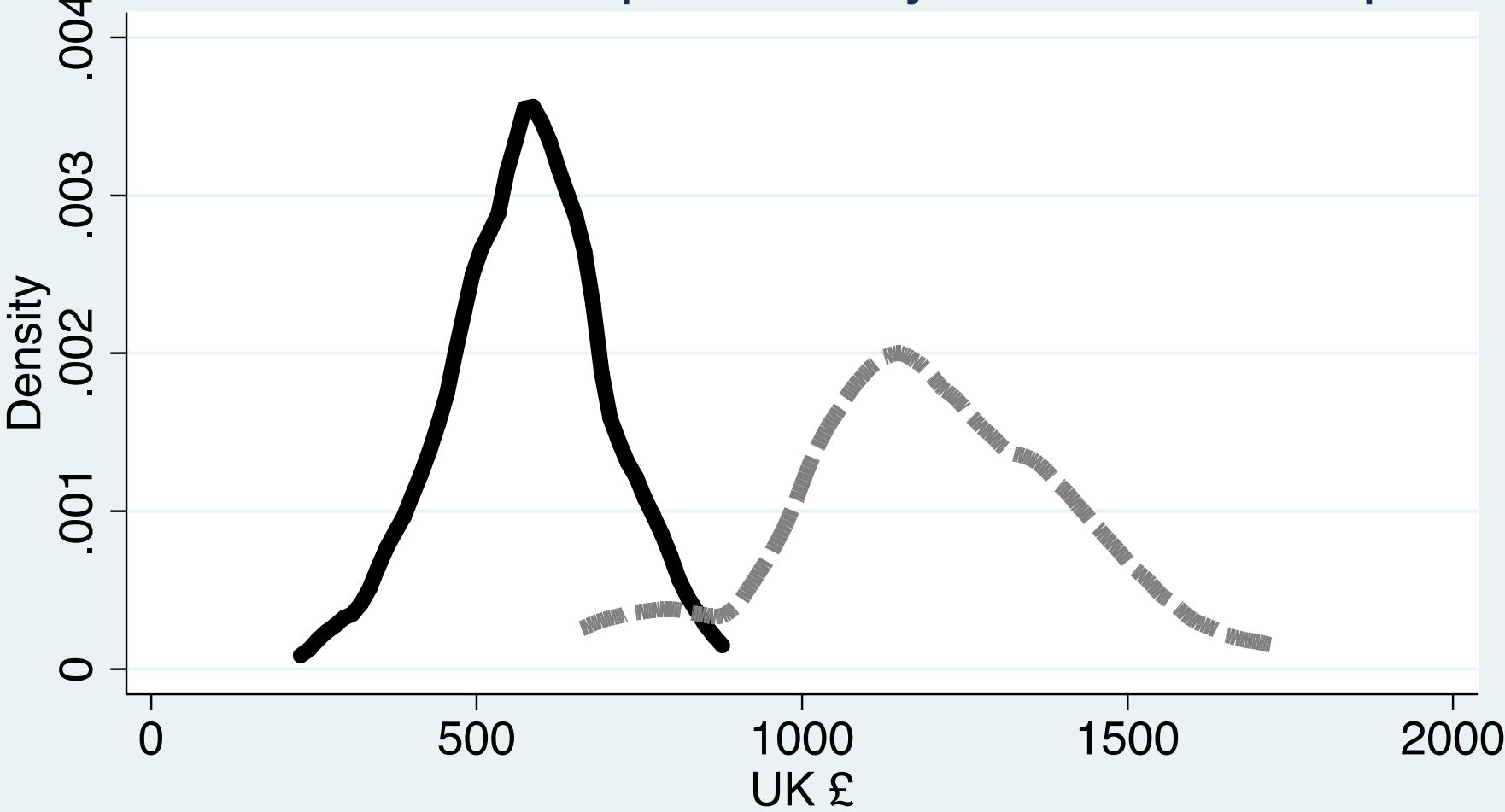
Proportions and adjusted odds ratios for physical activity, losing weight and progression to diabetes

Outcome	Intervention group	Control group	Odds ratio (95% CI)
Reporting 150 min of physical activity per week	55%	45%	1.19 (0.55, 2.55)
Losing ≥ 2.5 kg	39%	14%	3.92 (1.68, 9.13)
Losing $\geq 5\%$ of body weight	25%	5%	6.57 (1.92, 22.44)
Progressing to diabetes	15%	21%	0.68 (0.27, 1.67)

Health economics

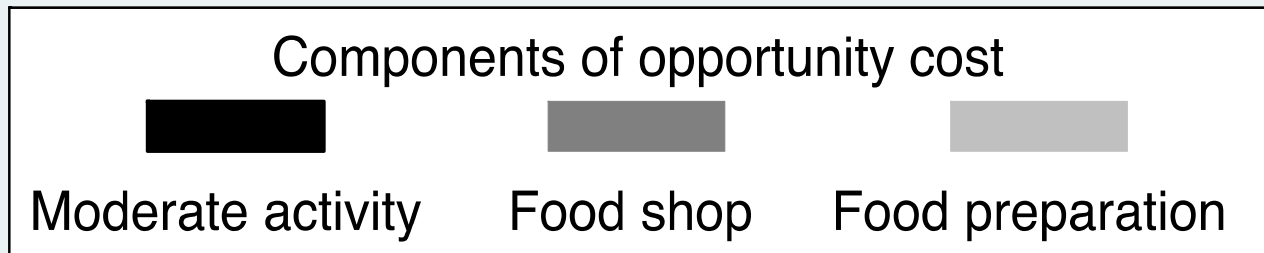
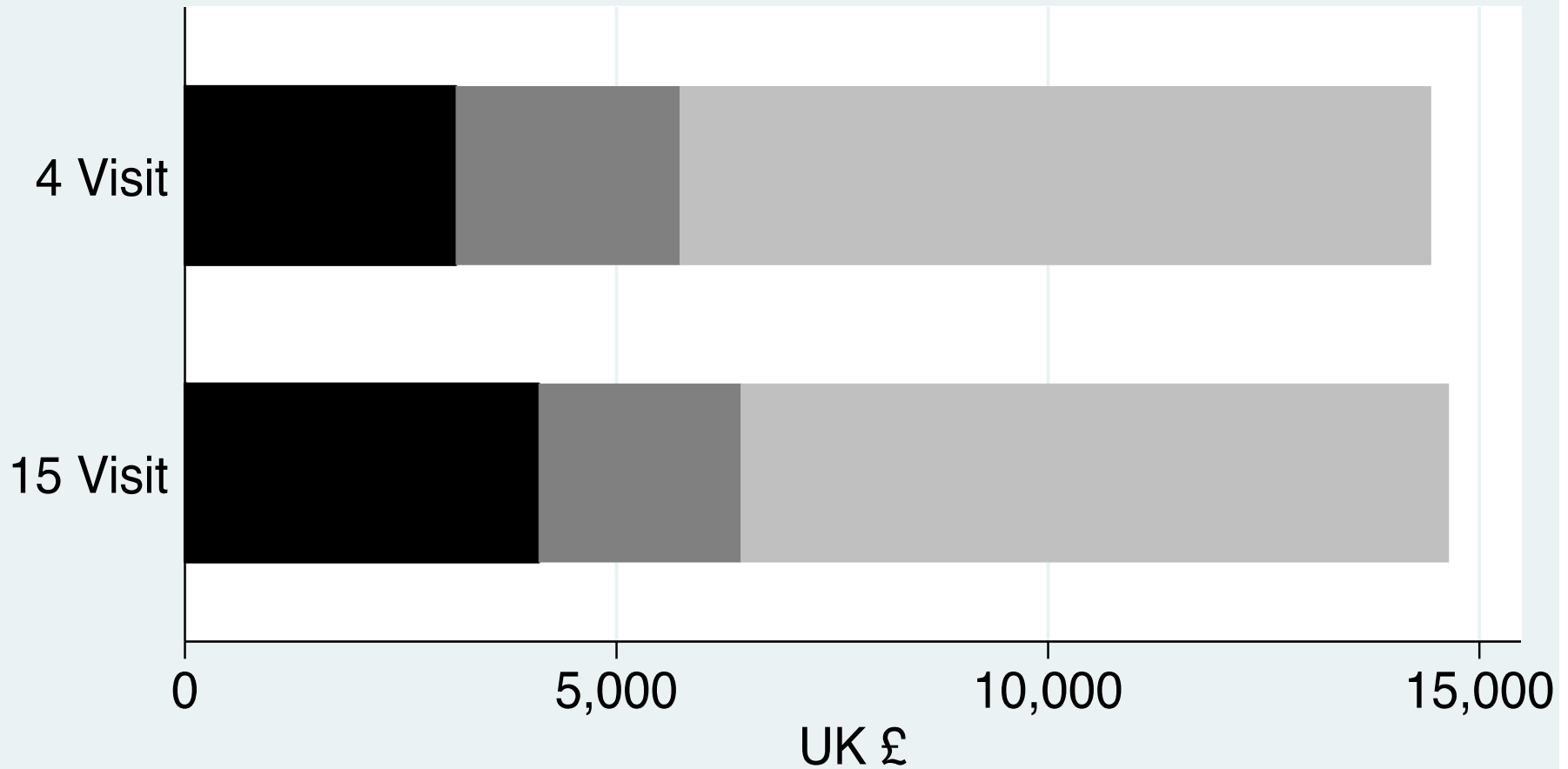
- * Cost effectiveness - requires disease outcome data (being collected via data linkage)
- * Within-trial analysis of cost differences between the two groups assessed

Dietitian cost up to three years of follow-up



Indirect (opportunity) cost

Use and value of participant time up to three years follow-up



Qualitative findings (21 interviews)

Recruitment

- * Prefer verbal communication
- * Altruism

Retention

- Trust & relationships
- People did not see themselves in a research project

Adherence

- Personal achievements –pride
- Social support was important

Summary of key results

- * Recruitment into screening was difficult but retention was extremely high
- * The effect on weight loss is demonstrably modest, though of potential importance
- * The cost per year of tailored intervention about £200 per year more than a simple information & measurement orientated annual home visit
- * The costs and clinical implications need consideration
- * Participants appreciated the intervention, and the dietitians' work

Lessons from the trial

- * Trials of this kind are feasible and strongly supported by professionals and the public (in principle)
- * Converting support to enrolment is harder than anticipated
- * Personal, face-to-face contact is the key to recruitment
- * Once recruited, retention is surprisingly high-perhaps because of the home-based intervention
- * Participants seem to appreciate the intervention
- * The trial has been a massive learning experience, including around adaptation processes

Interpretation

- * Intensive interventions to prevent progression of IGT/IFG to diabetes are effective and cost effective.
- * The literature shows that weight loss (none in the Indian DPP) and increase physical activity in South Asians is difficult to achieve
- * This medium-intensity, translational intervention lead to modest but sustained weight loss in South Asians.
- * Meta-analysis of studies on South Asians needed after D-CLIP and DHIANN report final-year results.

Implications of PODOSA for policy and practice

- * Pending further research, PODOSA materials and approaches may help in combating adiposity related diseases but, alone, comprise an insufficient strategy.

Next steps

- * Meta-analysis with trials including South Asians
- * Refinement and further development of interventions
- * Examine effects on disease outcomes in long-term
- * Policy and community-based interventions need to be designed and evaluated, to complement individual-based interventions
- * PODOSA investigators have established an international group to consider the next steps in the goal of preventing diabetes in South Asians

Publications so far

- * Is there a divergence in time trends in the prevalence of impaired glucose tolerance and diabetes? International Journal of Epidemiology 2011 Oct 26.
<http://ije.oxfordjournals.org/content/early/2011/10/25/ije.dyr159.full.pdf+html>
- * Recruiting South Asians to a lifestyle intervention trial: experiences and lessons from PODOSA (Prevention of Diabetes & Obesity in South Asians). Trials 2011;12(1):220.
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<http://heapro.oxfordjournals.org/content/early/2013/04/10/heapro.dato15.full.pdf+html>
- * Challenges in recruiting South Asians into prevention trials. Public Health 2011 Mar 28;125:201-9. http://www.sciencedirect.com/science?_ob=ArticleURL&
- * Morrison Z, Douglas A, Bhopal R, Sheikh A. Understanding experiences of participating in a weight loss lifestyle intervention trial: a qualitative evaluation of South Asians at high risk of diabetes. BMJ Open 2014;4(6):e004736
- * Bhopal RS, Douglas A, Wallia S, Forbes JF, Lean MEJ, Gill JMR, 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. The Lancet Diabetes & Endocrinology. 2013; 2: 218-227