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

Presentation to UK SBM 2014

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For the PODOSA Investigators Group
A community-based trial

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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National Prevention Research Initiative: PODOSA funders

Additional support from NHS Lothian and NHS Greater Glasgow & Clyde R&D, Chief Scientist Office, NHS Health Scotland, NHS National Services for Scotland
Acknowledgements

* SPCRN
* SDRN
* WTCRF Edinburgh
* Diabetes MCNs
* GRI retinal screening
* GPs
* Counterweight
* Oceanic Consulting

Many other individuals helped, especially support staff

* 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
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

Deaths per 100,000 (log scale)

- Asian females
- Asian males
- White females
- White males

(Whites: Mean 1654–58. 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.

Middle/old-age

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

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

Enrollment

Screened to check eligibility (n=1,319)

- Ineligible (n=1,123)
  - normoglycaemic (n=972)
  - diabetes (n=102)
  - other (n=49)

Eligible for trial (n=196)

- Excluded (n=25)
  - Not meeting inclusion criteria (n=16)
  - Declined to participate (n=9)

Randomised (n=171 plus 124 family volunteers)

Allocation

Allocated to 15 visit group (n= 85 plus 55 family volunteers representing 78 families)

Allocated to 4 visit group (n= 86 plus 69 family volunteers representing 78 families)

Retention rate = >97%
Eligibility Criteria

* Pakistani/Indian origin
* Age $\geq 35$ years
* Waist $\geq 90$ cm men / $80$ cm 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 $\geq 3.5$ kg;
- increase in moderate physical activity to $\geq 30$ 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
<table>
<thead>
<tr>
<th></th>
<th>Referrals or responses (% of total)</th>
<th>Initial target (%)</th>
<th>% of total screened</th>
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<tbody>
<tr>
<td><strong>NHS</strong></td>
<td></td>
<td></td>
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<tr>
<td>Direct referrals</td>
<td>55 (3)</td>
<td>25</td>
<td>1</td>
</tr>
<tr>
<td>Written invitations via GPs</td>
<td>265 (13)</td>
<td>25</td>
<td>11</td>
</tr>
<tr>
<td><strong>Community</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Snowball/contacts</td>
<td>630 (30)</td>
<td>50</td>
<td>47</td>
</tr>
<tr>
<td>Community groups etc</td>
<td>618 (29)</td>
<td></td>
<td>26</td>
</tr>
<tr>
<td>Research team recruitment</td>
<td>480 (23)</td>
<td></td>
<td>14</td>
</tr>
</tbody>
</table>
Baseline characteristics (167/171-97%- completed trial)

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
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<tbody>
<tr>
<td>Indian/Pakistani (%)</td>
<td>34/66</td>
<td>33/67</td>
</tr>
<tr>
<td>Family volunteers (%)</td>
<td>53</td>
<td>56</td>
</tr>
<tr>
<td>Family history DM (%)</td>
<td>71</td>
<td>70</td>
</tr>
<tr>
<td>Mean years in UK</td>
<td>32</td>
<td>31</td>
</tr>
<tr>
<td>Age (mean)</td>
<td>53</td>
<td>52</td>
</tr>
<tr>
<td>Waist (mean &amp; SD)</td>
<td>102.7 (11.2)</td>
<td>103.3 (11.0)</td>
</tr>
<tr>
<td>BMI (mean &amp; SD)</td>
<td>30.6 (5.0)</td>
<td>30.5 (4.6)</td>
</tr>
<tr>
<td>2-hour plasma glucose (mmoles/l &amp; SD)</td>
<td>8.2 (1.6)</td>
<td>8.3 (1.5)</td>
</tr>
</tbody>
</table>
### Adjusted mean difference between intervention and control group at three years

<table>
<thead>
<tr>
<th>Measure</th>
<th>Difference</th>
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<tbody>
<tr>
<td>Weight (kg)</td>
<td>-1.64 (-2.83, -0.44)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>-0.60 (-1.06, -0.14)</td>
</tr>
<tr>
<td>Waist (centimetre)</td>
<td>-1.89 (-3.27, -0.52)</td>
</tr>
<tr>
<td>Hip (centimetre)</td>
<td>-1.54 (-2.71, -0.37)</td>
</tr>
<tr>
<td>Fasting glucose: 2-hour post OGTT (mmole/l)</td>
<td>-0.13 (-0.39, 0.13)</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>-1.19 (-5.50, 3.12)</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intervention group</th>
<th>Control group</th>
<th>Odds ratio (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>Reporting 150 min of physical activity per week</td>
<td>55%</td>
<td>45%</td>
<td>1.19 (0.55, 2.55)</td>
</tr>
<tr>
<td>Losing &gt;2.5 kg</td>
<td>39%</td>
<td>14%</td>
<td>3.92 (1.68, 9.13)</td>
</tr>
<tr>
<td>Losing ≥5% of body weight</td>
<td>25%</td>
<td>5%</td>
<td>6.57 (1.92, 22.44)</td>
</tr>
<tr>
<td>Progressing to diabetes</td>
<td>15%</td>
<td>21%</td>
<td>0.68 (0.27, 1.67)</td>
</tr>
</tbody>
</table>
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

Density

UK £

4 Visit 15 Visit
Indirect (opportunity) cost
Use and value of participant time up to three years follow-up

Components of opportunity cost
- Moderate activity
- Food shop
- Food preparation

UK £

4 Visit

15 Visit

0 5,000 10,000 15,000
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
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.
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


