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**WP4: Deliverable 7 D4.1 Draft scientific paper on differential effectiveness population subgroups.**

**Effectiveness of dietary and physical activity interventions to reduce the risk of type 2 diabetes in South Asians living in Europe across population subgroups: individual participant data meta-analysis of European randomized controlled trials identified in a systematic review** (First summary based on four European studies)

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## **Abstract**

**Background:** Randomized controlled intervention trials (RCTs) in South Asians to prevent type 2 diabetes seem to be less effective than in populations with European origin.

**Aims:** To assess the effect of dietary and/or physical activity interventions to prevent type 2 diabetes among South Asians in Europe, overall, and for pre-specified subgroup analyses.

**Methods:** Primary outcomes: fasting glucose, 2 hour-glucose. Secondary outcomes: weight, waist circumference. A systematic review was performed to identify relevant RCTs worldwide and thereafter those from Europe. The study quality was assessed by the Quality Assessment Tool for Quantitative studies. Individual participant data (IPD) meta-analysis is the gold-standard for synthesizing evidence of effect across clinical studies. Compared with meta-analyses from aggregate data from published papers, IPD increases the precision in the estimates, facilitates standardization of analyses and increases the quality of sub-group analyses. Anonymous data for all studies (study duration 36, 24, 7 and 5 months), were received. The IPD meta-analyses proceeded in two stages: 1) Multilevel linear regression models with random effects at individual level and group allocation as fixed effect, were used to analyse pooled individual data, adjusted for age and gender, and baseline values for the outcome variable of interest, using Stata 13. For studies with only one follow-up, GLM was used. 2) Model estimates obtained from the multilevel models were used to estimate weighted averages across the studies by accounting for between-study heterogeneity using Review Manager (Revman 5.3). Subgroup analyses were performed for gender, baseline age  $\pm 44$  years, BMI  $\pm 27.5$  kg/m<sup>2</sup> and by study duration (short- and long-term).

**Results:** Of the fourteen RCTs identified by a systematic review, four were from Europe (The PODOSA study (Scotland) of 3 years duration, the DHIAAN study of two years duration (The Netherlands), the INNVA-Dia study of 7 months duration with women only (Norway) and the PAMH study of 5 months duration with men only (Norway)). The interventions combined dietary and physical activity in all but the PAMH study which used physical activity only. The study quality was found to be strong to moderate. Individual participant data for 775 South Asians were included. Significant reductions in the intervention groups compared to controls (Figure 1) for fasting glucose (-0.11 (95% confidence interval: -0.22 to 0.00); P 0.04, I<sup>2</sup> 0%), 2hour glucose (0.27 mmol/l (-0.53 to -0.01); P: 0.04, I<sup>2</sup> 0%), weight (1.13 kg (-1.81 to -0.46); P: 0.0009, I<sup>2</sup> 62%) and waist circumference (-1.59 cm (-2.94 to -0.24); P: 0.02, I<sup>2</sup> 77%) were found. A subgroup effect was found only for gender (Figure 3) for weight ((men 1.91 kg (-2.61 to -1.22), women (0.34 kg (-0.90 to 0.22), P for interaction: 0.0005)) (Figure 2).

**Conclusions:** IPD meta-analyses of all RCT's among South Asians in Europe revealed clinically small, but consistent effects on glucose measures, weight and waist circumference, and a stronger effect on weight reduction in men than in women.

Update of abstract based on extended analyses as per May 29.th 2018;

Previous analysis, extended with two eligible trials from India, with new title:

**Effects of dietary and physical activity interventions on the risk of type 2 diabetes in South Asians: individual participant data meta-analysis of randomised controlled trials**  
*(Paper in progress, full paper will be submitted soon)*

**Background:** The effectiveness of diet and/or physical activity lifestyle modification interventions on prevention of type 2 diabetes in South Asians is unclear. We performed an individual participant data meta-analysis of randomised controlled trials (RCTs) in this high-risk population.

**Methods:** We searched PUBMED, Embase, Cochrane Library and Web of Science (to September 30<sup>th</sup> 2017) for RCTs on lifestyle modification interventions in South Asian adults, and obtained individual participant data on 1816 participants from all six eligible trials (from Europe and India) identified. Applying a 2-step approach, we generated hazard estimates for incident diabetes and mean differences for fasting glucose, 2-hour glucose, weight and waist circumference, using fixed-effect meta-analysis overall, and by pre-specified subgroups. We applied the GRADE system to rate the quality of evidence. (PROSPERO registration CRD4217078003).

**Results:** In high-risk South Asian populations, lifestyle modification interventions resulted in modest adiposity and postprandial glucose changes, but a 35% relative reduction in diabetes incidence, consistent across subgroups.

**Implication:** Given the increasing global burden of disease from diabetes, lifestyle modification interventions strategies should be more widely used to improve the diet and promote physical activity, and through so doing substantially reduce the risk of diabetes in populations of South Asian origin, known to be at high risk. We also need to find better ways or adapt interventions to try to achieve greater benefits.