

Supplementary Table 6 - Estimated natural direct and indirect effects using sequential mediation analysis, analyses excluded women categorized as overweight, complete case analysis

Number of cases/ number of controls	Body Mass Index ≥ 30 vs. ≥ 18.5 & < 25 kg/m ²			Waist Circumference > 88 vs. ≤ 80 cm		
	83/155			105/183		
	Odds Ratio (95% CI)		% mediated on log odds scale	Odds Ratio (95% CI)		% mediated on log odds scale
Total effect (estimated as the product of natural direct and indirect effects)	2.37	(1.07 to 5.23)		2.19	(1.20 to 4.01)	
Natural indirect effect through all the biomarkers	2.00	(0.99 to 4.04)	81%	1.63	(0.91 to 2.89)	62%
Natural indirect effect through reduced adiponectin and increased inflammation	1.52	(0.86 to 2.69)	49%	1.44	(0.88 to 2.36)	47%
Natural indirect effect through reduced adiponectin levels	1.22	(0.97 to 1.53)	23%	1.25	(0.97 to 1.61)	29%
Natural indirect effect through increased inflammation, beyond the potential influence of adiponectin	1.25	(0.74 to 2.10)	25%	1.15	(0.76 to 1.75)	18%
Natural indirect effect through increased c-peptide levels, beyond the potential influences of adiponectin and inflammation	1.07	(0.88 to 1.30)	8%	1.05	(0.89 to 1.24)	6%
Natural indirect effect through increased free estradiol and estrone levels, beyond the potential influences of adiponectin, inflammation, and c-peptide	1.23	(0.84 to 1.80)	24%	1.07	(0.84 to 1.37)	9%
Natural direct effect not through any of the biomarkers	1.18	(0.46 to 3.06)		1.35	(0.62 to 2.95)	

Confounders included age at blood collection, country region, age at menarche, number of full-term pregnancies, history of oral contraceptive use, history of hormone therapy, physical activity, and smoking status. The reported 95% CIs are constructed from 1,000 bootstrap draws.