Supplementary Materials

Subcutaneous fat mass in infancy and cardiovascular risk factors at school-age. The Generation R Study

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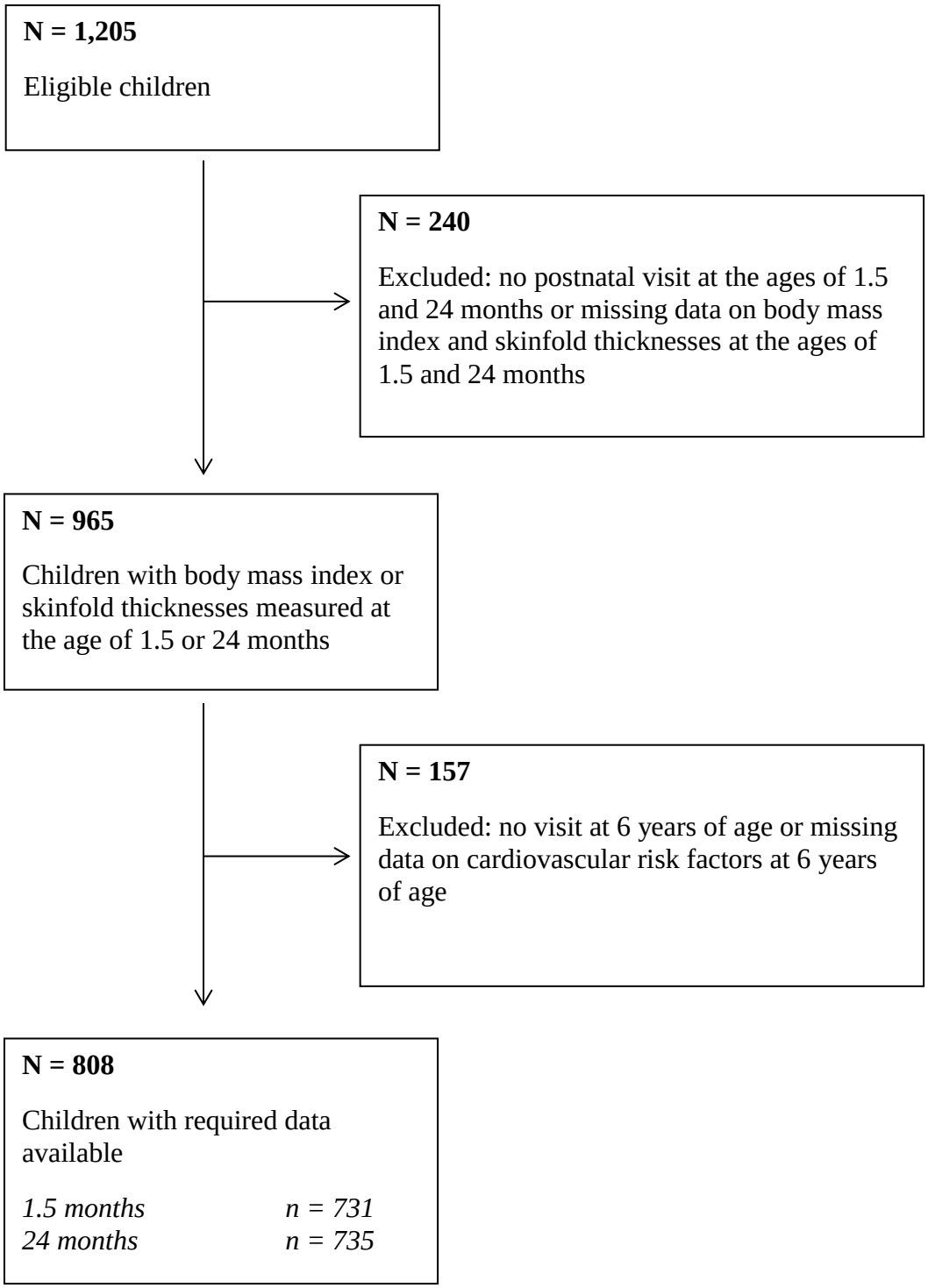
Figure S1 Flow chart of participants in study



Supplemental Methods

Log-log regression analyses

The relationships between total subcutaneous fat mass and length or height, and between central subcutaneous fat mass and total subcutaneous fat mass were assessed using log-log regression analyses. Total and central subcutaneous fat mass measures as well as length or height were all log-transformed. Log-total subcutaneous fat mass was regressed on log-length or height. The regression slope corresponds to the power P by which length or height should be raised in order to calculate an index uncorrelated with length or height (total subcutaneous fat mass/length or height^{P}). A similar calculation was undertaken for log-central and -total subcutaneous fat mass (1).

Conditional analysis

We performed conditional analysis to enable inclusion of body mass index measures at different ages in the same linear regression model, without problems regarding the correlations between the measures. First, we calculated the expected body mass index at the age of 6 years based on body mass index at 1.5 or 24 months by performing a linear regression model of body mass index at 1.5 or 24 months regressed on body mass index at 6 years. The standardized residuals obtained from these regression models correspond to the difference between the expected and the actual body mass index at 6 years and thus are entirely uncorrelated with body mass index at 1.5 or 24 months. Then, we added the standardized residuals to the models in order to assess the associations of infant body mass index with childhood cardiovascular risk factors, independently of body mass index at 6 years (2).

References

1. Wells JC, Cole TJ, ALSPAC study team. Adjustment of fat-free mass and fat mass for height in children aged 8 y. *Int J Obes Relat Metab Disord* 2002;26:947-952.

2. Keijzer-Veen MG, Euser AM, van Montfoort N, Dekker FW, Vandenbroucke JP, Van Houwelingen HC. A regression model with unexplained residuals was preferred in the analysis of the fetal origins of adult diseases hypothesis. *J Clin Epidemiol* 2005;58:1320-4.

Table S1 Comparison of maternal and child's characteristics between children included and not included in the analyses[1]

	Participants (n = 808)	Non-participants (n = 157)	P-value
Maternal characteristics			
Age (years), mean (SD)	32.0 (3.8)	30.9 (4.9)	0.008
Highest completed education, n (%)			
Primary school	10 (1.2)	8 (5.2)	<0.001
Secondary school	261 (32.5)	62 (40.0)	
Higher education	533 (66.3)	85 (54.8)	
Parity, n (%) nulliparous	512 (63.4)	84 (53.5)	0.020
Pre-pregnancy body mass index (kg/m^2), mean (SD)	23.6 (4.2)	22.8 (3.4)	0.040
Total energy intake (kcal), mean (SD)	2131 (499)	2091 (533)	0.391
Total weight gain during pregnancy (kg), mean (SD)	10.2 (4.6)	10.4 (4.7)	0.477
Smoking habits during pregnancy, n (%)			
No	575 (78.7)	100 (67.6)	0.004
Yes	156 (21.3)	48 (32.4)	
Gestational diabetes, n (%)	9 (1.1)	2 (0.5)	0.318
Gestational hypertensive disorders, n (%)	64 (8.1)	19 (5.0)	0.056
Child's characteristics			
Boys, n (%)	405 (50.1)	91 (58.0)	0.072
Birth weight (g), mean (SD)	3535 (517)	3403 (624)	0.014
Gestational age at birth (weeks), median (95% range)	40.3 (36.4-42.4)	39.9 (34.8-42.4)	0.003
Breastfeeding duration (months), mean (SD)	4.7 (3.9)	3.3 (3.5)	<0.001
Introduction of solid foods, n (%)			
<3 months	41 (5.5)	7 (6.1)	0.417
3 to 6 months	569 (76.6)	81 (71.1)	
>6 months	133 (17.9)	26 (22.8)	
TV watching time, n (%)			
< 2 hours/day	668 (91.3)	64 (92.8)	0.672
≥ 2 hours/day	64 (8.7)	5 (7.2)	
1.5 months			
Body mass index (kg/m^2), mean (SD)	15.2 (1.4)	15.2 (1.3)	0.989
Total subcutaneous fat mass (mm), mean (SD)	23.9 (7.0)	24.9 (9.1)	0.235
Central-to-total subcutaneous fat mass ratio, mean (SD)	0.50 (0.05)	0.50 (0.04)	0.297
24 months			
Body mass index (kg/m^2), mean (SD)	16.0 (1.3)	15.9 (1.2)	0.504
Total subcutaneous fat mass (mm), mean (SD)	27.4 (7.5)	26.8 (6.0)	0.488
Central-to-total subcutaneous fat mass ratio, mean (SD)	0.43 (0.06)	0.44 (0.07)	0.123

[1]Values are observed data and represent means (SD), medians (95% range) or numbers of subjects (valid %). Differences were tested using Student's t-tests and Mann-Whitney tests for normally and non-normally distributed variables, respectively and χ^2-test for dichotomous variables. SD, standard deviation.

Table S2 Associations of infant subcutaneous fat mass measures with cardiovascular risk factors at 6 years old[1-2]

Fat mass measures	Cardiovascular risk factors at 6 years in standard-deviation scores Difference (95% Confidence Interval)						
	Systolic blood pressure	Diastolic blood pressure	Total-cholesterol	HDL-cholesterol	LDL-cholesterol	Triglycerides	Insulin
1.5 months							
Body mass index	0.03 (-0.04,0.11)	-0.01 (-0.08,0.06)	0.02 (-0.07, 0.11)	0.03 (-0.06,0.12)	-0.01 (-0.10,0.08)	0.01 (-0.08,0.10)	-0.01 (-0.10,0.08)
Total subcutaneous fat mass	0.03 (-0.04,0.11)	-0.02 (-0.10,0.05)	-0.05 (-0.14,0.05)	0.02 (-0.08,0.11)	-0.10 (-0.19,-0.01)*	-0.02 (-0.11,0.08)	0.05 (-0.04,0.15)
Central-to-total subcutaneous fat mass ratio	-0.01 (-0.09,0.06)	-0.03 (-0.10,0.05)	0.06 (-0.03,0.15)	0.02 (-0.06,0.12)	0.02 (-0.06,0.12)	0.09 (-0.01,0.18)	0.02 (-0.07,0.11)
24 months							
Body mass index	-0.03 (-0.10,0.05)	-0.06 (-0.14,0.02)	-0.05 (-0.15,0.04)	-0.10 (-0.19,-0.01)*	0.00 (-0.10,0.09)	-0.01 (-0.10,0.09)	-0.06 (-0.15,0.04)
Total subcutaneous fat mass	0.01 (-0.07,0.08)	0.02 (-0.06,0.09)	0.14 (0.05,0.24)**	0.01 (-0.08,0.10)	0.13 (0.04,0.22)**	0.03 (-0.06,0.12)	0.03 (-0.06,0.13)
Central-to-total subcutaneous fat mass ratio	0.04 (-0.04,0.11)	0.04 (-0.04,0.11)	0.05 (-0.04,0.15)	-0.10 (-0.19,-0.01)*	0.10 (0.01,0.20)*	0.04 (-0.06,0.14)	-0.01 (-0.11,0.09)
Change from 1.5 to 24 months							
Body mass index	-0.05 (-0.11,0.02)	-0.04 (-0.11,0.02)	-0.05 (-0.13,0.03)	-0.06 (-0.14,0.02)	-0.01 (-0.10,0.07)	-0.02 (-0.10,0.06)	-0.01 (-0.10,0.07)
Total subcutaneous fat mass	-0.01 (-0.06,0.05)	0.02 (-0.04,0.08)	0.10 (0.03,0.17)**	0.00 (-0.07,0.07)	0.10 (0.03,0.18)**	0.03 (-0.04,0.11)	0.01 (-0.06,0.09)
Central-to-total subcutaneous fat mass ratio	0.02 (-0.04,0.08)	0.04 (-0.02,0.10)	-0.04 (-0.12,0.03)	-0.06 (-0.13,0.01)	0.02 (-0.06,0.10)	-0.04 (-0.12,0.03)	-0.01 (-0.09,0.06)

[1]Values are standardized regression coefficients (95% confidence interval) and represent the difference in standard-deviation scores for cardiovascular risk factors at 6 years per 1-standard-deviation scores increase in body mass index and subcutaneous fat mass measures. Body mass index = weight/height^2. Total subcutaneous fat mass = biceps + triceps + suprailiacal + subscapular skinfold thicknesses. Central-to-total subcutaneous fat mass ratio = (suprailiacal + subscapular skinfold thicknesses)/total subcutaneous fat mass. HDL-cholesterol, high-density lipoprotein-cholesterol; LDL-cholesterol, low-density lipoprotein-cholesterol.

[2]Unadjusted model.

*P-value<0.05; **P-value<0.01.