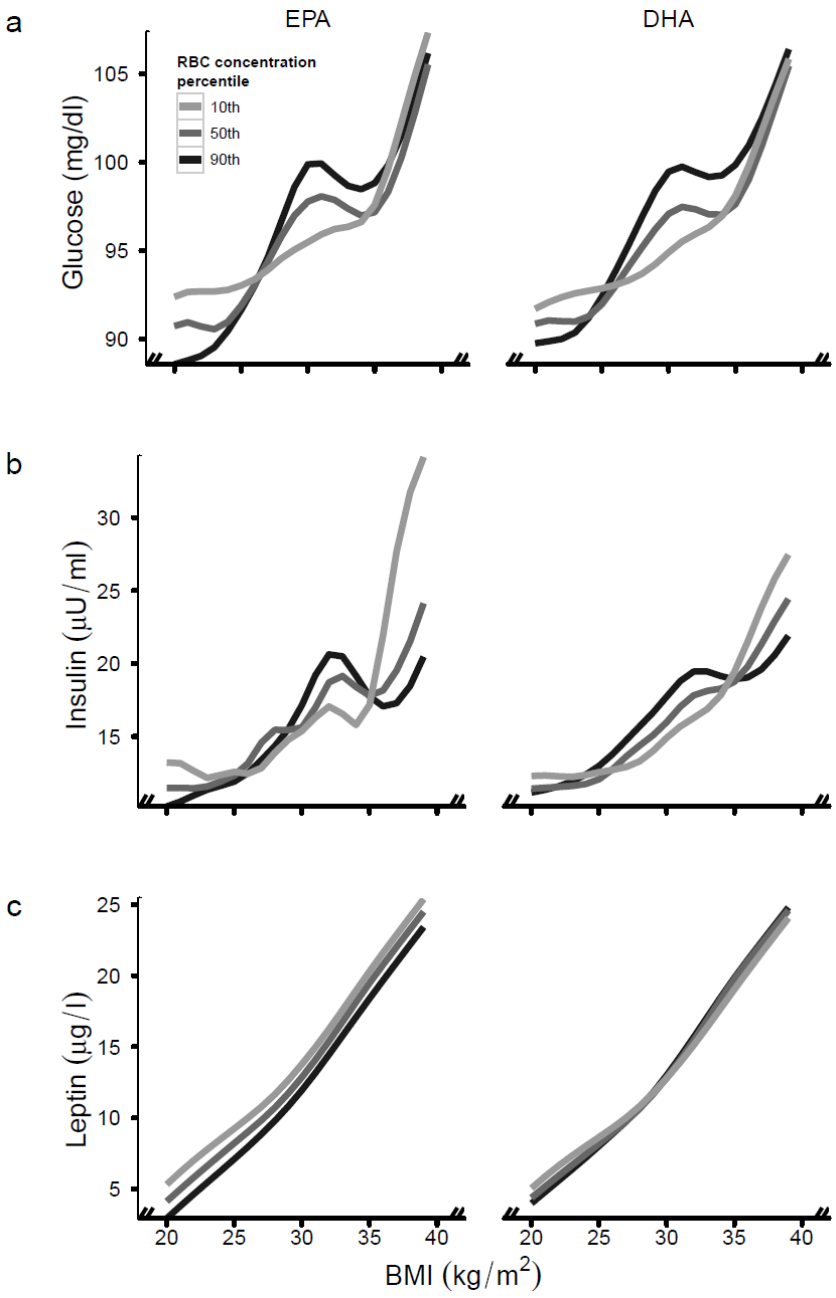
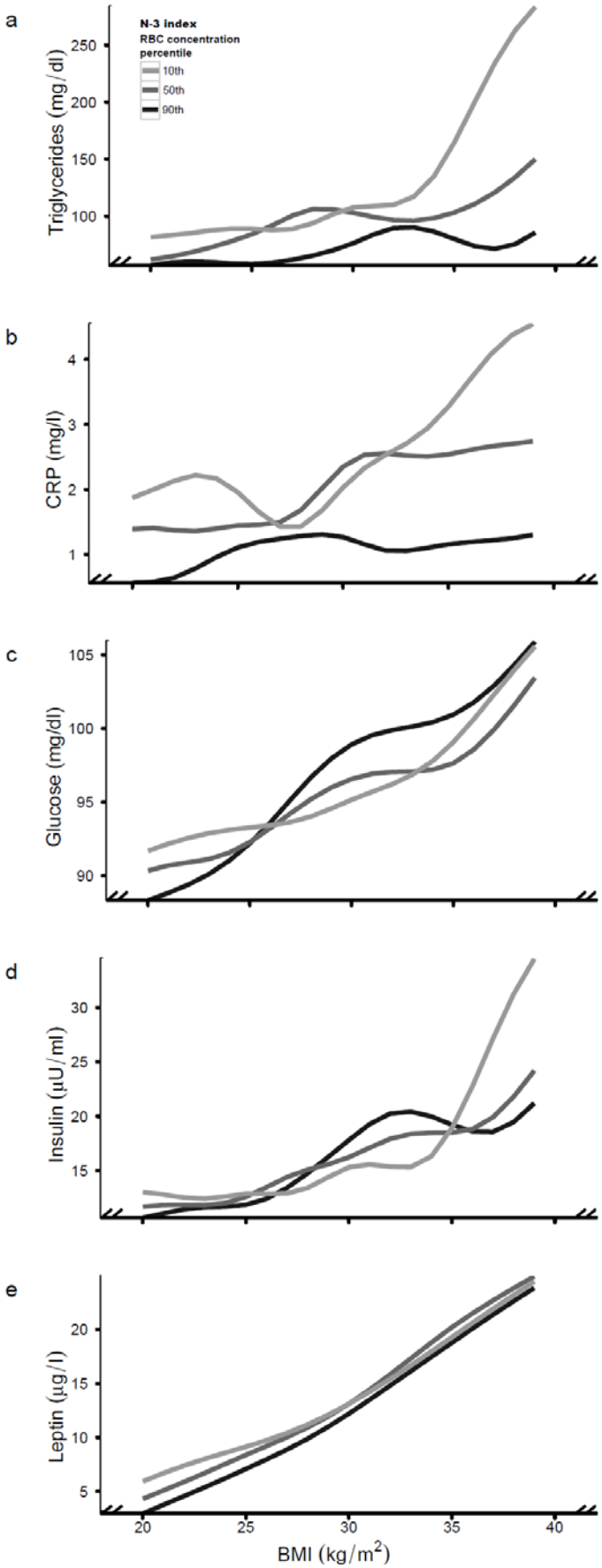
Supplemental Information



Supplementary Figure 1 Generalized Additive Models (GAM) of the associations of BMI with glucose (a), insulin (b) and leptin (c) by eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), as percentages of total fatty acids in RBC. The GAM include a bivariate smooth surface over EPA or DHA and BMI (all continuous). The estimated GAM were evaluated at mean values of age, gender and current smoking status and at the 10th (light grey line), 50th (dark grey line) and 90th (black line) percentiles of RBC EPA (1%, 3% and 5% of total fatty acids) and DHA (4%, 7% and 9% of total fatty acids). To convert glucose from mg/dl to mmol/l, multiply by 0.0555. To convert insulin from µU/l to pmol/l, multiply by 6.945.


a
N-3 index
RBC concentration percentile
10th
50th
90th
Triglycerides (mg/dl)
250
200
150
100
b
CRP (mg/l)
4
3
2
1
c
Glucose (mg/dl)
105
100
95
90
d
Insulin (µU/ml)
30
25
20
15
e
Leptin (µg/l)
20
15
10
5
20
25
30
35
40
BMI (kg/m^2)

Supplementary Figure 2 Generalized Additive Models (GAM) of the associations of BMI with triglycerides (a), CRP (b), glucose (c), insulin (d) and leptin (e) by n-3 index (RBC eicosapentaenoic acid + docosahexaenoic acid), as percentage of total fatty acids in RBC. The GAM include a bivariate smooth surface over n-3 index and BMI (all continuous). The estimated GAM were evaluated at mean values of age, gender and current smoking status and at the 10th (light grey line), 50th (dark grey line) and 90th (black line) percentiles of n-3 index (5%, 10% and 14% of total fatty acids). To convert triglycerides from mg/dl to mmol/l, multiply by 0.0113. To convert glucose from mg/dl to mmol/l, multiply by 0.0555. To convert insulin from μU/l to pmol/l, multiply by 6.945.

Supplementary Table Associations of BMI with biomarkers of chronic disease risk by n-3 index, as percentages of total fatty acids in RBC[a]

	N-3 index[b] (% *of total fatty acids)*						
	<7.0 (*n* = 83)		7.0–12.1 (*n* = 164)		>12.1 (*n* = 83)		*P*[c]
	β ± SE	*P*	β ± SE	*P*	β ± SE	*P*	
SBP (*mm Hg)*	0.4 ± 0.4	0.25	0.5 ± 0.2	0.06	0.7 ± 0.3	0.04	0.85
DBP (*mm Hg)*	0.9 ± 0.2	<0.001	0.5 ± 0.1	<0.001	0.8 ± 0.2	<0.001	0.25
Triglycerides[d, e] (*mg/dl)*							
Model 1	0.06 ± 0.01	<0.001	0.04 ± 0.01	<0.001	0.02 ± 0.01	0.005	0.05
Model 2							
Linear	−0.29 ± 0.11	0.012	0.13 ± 0.07	0.06	0.01 ± 0.09	0.87	<0.001
Quadratic	0.006 ± 0.002	0.003	−0.001 ± 0.001	0.19	0.0002 ± 0.001	0.91	
Total cholesterol[f] (*mg/dl)*	0.5 ± 1.0	0.60	−0.9 ± 0.7	0.18	−1.7 ± 0.9	0.07	0.27
LDL cholesterol[f] (*mg/dl)*	−0.2 ± 0.9	0.86	−0.2 ± 0.6	0.78	−0.3 ± 0.8	0.74	0.99
HDL cholesterol[f] (*mg/dl)*	−1.5 ± 0.4	<0.001	−1.4 ± 0.2	<0.001	−1.8 ± 0.3	<0.001	0.61
ApoA1 (*g/l)*	−0.02 ± 0.005	<0.001	−0.01 ± 0.003	<0.001	−0.02 ± 0.004	<0.001	0.58
Glucose[g] (*mg/dl)*	0.5 ± 0.2	0.03	0.5 ± 0.2	0.002	1.1 ± 0.2	<0.001	0.09
Insulin[h] (*μU/ml)*							
Model 1	0.7 ± 0.1	<0.001	0.6 ± 0.1	<0.001	0.6 ± 0.1	<0.001	0.76
Model 2							
Linear	−6.0 ± 1.8	0.001	0.3 ± 1.1	0.81	1.7 ± 1.4	0.23	0.01
Quadratic	0.12 ± 0.03	<0.001	0.006 ± 0.019	0.76	−0.02 ± 0.02	0.44	
HOMA-IR[d]	0.05 ± 0.01	<0.001	0.05 ± 0.01	<0.001	0.05 ± 0.01	<0.001	0.99
IGF1[i] (*μg/l)*	−4.3 ± 1.8	0.02	−1.7 ± 1.2	0.14	−2.6 ± 1.6	0.10	0.48
IGFBP3 (*μg/l)*	38.7 ± 22.9	0.09	40.1 ± 15.1	0.008	59.1 ± 20.2	0.004	0.71
CRP[d] (*mg/l)*	0.08 ± 0.03	0.007	0.06 ± 0.02	0.003	0.04 ± 0.02	0.09	0.67
IL6[d], ng*/l*	0.05 ± 0.03	0.13	0.02 ± 0.02	0.35	0.02 ± 0.03	0.45	0.75

sTNFR2[d] (ng*/l)*	−0.006 ± 0.015	0.71	0.008 ± 0.01	0.40	0.008 ± 0.013	0.56	0.73
Leptin[d] (µg*/l)*	0.11 ± 0.01	<0.001	0.11 ± 0.01	<0.001	0.08 ± 0.01	<0.001	0.08
Adiponectin (*mg/l)*	−0.35 ± 0.10	<0.001	−0.46 ± 0.06	<0.001	−0.34 ± 0.09	<0.001	0.47

[a] Values are β coefficients ± SE and corresponding *P* values from linear (Model 1) and quadratic (Model 2) regression models controlling for age (continuous), sex and current smoking status (yes, no). Quadratic models are reported only when statistically significant.

[b] Categories are <25th percentile, 25th to 75th percentiles and >75th percentile.

[c] *P* values for interaction are based on the likelihood ratio *F*-test test comparing linear regression models with and without interaction of BMI (continuous) with n-3 index (categorical).

[d] Log-transformed values were used for the regression analysis.

[e] To convert triglycerides from mg/dl to mmol/l, multiply by 0.0113.

[f] To convert cholesterol (total, HDL and LDL) from mg/dl to mmol/l, multiply by 0.0259.

[g] To convert glucose from mg/dl to mmol/l, multiply by 0.0555.

[h] To convert insulin from µU/ml to pmol/l, multiply by 6.945.

[i] Regression model additionally adjusted for IGFBP3.