Online Supplement

Long-term Adiposity and Midlife Carotid Intima-media Thickness Are Linked Partly through Intermediate Risk Factors

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Running Title: Obesity-Atherosclerosis via Third Variables

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Table S1. Mediation effect parameters in one model with parallel multiple mediators and with cIMT as the outcome

Predictor	Mediator	c	β_1	β_2	β_{Ind}	c'	Mediation effect (%)
Childhood BMI	Adult SBP	0.138 (0.025)*	0.080 (0.025)*	0.141 (0.027)*	0.011 [0.004, 0.021]*	0.116 [0.057, 0.174]*	8.0 [0.9, 15.1]*
	Adult LDLC	0.138 (0.025)*	0.004 (0.027)	0.089 (0.025)*	0.000 [-0.006, 0.006]	0.116 [0.057, 0.174]*	0.0 [-4.3, 4.3]
	Adult AIP	0.138 (0.025)*	0.106 (0.025)*	0.047 (0.028)	0.005 [-0.001, 0.011]	0.116 [0.057, 0.174]*	3.6 [-0.7, 7.9]
	Adult Glucose	0.138 (0.025)*	0.094 (0.026)*	0.063 (0.026)*	0.006 [0.000, 0.013]*	0.116 [0.057, 0.174]*	4.3 [0.0, 8.7]*
Adult BMI	Adult SBP	0.111 (0.025)*	0.185 (0.025)*	0.142 (0.027)*	0.026 [0.013, 0.043]*	0.046 [-0.025, 0.124]	23.4 [9.7, 37.1]*
	Adult LDLC	0.111 (0.025)*	0.095 (0.027)*	0.084 (0.025)*	0.008 [0.002, 0.017]*	0.046 [-0.025, 0.124]	7.2 [-0.1, 14.5]
	Adult AIP	0.111 (0.025)*	0.299 (0.024)*	0.046 (0.029)	0.014 [-0.003, 0.032]	0.046 [-0.025, 0.124]	12.6 [-2.2, 27.4]
	Adult Glucose	0.111 (0.025)*	0.264 (0.026)*	0.063 (0.027)*	0.017 [0.001, 0.034]*	0.046 [-0.025, 0.124]	15.3 [1.7, 28.9]*
BMI AUC	Adult SBP	0.150 (0.025)*	0.166 (0.024)*	0.135 (0.027)*	0.022 [0.011, 0.037]*	0.103 [0.037, 0.180]*	14.7 [5.6, 23.7]*
	Adult LDLC	0.150 (0.025)*	0.037 (0.027)	0.087 (0.025)*	0.003 [-0.002, 0.010]	0.103 [0.037, 0.180]*	2.0 [-1.9, 5.9]
	Adult AIP	0.150 (0.025)*	0.222 (0.024)*	0.039 (0.028)	0.009 [-0.003, 0.022]	0.103 [0.037, 0.180]*	6.0 [-1.6, 13.6]
	Adult Glucose	0.150 (0.025)*	0.270 (0.025)*	0.049 (0.027)	0.013 [-0.002, 0.031]	0.103 [0.037, 0.180]*	8.7 [-2.4, 19.7]

c, β_1, and β_2 are standardized regression coefficients (standardized errors). β_{Ind} and c' are standardized regression coefficients [95% confidence intervals]. Mediation effects are percentages [95% confidence intervals].
c=total effect; c'=direct effect; β_1=indirect effect 1; β_2=indirect effect 2; β_{Ind}=indirect effect ($\beta_1 \times \beta_2$)
*, $P < 0.05$ for being different from 0
cIMT=carotid intima-media thickness; BMI=body mass index; SBP=systolic blood pressure; LDLC=low-density lipoprotein cholesterol; AIP=atherogenic index of plasma; AUC=area under the curve
Covariates in the models were race, sex, follow-up years, adult age, smoking and alcohol drinking.

Table S2. Mediation effect parameters in one model with parallel multiple mediators and with cIMT as the outcome

Predictor	Mediator	c	β_1	β_2	β_{Ind}	c'	Mediation effect (%)
Childhood BMI	Adult SBP	0.121 (0.025)*	0.065 (0.024)*	0.137 (0.027)*	0.009 [0.002, 0.018]*	0.105 [0.049, 0.164]*	7.4 [0.7, 14.1]*
	Adult LDLC	0.121 (0.025)*	0.009 (0.027)	0.095 (0.025)*	0.001 [-0.005, 0.007]	0.105 [0.049, 0.164]*	0.8 [-4.0, 5.7]
	Adult AIP	0.121 (0.025)*	0.088 (0.025)*	0.038 (0.028)	0.003 [-0.001, 0.009]	0.105 [0.049, 0.164]*	2.5 [-2.4, 7.3]
	Adult Glucose	0.121 (0.025)*	0.067 (0.026)*	0.048 (0.026)	0.003 [-0.001, 0.009]	0.105 [0.049, 0.164]*	2.5 [-2.4, 7.3]
Adult BMI	Adult SBP	0.084 (0.026)*	0.161 (0.025)*	0.140 (0.027)*	0.022 [0.011, 0.037]*	0.030 [-0.042, 0.106]	26.2 [6.7, 45.7]*
	Adult LDLC	0.084 (0.026)*	0.109 (0.028)*	0.091 (0.025)*	0.010 [0.003, 0.020]*	0.030 [-0.042, 0.106]	11.9 [1.0, 22.8]*
	Adult AIP	0.084 (0.026)*	0.276 (0.025)*	0.039 (0.028)	0.011 [-0.005, 0.028]	0.030 [-0.042, 0.106]	13.1 [-4.8, 31.0]
	Adult Glucose	0.084 (0.026)*	0.228 (0.026)*	0.050 (0.027)	0.011 [-0.002, 0.026]	0.030 [-0.042, 0.106]	13.1 [-3.0, 29.2]
BMI AUC	Adult SBP	0.126 (0.025)*	0.144 (0.025)*	0.133 (0.027)*	0.019 [0.009, 0.032]*	0.088 [0.021, 0.161]*	15.1 [5.3, 24.8]*
	Adult LDLC	0.126 (0.025)*	0.047 (0.027)	0.093 (0.025)*	0.004 [-0.001, 0.012]	0.088 [0.021, 0.161]*	3.2 [-1.5, 7.9]
	Adult AIP	0.126 (0.025)*	0.197 (0.025)*	0.032 (0.028)	0.006 [-0.005, 0.018]	0.088 [0.021, 0.161]*	4.8 [-4.3, 13.8]
	Adult Glucose	0.126 (0.025)*	0.236 (0.025)*	0.037 (0.027)	0.009 [-0.005, 0.025]	0.088 [0.021, 0.161]*	7.1 [-4.7, 19.0]

c, β_1, and β_2 are standardized regression coefficients (standardized errors). β_{Ind} and c' are standardized regression coefficients [95% confidence intervals]. Mediation effects are percentages [95% confidence intervals].
c=total effect; c'=direct effect; β_1=indirect effect 1; β_2=indirect effect 2; β_{Ind}=indirect effect ($\beta_1 \times \beta_2$)
*, $P < 0.05$ for being different from 0
cIMT=carotid intima-media thickness; BMI=body mass index; SBP=systolic blood pressure; LDLC=low-density lipoprotein cholesterol; AIP=atherogenic index of plasma; AUC=area under the curve
Covariates in the models were race, sex, follow-up years, adult age, smoking, alcohol drinking, antihypertensive, lipid-lowering and antidiabetic medications.
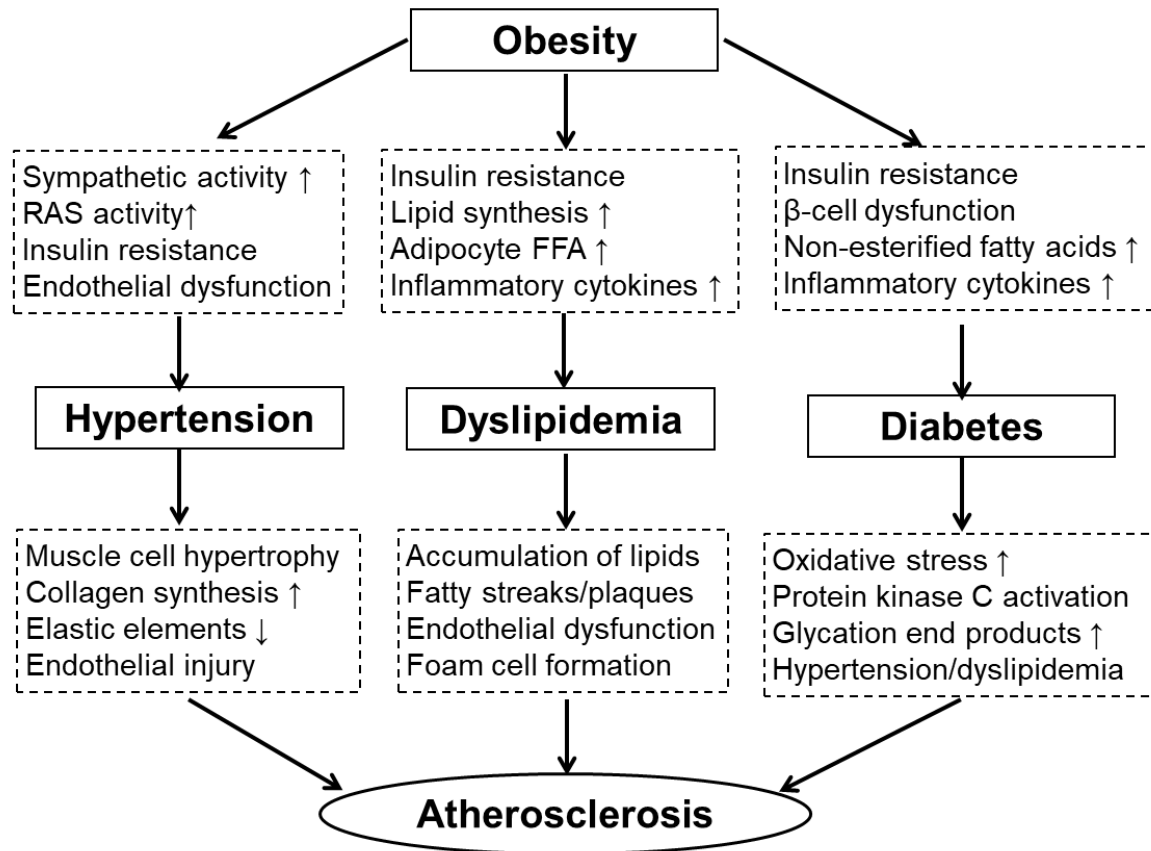
Figure S1. Biological mechanisms underlying the relationships between obesity, hypertension, dyslipidemia, diabetes and atherosclerosis

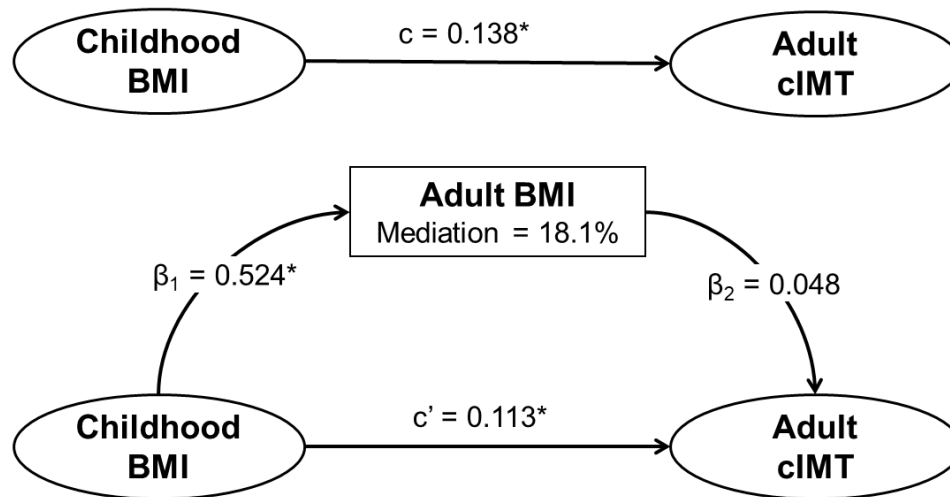RAS=renin angiotensin system; FFA=free fatty acid

Figure S2. Mediation effect of adult BMI on the childhood BMI-adult cIMT association

β, c and c' are standardized regression coefficients.

c=total effect; c'=direct effect; β_1=indirect effect 1; β_2=indirect effect 2; β_{Ind}=indirect effect ($\beta_1 \times \beta_2$); BMI=body mass index; cIMT=carotid intima-media thickness

β_{Ind}= 0.025, P = 0.242
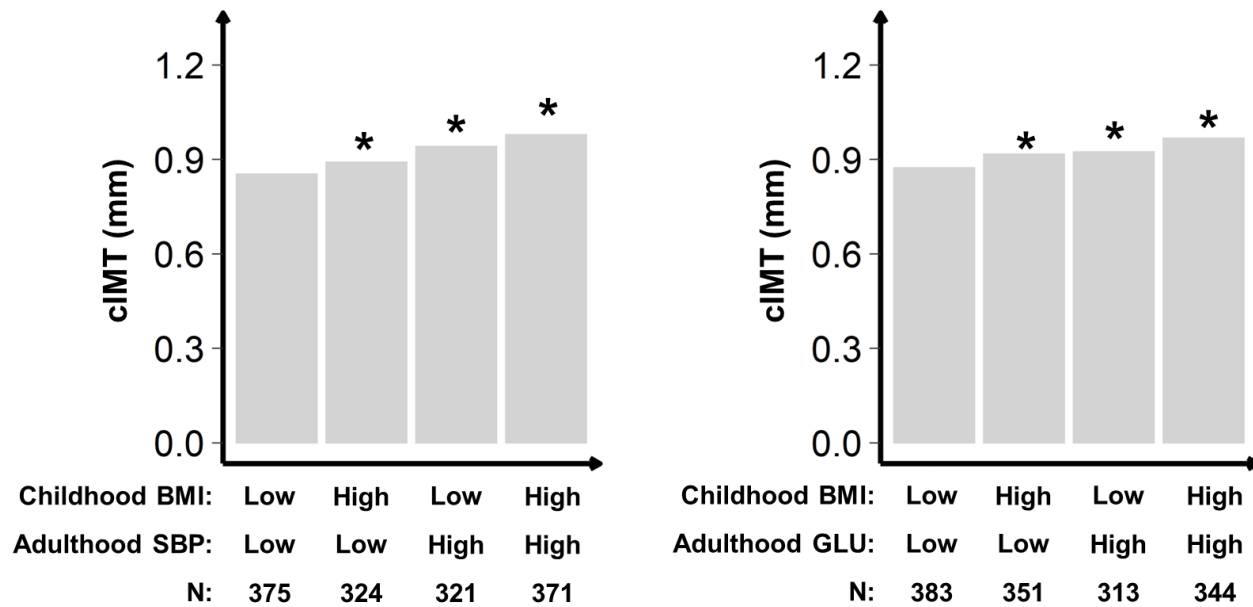
* P < 0.01 for being different from 0

Figure S3. Least square means of adult cIMT, adjusted for race, sex, follow-up years, adult age, smoking and alcohol drinking, by subgroups
BMI=body mass index; SBP=systolic blood pressure; GLU=glucose; cIMT=carotid intima-media thickness
Low and high levels were defined by their race- and sex-specific medians.
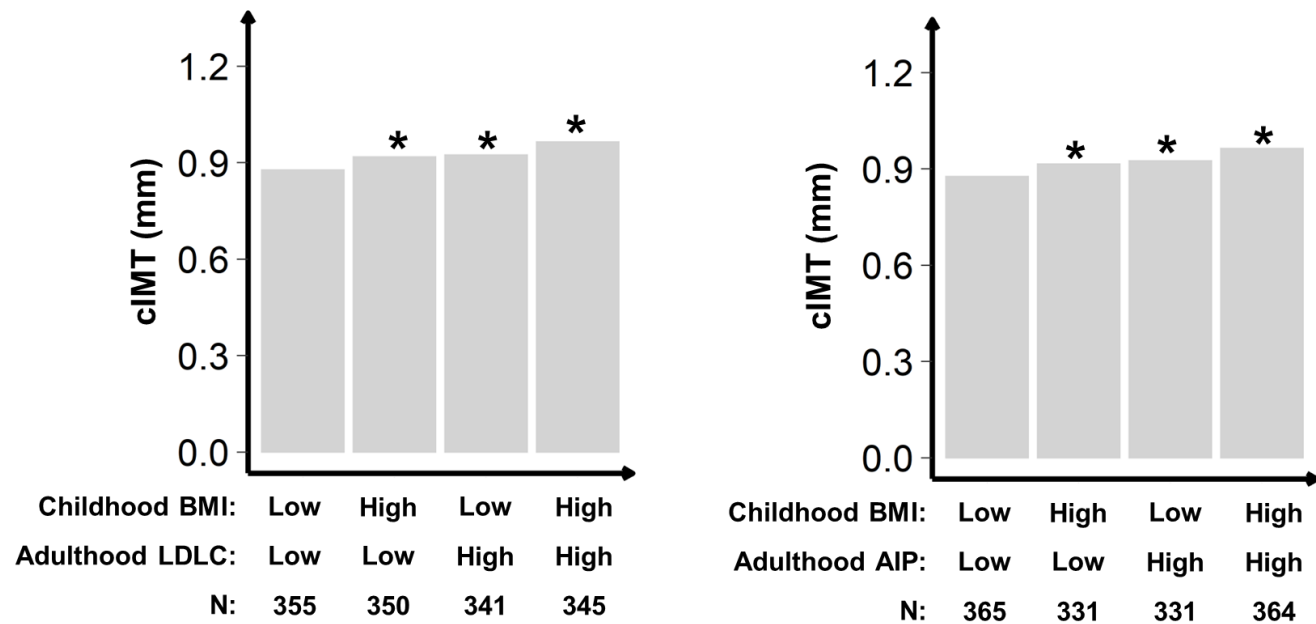*, Bonferroni adjusted $P<0.05$ compared to the low-low group

Figure S4. Least square means of adult cIMT, adjusted for race, sex, follow-up years, adult age, smoking and alcohol drinking, by subgroups
BMI=body mass index; LDLC=low-density lipoprotein cholesterol; AIP=atherogenic index of plasma; cIMT=carotid intima-media thickness
Low and high levels were defined by their race- and sex-specific medians.
*, Bonferroni adjusted *P*<0.05 compared to the low-low group