

Original Contribution

Relation of Childhood Obesity/Cardiometabolic Phenotypes to Adult Cardiometabolic Profile

The Bogalusa Heart Study

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Not all obese adults have cardiometabolic abnormalities. It is unknown whether this is true in children and, if true, whether children who have metabolically healthy overweight/obesity (MHO) will also have favorable cardiometabolic profiles in adulthood. These aspects were examined in 1,098 individuals who participated as both children (aged 5–17 years) and adults (aged 24–43 years) in the Bogalusa Heart Study between 1997 and 2002 in Bogalusa, Louisiana. MHO was defined as being in the top body mass index quartile, while low density lipoprotein cholesterol, triglycerides, mean arterial pressure, and glucose were in the bottom 3 quartiles, and high density lipoprotein cholesterol was in the top 3 quartiles. Forty-six children (4.2%) had MHO, and they were more likely to retain MHO status in adulthood compared with children in other categories ($P < 0.0001$). Despite markedly increased obesity in childhood and in adulthood, these same MHO children and adults showed a cardiometabolic profile generally comparable to that of nonoverweight/obese children ($P > 0.05$ in most cases). Moreover, there was no difference in carotid intima-media thickness in adulthood between MHO children and nonoverweight/obese children. Further, carotid intima-media thickness in adulthood was lower in MHO children than in metabolically abnormal, overweight/obese children ($P = 0.003$). In conclusion, the MHO phenotype starts in childhood and continues into adulthood.

carotid intima-media thickness; longitudinal studies; metabolism; obesity; risk factors

Abbreviations: BMI, body mass index; CI, confidence interval; CIMT, carotid intima-media thickness; HDL, high density lipoprotein; MHO, metabolically healthy overweight/obesity.

Obesity has reached epidemic proportions in children as well as adults over the last few decades in developed countries and more recently in developing countries (1–4). Obesity is associated with increased risk of insulin resistance, dyslipidemia, elevated blood pressure, and inflammation (5, 6), which is linked to increased risk of type 2 diabetes and cardiovascular disease, among others (7, 8).

However, there exists substantial heterogeneity in the prevalence of cardiometabolic risk factors in obese individuals (9, 10); that is, not all obese individuals present adverse metabolic profiles (11–15). In a national representative survey, Wildman et al. (12) reported that, overall, 16.6% of the obese had no cardiometabolic abnormalities

for the risk factors considered (blood pressure, triglycerides, fasting plasma glucose, C-reactive protein, homeostasis model assessment of insulin resistance, and high density lipoprotein cholesterol). Obese individuals who do not have an adverse cardiometabolic profile have been referred to as having “metabolically healthy obesity.” Because there has been no consensus on the definition of metabolically healthy obesity, the prevalence of metabolically healthy obesity varies depending on how metabolically healthy obesity is defined (16).

Observations on metabolically healthy obesity have been made only in adult populations and are mostly cross-sectional. Whether metabolically healthy obesity also exists

in childhood and, if so, whether metabolically healthy obesity persists into adulthood are not known. Such information will provide insight into our understanding of the evolution of the metabolically healthy obesity phenotype from childhood to adulthood.

We hypothesized that metabolically healthy obesity exists in children and that metabolically healthy obese children may not necessarily present an adverse cardiometabolic risk profile in adulthood. The Bogalusa Heart Study, a community-based, black-white, longitudinal study, provides a unique opportunity to examine metabolically healthy obesity in children and its cardiometabolic profile in adulthood.

MATERIALS AND METHODS

Study population

Between 1973 and 2002, 7 cross-sectional surveys of children aged 4–17 years and 7 surveys of young adults aged 18–43 years who participated earlier as children and remained accessible were conducted in the biracial (65%

whites, 35% blacks) community of Bogalusa, Louisiana. The participation rates ranged from 80% to 92% for children and from 60% to 65% for young adults. During the 2000–2002 survey of young adults ($n = 1,203$, aged 24–43 years), B-mode ultrasound examination of the carotid artery was conducted in 1,148 subjects. Of those, 1,098 individuals who were previously examined for traditional cardiovascular risk factors at least 2 times in childhood (ages 4–17 years) and had all of the risk factors measured formed the cohort in this study. The average follow-up period was 24.2 (range: 14.1–28.6) years. Characteristics of the study cohort are presented in Table 1.

Written, informed consent was obtained from parents or guardians in childhood and from the participants in adulthood. The protocol was approved by the Institutional Review Board of the Tulane University Health Sciences Center.

Examinations

All examinations followed essentially the same protocols. Subjects were instructed to fast for 12 hours before

Table 1. Characteristics (Mean (SD)) of the Study Cohort: The Bogalusa Heart Study, Bogalusa, Louisiana, 1973–2002

Variable	White		Black		<i>P</i> _{difference}	
	Men ($n = 351$)	Women ($n = 408$)	Men ($n = 131$)	Women ($n = 208$)	Race	Sex
Childhood						
Age, years	11.93 (3.79)	11.74 (3.80)	11.92 (3.77)	11.51 (3.74)	>0.05	>0.05
Body mass index ^a	19.28 (4.36)	18.69 (3.62)	19.26 (4.51)	19.32 (4.56)	>0.05	>0.05
HDL cholesterol, mg/dL	57.81 (19.24)	59.13 (17.25)	64.40 (18.31)	63.86 (17.42)	<0.001	>0.05
LDL cholesterol, mg/dL	83.98 (23.38)	87.47 (25.82)	83.60 (24.60)	89.33 (25.29)	>0.05	>0.05
Triglycerides, mg/dL	73.45 (41.68)	73.36 (33.14)	62.15 (28.56)	62.14 (22.74)	<0.001	>0.05
Systolic blood pressure, mm Hg	103.77 (11.44)	101.70 (9.89)	103.29 (12.00)	101.83 (11.37)	>0.05	>0.05
Diastolic blood pressure, mm Hg	62.74 (9.95)	63.43 (9.50)	62.73 (9.63)	63.78 (10.58)	>0.05	>0.05
Glucose, mg/dL	89.11 (8.35)	86.69 (8.24)	87.89 (10.09)	85.25 (9.86)	0.02	<0.001
Adulthood						
Age, years	36.19 (4.26)	35.96 (4.39)	36.35 (4.36)	35.38 (4.75)	>0.05	>0.05
Body mass index ^a	29.32 (5.93)	28.37 (7.05)	29.87 (7.44)	31.59 (8.51)	<0.001 ^b	<0.05 ^c
Waist, cm	99.59 (15.46)	87.23 (16.39)	98.24 (18.24)	94.16 (18.32)	<0.001 ^b	<0.05
HDL cholesterol, mg/dL	41.21 (12.00)	50.34 (12.89)	49.27 (15.88)	51.61 (12.81)	<0.001 ^d	<0.001 ^c
LDL cholesterol, mg/dL	128.80 (33.93)	124.55 (32.39)	124.79 (44.07)	115.14 (31.98)	>0.05	>0.05
Triglycerides, mg/dL	164.56 (131.04)	122.13 (71.56)	130.33 (108.62)	89.52 (39.26)	<0.001	<0.001
Systolic blood pressure, mm Hg	118.34 (10.97)	111.20 (11.21)	128.47 (16.63)	118.57 (14.86)	<0.001	<0.001
Diastolic blood pressure, mm Hg	80.22 (7.99)	75.03 (8.49)	86.76 (12.32)	79.41 (10.61)	<0.001	<0.001
Insulin, μ U/mL	13.41 (10.37)	11.55 (8.21)	12.55 (9.37)	15.94 (19.84)	<0.001 ^b	<0.001 ^e
Glucose, mg/dL	88.85 (23.78)	82.66 (15.91)	90.63 (32.38)	88.90 (32.54)	<0.01	<0.01
Carotid IMT, mm	0.85 (0.19)	0.76 (0.13)	0.89 (0.22)	0.80 (0.16)	<0.001	<0.001

Abbreviations: HDL, high density lipoprotein; IMT, intima-media thickness; LDL, low density lipoprotein; SD, standard deviation.

^a Body mass index: weight (kg)/height (m)².

^b Only in women.

^c Only in whites.

^d Only in men.

^e Different directions in blacks versus whites.

the screening, with compliance ascertained by interview on the morning of the examination. Height, weight, and waist circumference were measured twice, and the mean values were used. Body mass index (BMI) was calculated as weight (kg)/height (m)².

Replicate blood pressure measurements were obtained on the right arm of the subjects in a relaxed, sitting position. Arm measurements, length and circumference, were made during the examination to ensure proper cuff size. Systolic and diastolic blood pressure levels were analyzed as the first, fourth (in children), and fifth (in adults) Korotkoff phases by using mercury sphygmomanometers. Blood pressure levels were reported as the mean of 6 replicate readings, 3 taken by each of 2 randomly assigned and trained observers.

Serum lipid and lipoprotein analyses

During 1973–1986, cholesterol and triglyceride levels were measured by the use of chemical procedures with a Technicon AutoAnalyzer II (Technicon Instrument Corporation, Tarrytown, New York) according to the Laboratory Manual of the Lipid Research Clinics Program (17). Since 1987, these variables were determined by using the Abbott VP instrument (Abbott Laboratories, North Chicago, Illinois) by enzymatic procedures (18). Both chemical and enzymatic procedures met the performance requirements of the Lipid Standardization Program of the Centers for Disease Control and Prevention, Atlanta, Georgia, which routinely monitors the accuracy of measurements of total cholesterol, triglycerides, and high density lipoprotein (HDL) cholesterol concentrations. Measurements on the Centers for Disease Control and Prevention-assigned quality control samples showed no consistent bias over time within or between surveys. Serum lipoprotein cholesterol levels were analyzed by using a combination of heparin-calcium precipitation and agar-agarose gel electrophoresis procedures (19). A commercial radioimmunoassay kit was used for measuring plasma immunoreactive insulin levels (Pharmacia Diagnostics, Piscataway, New Jersey). Plasma glucose levels were measured as part of a sequential multi-channel analysis with computer-20 (SMA20) chemistry profile by a glucose oxidase method.

Carotid ultrasonography

Trained sonographers performed ultrasound examinations with a Toshiba Sonolayer SSH160A (Toshiba Medical, Tokyo, Japan), a 7.5-MHz linear array transducer on subjects in the supine position with the head slightly extended and turned to the opposite direction of the carotid artery being studied. Images were recorded at the common carotid, carotid bulb (bifurcation), and internal carotid arteries bilaterally according to previously developed protocols for the Atherosclerosis Risk in Communities Study (20). Images were recorded on super-video home system (S-VHS) tapes and read by certified readers from the Division of Vascular Ultrasound Research using a semiautomatic ultrasound image processing program developed by the California Institute of Technology Jet Propulsion Laboratory

(Pasadena, California) according to strict protocols (20, 21). The mean of the maximum carotid intima-media-thickness (CIMT) readings of 3 right and 3 left far walls for common, bulb, and internal segments was used.

Statistical methods

Data analyses were performed by using SAS, version 9.2 (SAS Institute, Inc., Cary, North Carolina), software. Average values of all measurements in childhood were used as the childhood values; values at the last examination were used as the adulthood values. To define metabolically healthy overweight/obesity (MHO), we first regressed these values on age, race, and sex, and the residuals were then standardized by inverse-normal transformation. MHO was defined as BMI in the top quartile, while low density lipoprotein cholesterol, triglycerides, mean arterial pressure, and glucose were in the bottom 3 quartiles, and HDL cholesterol was in the top 3 quartiles, for both childhood and adulthood; metabolically abnormal overweight/obesity was defined as BMI in the top quartile but not MHO. Metabolically healthy nonoverweight/obesity was defined as BMI, low density lipoprotein cholesterol, triglycerides, mean arterial pressure, and glucose in the bottom 3 quartiles and HDL cholesterol in the top 3 quartiles; metabolically abnormal nonoverweight/obesity was defined as BMI in the bottom 3 quartiles but not belonging to the previous group. For the definition of MHO in adulthood, subjects with type II diabetes and taking blood pressure medications were considered to be in the top quartile of glucose and mean arterial pressure, respectively, in adulthood; subjects taking lipid-lowering drugs were considered to be in the top quartile of triglycerides and low density lipoprotein cholesterol and in the bottom quartile of HDL cholesterol. We also defined MHO in adulthood, according to the latest definition of metabolic syndrome (22), as waist circumference ≥ 102 cm for men or 88 cm for women, triglycerides ≥ 150 mg/dL or taking lipid-lowering drugs, systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg, or taking blood pressure-lowering drugs, plasma glucose ≥ 100 mg/dL or being diabetic, and HDL cholesterol less than 40 mg/dL for men or 50 mg/dL for women or taking lipid-lowering drugs. Metabolically abnormal obesity, metabolically healthy nonobesity, and metabolically abnormal nonobesity were defined accordingly. Because findings were similar for the 2 definitions of MHO, we focused on findings from quartile splits only. Triglycerides, insulin, and CIMT were log transformed to increase normality before further data processing.

The chi-square test was used to examine tracking of MHO status from childhood to adulthood. The general linear model was used to examine the differences in cardiometabolic risk factors in childhood as well as in adulthood among children with different obesity status.

RESULTS

In childhood, 46 (4.2%) had MHO; 228 (20.8%) were metabolically abnormal, overweight/obese; 514 (46.8%) were metabolically abnormal, nonoverweight/obese; and

Table 2. Tracking of Obesity Status According to Quartile Splits From Childhood to Adulthood: The Bogalusa Heart Study, Bogalusa, Louisiana, 1973–2002*

Childhood ^a	Adulthood ^a								Total	
	MHNO		MANO		MAO		MHO			
	No.	% ^b	No.	% ^b	No.	% ^b	No.	% ^b	No.	% ^c
MHNO	138	44.5	135	43.6	27	8.7	10	3.2	310	28.2
MANO	157	30.5	300	58.4	50	9.7	7	1.4	514	46.8
MAO	20	8.8	60	26.3	137	60.1	11	4.8	228	20.8
MHO	9	19.6	15	32.6	16	34.8	6	13.0	46	4.2
Total	324	29.5	510	46.4	230	21.0	34	3.1	1,098	100.0

Abbreviations: MANO, metabolically abnormal nonoverweight/obesity; MAO, metabolically abnormal overweight/obesity; MHNO, metabolically healthy nonoverweight/obesity; MHO, metabolically healthy overweight/obesity.

* $P < 0.0001$ according to χ^2 test.

^a MHO was defined as body mass index in the top quartile, while low density lipoprotein cholesterol, triglycerides, mean arterial pressure, and plasma glucose were in the bottom 3 quartiles, and high density lipoprotein cholesterol was in the top 3 quartiles in both childhood and adulthood; medication use in adulthood was taken into account.

^b “%” indicates proportions in the row.

^c “%” indicates proportions in the column.

310 (28.2%) were metabolically healthy, nonoverweight/obese. Of the 46 children, 24 (52.2%) became nonoverweight/obese as adults, 9 (37.5%) of whom were metabolically healthy, and 16 (34.8%) became metabolically abnormal, overweight/obese. Although only 6 (13%) retained MHO status in adulthood, MHO children were 2.7–9.3 times more likely to retain the MHO status as adults compared with children in other categories ($P < 0.0001$) (Table 2). Of note, 67.4% (31/46) of those who were classified as MHO in childhood became metabolically abnormal in adulthood; 52.3% (162/310) of those who were classified

as metabolically healthy nonoverweight/obese in childhood became metabolically abnormal. In addition, 62.0% (against 25% expected) of children in the top BMI quartile remained in the top BMI quartile in adulthood, indicating strong BMI tracking, even after an average period of 24.2 years.

If cutoff points for metabolic syndrome components were used to define MHO in adults, 5.2% (57/1,098) had MHO as adults. Results for tracking (or otherwise changing) of MHO status from childhood to adulthood were similar to those observed if quartile splits were used in adulthood (Table 3).

Table 3. Tracking of Obesity Status From Childhood (According to Quartile Splits) to Adulthood (According to Cutoff Points for Proposed Metabolic Syndrome^a): The Bogalusa Heart Study, Bogalusa, Louisiana, 1973–2002*

Childhood ^b	Adulthood ^c								Total	
	MHNO		MANO		MAO		MHO			
	No.	% ^d	No.	% ^d	No.	% ^d	No.	% ^d	No.	% ^e
MHNO	119	38.4	109	35.1	65	21.0	17	5.5	310	28.2
MANO	136	26.5	217	42.2	145	28.2	16	3.1	514	46.8
MAO	18	7.9	23	10.1	170	74.6	17	7.4	228	20.8
MHO	5	10.9	7	15.2	27	58.7	7	15.2	46	4.2
Total	278	25.3	356	32.4	407	37.1	57	5.2	1,098	100.0

Abbreviations: MANO, metabolically abnormal nonoverweight/obesity; MAO, metabolically abnormal overweight/obesity; MHNO, metabolically healthy nonoverweight/obesity; MHO, metabolically healthy overweight/obesity (for children) or metabolically healthy obesity (for adults).

* $P < 0.0001$ according to χ^2 test.

^a According to Alberti et al. (*Circulation*. 2009;120(16):1640–1645) (22).

^b MHO was defined as body mass index in the top quartile, while low density lipoprotein cholesterol, triglycerides, mean arterial pressure, and plasma glucose were in the bottom 3 quartiles, and high density lipoprotein cholesterol was in the top 3 quartiles.

^c MHO was defined as waist circumference ≥ 102 cm for men or 88 cm for women, triglycerides ≥ 150 mg/dL, systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg, plasma glucose ≥ 100 mg/dL, and HDL cholesterol < 40 mg/dL for men or 50 mg/dL for women; medication use was taken into account.

^d “%” indicates proportions in the row.

^e “%” indicates proportions in the column.

Despite substantially higher BMI, MHO children had similar cardiometabolic risk factors compared with metabolically healthy, nonoverweight/obese children except for HDL cholesterol (Table 4). Further, MHO children had more favorable levels of risk factors than metabolically abnormal, nonoverweight/obese children and, to a much higher degree, metabolically abnormal, overweight/obese children (Table 4).

Overall, MHO children showed substantially increased BMI and waist circumference in their adulthood compared with nonoverweight/obese (either metabolically healthy or abnormal) children (Table 5). Despite this striking difference in obesity measures in their adulthood (amounting to ~7 BMI units or ~20 cm in waist circumference) between MHO children and metabolically abnormal, nonoverweight/obese children, MHO children had comparable or even favorable cardiometabolic risk factors as adults (Table 5). Moreover, MHO children and metabolically healthy, nonoverweight/obese children had comparable cardiometabolic risk profiles in adulthood, except that the former had higher blood pressure and, to a lesser degree, higher levels of insulin and glucose than the latter in adulthood (Table 5). MHO children showed a very favorable cardiometabolic profile in their adulthood, compared with metabolically abnormal, overweight/obese children (Table 5).

MHO children showed lower CIMT in adulthood compared with metabolically abnormal, overweight/obese children (0.794 (95% confidence interval (CI): 0.748, 0.841) mm vs. 0.859 (95% CI: 0.829, 0.889) mm) ($P=0.003$) (Figure 1). Notably, CIMT in adults was comparable between MHO children and metabolically healthy, nonoverweight/obese children (0.794 (95% CI: 0.748, 0.841) mm vs. 0.783 (95% CI: 0.768, 0.798) mm) ($P=0.88$) and between MHO children and metabolically abnormal, nonoverweight/obese children (0.794 (95% CI: 0.748, 0.841) mm vs. 0.816 (95% CI: 0.801, 0.831) mm) ($P=0.42$) (Figure 1), despite the striking difference in obesity measures in childhood and in adulthood (Tables 4 and 5).

DISCUSSION

In this community-based, black-white cohort, we showed that MHO children had considerably favorable cardiometabolic profiles as adults compared with metabolically abnormal, overweight/obese children. Further, their adulthood cardiometabolic profiles were, overall, comparable to those of metabolically healthy, nonoverweight/obese children despite substantially increased obesity in adulthood. Such observations are in agreement with previous findings that there exist substantial heterogeneities in the metabolic consequences of obesity. Importantly, our findings indicate that MHO in adults has its origin in the childhood years.

Our results support the argument by Gerald Reaven that “all obese individuals are not created equal” (10, p. 105), with observations that MHO children showed a comparable cardiometabolic profile compared with their metabolically healthy, nonoverweight/obese counterparts, and that metabolically abnormal, overweight/obese children had the most adverse cardiometabolic profile in adulthood. Our observations clearly show that such “inequality” in cardiometabolic consequences starts in childhood. Although only 13% of

Table 4. Childhood Characteristics of the Study Sample by Obesity Status in Childhood: The Bogalusa Heart Study, Bogalusa, Louisiana, 1973–2002

Variable in Childhood	MHO			MAO			MHO		
	Mean	95% CI	P Value ^b	Mean	95% CI	P Value ^b	Mean	95% CI	P Value ^b
Age, years	13.58	13.31, 13.85	0.62	13.88	13.67, 14.08	0.77	13.68	13.38, 13.98	0.83
Body mass index ^c	18.25	18.03, 18.47	<0.0001	18.95	18.77, 19.13	<0.0001	25.80	25.28, 26.32	<0.0001
LDL cholesterol, mg/dL	77.46	75.78, 79.14	0.69	92.84	90.72, 94.96	<0.0001	101.90	98.11, 105.68	<0.0001
HDL cholesterol, mg/dL	63.94	62.70, 65.17	0.04	55.52	54.13, 56.91	0.09	51.25	48.98, 53.56	0.001
Triglycerides, mg/dL	55.56	54.03, 57.08	0.07	74.46	72.05, 76.88	0.0003	90.68	85.73, 95.62	<0.0001
Glucose, mg/dL	83.10	82.55, 83.65	0.68	86.80	86.13, 87.47	<0.0001	87.02	86.07, 87.97	<0.0001
Systolic blood pressure, mm Hg	102.86	102.04, 103.68	0.06	107.39	106.61, 108.18	0.13	110.59	109.53, 111.66	<0.0001
Diastolic blood pressure, mm Hg	63.24	62.54, 63.95	0.39	67.39	66.67, 68.12	0.009	68.18	67.31, 69.05	0.0001
Mean arterial pressure, mm Hg	76.45	75.81, 77.09	0.16	80.73	80.04, 81.41	0.01	82.32	81.50, 83.14	<0.0001

Abbreviations: CI, confidence interval; HDL, high density lipoprotein; LDL, low density lipoprotein; MAO, metabolically abnormal nonoverweight/obesity; MHO, metabolically abnormal nonoverweight/obesity; MHO, metabolically healthy overweight/obesity.

^a MHO was defined as body mass index in the top quartile, while LDL cholesterol, triglycerides, mean arterial pressure, and plasma glucose were in the bottom 3 quartiles, and HDL cholesterol was in the top 3 quartiles.

^b Compared with the MHO group, adjusted for race and sex (and age) in a general linear model.

^c Body mass index: weight (kg)/height (m)².

Table 5. Adulthood Characteristics of the Study Sample by Obesity Status in Childhood: The Bogalusa Heart Study, Bogalusa, Louisiana, 1973–2002

Variable in Adulthood	Healthy Obesity Status in Childhood ^a							
	MHNO		MAO		MHO			
	Mean	95% CI	P Value ^b	Mean	95% CI	P Value ^b	Mean	95% CI
Age, years	35.71	35.23, 36.19	0.77	36.39	36.02, 36.76	0.46	35.39	34.78, 36.00
Body mass index ^c	26.77	26.18, 27.37	<0.0001	27.35	26.88, 27.82	<0.0001	36.85	35.92, 37.79
Waist, cm	87.99	86.47, 89.51	<0.0001	88.97	87.75, 90.19	<0.0001	109.88	107.57, 112.18
LDL cholesterol, mg/dL	115.87	112.54, 119.20	0.95	126.61	123.52, 129.69	0.04	131.68	126.80, 136.55
HDL cholesterol, mg/dL	49.99	48.39, 51.59	0.70	47.57	46.40, 48.73	0.24	43.66	42.27, 45.05
Triglycerides, mg/dL	115.05	105.35, 124.76	0.79	134.04	124.90, 143.18	0.13	147.23	134.32, 160.13
Insulin, μ U/mL	11.09	10.24, 11.95	0.10	12.23	11.03, 13.43	0.21	17.71	16.15, 19.26
Glucose, mg/dL	83.43	80.90, 85.96	0.21	85.55	83.87, 87.23	0.39	93.64	89.29, 97.98
Systolic blood pressure, mm Hg	113.78	112.42, 115.14	0.01	116.16	115.05, 117.28	0.09	122.37	120.37, 124.37
Diastolic blood pressure, mm Hg	76.68	75.68, 77.68	0.04	78.58	77.75, 79.40	0.26	82.42	80.99, 83.85

Abbreviations: CI, confidence interval; HDL, high density lipoprotein; LDL, low density lipoprotein; MANO, metabolically abnormal nonoverweight/obesity; MAO, metabolically abnormal overweight/obesity; MHNO, metabolically healthy nonoverweight/obesity; MHO, metabolically healthy overweight/obesity.

^a MHO was defined as body mass index in the top quartile, while LDL cholesterol, triglycerides, mean arterial pressure, and plasma glucose were in the bottom 3 quartiles, and HDL cholesterol was in the top 3 quartiles.

^b Compared with the MHO group, adjusted for race and sex (and age) in a general linear model.

^c Body mass index: weight (kg)/height (m)².

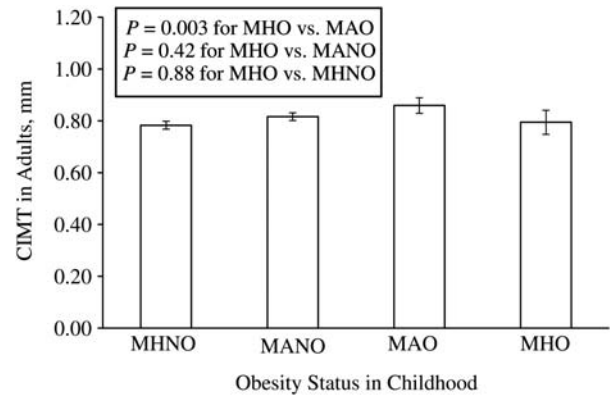


Figure 1. Carotid intima-media thickness (CIMT) in adults by childhood obesity status: The Bogalusa Heart Study, Bogalusa, Louisiana, 1973–2002. MANO, metabolically abnormal nonoverweight/obesity; MAO, metabolically abnormal overweight/obesity; MHNO, metabolically healthy nonoverweight/obesity; MHO, metabolically healthy overweight/obesity. A general linear model was used, with *P* values adjusted for adult age, race, and sex.

MHO children retained MHO status as adults, MHO children were 2.7–9.3 times more likely to be MHO adults compared with children in other categories. Importantly, MHO children did not show increased CIMT, a surrogate marker of atherosclerosis, in adulthood compared with nonoverweight/obese children, suggesting that MHO children may not have increased risk of cardiovascular disease in their adulthood. It should be noted, however, that MHO children seemed to have intermediate levels of blood pressure and insulin and glucose in adulthood, compared with metabolically healthy, nonoverweight/obese children and metabolically abnormal, overweight/obese children. This indicates that MHO children may be at intermediate risk of developing hypertension and type 2 diabetes as adults. It should also be noted that metabolically healthy, nonoverweight/obese children had the best risk profile in adults. Interestingly, 62.0% of MHO children were nonoverweight/obese in adulthood, indicating that the majority of MHO children are not destined to have increased weight in adulthood.

There is compelling evidence that obesity in childhood is a predictor of cardiovascular risk in adulthood (23, 24), and it is strongly recommended to adopt weight-loss interventions for overweight/obese children (25). Our observations, however, raise an important question as to whether MHO children would benefit from weight-loss interventions, from either increased physical activity or a healthy diet or both. It has been reported that obese adults respond differently to dietary intervention or physical activity intervention for weight loss, and MHO individuals may not benefit, or even suffer, metabolically from these interventions (26–28). Whether this is true for MHO children is not known and cannot be addressed in this study, because we did not have enough information on physical activity and dietary intake in children. Studies addressing this question

should have important public health implications in promoting health in obese children. It has to be noted, however, that there is no doubt that interventions should target those metabolically abnormal, overweight/obese children and that these children may benefit the most from such interventions.

Determinants of the MHO phenotype are not very clear. Studies have shown that insulin resistance, visceral fat, and inflammation are strongly associated with metabolic consequences of obesity (9, 13, 15, 29). Other factors, such as fitness and physical activity, may also play a part (30). Although in our study waist circumference in adulthood of MHO children was increased ($P < 0.001$) compared with nonoverweight/obese children and was comparable to that of metabolically abnormal, overweight/obese children, waist circumference per se cannot differentiate visceral fat from subcutaneous fat in the abdomen. Previously in the Bogalusa Heart Study, subjects were showed that a high waist/height ratio is associated with adverse cardiometabolic risk among normal weight children and adults (31, 32). Whether or not this ratio can be used among obese children and adults remains to be addressed. Other factors, such as genetic factors, have been proposed to be determinants of the MHO phenotype (33). In this regard, Kilpelainen et al. (34) have recently reported that variants near the insulin receptor substrate 1 gene (*IRS1*) are associated with reduced adiposity and an impaired metabolic profile.

Some limitations of our study need to be addressed. First, we arbitrarily defined the MHO phenotype by quartiles, because there is no consensus on the definition of MHO, especially in childhood. Second, grouping children based on extreme values of multiple variables might have subjected our results to be influenced by the effect of “regression to the mean” (35–37). However, we expect such an effect might have been mitigated by using the average values of at least 2 measurements to define the MHO phenotype in children. Finally, we recognize that the sample size of our study was relatively small, and the findings should be interpreted with caution. Future studies with large sample sizes are needed to confirm our findings.

In conclusion, MHO children have favorable cardiometabolic profiles and CIMT in adulthood compared with metabolically abnormal, overweight/obese children. Further, their cardiometabolic profiles and CIMT are comparable to those of nonoverweight/obese children. Such observations provide important evidence that the MHO phenotype starts in childhood and continues into adulthood. Whether MHO children should be targeted with weight-loss interventions needs to be addressed in future studies.

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