NHLBI Evidence Table: State of the Science: CV Risk Factors and the Development of Atherosclerosis in Childhood-OB

PMID	First Author	Title	Year	Study Type	Prospect./ Restrospect.	Study	CVD	RF by CQ	Country	Setting	Main Study Objective	N at Baseline (N at Follow-up)	Target Population	Eligibility Criteria	Patient Characteristics	Study Groups	n at Baseline (n at Follow-up) for Study Groups	Total Follow-up Duration	Outcomes Measured	Results	Main Reported Findings by Critical Question
758999	Schrott HG	Increased coronary mortality in relatives of hypercholesterolemic school children: the Muscatine study	1979	CrS	Retrospective	Muscatine	Atherosclerosis	Q4 (RF1,RF5)	USA	Community (other)	To evaluate hx of coronary mortality & lipid levels in families of children with varying levels of TC	146 index cases	Parental/ Family/ Caregiver	1st & 2nd degree relatives of 3 groups of index cases from Muscatine population: 67 children with TCs > 95th%ile (=HTC); 60 children with TCs < 10th%ile (=LTC) ; 46 randomly selected children with TC btwn 5th & 95th%iles(=MTC), tested on 2 occasions, 2 y apart.	56/ 67 children (26 M/30 F) with TCs > 95th%ile (=HTC); 46/60 children with TCs < 10th%ile (=LTC)(22 M/ 24 F); 45/ 46 randomly selected children with TC btwn 5th & 95th%iles(=MTC), tested on 2 occasions, 2 y apart.	HTC=56 index cases; 210 first degree relatives, 395 second degree relatives LTC=46 index cases;192 first degree relatives, 313 second degree relatives MTC=44 index cases; 169 first degree relatives, 271 second degree relatives	N/A	N/A	Non-lipid RF profiles Lipid profiles CAD death certificate information	No difference in non-lipid RF profiles between index cases, first or second degree relatives in the 3 groups For siblings and parents, TC & TG levels between the 3 groups varied in a statistically significant stepwise fashion. For grandparents, there was a statistically significant difference between TC levels in the HTC v. MTC & LTC groups but MTC & LTC grps did not differ & there was no difference in TG levels between the 3 grps. Mortality among relatives of the HTC group was significantly greater (p=S) than among the MTC & LTC groups. More MIs occurred between 30-59 y in the HTC group v. MTC & LTC groups (p=S*). No difference in cancer mortality between groups. Death from MI was 2X as frequent among males 30 -59 y in the HTC group v. their counterparts in MTC & LTC groups. Death from MI was 10X greater in females in the HTC group vs. females in the MTC & LTC groups.	Familial elevation of TC levels appears to confer an increased risk of premature atherosclerosis and death from CAD.
1529936	Berenson GS	Atherosclerosis of the aorta and coronary arteries and cardiovascular risk factors in persons aged 6 to 30 years and studied at necropsy (The Bogalusa Heart Study)	1992	CrS		Bogalusa	Atherosclerosis	Q1(RF2,3,4,5,8) Q2(RF2,3,4,5,8) Q3(RF2,3,4,5,8) Q5(RF2,3,4,5,8)	USA	Community (other)	To relate C-V RFs measured in life to atherosclerotic extent at autopsy after unexpected death in childhood or young adult life.	66	Pediatric/ Young adult	Since 9/89, 150 individuals have died unexpectedly at 3-31 y of age in Washington county, Bogalusa - 66 of the group had been evaluated previously at least once as part of a Bogalusa screening.	Community-based cohort of B & W children and young adults - originally examined at 5-17 yrs; 52% F, 44% B. For this study, autopsy findings of 150 study subjects who died unexpectedly are correlated with pre-mortem RFs.	N/A	N/A	N/A	Age Race Gender Ht Wt Ponderal index (PI) BMI SBP DBP TC TG HDL LDL VLDL TC/HDL Fasting glucose (FG) Fasting insulin (INS)	Age at death ranged from 6-30y(mean=20y) with 75% occurring between 17 & 27y. Interval from last CV RF evaluation ranged from 3 wk to 16 yrs. Intimal fatty streaks were common and extensive, more prevalent in males and more in Bs than Ws (32% vs 20%,p=S**), increasing with increasing age. Fibrous plaques were rare but increased with age, with greater extent in males. Fatty streaks and fibrous plaques correlated best in the coronary arteries, less well in the aorta. With all subjects combined, aortic and coronary fatty streaks correlated (+)ly with TC & LDL-C (r=.63,p=S**); (-)ly with TC/HDL(r=.30 and (+)ly with ponderal index (r=.35,p=S). In Ws, coronary fatty streaks correlated (+)ly with TGs (r=.48, p=S), VLDL(r=.36,p=S), SBP(r=.54,p=S*), DBP(r=.47,p=S) & ponderal index(r=.37,p=S); correlations were less strong in the aorta. In Bs, aortic fatty streaks correlated (+)ly with TC(r=.74,p=S*) & LDL-C(r=.64,p=S); there were no correlations with coronary lesions in Bs. Fatty streak intimal surface involvement increased significantly with increasing quartile of LDL in the aorta & coronary arteries.	Q1,2,3 Atherosclerosis begins in childhood and extent is related to the presence & intensity of known RFs. Q%. There are race & gender differences in the development of atherosclerosis and the impact of C-V RFs.
1579553	Kikuchi DA	Relation of serum lipoprotein lipids and apolipoproteins to obesity in children: the Bogalusa Heart Study	1992	CrS	Retrospective	Bogalusa	None	Q5 (RF5, RF8) Q6 (RF5, RF8)	USA	Community (other)	Correlate serum lipid/ lipoprotein levels with obesity measures in children	2,816	Pediatric/ Young adults	Age: 5-17 yr All children screened as part of the Bogalusa study in 1981-82 with fasting lipid profile results.	Community-based cohort of black(B) and white (W) children and young adults - originally examined at 5-17 yrs; 52% female(F), 48% male (M); 44% B.	49% M 36% B	N/A	N/A	TC TG HDL VLDL LDL Apo B Apo A1 Skinfolds (SFs) Ponderal index (PI) Glucose Insulin	Overall, Fs had higher levels of TC,TG,VLDL & LDL, and lower levels of HDL than Ms. Ms were thinner than Fs and BMs were thinner than WMs. In all race & sex grps: TG & VLDL correlated postively with glucose & insulin. HDL & apoA1 correlated negatively with insulin. LDL & apoB correlated postively with insulin. TG & VLDL correlated negatively with HDL, more than with apoA1. LDL related strongly to apoB; HDL related moderately to apoA1. Spearman correlations of lipid variables & obesity measures: Subscapular SFs correlated postively with insulin(r=0.29),TGs (0.26), LDL (0.18) & apoB (0.19)(all,p=S**) & negatively with HDL (-0.13,p=S**) & apoA1(-0.05;p=S). After adjustment for insulin & TGs, correlations are much less strong but still significant. When analyzed by quintiles of SFs, major positive effects noted in TGs & negative effects for HDL, for top 2 quintiles, greatest after 10 yr of age. LDL & apoB increased with increasing obesity but not nearly as strong a difference. With MRA, strongest correlation consistently seen between SFs and insulin & TGs, rather than LDL, HDL, apoB & apoA1.	Q1,2,3 Atherosclerosis begins in childhood and extent is related to the presence & intensity of known RFs. Q%. There are race & gender differences in the development of atherosclerosis and the impact of C-V RFs.
1919885	Stuhldreher WL	Cholesterol screening in childhood: sixteen-year Beaver County Lipid Study experience	1991	Cohort	Prospective	Beaver	None	Q8(RF5)	USA	Community (schools)	Evaluate prediction of adult cholesterol levels from pediatric results.	2448/ 295	Pediatric/ Young adults	Of 2448 7th grade subjects who underwent cholesterol screening in 1972-73, 295 of a possible 384 eligible subjects were re-tested in 1988-89.	Population-based study of a county-wide cohort of all 7th graders in Beaver City in 1981-82, aged 11-14 y at entry. For this study, mean age = 28 y, all had participated as children at 11 -14 y in cholesterol screening. 49% male. Lab methods changed between the 2 sample times so results for gender-specific cholesterol distributions were compared.	n=298 subjects, 49% male.	N/A	15 y	TC quintile at baseline and follow-up	38% of males & 42% of females who were in the top quintile at F/U (TC=223-316 for M, 210-301 for F) were in the top quintile at first evaluation (TC=189-362 in M, 194-275 in F). 37% of males & 45% of females in the top quintile as children were still in the top quintile and 65% in the top 2 quintiles at F/U. Using NCEP cutpoints, sensitivity of screening at age 12 y to predict elevated TC as an adult was 63%, specificity was 67% and PP(+) was 47%. Males with false positive results smoked significantly less than those with false negative results (p=S) and had a greater improvement in diet assessed by nutrition score change. Females with false positive results smoked significantly less than those with false negative results, were less overweight (both, p=S) and had lower prevalence of OC use (p=S*).	Overall correlation between baseline and follow-up TC was moderate but significant (r=.44; p=S**). Women had a higher correlation than men (r=.51 vs r=.38).
1929690	Wattigney WA	Increasing impact of obesity on serum lipids and lipoproteins in young adults. The Bogalusa Heart Study	1991	CrS		Bogalusa	None	Q5 (RF5,8) Q6 (RF5,8)	USA	Community (other)	Evaluate impact of obesity on serum lipids with increasing age beginning in childhood.	3,311	Pediatric/ Young adult	Subjects from 3 of the Bogalusa CrS surveys were included - 1983 through 1986 - with exclusion of pregnant Fs and those on OCs. 4 age groups: 5-10 y;11-16 y;17-22 y;23-26 y.	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. For this study: Age:5-22 yrs.	4 age groups: 5-10 y; 11-16 y; 17-22 y; 23-26 y.	N/A	N/A	Age Race Sex SBP DBP Ht Wt Tanner stage Rohrer index (kg/m cubed) (RI) Waist circumference Skin-fold thicknesses (mean of 7 sites) (SSFs) TC TG VLDL HDL LDL HDL/LDL + VLDL LDL/HDL Smoking status Alcohol use OC use	Prevalence of obesity increased with increasing age, most prominently in black females with 37% of 23-26 y old BFs classified as obese. (+) association of obesity with increasing LDL-C, greater as age increases, especially in white males; no such association in BFs. VLDL levels correlated significantly with RI with r=0.17 to 0.31 for different age & sex groups (p=S-S*) (-) association between ponderosity and HDL-C, maximal in 23-26 y old WMs (r=-0.39,p=S**). Lipid correlations with SSFs inconsistent. Based on NCEP criteria, 28% of WMs were defined as borderline high and 12% as high for LDL-C.	Adiposity in childhood correlates with adverse lipid profile findings, increased as age increases. There are race and sex differences in both fat patterning and lipid profile findings.

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2028978	Webber LS	Tracking of serum lipids and lipoproteins from childhood to adulthood. The Bogalusa Heart Study	1991	Cohort	Prospective	Bogalusa	None	Q6 (RF5) Q7 (RF5) Q8 (RF5)	USA	Community (other)	Describe serial lipid levels in a bi-racial cohort from childhood to late adolescence/ early adulthood.	2 179/1 586	Pediatric/ Young adults	All members of the community of Bogalusa. LA are potentially eligible for study. In 1973-74, 3 524 children aged 5-14 y were studied + 714 pre-school children. Repeat evaluations occurred annually with roughly half to 2/3's of group returning. Results represent a series of cross sectional surveys from the same community group but results are not subject-specific. Evaluation of those not present at baseline but present at F/U, and of those present at baseline but not at F/U showed no difference so study group is felt to be representative of both the baseline & late F/U population.	Community-based cohort of black(B) and white (W) children and young adults - originally examined at 5-17 yrs; 52% female(F), 48% male (M); 44% B. For this study: 36% B, 64% W. Age at initial evaluation: 2-14 y Age at final evaluation:14-26 y	Age at initial evaluation: 2-14 y Age at final evaluation:14-26 y 36% B, 64% W.	2 179/1 586	12 yrs	TC TG HDL LDL VLDL Race/ Age/ Sex Wt/ Ht cubed = Rorher's Index (RI)	TC was stable from 2-10 y, then decreased until 18 y, followed by a steady increase until final study values at 26y - in BMs, increase began at 17y and in BFs, decrease with puberty was less striking. LDL pattern was similar to TC but change was less; magnitude of increase over time greater for WMs & all Fs than in BMs. TGs and VLDL increased progressively with age in WMs & WFs but this was much less apparent in BMs & BFs. In Ws, HDL was stable until mid-puberty with progressive subsequent decline, greater in WMs (20 mg/dl drop from 14-16 y to 25-26 y, than in WFs (10 mg/dl decline). In Bs, HDL levels were higher throughout and decline over time was much less apparent. With tracking by quartile, ~ 50% of those with TC & ~ 55% of those with LDL >age/race/sex-specific 75th%ile at baseline had TC or LDL > 75%ile 12 y later, 2X as many as would be expected by chance. Persistence of elevated levels was greater in 9-14y olds than in the 2-8y olds. Tracking was less good for TGs & VLDL.	TC and LDL-C levels decrease during adolescence, more in boys than in girls and in Ws than Bs. After adolescence, TC and LDL-C levels rise continuously until 26 yrs. After adolescence, HDL-C levels continue to drop, most in W males. Tracking was evident for all lipids & lipoproteins: 12 yr correlation coefficients were greatest for LDL-C. Tracking for HDL was better after age 9, especially in W males. 50% of children who had TC or LDL-C levels > 75th%ile at baseline remained elevated 12 yrs later. For HDL, a trend with age was noted for W boys: 42% of those with HDL in the lowest quartile at 9-14 yrs remained in this quartile 12 yrs later. (7)
2028978	Webber LS	Tracking of serum lipids and lipoproteins from childhood to adulthood. The Bogalusa Heart Study	1991																	For HDL, 42% of WMs in the lowest quartile at baseline at 9-14 y remained in this quartile 12 y later. No tracking for HDLs measured at earlier ages. Best predictor of year 12 TC was baseline TC with R squared ranging from 18-48% for TC & 26-57% for LDL. For HDL, there was a strong inverse correlation with increase in obesity over time. Using NCEP cutpoints, of 35 subjects with TC > 240 mg/dl as adults, 23 were > 75th%ile as children & 4 more were obese.	The best predictor of F/U lipid level was baseline level.
2243431	Lauer RM	Use of cholesterol measurements in childhood for the prediction of adult hypercholesterolemia. The Muscatine Study	1990	Cohort	Prospective	Muscatine	None	Q8 (RF5)	USA	Community (other)	Evaluate the validity & utility of screening tests for TC in school-age children to predict adult TC levels above the NCEP cut-points for intervention.	2,367	Pediatric/ Young adults	A group of 2 367 subjects who underwent multiple TC screenings in childhood and had F/U evaluation at 20-30 y of age.	Longitudinal cohort study based in Muscatine, IA of children aged 8-18 y at enrollment between 1971 & 1981, followed with biennial school surveys. into adult life. A total of 14,066 children have undergone 32,636 evaluations. For this study, age at baseline: 8 - 18 y; serial lipid evaluation + F/U at 20-30 yrs. 1234 F/ 1133M.	N/A	N/A	12- 22 y	TC TC %ile for age/ sex	If 2 childhood TCs >75th%ile, sensitivity=45% and specificity=90% for adult TC > 200 mg/dl in both Ms & Fs. For Ms, PP(+) = 45% & PP(-) = 89%. For Fs, PP(+)=57% & PP(-) = 86%. If 2 childhood TCs> 90th%ile, sensitivity = 16% for Fs & 21% for Ms for adult TC > 200 mg/dl. PP(+)=75% for Ms & Fs. PP(-)=81`% for Fs & 87% for Ms. With two consecutive childhood TC levels ≥75th%ile, 57% of Fs & 45% of Ms would be correctly labeled as future high TC. With 2 consecutive TC > 90th%ile, 75% of both girls & boys were correctly identified as high adult TC & 25% were incorrectly labeled. In young adults, prevalence of smoking, obesity, low HDL, DM & HTN increased as adult TC level increased especially among Ms: ~ 88 % of Ms with TC > 240 mg/dl had ≥2 other RFs vs. 26.9% of Fs. Results for LDL paralleled those with TC.	While in general, TC levels track from childhood to adult life, screening for TC in children misidentifies many children as being high risk for requiring treatment for high LDL as adults. Of children with TC > 75th%ile on 2 occasions, 75% of girls & 56% of boys would not qualify for intervention as adults. Of children with TC > 90th %ile on 2 occasions, 57% of girls & 30% of boys would not qualify for intervention as adults.
2302349	Raekallio J	Histological and histochemical studies on local coronary wall thickenings (cushions) in Finnish children who died violently. Cardiovascular risk in young Finns?	1990	CrS	Retrospective	Young Finns	Atherosclerosis	Q1	Finland	Clinical	Evaluate histologically the coronary arteries of children who died traumatically	93	Pediatric/ Young adults	Coronary artery specimens collected at 93 sequential autopsies of victims of violent death aged birth - 15 y.	68%M, all W.	N/A	N/A	N/A	Histologic and histochemical findings in CAs at autopsy.	In 47% of the children of both sexes, thickenings of the coronary arteries were seen associated with splitting of the elastic membrane and accumulation of smooth muscle cells plus histochemical evidence of degeneration. Histologically, this was associated with presence of splitting of the internal elastic membrane creating a new layer between the intima & media. Clinical significance of these findings is unknown.	Q1. No definitive findings.
2683750	Folsom AR	Relation of body fatness and its distribution to cardiovascular risk factors in young blacks and whites. The role of insulin	1989	CrS		CARDIA	None	Q6 (RF4,5,8,14)	USA	Community (other)	Examine the cross-sectional relation of % body fat and fat distribution to C-V RFs in CARDIA cohort at baseline.	5115	Pediatric/ young adult	All subjects evaluated at baseline in whom complete fasting data and all anthropometric measures were recorded.	Population-based, prospective observational study with participants recruited from 4 metropolitan areas (Birmingham, Ala; Chicago, Ill, Minneapolis, Minn; & Oakland, Calif) in 1985-1986 at 18-30 yrs of age (44.9% black(B), 55.1% white(W); 53.9% female(F),46.1% male(M). Body composition measures and assessment of C-V RFs performed at baseline assessment.	N/A	N/A	N/A	Age Race Gender Ht Wt BMI (>25kg/m squared = overweight) Waist circumference (WC) Hip circumference (HC) Waist to hip ratio (WC/HC) Subcapular,triceps & supra-iliac SFs % body fat (calculated from SFs) SBP DBP TC TG HDL LDL TC/HDL Fasting glucose (FG) Fasting insulin (INS) Smoking status Education level Alcohol use OC use Physical activity	WMs were slightly older and taller than BMs and BFs were shorter,fatter & had a greater W/H ratio than WFs.% body fat from SFs was associated significantly with all measured lipids, lipoproteins, apolipoproteins, uric acid & BP. Compared with WMs, BMs had higher INS, HDL and apoA1, & lower FG,TG,apoB & uric acid. Compare with WFs, BFs had higher INS & lower TGs than WFs. WC was strongly associated with % BF(r=0.75-0.8) but the latter was uniformly & more strongly associated with all other RF measures; strongest associations with increased body fat were TGs, HDL (inversely), apoB & uric acid. All these measures were also significantly associated with INS. Waist-to-hip ratio was significantly but more weakly associated with TGs, HDL-C, HDL2-C, apolipoproteins A1 and B, LDL-C (in women only), uric acid and SBP, but was not associated with TC, HDL3-C or DBP. Fasting insulin levels were significantly associated with % body fat, waist to hip ratio and most of the physiologic RFs. With MVA, inclusion of fasting insulin reduced but did not eliminate the associations between waist to hip ratio and C-V RFs.	Q6. C-V RFs cluster together and are strongly associated with overall body fatness. They are also associated with W/H ratio suggesting that abdominal obesity confers excess C-V risk. Physiologic effects of fatness are only partially mediated by insulin. Q5. There are racial and gender differences in the physiologic response to increasing adiposity.
2816800	Freedman DS	Relation of body fat patterning to lipid and lipoprotein concentrations in children and adolescents: the Bogalusa Heart Study	1989	CrS		Bogalusa	None	Q6 (RF 5,8)	USA	Community (other)	Correlate serum lipids with anthropometric measures of fat distribution	361	Pediatric/ Young adult	Based on the average of 2 VLDL & LDL measurements from previous surveys in 1973-4 & 1976-77, subjects were placed in 4 groups: Group 1: Low VLDL, low LDL; Group 2: Low VLDL, high LDL; Group 3: High VLDL, high LDL Group 4: High VLDL, low LDL High & low cut-offs were based on the 20th& 80th%iles (groups 1 & 3) or the 25th & 75th%iles (groups 2 & 4).	Community-based cohort of B & W children and young adults - originally examined at 5-17 yrs; 52% F, 44% B. For this study: B & W children with extreme measures of VLDL and LDL-C underwent measurement of truncal and peripheral fat. 32% WMs, 28% WFs,21% BMs,19% BFs.	Group 1: Low VLDL, low LDL; Group 2: Low VLDL, high LDL; Group 3: High VLDL, high LDL Group 4: High VLDL, low LDL	N/A	N/A	Race Sex SBP DBP Ht Wt Tanner stage Rohrer index (kg/m cubed) (RI) Waist circumference Skin-fold thicknesses (mean of 7 sites) (SSFs) TC TG VLDL HDL LDL HDL/LDL + VLDL LDL/HDL Apolipoprotein A1 Apolipoprotein B Smoking status Alcohol use OC use	Anthropometric variables were highly correlated but association decreased after controlling for generalized obesity. Low VLDL/low LDL group had the lowest RI (p=S**), WC(p=S**) and SSFs(p=S**) vs highest for all 3 measures in high VLDL/high LDL group. There was no significant difference in anthropometrics between low VLDL/low LDL goup and low VLDL/high LDL group. High VLDL/low LDL group vs low VLDL/low LDL group had significantly greater WC(p=S*) and SSFs(p=S*) but no difference in RI. Mean of WC + subscapular & suprailiac SFs was used to estimate truncal obesity; mean of triceps, biceps, femoral & calf SFs was used as an index of peripheral obesity. Increased truncal fat correlated significantly with higher TGs (r=0.17, p=S*); VLDL(r=0.19,p=S**); LDL(r=0.11,p=S) & apoB(r=0.14,p=S*); and with lower HDL(r=-0.19,p=S**) and apoA1(r=0.25,p=S**). In obese children, higher truncal fat strongly correlated with elevated TGs & VLDL and lower apoA1;correlations with peripheral fat were less strong.	In children, truncal distribution of fat is associated with adverse lipid, lipoprotein cholesterol & apolipoprotein levels. Q6. Obesity & adverse lipid profile measurements cluster together.
2816800	Freedman DS	Relation of body fat patterning to lipid and lipoprotein concentrations in children and adolescents: the Bogalusa Heart Study	1989																	Increasing WC correlated directly with lower HDL & apoA1 levels.	

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3258194	Freedman DS	Black-white differences in aortic fatty streaks in adolescence and early adulthood: the Bogalusa Heart Study	1988	Case series		Bogalusa	Atherosclerosis	Q1 (RF2,4,5,8,10) Q2 (RF2,4,5,8,10) Q3 (RF2,4,5,8,10) Q4 (RF2,4,5,8,10) Q5 (RF2,4,5,8,10)	USA	Community (other)	Evaluate racial differences in the correlation of pre-mortem C-V RFs with post mortem evidence of atherosclerosis	44	Pediatric/ Young adult	Of 104 deaths in individuals eligible to have participated in the Bogalusa study, 44 had participated in at least one C-V RF evaluation. Post-mortem data in these subjects is the basis of this study.	Community-based cohort of B & W children and young adults - originally examined at 5-17 yrs; 52% F, 44% B. For this study, 44 subjects with age at death: 6-27 yrs (mean=18 yrs). 25% B. Mean time from last C-V RF measurement = 3.5 yrs(range: <1 y to 12 y)	N/A	N/A	N/A	Race Sex SBP DBP Ht Wt Ponderal index (PI) TC TG VLDL HDL LDL HDL/LDL + VLDL LDL/HDL Smoking status	Bs consistently had more extensive fatty streaks than Ws (31% vs 20%,in both sexes, p=S**) in the aorta independent of sex and age at death; this was not seen in the coronary arteries. . By univariate analysis, premortem C-V RFs correlated significantly with aortic fatty streaks with significant differences between Bs & Ws: LDL= 0.49 in Ws, 0.73 in Bs (p=S*); HDL=-0.29 in Ws, -0.23 in Bs (p=NS); TC=0.46 in Ws,0.59 in Bs(p=S);PI=0-.41 in Ws , 0.14 in Bs. The extent of aortic fatty streaks increased at adverse levels of each RF and this was strongest for LDL, but B/W difference persisted. Even after controlling for antemortem RFs, Bs had an additional 16% involvement of the aorta with fatty streaks as compared with Ws (p=S**).	Q1. Atherosclerosis begins in childhood. Q2. Presence of RFs in childhood affects the development of atherosclerosis in childhood. Q3. Presence of RFs in childhood affects the development of atherosclerosis in adult life. Q4. Childhood LDL showed the highest correlation with post-mortem fatty streaks; correlation with BP was very low. Q.5 Bs had consistently more fatty streaks than Ws regardless of all other RFs.
3498363	Baumgartner RN	Associations between plasma lipoprotein cholesterols, adiposity and adipose tissue during adolescence	1987	CrS		Fels	None	Q6 (RF5,8)	USA	Community (other)	Evaluate the association of body fat pattern with plasma lipids and BP	214		All subjects between 11 & 18 y who were participants in the Fels study and who were willing to participate in this sub-study were eligible. Each had an average of 3 measurements during this age period.	Longterm serial study of human growth initiated in 1929 in southwestern Ohio. Subjects are enrolled shortly after birth and followed q.3 mos until 2 y, then q.6 mos from 2-18 y of age, q. 3-5 y as adults. For this study, a cross-sectional sample of white males(M) & females(F) aged 11-18 y were evaluated. 108 Ms/106 Fs.	N/A	N/A	N/A	Age Race Gender Ht Wt BMI (>25kg/m squared = overweight) Waist circumference (WC) Hip circumference (HC) Waist to hip ratio (WC/HC) Subscapular,triceps,biceps, midaxillary,supra-iliac,lateral calf SFs --> 2 ratios of adipose tissue distribution: Subscapular/ Triceps (S/TR)= centripetal fat; Subcapular/Lateral calf = extremity fat (S/LC) % body fat (calculated from hydrostatic weighing)) TC TG HDL LDL TC/HDL	**CrS analysis by age**: % BF decreased with age in Ms but was constant across age groups in Fs. S/LC indicated a dominant peripheral fat pattern until 15 y in Ms and 16 y in Fs. S/TR scores increased with age in Ms & Fs but after age 15, S/TR was (+) in Ms indicating a dominant cenrtripetal pattern. HDL decreased with age in Ms and was constant in Fs. **Longitudinal analysis:** Baseline vs 5 y F/U HDL decreased significantly in Ms(p=S) and was constant in Fs. %BF decreased in Ms & increased in Fs. S/TR increased only in Ms. All variables tracked moderately well (r=0.55-0.70) There was a significant inverse relationship between S/TR (r= - 0.62,p=S)and S/LR(r=0.68,p=S) and HDL, only in Ms In MVA, centripetal fat pattern had a small but significant association with SBP in men. (R2=.02; p=S). (3) In women, centripetal fat pattern had a small but significant (+) association with TGs (R2=.05; p=S*) and a (-) association with HDL (R2=.08; p=S**).	In childhood, there is a predominant peripheral fat pattern until the mid-teens when a centripetal fat pattern develops. Q6. Centripetal obesity and adverse levels of TG and HDL cluster together. There are sex difference for fat patterning and lipids which appear during adolescence.
3544817	Smoak CG	Relation of obesity to clustering of cardiovascular disease risk factors in children and young adults. The Bogalusa Heart Study	1987	Cohort	Prospective	Bogalusa	None	Q6,7 (RF4, RF5, RF6)	USA	Community (other)	Investigate the relationship of obesity to clustering of systolic blood pressure, fasting insulin, and ratio of low and very low density lipoprotein cholesterol to high density lipoprotein cholesterol	3503	Pediatric/ Young adults	Individuals between 5 and 24 years of age Exclusions: No blood drawn Missing height, weight, or skinfold data Nonfasting participants	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. For this study: 1664 male 1802 female 2260 white 1206 black	NA	NA	NA	Rohrer index(kg/m cubed) (RI) HDL cholesterol LDL cholesterol VLDL cholesterol Blood pressure(systolic[S] & diastolic [D]) Subscapular SF(SSF)	Comparing the # of individuals with top tertile results for SSF, insulin, LDL-C + VLDL-C/HDL-C and SBP to the expected number, there was strong evidence of clustering (RR=3.1,p=S**). After adjustment for SSF, RR was reduced to 1.3 (p=S*) . In lean subjects, the degree of clustering was less than expected (RR=0.4) while more obese subjects had a greater degree of clustering (RR=3.1;p=S**)	Obesity assessed by SSF correlated strongly with fasting insulin, dyslipidemia (LDL-C + VLDL-C/HDL-C) and SBP. After adjustment for SSF, the correlation was reduced. Strongest effect of obesity was shown in the highest tertile of SSF. Significant clustering was also shown for low levels of CV RFs in primarily lean individuals.
3728436	Clarke WR	Changes in ponderosity and blood pressure in childhood: the Muscatine Study	1986	Cohort	Retrospective	Muscatine	None	Q6 (RF4,8) Q7 (RF4,8) Q10 (RF4,8)	USA	Community (other)	Describe longitudinal changes in BP relative to changes in ponderosity in childhood.	2,925	Pediatric/ young adult	All 2,925 subjects who were screened at 15-18y of age as part of the Muscatine study and who had also participated in at least 1 additional screening in childhood.	Longitudinal cohort study based in Muscatine, IA of children aged 8-18 y at enrollment between 1971 & 1981, followed with biennial school surveys into adult life. A total of 14,066 children have undergone 32,636 evaluations. For this study, baseline age = 6-15 y; F/U age = 15-18 y. 1,530 F/ 1395 M.	4 ponderosity groups based on QI at 2 visits: Upper quintile = High, lower 4 quintiles = low--> High/High(H/H) High/ Low (H/L) Low/ High (L/H) Low/ Low (L/L)	N/A	9-12 y	Ht Wt Quetelet index (Wt/Ht squared) = QI Triceps skin fold SBP DBP	All ponderosity measures correlated at roughly the same level with SBP(r=0.25-0.31) and DBP(r=0.11-0.15). BP is significantly correlated with body size. When 2 measurements taken on the same child from 2-10 y apart are considered, correlations between measurements decrease as the time between measurement increases. (SBP: r=0.44 at 2y --> 0.24 at 10 y; QI: r=0.86 at 2 y--> 0.67 at 10 y). By ANOVA of BP in the 4 ponderosity groups, children whose ponderosity decreased showed a decrease in SBP & DBP while children who gained in ponderosity showed an increase in SBP & DBP, independent of initial BP. The LOW/LOW group showed little change in BP. Magnitude of change correlated with change in ponderosity and not to baseline BP.	Q 10. A decrease in ponderosity is associated with a decrease in BP in childhood. Q6,7. BP and body size are significantly and consistently correlated.
3728437	Freedman DS	Cigarette smoking initiation and longitudinal changes in serum lipids and lipoproteins in early adulthood: the Bogalusa Heart Study	1986	Cohort	Retrospective	Bogalusa	None	Q5 (RF 5,10) Q6 (RF 5,10)	USA	Community (other)	Evaluate changes in serum lipid & lipoproteins post initiation of cigarette smoking.	1978/ 747 162 smokers at follow-up	Pediatric/ Young adults	From 2,543 9-17 y olds examined in 1976-77, 347 smokers, 98 with no smoking information & 28 OC users were excluded --> 1,978 non-smokers at baseline. At F/U at 14-23 yrs, 568 did not smoke & 162 were smokers.	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. For this study, 1,978 non-smoking 9-17 yr olds underwent fasting lipid testing; at re-evaluation, 5-6 yrs later, all were re-evaluated; 162 reported now smoking cigarettes. 45% M; 62% W.	Smokers: n= 162 Non-smokers:n= 568	1978/747	5-6 yrs	# of cigarettes smoked Age Sex Wt Ht Ponderal index (PI) Triceps skin fold (TSF) TC TG VLDL HDL LDL Thiocyanate levels	20 % of the cohort were smokers at F/U with median # of cigarettes smoked/ week of 20. Ws were more frequently smokers than Bs (23% vs 16%, p=S). BFs had lowest prevalence of smoking; BFs who smoked used a significantly lower # of cigarettes /wk, 10 vs 20. Compared with non-smokers, WM smokers had significantly higher TGs (p=S*) & VLDL (p=S**) & significantly lower HDL (p=S**). Differences occurred in the same direction in WFs, BMs & BFs but were less striking. In WM smokers, changes were exaggerated when associated with increased ponderosity. Compared with change from baseline in non-smokers, W males and females smoking ≥ 3 packs/wk, LDL-C increased an additional 13.2 and 11.6 mg/dl, TGs increased an additional 5.9 & 2.4 mg/dl and HDL-C decreased an additional 15.6 & 9.2 mg/dl. In B smokers, there were larger increases in TGs and VLDL-C levels than in B non-smokers.	Cigarette smoking is associated with adverse lipid profile changes, greatest in WMs, which are exaggerated by association with obesity. Adverse lipid profile changes increase as the # of cigarettes smoked increases. There are race & gender differences in the lipid response to cigarette smoking.
7572972	Myers L	Prediction of adult cardiovascular multifactorial risk status from childhood risk factor levels. The Bogalusa Heart Study	1995	Cohort	Retrospective	Bogalusa	None	Q6 (RF4,5,8) Q7 (RF4,5,8) Q8 (RF4,5,8)	USA	Community (other)	Correlation of C-V RFs (Ponderal index/ SBP/ TC) measured in childhood in 1973 and again 15 yrs later.	1,457	Pediatric/ Young adult	Two groups: 1,864 young adults aged 19-32 y, were screened in 1988-91 & at least once in childhood = young adult sample; 68.2% W, 55.4% F. Among 3,633 subjects screened at 5-15 y of age in 1973-4, 1,457 were screened as adults in 1988-91 = longitudinal sample; 45% M, 33.7% B.	Community-based cohort of B & W children and young adults - originally examined at 5-17 yrs; 52% F, 44% B.	N/A	N/A	15 yrs	Age Race Gender Ht Wt Ponderal index (PI) BMI SBP DBP TC TG HDL LDL TC/HDL Fasting glucose (FG) Fasting insulin (INS) * 3 RFs defined as criteria = TC, SBP, PI - adverse level defined as ≥75th%ile for age/ race/sex. * Clustered = All 3 RFs ≥75th%ile	In children, there was a significant (+) relationship between PI & TC (p=S**) and between SBP & PI (p=S**) but not between TC & SBP. In adults, all 3 RFs were significantly correlated (all,p=S**). 3.7% of children were clustered vs 4.1% of young adults. Of children who were in the top quartile for 3 RFs, 21.8% were clustered as adults. Of children with no RFs in the top quartile, only 1.1% were clustered as adults. In the longitudinal sample, 4% were clustered as adults and in this group, not only TC, SBP & PI were significantly higher but also TGs, LDL, VLDL, DBP & INS. Individuals who clustered were also significantly more obese by PI (p=S**), BMI & SFs. Strong (+) correlations were demonstrated between childhood & young adult levels of the 3 RF variables (SBP: r=0.41; PI: r = 0.62; TC:r = 0.53; all, p=S***). Among clustered adults, all RF levels were significantly higher in childhood.	Q6,Q7,Q8 RFs cluster in childhood and clustering persists from childhood into young adult life. Presence of RF clustering predicts adverse levels of other RFs and therefore, a more adverse overall risk profile. RF clustering in childhood predicts a clustered & adverse RF profile in adult life.
7572972	Myers L	Prediction of adult cardiovascular multifactorial risk status from childhood risk factor levels. The Bogalusa Heart Study	1995																	A model was developed to predict adult cluster status from childhood RF levels with best-fitting model including all 3 variables: as levels for any one of the 3 RF variables increase in childhood, the risk of adult clustering increases in a multiplicative manner.	

NHLBI Evidence Table: State of the Science: CV Risk Factors and the Development of Atherosclerosis in Childhood-OB

PMID	First Author	Title	Year	Study Type	Prospect./ Restrospect.	Study	CVD	RF by CQ	Country	Setting	Main Study Objective	N at Baseline (N at Follow-up)	Target Population	Eligibility Criteria	Patient Characteristics	Study Groups	n at Baseline (n at Follow-up) for Study Groups	Total Follow-up Duration	Outcomes Measured	Results	Main Reported Findings by Critical Question
7749853	McGill HC, Jr.	Relation of glycohemoglobin and adiposity to atherosclerosis in youth. Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group	1995	CrS		PDAY	Atherosclerosis	Q1,2,4,9 (R5,6, 8, 10)	USA	Clinical	Assess the association of hyperglycemia, as indicated by glycohemoglobin levels, and adiposity with the extent and severity of atherosclerosis at autopsy in 15 - 34 y old subjects after death from external causes.	1692 (1532)	Pediatric/ Young adults	Participants in the PDAY study: young persons 15-34 yr who died of external causes and were autopsied in medical examiners' laboratories. Exclusions: Persons of race other than black or white, presence of congenital heart disease, Down's syndrome, acquired immunodeficiency syndrome, or hepatitis.	NR	NA	NA	NA	Estimation of intimal surface involved with fatty streaks, fibrous plaques, complicated lesions, and calcified lesions. Glycohemoglobin levels. BMI Thickness of panniculus adiposus Serum cholesterol,HDL-C, VLDL-C Thiocyanate levels	Elevated glycohemoglobin levels are substantially and significantly associated with more extensive and more advanced atherosclerosis in the aorta and right coronary artery in persons 25 - 34 y of age. Adiposity, as measured by either BMI or thickness of the panniculus adiposus, is associated with more extensive and more advanced atherosclerosis of the right coronary artery in persons aged 15-34 y. Association of lesions with adiposity is not explained by serum lipoprotein cholesterol levels or smoking exposure.	Q1,2,4,9: Elevated glycohemoglobin levels are associated with accelerated atherogenesis in the third and fourth decades of life. Q1,2,4,9: Adiposity is associated with more extensive and advanced atherosclerosis at 15 - 34 y of age. Association of lesions with adiposity is not explained by serum lipoprotein cholesterol levels or smoking exposure.
7811129	Jiang X	Association of fasting insulin level with serum lipid and lipoprotein levels in children, adolescents, and young adults: the Bogalusa Heart Study	1995	CrS		Bogalusa	None	Q5 (RF5,8,14) Q6 (RF5,8,14) Q7 (RF5,8,14) Q8 (RF5,8,14)	USA	Community (other)	Correlate insulin levels with lipid profile results in children and young adults.	4,136	Pediatric/ Young adult	Findings from a CrS survey of 3,256 children, age 5-17y, from the Bogalusa study evaluated in 1987-88 and 1,881 young adults, age 19-30 y, evaluated in 1988-91.	Community-based cohort of B & W children and young adults - originally examined at 5-17 yrs; 52% F, 44% B. For this study: Age: 5-30 yrs; 63.9% W; 52% F.	5-11 y : n= 1650 12-17 y: n=968 19-24 y: n=679 25-30 y: n=839	N/A	N/A	Age Race/ Ethnicity Gender Ht Wt BMI Subscapular Skinfolds (SSFs) SBP DBP TC TG VLDL HDL LDL TC/HDL ApoA1 ApoB Fasting glucose (FG) Fasting insulin (INS) HOMA-IR Smoking status Alcohol use OC use	In general, marked increases in TC, LDL & TGs occurred with increasing age in all race/ sex groups while HDL decreased, most strikingly in WMs. In univariate analysis, INS correlated strongly and (+)ly with TG & VLDL-C levels and (-)ly with HDL-C levels in all age groups. An increasing association with LDL was seen in young adults. In MVA, INS was significantly associated with VLDL-C for most age grps independent of age/sex/glucose/obesity/ smoking & alcohol intake. In MVA, INS correlated inversely with HDL In WMs and WFs aged 5-17 y and in Bs and Ws aged 19-24 y. In analysis stratified by INS and SSFs, WMs and WFs had lower HDL & higher VLDL and LDL levels than did B subjects at the same level for obesity & INS. The magnitude of the association between insulin and lipoprotein fractions was stronger in obese than lean subjects.	Obesity, elevated INS and adverse lipid levels cluster together. There are race and sex differences in the interaction between INS and lipids. The adverse association between lipid levels and INS increased with increasing levels of obesity.
7998592	Porkka KV	Tracking and predictiveness of serum lipid and lipoprotein measurements in childhood: a 12-year follow-up. The Cardiovascular Risk in Young Finns study	1994	Cohort	Prospective	Young Finns	None	Q6 (RF5) Q8 (RF5)	Finland	Clinical	Evaluate tracking of serum lipoproteins in childhood over a 12y period	883	Pediatric/ Young adults	The Cardiovascular Risk in Young Finns Study is a collaborative effort of all university departments of pediatrics + several other Finnish institutions to study C-V RFs and their determinants in children and adolescents. The main cross-sectional study carried out in 1980 included 3596 3-18-year-old subjects with F/U studies in 1983, '86,'89 and '92, the last when the subjects were 15-30 years old.	Finnish cohort enrolled at 3-18 yr of age in 1980 and followed with serial lipid evaluation over time. 47% male.	All 883 subjects who had complete data on serum lipids in 1980 & 1992	883/ 883 by design	12 yr	TC TG HDL (incl HDL2 & HDL3) LDL VLDL Apo A1 ApoB BP SFs Diet Smoking status Alcohol use	Significant tracking was present for each lipid variable. 12 yr correlation coefficients: TC = 0.48-0.58; LDL = 0.53-0.58; HDL = 0.57-0.59; LDL/HDL = 0.57-0.59; TG = 0.33-0.37. Longterm tracking was better in Ms than Fs, especially for TC. Best correlation achieved for TC & LDL in 18 y old Ms. Apo A-1 and B showed similar tracking to LDL and HDL. 50% of extreme quintile TC, LDL and HDL subjects were still in that quintile 12 yrs later. In MVA, addition of BMI, exercise, diet and smoking did not change lipid correlations. Initial childhood or adolescent lipid value was the most significant predictor of the adult value. Tables for 95% CIs for adult lipid values based on single childhood value provided.	Significant tracking was present for each lipid variable with 12 yr correlation coefficients: TC = 0.48-0.58; LDL = 0.53-0.58; HDL = 0.57-0.59; LDL/HDL = 0.57-0.59; TG = 0.33-0.37. HDL tracking is considerably better than in other studies.
8030623	Raitakari OT	Effects of persistent physical activity and inactivity on coronary risk factors in children and young adults. The Cardiovascular Risk in Young Finns Study	1994	Cohort	Prospective	Young Finns	None	Q6 (RF5, RF8, RF9, RF10, RF11, RF14) Q7 (RF5, RF8, RF9, RF10, RF11, RF14)	Finland	Community (other)	Correlate physical activity levels with C-V RFs over 6 yr of follow-up	1,159/ 961	Pediatric/ Young adults	All subjects with complete data on physical activity who participated in the first & second surveys of the C-V Risk in Young Finns study in 1980 & 1983. Subjects were 12,15 & 18 y at baseline. Follow-up conducted X 6 y.	Finnish cohort enrolled at 3-18 yr of age in 1980 and followed with serial RF evaluation q 3 y over time. Physical activity assessed by questionnaire in a subset of the cohort, aged 12,15 and 18 yr at baseline, and correlated with other CV RFs. 58% F.	N/A	1,159/961	6 yr	BMI Subscapular skin folds (SSFs) TC TG HDL LDL VLDL ApoA1 ApoB HDL2 HDL3 Fasting glucose(FG) Fasting insulin (INS) Physical activity index (PAI) --> 3 groups : Physically active = PAI ≥85 on all 3 exams(ACT); Moderately active (MOD) =PAI>15,<85 on all 3 exams; Physically inactive (INACT)= PAI</=15 on all 3 exams. Current smoking habit 48-h dietary recall	At 6 y evaluation, Ms had higher PAI scores than Fs(p=S**) and higher BMI (p=S*); Fs had greater SSFs, HDL ,HDL2, HDL3, ApoA1, HDL/TC(all,p=S**); LDL(p=S); and lower FG(p=S**). At 6 y evaluation, more Ms smoked (p=S*) and more Ms had started smoking during the F/U period (p=S**). Proportion of ACT subjects remained the same on F/U; %age of sedentary subjects increased from baseline, from 38.7% to 47.2% in Fs and from 29.1% to 43.8% in Ms. Activity patterns tracked with 57% of INACT subjects remaining inactive vs. 44% of ACT subjects. Probabilty of remaining sedentary was significantly stronger than probabilty of remaining active (p=S*). Persistently ACT Fs had lower TGs (p=S) and SSFs (p=S*)compared with persitently INACT Fs. SSFs, INS and TG were lower(all, p=S) and HDL higher (p=S) in persistently ACT vs. persistently INACT Ms. INACT Fs began smoking at a higher rate than did ACT Fs (p=0.053) and %age of smokers was higher in INACT Fs at 6 y F/U (45.5% vs 8.7%,p=S*)	Physical activity patterns tracked during 6 y F/U; tracking was better for sedentary behavior than for active behavior. C-V RFs clustered together at lower & higher levels in ACT & INACT subjects. Smoking was significantly more common in INACT subjects.
8030623	Raitakari OT	Effects of persistent physical activity and inactivity on coronary risk factors in children and young adults. The Cardiovascular Risk in Young Finns Study	1994																	ACT Ms never started to smoke during F/U while 33.3% of INACT Ms began smoking (p=S**). %age of smokers was 9.3% among ACT Ms vs 46.9% in INACT Ms(p=S**). In MVA, change in activity was associated with changes in INS & TGs in Ms (both,p=S).	
8326345	Bao W	Tracking of serum apolipoproteins A-I and B in children and young adults: the Bogalusa Heart Study	1993	Cohort	Prospective	Bogalusa	None	Q8 (RF5)	USA	Community (other)	Assess tracking of apoB and apoA1 in children and young adults examined 4 yrs apart.	1 728	Pediatric/ Young adults	All 1,728 children and young adults aged 7-22 y at F/U who had fasting lipid profiles evaluated 4 yrs apart were included.	Community-based cohort of black(B) and white (W) children and young adults - originally examined at 5-17 yrs; 52% female(F), 48% male (M); 44% B. For this study, 1,728 children and young adults aged 7-22 y at F/U who had fasting lipid profiles evaluated 4 yrs apart were included.	1728 subjects; aged 7 - 22 y at F/U; 38% B; 53% F.	1728/1728 (by definition)	4 yrs	TC TG HDL LDL Apo B Apo 1 Ponderal index (PI) Smoking & drinking habits by questionnaire Parental hx of MI by self-report.	In general, Bs had higher apo A1 than Ws. Over time, apo A1 decreased except for the youngest age grp. Over time, apo B increased with age in all race-sex grps. Yr 1 vs yr 4 correlation coefficients ranged from .24-.45 for apoA1 and .57-.59 for apoB among different race and sex grps. (p=S** for all race-sex grps). Corresponding values for HDL & LDL were .39-.46 and .64-.67 respectively. Highest yr 1 vs yr 4 correlations were for TC(0.61-0.68) & LDL(0.64-0.67). No change after adjustment for age, height or PI. 31% of those with apoA1 in the highest quintile in yr 1 remained there in yr 4. For apoB, 50% of those in the highest quintile in yr 1 remained there in yr 4. For those in the lowest quintile in yr 1, 36% for apoA1 and 53% for apoB remained in this rank at F/U.	Yr 1 vs yr 4 correlation coefficients ranged from .24-.45 for apoA1 and .57-.59 for apoB among different race and sex grps. Corresponding values for HDL & LDL were .39-.46 and .64-.67 respectively. 31% of those with apoA1 in the highest quintile in yr 1 remained there in yr 4. For apoB, 50% of those in the highest quintile in yr 1 remained there in yr 4. For those in the lowest quintile in yr 1, 36% for apoA1 and 53% for apoB remained in this rank at F/U. Tracking of apolipoproteins offers no advantage over standard lipoprotein cholesterol measurements.
8357505	Clarke WR	Does childhood obesity track into adulthood?	1993	Cohort	Prospective	Muscatine	None	Q8 (RF8)	USA	Community (schools)	Evaluate tracking of body anthropometry from childhood into young adult yrs.	2631		All those surveyed as children between 1971-1981 and again as young adults between 1981-1990. Total # of subjects with data in both time periods=2631.	Longitudinal cohort study based in Muscatine, IA of children aged 8-18 y at enrollment between 1971 & 1981, followed with biennial school surveys into adult life. A total of 14,066 children have undergone 32,636 evaluations. For this study, age at baseline: 9 - 18 y; Age at F/U: 23, 28 & 33 y.	All those surveyed as children between 1971-1981 and again as young adults between 1981-1990.	N/A	15 y	Height Weight BMI Triceps skin fold (SF)	Pearson correlations were used to assess tracking for childhood to adult anthropometric measures: Ht: 0.41-0.97; Wt:0.51 - 0.88; BMI: 0.58 - 0.91;SFs: 0.26 - 0.58. From 57.3-68.5% of children in the top quintile for weight were in the top quintile as adults; from 50-87.5% of F children & 47.8-75.0% of M children in the top quintile of BMI were again in the top quintile as adults; from 25-57% of children in the top quintile of triceps SFs were again in the top quintile as adults. 31% of children from the upper quintile of BMI become adults with BMIs below this level & a similar # of lean children become obese adults.	Weight, BMI and triceps SFs track strongly from childhood into young adult life. However, ~30% of individuals in the top quintile for BMI in childhood become adults with BMI in the lower 3 quintiles. Equally,~ 30% of individuals with BMI in the lower 3 quintiles as children become adults with BMI in the top quintile.

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PMID	First Author	Title	Year	Study Type	Prospect./ Restrospect.	Study	CVD	RF by CQ	Country	Setting	Main Study Objective	N at Baseline (N at Follow-up)	Target Population	Eligibility Criteria	Patient Characteristics	Study Groups	n at Baseline (n at Follow-up) for Study Groups	Total Follow-up Duration	Outcomes Measured	Results	Main Reported Findings by Critical Question
8427537	Jiang X	Association of fasting insulin with blood pressure in young individuals. The Bogalusa Heart Study	1993	CrS	Retrospective	Bogalusa	None	Q5 (RF4,8,14) Q6 (RF4,8,14) Q7 (RF4,8,14)	USA	Community (other)	Evaluate the relationship btwn fasting insulin and BP in a biracial population of children & young adults	3518	Pediatric/ Young adults	All participants in the Bogalusa study for whom fasting insulin, glucose & BP data were available.	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. For this study, 4 age groups: 5-8, 9-12,13-17,& 18-26 yrs. were evaluated.	4 age groups: 5-8: n=717 9-12: n=939 13-17: n=1846 18-26: n=814	N/A	N/A	Ht Wt Ponderal index BMI SBP DBP Fasting glucose(FG) Triceps SF Subscapular SF Fasting insulin(INS)	A marked & consistent increase in INS & SBP occurs at puberty in early adolescence, greatest in WMs & WFs. INS then declines until ~ 17 y when it plateaus across young adult yrs. Overall, INS levels were highest in BFs. INS was significantly and (+)ly asst'd with SBP & DBP for all age groups except 13-17 y olds, but correlation was highest in younger age groups and post puberty. Strongest simple correlation was 0.38 for INS and SBP in 9-12 y group. Strongest overall correlation with SBP& DBP was BMI. With MVA, INS remained independently correlated with BP after controlling for glucose, BMI and SFs in 5-8 y group (r=0.13), 9-12 y group (r=0.22) & young adult group (r=0.08) but not in adolescents.	Q6,7. Insulin, SBP & BMI cluster together throughout childhood and into young adult life . There is a (+) correlation between fasting insulin & SBP except in adolescence but the association is substantially weakened with inclusion of BMI.
8501577	Gillman MW	Identifying children at high risk for the development of essential hypertension	1993	Cohort	Prospective	East Boston	None	Q8 (RF4)	USA	Community (other)	Evaluate the prediction of adult BP from serial childhood values.	337/ 317	Pediatric/ Young adults	All available participants in the East Boston BP study.	Cohort study of 339 schoolchildren from a single school in east Boston beginning in 1978 with annual F/U until 1981 and then reassembly of 317 of the original cohort in 1989-1990. 177F/ 139M. 315 W; 2 Asian.	N/A	N/A	12 yr	Age Sex Ht Wt BMI SBP DBP History of HTN dx History of parental HTN dx Medication use Cigarette use Alcohol use * BPs were measured weekly X 3 wks using a standard protocol in 1978, 1979, 1980 & 1981 and then again in 1989-90.	BPs were higher in Ms than Fs, as expected. Nearly half of subjects had at least one parent with HTN. Tracking correlations based on single visit BP measurements ranged from 0.23-0.37, as reported by others. Tracking correlations corrected for within-person variability and adjusted for age/sex/BMI/HR & parental HTN were 0.55(CI=0.45-0.63) for SBP and 0.41 (CI=0.30-0.50) for DBP. Predictive values for ranges of BP at age 10 y are presented.	SBP over several visits in childhood is a modest predictor of adult BP. While there is statistically significant tracking from childhood to adult BP, screening for adult HTN based on childhood BP readings is not highly effective.
8557894	Mahoney LT	Coronary risk factors measured in childhood and young adult life are associated with coronary artery calcification in young adults: the Muscatine Study	1996	Cohort		Muscatine	Coronary Ca	Q3 (RF4,5,8) Q4 (RF4,5,8) Q9 (RF4,5,8)	USA	Community (other)	Correlate prevalence of CAC in young adults with RFs for coronary disease measured in childhood.	197 men, 187 women	Pediatric/ young adult	Subjects who had participated during childhood in one of the Muscatine School Surveys and in one Muscatine Young Adult Follow-up Survey between the ages of 20 & 34 y. Of 284 M & 272 eligible Fsubjects, 197 M & 187 Fs participated.	Longitudinal cohort study based in Muscatine, IA of children aged 8-18 y at enrollment between 1971 & 1981, followed with biennial school surveys into adult life. A total of 14,066 children have undergone 32,636 evaluations. For this study, subjects were 29-37 y old and had participated during childhood in one of the Muscatine School Surveys and in one Muscatine Young Adult Follow-up Survey between the ages of 20 & 34 y. 50% M; all W.	N/A	N/A	20-30 y	Ht Wt BMI (>25kg/m squared = overweight) Waist circumference (WC) Hip circumference (HC) Waist to hip ration (WC/HC) Triceps SFs SBP DBP TC TG HDL LDL TC/HDL Apolipoprotein A Apolipoprotein B Lp(a) Homocysteine EBCT assessment of CAC - read as (+) or (-).	Subjects had C-V RFs measured at mean ages of 15 y, 27 y & 33 y. EBCT/CAC was performed at a mean age of 33 yrs. Prevalence of CAC was 31% in Ms & 10% in Fs(p=S**) In Ms, childhood wt, BMI & TSFs were significantly higher in CAC (+) group; there was no difference in childhood RFs for Fs. Among young adult & current RF measures, wt, BMI, TSFs , SBP, DBP, apoB, LDL/HDL & TC/HDL were consistently higher and apoA and HDL consistently lower in the CAC(+) group. Significant ORs for CAC relative to upper decile of the RFs: <u>In childhood</u>: 2.9 for wt in Ms; <u>In young adults</u>: 4.9 and 13.6 for wt in Ms & Fs, 6.5 & 4.7 for BMI in Ms & Fs; 2.9 & 6.8 for TSFs in Ms & Fs; 4.4 & 4.2 for SBP in Ms & Fs; 3.4 & 4.5 for DBP in Ms & Fs; 2.7 for TC in Ms; 4.7 for TGs in Fs; 8.9 for HDL in Fs; 3.7 for LDL in Ms. <u>At CAC</u>: 8,7 & 19.6 for wt in Ms& Fs; 6.4 & 13.6 for BMI in Ms & Fs; 2.9 for WC/HC in Ms; 6.4 & 6.4 for SBP in Ms & Fs; 2.9 for TC in Ms; 4.3 & 4.7 for lowest decile of HDL in Ms & Fs. 62% of Ms & 31% of Fs who were in the upper tertile for both BMI & SBP had (+)CAC vs 10% of Ms & 0% of Fs in the lower tertile for both variables.	Q3. Increased childhood wt, BMI & TSFs in Ms are significant predictors of early atherosclerosis assessed by CAC in young adult life. Measures of obesity, BP & decreased HDL in early young adult life are significantly associated with (+) CAC on EBCT. Q4. In all age groups, measures of obesity are the most consistent & strongest predictors of (+) CAC.
8651840	Bao W	Usefulness of childhood low-density lipoprotein cholesterol level in predicting adult dyslipidemia and other cardiovascular risks. The Bogalusa Heart Study	1996	Cohort	Prospective	Bogalusa	None	Q6 (RF4,5,8) Q7 (RF4,5,8) Q8 (RF 5)	USA	Community (other)	Examine the usefulness of childhood LDL-C for predicting dyslipidemia in adulthood and the association of dyslipidemia with other C-V RFs.	1 169 (by definition)	Pediatric/ Young adults	All 1169 individuals who underwent baseline fasting lipid profile assessment in 1973-74 and then again in 1988-91 were identified from 2 CrS surveys and defined as a longitudinal cohort.	Community-based cohort of black(B) and white (W) children and young adults - originally examined at 5-17 yrs; 52% female(F), 48% male (M); 44% B. For this study, age at initial evaluation = 5-14y & at F/U evaluation =20-29y; 34% B	N/A	N/A	15 yrs	TC TG VLDL HDL-C LDL-C BMI BP	In general, lipid/ lipoprotein results tracked from childhood into adult life: LDL-C - r =.4-.6, p=S**TGs/ HDL - r = .1-.4, p=S** When subjects were ranked by quintile, among those with TC or LDL-C > 80th %ile as children, 40% had similar elevation 15 y later, more than 2X the expected rate. In stepwise MRA, incremental increases in childhood TC & BMI independently predicted incremental increases in adult values. Best predictor of adult lipoprotein level was childhood level, better for TC & LDL-C than TGs and HDL; next most predictive was change in BMI. If adult subjects were classified as having dyslipidemia by NCEP criteria,childhood LDL-C was most predictive of adult dyslipidemia:a 29 mg/dl higher childhood LDL= 2.5X greater risk by stepwise regression. Based on childhood LDL-C, children were classified as acceptable (AC:<110 mg/dl; = 977/ 84% of subjects), borderline (BO:110-129 mg/dl; =121/ 10%) or HR (≥130 mg/dl; = 71/ 6%).	In general, lipid/ lipoprotein results tracked from childhood into adult life: LDL-C - r =.4-.6, p=S**TGs/ HDL - r = .1-.4, p=S** In MRA, childhood level was most predictive followed by change in BMI. Adult dyslipidemia was best predicted by childhood LDL-C. Compared with subjects with childhood LDL<110 mg/dl, those with childhood LDL > 130 mg/dl had significantly higher prevalence of elevated TC, TGs and reduced HDL level + higher prevalence of obesity and HTN. If elevated LDL persisted > 90th%ile in childhood, presence of adult dyslipidemia was markedly increased (p<.001).
8651840	Bao W	Usefulness of childhood low-density lipoprotein cholesterol level in predicting adult dyslipidemia and other cardiovascular risks. The Bogalusa Heart Study	1996																	In adult subjects who were HR vs.AC, obesity was 1.6X (38%) as prevalent (p=S); HTN was 2.4X as prevalent(p=S*); adult dyslipidemia was 8.3X as prevalent: 24% (8.3X) had high TC, 28% (5.4X) & 13% (2.4X) had low HDL. In 883 subjects with repeated childhood measurements, prevalence of adult dyslipidemia was highest(>50%) in those with 2 LDL-C>90th %ile in childhood; if child had no LDL-C > 90th%ile, chance of adult dyslipidemia was < 10%.	
8686692	Folsom AR	Increase in fasting insulin and glucose over seven years with increasing weight and inactivity of young adults. The CARDIA Study. Coronary Artery Risk Development in Young Adults	1996	Cohort	Prospective	CARDIA	None	Q5 (RF 8,10,11,14) Q6 (RF 8,10,11,14) Q7 (RF 8,10,11,14) Q8 (RF 8,10,11,14)	USA	Community (other)	Characterize 7 yr changes in fasting insulin & glucose.	5,115/ 4,086	N/A	All subjects from the original CARDIA cohort who returned for year 7 examination.	Population-based , prospective observational study with participants recruited from 4 metropolitan areas (Birmingham, Ala; Chicago, Ill, Minneapolis, Minn; & Oakland, Calif) in 1985-1986 at 18-30 yrs of age (44.9% black, 53.9% women). Insulin & glucose measurements from baseline & 7 yr F/U data.			7 yrs	Age Race Gender Ht Wt BMI (>25kg/m squared = overweight) Waist circumference (WC) Hip circumference (HC) Waist to hip ratio (WC/HC) Subcapular,triceps & supra-iliac SFs % body fat (calculated from SFs) Fasting glucose (FG) Fasting insulin (INS) Diet Smoking status Education level Alcohol use OC use Physical activity	Mean fasting insulin increased substantially over all race/sex groups, from 10% in WFs to 25% in BMs. FG increased across all race/sex groups from 7% in WFs to 10% in BMs. BMI increased in all groups, from 7% in WFs to 12% in BFs. Persons who lost weight had decreased insulin levels. Those with baseline W/H ratio above the median and highest BMI exhibited greater change in INS with wt change than did those with W/H ratio/BMI below the median. Greater wt gain was asst'd with greater increase in FG & INS. Decreases in activity were associated with greater wt gain, increase in W/H ratio and rise in FG/INS. By MVA, strongest predictor of both increase in fasting insulin & in FG was an increase in BMI and in W/H ratio. Insulin decreased longitudinally with age in the youngest members of the cohort.	In all race/sex groups, an individual's level & changes in INS & FG were linked strongly and (+)ly to level and change in BMI. There is clustering of adverse RFs with obesity and with increase in obesity. Decrease in activity is associated with higher INS levels.

NHLBI Evidence Table: State of the Science: CV Risk Factors and the Development of Atherosclerosis in Childhood-OB

PMID	First Author	Title	Year	Study Type	Prospect./ Restrospect.	Study	CVD	RF by CQ	Country	Setting	Main Study Objective	N at Baseline (N at Follow-up)	Target Population	Eligibility Criteria	Patient Characteristics	Study Groups	n at Baseline (n at Follow-up) for Study Groups	Total Follow-up Duration	Outcomes Measured	Results	Main Reported Findings by Critical Question
9268963	Raitakari OT	Associations between physical activity and risk factors for coronary heart disease: the Cardiovascular Risk in Young Finns Study	1997	CrS	Prospective	Young Finns	None	Q6 (RF4,5,8,11,14) Q10 (RF 4,5,8,11, 14)	Finland	Community (other)	Analyze the association between physical activity levels and CV RFs in children and young adults	2,358		All subjects from the C-V Risk in Young Finns study who underwent evaluation in 1986 - year selected because widest # of biochemical measures available at that time.	Finnish cohort enrolled at 3-18 yr of age in 1980 and followed with serial RF evaluation over time, including activity level assessment by questionnaire. In this cross-sectional sub-study, a cohort aged 9-24 yr were evaluated for physical activity and other C-V RFs. F=1,244; M=1,114.	N/A	N/A	N/A	BMI Subscapular skin folds (SSFs) Tanner stage SBP DBP TC TG HDL LDL ApoA1 ApoB HDL2 HDL3 Insulin (INS) Serum lecithin:cholesterolacyltransferase(LCAT) Physical activity index (PAI) --> 3 groups : Physically active (ACT); Moderately active (MOD); Physically inactive (INACT)	Study cohort was younger, thinner & more active than those lost to F/U. Among Ms, higher PA was associated with lower BMI and SSFs. In Fs, higher PA was associated with lower SSFs but no difference in BMI. No relation between activity level & BP for Ms or Fs. Among Ms, apoB levels were significantly lower among ACT Ms with a significant dose effect. No difference in TC, LDL, HDL or apoB with activity in Fs. HDL-C, HDL/TC and apoA!/apoB were significantly higher in ACT Ms with a significant dose effect; high HDL2 levels were associated with activity but there was no association with HDL3. There was no association between activity & LCAT levels. In Ms & Fs, ACT was associated with low TGs in a dose-related manner. In Ms, INS were significantly lower in ACT group compared with INACT. No relationship between activity & INS in Fs.	High levels of physical activity were associated with high HDL, low TGs, low apo B and low insulin in males, but only low TGs in women. For both males and females, high physical activity levels were inversely associated with adiposity. There was no association between physical activity and BP. Q10. RFs in children are decreased with high levels of physical activity. Q6. Low levels of physical activity are associated with a cluster of C-V RFs including adiposity and dyslipidemia.
9388151	Bao W	Longitudinal changes in cardiovascular risk from childhood to young adulthood in offspring of parents with coronary artery disease: the Bogalusa Heart Study	1997	Cohort	Retrospective	Bogalusa	None	Q5 (RF 1,3,4,5,8,14) Q6 (RF 1,3,4,5,8,14) Q8 (RF 1,3,4,5,8,14)	USA	Community (other)	Examine the association btwn parental CAD and longitudinal changes in RF profile from childhood to young adulthood in offspring.	1,524	Pediatric/ Young adult	From the sample of young adults evaluated in Bogalusa in 1988-1991, history of parental CAD was verified --> identification of 271 individuals with verified parental hx of CAD in 1 (n=230) or both (n=41) parents. Their RF results were compared with those of 1253 subjects with no hx of parental CAD on serial evaluations beginning at mean age of 10 y.	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. For this study: 271 subjects with (+) parental hx for early CAD; 1,253 subjects with (-) parental hx. Mean age at first CAD event was 50 yrs in fathers and 52 yrs in mothers.	(+) CAD hx = 271 (-) CAD hx = 1253	N/A	18 y - serial CrS evaluations with 56-86% participation in 5 previous surveys,	Age Race Gender Ht Wt BMI SBP DBP TC (>240 mgm/dl = dyslipidemia) TG HDL LDL TC/HDL Fasting glucose (FG) Fasting insulin (INS) Family hx of CAD	Offspring of parents with CAD were overweight beginning in childhood, significantly different from a mean age of 10 y (p=S*). Levels of TC, LDL-C, glucose & insulin became significantly higher at older ages (TC at 15y, LDL & FG at 18y, INS at 21 y). The earlier the age of onset of parental CAD, the greater the RF levels at younger ages in offspring. Rates of increase in TC & LDL were significantly higher in (+) parental hx group even after adjustment for age/ race/ BMI. In adulthood, offspring with a (+) family hx had a higher prevalence of obesity (35% vs 26%, p=S**); elevated TC (8.4% vs 4.8%, p=S); elevated LDL-C (12.4% vs 4.7% (p=S*); and hyperglycemia (2.7% vs 0.4%,p=S**). Subjects with parental CAD were significantly more likely to have multiple RFs. Prevalence of dyslipidemia of any kind was significantly higher in adult offspring with (+) parental hx for CAD. By logistic regression, higher LDL in Ws, higher DBP in Bs and higher INS in Bs were most associated with hx of parental CAD. In both Bs & Ws, increased BMI in offspring was strongly associated with parental CAD.	Q5. There are race & sex differences in the prevalence of C-V RFs associated with parental CAD. Offspring of parents with CAD were overweight beginning in early childhood and significantly different from a mean age of 10 y, with other RFs becoming more apparent with increasing age. Q. 6 There is an increased prevalence of clustered RFs in offspring with (+) hx of parental CAD. There is an accelerated progression of C-V RFs in offspring of parents with early CAD.
9544768	Andersen RE	Relationship of physical activity and televiseh. Watching with body weight and level of fatness among children: results from the Third National Health and Nutrition Examination Survey	1998	CrS	Retrospective	NHANES III	None	Q5 (RF11) Q6 (RF2, RF8, RF11)	U.S.A	Clinical	Assess participation in vigorous activity and television watching habits and their relationship to body weight and fatness in U.S. children.	4,063	Pediatric/ Young adults	8-16 yr	Patient characteristics from NHANES III	Non-Hispanic white Non-Hispanic black Mexican-American	1,063 (NR) 1,424 (NR) 1,386 (NR)	NR	Weekly play or exercise that results in sweating or hard breathing Mean BMI [kg/m2] Mean sum of the subscapular or suprailiac skinfolds Television watched [hr/d]	Eighty percent of US children reported performing 3 or more bouts of vigorous activity each week. This rate was lower in non-Hispanic black and Mexican American girls (69% and 73%, respectively). Twenty percent of US children participated in 2 or fewer bouts of vigorous activity per week, and the rate was higher in girls (26%) than in boys (17%). Overall, 26% of US children watched 4 or more hours of television per day and 67% watched at least 2 hours per day. Non-Hispanic black children had the highest rates of watching 4 or more hours of television per day (42%). Boys and girls who watch 4 or more hours of television each day had greater body fat (P<.001) and had a greater body mass index (P<.001) than those who watched less than 2 hours per day.	Q5: Eighty percent of US children reported performing 3 or more bouts of vigorous activity each week. This rate was lower in non-Hispanic black and Mexican American girls (69% and 73%, respectively). Non-Hispanic black children had the highest rates of watching 4 or more hours of television per day (42%). Q6: Twenty percent of US children participated in 2 or fewer bouts of vigorous activity per week, and the rate was higher in girls (26%) than in boys (17%). Boys and girls who watch 4 or more hours of television each day had greater body fat (P<.001) and had a greater body mass index (P<.001) than those who watched less than 2 hours per day.
9614255	Berenson GS	Association between multiple cardiovas.cular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study	1998	CrS		Bogalusa	Atherosclerosis	Q1(RF 4,5,8,10) Q2(RF 4,5,8,10) Q3(RF 4,5,8,10) Q9(RF 4,5,8,10)	USA	Community (other)	Compare pre-mortem measurement of C-V RFs with postmortem evidence of atherosclerosis in children and young adults.	93	Pediatric/ Young adult	Of 204 deaths in individuals eligible to have participated in the Bogalusa study, 93 had participated in at least one C-V RF evaluation. Correlation of post-mortem data with premortem C-V RFs in these subjects is the basis of this study.	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. For this report, there were 41 WMs, 19 WFs, 23 BMs & 10 BFs.	N/A	N/A	N/A	Age Race Gender Ht Wt BMI SBP DBP TC TG HDL LDL TC/HDL Smoking status	All autopsied individuals in this series had fatty streaks in the aorta. Prevalence of fatty streaks in the coronary arteries increased with age, from ~ 50% at 2-15 y of age to ~ 85% at 21-39 y of age (p=S*) Aortic surface involved with fatty streaks increased from 13.8 +/- 5.5 % at 2-15 y of age to 28.8+/-15.3% at 26-39 yrs.(p=S**); aortic surface involved with fibrous plaques increased from 0.2+/-0.5% at 2-15 y of age to 4.0+/-7.4%% at 26-39 y of age (p=S**). Involvement in the coronary arteries was much less extensive for both fatty streaks and fibrous plaques but still increased significantly with aging. Fatty streaks strongly correlated with fibrous plaques in the coronary arteries(r=.60),less in the aorta (r=.23). With simple regression, the extent of atherosclerotic lesions correlated significantly with BMI, SBP, DBP,TC, LDL & TGs. BMI, BP, TC, TGs, LDL-C and HDL-C as a group were strongly asst'd with the combined extent of lesions in the coronary arteries and aorta; r=0.70;p=S**).	Q1. Atherosclerosis begins in childhood. Q2. Presence of RFs in childhood affects the development of atherosclerosis in childhood. Q3. Presence of RFs in childhood affects the development of atherosclerosis in adult life. Q4. Cigarette smoking powerfully increases the extent of atherosclerotic lesions. Q9. The percentage of involved surface increased exponentially as the # of RFs increased, especially for fibrous plaques in the coronary arteries.
9614255	Berenson GS	Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study	1998																	Cigarette smoking increased the % of intimal surface with fibrous plaques in the aorta (1.22% vs.0.12%;p=S) and fatty streaks in the coronary arteries(8.27% vs 2.89%;p=S) Subjects with 0,1,2, & 3 or 4 RFs had 19.1%, 30.3%, 37.9% & 35% of the intimal surface of the aorta covered with fatty streaks (p for trend =S*). For the coronary arteries, this was 1.3%, 2.5%, 7.9% & 11% for fatty streaks & 0.6%, 0.7%, 2,4% and 7.2% for fibrous plaques.	
9922071	Hickman TB	Distributions and trends of serum lipid levels among United States children and adolescents ages 4-19 years: data from the Third National Health and Nutrition Examination Survey	1998	CrS	Retrospective	NHES III, NHANES I, NHANES III	None	Q5 (RF2, RF5)	USA	Clinical	Examine lipid distributions among children and adolescents using the most recent nationally representative data	7,499	Pediatric/ Young adults	NHES III, NHANES I, and NHANES III eligibility criteria	Patient characteristics from NHES III, NHANES I, and NHANES III	Groups were studied by age, sex, and race/ethnicity	Sample sizes are stratified by age	NR	Mean TC [mg/dL (SE)] HDL-C [mg/dL (SE)] LDL-C [mg/dL (SE)] TG [mg/dL (SE)]	In national data for the US population ending in 1994, for children and adolescents 4 to 19 years of age, the 95th percentile for serum total cholesterol was 216 mg/dL and the 75th percentile was 181 mg/dL. Mean age-specific total cholesterol levels peaked at 171 mg/dL at 9-11 years of age and fell thereafter. Females had significantly higher mean total cholesterol and LDL-C levels than did males (P < 0.005). Non-Hispanic black children and adolescents had significantly higher mean total cholesterol, LDL-C, and HDL-C levels compared to non-Hispanic white and Mexican American children and adolescents. The mean total cholesterol level among 12- to 17-year-olds decreased by 7 mg/dL from 1966-1970 to 1988-1994 and is consistent with, but less than, observed trends in adults. Black females have experienced the smallest decline between surveys.	In national data for the US population ending in 1994, for children and adolescents 4 to 19 years of age, the 95th percentile for serum total cholesterol was 216 mg/dL and the 75th percentile was 181 mg/dL. The mean total cholesterol level among 12- to 17-year-olds decreased by 7 mg/dL from 1966-1970 to 1988-1994. This is consistent with, but less than, observed trends in adults. Black females have experienced the smallest decline between surveys. Q5: Non-Hispanic black children and adolescents had significantly higher mean total cholesterol, LDL-C, and HDL-C levels compared to non-Hispanic white and Mexican American children and adolescents.

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PMID	First Author	Title	Year	Study Type	Prospect./ Restrospect.	Study	CVD	RF by CQ	Country	Setting	Main Study Objective	N at Baseline (N at Follow-up)	Target Population	Eligibility Criteria	Patient Characteristics	Study Groups	n at Baseline (n at Follow-up) for Study Groups	Total Follow-up Duration	Outcomes Measured	Results	Main Reported Findings by Critical Question
10052443	Strong JP	Prevalence and extent of atherosclerosis in adolescents and young adults: implications for prevention from the Pathobiological Determinants of Atherosclerosis in Youth Study	1999	CrS		PDAY	Atherosclerosis	Q1(RF2,3) Q5(RF2,3)	USA	Clinical	Describe the pathologic extent & severity of atherosclerosis in adolescents & young adults.	2,876	Pediatric/ young adult	Autopsy results of 2,876 cases evaluated for extent & severity of atherosclerotic lesions	3,201 15-34 y olds who died accidentally in 15 different cities in the U.S. between 6/1/87 & 8/31/94. In this study, results of 2,876 cases are evaluated.	N/A	N/A	N/A	Extent of intimal surface of RCA & abd Ao with fatty streaks and raised lesions evaluated by pathologists and by computerized image analysis.	Mean % of surface area involved increased with age (p=S**) and was greater in Bs than Ws in all arterial segments. (p=S**). Involvement was greater in Ms than Fs for the CAs(p=S**) and thoracic Ao(p=S*) but less in the abd Ao(S**). Ms have a greater extent of advanced lesions in the RCA. Intimal lesions appeared in all the aortas & more than half the RCAs of the youngest grp, 15-19 y old, and increased in prevalence & extent through the oldest age grp (30-34 y). Fatty streaks were more common in Bs than Ws but raised lesions did not differ between these groups. Raised lesions were similar in the aortas of men & women but raised lesions in the RCA in Fs were less than those of men. Prevalence of total lesions was lower in the RCA than in the aorta, but the proportion of raised/ total was higher in the RCA.	There are distinct regional differences to atherosclerotic extent in the aorta and CAs. Q1. Atherosclerosis begins in childhood. Q5. There are race and gender differences in the development of atherosclerosis.
10086972	Sinaiko AR	Relation of weight and rate of increase in weight during childhood and adolescence to body size, blood pressure, fasting insulin, and lipids in young adults. The Minneapolis Children's Blood Pressure Study	1999	Cohort	Prospective	Minn	None	Q6 (RF4,5,8,14) Q7 (RF4,5,8,14) Q8 (RF4,5,8,14) Q11 (RF4,5,8,14)	USA	Community (other)	Assess the impact of rate of weight gain on the development of insulin resistance from childhood to young adult life.	1207/ 817/ 679	Pediatric/ young adult	From a longitudinal cohort of 1207 children examined first in 1st-3rd grade and followed through high school with serial exams, 879 returned for a post high school evaluation and 679 at a mean of 23.6 y for young adult F/U.	Subjects followed from 7.7+/- 0.1 yrs to 23.6+/- 0.2 yrs with repeated measures of ht, wt & SBP. At study end, insulin & lipids were measured. 52% male(M); 48% female(F) 66% white(W); 25% black(B); 4% Native American(N-A).	N/A	1207 /817/ 679	16 yrs	Age Race/ Ethnicity Gender Ht Wt BMI (>25kg/m squared = overweight) Waist circumference (WC) Hip circumference (HC) Waist to hip ratio (WC/HC) Triceps SFs (TSF) % body fat (calculated from SFs) SBP TC TG HDL LDL TC/HDL Fasting glucose (FG) Fasting insulin (INS)	At baseline, 7.4% of the cohort were obese vs 24.3% at late F/U. At young adult evaluation, wt, BMI, WC/HC and TSFs were (+)ly correlated with INS, TC, TGs, & LDL and (-)ly correlated with HDL (all, p=S**); ht was (+)ly correlated with TGs and (-)ly with HDL (both, p=S**); INS was (+)ly correlated with TC, TGs & LDL and (-) correlated with HDL(all, p=S**). Initial childhood wt, BMI, & ht were significantly correlated with young adult wt, ht and BMI (all, p=S**). Young adult INS, TGs, HDL & SBP were significantly related to initial childhood wt, BMI and ht(all,p=S**) but relationships of TC and LDL to childhood body measurements were not significant. Rates of increase in wt & BMI but not ht during childhood were significantly related to young adult levels of insulin, all lipids & SBP. Rates of increase in wt & BMI but not ht during adolescence were significantly related to INS,HDL & SBP. With MRA, young adult INS was significantly related to both childhood and adolescent rates of wt gain (p=S**)	Ht, wt and BMI measured early in childhood are significantly associated with body size in adult life. Childhood wt and BMI are significantly related to INS, TG, HDL and SBP in adult life. Wt gain in excess of constitutional gain is a major constituent of young adult C-V risk. Excess rate of increase in wt or BMI in childhood and/ or adolescence is associated with adverse INS, SBP, TG & HDL in young adult life. Conversely, below average increase in wt or BMI in childhood and adolescence is associated with advantageous C-V risk profile in young adult life. The degree of excess wt gain and the duration are both directly related to adult C-V risk factors.
10086972	Sinaiko AR	Relation of weight and rate of increase in weight during childhood and adolescence to body size, blood pressure, fasting insulin, and lipids in young adults. The Minneapolis Children's Blood Pressure Study	1999																	In 2 X 2 analysis with subjects divided according to their position above or below the median for childhood & adolescent rates of wt gain, subjects with above median wt gain in both time periods (190.1+/-7.2 pmol/L) had significantly greater INS than those below the median in both periods(116.2 +/- 7.2 pmol/L); below the median during childhood and above in adolescence (134.9 +/- 5.7 pmol/L); or above the median in childhood and below in adolescence (135.6 +/-5.7 pmol/L)(all,p=S**). Results were similar for lipid & SBP and when analysis was performed for BMI.	
10353925	Freedman DS	The relation of overweight to cardiovascular risk factors among children and adolescents: the Bogalusa Heart Study	1999	CrS	Retrospective	Bogalusa	None	Q5 (RF 4,5,8,14) Q6 (RF 4,5,8,14)	USA	Community (other)	Examine the relationship btwn overweight & C-V RFs + RF clustering in childhood.	9167 (no loss to F/U by study design)	Pediatric/ Young adults	All child participants in 7 CrS surveys with fasting blood work. If a subject participated in more than 1 survey, only final data was included --> 9167 subjects	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. For this study, subjects were evaluated in 7 cross-sectional surveys btwn 1973 & 1994; 52% M; 36% B.	N/A	N/A	N/A	Ht Wt Quetelet index (Wt (kgs)/ Ht (meters squared) (QI) Rohrer index (Wt in kgs/ Ht in meters cubed) Subscapular & triceps skin fold (SFs) SBP DBP MAP = DBP + (SBP-DBP/3) TC (< 200 mg/dl = high) TG (≥ 130 mg/dl = high) HDL-C (< 35 mg/dl = low) LDL-C (> 130 mg/dl = high) Fasting insulin (INS) (> 95th %ile for age/race/sex = high) Results grouped by age: 5-10y & 11-17y. Overweight defined as QI > 95th%ile for age/sex.	Based on Quetelet Index(QI) > 95th%ile, 10.8% of children were overweight (OW). For QI from below the 25th%ile to the 84th%ile, there was little variation in the prevalence of C-V RFs. Above the 85th%ile for QI, the prevalence of C-V RFs increased substantially and progressively. For children with QI > 95th%ile vs. < 75th%ile, OR was 2.4 for elevated TC (CI:2.0-3.0), 2.4 for high DBP(CI:1.8-3.0), 3.0 for elevated LDL-C(CI:2.4-3.6), 3.4 for low HDL-C(CI:2.8-4.2), 4.5 for high SBP(CI:3.6-5.8),7.1 for high TGs (CI:5.8-8.6)& 12.6 for high fasting insulin(CI:10-16). Among those with QI>95th%ile, 58% of 11-17 y olds & 61% of 5-10 y olds had at least 1 C-V RF. Using QI≥95th%ile as a screening tool identified 50% of those with ≥2 RFs.	Q6. Overweight children & adolescents have increased levels of multiple C-V RFs. Overweight was most strongly associated with elevated levels of insulin, triglycerides and SBP. Overweight appeared in a cluster with multiple other RFs, with prevalence increasing as the degree of overweight increased. Screening for C-V RFs based on overweight should be considered since this identified 50% of those with ≥ 2 C-V RFs.
10385774	Urbina EM	Association of fasting blood sugar level, insulin level, and obesity with left ventricular mass in healthy children and adolescents: The Bogalusa Heart Study	1999	CrS	Retrospective	Bogalusa	LV mass	Q1 (RF4,8,14) Q2 (RF4,8,14) Q4 (RF4,8,14) Q6 (RF4,8,14)	USA	Community (other)	Correlate fasting glucose (FG) & insulin levels with echo estimate of LVM.	216	Pediatric/ Young adults	Subjects who had participated in previous Bogalusa screenings and in whom echo measurement of LVM was obtained.	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. For this study, subjects were: Age: 13-27 yrs;51%M;61%W.	N/A	N/A	N/A	Ht Wt Ponderal index (Wt/Ht cubed) Triceps & subscapular SFs LVM from 2D echo imaging LVMC = LVM/Ht to the 2.7 power	In univariate analysis, FG levels correlated with LVMI with all race/sex grps combined (r=.17,p=S). By MVA, there was no correlation btwn LVMI, FG and insulin levels when race/sex/age/BMI/BP included. When subjects were ranked by tertiles for fasting insulin & wt/ adiposity, increasing LVMI correlated with increasing insulin level in the grps with highest adiposity with the only significant difference seen btwn the high & low insulin grps (p=S). When grouped by increasing BP level, there was no difference in LVMI with increasing insulin level.	Q6. For adolescents & young adults of normal wt, there is no direct independent effect of insulin on LVM. Q1. For heavier and/or more obese subjects, increasing INS was associated with greater heart mass.
10421238	Srinivasan SR	Temporal association between obesity and hyperinsulinemia in children, adolescents, and young adults: the Bogalusa Heart Study	1999	Cohort	Prospective	Bogalusa	None	Q6 (RF8,14) Q7 (RF8,14) Q8 (RF8,14)	USA	Community (other)	Evaluate the temporal nature of the relationship btwn obesity & hyperinsulinemia in children, adolescents & young adults.	1,497	Pediatric/ Young adults	For this study, subjects examined between 1981 &1993 were eligible and 1,497 were selected: 427 children (5-7 y); 674 adolescents(12-14 y) 396 adults (20-24 yrs) were selected retrospectively with F/U periods of ~ 3 y.	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. Seven CrS surveys of school children & 4 surveys of previously examined young adults were performed between 1978 & 1993. For this study, subjects examined between 1981 &1993 were eligible. 427 children (5-7 y)/ 674 adolescents (12-14 y)/ 396 adults (20-24 y) were selected	427 children (5-7 y) 674 adolescents (12-14 y) 396 adults (20-24 y)	N/A	3 yrs	Ht Wt BMI (≥30=obese) Fasting insulin (INS)	Baseline BMI correlated with F/U insulin levels in all grps. Logistic regression analysis indicated that the proportion of subjects who developed BMI > 75th%ile at F/U increased significantly across baseline quintiles of insulin only among adolescents, irrespective of race/gender. This relationship disappeared after adjusting for baseline BMI. By contrast, a significant (+) trend btwn baseline top quintile of BMI & incidence of hyperinsulinemia (> 75th%ile) persisted after adjustment for race/ gender and baseline insulin: children, adolescents & adults in the top quintile for BMI were 3.7-8.4 X more likely to develop hyperinsulinemia on follow-up. In MVA, the best predictor of F/U insulin level was baseline BMI in children & adults / baseline insulin in adolescents. Baseline BMI was the best predictor of F/U BMI in all 3 age grps.	Q6. There is a significant (+) association between baseline obesity & incidence of hyperinsulinemia at subsequent F/U in children, adolescents & adults, independent of race, gender & baseline insulin level. Baseline BMI is the best predictor of insulin level at F/U in children, adolescents & adults.
10512420	Chen W	Cardiovascular risk factor clustering features of insulin resistance syndrome (Syndrome X) in a biracial (Black-White) population of children, adolescents, and young adults: the Bogalusa Heart Study	1999	CrS	Retrospective	Bogalusa	None	Q5 (RF4,5,8,14) Q6 (RF4,5,8,14)	USA	Community (other)	Evaluate clustering characteristics of RFs associated with Met S (Ponderal index/insulin levels/glucose/ TGS/ HDL/ BP) in children, adolescents and young adults in a longitudinal cohort study	4522 - no loss to F/U by study design	Pediatric/ Young adults	All subjects who participated in 1 or more of the 5 CrS surveys in the Bogalusa study conducted between 1981 & 1996. Subjects with missing study values, who were non-fasting, had HTN or were taking anti-hypertensive meds were excluded. Total n = 4,522	Community-based cohort of black(B) & white(W)W children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. For this study, subjects were divided into 3 age groups, 5-11y,12-17y & 18-38y; 63.7%W, 36.3%B.	5-11y: n=1,088 12-17y: n=1,427 18-38y: n= 2,007	N/A	N/A	Ht Wt Ponderal index (Wt (kg)/Ht(m) cubed) SBP DBP Mean BP = DBP + 1/3(SBP-DBP) = MBP TC TG HDL-C LDL-C Fasting glucose (FG) Fasting insulin (INS) IRI (= INS X FG/ 22.5; aka HOMA-IR) For subjects with multiple exams, the data from the most recent evaluation was used. Abnormal defined as > 75%ile for race/sex/age.	Prevalence of Syndrome X consisting of HTN, dyslipidemia (high TGs +/- low HDL), high INS and obesity ranged from 2.4 - 4.8%, 8 to 30X the expected prevalence by age group. Factor analysis yielded 2 uncorrelated factors (factor 1 = insulin/ITGs/HDL/glucose/ponderal index; factor 2 = insulin/BP). These 2 factors explained 54.6% of the total variance in the entire sample. Factor patterns were similar in Ws & Bs and in all 3 age groups.	Q6. Factor analysis suggests the presence of 2 distinct physiologic processes characterizing the clustering of RFs related to Syndrome X: a distinct metabolic entity characterized by hyperinsulinemia/insulin resistance, dyslipidemia & obesity linked to hypertension through hyperinsulinemia.

NHLBI Evidence Table: State of the Science: CV Risk Factors and the Development of Atherosclerosis in Childhood-OB

PMID	First Author	Title	Year	Study Type	Prospect./ Restrospect.	Study	CVD	RF by CQ	Country	Setting	Main Study Objective	N at Baseline (N at Follow-up)	Target Population	Eligibility Criteria	Patient Characteristics	Study Groups	n at Baseline (n at Follow-up) for Study Groups	Total Follow-up Duration	Outcomes Measured	Results	Main Reported Findings by Critical Question
10553393	Morrison JA	Sex and race differences in cardiovascular disease risk factor changes in schoolchildren, 1975-1990: the Princeton School Study	1999	CrS		Princeton	None	Q5(RF4,5,8) Q6(RF4,5,8)	USA	Community (schools)	Compare obesity & C-V RFs in B & W children assessed in 1973-1975 and in 1989-990 in a biracial community.	300 + 1456	Pediatric/ young adult	From a pool of 3rd -5tg grade students in Princeton, Ohio participating in the LRL study in 1973-1975, 15% were randomly selected for treating. Their results are compared to those of a group recruited from the same grades in 1989-1990.	Population-based , prospective observational study with participants recruited from 4 metropolitan areas (Birmingham, Ala; Chicago, Ill, Minneapolis, Minn; & Oakland, Calif) in 1985 1986 at 18-30 yrs of age (44.9% black, 53.9% women) & followed up ≥ 15 yrs later in 2000-2001 @ 33-45 yrs of age. For this CrS study, 300 3rd - 5th grade students from the LRC study in 1973-75 + 1456 3rd - 5th grade students in the same grades & school district in 1989-1990 were compared.	1973-75: 300 1989-90-: 1456	N/A	N/A	Age Race Gender Ht Wt BMI (> 85th%ile=overweight) TC (>200 mg/dL = elevated) HDL TG LDL SBP (> 95th%ile for sex-age-ht = elevated) DBP (> 95th%ile for sex-age-ht = elevated) 3 d diet record	Overall, students in the 1989-90 study had significantly higher BMI, TC, TGs, SBP and DBP than those in the earlier study. Prevalence of obesity increased from 12.5 to 25.3% and of hypercholesterolemia from 8.0 to 14.8%. Increases in wt & BMI were greatest in the top deciles. B females had the greatest increase in BMI & the highest prevalence of elevated TC in '89-'90 study. By subgroup, there was an increased prevalence of hypercholesterolemia in W & B Fs but not in W or B Ms; BMs had a significant increase in SBP not seen in other groups. Calories consumed were unchanged but '89-'90 students reported consuming fewer calories from fat & sat fat.	There is a secular trend towards increased obesity in elementary school-aged children over a 15 y period. Increases in BMI cluster with increases in TC and BP. There are race and sex differences in the change in C-V RFs over this time period.
10656167	Fernandez-Britto JE	Pathomorphometrical characteristics of atherosclerosis in youth. A multinational investigation of WHO/World Heart Federation (1986-1996), using atherometric system	1999	CrS	Retrospective	PDAY	Atherosclerosis	Q1	Multiple	Clinical	Study autopsy data for the development of atherosclerotic lesions in a young population	1,339 autopsies	Pediatric/ Young adults	Age: 5-34 yr	NR	5-14 yr age group 15-24 yr age group 25-34 yr age group	NR	N/A	Amount of intima surface occupied by any kind of atherosclerotic lesion (measured using a digitizer and the software Atherosoft)	Atherosclerosis increases with age. Fatty streaks were present already at 5 yr of age, independent of the country, climate, state of nourishment, type and amount of foods and the habits and lifestyle of the population studied. Fatty streaks progressed most rapidly from 15-24 yr. Fibrous plaques began to appear slowly at the end of the second and rapidly progressed after the third decades. = Severe plaque was rarely observed before 30 yr; it appeared in the fourth decade and then progressed slowly, but steadily.	Q1: Fatty streaks were always present at 5 yrs of age, independent of the country, climate, state of nourishment, type and amount of foods and the habits and lifestyle of the population studied. Fatty streaks progressed most rapidly from 15 to 24 yr. Atherosclerosis progresses with increasing age with severe plaque rarely seen before 30 yrs of age.
10656168	Kadar A	World Health Organization (WHO) and the World Heart Federation (WHF) pathobiological determinants of atherosclerosis in youth study (WHO/WHF PBDAY Study) 1986-1996. Histomorphometry and histochemistry of atherosclerotic lesions in coronary arteries and the aorta in a young population	1999	CrS		PDAY	Atherosclerosis	Q2 (RF2,3,4,10) Q3 (RF2,3,4,10) Q9 (RF2,3,4,10)	Hungary,Cuba, Germany,Mexico, SriLanka	Clinical	Study the development of atherosclerotic lesions in a young population with known pre-mortem RFs.	214	Pediatric/ young adult	All subjects aged 15-34 y who died suddenly in 5 international collaborating centers. Pre-mortem RF data obtained when possible. Path analysis identical to US PDAY study.	Subjects aged 15-34 yrs who died traumatically in Germany/ Hungary/ Cuba/ Mexico City/ Sri Lanka.	15-24 y = 81 25-34 y = 133	N/A	N/A	Sections of proximal LAD and thoracic & desc. Ao evaluated for intima/media (I/M) ratio and grades 1-6 intimal lesions. BP Smoking status	Intima/ media ratio and extent of grade 3-4 lesions increased in all arteries with age. Geographic region had little impact on findings. I/M ratio in the LAD was significantly greater in Ms than Fs (p=S) Atherosclerotic lesions were more prevalent in men, especially in the LAD. HTN was asst'd with higher prevalence of gr 3 & 4 lesions in all arteries but significantly only in the thoracic aorta (p=S). Smoking was asst'd with higher prevalence of gr 3 & 4 lesions in all arteries but this was only significant in the ascending aorta (p=S).	Q2,3,9. Atherosclerosis begins in childhood and the presence and extent of RFs affects atherosclerotic extent in children.
10712411	McGill HC, Jr.	Effects of coronary heart disease risk factors on atherosclerosis of selected regions of the aorta and right coronary artery. PDAY Research Group. Pathobiological Determinants of Atherosclerosis in Youth	2000	CrS		PDAY	Atherosclerosis	Q1(RF2,3,4,6,8,10,14) Q2(RF2,3,4,6,8,10,14) Q4(RF2,3,4,6,8,10,14) Q5(RF2,3,4,6,8,10,14) Q9(RF2,3,4,6,8,10,14) Q14a(RF2,3,4,6,8,10,14)	USA	Clinical	Evaluate the topographic distribution of atherosclerosis in relation to RFs for adult C-VD.	2,000	Pediatric/ young adult	All subjects aged 15-34 y who died suddenly in 15 US collaborating centers. Topography of atherosclerotic lesions evaluated in light of RF status. In this study, information on > 2000 autopsies was used,.	3,201 15-34 y olds who died accidentally in 15 different cities in the U.S.; information on age/ gender/ lipids/ smoking / HTN / obesity / hyperglycemia was available.	N/A	N/A	N/A	Extent of intimal surface of RCA & abd Ao with fatty streaks and raised lesions evaluated by pathologists and by computerized image analysis. C-V RFs: Age Race Gender HDL < 35 mgm/dl Non-HDL-C = TC - HDL (LDL cutpoints + 30mgm/dL = non- HDL cutpoints) = > 160 mg/dl Thiocyanate level ≥ 90mmol/L Intimal thickness of small renal arteries = Mean BP estimate >110 mmHg BMI > 30 kg/ m squared HbA1C ≥ 8%	There are distinct regional differences to atherosclerotic extent in the aorta and CAs. With increasing age, fatty streaks decrease or remain stable and raised lesions increase in all regions with raised lesions in the RCA beginning in the 20-24 y old age group. RF effects on arterial regions that are vulnerable to lesions are 25% greater than RF effects assessed over entire arterial segments. In subjects with multiple RFs, extent of fatty streaks and raised lesions is greater in all regions of the aorta at all ages compared with low risk group, with increasing divergence between the 2 groups over time. In the RCA, differences between the low & high risk groups become apparent after age 25 with the difference between groups increasing in 30-34 y olds. Smoking selectively affects atherosclerosis in the abd Ao at a younger age than the CAs.	There are distinct regional differences to atherosclerotic extent in the aorta and CAs. Q1. Atherosclerosis begins in childhood. Q2. The presence of RFs correlates with the extent of atherosclerotic lesions at autopsy. Q9. An increase in the number of RFs is associated with increased prevalence and severity of atherosclerotic lesions at autopsy. Q14a. A low risk state is associated with decreased development & progression of atherosclerotic lesions.
10866058	Chen W	Age-related patterns of the clustering of cardiovascular risk variables of syndrome X from childhood to young adulthood in a population made up of black and white subjects: the Bogalusa Heart Study	2000	CrS	Retrospective	Bogalusa	None	Q5 (RF3, 4, 5, 8, 14) Q6 (RF3, 4, 5, 8, 14)	USA	Community (other)	Evaluate age-related clustering of RFs for Met S (insulin res index, BMI, TG/HDL, mean BP) in 3 age groups: 5-10 y,11-17 y, and 18-37 y in a longitudinal cohort.	8,875 (no loss to F/U by design)	Pediatric/ Young adults	All subjects who participated in 1 or more of the 5 CrS surveys in the Bogalusa study conducted between 1981 & 1996. Subjects with missing study values, who were non-fasting, had HTN or were taking anti-hypertensive meds were excluded. Total n = 8,875.	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. For this study, 3 different age groups (5-10y) (11-17 y) (18-37 y) were evaluated.	5-10y = 2,389; 50%M;37%B 11-17y =3,371;52%M;37%B 18-37y =2,115;43%B;33%B	N/A	N/A	Ht Wt BMI (≥30=obese) SBP DBP Mean BP = DBP + 1/3(SBP-DBP) = MBP TC TG HDL-C LDL-C Fasting glucose (FG) Fasting insulin (INS) Insulin resistance index (IRI= INS X FG/ 22.5; aka HOMA-IR) For subjects with multiple exams, the data from the most recent evaluation was used. Abnormal defined as > 75%ile for race/sex/age. MetS cluster = IRI; BMI; TG/HDL; MBP	Ratios of observed to expected were used to assess the degree of clustering of adverse levels of the 4 RFs by race & age group. RRs were significantly different than 1 for all race & sex groups (p=S*). RRs were higher in pre-pubertal & young adult age groups, lowest during puberty, regardless of race. Overall RR for clustering of adverse levels of all 4 variables was 9.8 for Ws and 7.4 for Bs (p=S). Intraclass correlations for 2,3 & 4 RF combinations for each race & sex group were calculated. For 2 & 3 RF combinations, correlation was strongest for combinations with IRI & BMI and lowest for those with TG/HDL & MBP. For 4-variable combinations with all the age-groups combined, Ws showed higher correlation(0.33 vs. 0.26 for B) with no overlap of CIs. Intraclass correlations were significant (p=S**) in all race and age groups, higher during pre-adolescence and young adult age than in adolescence. Intraclass correlations increased continuously with age during adulthood. When adjusted for BMI, intraclass correlations involving the other 3 variables were reduced by 50% and age-related pattern disappeared.	Q5. Clustering of RFs typical of the MetS was consistently stronger in Bs than Ws. Q6. RRs generated from observed to expected observation demonstrate strong evidence of clustering of BMI, IRI, TG/HDL & MBP at all ages but less during puberty. Q6. When adjusted for BMI, intraclass correlations for the other 3 variables decreased by 50% and age-related pattern disappeared suggesting that age-related changes in obesity may be the dominant factor accounting for RF clustering in MetS.
10912890	Janz KF	Tracking physical fitness and physical activity from childhood to adolescence: the Muscatine study	2000	Cohort	Prospective	Muscatine	None	Q8 (RF 4,5,8,11)	USA	Community (other)	To evaluate tracking of physical activity & fitness from childhood into adolescence	126/110	Pediatric/ Young adults	From a subset of 150 children from the Muscatine study group, 150 were contacted and ultimately 126 prepubertal subjects were enrolled.	M: n=61; mean age=10.6y F:n=62; mean age=10.3y.	N/A	126/110	5 y	Ht Wt BMI Tanner stage Skin folds (SFs) Waist circumference Body composition Maximal VO2 by bicycle ergometry Peak grip Activity questionnaire - TV/video game recall SBP DBP TC TG HDL LDL	VO2 values were greater in Ms than Fs throughout. In Ms, VO2 continued to increase throughout the study period; in Fs, VO2 was unchanged in y 5. Peak HR in Fs was consistently higher than in Ms; y-1 to y-5 HRs did not differ in Ms or Fs. Peak grip increased in Ms & Fs throughout the study. Weight-dependent variables showed the best tracking in both Ms & Fs. In Ms, peak grip tracked best with r ranging from 0.68 to 0.90 In Fs, peak grip also tracked well with r ranging from 0.52 to 0.80. In Ms, VO2max tracked well with r ranging from 0.48 to 0.86. In Fs, VO2max tracked well with r ranging from 0.43 to 0.74. 60% of Ms & 59% of Fs who were in the top tertile for VO2max at baseline were still there after 5 yrs.	.Physical fitness & physical activity variables tracked well throughout the 5 yrs in Ms & Fs. Boys who were sedentary at baseline were 2.2 X more likely to be sedentary at F/U. Sedentary behavior tracked better in boys while vigorous activity tracked better in girls

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PMID	First Author	Title	Year	Study Type	Prospect./ Restrospect.	Study	CVD	RF by CQ	Country	Setting	Main Study Objective	N at Baseline (N at Follow-up)	Target Population	Eligibility Criteria	Patient Characteristics	Study Groups	n at Baseline (n at Follow-up) for Study Groups	Total Follow-up Duration	Outcomes Measured	Results	Main Reported Findings by Critical Question
10938023	McGill HC, Jr.	Associations of coronary heart disease risk factors with the intermediate lesion of atherosclerosis in youth. The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group	2000	CrS		PDAY	Atherosclerosis	Q1(RF2,3,4,6,8,10,14) Q2(RF2,3,4,6,8,10,14) Q4(RF2,3,4,6,8,10,14) Q5(RF2,3,4,6,8,10,14) Q9(RF2,3,4,6,8,10,14) Q14a(RF2,3,4,6,8,10,14)	USA	Clinical	Assess the presence of raised fatty streaks, the intermediate lesion of atherosclerosis, in a population of adolescents and young adults.	2,876	Pediatric/ young adult	2,876 cases collected in the PDAY study between 1987&1994 with corresponding RF information.	3,201 15-34 y olds who died accidentally in 15 different cities in the U.S.; information on age/ gender/ lipids/ smoking / HTN / obesity / hyperglycemia was available. In this study, results of 2,876 cases were included. 25% F; 54% B.	N/A	N/A	N/A	Extent of intimal surface of RCA & abd Ao with fatty streaks and raised lesions evaluated and AHA grading (grades 1-6) of stained sections of CAs and abd Ao performed. Raised fatty streak = Intermediate lesion between simple fatty streak and raised lesions. Defined as a type III lesion in AHA classification. C-V RFs: Age Race Gender HDL < 35 mgm/dl Non-HDL-C = TC - HDL (LDL cutpoints + 30mgm/dL = non- HDL cutpoints) = > 160 mg/dl Thiocyanate level ≥ 90mmol/L Intimal thickness of small renal arteries = Mean BP estimate >110 mmHg BMI > 30 kg/ m squared HbA1C ≥ 8%	In the abdominal aorta, raised fatty streaks were more prevalent in Ms than Fs and in Bs vs Ws, present in 20% of 15-19 y old's and 40% of 30-34 y olds. In the RCA, raised fatty streaks were more prevalent in Ms than in Fs and in Bs vs Ws, found in 10% of 15-19 y olds & 30% of 30-34 y olds. Associations of RFs with fatty streaks began in the late teens while association with raised fatty streaks became evident in subjects > 25 y. The % of intimal surface involved with fatty streaks increased with age in both arteries & was asst'd with high non-HDL-C and low HDL in the abd aorta & RCA, with HTN in the abdominal aorta, with obesity in the RCA of Ms, & with impaired GT in the RCA. When subjects with multiple RFs (HTN+smoking+non-HDL>160 mg/dl+HDL < 35 mg/dl + BMI > 30) were compared with low risk subjects with none of these RFs, high-risk level was associated with more extensive flat fatty streaks, raised fatty streaks & raised lesions in the abdAo & RCA in all age groups (p=S). The impact of combined RFs increased with increasing age in both abd Ao and RCA.	The raised fatty streak represents a transitional lesion between the flat fatty streak and advanced raised lesions (fibrous plaques) Q1. Atherosclerosis begins in childhood. Q2. The presence of RFs correlates with the extent and severity of atherosclerotic lesions at autopsy. Q9. An increase in the number of RFs is associated with increased prevalence and severity of atherosclerotic lesions at autopsy. Q14a. A low risk state is associated with decreased development & progression of atherosclerosis.
10949011	Kimm SY	Longitudinal changes in physical activity in a biracial cohort during adolescence	2000	Cohort	Prospective	Growth	None	Q13 (RF11)	USA	Community (other)	Assess longitudinal changes in activity in a large biethnic cohort of girls from childhood through adolescence	2379	Pediatric/ Young adults	Physical activity self-reports completed at baseline. 3-d activity diary completed in 8 of 10 y of the study; habitual activity questionnaire completed as a structured interview in y 1, 3 & 5 and self-administered for y 7-10. Caltrac activity monitor was used to measure daily activity for 3-d coincident with the 3-d food record & activity diary, for the whole cohort in y 3-5.	1166 W girls, 1213 B girls from 3 geographic locations enrolled at age 9-10 y and followed annually X 10 y.	B girls: n=1213 W girls: n=1166	N/A	10 y	Activity diary scores - MET-min-d (-1 Power) Habitual activity questionnaire scores - MET-times-wk(-1 power) Caltrac scores - counts/d (-1 power)	For the group, activity scores were highly skewed with the majority of subjects reporting minimal activity. There was a consistent decline in level of reported activity from baseline to year 10 as indicated by 3-day diary scores (35% decrease;p=S**) and habitual patterns questionnaire (83%).(p=S**) There was a similar decline in activity as assessed by Caltrac accelerometer in years 3 - 5 when this data was available: 10% & 13% decrease by Caltrac in y3-4 & 4-5. When reports were available for all 3 methods from y 3 to y 5, consistent change was demonstrated: the AD score decreased by 22% and HAQ & Caltrac by 21%.	Activity levels decreased significantly from 9 - 19 y of age in this longitudinal cohort.
11257083	McGill HC, Jr.	Effects of nonlipid risk factors on atherosclerosis in youth with a favorable lipoprotein profile	2001	CrS		PDAY	Atherosclerosis	Q1(RF2,3,4,6,8,10,14) Q2(RF2,3,4,6,8,10,14) Q4(RF2,3,4,6,8,10,14) Q5(RF2,3,4,6,8,10,14) Q9(RF2,3,4,6,8,10,14) Q14a(RF2,3,4,6,8,10,14)	USA	Clinical	Evaluate the extent of atherosclerosis at autopsy in adolescents and young adults with a favorable lipid profile	856	Pediatric/ young adult	In this study, among 2,876 autopsies performed between 1987-91, 629 males/ 227 females with non-HDL-C < 160 mg/dl & HDL >/= 35 mg/dl; age range = 15-34 y were evaluated.	3,201 15-34 y olds who died accidentally in 15 different cities in the U.S.; information on age/ gender/ lipids/ smoking / HTN / obesity / hyperglycemia was available. In this study, among 2,876 autopsies performed between 1987-91, 629 males/ 227 females with non-HDL-C < 160 mg/dl & HDL >/= 35 mg/dl; age range = 15-34 y were evaluated.	N/A	N/A	N/A	Extent of intimal surface of RCA & abd Ao with fatty streaks and raised lesions was evaluated and AHA grading (grades 1-6) of stained sections of CAs and abd Ao was performed. C-V RFs: Gender Race Age Thiocyanate level ≥ 90mmol/L Intimal thickness of small renal arteries = Mean BP estimate >110 mmHg BMI > 30 kg/ m squared HbA1C ≥ 6.9%	Prevalence of smoking was high at 44% for the whole cohort & for those with favorable lipid profile. Of those with favorable lipid profile, 38.8% had no RFs, 47.3% had 1 non-lipid RF, 13.1% had 2 non-lipid RFs, 0.7% had 3 non-lipid RFs and 0.1% had all 4 non-lipid RFs. Those with favorable lipid profile and no other RFs had much less RCA involvement with raised lesions from the youngest age and extent of atherosclerosis progressed much less rapidly with increasing age vs those who smoked, had HTN, were obese and had hyperglycemia - for example, in 15-19 y Ms, low risk group had 0.5% raised lesions vs 1.3% in high non-lipid RF group; by 30-34 y, low risk group had 1% involvement with raised lesions vs 4% for high non-lipid RF group. This difference persisted in all race/sex groups. In the abd. aorta, smokers had more extensive fatty streaks & raised lesions than non-smokers and Bs with HTN had more raised lesions than normotensive Bs. In the RCA, Bs with HTN had more raised lesions than normotensive Bs, obese M had more extensive fatty streaks than non-obese men, and individuals with elevated HbA1c had more extensive fatty streaks. In the LADCA, obese men had more severe lesions.	Q9. Non-lipid RFs significantly accelerate atherosclerosis beginning in childhood. Progression of atherosclerosis is accelerated in Ms compared with Fs. Q5. There are race and gender differences in RF impact on the development of atherosclerosis. Q9. An increase in the number of RFs is associated with increased prevalence and severity of atherosclerotic lesions at autopsy even in the absence of dyslipidemia. Q14a. Preservation of a low risk state is associated with decreased development & progression of atherosclerosis.
11347739	Fagot-Campagna A	Diabetes, impaired fasting glucose, and elevated HbA1c in U.S. adolescents: the Third National Health and Nutrition Examination Survey	2001	CrS	Retrospective	NHANES	None	Q5 (RF6) Q6 (RF6)	US	Clinical	Estimate the prevalence of diabetes, impaired fasting glucose, and elevated HbA_{1c} (>6%) levels in US adolescents.	2,867	Pediatric/ Young adults	12-19 yr old participants in the NHANES III survey for 1988-1994 in whom fasting serum glucose had been measured	Nationally representative sample.	Group 1: All adolescents who had glucose measured Group 2: Subsample of adolescents assigned to morning examinatiion and fasting glucose	Group 1: 2,867 Group 2: 1,083	N/A	Fasting glucose (FG) HbA1c level BMI	(1) 13 of 2,867(0.41%[CI:0-0.86]) adolescents had a diagnosis of DM. 31% had T2DM and 69% had T1DM. (2) Of those 1,083 adolescents without DM, 20 had impaired FG and 22 of 2,852 had HbA1c > 6%. Both IFG and elevated HbA1c were more prevalent among non-Hispanic Bs and in males. 10 adolescents had both IFG & elevated HbA1c, all with BMI > 30 and all from minority groups. (3) Extrapolating from these data, 1.76% (CI:0.02-3.5) of adolescents have IFG and 0.39% (CI:0.04-0.74) have elevated HbA1c.	NHANES III data shows a very low prevalence of T2DM. Cases were all in obese adolescents and were non-Hispanic B or M-A.
11395036	Homma S	Histopathological modifications of early atherosclerotic lesions by risk factors--findings in PDAY subjects	2001	CrS		PDAY	Atherosclerosis	Q4(RF3,4,5,10) Q9(RF3,4,5,10)	USA	Clinical	Evaluate histopathological modifications of atherosclerotic lesions in light of pre-mortem RFs.	140	Pediatric/ young adult	From the 151 male PDAY cases collected from 1987-1989, 140 cases without significant branch artifacts or intimal damage were evaluated.	3,201 15-34 y olds who died accidentally in 15 different cities in the U.S.; information on age/ gender/ lipids/ smoking / HTN / obesity / hyperglycemia was available. Males from the PDAY study examined in 1987-89 for whom pre-mortem RF results were available were included in this study.	N/A	N/A	N/A	Extent of intimal surface of RCA & abd Ao with fatty streaks and raised lesions was evaluated and AHA grading (grades 1-6) of stained sections of CAs and abd Ao was performed. AHA grading of gross specimens + intimal thickness + status of foam cells + density of fibrosis reviewed. Age TC HDL Non-HDL-C = TC - HDL (LDL cutpoints + 30mgm/dL = non-HDL cutpoints) Thiocyanate level ≥ 90mmol/L Intimal thickness of small renal arteries = Mean BP estimate >107 mmHg BMI > 30 kg/ m squared HbA1C ≥ 8%	A pair-matched control was selected for each RF. Extent of gross atherosclerotic lesions did not progress differently by individual RFs. In both aorta and LCA, intimal thickness of subjects with HTN was greater than for normotensives with no proliferation of foam cells. In aortas, hypercholesterolemia was asst'd with an increase in foam cells but not with an increase in intimal thickness. HDL-C correlated inversely with # of foam cells in the aorta & LCA and the degree of thickness in the LADCA where early appearance of advanced lesions such as preatheroma or atheroma was also indicated in the low HDL-C grp. Smokers had fewer foam cells in both aorta and CAs and more intensive fibrosis in the LADCA than non-smokers.	Q4. Histopathologic changes of atherosclerosis vary with individual RF extent and severity.
11733400	Davis PH	Carotid intimal-medial thickness is related to cardiovascular risk factors measured from childhood through middle age: The Muscatine Study	2001	CrS		Muscatine	IMT	Q3 (RF2,3,4,5,8) Q9 (RF2,3,4,5,8)	USA	Community (other)	Correlate CIMT in young adult life with C-V RFs measured in childhood, currently and as a "load" from childhood to adulthood.	725	Pediatric/ young adult	Subjects from the Muscatine study who had participated in at least 1 childhood survey, 1 young adult survey and in the CAC study were eligible - 725 subjects, 33-42 y, 52% F participated.	Longitudinal cohort study based in Muscatine, IA of children aged 8-18 y at enrollment between 1971 & 1981, followed with biennial school surveys into adult life. A total of 14,066 children have undergone 32,636 evaluations. For this study, 346 men/ 379 women; aged 33 - 42 yrs; from the cohort followed from childhood were evaluated.	N/A	769/725	N/A	Ht Wt BMI (>25kg/m squared = overweight) Waist circumference (WC) Hip circumference (HC) Waist to hip ration (WC/HC) Triceps SFs SBP DBP TC TG HDL LDL TC/HDL Lp(a) Fasting glucose (FG) Fasting insulin (INS) Mean cIMT from carotid U/S average of 12 measurements from near & far wall of each CCA, carotid bifurcation and internal carotid artery.	Mean maximum CIMT was 0.79 +/- 0.12 in men & 0.72 +/- 0.10 in women (p=S**) In Ms, the only childhood RF to correlate with cIMT was TC (r=0.17, p=S*); in Fs, childhood BMI (r=0.18), TSFs (r=0.09), TC (r=0.14), SBP (r=0.15), DBP(r=0.10) & TGs (r=0.12) all correlated with cIMT in univariate analysis (all, p=S-S**). With MVA, significant current predictors of CIMT were age & LDL-C in both sexes and DBP in women. With MVA, significant childhood predictors were TC in both sexes & childhood BMI only in women. In a risk factor load model, LDL-C, HDL-C & DBP predicted CIMT; in women, LDL-C, BMI & TGs were predictive. In a MVA with cIMT in upper quartile vs lower 3 quartiles, childhood TC was a significant RF in Ms (OR=1.47,CI=1.02,2.13) and in Fs (OR=1.71, CI=1.16,2.50). Smoking & DM did not correlate with cIMT but the # of subjects with DM was very small and pack-yrs of smoking low compared with other studies.	Q 3. RFs present in childhood and in adult life correlate with atherosclerosis measured by cIMT in young adult life.

NHLBI Evidence Table: State of the Science: CV Risk Factors and the Development of Atherosclerosis in Childhood-OB

PMID	First Author	Title	Year	Study Type	Prospect./ Restrospect.	Study	CVD	RF by CQ	Country	Setting	Main Study Objective	N at Baseline (N at Follow-up)	Target Population	Eligibility Criteria	Patient Characteristics	Study Groups	n at Baseline (n at Follow-up) for Study Groups	Total Follow-up Duration	Outcomes Measured	Results	Main Reported Findings by Critical Question
11735090	Youssef AA	Trends of lipoprotein variables from childhood to adulthood in offspring of parents with coronary heart disease: the Bogalusa Heart Study	2001	Cohort	Prospective	Bogalusa	None	Q6 (RF1,5)	USA	Community (other)	Evaluate association of (+)FamHx with development of adverse lipid profile in children and young adults.	1,076	Pediatric/ Young adults	Data from 6 cross-sectional surveys in children and 4 in young adults pooled for analysis of lipoprotein variables over time in subjects with & without (+) fam hx of CAD.	Community-based cohort of black(B) and white (W) children and young adults - originally examined at 5-17 yrs; 52% female(F), 48% male (M); 44% B. For this study, 271 children with (+) famHx for CAD/ 805 without.	Fam hx(+) = 271 Fam hx(-) = 805	N/A - data pooled on fam hx(+) & fam hx (-) subjects assessed at each time interval	18 y	LDL TG VLDL HDL Correlated with age, sex, BMI, insulin & glucose in MVA	In (+) fam hx group, LDL was higher in early childhood from 4-15 y and then after age 20 y v. (-) fam hx group. LDL increased steeply in both groups during adolescence. VLDL & TG curves were similar in shape to LDL curves but differences btwn groups less impressive. For HDL, inverse association with age noted btwn ages 4 & 20 in both groups with trend for lower HDL in (+) fam hx group. With MVA, (+) fam hx was consistently correlated with higher VLDL with no interaction with age. Differences in LDL & TG btwn groups were significant after age 20. (+) fam hx correlated inversely with HDL and with age(p=.08) When BMI, insulin or glucose added to model, adverse association with VLDL & TGs was no longer significant. With LDL, adverse relationship disappeared only when glucose added to model. For all analyses, interactions were independent of race & sex.	With MVA, (+) fam hx was consistently correlated with higher VLDL with no interaction with age. In MVA adjusted for race and sex, parental CAD was (+)ly ass'd with LDL and TGs at young adult age and with VLDL during early childhood and young adulthood. Addition of obesity mediated measures alters relationship between (+) fam hx & lipids: (+) association between LDL and parental CAD persists with BMI and insulin in the model but disappears when FG is included; for TGs and VLDL, inclusion of BMI, insulin or FG eliminates the association with parental CAD.
11756342	Srinivasan SR	Predictability of childhood adiposity and insulin for developing insulin resistance syndrome (syndrome X) in young adulthood: the Bogalusa Heart Study	2002	Cohort	Prospective	Bogalusa	None	Q6 (RF4,5,8,14) Q7 (RF4,5,8,14) Q8 (RF4,5,8,14)	USA	Community (other)	Examine the relative contribution of childhood adiposity & insulin to adult risk for development of syndrome X.	745 (No loss to F/U by study design)	Pediatric/ Young adults	For this study, subjects must have participated in at least 1 survey at age 8-17 yrs.and one at age>/= 19yrs and have no missing data among the variables of interest.	Community-based cohort of B & W children and young adults - originally examined at 5-17 yrs; 52% F, 44% B. Five CrS surveys of school children & 5 surveys of previously examined young adults were performed were performed between 1978 & 1996. For this study, subjects must have participated in at least 1 survey at age 8-17 yrs.and one at age>/= 19yrs.	n=745 39% M, 67% W.	N/A	11.6 +/- 3.4 yrs	Ht Wt BMI (≥30=obese) Subscapular skin fold (SSF) Waist circumference (WC) (>100cm=obese) SBP DBP TC TG (>150 mg/dl=high) HDL-C (< 40 mg/dl in M,< 50 mg/dl in F = low) LDL-C (>160 mg/dl = high) Fasting glucose (FG) (>110-125 mg/dl = impaired; ≥126 mg/dl = DM) Fasting insulin (INS) (>18 uU/ml= high) HOMA-IR (= INS X FG/ 22.5) To maximize F/U when subject participated in multiple screenings, earliest childhood and latest adult data used. Syndrome X cluster variables=Highest quartile for BMI, fasting insulin, SBP or mean BP, and TC/HDL or TG/HDL. Clustering = All 4 variables	6.4% of adults had Syndrome X cluster. In cluster(+) adults, BMI, INS, FG, SBP, DBP, TC, LDL, TGs, TC/HDL & TG/HDL were all significantly higher and HDL significantly lower than in cluster(-) group (all, p=S**). For the entire cohort, as the # of cluster variables present in adult life increased, childhood values increased significantly. Proportion of subjects who developed clustering as adults increased across childhood BMI & INS levels - children in the top quartile for BMI & INS were 11.7X (CI 3.4-39.7) (p=S**) & 3.6 X (CI 1.5-8.7) (p=S*) more likely to develop (+) clustering as adults. Relationship of clustering to childhood BMI persisted after correction for insulin (OR=10.0 ;CI 2.8-35.5, p=S**) but insulin was no longer predictive after BMI entered into the analysis. No difference by race or sex.	Childhood obesity is the strongest predictor of development of syndrome X in adult life. As BMI increases, # of cluster variables present increases.
11976155	Freedman DS	Differences in the relation of obesity to serum triacylglycerol and VLDL subclass concentrations between black and white children: the Bogalusa Heart Study	2002	CrS		Bogalusa	None	Q5 (RF5,8) Q6 (RF5,8)	USA	Community (other)	Evaluate the relationship of obesity to VLDL subclasses in children.	916	Pediatric/ Young adult	All 10-17 y olds examined in the Bogalusa study in 1992-4 in whom lipoprotein sub-classes were obtained.	Community-based cohort of B & W children and young adults - originally examined at 5-17 yrs; 52% F, 44% B. For this study: Age: 10-17y; 40% AA/ 60% white	N/A	N/A	N/A	Age Gender Race Ht Wt BMI Rohrer Index (RI) Waist circumference (WC) Subscapular & triceps skinfolds TC TG HDL LDL VLDL VLDL/ TG sub-classes	In a large background sample, BMs were shown to be thinner than WMs and BFs were shown to be heavier than WFs, with consistently higher HDL & lower TGs in Bs vs Ws. Mean TGs were 25 mg/dl higher in white than black children due to a 140% difference in large VLDL. Small VLDL was 29% higher in whites. For the entire sample, VLDL + TGs correlated with all measures of obesity, most strongly with WC (r=0.36, p= S**). This association was curvilinear and was 2 to 6 X stronger in whites than blacks. As WC increased, the proportion of large VLDL increased. WC was not related to small VLDL.	Q 5. There are racial differences in TG/VLDL levels between W and B children with higher large VLDL sub-class largely responsible for the difference. Q 6. For the entire sample, VLDL/TGs correlated with all measures of obesity, most strongly with WC. The association with WC was 6X stronger in W children. Measurement of VLDL sub-classes may provide information on the role of race and obesity in the process of atherosclerosis.
12012257	Janz KF	Increases in physical fitness during childhood improve cardiovascular health during adolescence: the Muscatine Study	2002	Cohort	Prospective	Muscatine	None	Q8 (RF4,5,8,11) Q10 (RF11) Q11 (RF11)	USA	Community (other)	Evaluate aerobic fitness, muscular strength & C-V RFs in a cohort of children followed longitudinally.	125/109	Pediatric/ Young adults	A group of 125 pre-pubertal subjects were selected from the Muscatine study population .	Longitudinal cohort study based in Muscatine, IA of children aged 8-18 y at enrollment between 1971 & 1981, followed with biennial school surveys. into adult life. A total of 14,066 children have undergone 32,636 evaluations. For this study, mean baseline age= 10.5 yrs; all pre- or early puberty at baseline	N/A	125/109	5 y	Ht Wt BMI Tanner stage Skin folds (SFs) Waist circumference Body composition Maximal VO2 by bicycle ergometry Peak grip Activity questionnaire SBP DBP TC TG HDL LDL	There was a weak to moderate correlation between change in fitness over the 5 y period & y-5 lipids, adiposity & WC. (LDL & decrease in VO2max: r = -0.24, p=S; TC/HDL & decrease in VO2max,r=-0.27, p=S; SSF & decrease in peak grip, r= - 0.32, p=S; WC & decrease in peak grip, r = 0.31, p=S. When adjusted for age,gender, FFM & Tanner stage, 5-y decrease in VO2 still correlated significantly with TC/HDL(- 0.27);LDL(- 0.28);SSF(r= - 0.33); & WC(r= - 0.33)(all,p=S). When adjusted for age,gender, FFM & Tanner stage, change in peak grip still correlated significantly with SBP(r=- 0.21);SSF(r=- 0.32); WC(r= 0.32)(all,p=S). Best correlation was increase in FFM with SBP (r=0.49); DBP(r=0.26),TC/HDL, r=-0.20;and WC (r=-0.47) (all, p=S) Average VO2 over 5 years correlated only with WC(r=0.38) & SSF(-0.49), both p=S. Average 5-y peak grip correlated with SBP(r= -0.20), SSF (r=-0.45) & WC (r=-0.48) (all, p=S) By MVA, change in muscular strength explained 4% of the variability in yr 5 SBP; change in aerobic fitness explained 11% of yr 5 TC/HDL & 5% of yr 5 LDL-C.	Maintaining high levels of physical fitness is associated with low levels of adiposity in adolescence. Small but significant amounts of lipid & BP outcomes in adolescence can be explained by fitness changes in the preceding 5 years.
12012257	Janz KF	Increases in physical fitness during childhood improve cardiovascular health during adolescence: the Muscatine Study	2002																	Changes in aerobic fitness & strength explained 15% of the variability in 5 y adiposity & abdominal adiposity.	
12355326	Schmitz KH	Association of physical activity with insulin sensitivity in children	2002	CrS	Retrospective	Minn	None	Q6 (RF4, 5, 8, 11, 14)	USA	Community (schools)	Evaluate insulin sensitivity by euglycemic hyperglycemic clamp relative to physical activity in children.	357	Pediatric/ Young adults	Pts were selected from BP screening of 12,043 eighth graders from which a random selection of 2915 black(B) and white(W) children stratified as upper 25% and lower 75% of the BP distribution was made. This group were offered participation in a euglemic clamp study and 357 children ultimately participated.	Age: 10-16 yrs !74 subjects were from the top 25% of the BP distribution - 54.5% male(M),19.5% B. 183 subjects were from the lower 75% of the BP distribution - 43.7% female(F), 21.3% B.	N/A	N/A	N/A	Ht Wt BMI (Obesity=>95th%ile until yr-10, then ≥30) Waist circumference (WC) Triceps & sub-scapular SFs (SSFs) (% body fat= BF%) Tanner stage SBP DBP Fasting insulin (INS) Insulin euglycemic clamp(Mffm = glucose utilization/ kg of FFM/min HOMA-IR TC TG HDL LDL Physical activity by questionnaire (kcla/d)	Bs & Ms had higher activity levels. Wt & BMI did not change across activity levels but body fat % decreased & FFM increased as activity level increased. There were no differences in BP or lipids across activity quartiles. Physical activity (PA) correlated significantly but not strongly with INS and insulin sensitivity (r=.12, p=S; & r=.13,p=S*). There was no correlation between activity & body fat %, BMI, WC, BP or lipids. There was no modification of the association of activity and Mffm by introduction of gender, Tanner stage, BMI, HDL, TGs or DBP. Correlation was slightly stronger in children with above-median BP or above median body fat % (r=.17,p=S; & r=.35,p=S**). Adjustment for age/sex/ race/Tanner stage/BMI/% body fat/waist circumference or lipids did not affect these results.	Q6. There is a correlation between physical activity & both INS & Mffm; association is stronger in children with higher BP. Physical activity is associated with lower INS & higher insulin sensitivity.

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PMID	First Author	Title	Year	Study Type	Prospect./ Restrospect.	Study	CVD	RF by CQ	Country	Setting	Main Study Objective	N at Baseline (N at Follow-up)	Target Population	Eligibility Criteria	Patient Characteristics	Study Groups	n at Baseline (n at Follow-up) for Study Groups	Total Follow-up Duration	Outcomes Measured	Results	Main Reported Findings by Critical Question
12495828	Youssef AA	Time-course of adiposity and fasting insulin from childhood to young adulthood in offspring of parents with coronary artery disease: the Bogalusa Heart Study	2002	Cohort	Prospective	Bogalusa	None	Q5 (RF 1, 8,14) Q6 (RF 1, 8,14) Q8 (RF 8,14)	USA	Community (other)	Correlate (+) Fam Hx for CHD with obesity and insulin levels.	1076 (by design)	Pediatric/ Young adults	Among the 1930 young adults aged 18-32 y who were evaluated between 1988-1991, 271 had a (+) confirmed fam hx for parental CAD vs 805 with confirmed (-) fam hx. These 1076 subjects represent the eligible subjects.	Community-based cohort of B & W children and young adults - originally examined at 5-17 yrs; 52% F. 44% B. For this study, subjects were chosen based on confirmed family hx of CAD from among the 1930 subjects who underwent evaluation as young adults in 1988-1991 and on whom childhood data were available.	(+) FAM HX = 271 (-) FAM HX = 805	No loss to F/U by study design	18 y	BMI Sub-scapular skin folds (SFs) Fasting insulin levels (IN)	Analysis used generalized estimation equations to allow for varying #s & unequal spacing of observations, plus correlations between repeated observations on the same individual. Trends of BMI & SFs were consistently higher for offspring with (+) fam hx of CAD, beginning in childhood. In both groups, BMI & SFs increased markedly with age in an almost linear fashion but SFs only showed this pattern until age 20. By MVA, BMI & SFs were consistently higher in (+) FAM HX group from childhood to adulthood (p=S0. With BMI in the model, no association seen between SFs & fam hx of CAD. Fasting insulin levels showed a significant interaction between age & (+) FAM HX, lower to age 20 (p=S*) and higher after age 20 (P=S*), even after controlling for BMI.	BMI, triceps and subscapular SFs were consistently higher from childhood to adulthood in offspring of parents with CAD. Insulin levels were lower in childhood in offspring with (+) Fam Hx; after age 20, (+) Fam Hx was asst'd with higher insulin levels even after adjustment for BMI.
12629565	Norman JE	The impact of weight change on cardiovascular disease risk factors in young black and white adults.	2003	Cohort	Prospective	CARDIA	None	Q6 (RF4,5,8,14) Q7(RF4,5,8,14) Q8(RF4,5,8,14) Q10 (RF4,5,8,14) Q13 (RF4,5,8,14)	USA	Community (other)	Quantify change in weight with change in BP, lipids & insulin levels by race & by baseline level of obesity in a longitudinal cohort of young B & W men & women.	5115/3325	Pediatric/ young adult	All subjects from the original cohort of 5,115 subjects available for evaluation at 10 y F/U with exclusion of those with incomplete data and pregnant women.	Population-based , prospective observational study with participants recruited from 4 metropolitan areas (Birmingham, Ala; Chicago, Ill, Minneapolis, Minn; & Oakland, Calif) in 1985-1986 at 18-30 yrs of age (44.9% black, 53.9% women) & followed up for 10 yrs.	N/A	N/A	10 yrs.	Age Race Gender Ht Wt BMI (>25kg/m squared = overweight) SBP DBP TC TG HDL LDL TC/HDL Fasting glucose (FG) Fasting insulin (INS) Smoking status	At baseline, 34.4% of WMs, 22.5% of WFs, 37% of BMs & 44.5% of BFs were overweight. Over 10 y F/U, % of subjects with abnormal RF values increased proportionately for all RFs and all groups; obesity increased from 11 to 27%. Mean(SD) of weight gained was 10.5 kgs (10.0) for B men, 11.7kg (11.0) for B women, 7.7 kgs(8.0) for W men & 7.2 kgs (10.0) for W women. Increase in wt was asst'd with adverse changes in all RFs for all race-sex groups. Change in TGs was greater for W than B participants (p=S); no other racial differences were found. Changes in TGs (p=S**) & fasting insulin (p=S*) were greater in men than women. Only for LDL-C was there a significantly greater change for baseline non-overweight vs. baseline overweight subjects (p=S**).	RFs cluster with excess wt gain and track from adolescence into adult life. There are strong correlations between wt gain over a 10 yr period from late adolescence/ early adult life with adverse changes in mean values of lipids, BP & insulin.
12629565	Norman JE	The impact of weight change on cardiovascular disease risk factors in young black and white adults.	2003																	A small group either lost weight or did not gain (12% of BM, 10% of BFs, 13% of WMs & 20% of WFs); mean levels of HDL, LDL & SBP improved in all those who did not gain or lost weight over the 10 yr period. Prevalence of cigarette smoking was significantly higher for this group vs those who gained wt (35 vs 26%,p=S**)	
12957690	Kieltyka L	Framingham risk score is related to carotid artery intima-media thickness in both white and black young adults: the Bogalusa Heart Study	2003	CrS		Bogalusa	IMT	Q5 (RF1,2,3,4,5,6, 8,10,11,14) Q9 (RF1,2,3,4,5,6, 8,10,11,14)	USA	Community (other)	Correlate FRS with CIMT in young adults	517	Pediatric/ Young adult	From a group of 1420 young adults evaluated in 1995-6 as part of the Bogalusa Post HS Survey, 517 subjects who were previously examined in childhood were selected for cIMT and LVM by ultrasound.	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. Age at CIMT = 20-37 y; 71% white; 39% M.	N/A	N/A	N/A	Age Gender Ht Wt BMI Waist circumference (WC) SBP DBP TC TG HDL LDL TC/HDL ApoA1 ApoB Fasting glucose (FG) Fasting insulin (INS) HOMA Metabolic syndrome (NCEP definition) Smoking status Alcohol use CRP Physical activity Diet Family hx of CHD/ stroke/ HTN/ DM Carotid IMT (CIMT) - mean of 3 maximum right and left carotid measurements from the common carotid, bulb & internal carotid segments. Carotid diameter LVM indexed to ht in meters squared from M-mode echo	CIMT is greater in Bs than Ws at the common carotid (p=S***) & carotid bulb (Fs only)(p=S**) Ms had higher CIMT than Fs in common carotid (p=S), internal carotid (p=S) & carotid bulb (Ws only) (p=S**) With respect to components of FRS, age, cigarette use & T2DM were similar in all race-sex groups. However, race and gender differences were significant for : SBP - Bs>Ws,p=S**; Ms>Fs, p=S** TC/HDL - Ws > Bs,p=S**; Ms> Fs,p=S** LVH - Bs > Ws, p=S**; Ms > Fs,p=S** Significant (+) linear relationship between race-and gender-specific tertiles tertiles of FRS and IMT of common, bulb and int carotid segments (p=S* for all). With MVA, FRS independently asst'd with CIMT in all 3 carotid segments after stratification by race. FRS as a main predictor variable explained more of the variance in IMT of the carotid bulb (9%) than in the common (5%) or internal (3%) carotid segments. There was no association between IMT and family hx of CHD.	Q9. The multivariate Framingham risk score correlated (+)ly and significantly with CIMT, irrespective of race in asymptomatic young adults. There are race- & gender-specific differences in CIMT.
14600185	Li S	Childhood cardiovascular risk factors and carotid vascular changes in adulthood: the Bogalusa Heart Study	2003	Cohort	Retrospective	Bogalusa	IMT	Q3 (RF2,3,4,5,8) Q4 (RF2,3,4,5,8) Q5 (RF2,3,4,5,8) Q9 (RF2,3,4,5,8)	USA	Community (other)	Correlate CIMT in young adulthood with CV RFs measured in childhood	486	Pediatric/ Young adult	From a group of 1,420 young adults who had U/S evaluation of cIMT,486 who had been examined >/= 3 X since childhood were included.	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. For this study, age at CIMT = 25-37 y; 71% white; 39% M. >/=3 measures of CV RFs in childhood.	N/A	N/A	23 y	Age Gender Ht Wt BMI SBP DBP TC TG HDL LDL TC/HDL ApoA1 ApoB Carotid IMT (cIMT) - mean of 3 maximum right and left carotid measurements from the common carotid, bulb & internal carotid segments. * RFs measured at the first childhood & last adulthood exam were used to represent childhood & adult values and were standardized to z scores specific for age, sex & race.	CIMT measurement: M vs F(0.757 vs 0.723 mm,p=S**) and B vs W (0.760 vs 0.723,p=S**). Bs had higher SBP & HDL and lower TGs & LDL than Ws; Ms had higher SBP, LDL & TGs and lower HDL than Fs; WMs & BFs had higher BMI than WFs; BFs had higher BMI than BMs. In univariate analysis, childhood LDL,BMI & SBP all correlated significantly with CIMT in young adult life with highest correlation for LDL. In adulthood, SBP, LDL,BMI, HDL(inversely) & TGs all correlated with CIMT, with highest correlation for LDL & SBP. In MVA for CIMT in the top quartile vs. lower 3 quartiles, childhood LDL [OR=1.42,CI=1.14-1.78] & BMI [OR=1.25;CI=1.01-1.54]; adult LDL [OR=1.46,CI=1.16-1.82], HDL [OR=0.67,CI=0.51-0.88] & SBP [OR=1.36,1.08-1.72] were all significant RFs for elevated cIMT. Long term burden of LDL [OR=1.58, CI=1.24-2.01] & HDL [OR=0.75.0.58-0.97] measured serially from childhood to adulthood also correlated significantly with top quartile vs lower 3 quartiles CIMT.	Q 3. C-V RFs identified in childhood (BMI,LDL) are associated with evidence of atherosclerosis-related target organ damage in in adult life. Q4.In this study, the strongest predictor of increased cIMT was LDL measured in childhood. Q 5. There are race- & gender-specific differences in cIMT.
14600185	Li S	Childhood cardiovascular risk factors and carotid vascular changes in adulthood: the Bogalusa Heart Study	2003																	Increasing trend in CIMT across quartiles of LDL in childhood was observed. Mean value of CIMT for those who were in the top quartile for LDL in childhood was 0.761mm(CI=0.743-0.780) vs 0.724 mm (CI=0.715-0.734) for those in the lower 3 quartiles (p=S**).	

NHLBI Evidence Table: State of the Science: CV Risk Factors and the Development of Atherosclerosis in Childhood-OB

PMID	First Author	Title	Year	Study Type	Prospect./ Restrospect.	Study	CVD	RF by CQ	Country	Setting	Main Study Objective	N at Baseline (N at Follow-up)	Target Population	Eligibility Criteria	Patient Characteristics	Study Groups	n at Baseline (n at Follow-up) for Study Groups	Total Follow-up Duration	Outcomes Measured	Results	Main Reported Findings by Critical Question
14600186	Raitakari OT	Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study	2003	Cohort	Prospective	Young Finns	IMT	Q3 (RF4,5,8,10) Q4 (RF4,5,8,10) Q9 (RF4,5,8,10)	Finland	Community (other)	Correlate carotid IMT in 24-39 yr old adults with CV RFs measured at 3-18 yr of age	3596/ 2229	Pediatric/ Young adult	All participants in the C-V Risk in Young Finns Study who had carotid U/S performed in 2001 and who also had been evaluated at least once in childhood.	Finnish cohort enrolled at 3-18 yr of age in 1980 and followed with serial RF evaluation over time. Carotid IMT assessed at 24-39 yr of age.	N/A	N/A	21 yr	Ht Wt BMI Sum of skin folds (SSFs) BP Smoking status TC TG HDL LDL Carotid intima media thickness (CIMT)	In MVA, adjusted for age and sex, CIMT in adulthood was significantly associated with childhood LDL-C (S**), SBP (S**), BMI (S*) & smoking (S*) In MVA , CIMT in adulthood was significantly associated with adult SBP (S**), BMI (S**), male sex (p=S**), age (S**) and smoking (S*). Age-adjusted CIMT was 0.013mm greater in smoking vs non-smoking Ms (p=S) The greater the number of abnormal RFs at 12-18 yr of age, the higher the CIMT at 33-39 yr (S**, after adjustment for adult RFs). In Ms, childhood LDL, TC, LDL/HDL,TGs, SBP, DBP & BMI measured at 12-18 y correlated significantly with CIMT; in Fs, SBP & BMI measured at 12-18 y correlated with adult cIMT. The number of abnormal RFs at 3-9 yr of age correlated weakly (S) with carotid IMT at 24-30 yr of age in men but not in women. When current RFs were entered into MVA, childhood SBP(p=S*) and LDL(p=S*) remained independently associated with CIMT.	Q.3 C-V RFs in childhood(LDL-C,SBP, BMI,smoking) are associated with atherosclerosis evidenced by increased CIMT in young adult life. Q.4 Strongest pediatric predictors were LDL and SBP followed by BMI and smoking. Q.9 The greater the number of abnormal RFs at 12-18 y of age, the higher the CIMT at 33-39 yr in both Ms & Fs, even after adjustment for current RF levels.
14709364	Cohen HW	Glucose interaction magnifies atherosclerotic risk from cholesterol. Findings from the PDAY Study	2004	CrS		PDAY	Atherosclerosis	Q1(RF2,3,4,5,6,8,10,14) Q2(RF2,3,4,5,6,8,10,14) Q4(RF2,3,4,5,6,8,10,14) Q6(RF2,3,4,5,6,8,10,14) Q9(RF2,3,4,5,6,8,10,14)	USA	Clinical	Evaluate impact of hyperglycemia on pathologic findings of atherosclerosis	1,530	Pediatric/ young adult	Autopsy specimens from 1,530 deaths in 15-34 y olds who died of external causes and who had valid values of HbA1c, TC & HDL-C - correlation of RFs with lesions in the coronary arteries and abdominal aorta.	3,201 15-34 y olds who died accidentally in 15 different cities in the U.S.; information on age/ gender/ lipids/ smoking / HTN / obesity / hyperglycemia was available. 25% F; 54% B.	N/A	N/A	N/A	Extent of intimal surface of RCA & abd Ao with fatty streaks and raised lesions was evaluated and AHA grading (grades 1-6) of stained sections of CAs and abd Ao was performed. AHA grading (grades 1-6) of CAs and abd Ao C-V RFs: Gender Age TC HDL Non-HDL-C = TC - HDL (LDL cutpoints + 30mgm/dL = non-HDL cutpoints) Thiocyanate level ≥ 90mmol/L Intimal thickness of small renal arteries = Mean BP estimate >110 mmHg BMI > 30 kg/ m squared HbA1C ≥ 6.9%	Subjects were grouped into quintiles by TC/HDL and dichotomized for HbA1C with top quartile vs. lower 3 quartiles. An interaction product term of TC/HDL X HbA1C was statistically significantly asst'd with raised lesions even after correction for sex/race/age/BMI/smoking/HBP. Higher TC/HDL was associated with B race, older age, higher HbA1c, higher TC and lower HDL but not with sex, HTN or smoking status. Elevated glucose as estimated by HbA1c significantly increased the probability of raised atherosclerotic lesions at autopsy beyond that associated with dyslipidemia alone. Findings were most striking in the 25-34 y old age group vs those < 24.	Q1. Atherosclerosis begins in childhood. Q2. The presence of RFs correlates with the extent of atherosclerotic lesions at autopsy. Q4. Addition of hyperglycemia to dyslipidemia substantially increases the extent of atherosclerosis at autopsy. Q9. An increase in the number of RFs is associated with increased prevalence and severity of atherosclerotic lesions at autopsy.
14744922	Li S	Childhood blood pressure as a predictor of arterial stiffness in young adults: the Bogalusa heart study	2004	CrS	Retrospective	Bogalusa	Distensibility	Q3 (RF4,5,10) Q5 (RF4,5,10) Q9 (RF4,5,10)	USA	Community (other)	Correlate arterial stiffness assessed by brachial-ankle pulse wave velocity (baPWV) with C-V RFs measured in childhood, adolescence and early adult life.	835	Pediatric/ Young adults	835 young adult Bogalusa subjects who underwent baPWV in 2000-2001 and who had RF data from at least 1 childhood & 1 adult CrS. 76% of subjects had at least 6 sets of RF measurements.	Community-based cohort of B & W children and young adults - originally examined at 5-17 yrs; 52% F, 44% B. For this study, 835 young adults aged 24-44 yrs, 72% W, 44% male with at least 4 RF measurements form childhood to adult life	**N/A**	**N/A**	N/A	Age Gender Ht Wt BMI SBP DBP TC TG HDL LDL Smoking status Brachial/ankle pulse wave velocity (baPWV)	In general, Bs had higher SBPs and HDLs & lower TGs than Ws. Ms vs Fs had higher SBPs, LDL,TGs & lower HDL; WMs & BFs had higher BMI than WFs & BMs respectively. In young adults, baPWV was higher in males than females (p=S** and Bs vs Ws (p=S**). In univariate regression, childhood SBP,BMI & HDL were significantly correlated with baPWV in young adults. In adulthood, SBP, TGs,BMI, HDL, & LDL were all significantly correlated with baPWV; highest correlation was with SBP (r = 0.471) In MVA, the only independent predictor of baPWV in young adults was SBP in childhood. SBP, HDL-C, TGs and smoking in adulthood were independent correlates of baPWV. In a 3rd model, cumulative burdens of SBP, TGs and smoking X yrs from childhood were independent predictors of baPWV. SBP beginning in childhood is a consistent predictor of arterial stiffness in young adults.	SBP from childhood is a consistent & independent predictor of arterial stiffness assessed by baPWV in young adult life. Race & gender impact arterial stiffness. Higher SBP and TGs plus lower HDL & smoking in adulthood combine to increase arterial stiffness. The cumulative burden of higher SBP & TGs and duration of smoking yrs from childhood independently predicts increased arterial stiffness.
14747217	Klein DJ	Obesity and the development of insulin resistance and impaired fasting glucose in black and white adolescent girls: a longitudinal study	2004	Cohort	Prospective	Growth	None	Q5 (RF6,8,14) Q6 (RF6,8,14) Q7 (RF6,8,14)	USA	Clinical	Examine the association between obesity and insulin resistance adjusted for race and pubertal stage.	955	Pediatric/ Young adults	From the total cohort of 1,491 girls, all those with BMI at baseline and yr-10 and fasting glucose at yr-10 were selected --> n=955.	1166 white(W) girls, 1213 black(B) girls enrolled in 3 geographic locations at age 9-10 y, evaluated annually X 10 yrs; 2/3 locations participated in this study. From the total cohort of 1,491 girls, all those with BMI at baseline and yr-10 and fasting glucose at yr-10 were selected --> n=955; 52% B.	B Fs - n=500 W Fs - n=455	N/A	10 y	Ht Wt BMI (Obesity=>95th%ile until yr-10, then ≥30) Tanner stage Fasting glucose (FG) (≥110 mg/dl=Impaired; ≥126 mg/dl=DM) Fasting insulin (INS) HOMA-IR	B girls had greater baseline BMI than W girls but not after adjusting for pubertal stage. B girls had a greater prevalence of obesity at baseline (17.6 vs 6.2%) and yr-10 (28.2 vs 11.2%) (both, p=S**). 10 yr incidence of obesity was 2.5 X greater in B vs W girls (13.2 vs 5.2%) BMI-INS correlations were (+) in both B & W girls at yr 1 (both, r=0.44 & p=S**) & yr 10 (r=0.48 & 0.55, both, p=S**) In B girls, INS and HOMA-IR were significantly higher in the prepubertal period, increased more during puberty and decreased less after puberty; FG levels were higher at yr-10. In MVA, BMI & race were significant independent predictors of INS as was pubertal stage at baseline. Baseline BMI predicted year 10 FG & the development of impaired FG in B girls; in W girls, rate of BMI increase predicted these outcomes. Obesity was more persistent in B than W girls; mean BMI was higher in B & W Fs when obesity was persistent.	Q6. Obesity & insulin resistance are strongly associated in B & W girls. Q5. Incidence of obesity is greater among B girls and obesity is more likely to persist. Q5. Baseline BMI predicted year 10 FG & the development of impaired FG in B girls; in W girls, rate of BMI increase predicted these outcomes. Q5. B/W differences exist in insulin resistance beginning before puberty: in B girls, INS and HOMA-IR were significantly higher in the prepubertal period, increased more during puberty and decreased less after puberty; FG levels were higher at yr-10 and only B Fs developed DM during the 10 yr F/U.
14747217	Klein DJ	Obesity and the development of insulin resistance and impaired fasting glucose in black and white adolescent girls: a longitudinal study	2004																	Across all participants, 10 yr changes in BMI correlated with changes in INS(r-0.26);HOMA-IR(r=0.24) & FG (r=0.16) (all,p=S**). 10-year incidence of DM in B girls was 1.4%; no W girls developed DM.	
15066605	Mzayek F	Differential association of birth weight with cardiovascular risk variables in African-Americans and Whites: the Bogalusa heart study	2004	Cohort		Bogalusa	None	Q5 (RF4,5,8,14)	USA	Community (other)	Evaluate the relationship between birth weight and subsequent C-V RF profile in Bs and Ws.	1155	Pediatric/ Young adult	189 of 228 newborns from 1973 Bogalusa community cohort + 966 schoolchildren from a possible 1242 in the 1987-1988 cohort for whom birth weights were known.	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. For this study, 730 Ws/ 425 Bs were evaluated at 7-21 yrs of age	N/A	N/A	N/A	Age Gender Ht Wt BMI SBP DBP TC TG HDL LDL TC/HDL ApoA1 ApoB Fasting glucose (FG) Fasting insulin (INS) HOMA-IR	Prevalence of low BW (< 2500 gms) was 4.5% among Ws and 10.6% among Bs. In MRA, low BW was (+) ly related to BMI and inversely related to SBP (p=S*), log HOMA-IR (p=S), LDL (p=S*) and TGs (p=S). Association of birth wt with LDL, TGs and HOMA-IR was stronger in Bs while the asst'n with SBP was stronger in Ws. Subjects with BW < 2500 g were at increased risk for upper quartile HOMA-IR (OR=2.4, CI 1.4,4.3)and LDL (OR=1.7, CI 1.02, 2.8) compared with those with birth wt > 2500 gms.	Low birth wt is associated with adverse C-V RF profile in later childhood & adolescence . Low birth wt is significantly more prevalent in Bs than in Ws.

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15144353	Saakslahti A	Physical activity as a preventive measure for coronary heart disease risk factors in early childhood	2004	Cohort	Prospective	STRIP	None	Q6 (RF4,5,8,11) Q7 (RF4,5,8,11) Q11 (RF11) Q13 (RF11)	USA	Community (other)	Correlate activity levels over time in young children with C-V RFs.	155/144	Pediatric/ Young adults	155 children aged 4-7 y were randomly selected from the STRIP cohort of 1062 subjects.	RCT of individualized counseling focusing on healthy low fat & low saturated fat diet & good exercise behaviors 2 X/ y beginning in infancy. At age 7 mos, 540 children randomized to intervention, 522 to control. For this study, a subset underwent assessment of physical activity using a special diary 2X /yr X 4yrs. C-V RFs were measured 1X /yr.	N/A	155/144	3 yrs	Ht Wt BMI Activity observation diary for 1 weekend, 2X/yr SBP DBP TC TG HDL LDL	Yr by yr tracking of activity varied considerably, with r varying from 0.15-0.61 in Ms & 0.04-0.39 in Fs. In constantly active Fs, TC decreased during F/U , lowest in the last 2 yrs (p=S*); HDL/TC increased for this sub-group (p=S**). HDL/TC was significantly higher in the constantly active vs inactive Fs in the last study yr(p=S). Among Fs, low activity correlated with BMI at age 4 y(p=S). In Fs at mean age of 6, high-activity was (-)ly related to TC (r=.32, p<.05) & TGs (r=.32,p<.05)) and (+)ly related to HDL/TC ratio (r=.37,p<.01). In Ms at 5 yrs, outdoor activity correlated (+)ly with SBP(r=0.23,p=S. and DBP(r=.25,p=S). When constantly active children are compared with constantly inactive group,TC & TGs were lower and HDL/TC was higher in Fs; effects were smaller in Ms.	In general, higher levels of activity were associated with better C-V risk profiles in Ms & Fs.
15308430	Ergin A	Secular trends in cardiovascular disease mortality, incidence, and case fatality rates in adults in the United States.	2004	Cohort F/U	Retrospective	NHANES	Multiple	Q14b (No RF)	USA	Clinical	Assess the effects of changes in cardiovascular disease incidence and case fatality rates on secular trends in mortality in the U.S. population between 1971-1982 and 1982-1992	1971-1982 cohort: 10,869 1982-1992 cohort: 9,774	Other	Age: 35-74 yr	NR	1971-1982 cohort 1982-1992 cohort	1971-1982 cohort: 10,869 1982-1992 cohort: 9,774	N/A	Age-standardized CVD mortality CVD incidence 28-d CVD case fatality rate	Between 1971-1982 and 1982-1992, age-standardized CVD mortality declined from 79.1 (95% CI: 75.2 to 83.0) to 53.0 (95% CI: 49.5 to 56.5) per 10,000 person-years, while CVD incidence rates decreased from 293.5 (95% CI: 284.5 to 302.4) to 225.1 (95% CI: 216.6 to 233.5) per 10,000 person-yr. The 28-d case fatality rate for CVD declined from 15.7% (95% CI: 14.5% to 16.8%) to 11.7% (95% CI: 10.3% to 13.0%). After adjustment for age, sex, and race, rates were 31% lower for CVD mortality, 21% lower for incidence, and 28% lower for 28-d case fatality in the 1982-1992 cohort than in the 1971-1982 cohort (each P <0.001).	The decrease in CVD mortality between 1971-1982 and 1982-1992 was due to declines in both the incidence and case fatality rates in this national sample. These findings suggest that both primary and secondary prevention and treatment contributed to the decline in CVD in the United States.
15451913	Duncan GE	Prevalence and trends of a metabolic syndrome phenotype among U.S. Adolescents, 1999-2000	2004	CrS	Retrospective	NHANES III, NHANES 1999-2002	None	Q6 (RF2, RF6, RF8, RF14)	USA	Clinical	Determine the prevalence of a metabolic syndrome phenotype among U.S. adolescents.	991	Pediatric/ Young adults	12-19 yr	Patient characteristics from NHANES 1999-2000	Number of metabolic syndrome risk factors	NR	NR	BMI status <85th BMI status 85th to <95th BMI status >95th Number of risk factors for metabolic syndrome	The overall prevalence of a metabolic syndrome phenotype among U.S. adolescents increased from 4.2% in NHANES III (1988-1992) to 6.4% in NHANES 1999-2000 (P < 0.001). The syndrome was more prevalent (P < 0.01) in male than female adolescents (9.1 vs. 3.7%) and was found in 32.1% of overweight adolescents (BMI > or = 95th percentile for age and sex), compared with 7.1% of adolescents at risk for overweight (BMI between 85th and 95th percentiles) (P < 0.001). Based on population-weighted estimates, > 2 million U.S. adolescents currently have a metabolic syndrome phenotype.	Q6: The overall prevalence of a metabolic syndrome phenotype among U.S. adolescents increased from 4.2% in NHANES III (1988-1992) to 6.4% in NHANES 1999-2000 (P < 0.001). Metabolic syndrome was more prevalent in male than female adolescents and was found in 32.1% of overweight adolescents (BMI > or = 95th percentile for age and sex), compared with 7.1% of adolescents at risk for overweight (BMI between 85th and 95th percentiles).
15616245	Chen W	Metabolic syndrome variables at low levels in childhood are beneficially associated with adulthood cardiovascular risk: the Bogalusa Heart Study	2005	Cohort	Retrospective	Bogalusa	IMT	Q3 (RF4,5,8,14) Q6 (RF4,5,8,14) Q7 (RF4,5,8,14) Q8 (RF4,5,8,14) Q9 (RF4,5,8,14) Q14a (RF4, 5, 8, 14)	USA	Community (other)	(1)Compare adult prevalence of Met S RFs in a group with low levels of Met S RFs in childhood; (2)Compare CIMT in adulthood in a group with low level Met S RF status in childhood	1474 - no loss to F/U by design	Pediatric/ Young adults	All Bogalusa subjects who had data on the Met S RFs in childhood and had subsequent evaluation as adults	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. For this study, 1,474 subjects with evaluation at 4-17 y and 19-41 y; 41.9% B/ 62.6% W.	n=1,474 subjects; Sub-group of 138 subjects underwent cIMT measurement at 25-41 y of age	N/A	15.8 yr (range:5-21.1 yr)	Ht Wt BMI (≥30=obese) SBP DBP TC TG (>200 mg/dl=high) HDL-C (< 40 mg/dl = low) LDL-C (>160 mg/dl = high) Fasting glucose (FG) (>110 mg/dl = high) Fasting insulin (INS) (>18 uU/ml = high) HOMA-IR (= INS X FG/ 22.5) Carotid IMT (cIMT) Metabolic syndrome variables=BMI; HOMA-IR; SBP; TC/HDL Low MetS clustering in childhood ≤25th%ile for 3 or 4 variables Adult dx of MetS ≥75th%ile for all 4 variables	In childhood, 9% of the cohort had 3 or 4 MetS RFs in the bottom quartile of BMI/ HOMA-IR/ SBP/ TC:HDL ratio(O/E, p=S*). Clustering was greatest for all 4 variables vs any combination of 3. With 3 (+) RFs, O/E was significantly greater when BMI & HOMA-IR were included. Overall prevalence of Met S in adulthood was 13.6%, higher in Ws than Bs (15.2% vs 11.1%, p=S). Using ATPIII definition of MetS,overall prevalence of MetS in adulthood for the cohort was 12.1%, higher in Ws than Bs (14.5% vs 8.2%,p=S**) As adults, low risk Met S group had lower prevalence of Met S compared with high risk group (3.8 vs 14.6%;p=S**). Using ATPIII definition of MetS, low risk MetS group had significantly lower prevalence of MetS (4.6 vs 12.9%,p=S*) In childhood, subjects with (-) fam hx of CHD & HTN had a significantly greater prevalence of low risk MetS cluster compared with high risk MetS cluster (9.4 vs 5%;p=S) and (10.5 vs. 6.6%; p=S). cIMT in adulthood decreased with increasing #s of RFs in the bottom quartile in childhood (p for trend=S).	Q6,7. Low levels of RFs for the MetS cluster together in childhood just as high levels do. The low risk MetS cluster is associated with negative fam hx of CAD & HTN. Q8. As adults, those with low MetS cluster in childhood have a significantly lower prevalence of MetS dx indicating tracking of the low risk pattern from childhood to adult life. Q14. Preservation of a low risk state is associated with decreased development of target organ damage.
15629977	Freedman DS	The relation of childhood BMI to adult adiposity: the Bogalusa Heart Study	2005	Cohort	Prospective	Bogalusa	None	Q6 (RF8) Q8 (RF8)	USA	Community (other)	Evaluate the association btwn childhood BMI and body fatness with adult adiposity.	2,610	Pediatric/ Young adults	Children who participated in at least 1 survey in childhood at 2-17 y of age and in one adult survey at 18-37 y of age.	Community-based cohort of B & W children and young adults - originally examined at 5-17 yrs; 52% F, 44% B. For this study, 2 examinations: baseline at 2-17 yrs & F/U at 18-37 yrs; 57% F;	N/A	N/A	17.6 yrs (range:10-24 y)	Childhood & adult BMI Childhood triceps skin folds (SFs) Adult triceps & sub-scapular SFs	Study cohort did not differ from group lost to F/U except for slightly higher prevalence of overweight in the study cohort (7% vs 6%,p=S) At follow-up, 23% of subjects were obese (BMI≥30) & 25% were overfat with mean SF in the upper quartile. Childhood levels of BMI-for-age & SFs correlated significantly with adult levels with r=0.44 - 0.64. Strongest associations were seen between childhood & adult BMI but childhood BMI also correlated significantly with adult SFs at all ages including the youngest, 2-5 y olds with r=0.41 for M, 0.33 for F. Childhood BMI correlated almost as well as childhood SFs with adult SFs. In general, correlations were stronger for Ms than Fs and for older children (9-17y) than younger children. As childhood BMI increased, the (+) predictive value for adult obesity (BMI≥30) or overfatness(upper quartile SFs) increased.	Childhood levels of both BMI & triceps skin folds were associated with adult levels of BMI & adiposity. Magnitude increased with increasing childhood age but BMI levels of even the youngest children were moderately associated with adult obesity. 2 - 5 yr olds with BMI for age ≥ 95th%ile were 4X as likely to be overfat adults as were children with BMI < 50th%ile. Controlling for skin folds, childhood BMI still correlated with adult adiposity
15629977	Freedman DS	The relation of childhood BMI to adult adiposity: the Bogalusa Heart Study	2005																	(+) predictive values for overweight BMI increased with increasing childhood age & were greater for adult obesity than for adult overfat. (+) predictive values for adult overfat varied little with age. Multiple regression models demonstrated statistically significant independent associations between childhood BMI-for-age & SFs with adult SFs (p=S**). Among severely obese adults with BMI>/=40, 46% had a childhood BMI >/=95th%ile & 70% had a childhood BMI >85th%ile.	
15761176	Field AE	Weight status in childhood as a predictor of becoming overweight or hypertensive in early adulthood	2005	Cohort	Prospective	East Boston	None	Q6 (RF4,8) Q8 (RF4,8)	USA	Community (other)	To assess the extent to which weight status in childhood predicts young adult overweight or hypertension.	337/ 314	Pediatric/ Young adults	All available participants in the East Boston BP study.	Cohort study of 339 schoolchildren from a single school in east Boston beginning in 1978 with annual F/U until 1981 and then reassembly of the original cohort in 1989-1990. 177F/ 139M. 315 W; 2 Asian.	N/A	N/A	12 yrs	Age Sex Ht Wt BMI SBP DBP History of HTN dx History of parental HTN dx Medication use Cigarette use Alcohol use * BPs were measured weekly X 3 wks using a standard protocol in 1978, 1979, 1980 & 1981 and then again in 1989-90.	Overweight/ Obesity: At baseline in childhood, the distribution of wt status was similar in Ms & Fs. At adult F/U, among subjects with BMI < 25 at first visit, 48.3% of Ms vs 23.5% of Fs became overweight or obese (p=S**). Of 103 children who were at risk for overweight or overweight at childhood evaluation (BMI>85th%ile), 75% were overweight as young adults. 13% of children with BMI < 50th %ile became overweight/ obese as young adults vs 33% of children with BMI between the 50th & 75th%ile. For Fs whose BMI was between the 50th & 75th%iles in childhood, OR for becoming overweight/ obese was 4.8(CI=0.9-26.6); for childhood BMI between the 75th& 84th%iles, OR for becoming overweight/ obese was 20.2(CI=3.4-121.6). Independent of baseline BMI, childhood gains in BMI or BMI %ile predicted adult overweight/ obesity. There was a strong (+) association between childhood & adult BMI.	Weight status at 11 yrs of age was strongly predictive of future overweight/ obesity in young adulthood. Overweight male children were at significant risk to become hypertensive as young adults. Males at the upper end of the normal weight range in childhood have increased risk of developing HTN as young adults.

NHLBI Evidence Table: State of the Science: CV Risk Factors and the Development of Atherosclerosis in Childhood-OB

PMID	First Author	Title	Year	Study Type	Prospect./ Restrospect.	Study	CVD	RF by CQ	Country	Setting	Main Study Objective	N at Baseline (N at Follow-up)	Target Population	Eligibility Criteria	Patient Characteristics	Study Groups	n at Baseline (n at Follow-up) for Study Groups	Total Follow-up Duration	Outcomes Measured	Results	Main Reported Findings by Critical Question
15761176	Field AE	Weight status in childhood as a predictor of becoming overweight or hypertensive in early adulthood	2005																	BP: Incidence of HTN was 12.3% in Ms vs 1.9% in Fs (p=S**). As young adults, Fs had lower mean SBPs (by 12.3 mmHg) & DBP (by 5.4 mmHg) than Ms. Among Ms, childhood BMI was predictive of BP in young adulthood but BMI was no longer a significant predictor after adjustment for height. Age-specific z-score of childhood BMI(OR=2.2,CI=1.2-3.9)or BMI itself (OR=1.1,CI-1.0-1.3)predicted development of HTN in young adult males. Ms with BMI ≥ 85th%ile at first childhood visit were 5X more likely (OR=5.1, CI=1.4-18.1) than those with BMI < 75th%ile to become hypertensive by young adulthood.	
15851639	McMahan CA	Risk scores predict atherosclerotic lesions in young people	2005	CrS		PDAY	Atherosclerosis	Q1(RF2,3,4,5,6,8,10,14) Q2(RF2,3,4,5,6,8,10,14) Q4(RF2,3,4,5,6,8,10,14) Q9(RF2,3,4,5,6,8,10,14)	USA	Clinical	Develop a risk score derived from CHD RF measurements in young people to predict the probability of advanced atherosclerotic lesions in the coronary arteries or abdominal aorta	1117 & 1458	Pediatric/ young adult	Autopsy specimens from 1,127 deaths in 15-34 y olds who died of external causes - 1117 cases had correlation of RFs with lesions in the coronary arteries and 1458 cases with lesions in the abdominal aorta.	3,201 15-34 y olds who died accidentally in 15 different cities in the U.S.; information on age/ gender/lipids/smoking/HTN/ obesity/ hyperglycemia was available. Autopsy findings in the RCA, LADCA and abdominal aorta were available with grade 4 or 5 lesions defined as target lesions for this study. 25% F; 54% B.	N/A	N/A	N/A	Extent of intimal surface of RCA & abd Ao with fatty streaks and raised lesions was evaluated and AHA grading (grades 1-6) of stained sections of CAs and abd Ao was performed. AHA grading (grades 1-6) of CAs and abd Ao C-V RFs: Gender Age TC HDL Non-HDL-C = TC - HDL (LDL cutpoints + 30mgm/dL = non-HDL cutpoints) Thiocyanate level ≥90mmol/L Intimal thickness of small renal arteries = Mean BP estimate >110 mmHg BMI > 30 kg/m² HbA1C > 8%	Multiple regression models demonstrated statistically significant independent associations between childhood BMI-for-age & SFs with adult SFs (p=S**).	Q1. Atherosclerosis begins in childhood. Q2. The presence of RFs correlates with the extent of atherosclerotic lesions at autopsy. Q9. An increase in the number of RFs is associated with increased prevalence and severity of atherosclerotic lesions at autopsy. The RF scoring system based on pathologic findings correlated with measured RFs can be used to estimate the probability of advanced atherosclerotic lesions in young subjects. The presence of abdominal aortic target lesions significantly increased the probability of an advanced CA lesion by 48%.
15925733	Urbina EM	Impact of multiple cardiovascular risk factors on brachial artery distensibility in young adults: the Bogalusa Heart Study	2005	CrS		Bogalusa	Distensibility	Q4 (RF4,5,8,10,14) Q5 (RF4,5,8,10,14) Q9 (RF4,5,8,10,14)	USA	Community (other)	Evaluate impact of multiple RFs on brachial distensibility (BrachD)	803	Pediatric/ Young adult	803 young adults who underwent BrachD measurement as part of the Bogalusa post high school F/U study.	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. For this study: Age: 19-37 y; 42% male; 72% white; Race, age, BP, lipids, anthropometrics, glucose status, smoking status	N/A	N/A	N/A	Age Gender Ht Wt BMI Waist circumference (WC) SBP DBP TC TG HDL LDL TC/HDL ApoA1 ApoB Fasting glucose (FG) Fasting insulin (INS) HOMA Metabolic syndrome (NCEP definition) Smoking status Alcohol use Brachial distensibility (BrachD)	BrachD was significantly higher in Ws than Bs (6.% vs 6.3%,p=S*)and was slightly higher in Fs than Ms. By trend analysis, BrachD consistently decreased as the number of RFs increased (p=S**).	Q5. There are racial differences in brachial distensibility in young adults. Q9. As the number of CV RFs present increased, brachial distensibility progressively & significantly decreased.
16129802	Juonala M	Risk factors identified in childhood and decreased carotid artery elasticity in adulthood: the Cardiovascular Risk in Young Finns Study	2005	Cohort	Prospective	Young Finns	Distensibility	Q3 (RF4,5,8,10)	Finland	Community (other)	Correlate carotid artery elasticity measured by ulyrasound in young adulthood with CV RFs measured in childhood	3956/ 2255	Pediatric/ Young adult	Finnish cohort enrolled at 3-18 yr of age in 1980 and followed with serial RF evaluation over time. At 24-39 yr of age, group underwent evaluation of carotid artery elasticity using compliance (COM), Young's elastic modulus (YEM) and stiffness index (SI). All participants in the childhood CrS studies from 1980 who returned for F/U study were eligible - 2255 participated.	n=2255; M=1012/ F=1243.	N/A	N/A	21 yr	Ht Wt BMI Sum of skin folds (SSFs) BP Smoking status TC TG HDL- C LDL-C CRP Fasting glucose (FG) Fasting insulin (INS) Carotid intima media thickness (CIMT) Carotid artery compliance (CAC) Young's elastic modulus (YEM) Stiffness index (SI) No major difference between subjects & drop-outs except slightly younger age of drop-outs.	Among severely obese adults with BMI ≥40, 46% had a childhood BMI ≥95th%ile & 70% had a childhood BMI >85th%ile. Adult LDL, SBP & INS were inversely related to CAC & directly related to YEM & SI. BMI correlated directly with YEM. With increasing # of childhood RFs, there was a significant decreasing trend in CAC (P=S**) and an increasing trend in YEM (p=S**). After adjustment for current RFs, effect of childhood RFs was attenuated ~ 50%. Childhood risk score remained highly significant (p=S*). When current BP was introduced, effect of childhood BP was borderline significant.	Q3. The presence of RFs in childhood correlates with subclinical measures of atherosclerosis in adult life. In MVA, childhood BP & adiposity correlated significantly with ultrasound measures of decreasing arterial elasticity. Increasing number of RFs including LDL, BP, HDL and smoking at adverse levels in childhood related significantly with ultrasound measures of decreasing arterial elasticity. These associations persisted after adjustment for adult RFs.
16263998	Williams DE	Prevalence of impaired fasting glucose and its relationship with cardiovascular disease risk factors in US adolescents, 1999-2000	2005	CrS	Retrospective	NHANES 1999-2000	None	Q5 (RF6) Q6 (RF2, RF4, RF5, RF6)	U.S.A	Clinical	Examine the prevalence of IFG and its relationship with overweight and CVD risk factors in a nationally representative sample of U.S. adolescents who were aged 12 to 19 yr.	915	Pediatric/ Young adults	12-19 yr	Patient characteristics from NHANES 1999-2000	Normal weight At risk for overweight Overweight Non-Hispanic white Non-Hispanic black Mexican-Americans	N/A	N/A	Percent overweight BMI Fasting glucose (FG) Fasting insulin (INS) Hemoglobin A1C(HbA1C) Fasting lipids: TC TG HDL-C LDL-C	In 1999-2000, the prevalence of IFG in US adolescents was 7.0% and was higher in boys than in girls (10.0% vs 4.0%). Prevalence of IFG was higher in overweight adolescents (17.8%) but was similar in those with normal weight and those who were at risk for overweight (5.4% vs 2.8%). The prevalence of IFG was significantly different across racial/ethnic groups (13.0%, 4.2%, and 7% in Mexican Americans, non-Hispanic black individuals, and non-Hispanic white individuals, respectively). Adolescents with IFG had significantly higher mean hemoglobin A1c, fasting insulin, total and low-density lipoprotein cholesterol, triglycerides, and systolic blood pressure and lower high-density lipoprotein cholesterol than those with normal fasting glucose concentrations.	Q5: The prevalence of IFG was high at 7% overall, and was significantly different across racial/ethnic groups (13.0%, 4.2%, and 7% in Mexican Americans, non-Hispanic black individuals, and non-Hispanic white individuals, respectively). Q6: Prevalence of IFG was higher in overweight adolescents (17.8%) but was similar in those with normal weight and those who were at risk for overweight (5.4% vs 2.8%). Adolescents with IFG had adverse CV risk profiles with significantly higher mean hemoglobin A1c, fasting insulin, total and low-density lipoprotein cholesterol, triglycerides and systolic blood pressure and lower high-density lipoprotein cholesterol than those with normal fasting glucose concentrations.
16264006	Morrison JA	Development of the metabolic syndrome in black and white adolescent girls: a longitudinal assessment.	2005	Cohort	Prospective	Growth	None	Q5 (RF 4,5,8,14) Q6 (RF 4,5,8,14) Q7 (RF 4,5,8,14) Q8 (RF 4,5,8,14)	USA	Clinical	Identify early predictors of the presence of the metabolic syndrome at 18 & 19 y in B and W girls.	1192/ 1078	Pediatric/ Young adults	624 black(B) girls & 773 white(W) girls evaluated at baseline for longitudinal cohort study at 3 sites and followed X 10 yrs. In 2 sites, insulin & glucose were measured along with other variables at baseline and F/U and these subjects constitute this study group.	624 B girls & 773 W girls evaluated at baseline at 9-10y for longitudinal cohort study at 3 sites & followed X 10y. In 2 sites, insulin & glucose were measured along with other variables at baseline and F/U and these subjects constitute this study group.	608 W Fs; 584 B Fs	W: 608/511 B: 584/567	10 yr	Ht Wt BMI (Obesity ≥95th%ile until yr-10, then ≥30) Waist circumference (WC) Tanner stage SBP DBP Fasting glucose (FG) (≥110 g/dl=Impaired; ≥126 mg/dl=DM) Fasting insulin (INS) HOMA-IR TC TG HDL LDL MetS = ATP definition: ≥3 of the following: WC >102 cm in Ms, 88 cm in Fs; HDL ≤40 mg/dl in Ms, 50 mg/dl in Fs; BP ≥130/85; FG ≥110 mg/dl. For baseline assessment. 10th & 90th %iles used to define abnormal except for BP & TGs.	At baseline, BFs had higher BMI, WC, INS, HOMA-IR, HDL FG & SBP but lower TGs. At baseline, only 1 B girl and 1 W girl had >/= 3 factors for MetS (0.2%). On F/U, BMI, WC & SBP increased significantly, more in Bs than in Ws; TGs increased only in Ws. At 18-19 y, Bs had significantly greater BMI, WC, INS, HOMA-IR, SBP & FG(all,p=S**) & HDL & DBP (p=S*) but lower TGs(p=S**). At 10 y, 20 B girls (3.5%) and 12 W girls (2.3%) had MetS; using the new definition of abnormal FG of 100 mg/dl, 31 BFs (3.6%) & 15 (3%) W Fs had MetS. Low HDL was prevalent throughout the period in B & W girls. In MVA, early measures of BMI, WC and TG level were significant predictors for development of metabolic syndrome. Tracking coefficient for WC was 0.83 from y-2 to y-10 indicating strong persistence of central obesity.	Q5. There are striking racial differences in the prevalence of the components of MetS with Bs having the greater prevalence for all factors except TGs. Q6,Q7,Q8. In this study, the MetS RFs cluster together beginning before puberty and persisting X 10 y. Q8. While the prevalence of MetS overall was 3%, it was 12.1% in girls with persistently increased WC. Components of the MetS become increasingly common during adolescence & the criteria for MetS are met in 3% of young adult Fs.

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16414945	Carnethon MR	Prevalence and Cardiovascular Disease Correlates of Low Cardiorespiratory Fitness in Adolescents and Adults	2005	Cohort	Retrospective	NHANES	None	Q6,8 (RF4,5,8,11)	USA	Community (other)	Describe the prevalence of low fitness in the US population aged 12 through 49 years and relate fitness to CVD risk factors in this population	3,110	Pediatric/ Young adults	Adolescent participants in NHANES for 1999-2000 and 2001-2002: 12-19 yr Completed submaximal treadmill exercise TEx) testing No previous CVD diagnosis No abnormal hemodynamic parameters No existing medical conditions No physical limitations	12-19 yr 50% F Nationally representative racial/ethnic sample	Adolescents(12-19y) and adults (20-49y; not reported here.	N/A	N/A	SBP DBP TC TG HDL-C LDL Fasting glucose HbA1c BMI Waist circumference Treadmill exercise fitness score: LOW <20th%ile; MOD 20th-59th%ile; HIGH ≥ 60th%ile.	(1) 33.6% of adolescents were in the LOW fitness category, 34.4% of Fs and 32.9% of Ms (p=NS). (2) LOW fitness was more prevalent in blacks(B) and Mexican-Americans(M-A) than in non-Hispanic whites (W). (3) BMI, WC & TC were consistently & inversely associated with fitness level. HDL was positively correlated with fitness in Ms but not in Fs. SBP was inversely asst'd with fitness level in Ms; no correlation in Fs. (4) When the LOW & HIGH fitness groups were compared, LOW participants had significantly higher BMI(p=S*,M & F)) & WC(p=S*, M&F) & significantly lower SBP(p=S for Fs,S* for Ms) & TC(p=S*, M&F). There were no significant differences for TG, HbA1C or FG. (5) When LOW fitness group was compared with MOD or HIGH for CV RFs: Overweight: OR F 2.27(1.64-3.15) M 2.88 (2.02-4.09) Obese: OR F 2.68(1.86-3.86) M 3.65 (2.32-5.75) HTN: OR F 1.35(0.68-2.70) M 1.03 (0.30-3.54) TC>200 OR F 1.89 (1.12-3.17) M 3.68 (2.55-5.31) Low HDL OR F 1.03 (0.74-1.43) M 1.25(0.7901.95) Abn FG OR F 1.95 (0.71-5.37) M 1.24 (0.79-1.95) Met S OR F 2.72 (0.85-8.74) M 4.20 (2.14-8.25)	Low fitness in adolescents is very common present in 1/3 of all subjects. Low fitness was significantly associated with a high prevalence of CV RFs including overweight/obesity, dyslipidemia & hypertension. Conversely, high fitness was associated with lower measures of all CV RFs except TGs, HbA1C and FG.
16530772	McMahan CA	PDAY risk score predicts advanced coronary artery atherosclerosis in middle-aged persons as well as youth	2007	CrS	Retrospective	PDAY	Atherosclerosis	Q2 (RF4, RF5, RF8, RF10) Q3 (RF4, RF5, RF8, RF10)	USA	Don't know/NR	Estimate the probability of advanced atherosclerosis using coronary heart disease risk factors by applying the PDAY risk score to autopsied individuals from the Community Pathology Study	NR (NR)	Pediatric/ Young Adult	PDAY is a post mortem study of 15-34 yr olds who died accidentally in 15 different cities in the U.S.; information on age/ gender/ lipids/ smoking/ HBP/obesity/ hyperglycemia available; this data was used to develop the PDAY risk score for coronary artery atherosclerosis. In this study, the PDAY risk score was applied to 212 autopsied young and middle-aged subjects in PDAY and in the Community Pathology Study (CPS).	24% F	Individuals who died from CHD Individuals who died from external causes (Basal) Individuals who died from related diseases such as systemic hypertension, stroke, chronic renal disease, diabetes, or dissecting aneurysm, or who had CHD although it was not the cause of death (Related)	N/A	N/A	PDAY risk score Extent of raised lesions in coronary arteries	In CPS cases 15-34 y of age, the PDAY risk score was significantly associated with extent of raised lesions in the LAD (p=S) and LCF(p=S*), less in the RCA(p=.0762) In CPS subjects 35-54 yr of age, the PDAY risk score computed from only the modifiable risk factors was significantly associated with extent of raised lesions in the LCF (p=S) but not significantly in the RCA and LAD. In both PDAY and CPS cases combined, RCA surface area with raised lesions varied with age with a significant risk score-age interaction (p=S**).	Q2: The PDAY risk score was associated with extent of raised lesions in the coronary arteries of cases 15-34 yr of age Q3: The PDAY risk score computed from only the modifiable risk factors was associated with extent of raised lesions in the coronary arteries of subjects 35-54 yr of age. This association in middle-aged subjects validates the PDAY risk score. The associations in both younger (15-34 yr) and older (35-54 yr) subjects suggest a seamless progression of the effects of the modifiable risk factors on atherosclerosis from 15 to 54 yr of age
16672846	Yang X	Risk of obesity in relation to physical activity tracking from youth to adulthood	2006	Cohort	Prospective	Young Finns	None	Q6 (RF8,11) Q7 (RF8,11) Q8 (RF8,11)	Finland	Community (other)	Correlate physical activity patterns from youth with young adult BMI	1665/ 1319	Pediatric/ Young adults	Finnish cohort enrolled at 9-18 yr of age in 1980 and followed with serial RF evaluation over time, including activity level assessment by questionnaire. At 24-39 yr of age, activity level evaluated relative to BMI.	626 M/ 693 F	Persistently active (PA): n = 130 M/ 138 F Increasingly active (IA): n = 216 M/ 225 F Decreasingly active (DA): n = 139 M/ 187 F Persistently inactive (PI): n = 141 M/ 143 F		21 yr	Physical activity index (PAI) from questionnaires based on frequency & intensity of participation in leisure-time activities, training, & competitions. Subset of 102 participants underwent maximal cycle ergometry with measurement of VO2max,mean workload during last 4 mins of testing (Wlast4) & hypothetical max workload for 6 mins (Wmax6). BMI SSFs Waist circumference (WC)	PA: 33.1% of Ms/ 32% of Fs IA: 27.3% of Ms/ 30.3% of Fs DA: 28.1% of Ms/ 30.3% of Fs PI: 11.5% of Ms/ 7.4% of Fs Prevalence of obesity was 14.7% in Ms & 12.0% in Fs. Physically active subjects(both M & F) had lower WC as adults compared with all other groups; active Fs had lower BMI (p=S*) compared with all other groups but this was not true for Ms. Physical activity in youth was not associated with adult obesity. Physical inactivity in youth was associated with obesity in youth in Fs but not in Ms. After adjustment for age, youth BMI & SSFs, SES measures & smoking, being DA in Fs was independently associated with risk of being overweight (OR=2.35, CI=1.16-4.78) or obese (OR=2.72, CI=1.04-7.09) but not in Ms. In Ms, decreases in physical activity over this time period were not associated with development of obesity. In both Ms & Fs, being persistently inactive was not associated with development of obesity.	Physically active subjects(both M & F) had lower WC as adults compared with all other groups & active Fs had lower BMI. Decreasingly active subjects were more likely to have abdominal obesity as adults. Physical activity in youth was inversely associated with obesity in youth in Fs. In both Ms & Fs, being persistently inactive was not associated with development of obesity.
16728658	Juonala M	Childhood C-reactive protein in predicting CRP and carotid intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study	2006	Cohort	Prospective	Young Finns	IMT	Q1 (RF4,5,7,8,10,14) Q2 (RF4,5,7,8,10,14) Q3 (RF4,5,7,8,10,14) Q4 (RF4,5,7,8,10,14) Q8 (RF4,5,7,8,10,14)	Finland	Community (other)	(1) Evaluate whether CRP in childhood predicts CRP in young adult life (2) Evaluate which childhood RFs including CRP predict carotid IMT in young adults	1617	Pediatric/ Young adults	Subjects from the CV Risk in Young Finns study who had CRP performed in 2001 as young adults and who were not pregnant or using OC and id not have DM, rheumatic disease or recent infection.	Finnish cohort enrolled at 3-18 yr of age in 1980 and followed with serial RF evaluation over time. At 24-39 yr of age, group underwent evaluation of carotid IMT and reassessment of CRP. 43% F; all W.	N/A	N/A	21 yr	Ht Wt BMI Sum of skin folds (SSFs) BP Smoking status TC TG HDL- C LDL-C CRP Fasting glucose (FG) Fasting insulin (INS) Carotid intima media thickness (CIMT)	Significant tracking was observed between childhood and adult CRP levels, best for the oldest age group at baseline (18 yr) (r=0.47 in females, 0.32 in males, p=S**), independent of lipids, BP, smoking, obesity indices, and insulin. In MVA, childhood RFs that independently associated with increased adult carotid IMT included elevated BP (p=S**), high LDL (p=S*),and smoking (p=S) but not CRP.	Q1,2. Atherosclerosis-related target organ damage begins in childhood and is significantly affected by the presence of RFs. Q3. Atherosclerosis-related target organ damage in young adult life is related significantly to CV RFs present in childhood. There is no correlation between childhood CRP and adult atherosclerosis-related target organ damage.
16769996	Srinivasan SR	Changes in metabolic syndrome variables since childhood in prehypertensive and hypertensive subjects: the Bogalusa Heart Study	2006	Cohort	Prospective	Bogalusa	None	Q6 (RF4,5,8,14) Q7 (RF4,5,8,14) Q8 (RF4,5,8,14)	USA	Community (other)	Evaluate serial changes in C-V RFs asst'd with Met S in a community-based cohort of normotensive, pre-hypertensive and hypertensive subjects as they age from childhood into adulthood.	3255 - no loss to F/U by design	Pediatric/ Young adults	Subjects from any of the 6 cross-sectional studies of children who had participated in at least 1 of 7 screenings in young adult life	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B. This study is a retrospective review of BP, adiposity, lipids and insulin resistance measured in childhood(4-11 yrs), adolescence (12-18 yrs) and adulthood (19-42 yrs) in 3 BP grps : normotensive (n=2206); pre-hypertensive (n=721); hypertensive (n=328).	BP at last evaluation --> 3 groups: Normotensive(NBP): 2206 Prehypertensive(PHTN): 721 Hypertensive(HTN): 328 Age at childhood study = 11.6 +/-3.9y Age at adult study= 27.0+/-6.5 81% of subjects were screened ≥3 times & 54%, 4-6 times.	3255 - by design	N/A	Ht Wt BMI (≥30=obese) Subscapular skin fold (SSF) Waist circumference (WC) (>100cm=obese) SBP DBP TC TG (>200 mg/dl=high) HDL-C (< 40 mg/dl = low) LDL-C (>160 mg/dl = high) Fasting glucose (FG) (>110 mg/dl = high) Fasting insulin (INS) (>18 uU/ml= high) HOMA-IR (= INS X FG/ 22.5) Mean levels of RFs fpr preadolescence(4-11 y),adolescence (12-18 y) & adulthood (≥19 y) were combined for the analysis.	Adult subjects with HTN vs NBP had higher adiposity, SBP & DBP, glucose and TGs beginning in childhood through into adulthood; higher insulin/ins resistance in childhood and adulthood; and lower HDL-C in adulthood. Adult subjects with dx of PreHTN vs NBP subjects had significantly higher BMI and SSFs, SBP & DBP, and TGs beginning in childhood through adulthood; higher glucose in adolescence; and higher LDL-C, insulin/ins resistance in adulthood. In MVA, PreHTN was independently asst'd with adverse changes in adiposity, SBP & DBP; HTN was independently asst'd adverse changes in adiposity, SBP & DBP, ins resistance index, LDL-C, HDL-C, and TGs with HTN. As young adults, PreHTN & HTN subjects showed significantly greater prevalence of obesity, hyperinsulinemia, hyperglycemia and dyslipidemia. Excess adiposity and higher BP beginning in childhood and accelerated adverse longitudinal changes in all Met S risk variables characterize the early natural hx of HTN.	Q6. Excess adiposity and higher BP beginning in childhood and accelerated adverse longitudinal changes in Met S risk variables characterize the early natural hx of HTN. Higher BMI, adiposity, SBP, DBP & FG cluster together beginning in adolescence; in adult life, they are joined by dyslipidemia, high INS & abnormal HOMA-IR. Adult subjects with HTN vs NBP had higher adiposity, SBP & DBP, glucose and TGs beginning in childhood; higher insulin/ins resistance in childhood and adulthood; and lower HDL-C in adulthood. Longitudinal changes with aging suggest a primary role for excess adiposity in the early natural history of hypertension.

NHLBI Evidence Table: State of the Science: CV Risk Factors and the Development of Atherosclerosis in Childhood-OB

PMID	First Author	Title	Year	Study Type	Prospect./ Restrospect.	Study	CVD	RF by CQ	Country	Setting	Main Study Objective	N at Baseline (N at Follow-up)	Target Population	Eligibility Criteria	Patient Characteristics	Study Groups	n at Baseline (n at Follow-up) for Study Groups	Total Follow-up Duration	Outcomes Measured	Results	Main Reported Findings by Critical Question
16818562	Friedman LA	Sensitivity and specificity of pediatric lipid determinants for adult lipid status: Findings from the Princeton Lipid Research Clinics Prevalence Program follow-up study	2006	Cohort	Prospective	Princeton	None	Q8 (RF1,5)	USA	Community (other)	Determine the diagnostic utility of lipid levels in childhood assessed by the NCEP guidelines for determining adult lipid status 30 years later.	1 741	Pediatric/ Young adults	Subjects who underwent lipid testing in grades 1-12 in Cincinnati in the Princeton school district between 1972-78 and who participated in the Princeton F/U study between 1999-2004.	Students in grades 1-12 in Cincinnati Princeton school district between 1972-78. 73% W/ 27% B.; 52.3% M/ 47.7% F.	73% W/ 27% B.; 52.3% M/ 47.7% F Childhood group: 5-19 y of age Adult group: 28-48 y of age	1 741/1 741 by definition	30 y	TC LDL (+) Fam hx of parental HC (TC > 240 mg/dl) (+) fam hx of CVD at </= 55 y	Overall, sensitivities were: LDL 43.1% (CI:34.8-51.6%) TC 44.2% (CI:35.1-53.5%) Overall, specificities were: LDL 86.1%(CI:83.4-88.6%) TC 84.8& (CI:82.1-87.3%) For LDL:(+) predictive value = 39%;(-) predictive value = 88%. For TC: (+) predictive value = 31%;(-) predictive value = 91% Sensitivities varied considerably with age, with lowest at 14-16 y and highest at 5-10 y and 17-19 y. Lowest mean cholesterol levels occurred consistently at 14-16 y of age, regardless of adult lipid status W subjects tended to follow the same trends in sensitivity as the whole population but this was not true for B subjects. Number of adult CVD events was small - only 19 for LDL & 20 for TC. Sensitivity of childhood LDL for prediction of adult CVD was 10.5% (CI:1.3-33.1%); specificity was 81% (CI: 78.1-83.6%). Sensitivity of childhood TC to predict adult CVD was 20% (CI: 5.7-43.7%) and specificity 81% (CI: 78.2-93.5%). Results improved slightly when (+) family hx of HC or CVD included, to sensitivity of 11.1% for LDL (CI: 0.3048.3%) and 30% for TC (CI: 6.7 - 65.2%). Specificities for both decreased to 77% (CI:73-82%).	Sensitivity and specificity for evaluating TC or LDL levels in childhood that are elevated in adulthood are not improved by selecting children with a (+) family hx for high cholesterol or C-V disease. Differences in overall sensitivity between the selected screening approach and universal screening were only 3% for LDL and 1% for TC. In evaluating TC levels throughout childhood, maturational changes with puberty result in marked variation in sensitivities with lowest mean cholesterol levels occurring consistently at 14-16 y of age, regardless of adult lipid status. Number of adult CVD events was small - only 19 for LDL & 20 for TC. Sensitivity of childhood LDL for prediction of adult CVD was 10.5% (CI:1.3-33.1%); specificity was 81% (CI: 78.1-83.6%). Sensitivity of childhood TC to predict adult CVD was 20% (CI: 5.7-43.7%) and specificity 81% (CI: 78.2-93.5%). Results improved slightly when (+) family hx of HC or CVD included, to sensitivity of 11.1% for LDL (CI: 0.3048.3%) and 30% for TC (CI: 6.7 - 65.2%). Specificities for both decreased to 77% (CI:73-82%).
16818566	Srinivasan SR	Utility of childhood non-high-density lipoprotein cholesterol levels in predicting adult dyslipidemia and other cardiovascular risks: the Bogalusa Heart Study	2006	Cohort	Prospective	Bogalusa	None	Q8 (RF5)	USA	Community (other)	Evaluate usefulness of non-HDL-C measured in childhood for prediction of future dyslipidemia in adult life.	1163	Pediatric/ Young adults	All subjects from 2 cross sectional surveys, one performed in 1973-4(n=3446) & one in 2001-2 (n=1163) for whom fasting blood samples were obtained at both assessments	Community-based cohort of black(B) and white (W) children and young adults - originally examined at 5-17 yrs; 52% female(F), 48% male (M); 44% B. For this study, 1,163 subjects who had fasting lipid profiles at 5-14 yrs & as adults 27 yrs later. 30% B, 55% F.	N/A	N/A	27 yrs	TC TG HDL LDL Non-HDL Defined RFs: BMI ≥ 30 LDL ≥ 160 mg/dl TG ≥ 150 mg/dl HDL< 40 mg/dl Glucose ≥ 126 mg/dl Insulin ≥ 18 uU/ml SBP ≥ 140 DBP ≥ 90 mmHg	Best predictor for adult LDL was childhood LDL(r=0.58,p=S**); next best predictor was change in BMI from childhood to adulthood. High risk childhood LDL predicts high adult prevalence of obesity, high LDL and High TGs. 38.5% of those in the top quintile as children remained in the top quintile as adults; 66.2% were in the top 2 quintiles as adults. Best predictor for adult non-HDL was childhood non-HDL(r=0.52,p=S**); next best predictor was change in BMI from childhood to adulthood High risk childhood non-HDL predicts high adult prevalence of obesity, high LDL, high TGs, low HDL, hyperinsulinemia & hyperglycemia. By logistic regression, compared to those in the lowest quartile, those in the age-,race- & gender-specific top quartile for non-HDL-C and LDL-C in childhood were 4.5 X (CI:2.51-8.04,p=S**) and 3.5 X (CI:2.02-6.07,p=S**) more likely to develop adult dyslipidemia (adverse levels of LDL, non-HDL,TGs or HDL), independent of baseline BMI and BMI change 27 yrs later.	Non-HDL tracked almost as well as LDL from childhood to young adult life. Childhood non-HDL-C was the best predictor of adult non-HDL-C.. High childhood non-HDL-C predicts adult dyslipidemia and other non-lipid RFs, including obesity, high LDL, high TGs, low HDL-C, hyperinsulinemia and borderline hyperglycemia. Adverse non-HDL-C in childhood is the best lipid predictor of adult dyslipidemia.
16880344	Juonala M	Elevated blood pressure in adolescent boys predicts endothelial dysfunction: the cardiovascular risk in young Finns study	2006	Cohort	Prospective	Young Finns	FMD	Q3 (RF4)	Finland	Community (other)	Evaluate whether SBP in childhood predicts endothelial-dependent dilation in young adult life	3596/2265	Pediatric/ Young adults	All participants in the C-V Risk in Young Finns study who had baseline & F/U measurement of SBP and brachial artery U/S studies in 2001.	5-center Finnish cohort enrolled at 3-18 yr of age in 1980 and followed with serial RF evaluation over time. At 24-39 yr of age, group underwent evaluation of FMD.	N/A	N/A	21 yr	Age Gender Ht Wt BMI Waist circumference (WC) SBP DBP TC TG HDL LDL ApoA1 ApoB Fasting glucose (FG) Fasting insulin (INS) HOMA Metabolic syndrome (NCEP definition) Smoking status CRP Physical activity Diet Carotid IMT (cIMT) Carotid diameter Carotid compliance (CAC) Brachial flow mediated dilation (FMD) Brachial artery diameter	In males, top quartile SBP in adolescence (12 -18 yr of age) was inversely related to FMD evaluated at 24-39 yr of age (p=S**), independent of brachial diameter and other childhood and adult RFs. BP quartiles in adolescence were associated with DBP & BMI in childhood & adulthood, and LDL & TGs in childhood. The association between adolescent BP & adult FMD was independent of brachial artery diameter & other childhood or adulthood RFs Childhood SBP (3-9 yr of age) did not correlate with adult FMD in men or women. Combining several childhood/adolescent BPs to create a "BP load" variable and comparision of those with consistently high SBP did not change results. In adulthood, in 24-39 y old subjects, SBP correlated inversely with FMD(r=0.09;p=S**). Subjects with SBP >140 mmHg had decreased FMD (7.1+/-4.1% vs 8.0+/-4.4%,n=2022; p=S). By MVA with adolescentt & adult SBP in the model, only adolescent SBP persisted as significant(p=S).	Adolescent BP in males predicts flow-mediated brachial arterial dilation in adult life measured 21 yrs later, independent of all other RFs. SBP measured in adolescence in males was a stronger correlate for endothelial function than SBP in adulthood.
16939740	Gunczler P	Coronary artery calcification, serum lipids, lipoproteins, and peripheral inflammatory markers in adolescents and young adults with type 1 diabetes	2006	Case control	Prospective	Other	Coronary Ca	Q1(RF4,5,6,7,8) Q2(RF4,5,6,7,8) Q9(RF4,5,6,7,8)	USA	Community (other)	To compare CAC, serum lipids and CRP + MMP-9 in young diabetics with same factors in age-matched controls.	32	Pediatric/ young adult	Consecutive recruits from diabetes & pediatric endocrine clinics	This study compared CAC in 32 Hispanic subjects with type 1 DM, mean age of 16.1+/-4.4 yrs vs. 15 healthy controls, mean age = 15.2+/-2.2 yrs.	T1DM: n = 32 Control:n =15	N/A	N/A	Age Sex BP BMI TC HDL TGs LDL Apolipoprotein A Apolipoprotein B CRP MMP-9 HbA1C	No CAC in T1DM subjects or controls at this age.. Mean RF levels did not differ between groups but 34.4% & 25% of T1DM subjects had elevated total & LDL-C vs 20% & 13.3% of CON; 15.6% of T1DM had elevated TGs vs 6.7% of CON; 28.1% of T1DM subjects had elevated apo B vs 13.3% of CON. 28.1% of T1DM had elevated CRP vs 6.7% of CON subjects. In diabetic group, TC, LDL, HDL, TGs, apoB and CRP correlated significantly with duration of disease (p=S** for TC, LDL, apoA, apoB, HDL; p=S* for CRP) and with HbA1C (p=S** for TC, S for LDL & TGs, S* for HDL & apoB, S** for apoA).	Q1, Q2, Q9 - No CAC was detected in adolescents with type 1DM. Association between disease duration and HbA1C with lipid and other RFs suggests that glycemic control may be an important modifier of C-V risk in this population.
17015535	McMahan CA	Pathobiological determinants of atherosclerosis in youth risk scores are associated with early and advanced atherosclerosis	2006	CrS		PDAY	Atherosclerosis	Q1(RF2,3,4,5,6,8,10,14) Q2(RF2,3,4,5,6,8,10,14) Q4(RF2,3,4,5,6,8,10,14) Q9(RF2,3,4,5,6,8,10,14)	USA	Clinical	Evaluate use of a risk score derived from CHD RF measurements in young people to predict the presence of advanced atherosclerotic lesions in the coronary arteries or abdominal aorta	1,127	Pediatric/ young adult	Autopsy specimens from 1,127 deaths in 15-34 y olds who died of external causes.	3,201 15-34 y olds who died accidentally in 15 different cities in the U.S.; information on age/ gender/lipids/smoking/HTN/ obesity/ hyperglycemia was available. Autopsy findings in the RCA, LADCA and abdominal aorta were graded using the AHA system plus an estimation of the extent of fatty streaks and raised lesions in the RCA and abdominal aorta was made independently by 3 pathologists. 25% F; 54% B.	N/A	N/A	N/A	Extent of intimal surface of RCA & abd Ao with fatty streaks and raised lesions was evaluated and AHA grading (grades 1-6) of stained sections of CAs and abd Ao was performed. AHA grading of LCA (grades 1-6) and independent blinded grading of RCA & abd Ao. C-V RFs: Gender Age Non-HDL-C = TC - HDL (LDL cutpoints + 30mgm/dL = non-HDL cutpoints) Thiocyanate level ≥ 90mmol/L Intimal thickness of small renal arteries =Mean BP estimate >110 mmHg BMI > 30 kg/ m squared HbA1C > 8%	Only ~ 20% of PDAY subjects had a risk score of 0 - 1, compatible with low prevalence of atherosclerosis. The extent of atherosclerotic lesions increased with age and with risk score. The prevalence of high-risk scores was unusual in Fs and the severity of atherosclerosis was lower for the same RF score. PDAY risk scores correlated with the entire range of atherosclerotic lesions predicting the prevalence of the earliest microscopically demonstrable lesions of atherosclerosis in the LADCA & with the extent of fatty streaks in the RCA and abdominal aorta. Risk scores were also correlated with prevalence of higher grade lesions in the LADCA & with extent of lesions of higher severity in the RCA & abd. aorta.	Q1. Atherosclerosis begins in childhood. Q2. The presence of RFs correlates with the extent of atherosclerotic lesions at autopsy. Q9. An increase in the number of RFs is associated with increased prevalence and severity of atherosclerotic lesions at autopsy.
17188605	Freedman DS	Cardiovascular risk factors and excess adiposity among overweight children and adolescents: the Bogalusa Heart Study	2007	Cohort	Prospective	Bogalusa	None	Q6 (RF4, RF5, RF8, RF14) Q8 (RF8)	USA	Community (other)	Explore the accuracy of various BMI cutpoints in identifying children who have excess adiposity (based on skinfold thicknesses), adverse levels of lipids, insulin, and blood pressures, and a high risk for severe adult obesity	10,999 (NR)	Pediatric/ Young Adult	Community-based cohort of B & W children and young adults - original group examined at 5-17 yrs; 52% F, 35% B. in 1982; serial cross-sectional studies performed from 1970 to present. For this study, participants were 5-17 yr, fasting and had recorded values for weight, height, and levels of six cardiovascular disease risk factors: TG, LDL-C, HDL-C fasting insulin, SBP and DBP Exclusions: Pregnant girls	Mean age: 11.4 yr	Childhood BMI percentile 1-49 Childhood BMI percentile 50-84 Childhood BMI percentile 85-89 Childhood BMI percentile 90-94 Childhood BMI percentile 95-98 Childhood BMI percentile ≥ 99	1,161 832 130 121 122 26	NR	Sum of skinfolds BMI Lipid levels Insulin levels Blood pressures * Adverse RF levels were based on the distribution of RFs in Bogalusa and were defined as: SSF ≥90th%ile TG, INS, LDL >90th%ile; HDL <10th %ile; SBP &/or DBP ≥90th %ile	12% of children had a BMI ≥ 95th%ile and 2% equaled or exceeded the 99th%ile. Of children with a BMI ≥ 95th percentile, 39% had at least 2 risk factors, 65% had excess adiposity, and 65% had an adult BMI of ≥ 35 kg/m². Of those with a BMI ≥ 99th percentile, 59% had at least 2 risk factors, 94% had excess adiposity, and 88% had an adult BMI of ≥ 35 kg/m² **Childhood BMI** **# of CV RFs** ≥1 ≥2 ≥3 ≥4 85th-94th%ile 51% 19% 5% 1% > 95th%ile 70% 39% 18% 5% > 99th %ile 84% 59% 33% 11% Only 5% of children with a BMI < 50th%ile were obese as adults; 84% of children with a BMI between the 95th & 98th %iles and all of those with a BMI≥99th%ile were obese as adults (mean age=27 yrs).	Q6,7,8. Of children with a BMI ≥ 95th percentile, 39% had at least 2 risk factors and 65% had excess adiposity. Only 5% of children with a BMI < 50th%ile were obese as adults; 84% of children with a BMI between the 95th & 98th %iles and all of those with a BMI>99th%ile were obese as adults (mean age=27 yrs). Q6,7,8. Of those with a BMI ≥ 99th percentile, 59% had at least 2 risk factors, 94% had excess adiposity, and 88% had an adult BMI of ≥ 35 kg/m². The 99th percentile of BMI-for-age may be appropriate for identifying children who are at very high risk for metabolic abnormalities and severe adult obesity

NHLBI Evidence Table: State of the Science: CV Risk Factors and the Development of Atherosclerosis in Childhood-OB

PMID	First Author	Title	Year	Study Type	Prospect./ Restrospect.	Study	CVD	RF by CQ	Country	Setting	Main Study Objective	N at Baseline (N at Follow-up)	Target Population	Eligibility Criteria	Patient Characteristics	Study Groups	n at Baseline (n at Follow-up) for Study Groups	Total Follow-up Duration	Outcomes Measured	Results	Main Reported Findings by Critical Question
17188606	Thompson DR	Childhood Overweight and Cardiovascular Disease Risk Factors: The National Heart, Lung, and Blood Institute Growth and Health Study	2007	Cohort	Prospective	NGHS	None	Q6,7,8 (RF 4,5,8)	USA	Community (schools)	Estimate the prevalence and incidence of overweight in black and white girls and examine associations between adolescent overweight and CVD risk	2379 (2054)	Pediatric/ Young adults	Participants in the NHLBI Growth and Health Study. Female. Self reported as black or white. 9-10 years of age at baseline. Living with parents/guardians with racial concordance.	Black: 1213 White: 1166	Black girls. White girls.	Black 1213 (1063) White 1166 (991)	10 yr	BMI Body fat by bioelectric impedance(BF) Sum of skin folds (SSF) Waist circumference (WC) BP Lipids (TC,HDL-C, TG, LDL-C) New onset of overweight (BMI>95th%ile for age)	Overweight was more prevalent in B girls than W girls at all ages (OR=4.9 CI:1.6-8.2);[B vs W % overweight 9-12 years old: 21.5% vs 10.3%; B vs W % overweight 13-18 years old: 23.3% vs 10.1%]. % of new onset overweight was 2-5% through age 12, then averaged 1-2%. Compared with non-overweight girls, girls who were overweight at age 9-18 were substantially more likely to be overweight as adults (p=S**). All adiposity indicators increased as BMI increased & all measures increased with increasing age (p=S**). %BF & WC were greater in B girls by approximately 5.7%(CI:4.4-7.1) and 2.8%(CI:1.9-3.7)(p=S** for both). Overweight was most strongly ass'd with SSFs & WC but also significantly with % BF. Compared with non-overweight girls, girls who were overweight were more likely to have high SBP & DBP (p=S*);to exhibit low HDL (p=S**) and high TG (p=S*). Overweight was not significantly associated with elevated TC or LDL-C. In a model that controlled for maturation, LDL was associated with overweight (p=S*).	Q5. Racial differences in obesity prevalence are present at age 9 with a significantly higher prevalence in B girls. B girls also showed higher incidence of overweight onset. % of new onset overweight was higher at 2-5% through age 12, then lower and stable through the rest of the F/U period. The association between overweight & CV RFs is already present in early childhood: girls who were overweight were 3 to 10 X more likely to be assessed in the high risk range for 4 of 6 CV indicators (SBP,DBP,HDL,TG)
17329668	Parker ED	Physical activity in young adults and incident hypertension over 15 years of follow-up: the CARDIA study	2007	Cohort	Prospective	CARDIA	None	Q6 (RF4, RF11)	USA	Don't know/NR	Examine the relation between physical activity and incident hypertension in young adults over 15 yr of follow-up	NR (3,993)	Pediatric/ Young Adult	Population-based , prospective observational study with participants recruited from 4 metropolitan areas (Birmingham, Ala; Chicago, Ill, Minneapolis, Minn; & Oakland, Calif) in 1985-1986 at 18-30 yrs of age (44.9% black, 53.9% women) & followed up 2,5,7,10 & 15 yrs later. Exclusions: Hypertension at baseline Missing BP data at more than 2 follow-up exams Missing data for any other co-variates Self-reported pregnancy	Black: 50% Mean years of education: 14.6 yr Prevalence of smoking: 28.8%	Black men Black women White men White women	815 1,101 967 1,110	15 yr	Cases of incident hypertension (BP> 140/90) Physical activity level by questionnaire	Baseline physical activity was greatest in BMs, then WMs, then WFs with much less in BFs. Over time, physical activity levels decreased in all groups except BFs where there was no change. There were 634 cases of incident HTN, most in BMs and BFs, least in WFs. With multivariable proportional hazards regression, those who were more versus less physically active experienced a reduced risk (hazard rate ratio = 0.83; 95% CI = 0.73, 0.93) for incident hypertension, after adjustment for race, sex, age, education, and family history of high blood pressure.	Q13: Consistent high levels of physical activity are associated with reduced risk of incident hypertension in young adults.
17512357	Loria CM	Early adult risk factor levels and subsequent coronary artery calcification: the CARDIA Study	2007	Cohort	Prospective	CARDIA	Coronary Ca	Q3 (RF2, RF4, RF5, RF10)	USA	Community (other)	Determine whether early adult levels of cardiovascular risk factors predict subsequent coronary artery calcium better than concurrent or average 15-yr levels and independent of a 15-yr change in levels	NR (3,043)	Pediatric/ Young Adult	Participants with a CT scan who completed the year 15 examination 18-30 yr African American or white Exclusions: Participants missing data on CAC or risk factors at year 0 or year 15 Participants who were pregnant or if weight was above CT scanner limits	Population-based , prospective observational study with participants recruited from 4 metropolitan areas (Birmingham, Ala; Chicago, Ill, Minneapolis, Minn; & Oakland, Calif) in 1985-1986 at 18-30 yrs of age (44.9% black, 53.9% women) & followed up >/= 15 yrs later in 2000-2001 @ 33-45 yrs of age. For this study: 33-39 yr: 1,464 40-45 yr: 1,579 Men: 1,383 African-American women: 800 African-American men: 576 White women: 860 White men: 807	Detectable levels of CAC Non-detectable levels of CAC	N/A	N/A	Race/ gender Age Cigarette smoking status BMI TC TG HDL-C LDL-C SBP DBP Fasting glucose (FG) Coronary Ca (CAC)(Agatson score)	9.6% of adults had any CAC, with a greater prevalence among men than women (15.0% vs. 5.1%), white than African American men (17.6% vs. 11.3%), and ages 40 to 45 years than 33 to 39 years (13.3% vs. 5.5%). Baseline levels predicted CAC presence (C = 0.79) equally as well as average 15-year levels (C = 0.79; p = 0.8262) and better than concurrent levels (C = 0.77; p = 0.019), despite a 15-year change in risk factor levels. Highest ORs for baseline RFs predicting CAC at year 15 were for LDL-C(1.42-1.43) and cigarettes/day(1.41) but were also significant for BMI, SBP and FG. Multivariate-adjusted OR of having CAC by ages 33-45 years were 1.5 (95% CI 1.3 to 1.7) per 10 cigarettes, 1.5 (95% CI 1.3 to 1.8) per 30 mg/dl LDL-C, 1.3 (95% CI 1.1 to 1.5) per 10 mmHg SBP, and 1.2 (95% CI 1.1 to 1.4) per 15 mg/dl glucose at baseline	Q2,3: RF levels in early adult life predicted CAC presence as well as did average 15-year levels and better than concurrent levels , despite a 15-year change in risk factor levels. Highest ORs for baseline RFs predicting CAC at year 15 were for LDL-C(1.42-1.43) and cigarettes/day (1.41) but were also significant for BMI, SBP and FG.
17548727	Kallio K	Tobacco smoke exposure is associated with attenuated endothelial function in 11-year-old healthy children	2007	Cohort	Prospective	STRIP	FMD	Q2 (RF13)	Finland	Community (other)	Study the effect of passive smoking on endothelial function in children	NR (402)	Pediatric/ Young Adult	Children who had cotinine measurements at 4 age points between 8 and 11 yrs and brachial artery measurements at 11 yr	Finnish RCT of individualized counseling focusing on healthy low fat & low saturated fat diet & good exercise behaviors 2 X/ y beginning in infancy. At age 7 mos, 540 children randomized to intervention, 522 to control. Serum lipids checked annually beginning at 13 mos of age For this study, no child reported active smoking and all subjects had cotinine measurements at 4 age points between 8 and 11 yrs plus brachial artery FMD assessment at 11 yr	Noncotinine Low cotinine Top decile cotinine	NR (229) NR (134) NR (39)	N/A	Cotinine concentration Attenuated peak FMD response Total dilation response	At age 11, elevated cotinine concentration was associated with attenuated peak FMD response (mean+/-SD: the no cotinine group 9.10+/-3.88%, the low-cotinine group 8.57+/-3.78%, and the top-decile cotinine group 7.73+/-3.85%; P=S for trend) Total dilation response (the area under the dilation response versus time curve between 40 and 180 sec after hyperemia) was affected by the cotinine level (p=S for trend) These trends were not explained by traditional atherosclerosis risk factors. Arterial measures and passive smoking showed even stronger association when longitudinal cotinine data were used (peak FMD, p=S* for trend; total dilation response, p=S** for trend)	Q2: Passive smoke exposure assessed by elevated cotinine concentration is associated with attenuated peak FMD response in 8-11 yr old children.
17573336	Chen W	Clustering of long-term trends in metabolic syndrome variables from childhood to adulthood in Blacks and Whites: the Bogalusa Heart Study	2007	Cohort	Prospective	Bogalusa	None	Q5 (RF5, RF8, RF14) Q6 (RF5, RF8, RF14)	USA	Community (other)	Evaluate long-term rates of change in metabolic syndrome variables from childhood to adulthood	1,020 (NR)	Pediatric/ Young Adult	Bogalusa subjects who had been examined at least once in childhood and at least once in adulthood - actual study group evaluated 3-6 times.	Community-based cohort of black(B) & white(W) children and young adults - originally examined at 5-17 yrs; 52% female(F),48% male(M); 44% B in 1982; serial cross-sectional studies performed from 1970 to present. For this study: Males: 40.9% Black: 389/ White: 631	N/A	N/A	Average of 16 yr	BMI HOMA-IR TG/HDL-C ratio Mean BP	Intraclass correlations, a measure of the degree of clustering among the variables were significant for childhood, adulthood, and incremental area values and were higher in adulthood than in childhood, more in Ms than Fs (p=S**for all 4 variables). Blacks showed a higher degree of clustering of long-term rates of change in risk variables than did Whites. Adjustment for body mass index reduced the degree of clustering by approximately 50%.	Results show that metabolic syndrome variables coexist in terms not only of their levels in childhood and adulthood but also the long-term rates of change. Q5: Blacks showed a higher degree of clustering of long-term rates of change in metabolic syndrome risk variables than did Whites. Q6: Intraclass correlations, a measure of the degree of clustering, among variables, were significant for childhood, adulthood, and incremental area values and were higher in adulthood than in childhood.
17599442	Frontini MG	Utility of non-high-density lipoprotein cholesterol versus other lipoprotein measures in detecting subclinical atherosclerosis in young adults (The Bogalusa Heart Study)	2007	CrS	Retrospective	Bogalusa	IMT	Q3 (RF5)	USA	Community (other)	Compare the utility of non-HDL cholesterol with the utility of LDL-C, HDL-C, TG, Apo B, Apo A-I, ratio of TC to HDL-C, and ratio of Apo B to Apo A-I in detecting increased carotid IMT in asymptomatic younger adults	1,203 (NR)	Pediatric/ Young Adult	Bogalusa subjects who had an ultrasound measurement of carotid IMT Exclusions: Subjects who lacked bilateral far wall carotic IMT measurements on any arterial segment Subjects who were nonfasting	Community-based cohort of black(B) and white (W) children and young adults - originally examined at 5-17 yrs; 52% female(F), 48% male (M); 44% B. Serial cross-sectional studies made from 1970 to present.. For this study: 24-43 yr White: 71% Men: 43%		N/A	N/A	Non-HDL-C LDL-C HDL-C TG Apo B Apo A-I Ratio of Apo B to Apo A-I Ratio of TC to HDL-C Carotid IMT	In multivariate logistic regression analysis for detecting increased carotid IMT only non-HDL-C,TC/HDL-C, and Apo B emerged as significant correlates with respective OR of 1.75 (95% CI 1.10 to 2.78), 2.02 (95% CI 1.27 to 3.19), and 2.13 (95% CI 1.38 3.29) after adjusting for body mass index, systolic blood pressure, and other lipoprotein measurements Regarding discriminating values of different lipoprotein measurements in detecting increased carotid IMT, area (c-value) under the receiver operating characteristic curve analysis for each lipoprotein measurement adjusted for age, race, gender, body mass index, and systolic blood pressure indicated that the c-value for non-HDL-C (0.73) was similar to those for LDL-C (0.76), TC/HDL-C (0.72), Apo B/Apo A-I (0.71), and HDL-C (0.70), but significantly (p <0.001) higher than that for Apo A-I (0.69), TG (0.64), and Apo B (0.64) Non-HDL cholesterol is as good as or better than other widely recommended lipoprotein measurements in the identification of subclinical atherosclerosis in young adults	Q3: Only non-HDL-C,TC/HDL-C, and Apo B emerged as significant correlates of increased carotid IMT

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17671060	Morrison JA	Metabolic Syndrome in Childhood Predicts Adult Cardiovascular Disease 25 Years Later: The Princeton Lipid Research Clinics Follow-up Study	2007	Cohort	Prospective	Princeton	CVD unspecified	Q8 (RF14) Q3 (RF 14) Q8 (RF14)	USA	Community (other)	Assess the association of metabolic syndrome in childhood with adult CVD 25 years later	771 (771)	Pediatric/ Young adults	Participants in the National Heart, Lung, and Blood Institute LRC Prevalence Study: Students in the Princeton School District of Greater Cincinnati in grades 1 through 12		NA	NA	25 yr	BMI. Waist Circumference(WC). Fasting Glucose (FG) HDL-C TG SBP & DBP Metabolic Syndrome(MS) = > 3 of: In adults: HDL< 50mg/dl in Fs, 40 mg/dl in Ms; TG >150mg/dl; SBP>130 +DBP> 85; FG >110mg/dl.; BMI>25. In children: TG >110mg/dl; BMI > 90th%ile for age/sex; SBP/DBP>age/sex-specific 90th%ile; HDL<50mg/dl in Fs, 40 mg/dl in Ms; FG >110mg/dl CVD: MI, CABG,angioplasty, stroke.	All MS components increased: High BMI:13.7% (LRC) to 25.4% (PFS); Large WC: NA (LRC) to 49.1% (PFS); High FG: 0.7% (LRC) to 6% (PFS); Low HDL: 13.0% (LRC) to 52.9% (PFS); High TG: 12.3% (LRC) to 28.3% (PFS); High BP: 11.9% (LRC) to 33.8% (PFS); CVD occurred in 2.2% of the adult subjects. MS: 4%(LRC) to 27.2% (PFS) MS was strongly asst'd with increased BMI - 95% of adults with MS were overweight or obese. 68% of pediatric MS had MS at follow-up;32% did not. In MVA with age, gender, and race, only ped MS predicted adult MS(OR=6.1;p=S**). When change in BMI was added, it was significant (OR=1.024,p=S**). For each 10%ile change in BMI, the MS prevalence increased 24%. 0% (LRC) to 2.2% (PFS). Among the ped MS subjects, the incidence of CVD was 19.4% vs 1.5% for those without ped MS. In MVA, ped MS (OR=14.7;p=S**) and age (OR=1.2;p=S) were significant predictors of adult CVD. Gender, race & fam hx of CVD were not.	Q8: Children with the cluster of risk factors defined as pediatric metabolic syndrome were significantly more likely to have CVD 25 years later as adults, compared with their peers. Metabolic syndrome was strongly associated with obesity. 68% of pediatric MS had MS at follow-up; 32% did not.
17884375	McMahan CA	Association of Pathobiologic Determinants of Atherosclerosis in Youth Risk Score and 15-Year Change in Risk Score With Carotid Artery Intima–Media Thickness in Young Adults (from the Cardiovascular Risk in Young Finns Study)	2007	Cohort	Retrospective	PDAY/ Young Finns	IMT	Q3 (RF2,3,4,5,6, 8,10)	Finland	Clinical	Calculate the PDAY risk score for the participants in the Cardiovascular Risk in Young Finns study population based on CV RF assessment in childhood adult life and correlate results with CIMT measured in adult life.	1279	Pediatric/ Young adults	Participants in the Young Finns Study who were over 12 years old in 1986 for whom risk factors were measured in 1986 and 2001 and IMT was measured in 2001. Exclusions: Subjects who were pregnant at either measurement.	NR	NA	NA	15 yr	Age Sex Smoking status Hyperglycemia/Diabetes mellitus (DM) BP BMI Non-HDL & HDL cholesterol CIMT by ultrasound imaging PDAY risk score from adolescence & adult CV RFs: Low risk = -1 or 0 Intermediate risk = 1- 4 High risk = ≥ 5 Risk score change: Improved ≤ -2 No change = -1 to 1 Worsened >2	CIMT and plaque presence increased with increasing age(p=S**) & were higher in Ms (p=S**). Child/adolescent RF score significantly predicted young adult CIMT with OR for a 1 point increase in score (= 1y of aging) of 1.106 (CI:1.056,1.158). The child/adolescent score predicted CIMT better but not significantly better than the young adult score (OR 1.007;CI: 1.004,1.010). The change in RF score - increase or decrease - significantly predicted CIMT.	Q3. CV RFs measured in adolescence predicted the presence of increased CIMT 15 years later using the PDAY RF score. The PDAY coronary artery risk score based on CV RFs determined at autopsy predicted CIMT in living young adults.
18071074	Magnussen CG	Utility of currently recommended pediatric dyslipidemia classifications in predicting dyslipidemia in adulthood: Evidence from Childhood determinants of adult health (CDAH) study, Cardiovascular risk in young Finns study, and Bogalusa heart study.	2008	CrS	Prospective	Bogalusa, Young Finns, CDAH	None	Q8 (RF5)	USA + Finland + Australia	Community (schools)	Apply current definitions for pediatric dyslipidemia to adolescent lipid results to assess strength as predictors of adult dyslipidemia.	NR	Pediatric/ Young adults	3 cohorts: CDAH: Australian study of CV RFs from childhood into adult life. Baseline data on 8498 subjects, 7 - 15 y of age; 2410 subjects evaluated again at 26-36 y. Bogalusa: Community-based cohort of B & W children and young adults - original group examined at 5-17 yrs; 52% F, 35% B. in 1982; serial cross-sectional studies performed from 1970 to present. This study, included 273 subjects who had baseline lipids done at 12 -17 y and who returned for repeat testing as young adults. Young Finns: Collaborative effort of all university departments of pediatrics + several other Finnish institutions to study C-V RFs and their determinants in children and adolescents. The main cross-sectional study carried out in 1980 included 3596 3-18-year-old subjects with F/U studies in 1983, '86,'89 and '92, the last when the subjects were 15-30 years old. For this study, there were 1185 subjects who had adolescent and young adult lipid data.	CDAH: Mean age at baseline testing: 13.5+/-1.5y Mean age at adult testing: 33.4+/-1.6 y 178 M/ 185 F Bogalusa: Mean age at baseline testing: 15.3 +/- 1.6y Mean age at adult testing: 32.4+/- 1.4 117 M/ 149 F Young Finns: Mean age at baseline testing: 14.9+/-2.4 y Mean age at adult testing: 35.9+/-2.4 y 523 M/ 657 F	CDAH: Mean age at baseline testing: 13.5+/-1.5y Mean age at adult testing: 33.4+/-1.6 y 178 M/ 185 F Bogalusa: Mean age at baseline testing: 15.3 +/- 1.6y Mean age at adult testing: 32.4+/- 1.4 117 M/ 149 F Young Finns: Mean age at baseline testing: 14.9+/-2.4 y Mean age at adult testing: 35.9+/-2.4 y 523 M/ 657 F	N/A	N/A	TC TG HDL-C LDL-C % high TC % high TG % low HDL % high LDL	Pooled calculation of adjusted RR for abnormal lipids as an adult based on adolescent results was significantly higher for adolescents with borderline high/high-risk levels compared to those with nl lipids. Stratified by study group, results were similar for TC, LDL & TG but differed for HDL-C, with RR significantly lower for Bogalusa subjects. Pooled data calculation of sensitivity & specificity of high-risk cut points indicated: - For TC, borderline- and high risk NCEP cutpoints were considerably moresensitive than were NHANES: of adults with elevated TC, 32.3% would not be identified from adolescent results with NCEP cutpoint vs 60.6% with NHANES cutpoints. - For LDL, the NCEP borderline- and high-risk cutpoints were more sensitive and less specific than NHANES. 55.4% of adults with elevated LDL were not identified by NHANES cutpoints vs 35% with NCEP. - For HDL, the NHANES borderline- and high-risk cutpoints were better than the NCEP cutpoints, but both were poor predictors with 83.3% of adults with low HDL missed with NHANES and 93.3% with NCEP. - For TG, both classification performed poorly with NCEP better than NHANES; 86% of adults with elevated TGs were not identified using NCEP cutpoints and 97.7% using NHANES.	Q 8. Using data from 3 prospective cohort studies, findings confirmed that the more abnormal the lipid results were in adolescence, the more likely they were to accurately predict abnormal lipids in adult life. Comparing the predictive capacity of NCEP and NHANES cutpoints, the NCEP cutpoints were more accurate predictors for TC,. LDL and TGs but the NHANES cutpoints were more accurate for HDL. The study indicated limitations with all screening approaches for clinical use in adolescents. Universal screening identified 75% of those with high LDL but false positives were high at 66.2% Current screening approaches based on cutpoints in adolescents were all poor in identifying adults with low HDL.
18071074	Magnussen CG	Utility of currently recommended pediatric dyslipidemia classifications in predicting dyslipidemia in adulthood: Evidence from Childhood determinants of adult health (CDAH) study, Cardiovascular risk in young Finns study, and Bogalusa heart study.	2008																	Using the Young Finns cohort and the best-performing cutpoints from the previous analyses, 3 different screening strategies were used: UNIVERSAL; positive FAM HX + cutpoints; OV/OB+ cutpoints; and positive FAM HX + OV/OB + cutpoints --> Universal screening identified 75% of those with high LDL but false positives were high at 66.2%. Results were simlar for positive FAM HX, OV/OB and positive FAM HX + OV/OB. 20% with high LDL as adults were not identified by any screening strategy. Regardless of cutpoints used, 71% of adults with low HDL: were not identified from adolescent results.	
18206683	Cook S	Metabolic syndrome rates in United States adolescents, from the National Health and Nutrition Examination Survey, 1999-2002	2008	CrS	Retrospective	NHANES 1999-2002	None	Q5 (RF2, RF3, RF8, RF14) Q6 (RF2, RF3, RF8, RF14)	U.S.A	Clinical	Report the prevalence rates of the metabolic syndrome in a nationally representative sample of adolescents in the U.S. using 4 previously reported definitions of the syndrome.	4,902	Pediatric/ Young adults	12-19 yr Exclusions: Pregnancy Inadequate fasting Taking medications that could interfere with test results for the components of the metabolic syndrome	Patient characteristics from NHANES 1999-2002	Groups were studied by sex, race/ethnicity, and BMI status, as well as the 4 following definitions for metabolic syndrome: Cook/Ford Cruz Caprio Adult	NR	NR	Abdominal obesity BP TG LDL-C Glucose	In NHANES 99-02, the prevalence of the metabolic syndrome varied from 2.0% to 9.4% of teens in the United States, depending on the definition used. In obese teens, these prevalence rates varied from 12.4% to 44.2%. In obese teens, application of the metabolic syndrome definition by Cruz produced a prevalence rate of 12.4%, that of Caprio produced a rate of 14.1%. However, none of the normal weight or overweight teens met either definition. Application of the definition by Cook produced a prevalence rate of 7.8% in overweight teens and 44% in obese teens. The adult definition of metabolic syndrome produced a prevalence rate of 16% in overweight teens and 26% in obese teens.	Q6: Prevalence rates for metabolic syndrome vary widely depending on the definition used. In obese teens, metabolic syndrome prevalence varied from 12.4% to 44.2%.
18206689	Morrison JA	Metabolic Syndrome in Childhood Predicts Adult Metabolic Syndrome and Type 2 Diabetes Mellitus 25 to 30 Years Later	2008	Cohort	Prospective	Princeton	None	Q8 (RF14) Q6 (RF 4,5,8,14)	USA	Mult settings	Assess the association of metabolic syndrome in childhood with adult metabolic syndrome and type 2 diabetes mellitus (T2DM) 25 to 30 years later	NR (814)	Pediatric/ Young adults	Participants in the National Heart, Lung, and Blood Institute LRC Prevalence Study: Students in the Princeton School District of Greater Cincinnati in grades 1 through 12	At the LRC the participants ranged in age from 5-19 yr; at follow-up, subjects ranged from 30 - 59 yr. Male: 45% White: 72% Black: 28%	NA	NA	25-30 yr	BMI Waist circumference (WC) Blood Pressure (BP) Lipid profile: TC,TG,HDL,LDL Fasting Glucose T2DM = FG > 126 mg/dl. Metabolic Syndrome(MS) = ≥ 3 of: In adults: HDL< 50mg/dl in Fs, 40 mg/dl in Ms; TG >150mg/dl; SBP>130 +DBP> 85; FG >110mg/dl.; BMI>25. In children: TG >110mg/dl; BMI > 90th%ile for age/sex; SBP/DBP>age/sex-specific 90th%ile; HDL<50mg/dl in Fs, 40 mg/dl in Ms; FG >110mg/dl	3.9% of baseline LRC participants met the definition for pediatric MS; of these 75% had BMI > 90th%ile. At follow-up, 25.4% of the cohort had BMI> 90th%ile for age; 28.1% had high TG; 52.5% had low HDL; 33.4% had abnormal BP;6% had abnormal FG. Prevalence of high WC was 48.9%. At follow-up, prevalence of MS was 26.6%. Adult MS was strongly asst'd with BMI at F/U: 95% of those with MS had BMI > 25 kg/m squared. In multivariate analysis, adult MS correlated with pediatric MS (OR=9.4,CI:1.6,3.5); parental history of DM (OR=2.4, CI:1.6,3.5); age at F/U: (OR=1.06,CI:1.01,1.11);and change in weight (OR=1.025,CI:1.018,1.033). Among adults with T2DM, 15.6% had pediatric MS vs 5% in those without MS in childhood (p=S**). In multivariate analysis, adult T2DM correlated with pediatric MS (OR= 11.5, p=S*); parental hx of DM(OR=1.12,p=S*);and black race (OR=2.2,p=S).	Q6. RFs cluster together in children as they do in adults. Children with the MS cluster are much more likely to have T2DM 25 - 30 yrs later as adults. Pediatric MS and a (+) parental hx of T2DM were major independent predictors of adult T2DM. Q5. There are racial differences in T2DM prevalence: Black Ms and Fs had 2X the risk of developing T2DM as did whites and for each 1 y increase in age, risk of DM increased 12.2%. Prevalence of MS increased from 4% in childhood to 27.2% at a mean age of 38 yrs asst'd primarily with changes in weight. For each 10%ile change in BMI, the MS prevalence increased 25%. (+) parental hx of T2DM correlated with high BMI as children and as adults.

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PMID	First Author	Title	Year	Study Type	Prospect./ Restrospect.	Study	CVD	RF by CQ	Country	Setting	Main Study Objective	N at Baseline (N at Follow-up)	Target Population	Eligibility Criteria	Patient Characteristics	Study Groups	n at Baseline (n at Follow-up) for Study Groups	Total Follow-up Duration	Outcomes Measured	Results	Main Reported Findings by Critical Question
18309111	Juonala M	Associations of dyslipidemias from childhood to adulthood with carotid intima-media thickness, elasticity, and brachial flow-mediated dilatation in adulthood: the Cardiovascular Risk in Young Finns Study	2008	Cohort	Prospective	Young Finns	Multiple	Q3 (RF5)	Finland	Don't know/NR	Examine in detail the effects of dyslipidemia phenotypes, including combined dyslipidemia, on risk of subclinical atherosclerosis in young adults.	3596 (2265)	Pediatric/ Young adults	Patients in the Cardiovascular Risk in Young Finns Study who completed the 21-year follow-up. Men and women between 3 and 18 at study onset.	Men and women between 3 and 18 yr at study onset	NA	NA	21 yr	**Arterial function:** cIMT; Elasticity; FMD. **CV RFs**: Serum Lipids, BP, BMI, smoking hx, fam hx of prem CAD, FG,Insulin or dx of DM, CRP Clinical characteristics.	(1) Adult cIMT was increased in subjects with childhood type IIb dyslipidemia after adjustment for sex/age/BP/BMI/CRP/ Ins/FG/DM/fam hx of CAD/smoking(p=S*). (2) Carotid compliance was decreased in type IIb but only in univariate analysis. (3) In type IIb subjects, increasing number of non-lipid RFs was significantly correlated with increased cIMT.(p=S**). cIMT increased with increasing number of non-lipid RFs but this was not significant in normolipidemic subjects. (4) Increased cIMT correlated significantly with presence of the metabolic syndrome only in type IIb subjects. (p=S) (5) In adulthood, subjects with type IIb or IV dyslipidemia had higher BP, BMI, insulin, and CRP levels, increased prevalence of metabolic syndrome and DM, and increased prevalence of positive family history of CAD compared to nondyslipidemic subjects. (6) HypoHDL-cholesterolemia was associated with increased prevalence of the metabolic syndrome. (7) In childhood, type IIb had increased BMI and type IV subjects had increased BMI and BP.	Q3: Type IIb dyslipidemia has deleterious effects on arterial vasculature beginning in childhood. Subjects with type IIb dyslipidemia were more vulnerable to the effects of cardiovascular risk factors and metabolic syndrome. The synergistic effect of the CV RFs begins in childhood.
18450895	Frontini MG	Usefulness of Childhood Non–High Density Lipoprotein Cholesterol Levels Versus Other Lipoprotein Measures in Predicting Adult Subclinical Atherosclerosis: The Bogalusa Heart Study	2008	Cohort	Retrospective	Bogalusa	Multiple	Q1,3 (RF5)	USA	Community (other)	Examine the usefulness of childhood non-high-density lipoprotein cholesterol level versus low-density lipoprotein cholesterol level, high-density lipoprotein cholesterol level, triglyceride level, apolipoprotein B level, apolipoprotein A-I level, total cholesterol/high-density lipoprotein cholesterol ratio, and apolipoprotein B/apolipoprotein A-I ratio in predicting adult excess carotid intimamedia thickness, an indicator of subclinical atherosclerosis.	437	Pediatric/ Young adults	Participants in the Bogalusa Heart Study as children 5-17 years of age and as adults 16-19 years later	White: 70% Male: 40% Mean age at F/U: 31.9 y(24-43 y)	NA	NA	16-19 yr	Non-HDL-C LDL-C HDL-C TG Apolipoprotein B Apolipoprotein A-I CIMT	By MVA, after adjustment for childhood BMI, SBP, other lipoprotein measures and F/U yrs, childhood non-HDL-C (OR=2.60), LDL-C (OR=2.95), TC/HDL-C ratio (1.78), apoB(OR=1.44) and apoB/apoA1 ratio (OR=1.69) were independent predictors of excess CIMT in young adulthood. HDL-C, TG and apoA! were not significant predictors. When evaluated by ROC analysis, childhood non-HDL was as effective as any other childhood lipid measure (c=0.62-0.66).	Childhood lipoprotein findings (non-HDL-C,LDL-C,TC/HDL-C,apoB and apoB/apoA1 ratio) were significant predictors of adult sub-clinical atherosclerosis assessed by CIMT. Childhood non-HDL was as effective a predictor as any other childhood lipid measure.
18505949	Ogden CL	High Body Mass Index for Age Among US Children and Adolescents, 2003-2006	2008	CrS	Retrospective	NHANES	None	Q5 (RF8) Q6 (RF8)	US	Clinical	Estimate the prevalence of high BMI for age among children and adolescents.	8,165	Pediatric/ Young adults	2-19 yr participants in the NHANES surveys, 1988-1994 and 1999-2004.	Nationally representative sample of US children and adolescents Group 1: 2-5 yr: 22% 6-11 yr: 34% 12-19yr: 43% Male: 51% Non-Hispanic white(W): 73% Non-Hispanic black(B): 17% Mexican American(M-A): 10% Group 2: 2-5 yr: 21% 6-11 yr: 34% 12-19yr: 46% Male: 51% Non-Hispanic white(W): 70% Non-Hispanic black(B): 17% Mexican American(M-A): 14%	Group 1: NHANES respondents 2003-2004 Group 2: NHANES respondents 2005-2006	Group 1: 4,207 Group 2: 3,958	N/A	Prevalence of BMI at or above the 85th, 95th and 97th %iles for age/sex and racial/ethnic group.	In 2003 - 06, 11.3% (CI:9.7%-12.9%) of children and adolescents aged 2 - 19 y were ≥ the 97th%ile of the 2000 BMI age-for-growth charts; 16.3% (CI:14.5% - 18.1%) were ≥ above the 95th%ile; and 31.9% (CI:29.4% - 34.4%) were ≥ the 85th%ile. There were no significant time trends over the 4 time periods (1999-2000,2001-2002,2003-2004,2004-2005) for Ms or Fs or by race/ethnicity. BMI > 97th%ile was more prevalent in 12-19 y olds than in 2-5 y olds (OR=0.59 for Ms, 0.65 for Fs). Non-Hispanic B(28%;CI:23.8-31.6%) and Mexican American (20%;CI:17.0 - 22.8%) girls were significantly more likely to have a BMI for age > 95th%ile than non-Hispanic W girls (14.5%;CI:10.4-18.6%). Among Ms, Mexican American boys were significantly more likely to have a high BMI for age than were non-Hispanic W boys; among non-Hispanic B boys, this was only true for BMI > 97th%ile.	Obesity prevalence in children and adolescents is high but stable over the time period from 1999 to 2005. Q5. There are significant difference by race and gender with higher prevalence of obesity in Fs, especially in non-Hispanic B and Mexican American girls. Obesity prevalence has increased with age in Ms and Fs.
18534237	Messiah SE	Relationship between body mass index and metabolic syndrome risk factors among US 8- to 14-year-olds, 1999 to 2002	2008	CrS	Retrospective	NHANES	None	Q5 (RF8) Q6 (RF2, RF3, RF4, RF6, RF8)	US	Clinical	Determine the prevalence of metabolic syndrome risk factors (MSRF) and examine the relationship between body mass index and the prevalence of 3 or more MSRF in children and adolescents.	1,698	Pediatric/ Young adults	Combined results from the nationally represented sample in the 1999-2002 NHANES survey for 8 - 11 yr olds and 12 - 14 yr olds. Exclusions: Race = "other" Diabetes mellitus Use of medications that alter blood pressure, lipid metabolism, or blood glucose	8-11 yr: 62.8% 12-14 yr: 37.2% Male: 49.8% Non-Hispanic white: 27.6% Non-Hispanic black: 34.4% Mexican American: 38%	Group 1: Younger (8-11 yr) Group 2: Older (12-14 yr)	Group 1: 1067 (N/A) Group 2: 631 (N/A)	N/A	Weight BMI Waist circumference SBP DBP HDL-C Fasting glucose (FG) TG Met S (MS) defined as ≥3 of the following: WC ≥90th%ile for age/sex (≥75th%ile for age/sex/ethnicity); FG ≥100 mg/dl; SBP +/- DBP ≥90th %ile for age/sex/ht.; TG >/= 110 mg/dl(≥90th%ile for age & ethnicity); HDL ≤40 mg/dl (≤10th %ile for age/ethnicity).	Based on BMI, 17.5% of Ms and 17% of Fs were ≥95th%ile for age/sex. Overall, 25% of non-Hispanic Bs, 22% of M-As and almost 15% of non-Hispanic Ws were overweight/ obese. For the older age group, 22% of non-Hispanic B, 27% of M-As and almost 15% of non-Hispanic Ws were overweight/ obese. As BMI increased, the % of those with abnormal CV RFs increased. For 8 - 11 yr olds, 35% of those who were overweight had ≥2 MS RFs present vs 2% of those with normal weight. For 12 - 14 yr olds, 29% of those who were overweight had ≥2 MS RFs present vs 8% of those with normal weight. ≥3 adjusted MS RFs were seen in 26.28%(CI:16.71 - 38.78) of 12 - 14 yr olds and 9.51% (CI:5.59 - 15.71) of 8 - 11 yr olds.	Q6. Among overweight/ obese children and young adolescents, the prevalence of a MS profile (≥3 MS RFs) is high, and greater with older age. The MS cluster occurred in almost 10% of 8 - 11 yr olds and 26% of 12-14 yr olds in the 1999-2002 NHANES survey.
18634985	Juonala M	Childhood Levels of Serum Apolipoproteins B and A-I Predict Carotid Intima-Media Thickness and Brachial Endothelial Function in Adulthood	2008	Cohort	Prospective	Young Finns	Multiple	Q3,4 (RF4,5,8,10,14)	Finland	Clinical	Determine whether CV RFs including apolipoproteins (apo) B and A-I measured in childhood and adolescence predict subclinical evidence of atherosclerosis in adulthood	1341 (879)	Pediatric/ Young adults	Participants in the Cardiovascular Risk in Young Finns Study aged 3,6,9,12,15, and 18 years old at the onset of the study in 1980.	Male: 45.7% Mean age (SD) at F/U: 31.9 yr (5.0;)	NA	NA	21 yr	**Baseline and F/U:** Apo B levels; Apo A-I levels; TC,LDL-C,HDL-C,TG BP Smoking status BMI Insulin CRP **Follow-up:** CIMT Brachial FMD	In bivariate analysis, baseline Apo B(p=S**) and ApoB/Apo A-I ratio(p=S**) were directly related and Apo A-I was inversely related(p=S*) with adulthood IMT in subjects aged 12-18 y at baseline. These associations were not significant for baseline measures at 3-9 y. LDL(p=S) and LDL/HDL ratio(p=S*) also correlated significantly with adulthood CIMT but the correlation was roughly half as strong. In MVA using age-and gender-specific z-scores at 12-18 y, the direct association with apoB(p=S**) and the apoB/A1 ratio and the inverse association with apoA1(p=S*) were independent of other RFs. The associations between adolescent apolipoproteins and adult CIMT remained significant when adult apolipprotein results were included (p=S). The c-value for the MV model predicting CIMT > 90th%ile or carotid plaque with lipid and non-lipid RFs included was higher for adolescent apoB/apoA1 compared with LDL/HDL and with non-HDL/HDL(p=S for both). In bivariate analysis, baseline Apo B(p=S) and ApoB/Apo A-I ratio(p=S**) were indirectly related and Apo A-I was directly related(p=S**) with adulthood FMD in subjects aged 3-18 y at baseline. LDL and LDL/HDL ratio were not related to adulthood FMD. The associations between childhood apolipoproteins and adult FMD remained significant when adult apolipprotein results were included (p=S).	Q3: Apo B and A-I measured in children and adolescents better predicted adult sub-clinical atherosclerosis than did conventional lipid measures. High levels of apoB and low levels of apoA1 measure in adolescence reflect a lipoprotein profile predisposing to the development of subclinical atherosclerosis in adult life.