NHLBI Evidence Table: RF1-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.
7053887	Schrott HG	Coronary artery disease mortality in relatives of hypertriglyceridemic school children: the Muscatine study.	1982	CrS	Retrospective	Muscatine	Atherosclerosis	Q4 (RF1,RF5)	USA	Community (other)	To evaluate coronary artery mortality and lipid profiles in first and second degree relatives of children with sustained high and low TGs.	538/605 1st degree; 840/1216 2nd degree	Parental/ Family/ Caregiver	1st & 2nd degree relatives of 75 children from Muscatine population with TGs > 90th%ile(HTG) and 47 children with TGs < 10th%ile(LTG) on 2 occasions, 2 y apart.	1st & 2nd degree relatives of 75 children (34 M/ 41 F) from Muscatine population with TGs > 90th%ile (=HTG) and 47 children with TGs < 10th%ile (+LTG) (20 M/ 27F) on 2 occasions, 2 y apart.	122 index cases + 538/605 1st degree relatives; 840/1216 2nd degree relatives	N/A	N/A	RF profiles of groups. Lipid profiles of family members Death certificate information medical history of CAD.	HTG v. LTG index cases were significantly heavier (Relative weight = 115.9+/-22.9 v. 99.9 +/-11.4;p=S); with higher TC (194.8+/-36.5 v. 160.9 +/-25.1;p=S*). HTG group was divided into HTG-HC & HTG-LC based on TC levels - criterion for HC & LC not given. When relatives of HTG-HC & HTG-LC sub-groups are compared, siblings, parents, aunts & uncles, and grandparents in the HTG-HC group all had significantly higher TC levels. When lipid results for HTG & LTG family members are compared, TC & TG values were significantly higher for the siblings, parents, aunts & uncles but not for grandparents. No difference in coronary mortality between groups (HTG=13.2% v. LTG = 14.2%) There was a trend towards higher mortality in the HTG-HC group v HTG-LC group in age group< 60y but difference NS.	Familial elevation of TG levels did not appear to increase coronary mortality suggesting that TG levels alone are not an important RF for ASHD. There is a suggestion that elevated TG levels combined with elevated TC levels increase risk for early CAD.
7805239	Bao W	The relation of parental cardiovascular disease to risk factors in children and young adults. The Bogalusa Heart Study	1995	CrS	Retrospective	Bogalusa	None	Q5 (RF4,5,8,14) Q6 (RF4,5,8,14)	USA	Community (other)	Correlate parental hx of CAD, HBP and DM with RF profiles in their offspring from childhood to young adult life.	8,276	Pediatric/ Young adults	All participants in 6 CrS surveys performed as part of the Bogalusa study for whom fam hx information had been provided by the subjects and/or their parents.	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 5-31 yrs old, 36% B, 64% W.	N/A	N/A	N/A	Ht Wt Ponderal index (PI) SBP DBP TC TG VLDL HDL LDL Fasting insulin (INS) Fasting glucose (FG) Fam hx of heart attack Fam hx of HTN Fam hx of stroke Fam hx of diabetes * Fam hx deemed (+) of one or both parents were reported to have disease.	Comparing 5-10 y old children to 25-31 y old young adults, prevalence of parental MI increased from 5 to 25%; parental stroke increased from 2 to 9% in Ws and 3 to 19% in Bs; parental DM increased from 7 to 19% in Ws and 9 to 33% in Bs; parental HTN increased from 26 to 59% in Ws and 40 to 72% in Bs. % of offspring with parental stroke was 2X as common in Bs. % of offspring with parental DM was 50% greater in Bs. Offspring with (+) fam hx of MI were significantly overweight after 10 yrs and showed elevated levels of TC, VLDL-C, LDL-C, insulin and glucose after 17 yrs, irrespective of weight. Offspring of parents with DM were significantly overweight regardless of age and showed significant increases in insulin, glucose, TGs, TC, VLDL-C,and LDL-C after 24 yrs, irrespective of weight. Offspring of parents with HTN were overweight regardless of age & had higher BP levels after 10 yrs and elevated TGs and VLDL-C after 24 yrs, irrespective of wt. By ANOVA for race and sex in 18-31 y olds, parental MI related strongly to higher LDL-C in W offspring, especially W males and to insulin in B males and females. By ANOVA for race and sex in 18-31 y olds, parental DM showed a strong asst'n with higher PI and higher FG in B females. By ANOVA for race and sex in 18-31 y olds, parental HTN was also related to greater PI, only in B females. By ANOVA for race/sex in 5-17 y olds, only significant association was between parental hx of diabetes and greater PI in BFs.	Parental hx of MI, DM, HTN or stroke is associated with adverse RF levels in offspring, increasing with age. There are race and sex differences in prevalence of parental disease with MI more common in Ws and HTN, stroke & DM more common in Bs. Offspring with a (+) hx of parental cardiovascular disease show adverse RF levels beginning in early childhood. RF patterns in offspring change adversely and selectively with parental disease and are significantly affected by race and sex.
8115204	Muhonen LE	Coronary risk factors in adolescents related to their knowledge of familial coronary heart disease and hypercholesterolemia: the Muscatine Study	1994	CrS		Muscatine	None	Q6 (RF1,4,5,8)	USA	Community(other)	Evaluate the utility of family hx of C-VD in identifying adolescents with adverse C-V RF levels.	599	Pediatric/ Young adults	All participants in the Muscatine study in 1990 who completed a fam hx questionnaire and underwent C-V RF assessment.	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, 9th - 12 th grade students completed a questionnaire re: family hx of coronary heart disease & a subset underwent subsequent C-V RF assessment	N/A	N/A	N/A	Fam hx of or early (30-55y) or later (>55y) MI / CABG/ cardiac death in parent or grandparent --> 3 groups: No heart disease - No parent or grandparent with MI, angina, CABG, or cardiac death; Early CHD - At least one parent or grandparent with MI, angina, CABG or cardiac death at < 55y; Later CHD - At least one parent or grandparent with MI, angina,CABG, or cardiac death at > 55y. Fam hx of high cholesterol --> 3 groups: ( ) No parent or grandparent with known hx of high cholesterol; (+) At least 1 parent or grandparent with known hx of high cholesterol; Unsure. Age Gender Ht Wt BMI Triceps skin fold (TSF) SBP DBP TC	(+) vs (-) parental hx of high cholesterol identified no statistically significant differences for RFs. (+) vs (-) grandparent hx of high TC predicted adverse levels of LDL (OR=2.46,CI=1.20-5.03,p=S) and LDL/HDL (OR=2.30,CI=1.06-5.01,p=S) 2.5% of subjects had a (+) parental hx of early CHD. Parental hx of early CHD was asst'd with significantly higher BMI than in CHD (-) group. Odds of having adverse RF level for (+)parental hx group were significant for high BMI (OR=5.15, CI=1.84-14.41,p=S*) and low apoA1 (OR=3.84,CI=1.25-11.84,p=S) 14% of subjects had a (+) grandfather hx of early CHD & 22% of later CHD. Subjects with early &/or later grandfather hx of CHD had significantly higher BMI, TSF, DBP & lower apoA1 levels than fam hx (-) subjects. Odds of having adverse RF level for (+)grandparental hx group were significant for high BMI (OR=2.47,CI=1.08-5.64,p=S), SBP(OR+2.28,CI=1.01-5.14,p=S) and low apoA1 (OR=2.53,CI=1.17-5.49,p=S).	(+) family hx of CHD in parents or grandparents identifies children at risk for adverse RF levels. However, the prevalence of early CHD is low and knowledge of fam hx is frequently incomplete so use of fam hx in screening is limited.
8115204	Muhonen LE	Coronary risk factors in adolescents related to their knowledge of familial coronary heart disease and hypercholesterolemia: the Muscatine Study	1994																TG HDL LDL ApoA1 ApoB		
9439456	Bachorik PS	Apolipoprotein B and AI distributions in the United States, 1988–1991: results of the National Health and Nutrition Examination Survey III (NHANES III)	1997	CrS	Retrospective	NHANES	None	Q5 (RF5) Q6 (RF5)	US	Clinical	Present the distribution of apo AI and apo B in persons aged 4 years or older.	16,619	Pediatric/ Young adults	> 4 y old participants in the NHANES III from 1988 - 1991, a nationally representative sample of the US population.	Male: 49.7% White: 7,148 Black: 4,205 Mexican-American: 5,007	N/A	N/A	N/A	Apo A-I Apo B LDL-C HDL-C Non-HDL-C TG TC	**APO B**: (1) There were no significant differences in apoB based on fasting state or sex. (2) By ethnic group, age-adjusted apoB levels were slightly but significantly lower in B adult males than Ws or M-As; means in females were the same for all 3 racial/ethnic groups. (3) Median apoB levels were stable from 4 to 19 y of age in males, then increased abruptly after 20 y of age & reached a plateau after age 60. (4) In females, apoB levels peaked twice, between 20-49 yrs and again after age 59 y. (5) There was a reasonably high correlation between apoB and LDL-C (r=0.87) similar in Ms & Fs. (6)There was a high correlation between apoB and non-HDL-C (r=0.92), similar in Ms & Fs. (7) By MVA, female sex, hormone use and black race were independently & inversely asst'd with apo B whereas BMI and current and past cigarette smoking were independently & directly related to apo B concentrations.	Norms for apo A1 and apo B from ~12,000 individuals > 4 yrs of age are provided. Age, gender & race-related differences are reported. Correlations with other CV RFs are similar for apo B and LDL, and for apo A1 and HDL.

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9439456	Bachorik PS	Apolipoprotein B and AI distributions in the United States, 1988–1991: results of the National Health and Nutrition Examination Survey III (NHANES III)	1997																	**APO A1:** (1) There were no significant differences in apoA1 based on fasting state. (2) ApoA1 levels were significantly higher in Fs. (3) ApoA1 levels in B males & females were significantly higher than in Ws & M-As. (4) For age, median apoA1 concentrations in Ms remained essentially constant with age except for 6-11y olds where they were significantly higher. (5) Median apoA1 levels in Fs increased with age until age 50. (6) The correlation between apoA1 and HDL was 0.74 in Ms and 0.78 in Fs. (7) By MVA, age, female sex, B race, alcohol consumption & yrs of education correlated independently & directly with apo A1. BMI & current cigarette smoking were independently & inversely asst'd with apo A1.	
16614318	Juonala M	Young adults with family history of coronary heart disease have increased arterial vulnerability to metabolic risk factors: the Cardiovascular Risk in Young Finns Study	2006	Cohort	Prospective	Young Finns	Multiple	Q3(RF1)	Finland	Community(other)	Correlate family history of coronary disease with subclinical measures of atherosclerosis	3596/2265	Pediatric/ Young adults	All participants in the 1990 C-V Risk in Young Finns study who were re-examined in 2001 at 24-39 y of age.	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, coronary calcium and FMD.	N/A	N/A	21 yr	Fam hx of CHD by questionnaire in 2001 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	Subjects with (+) fam hx of CHD were older (p=S*) and had higher TGs in childhood(p=S*) and higher LDL(p=S**), apoB (p=S*) and apoB/apoA1 ratios(p=S*) in adulthood Subjects with a positive family history of coronary disease had greater IMT compared with those with negative family history (0.600+/-0.006 vs. 0.578 +/-0.002, p=S*after age & sex adjustment). No differences were observed with CAC or FMD. Difference in IMT persisted after adjustment for current risk factors or childhood RFs measured 21 yr earlier. Analysis of associations between RFs & cIMT separately in subjects with (+) & (-) fam hx revealed significant associations for lower HDL,higher TGs & higher FG in the fam hx (+) group but not in the fam hx (-) group. cIMT was associated with (+) metS dx in both groups but significance was greater for the (+) fam hx group. By MVA, independent determinants of cIMT were WC(p=S**), SBP (p=S**), age (p=S**),the interaction term family risk-MetS (p=S*) & smoking (p=S).	Young adults with (+) fam hx of CHD have increased cIMT, not fully explained by current or childhood RFs. Metabolic RFs(low HDL, highTGs, high FG & NCEP MetS components) clustered together and their effects were stronger among those with (+) fam hx.