NHLBI Evidence Table: RF5-RCT

PMID	First Author	Title	Year	Study Type	CVD	RF by CQ	Country	Setting	Int Length	Total Study Duration	Main Study Objective	Total N	Target Population	Eligibility Criteria	Patient Characteristics	Int. n at Baseline (n at Final Follow-up)	Int Type	Specific Intervention	Control n at Baseline (n at Final Follow-up)	Specific Control	Outcomes Measured	Results/CI	Significance S (p<0.05 or non-overlapping CI); S* (p<0.01); S** (p<0.001); NS (p≥0.05 or overlapping CI)	Safety and Adverse Events	Additional findings	Summary	Main Reported Findings by Critical Question
1619204	Jacques H	Influence of diets containing cow's milk or soy protein beverage on plasma lipids in children with familial hypercholesterolemia	1992	RCT (crossover)	None	Q10 (RF5)	Canada	Clinical	4 wk	18 wk Includes 6 wk stabilization phase and 4 wk washout phase	Examine the effects of diets containing either cow's milk or soy protein beverage on plasma lipids and lipoproteins in children with FH	10	Pediatric/ Young Adults	6-12 yr HeFH	Boys: 6	10 (NR)	Behavioral	Intervention: Diet containing soy protein beverage (SOY) Diet contained 20%E as protein, of which 35% was replaced by protein from soy protein beverage	10 (NR)	Control: Diet containing cow's milk (COW) Diet contained 20%E as protein, of which 35% was replaced by protein from cow's milk	**Primary:** TC mmol/L TG mmol/L Phospholipids mmol/L VLDL-C LDL-C HDL-C HDL2-C HDL3-C	**Primary:** No difference between groups SOY: 0.80(0.08) vs COW: 1.02(0.11) No difference between groups SOY: 0.35(0.04) vs COW: 0.45(0.05) No difference between groups SOY: 1.20(0.07) vs COW: 1.15(0.06) No difference between groups SOY: 0.66(0.02) vs COW: 0.60(0.03)	**NS** **S** **NS** **S** **NS** **S** **NS** **S**	No differences in growth by physical growth charts. No significant differences were observed in body weight, height, or body mass index between the two diet groups.	None	In a small study of 6-12 yr old children, short term replacement of cow's milk with soy beverage had no effect on TC or LDL-C but those on soy milk had significantly lower TG and VLDL-C and higher HDL-C and HDL3-C.	Q10. VLDL-C and triglycerides can be lowered by soy milk substitution for cow's milk and HDL-C and HDL-3-C can be increased. There is no effect on LDL-C.
2058593	Laurin D	Effects of a soy-protein beverage on plasma lipoproteins in children with familial hypercholesterolemia	1991	RCT (crossover)	None	Q10 (RF5, RF9)	Canada	Mult settings	4 wk	12 wk Includes 4 wk washout period	Determine the effects of soy protein given as a beverage and those of cow-milk proteins on plasma lipoprotein concentrations in children with FH	10	Pediatric/ Young Adults	6-12 yr HeFH Hypercholesterolemia in at least 2 first-degree relatives Tendinous anthomas or type II-A lipoprotein pattern in 3 generations of relatives Exclusions: Fasting hyperchylomicronemia or type III hyperlipoproteinemia Recent history of weight loss (within 6 mo) Acute disease or major surgery in past 3 mo	Mean age (SE): 8 yr (1) Boys: 6	10 (9)	Behavioral	Intervention: Soy-beverage + diet Beverage formulated to provide similar amounts of protein, CHO, fat, calcium, and phosphorus as 2% cow milk and minimum of 20% of US recommended dietary allowances of 16 other vitamins and minerals (per 250-mL serving) Diet consisted of rotating menu for 5-7 d developed to reflect food preferences and energy intake reported by children and parents in diet history and in 3 d food intake diary Daily dietary intakes ensured approx. 20% energy from protein; about 1/3 (35%) of this protein energy consumed as dairy source	10 (9)	Control: Cow-milk + diet Diet consisted of rotating menu for 5-7 d developed to reflect food preferences and energy intake reported by children and parents in diet history and in 3 d food intake diary Daily dietary intakes ensured approx. 20%E from protein; about 1/3 (35%) of this protein energy consumed as dairy source	**Primary:** Mean HDL-C [mmol/L (SE)] Mean TG [mmol/L (SE)] Mean VLDL-C [mmol/L (SE)] Mean TC [mmol/L (SE)] Mean apo A-I [g/L (SE)] Mean apo B [g/L (SE)] Mean LDL-C [mmol/L (SE)]	**Primary:** INT: 1.15(0.06) to 1.20(0.07) CON: 1.11(0.07) to 1.15(0.06) INT: 0.99(0.09) to 0.80(0.08) CON: 0.96(0.11) to 1.02(0.11) INT: 0.44(0.04) to 0.35(0.04) CON: 0.42(0.05) to 0.45(0.05) No significant difference between groups for any of these measures.	**S between groups post intervention.** **S between groups post intervention.** **S between groups post intervention.**	Not reported.	Dietary components were maintained at equivalent levels in the 2 groups. Short term trial.	In children with FH, a month long substitution of soy-protein milk for cow's milk resulted in lower levels in TG and VLDL and higher levels of HDL.	Q10,13. In children with FH, a month long substitution of soy-protein milk for cow's milk resulted in lower levels in TG and VLDL and higher levels of HDL.
3882058	Wheeler KA	Double blind trial of bezafibrate in familial hypercholesterolaemia	1985	RCT (crossover)	None	Q10 (RF5)	NR	Clinical	3 mo	6 mo	Assess the efficacy of bezafibrate in children with FH	14	Pediatric/ Young Adults	HeFH Prior treatment by dietary measures (low saturated fat and increased polyunsaturated fat) had proven inadequate and children given cholestyramine for variable periods before refusing to take the drug All children had stopped taking any hypolipidaemic drugs at least 3 mo before entry into the trial	4-15 yr Boys: 6	14(14)	Pharmacologic	Intervention: Bezafibrate 10-20 mg/kg/d bid During the trial period patients were asked not to change their routine diets	14 (14)	Control: Placebo During the trial period patients were asked not to change their routine diets	**Primary:** Efficacy: TC mmol/L HDL-C mmol/L TG mmol/L	**Primary:** Efficacy -22% Bezaf vs placebo +15% Bezaf vs placebo -23% Bezaf vs placebo	**S** **S** **NS**	Growth was satisfactory and there were no reported side effects. One child had a transient increase in alkaline phosphatase and another a slight transient rise in alanine transaminase on bezafibrate.	All except one patient were excreting bezafibrate in all samples of urine analyzed during the active drug period.	Bezafibrate produced a significant reduction of 22% in TC and a significant increase of 15% in HDL-C; TG also fell 22% on bezafibrate but were NS.No major side effects were detected.	Q10 RF5 Bezafibrate treatment produced a significant reduction of 22% in TC and a significant increase of 15% in HDL-C; TG also fell 22% on bezafibrate but this was not significant. No major side effects were detected.
7595101	Gylling H	Sitostanol ester margarine in dietary treatment of children with familial hypercholesterolemia	1995	RCT (crossover)	None	Q10 (RF5) Q13 (RF8, RF9)	Finland	Clinical	6 wk	12 wk	Study the effects of sitostanol ester margarine in dietary treatment of children with FH	14	Pediatric/ Young Adults	FH	Mean age (SE): 9.1 yr (1.1) Boys: 7	14 (14)	Dietary Supplements	Intervention: Margarine + sitostanol ester Children had 24 g of their normal daily fat intake replaced by the same amount of a rapeseed oil-rich margarine with sitostanol (3 g/d) ester Sitostanol was a sterol mixture containing 81% sitostanol, 7% campestanol, 10% sitosterol, and 2% campesterol Children and their families had been advised to use a low animal fat-low cholesterol diet for years	14 (14)	Control: Margarine Children had 24 g of their normal daily fat intake replaced by the same amount of a rapeseed oil-rich margarine without sitostanol ester Children and their families had been advised to use a low animal fat-low cholesterol diet for years	**Primary:** Per cent change in mean TC [%] Per cent change in mean VLDL-C [%] Per cent change in mean LDL-C [%] Per cent change in mean HDL-C [%] Per cent change in HDL/LDL ratio [%] Per cent change in mean TG [%] Per cent change in mean phospholipids [%]	**Primary:** -10.6% -3.8% -25.9% -15.0% +26.8%. -10.7% -7.0% **Secondary:** There were significant changes in on-cholesterol sterol proportions in the serum, with increased deltat-cholesterol, lathosterol, desmosterol, & reduced cholestanol, campesterol and sitosterol, suggesting that cholesterol absorption was decreased and synthesis increased. Relationships between changes in lipid values and changes in sterol proportions explored: high basal levels of precursor sterol proportions predicted a greater decrease in LDL levels.	**S** **NS** **S** **NS** **S** **NS** **S**	Not reported. No washout period.	Significant changes in on-sitostanol sterol proportions in the serum, with increased deltat8-cholesterol, lathosterol, desmosterol, & reduced cholestanol, campesterol and sitosterol, suggesting that cholesterol absorption was decreased and synthesis increased. High basal levels of precursor sterol proportions predicted a greater decrease in LDL levels.	Partial replacement of dietary fat consumption by sitostanol ester margarine appears to be effective in reducing TC, LDL-C and IDL levels.	Q10,13. Partial replacement of dietary fat consumption by sitostanol ester margarine appears to be effective in reducing TC, LDL-C and IDL levels.
7606644	Hardman AE	Walking during the postprandial period decreases alimentary lipaemia	1995	RCT (crossover)	None	Q6 (RF2, RF5) Q13 (RF5, RF9, RF11)	United Kingdom	Clinical	6 hr	9 d Includes 2 d of food intake recording prior to 1st phase and 7 d between phases	Examine the effect of a single period of low-intensity walking on alimentary lipaemia	12	Pediatric/ Young adults	Normolipidemic Regular participation in recreational physical activity Non-smokers	Mean age (SEM): Women: 24.7 yr (1.4) Men: 27.2 yr (1.6) Men: 6	12 (12)	Behavioral	Intervention: High-fat meal + exercise High-fat meal followed by resting for 1.5 h, walking for 1.5 hr on a treadmill at 40% maximal oxygen uptake, and then resting for 3.0 hr	12 (12)	Control: High-fat meal + rest High fat meal followed by 6 hr resting period	**Primary:** Triacylglycerol time curve **Secondary:** Mean fasting triacylglycerol [mmol/L (SEM)] Mean HDL-C [mmol/L (SEM)] Mean apo-AI [g/L (SEM)] Mean apo-B [g/L (SEM)] Mean TC [mmol/L (SEM)]	**Primary:** Area under the curve was significantly lower at 3-6 hrs and overall 0-6 hours post prandially (3.22[0.48] vs 4.48[0.62]) for the exercise vs. control group. **Secondary:** No significant differences in glucose, total cholesterol, HDL or HDL-2 levels or apoB. Higher apoAI levels at 2 hours and lower insulin levels at 3 and 6 hours in the exercise group - results shown only as figures.	**S**	Not reported.	Study is in young adults.	In young adults, prolonged walking (90 minutes) after a fatty meal attenuates post-prandial lipemia.	In young adults, prolonged walking (90 minutes) after a fatty meal attenuates post-prandial lipemia.
7665996	Mize CE	Lipoprotein-cholesterol responses in healthy infants fed defined diets from ages 1 to 12 months: comparison of diets predominant in oleic acid versus linoleic acid, with parallel observations in infants fed a human milk-based diet	1995	RCT	None	Q13 (RF5)	USA	Home	1 yr	1 yr	Compare effects of 2 different types of predefined unsaturated fatty acids in vegetable oil-based formulas, monosaturated and polyunsaturated, on the concentrations of lipoprotein lipids in plasma in 2 groups of infants	67	Pediatric/ Young Adults	Exclusions: Infants from families with a self-reported history of early heart attack or known cholesterol levels	Males: 30	42 (39) Arm 1: 20 (19) Arm 2: 22 (20)	Dietary Supplements	Arm 1: Formula high in MUFA Arm 2: Formula high in PUFA Both formulas contained 48% of total calories as fat, 9% as protein, and the remaining as CHO All infants received 109 to 120 kcal/kg/d and 2.4 to 2.9 g protein/kg/d. Total intakes were increased as a function of increasing age Composition of solid food diets was progressively adjusted to age 12 mo to maintain a relative fatty acid composition similar to that of the initial formula	25 (23)	Control Arm: Human milk Control Arm was not randomized After weaning at mean age of 6.2 mo, infants received a mixed diet resembling human milk both in general nutrient and fatty acid composition, as well as TC content (100-140 mg/d)	**Primary:** Mean TC [mg/dL (SD)] Mean LDL-C [mg/dL (SD)] Mean HDL-C [mg/dL (SD)] Mean TG [mg/dL (SD)]	**Primary:** **Hi-Mono Hi-Poly Breast Fed** 4m 136(30) 135(19) 164(33) 9m 147(18) 139(20) 158(24) 12m 156(31´) 128(20) 156(30) 4m 72(22) 77(14) 100(34) 9m 88(20) 84(25) 98(24) 12m 98(24´) 79(16) 96(28) 4m 50(12) 46(10) 50(13) 9m 43(10) 39(10) 45(8) 12m 44(10´) 35(8) 42(11) 4m 169(67) 97(60) 129(93) 9m 102(50) 114(79) 107(58) 12m 98(24) 35(8) 151(108)	**BF vs both other groups: S** **BF vs HiPoly: S** **BF & HiMono vs HiPoly: S** **BF vs both other groups: S** **NS between groups** **BF & HiMono vs HiPoly: S** **NS between groups** **NS between groups** **S between HiMono & HiPoly** **S between HiMono & HiPoly**	Not reported	TG tended to be lower in the high poly unsaturated fat diet group throughout but differences were not significant.	In infants, a high poly unsaturated fat diet for 12 mos resulted in significantly lower TC and LDL-C than a high monounsaturated fat diet or breast feeding. The high poly unsaturated fat diet also resulted in lower HDL than the high monounsaturated fat diet but did not differ significantly from the breast fed group.	Q10,13.In infants, a high poly unsaturated fat diet for 12 mos resulted in significantly lower TC and LDL-C than a high monounsaturated fat diet or breast feeding. The high poly unsaturated fat diet also resulted in lower HDL than the high monounsaturated fat diet but did not differ significantly from the breast fed group.
7706601	Agostoni C	Effects of diet on the lipid and fatty acid status of full-term infants at 4 months	1994	RCT	None	Q10,13 (RF5)	Italy	Clinical	4 mo	4 mo	Compare the effects of the exogenous supply of LC-PUFA and cholesterol on the lipid and fatty acid status in full-term, 4-mo old infants	44	Pediatric/ Young Adults	Infants	Mean gestational age (SD): Arm 1: 38.9 wk (1.5) Control Arm: 39.3 wk (1.4) Males: Arm 1: 11 Control Arm: 14	21 (NR)	Dietary Supplements	Arm 1: Formula enriched with a mixture of LC-PUFA and cholesterol (LCP) No infants were given any supplementary food during the study period except on medical advice 15 infants that were breastfed exclusively from the first day of life up to 4 mo were included as a reference group (BF)	23 (NR)	Control Arm: Standard infant formula (STD) No infants were given any supplementary food during the study period except on medical advice	**Primary:** Mean TC [mg/dL (SD)] Mean LDL-C [mg/dL (SD)] Mean HDL-C [mg/dL (SD)] Mean TG [mg/dL (SD)] **Secondary:** Fatty acid composition of erythrocyte phospholipids	**Primary: 4 mos** **LCP STD BF** Male 149(17) 142(22) 136(10) Female 171(35) 159(30) 184(51) Male 75(14) 66(23) 80(10) Female 99(36) 84(24) 101(47) Male 54(14) 50(8) 35(3) Female 48(12) 48(14) 51(13) Male 100(58) 125(51) 106(21) Female 117(58) 132(100) 162(99) **Secondary:** In the STD grp, levels of fatty acid derived from LCP were less than 50%of LCP & BF grps.	**NS between groups** **S*, females vs males** **NS between groups** **S*, females vs males** **NS between groups** **NS between sexes** **NS between groups** **NS between sexes** **S****	No differences in growth parameters other adverse events not reported	Female infants had significantly higher TC and LDL-C levels than males in all 3 feeding groups.	In newborns, a formula supplemented with long chain polyunsaturated fatty acids achieved erythrocyte fatty acid status similar to that of breast fed infants. There were no significant differences in serum lipids.	RF10,13. In newborns, a formula supplemented with long chain polyunsaturated fatty acids achieved erythrocyte fatty acid status similar to that of breast fed infants. There were no significant differences in serum lipids.
7723156	[No authors listed]	Efficacy and safety of lowering dietary intake of fat and cholesterol in children with elevated low-density lipoprotein cholesterol. The Dietary Intervention Study in Children (DISC). The Writing Group for the DISC Collaborative Research Group.	1995	RCT	None	Q10 (RF5)	USA	Clinical	3 yr	3 yr	Assess the efficacy and safety of lowering dietary intake of total fat, saturated fat, and cholesterol to decrease LDL-C levels in children	663	Pediatric/ Young Adults	8-10 yr Prepubertal LDL-C levels greater than or equal to the 80th and less than the 98th percentiles for age and sex	Boys: 362 Girls: 301	334	Behavioral	Arm 1: Behavioral intervention to promote adherence to a diet providing 28% of energy from total fat, less than 8% from saturated fat, up to 9% from polyunsaturated fat, and less than 75 mg/4200 kJ (1000 kcal) per day of cholesterol (not to exceed 150 mg/d)	329	Control arm: Usual care	**Primary:** Mean serum LDL-C [mg/dL(SD)] Mean serum total cholesterol [mg/dL(SD)] Mean serim HDL-C [mg/dL(SD)] Mean serum triglycerides [mg/dL(SD)] **Secondary:** Dietary total fat [% of energy(SD)] Dietary saturated fat [% of energy(SD)] Dietary cholesterol (mg/kJ) Polyunsaturated fat [% of energy(SD)] Protein [% of energy(SD)] Carbohydrate [% of energy(SD)] Energy [kJ(SD)]	**Primary: (At 3 yrs)** INT: 130.6(12.2) to 115.3(18.7) CON: 130.5(11.6) to 118.6(19.4) INT: 200.0(14.6) to 183.3(21.5) CON: 200.0(14.6) to 186.4(22.3) No change from B/L; no difference between groups No change from B/L; no difference between groups **Secondary:** INT: 33.4(5.5) to 28.6(5.8);CON:34.0(4.9) to 33.0(4.7) INT: 12.5(2.7) to 10.2(2.6); CON:12.7(2.5) to 12.3(2.2) INT: 0.028(0.013) to 0.0-23(0.011) CON: 0.027(0.013) to 0.027(0.011) INT: 5.7(1.5) to 5.5(1.9); CON: 6.0(1.6) to 5.9(1.8) INT: 14.8(2.8) to 16.0(3.5); CON: 14.6(2.7) to 15.1(3.0) INT:53.0(6.7) to 56.2(6.8); CON:52.8(6.2) to 52.9(6.3) INT: 7364(1832) tyo 7220(2042) CON: 7229(1841) to 7822(2207)	**S** **S** **NS** **NS** **S**** **S**** **S**** **S** **S**** **S**** **S****	No significant differences between the groups in adjusted mean height or serum ferritin levels or other safety outcomes		A low fat, low saturated fat and reduced cholesterol diet modestly but significantly decreased total and LDL-C levels in hypercholesterolemic children with no adverse effects.	Q10: In hypercholesterolemic children, a low fat, low saturated fat and reduced cholesterol diet achieved modest lowering of LDL-C levels over 3 years while maintaining adequate growth, iron stores and nutritional adequacy during the critical growth period of adolescence.

NHLBI Evidence Table: RF5-RCT

PMID	First Author	Title	Year	Study Type	CVD	RF by CQ	Country	Setting	Int Length	Total Study Duration	Main Study Objective	Total N	Target Population	Eligibility Criteria	Patient Characteristics	Int. n at Baseline (n at Final Follow-up)	Int Type	Specific Intervention	Control n at Baseline (n at Final Follow-up)	Specific Control	Outcomes Measured	Results/CI	Significance S (p<0.05 or non-overlapping CI); S* (p<0.01); S** (p<0.001); NS (p≥0.05 or overlapping CI)	Safety and Adverse Events	Additional findings	Summary	Main Reported Findings by Critical Question
7971012	Shannon BM	Reduction of elevated LDL-cholesterol levels of 4- to 10-year-old children through home-based dietary education	1994	RCT	None	Q10 (RF5) Q13 (RF9)	USA	Mult settings	3 mo	3 mo	Assess the effects of a home-based, parent-child autotutorial (PCAT) dietary education program on the dietary knowledge, lipid consumption, and LDL-C of 4-10 yr old children with elevated plasma LDL-C	352	Parental/ Family/ Caregiver	3.9-9.9 yr Plasma TC levels > 4.55 mmol/L No history of diseases that would explain hypercholesterolemia Body weight ≥ 85% but not > 130% of ideal body weight Mean fasting plasma LDL-C for boys between 2.77 mmol/L and 4.24 mmol/L Mean fasting plasma LDL-C for girls between 2.90 mmol/L and 4.24 mmol/L Children receiving care in suburban Philadelphia clinics	Mean age (SE): Arm 1: 6.3 yr (0.19) Arm 2: 6.2 yr (0.19) Control Arm: 6.4 yr (0.19) Males: Arm 1: 43 Arm 2: 43 Control Arm: 45 White: Arm 1: 77 Arm 2: 77 Control Arm: 73 African-American: Arm 1: 9 Arm 2: 7 Control Arm: 10	Arm 1: 92 (75) Arm 2: 90 (78)	Behavioral	Arm 1: PCAT program Included 10 talking-book lessons and follow-up paper-pencil games for children along with a manual for parents No dietary instruction Arm 2: Counseling program Received 45-60 min counseling session with a registered dietician and take-home materials for children and parents Study dietician was available via telephone to answer questions	87 (NR)		**Primary:** LDL-C mg/dL PCAT vs At-Risk Control PCAT vs Counseling Knowledge Scores (%) PCAT vs At-risk control PCAT vs Counseling Dietary Intake Total Fat PCAT vs At-Risk Control PCAT vs Counseling Saturated Fat PCAT vs At-Risk Control PCAT vs Counseling Cholesterol PCAT vs At-Risk Control PCAT vs Counseling Total Calories PCAT vs At-Risk Control PCAT vs Counseling	**Primary:** LDL-C mg/dL -10.1 vs -3.4 -10.1 vs -4.1 Knowledge Scores (%) +29.4 vs +8.2 +29.4 vs +8.2 Dietary Intake Total Fat (g) -4.5 vs +4.0 -4.5 vs -4.8 Saturated Fat (g) -2.2 vs +1.6 -2.2 vs -2.6 Cholesterol (mg) -23.3 vs + 6.6 -23.3 vs -24.4 Total Calories -58.8 vs +56.7 -58.8 vs -43.1	**S** **NS** **S** **S** **S** **NS** **S** **NS** **NS** **NS** **S** **NS**	None reported Not part of study design	Of the 3,667 children who were screened, 997 tested positive, i.e., had a total cholesterol level > 176 mg/dL. This is the approximate 75th%. Of the 924 who met eligibility criteria, 458 agreed to participate, of whom 271 confirmed positive (LDL-C between 107 and 164 mg/dL for boys, and between 112 and 164 mg/dL for girls.	At risk children with high normal LDL-C who were given home-based dietary education had significantly better LDL-C reduction, decreased total fat, saturated fat, total calories and improved dietary knowledge scores than a control at-risk group with similar B/L levels. Those who received individual dietary counseling session did as well as the home-based group in all the primary endpoints with the exception of dietary knowledge scores, which were significantly better in the home based group.	Q 10,13 Low fat diet implement through home-based training or RD counseling reduces LDL-C in 4-10 yr old children with high normal baseline LDL-C.
8018689	McGowan MP	Intervention in hypercholesterolemic college students: a pilot study	1994	RCT	None	Q10 (RF5) Q13 (RF4, RF8, RF9)	USA	Clinical	7 wk	8 mo	Test the effectiveness of a health education intervention in hypercholesterolemic college students	39	Pediatric/ Young Adults	University students Average LDL-C ≥ 75th percentile (2.84 mmol/L) in 2 samples after overnight fast	Mean age (SD): Arm 1: 18.6 yr (0.7) Control Arm: 18.6 yr (0.7) Male: Arm 1: 70% Control Arm: 42% White: Arm 1: 60% Control Arm: 74% Smoking: Arm 1: 10% Control Arm: 10% Family history of: High cholesterol: Arm 1: 70% Control Arm: 89% Heart attack before 55 yr: Arm 1: 35% Control Arm: 17% Stroke: Arm 1: 5% Control Arm: 11% Hypertension: Arm 1: 50% Control Arm: 89%	20 (NR)	Behavioral	Arm 1: 7-session course Course included lectures and small group discussions focusing on nutrition, cholesterol, saturated fat, as well as tastings of low-fat food and behavioral modification techniques (e.g., role playing, pre-meal menu review)	19 (NR)	Control Arm: 30-min lecture on diet and nutrition + 30-min video about cholesterol and saturated fat	**Primary:** Nutritional knowledge [score(SD)] Heart healthy attitude [score(SD)] Mean LDL-C (mmol/L) **Secondary:** Mean TC (mmol/L) Mean HDL-C (mmol/L) Mean TG (mmol/L) Mean BMI [kg/m2 (SD)] Mean weight [kg (SD)] Mean SBP [mmHg (SD)] Mean DBP [mmHg (SD)]	**Primary:** INT: 19.6(5.6) to 26.9(5.2) *vs* CON: 17.0(6.6) to 20.0(3.5) INT: 47.3(2.8) to 50.2(3.3) vs CON:48.0(5.0) to 49.4(3.0) **B/L** **8w** **8m** INT 3.39(0.52) 3.18(0.46) 3.41(0.62) CON 3.34(0.44) 3.26(0.49) 3.67(0.75) **Secondary:** No significant difference between groups over time for any of these variable.	**S**** **NS(p=0.11)** **S between groups at 8m.**	Not reported.	Of note, both groups increased alcohol consumption and decreased activity levels during the intervention period.	In college age students, a healthy lifestyle educational intervention may have some benefit in terms of LDL lowering particularly in those with higher levels.	Q13. In college age students, a healthy lifestyle educational intervention may have some benefit in terms of LDL lowering particularly in those with higher levels.
8391569	Dennison BA	Randomized, double-blind, placebo-controlled, two-period crossover clinical trial of psyllium fiber in children with hypercholesterolemia	1993	RCT (crossover)	None	Q10 (RF5, RF9)	USA	Clinical	4-5 wk	12 wk Includes a 2 wk washout phase	Test the efficacy of psyllium fiber in lowering elevated LDL-C levels in children	25	Pediatric/ Young Adults	5-17 yr LDL-C levels > 2.84 mmol/L (110 mg/dL) Completion of at least 3 mo of a diet consisting of < 30% calories as total fat, < 10% calories as saturated fat, and < 200 mg dietary cholesterol per day Exclusions: Hyperlipidemia with a secondary cause	Mean age (SD): Completed study: 11.1 yr (3.8) Did not complete study: 12.9 yr (4.0) Males: Completed study: 11 Did not complete study: 1	25 (20)	Dietary Supplements	Intervention: Cereal containing 3 g water-insoluble fiber and 3 g water-soluble fiber per serving All children were instructed to eat 2 28 g servings of cereal/d All patients continued to follow the same low fat, low saturated fat, low cholesterol diet from the period before randomization	25 (20)	Control: Cereal containing 5 g water-insoluble wheat fiber per serving All children were instructed to eat 2 28 g servings of cereal/d All patients continued to follow the same low fat, low saturated fat, low cholesterol diet from the period before randomization	**Primary:** Efficacy: LDL-C mmol/L Safety: Growth (height, weight, skin folds) **Secondary:** Efficacy: TC mmol/L HDL-C mmol/L TG mmol/L TC/HDL-C LDL-C/HDL-C Safety Folic acid Fat soluble vitamins A D E	**Primary:** No difference No difference **Secondary:** No difference No difference + 0.68 (26 mg/dL) CON cereal No difference No difference No difference No difference No difference	**NS** **NS** **NS** **S** **NS** **NS** **NS** **NS** **NS**	No difference in growth, folate, fat soluble vitamins or minerals. Transient increase in stool frequency in one child on control cereal	None	In 5-17 yr olds, psyllium supplements did not influence lipids, lipoproteins growth, vitamin or mineral levels in a short term study	Q 10 RF 5 Dietary psyllium supplementation had no effect on serum lipids.
8391569	Dennison BA	Randomized, double-blind, placebo-controlled, two-period crossover clinical trial of psyllium fiber in children with hypercholesterolemia	1993																		Mineral levels Iron Zinc Calcium	No difference No difference No difference	**NS** **NS** **NS**				
8483855	Kuehl KS	Effective control of hypercholesterolemia in children with dietary interventions based in pediatric practice	1993	RCT	None	Q10,13 (RF5, RF9)	USA	Clinical	Arm 1: 90-min session Arm 2: 4 90-min sessions over 8 wk	Arm 1: 21 wk Arm 2: 33 wk Includes time from baseline to follow-up interval 1 (intended to take place at 8 wk) to follow-up interval 2 (intended to take place at wk 16)	Evaluate effectiveness of 2 programs of office-based nutritional education therapy	295	Parental/ Family/ Caregiver	TC ≥ 185 mg/dL	Mean age: 7 yr	295 (215) Arm 1: 167 (108) Arm 2: 128 (107)	Behavioral	Arm 1: 90-min session of family oriented nutritional education (SSI) Slide presentation with participant interaction; children prepared low-fat recipe while parents received further information; tasted recipe and low-fat snack foods; distributed fruit and cereal to reinforce starting low-fat diet immediately Arm 2: 4 90-min nutritional education sessions (MSI) Food preparation for breakfast, snacks, lunch and dinner; received notebooks with nutritional information and recipes and incentive awards for attendance and completion of behavioral contracts (eating low-fat meals)	NA	N/A	**Primary:** Mean total & sat fat intake [%E (SEM)] Mean cholesterol intake [mg/d (SEM)] Mean TC [mg/dL (SEM)] Mean HDL-C [mg/dL (SEM)] Mean LDL-C [mg/dL (SEM)] Mean TG (mg/dL (SEM)] **Secondary:** Mean total calories (SEM) Mean protein intake [%E (SEM)] Mean iron intake [% RDA (SEM)] Mean calcium intake [% RDA (SEM)] Mean weight [lb]	**Primary:** At early F/U, both groups had decreased total & sat fat intake from baseline and sustained this to late F/U. At early F/U, both groups had decreased cholesterol intake from baseline, not sustained at late F/U. **B/L** **Early F/U** **Late F/U** MSI 207.9(3.2) 191.6(3.6) 193.2(3.0) SSI 206.1(3.3) 194.4(3.6) 198.5(3.3) MSI 53.7(1.4) 50.1(1.7) 51.6(1.4) MSI: 137.0(3.6) 123.6(3.5) 124.9(3.3) MSI: 88.5(6.8) 87.9(6.0) 83.5(5.1) **Secondary:** Decreased from baseline in both groups Increased from baseline in both groups No change from baseline in either group. No change from baseline in either group. No difference between groups	**S** for MSI, S* for SSI** **S* for MSI at early F/U, S for SSI.** **NS for both at late F/U.** **S**, B/L to early F/U in both groups** **S** for MSI, S* for SSI, B/L to late F/U** **NS from B/L** **S**, B/L to early F/U; S*, B/L to late F/U.** **NS from B/L** **S from B/L for both groups.** **S from B/L for both groups.** **NS** **NS** **NS**	None reported	Significant drop-out(35%) in the single intervention session group with no intention-to-treat analysis.	A family-based intervention in pediatrician's offices to lower fat and cholesterol intake in hypercholesterolemic children was successful at 4 month follow-up in sustaining diet change and change in plasma lipids whether a single session or multiple sessions of diet training were provided.	Q10: A family-based intervention in pediatrician's offices to lower fat and cholesterol intake in hypercholesterolemic children was successful at 4 month follow-up in sustaining diet change and change in plasma lipids whether a single session or multiple sessions of diet training were provided.
8586774	Williams CL	Soluble fiber enhances the hypocholesterolemic effect of the Step I diet in childhood	1995	RCT	None	Q10 (RF5, RF9)	USA	Mult settings	12 wk	12 wk	Test the effectiveness of psyllium in lowering TC and LDL-C in children with borderline high and high blood cholesterol levels	58	Parental/ Family/ Caregiver	2-11 yr Serum cholesterol > 170 mg/dL LDL-C > 110 mg/dL Exclusions: Significant medical problems	Mean age (SD): Arm 1: 82.6 mo (30.1) Control Arm: 94.7 mo (26.7) Parent with premature onset of coronary heart disease defined as onset before 55 yr: 5% Grandparent with premature onset of coronary heart disease defined as onset before 55 yr: 52%	NR (26)	Dietary Supplements	Arm 1: Diet + psyllium-enriched cereal (3.2 g soluble fiber) Step 1 diet consists of reducing intake of saturated fat < 10% of calories, maintaining protein intake, and increasing intake of complex CHO; cereal enriched with 3.2 g soluble fiber (psyllium) Participants attended group nutrition counseling sessions that emphasized Step 1 diet; parents kept food diaries for children	NR (24)	Control Arm: Diet + placebo cereal Step 1 diet consists of reducing intake of saturated fat < 10% of calories, maintaining protein intake, and increasing intake of complex CHO; cereal contained 0.5 g soluble fiber Participants attended group nutrition counseling sessions that emphasized Step 1 diet; parents kept food diaries for children	**Primary:** Efficacy: % change in LDL-C mmol/L Safety: Growth & Body Fatness **Secondary:** Efficacy % change in TC mmol/L % change in HDL-C mmol/L % change in TG mmol/L % change in TC/HDL-C ratio % change in LDL/HDL ratio	**Primary: (At 12 weeks):** Efficacy: INT: -15.7% vs CON: -6.4% Safety: No difference between groups **Secondary:** Efficacy: INT: - 9.6% vs -5.5% INT: +9.96%vs CON: +3.1% INT: -8.9% vs CON:-15.3% INT: -17.9% vs CON: -4.7% INT: -21.1% vs CON: -7.4%	**S*** **NS** **S** **NS** **NS** **S**** **S****	Safety assessed by growth & body fatness (no difference) and AE (limited to mild upset stomach or gas)	None	In hypercholesterolemic children aged 2-11 yrs, modest amounts of psyllium fiber supplementation produced significantly greater decreases in total and LDL-C when compared with diet alone. HDL and TG did not change significantly. There were no differences in growth or body fatness.	Q10 In hypercholesterolemic children aged 2-11 yrs, modest amounts of psyllium fiber supplementation produced significantly greater decreases in total and LDL-C when compared with diet alone. HDL and TG did not change significantly. There were no differences in growth or body fatness.

NHLBI Evidence Table: RF5-RCT

PMID	First Author	Title	Year	Study Type	CVD	RF by CQ	Country	Setting	Int Length	Total Study Duration	Main Study Objective	Total N	Target Population	Eligibility Criteria	Patient Characteristics	Int. n at Baseline (n at Final Follow-up)	Int Type	Specific Intervention	Control n at Baseline (n at Final Follow-up)	Specific Control	Outcomes Measured	Results/CI	Significance S (p<0.05 or non-overlapping CI); S* (p<0.01); S** (p<0.001); NS (p≥0.05 or overlapping CI)	Safety and Adverse Events	Additional findings	Summary	Main Reported Findings by Critical Question
8598593	Luepker RV	Outcomes of a field trial to improve children's dietary patterns and physical activity: The Child and Adolescent Trial for Cardiovascular Health (CATCH)	1996	RCT	None	Q13 (RF4, RF5, RF8, RF9, RF11)	USA	Mult settings	3 school yr	3 school yr	Assess the outcomes of health behavior interventions, focusing on the elementary school environment, classroom curricula, and home programs, for the primary prevention of CVD	5,106 (96 schools)	Parental/ Family/ Caregiver	3rd grade Public schools located in California, Louisiana, Minnesota, and Texas	Mean age: 8.76 yr White: Boys: 1,894 Girls: 1,636 African American: Boys: 313 Girls: 361 Hispanic: Boys: 345 Girls: 363 Other race: Boys: 93 Girls: 101	Arm 1: 28 schools (28 schools) Arm 2: 28 schools (28 schools)	Behavioral	Arm 1: CATCH school-based program CATCH school-based program consisted of the Eat Smart school food service intervention, CATCH physical education (PE) intervention, and the CATCH curricula Eat Smart provided children with meals that were lower in total fat (to 30%E), saturated fat (to 10%E), and sodium (600-1,000 mg/serving) CATCH PE intervention sought to increase the amount of enjoyable MVPA during PE classes at school to 40% of PE class CATCH curricula consisted of 15, 24, and 16 30-40 min lessons during grades 3, 4, and 5, respectively Arm 2: CATCH school-based program + family-based program Home curriculum involved activity packets for children to complete with parents and "family fun nights" during grades 3 and 4	40 schools (40 schools)	Control Arm: Usual food service programs, PE, and health curricula	**Primary:** **School Lunch Menu analysis:** Total energy content [MJ(SE)] Energy from total fat [%(SE)] Energy from saturated fat [%(SE)] Cholesterol content [mg(SEM)] **Physical education classes:** MVPA (% of time) VPA (% of time) Change in 9 min run distance(yards(SE)] **24 hr diet recall:** Change in total energy intake[MJ(SE)] Change in total fat intake[%(SE)] Change in saturated fat intake[%(SE)] Change in polyunsaturated fat intake[%(SE)] Change in carbohydrate intake[%(SEM)]	**Primary:** INT: 3.01(.04) to 2.86(0.04) CON: 2.97(0.04) to 3.12(0.04) INT: 38.7(0.4) to 31.9(0.4);CON:38.9(0.5) to 36.2(0.5) INT: 14.8(0.2) to 12.0(0.2);CON:15.1(0.3) to 13.7(0.3) INT: 77.7(2.0) to 74.9(2.0);CON:80.3(2.4) to 83.2(2.4) INT: 1991(B/L): 38% to 1994: 50% CON: 1991(B/L): 36% to 1994: 42% INT: 1991(B/L): 18% to 1994: 20% CON:1991(B/L): 17% to 1994: 19% INT: +100 yds vs CON: +84 yds INT: +0.14(0.12); CON:+0.60(0.15) INT: -2.3(0.3); CON:-0.5(0.4) INT:-1.1(0.1); CON: -0.4(0.2) INT:-0.1(0.1); CON: +0.3(0.1) INT: +2.2(0.4); CON: +1.0(0.5)	**S** between groups** **S** between groups** **S*** **NS** **S** **S** **NS** **S*** **S**** **S*** **S*** **p=.06**	No differences in growth parameters no other adverse events reported.	Dietary knowledge, dietary intentions and self-reported food choices all significantly improved in intervention schools.	An intensive school-based intervention was successful in decreasing dietary energy from fat and saturated fat and increasing time spent in PE classes in MVPA and VPA. There were no changes in any physiologic measure.	Q10,13. An intensive school-based intervention was successful in decreasing dietary energy from fat and saturated fat and increasing time spent in PE classes in MVPA and VPA. There were no changes in any physiologic measure.
8598593	Luepker RV	Outcomes of a field trial to improve children's dietary patterns and physical activity: The Child and Adolescent Trial for Cardiovascular Health (CATCH)	1996																		Change in cholesterol intake[mg(SE)] **Secondary:** Measures of body size: Ht, Wt, BMI, Triceps skin folds, Subscapular skin folds Physiologic measures: HR, SBP,DBP,TC,HDL-C,apolipoprotein B	INT: -15(6); CON:+5(8) **Secondary:** No difference between groups for any of these measures	**S**			
8604676	Davidson MH	A psyllium-enriched cereal for the treatment of hypercholesterolemia in children: a controlled, double-blind, crossover study	1996	RCT (crossover)	None	Q10 (RF5) Q13 (RF9)	USA	Clinical	6 wk	26 wk Includes 8-wk diet-stabilization period and 6 wk washout period	Investigate the hypocholesterolemic effect of a psyllium-enriched breakfast cereal in children with documented hyperlipidemia	32	Pediatric/ Young Adults	6-18 yr LDL-C concentration > 90th percentile for age and sex Exclusions: Height and weight > 75th percentile Chronic medical conditions, including diabetes Triacylglycerol concentrations > 300 mg/dL	FH: 6 FCH: 16 Polygenic hypercholesterolemia: 3	32 (25)	Dietary Supplements	Intervention: Diet + psyllium-enriched cereal 58 g/d Each serving of psyllium contained 3.2 g soluble fiber. Children were instructed to consume 2 28-g boxes of cereal daily for a total daily dose of 6.4 g soluble fiber from psyllium All children were instructed to follow a low-fat diet based on NCEP Step 1 dietary guidelines for the total study duration; children were counseled about compliance with a low-fat diet by a registered nurse dietitian at each visit	32 (25)	Control: Diet + placebo cereal All children were instructed to follow a low-fat diet based on NCEP Step 1 dietary guidelines for the total study duration; children were counseled about compliance with a low-fat diet by a registered nurse dietitian at each visit	**Primary:** Change in mean LDL levels [mmol/L (SD)] **Secondary:** Change in mean TC [mmol/L (SD)] Change in mean HDL-C [mmol/L (SD)] Change in mean TG [mmol/L (SD)]	**Primary:** INT: -0.28 (0.38) vs. PLAC: 0.0mmol/L(0.29) **Secondary:** INT: -0.31(0.46) vs. PLAC: -0.01(0.36) No significant changes in HDL, triacylglycerols	**S*** **S** **NS**	None reported	No differences regarding dietary composition other than dietary fiber. There were no carry-over effects except for total cholesterol levels.	In children with hypercholesterolemia, psyllium-enriched cereal consumption resulted in a significant decrease in TC and LDL-C.	Q10,13. In children with hypercholesterolemia, psyllium-enriched cereal consumption resulted in a significant decrease in TC and LDL-C.
8628597	Lambert M	Treatment of familial hypercholesterolemia in children and adolescents: effect of lovastatin. Canadian Lovastatin in Children Study Group	1996	RCT	None	Q10 (RF5, RF9)	Canada	Clinical	8 week	12 wk Includes 4 wk placebo period	Determine the efficacy, safety, and tolerance of the short-term use of lovastatin, a 3-hydroxy 3-methylglutaryl coenzyme A reductase inhibitor, in the control of severe FH in a male pediatric population and to evaluate the dose-response relationship	69	Pediatric/ Young Adults	Male Severe FH Plasma LDL-C > 95th percentile for age Maintaining a lipid-lowering diet Positive family history of atherosclerosis at or before age 50 Documented family history of hyperlipidemia Exclusions: Concomitant conditions such as diabetes Weight or height < 3rd or > 97th percentile for age	Mean age (SD): Arm 1: 12.5 yr (2.4) Arm 2: 12.7 yr (1.6) Arm 3: 13.3 yr (2.7) Arm 4: 12.9 yr (2.7) White: Arm 1: 94.1% Arm 2: 100% Arm 3: 94.7% Arm 4: 93.3% No cigarette smoking: Arm 1: 100% Arm 2: 100% Arm 3: 89.5% Arm 4: 100%	Arm 1: 17 (NR) Arm 2: 18 (NR) Arm 3: 19 (NR) Arm 4: 15 (NR)	Multiple Interventions	Arm 1: 10 mg/d lovastatin + diet Arm 2: 20 mg/d lovastatin + diet Arm 3: 30 mg/d lovastatin + diet Arm 4: 40 mg/d lovastatin + diet Diet included fat intake restricted to 30% of total calories, saturated fats restricted to 10% global caloric intake, moderate use of polyunsaturated fats (maximum 10% of total daily caloric intake), and reduced cholesterol intake of < 125 mg/1,000 kcal/d or < 300 mg/d, whichever was less	N/A	N/A	**Primary:** Mean % change in TC (95% CI) Mean % change in LDL-C (95% CI) Mean % change in apo B (95% CI) Mean % change in HDL-C (95% CI) Mean % change in apo A1 (95% CI) Mean % change in TG (95% CI) **Secondary:** Cortisol [nmol/L] DHEAS [umol/L]	**Primary: Week 8** **10 mg 20 mg 30 mg 40 mg** -17(-22,-12) -19(-23,-15) -21(-28,-14) -29(-32,-26) -21(-27,-15) -24(-29,-19) -27(-35,-19) -36(-39,-33) -19(-26,-12) -20(-25,-15) -22(-29,-15) -28(-33,-23) +9(+4,+14) +2(-3,+7) +11(+3,+19) +3(-2,+8) +11(+2,+16) +4(0,+8) +5(0,+10) +1(-4,+6) No differences within or between groups. **Secondary:** No significant differences within or between groups.	**S** at all doses** **S** at all doses** **S** at all doses** **S* at 10 mg,S at 30 mg; NS at 20 & 40 mg** **S at 10 & 20 mg; NS at 30 & 40 mg.** **NS**	CK significantly increased in 3 pts, all in 30 mg dose group - all returned to baseline spontaneously with no interruption in therapy. Mean AST significantly increased in lovastatin groups compared with placebo.	No change in dietary intake between groups. There were trends towards increases in HDL-C and apoA1.	Lovastatin therapy significantly lowers TC, LDL-C and apo-B levels in hypercholesterolemic male adolescents - dose response relationship for 10,20 & 30 mg doses, no additional decrease with 40 mg. No clinically significant AEs.	Q10. Lovastatin therapy significantly lowers TC, LDL-C and apo-B levels in hypercholesterolemic male adolescents
8660081	Tonstad S	Low dose colestipol in adolescents with familial hypercholesterolaemia	1996	RCT	None	Q6 (RF5, RF8) Q10 (RF5) Q13 (RF8)	Norway	Clinical	52 wk Includes 44-52 wk of open treatment	66 wk Includes 6 wk stabilization phase	Examine the effects of orange flavored colestipol granules in children with FH	66	Pediatric/ Young Adults	10-16 yr FH 2 or more TC concentration measurements ≥ 6.2 mmol/L and TG < 3.0 mmol/L	Mean age (SD): Arm 1 & 2 : 12.5 yr (1.5) Control Arm: 13.8 yr (1.6) Boys: 37	33 (29)	Pharmacologic	Arm 1: Diet + colestipol 10 g qd Arm 2: Diet + colestipol 5 g bid All the subjects were instructed to follow a diet containing ≤ 30%E from fat, < 10%E from saturated fat, and < 200 mg/d of cholesterol	33 (30)	Control Arm: Diet + placebo Period 1: Placebo controlled Placebo wk 0-7 Period 2: Open treatment Colestipol 10 g/d wk 8-60 All the subjects were instructed to follow a diet containing ≤ 30%E from fat, < 10%E from saturated fat, and < 200 mg/d cholesterol	**Primary:** Efficacy: LDL mmol/L Safety: Height Velocity **Secondary:** Efficacy TC mmol/L HDL-C mmol/L TG mmol/L ApoB gm/L ApoA-I Safety: Erythrocyte folate(nmol/L) Serum folate(nmol/L) Fat-soluble vitamins Vitamin A(umol/L) 25 OH vitamin D(nmol/L) Vitamin E/TC Carotenoids/TC	**Primary:** Efficacy: -19.5% vs -1.0% Safety: No difference **Secondary** Efficacy -14.2% vs 1.0% No difference +16.2% vs -12.5% -9.0% vs -1.0% No difference Safety: No difference -10.4% vs +18.0% Fat soluble vitamins No difference No difference No difference No difference	**S*** **NS** **S*** **NS** **NS** **S*** **NS** **NS** **S*** **NS** **NS** **NS**	Gastrointestinal side effects (constipation, dyspepsia, flatulence, nausea, abdominal pain) in the course only 1/3 patients adhered completely with the drug. Unpalatability was the major reason. At one year only 2/3 patients were still in the study	At one year 25 OH vitamin D decreased more in the most compliant patients	In hypercholesterolemic adolescents, low dose colestipol lowered LDL-C by almost 20% There were no adverse effects on linear growth velocity or fat soluble vitamins. Folate was decreased significantly.	Q10. In hypercholesterolemic adolescents, low dose colestipol lowered LDL-C by almost 20% There were no adverse effects on linear growth velocity or fat soluble vitamins. Folate was decreased significantly.
8726243	Knipscheer HC	Short-term efficacy and safety of pravastatin in 72 children with familial hypercholesterolemia	1996	RCT	None	Q10 (RF5)	Netherlands	Clinical	12 wk	20 wk Includes 8 wk diet and placebo run-in period	Evaluate the safety, tolerability, and efficacy of a 12 wk treatment with pravastatin	72	Pediatric/ Young Adults	HeFH Hypercholesterolemia present in siblings, parents, or grandparents, or clinical manifestations of premature atherosclerosis present before the age of 50 yr in first or second degree relatives Exclusions: Hepatic or renal dysfunction	Mean age (range): Arm 1: 12.1 yr (8-16) Arm 2: 12.0 yr (8-16) Arm 3: 11.9 yr (8-16) Control Arm: 12.1 yr (8-16) Males: Arm 1: 7 Arm 2: 7 Arm 3: 7 Control Arm: 4 White: Arm 1: 17 Arm 2: 18 Arm 3: 16 Control Arm: 15 Oriental: Arm 1: 0 Arm 2: 0 Arm 3: 1 Control Arm: 0 Black: Arm 1: 1 Arm 2: 0 Arm 3: 1 Control Arm: 3	54 (54) Arm 1: 18 (18) Arm 2: 18 (18) Arm 3: 18 (18)	Pharmacologic	Arm 1: Pravastatin 5 mg/d + diet Arm 2: Pravastatin 10 mg/d + diet Arm 3: Pravastatin 20 mg/d + diet Pre-study diet was adjusted to comply with a CHO intake of 50%E, protein intake of 20%E, and fat intake of 20%E; total daily intake of cholesterol was limited to < 300 mg	18 (18)	Control Arm: Placebo + diet Pre-study diet was adjusted to comply with a CHO intake of 50%E, protein intake of 20%E, and fat intake of 20%E; total daily intake of cholesterol was limited to < 300 mg	**Primary:** Efficacy: LDL-C [% change(95%CI)] TC [% change(95%CI)] HDL-C [% change(95%CI)] TG [% change(95%CI)] VLDL [% change(95%CI)] Apo B Apo A1 Lp(a) Safety: Adverse Events Safety: LFTs U/L CK U/L TSH (mU/L ACTH ng/L Cortisol umol/L	**Primary:** **5 mg 10 mg 20 mg** -23.3(-21.9,-14.2) -23.8(-28.5,-18.8) -32.9(-37.0,-28.6) -18.2(-21.9,-14.2) -17.2(-21.1,-13.1) -24.6(-28.1,-21.0) +3.8(-3.1,+11.2) +5.5(-1.7,+13.2) +10.8(+3.4,+18.8) No difference -23.8(-34.4,-11.6) -17.9(-29.6,-4.3) -24.5(-35.0,-12.3) -18.0(-23.3,-12.2) -19.2(-24.6,-13.4) -26.8(-13.2,-21.7) No difference -7.3(-26.2,+16.4) -4.4(-24.0,+20.1) +4.0 (-17.4,+30.8) Safety: No difference Safety: No difference	**S** at each dose level vs B/L** **S** at each dose level vs B/L** **NS at each dose level vs B/L** **NS at each dose level vs B/L** **S**; S; S*** **S** at each dose level vs B/L** **NS** **NS at each dose level vs B/L** **NS** **NS** **NS** **NS**	No difference in adverse events between pravastatin and placebo. Adverse events such as dermatologic, fatigue, headache, diarrhea, dyspepsia, nausea, vomiting, abdominal pain, myalgia as well as laboratory safety measures (see also outcomes).	100% completed with drug compliance of 93%.	In adolescents with FH, pravastatin was well-tolerated, safe and efficacious in short term therapy.	Q10 In adolescents with FH, pravastatin was well-tolerated, safe and efficacious in short term therapy.

NHLBI Evidence Table: RF5-RCT

PMID	First Author	Title	Year	Study Type	CVD	RF by CQ	Country	Setting	Int Length	Total Study Duration	Main Study Objective	Total N	Target Population	Eligibility Criteria	Patient Characteristics	Int. n at Baseline (n at Final Follow-up)	Int Type	Specific Intervention	Control n at Baseline (n at Final Follow-up)	Specific Control	Outcomes Measured	Results/CI	Significance S (p<0.05 or non-overlapping CI); S* (p<0.01); S** (p<0.001); NS (p≥0.05 or overlapping CI)	Safety and Adverse Events	Additional findings	Summary	Main Reported Findings by Critical Question
8757561	Tonstad S	Efficacy and safety of cholestyramine therapy in peripubertal and prepubertal children with familial hypercholesterolemia	1996	RCT	None	Q10 (RF5) Q13 (RF9)	Norway	Clinical	1 yr	2 yr Includes low-fat, low-cholesterol diet (following the NCEP recommendations) for 1 yr for all participants prior to randomization	Determine the efficacy and safety of cholestyramine therapy in young children with FH	96 during dietary phase prior to randomization 72 at randomization 1 yr later	Pediatric/ Young Adults	Prepubertal boys 6-11 yr Prepubertal girls 6-10 yr FH LDL-C levels ≥ 4.9 mmol/L (190 mg/dl) and positive family history of premature CVD or LDL-C levels ≤ 4.1 mmol/L (160 mg/dl) without positive family history after 1 yr low-fat, low-cholesterol diet	Mean age (SD): 8.4 yr (1.4) (during dietary phase prior to randomization) Boys: Arm 1: 56% Control Arm: 67%	36 (22)	Pharmacologic	Arm 1: Low fat, low cholesterol diet + cholestyramine 8 g/d Initial 1-wk buildup phase of cholestyramine 4 g/d Low fat, low cholesterol diet common to all participants for 1 yr followed by cholestyramine for 1 yr	36 (20)	Control Arm: Low fat, low cholesterol diet + placebo Low fat, low cholesterol diet common to all participants for 1 yr followed by placebo for 1 yr	**Primary:** Efficacy: Change in LDL-C [%(95%CI)] Safety: Height velocity [SD] **Secondary:** TC mmol/L HDL-C mmol/L TG mmol/L ApoB gm/L ApoA-I Safety: Erythrocyte folate(nmol/L) Homocysteine(mmol/L) Fat-soluble vitamins Vitamin A(umol/L) 25 OH vitamin D(nmol/L) Vitamin E/TC Bone Age Tanner Stage	**Primary: (At 12 months)** **INT** **PLACEBO** -16.9%(-10.8,-22.9) +1.4%(-4.4,+7.2) + 0.24(1.14) +0.11(0.68) **Secondary:** -11.5% +3.0% (CI not given) +8.2 to 13.4% +2.4 to 8.8% Unchanged Unchanged -12.7% Unchanged (CI not given) +7.7% +8.3% -3.3% +9.8% +13.2% +1.9% No difference -30.9% -18.6% +39.3% +13.3% No difference No difference	S** NS S** NS NS S** NS NS S NS S S* NS NS	Safety- see outcomes; Adverse effects: Unpalatability, vomiting, headache; intestinal obstruction 3 months after appendectomy for one child	Only 50% of the children completed 12 months of therapy taking the full prescribed dose of placebo or resin. Insulin-growth factor I and thyroid function- no difference between the prescribed diet between the two groups.	When low dose cholestyramine (8 gm /day) was added to a low fat diet, a significant fall in total and LDL-C and apoB occurred. This decrease was maintained over one year and treatment was not associated with any difference in height velocity compared to placebo. Those treated with resin had significantly lower 25-OH vitamin D but higher vitamin E/TC and higher homocysteine. Unpalatability and compliance were an issue, and only 50% of the children on resin or placebo were taking the full prescribed dose after 12 months.	Q10 (RF 5) A relatively low dose of a bile acid sequestrant can produce significant sustained decreases in LDL-C but compliance is poor.
8885957	Lapinleimu H	Apolipoprotein E (apoE) polymorphism and serum lipids in a randomized, prospective trial of an infant diet with reduced saturated fat and cholesterol	1996	RCT	None	Q6 (RF2, RF5) Q13 (RF5, RF9)	Finland	Clinical	6 mo	6 mo	Analyze the effects of apoE phenotypes on changes in serum lipid concentrations	1062 (1054 families)	Pediatric/ Young Adults	7 mo	NR	540 (NR)	Behavioral	Arm 1: Dietary counseling Recommended 30-35%E intake to be derived from fat with a PUFA/MUFA/SFA ratio of 1:1:1, daily cholesterol intake to be < 200 mg, proteins to constitute 15%E intake, and CHO to constitute 55%E intake Detailed suggestions were made about the amounts and composition of food products as well as food preparation All mothers were encouraged to continue breastfeeding or fo use commercial infant formula until infant was 1 yr, after which the daily consumption of 0.6 L of dairy-processed skim cow milk was recommended	522 (NR)	Control Arm: General health education No detailed suggestions were made All mothers were encouraged to continue breastfeeding or to use commercial infant formula until infant was 1 yr, after which the daily consumption of 0.6 L of dairy-processed skim cow milk was recommended	**Primary:** Mean TC [mg/dL (95% CI)] Mean HDL-C [mg/dL (95% CI)] Mean non-HDL-C [mg/dL (95% CI)] Mean apo-B [g/L (95% CI)] Mean apo-A1 [g/L (95% CI)]	**Primary:** **INT E4+ INT E4- CON E4+ CON E4-** 7m 161.6(34.0) 150.4(30.2) 155.8(28.6) 150.8(26.7) 13m 162.0(27.6) 149.3(25.9) 166.3(26.7) 159.3(30.2) 7m 33.6(7.73) 35.6(7.73) 34.0(7.73) 35.2(6.57) 13m 32.5(6.96) 34.0(7.35) 34.4(7.35) 35.6(7.35) 7m 128.0(32.9) 115.2(28.6) 121.4(27.8) 115.6(25.9) 13m 129.5(26.3) 115.2(25.1) 132.3(25.1) 123.7(28.6) 7m 0.74(0.19) 0.65(0.17) 0.70(0.17) 0.66(0.16) 13m 0.78(0.16) 0.69(0.17) 0.79(0.16) 0.73(0.18) No difference between apoE4 group status or intervention status at either time.	**E4+ vs E4-: S** at 7m & 13m.** **INT vs CON: NS for 7m, S** for 13m.** **E4+ vs E4-: S at 7m & 13m.** **INT vs CON: NS at 7m, S** at 13m.** **E4+ vs E4-: S** at 7m & 13m** **INT vs CON: NS at 7m, S* at 13m.** **E4+ vs E4-: S** at 7m & 13m.** **INT vs CON: NS at 7m & 13m.**	Not assessed.		A low fat, low saturated fat diet decreases serum cholesterol in infancy irrespective of apo E4 phenotype. Infants who were apo E4+ had significantly higher cholesterol and non-HDL cholesterol levels regardless of diet.	A low fat, low saturated fat diet decreases serum cholesterol and non-HDL cholesterol in infancy irrespective of apo E4 phenotype. Infants who were apo E4+ had significantly higher cholesterol and non-HDL cholesterol levels regardless of diet.
8942411	Katoku Y	Effect of the cholesterol content of a formula on the lipid compositions of plasma lipoproteins and red blood cell membranes in early infancy	1996	RCT	None	Q13 (RF5, RF8)	Japan	Clinical	6 mo	6 mo	Investigate whether or not a regular formula supplemented with cholesterol would increase the plasma cholesterol concentration and alter the red blood cell membrane lipid composition in healthy full-term infants compared with their breastfed counterparts	32 (plus 13 in the control breast-fed group for a total of 45)	Pediatric/ Young Adults	Newborn infants	NR	19 (17)	Dietary Supplements	Arm 1: Cholesterol-fortified formula Solid food was added at or after age 4 mo	13 (12)	Control Arm: Cholesterol-unfortified formula Solid food was added at or after age 4 mo 13 nonrandomized infants who were exclusively breastfed served as a reference group. Solid food was added at or after age 4 mo	**Primary:** Total cholesterol [mmol/L] LDL-C [mmol/L] TG [mmol/L] **Secondary:** Red cell membrane cholesterol :protein, and phospholipid-choline: protein ratios Mean body length Mean body weight [g]	**Primary:** Results shown only as a figure. Higher TC and LDL-C levels in breast fed infants at 1 and 3 mos of age; no difference at 6 mos. No difference between feeding methods for TG. **Secondary:** Lower DHA and EPA in RBC membranes with cholesterol-unfortified formula. No difference in ratio of cholesterol to protein or the ratio of phospholipid choline to protein in the RBC membrane of the 3 grps at any time. No differences between groups No differences between groups	**S at 1 and 3 m, NS at 6 m for BF vs both formula fed groups.**	Not reported	Very small study groups.	Cholesterol fortification of formula led to EPA and DHA concentrations in the RBC membrane similar to those in breast fed babies.	None.
9042130	McCrindle BW	Acceptability and compliance with two forms of cholestyramine in the treatment of hypercholesterolemia in children: a randomized, crossover trial	1997	RCT (crossover)	None	Q10 (RF5)	Canada	Clinical	8 wk	28 wk Includes 2 6-wk washout periods	Compare the acceptability, compliance, and therapeutic effectiveness of 2 formulations of cholestyramine resin, pills and powder, in the treatment of children with FH	40	Pediatric/ Young Adults	10-18 yr At least 1 parent documented to have HeFH type IIA or IIB Fasting serum LDL-C ≥ 3.4 mmol/L (> 95th percentile for age and sex) while on an American Heart Association step 2 diet	Median age (range): 13 yr (10-18) Males: 23 Fathers with myocardial infarctions at a median age of 39 yr: 17	40 (38)	Pharmacologic	Intervention 1: Cholestyramine powder 8 g/d (4 g packets) Intervention 2: Cholestyramine pills 8 g/d (1 g tablets)	N/A	N/A	**Primary** Patient Preference Compliance [% prescribed amount taken(SD)] Mean daily dose [gm/m2(SDF)] Change in TC [%(SD)] Change in LDL-C [%(SD)] Change in HDL-C [%(SD)] Change in TG [%(SD)]	Pills: 82%; Powder: 16% Pills: 61%(31); Powder: 50%(30) Pills: 3.2(1.7); Powder: 2.7(1.7) Pills: -7(13); Powder: -11(13) Pills: -10(20); Powder: -15(17) No change No change	**Not reported** **S* between groups** **S between groups** **S** from B/L for both' ns between groups** **S* for pills, S** for powder from B/L; NS between groups** **NS from B/L for both groups; NS between groups** **NS from B/L for both groups; NS between groups**	Constipation, Bloating/gas, stomach ache and headache comparable between the two groups.	Only 8% of these affected children achieved a LDL-C < 130 mg/dL	Pill form was clearly preferred by most children and was associated with a significant difference in compliance between the pill and powder forms. Absolute compliance was still low (50 to 60%) indicating problems with the sequestrants regardless of the form. Both preparations produced a significant LDL-C reduction, no greater in the pill group, despite a significantly greater mean daily dose in the pill group.	Q10 In adolescents with severe hypercholesterolemia, bile acid resin therapy in pill or powder form is associated with a significant reduction in LDL-C despite problems with compliance.
9177986	Decsi T	Plasma lipid and apolipoprotein concentrations in full term infants fed formula supplemented with long-chain polyunsaturated fatty acids and cholesterol	1997	RCT	None	Q13 (RF5)	Hungary	Clinical	NR	120 d	Investigate the biochemical consequences of feeding formula supplemented with egg lipids to provide long-chain PUFA	22	Pediatric/ Young Adults	Full-term infants Not being breastfed	NR	12 (12)	Dietary Supplements	Arm 1: Infant formula + supplements Conventional infant formula based on cow's milk protein and vegetable fat supplemented with egg lipids and evening primrose oil	10 (10)	Control Arm: Infant formula Conventional infant formula based on cow's milk protein and vegetable fat	**Primary:** Median TC [mmol/L (IQR)] Median TG [mmol/L (IQR)] Median non HDL-C [mmol/L (IQR)] Median HDL-C [mmol/L (IQR)] Median apo A-I [g/L (IQR)] Median apo B [g/L (IQR)] Phospholipid [mmol/L (IQR)]	**Primary:** **D5 D30 D60 D90 D120** **STD** 2.15(.56) 2.70(.6) 2.80(.97) 3.10(.62) 3.45(.15) **LCP** 3.15(.37) 3.25(.65) 3.40(.77) 3.60(.75) 3.80(.65) **STD** 1.05(.29) 1.00(.27) 1.00(.17) 1.00(.37) 1.45(.40) **LCP** 1.85(.47) 1.45(.32) 1.40(.35) 1.10(.25) 1.40(.25) **STD** 1.20(.15) 1.30(.46) 1.70(.60) 1.80(.67) 2.30(.15) **LCP:** 2.30(.37) 1.70(.70) 2.70(.67) 2.50(.67) 2.65(.95) No significant difference between groups or over time for any of these measures.	**S D5 only** **S D5,D30** **S D5**	Not reported.	No significant differences between groups after 1 month of age.	Neonates fed formulas supplemented with omega-3 and omega-6 long-chain polyunsaturated fatty acids showed higher total cholesterol and triglycerides levels only in the first month of life with no sustained change on follow-up in infancy.	Neonates fed formulas supplemented with omega-3 and omega-6 long-chain polyunsaturated fatty acids showed higher total cholesterol and triglycerides levels only in the first month of life with no sustained change on follow-up in infancy.
9355889	Kwiterovich PO	Effects of diet and sexual maturation on low-density lipoprotein cholesterol during puberty: the Dietary Intervention Study in Children (DISC)	1997	RCT	None	Q6 (RF2, RF5, RF8, RF9) Q10 (RF5) Q13 (RF8, RF9)	USA	Clinical	3 yr	3 yr	Examine the efficacy and safety of a dietary intervention to reduce serum LDL-C in children with elevated LDL-C	663	Parental/ Family/ Caregiver	TC ≥ age- and sex-specific 75th percentile and below the 98th percentile LDL-C on two subsequent screenings between the age- and sex-specific 80th and 98th percentiles	Mean age (SD): Arm 1: Boys: 9.9 yr (0.6) Girls: 9.2 yr (0.6) Control Arm: Boys: 9.9 yr (0.6) Girls: 9.1 yr (0.6) Patient characteristics pertain only to the 566 children with complete data at 3 yr follow-up	NR (296)	Behavioral	Arm 1: Diet Diet included 28%E from total fat, < 8%E from saturated fat, up to 9%E from polyunsaturated fat, and < 75 mg/4.2 MJ/d of dietary cholesterol not exceeding 150 mg/d 6 weekly group sessions including child's family, followed by 5 biweekly group sessions and 2 individual sessions during the first 6 mo 4 group sessions and 2 individual sessions during 2nd 6 mo Group and individual maintenance sessions 4-6 times/yr plus monthly telephone contacts during second and third yr	NR (270)	Control Arm: Usual care Families provided with educational publications on healthy eating and informed of child's elevated blood cholesterol, but given no specific recommendations to see a physician	**Primary:** Mean change in LDL[mmol/L] per change in dietary cholesterol[mg/MJ] Mean BMI [kg/m2 (SD)] LDL-C[mmol/L] Tanner stage	**Primary: Multiple linear regression:** Males: - 0.018mmol/L per 10 mg/4.2MJ decrease; no single nutrient effect in girls but group effect is significant For males and females, BMI at 3 y was a significant (+) predictor of LDL-C. For both males & females, LDL-C at B/L was a significant (+) predictor of LDL-C. In males, LDL-C was 0.603 mmol/L lower at Tanner stage 4+ than at Tanner stage 1. In females, LDL-C was 0.274 mmol/L lower at Tanner stage 4+ than at Tanner stage 1.	**S for males and females** **S** **S** **S*** **S**	No adverse events reported - had been reported in detail in the primary outcome paper of this trial	As reported previously, dietary fat and cholesterol also affect LDL-C levels.	Puberty exerts powerful effects on LDL-C. In pubertal children, sexual maturation and BMI were shown to be the most significant predictors of LDL-C.	Q10. Puberty exerts powerful effects on LDL-C. In pubertal children, sexual maturation and BMI were shown to be the most significant predictors of LDL-C.
9360208	Weizman Z	Whey deionization method of infant formula affects plasma lipids	1997	RCT	None	Q13 (RF5)	Israel	Clinical	60 d	60 d	Explore whether different methods of whey deionization also affect levels of plasma lipids	35	Pediatric/ Young Adults	Newborn infants	Mean age (SD): Arm 1: 8.6 d (4.1) Arm 2: 7.6 d (4.5) Males: Arm 1: 13 Arm 2: 10 Asian or African: Arm 1: 7 Arm 2: 6 European or American: Arm 1: 9 Arm 2: 8	35 (30) Arm 1: 18 (16) Arm 2: 17 (14)	Dietary supplement	Arm 1: Ultrafiltrated whey formula Arm 2: Electrodialyzed whey formula	N/A	N/A	**Primary:** Mean TC [mg/dL (SD)] Mean LDL-C [mg/dL (SD)] Mean VLDL-C [mg/dL (SD)] Mean HDL-C [mg/dL (SD)] Mean TG [mg/dL (SD)]	**Primary:** **ULTRA ELECTRO** 140.8(18.1) 113.5(14.3) 70.6(10.9) 49.7(8.4) 36.6(16.1) 43.2(15.3) 29.3(4.7) 23.4(11.3) 122.7(20.6) 138.8(24.5)	**S**** **S**** **NS** **NS** **NS**	not presented		Newborns fed ultrafiltrated whey formula had higher total cholesterol and LDL-C than those fed electrodialyzed whey formula.	Q13. Newborns fed ultrafiltrated whey formula had higher total cholesterol and LDL-C than those fed electrodialyzed whey formula.
9470006	Estevez-Gonzalez MD	Reduction of serum cholesterol and low-density lipoprotein cholesterol levels in a juvenile population after isocaloric substitution of whole milk with a milk preparation (skimmed milk enriched with oleic acid)	1998	RCT (crossover)	None	Q13 (RF5)	Spain	Clinical	7 mo	14 mo	Study the effects of serum lipid levels by isocaloric substitution of whole milk intake in a group of children with a milk preparation consisting of fat-free milk enriched with oleic acid containing a small amount of cholesterol	88	Pediatric/ Young adults	3-9 yr No family history of heart disease No history of metabolic disease No history of hyperlipidemia Exclusions: Older than 9 years	Mean age for 3-5 yr (SD): Group receiving intervention 1st: 4.25 yr (0.75) Group receiving control 1st: 4.39 yr (0.72) Mean age for 6-7 yr (SD): Group receiving intervention 1st: 6.54 yr (0.53) Group receiving control 1st: 6.56 yr (0.4) Mean age for 8-9 yr (SD): Group receiving intervention 1st: 8.55 yr (0.52) Group receiving control 1st: 8.12 yr (0.35) Males: 48	88 (88)	Behavioral	Intervention: Milk substitute (FFM) Milk substitute consisted of reconstituted skimmed powdered milk enriched with vegetable oils (60% olive, 20% peanut, and 20% new sunflower) and vitamins A, D, and E, in accordance with Spanish food regulations The milk substitute was composed of 30% monounsaturated fatty acids, 3% polyunsaturated fatty acids, 67% saturated fatty acids, and 107 mg/dL saturated fatty acids	88 (88)	Control: Normal whole milk (WM) The whole milk was composed of 70% monounsaturated fatty acids, 15% polyunsaturated fatty acids, 15% saturated fatty acids, and 22 mg/dL saturated fatty acids	**Primary:** TC [mg/dL(SD)] TG [mg/dL(SD)] LDL-C [mg/dL(SD)] HDL-C [mg/dL(SD)] ApoA-I [mg/dL(SD)] ApoB [mg/dL(SD)] Lp (a) [mg/dL(SD)]	**Primary:** WM: 175.25(34.91) vs FFM: 162.65(25.94) WM: 73.98(34.64) vs FFM: 64.15(21.43) WM: 105.9(28.49) vs FFM: 95.86(21.32) No change No change No change No change	**S**** **S*** **S**** **NS** **NS** **NS** **NS**	None reported.	Variation of cholesterol and LDL-C is more marked after dietary modification in those children with raised TC levels.	Substitution of a fat-free beverage enriched with oleic acid for whole milk produced significant but moderate reductions in total and LDL-C and TG.	Q13 Use of a fat-free beverage vs whole milk is associated with significant moderate reductions in TC, LDL-C and TG.

NHLBI Evidence Table: RF5-RCT

PMID	First Author	Title	Year	Study Type	CVD	RF by CQ	Country	Setting	Int Length	Total Study Duration	Main Study Objective	Total N	Target Population	Eligibility Criteria	Patient Characteristics	Int. n at Baseline (n at Final Follow-up)	Int Type	Specific Intervention	Control n at Baseline (n at Final Follow-up)	Specific Control	Outcomes Measured	Results/CI	Significance S (p<0.05 or non-overlapping CI); S* (p<0.01); S** (p<0.001); NS (p≥0.05 or overlapping CI)	Safety and Adverse Events	Additional findings	Summary	Main Reported Findings by Critical Question
9491017	Tershakovec AM	One-year follow-up of nutrition education for hypercholesterolemic children	1998	RCT	None	Q10 (RF5, RF9) Q11 (RF5, RF9)	USA	Home	12 mo	12 mo	Evaluate retention of the effect of a home-based, practitioner-initiated nutrition education model	261	Parental/ Family/ Caregiver	4-10 yr "At-risk", defined by TC > 176 mg/dL (75th percentile); no secondary cause of hypercholesterolemia and 85% to 130% of ideal body weight Elevated mean fasting LDL-C: Boys: 107-164 mg/dL Girls: 112-164 mg/dL	Mean age (SE): Arm 1: 6.3 yr (0.2) Arm 2: 6.2 yr (0.2) Control Arm: 6.4 yr (0.2) Males: Arm 1: 49% Arm 2: 50% Control Arm: 52% White: Arm 1: 88% Arm 2: 90% Control Arm: 84%	174 (139) Arm 1: 88 (66) Arm 2: 86 (73)	Behavioral	Arm 1: Parent-Child auto tutorial Parent-Child auto tutorial included 10 talking book lessons and a follow-up paper-pencil activity for children, along with a parent's manual Arm 2: Counseling Children and parents in the counseling program attend a 45-60 min counseling session with a registered dietitian Both intervention programs comply with NCEP recommendations	87 (76)	Control Arm: No treatment (CON) 81 not-at-risk children, matched on age and gender, were included as a reference group	**Primary:** **Measured at 3, 6 & 12 m:** Increase in LS mean fat and cholesterol knowledge score [%] LS mean total fat intake [% calories (SE)] LS mean cholesterol intake [mg/1000 kcal (SE)] LS mean LDL-C [mmol/l (SE)]	**Primary:** Greatest in parent-child autotutorial group; intermediate increase in counseling group, least in CON groups. Greatest decreases in parent-child autotutorial & counseling groups, no change in CON groups. Decrease only in parent-child autotutorial group Decrease in parent-child autotutorial & counseling groups, significant only for the former. *Results shown only as figures.	**S from baseline in parent-child autotutorial & counseling groups** **S from baseline in parent-child autotutorial & counseling groups** **S from baseline in parent-child autotutorial group** **S from baseline in parent-child autotutorial & counseling groups**	None		Two nutrition intervention programs significantly increased parent & child knowledge re:fat & cholesterol, decreased fat intake and lowered LDL-C levels with results sustained over 12 m F/U.	Q10, 11: Two nutrition intervention programs significantly increased parent & child knowledge re:fat & cholesterol, decreased fat intake and lowered LDL-C levels with results sustained over 12 m F/U.
9633944	Couture P	Association of specific LDL receptor gene mutations with differential plasma lipoprotein response to simvastatin in children and adolescents with heterozygous familial hypercholesterolemia	1998	RCT	None	Q6 (RF2, RF5, RF8) Q10 (RF5)	Canada	Clinical	6 wk	10 wk Includes 4 wk run-in period in which all participants received placebo	Determine whether the nature of the LDL-receptor mutation affects the response to simvastatin	63	Pediatric/ Young Adults	8-17 yr Weight > 27 kg HeFH Plasma LDL-C levels persistently > 95th percentile for age and sex while maintaining a lipid-lowering diet Exclusions: Concomitant conditions (e.g., diabetes mellitus, liver disorder)	Mean age (SD): HeFH with ∆15kb gene mutation: 12.4 yr (2.3) HeFH with C646Y gene mutation: 12.4 yr (2.4) HeFH with W66G gene mutation: 12.9 yr (2.2) Boys: 37	47 (NR)	Pharmacologic	Arm 1: 20 mg/d simvastatin + diet counseling Consisted of participants from each of the 3 gene mutation groups All participants received counseling from a dietician to follow a cholesterol-lowering diet (American Heart Association phase I diet)	16 (NR)	Control Arm: Placebo + diet counseling Consisted of participants from each of the 3 gene mutation groups All participants received counseling from a dietician to follow a cholesterol-lowering diet (American Heart Association phase I diet)	**Primary:** Mean change in LDL-C[%(95%CI)] Mean change in TC[%(95%CI)] Mean change in TG[%(95%CI)] Mean change in HDL-C[%(95%CI)]	**Primary:** Del>15kb -38% (-43,-33) C646Y -42% (-49,-35) W66G -31% (-37,-25) Del>15kb -30% (-35,-26) C646Y -33% (-39,-28) W66G -24% (-28,-20) Del>15kb -12% (-26,+2) C646Y -12% (-33,+8) W66G -23% (-44,-2) Del>15kb +6% (-2,+13) C646Y +3% (-2,+9) W66G +11% (+4,+17)	**S** from baseline; NS between groups** **S** from baseline **S** from baseline **S** from baseline **S** from baseline **S** from baseline **S btwn W66G & other grps **S from baseline; NS between groups **NS** **S** from baseline **NS from baseline; NS between groups **NS from baseline **S** from baseline	Not reported		In children with FH, there were some differences in response to simvastatin by genotype but overall, simvastatin treatment resulted in significant reductions in LDL-C, and total cholesterol for all LDL-receptor genotypes	Q10,13. In children with FH, there were some differences in response to simvastatin by genotype but overall, simvastatin treatment resulted in significant reductions in LDL-C, and total cholesterol for all LDL-receptor genotypes
9811286	McCrindle BW	Garlic extract therapy in children with hypercholesterolemia	1998	RCT	None	Q10 (RF5)	Canada	Clinical	8 wk	8 wk	Determine whether garlic extract therapy is efficacious and safe in children with hypercholesterolemia	30	Pediatric/ Young Adults	8-18 yr Positive family history of hypercholesterolemia or premature atherosclerotic CVD in first-degree relatives Minimum fasting TC level > 4.8 mmol/L (> 185 mg/dL) Participation in a dietary counseling program Compliance with a NCEP Step II diet for ≥ 6 mo Exclusions: Presence of secondary causes of hyperlipidemia	Mean age (SD):14.0 yr (2.3) Males:16	15 (15)	Dietary Supplements	Arm 1: Garlic extract tablet 300 mg containing allicin 0.6 mg tid	15 (15)	Control Arm: Placebo	**Primary:** Mean change in TC [mg/dL (CI)] Mean change in LDL-C [mg/dL (CI)] Mean change in HDL-C [mg/dL (CI)] Mean change in TG [mg/dL (CI)] Mean change in apo A-1 [mg/dL (CI)] Mean change in apo B-100 [mg/dL (CI)] Mean change in Lp(a) [mg/dL (CI)] Mean change in fibrinogen [mg/dL (CI)] Mean change in homocysteine [umol/L(CI)] Mean change in systolic Blood Pressure [mm Hg (CI)] Diastolic Blood Pressure [mm Hg(CI)]	**Primary** +0.6(-5.8,+6.9) No change No change No change +10.0%(+1.2,+14.%) No change No change No change No change No change	**NS** **NS** **NS** **NS** **S** **NS** **NS** **NS** **NS** **NS**	No difference in adverse effects between garlic and placebo nor difference in height, weight, or blood pressure. Serum albumin (p = 0.002) and hemoglobin (p = 0.02) were both higher in garlic group.		Garlic extract had no significant effect on multiple lipid measures, fibrinogen or BP in hypercholesterolemic children.	Q10 Garlic extract had no significant effect on multiple lipid measures, fibrinogen or BP in hypercholesterolemic children.
9917116	Stein EA	Efficacy and safety of lovastatin in adolescent males with heterozygous familial hypercholesterolemia: a randomized controlled trial	1999	RCT	None	Q10 (RF5)	USA, Finland	Clinical	48 wk	56 wk Includes run in period with American Heart Association diet (wk -8 to wk 0) and placebo (wk -4 to wk 0)	Assess lipid-lowering efficacy, biochemical safety, and effect on growth and sexual development of lovastatin in adolescent boys with heFH	132	Pediatric/ Young Adults	10-17 yr Boys HeFH Subjects who had followed the American Heart Association pediatric diet for ≥ 4 mo Exclusions: Subjects weighing < 32 kg Subjects weighing less than the 10th or greater than the 95th weight percentiles for age Homozygous FH U	Mean age (SE): Arm 1: 13.3 yr (0.3) Control Arm: 13.1 yr (0.3) White: 93% Smokers: Arm 1: 3.0% Control Arm: 3.1% Parental evidence of coronary artery disease: 36	67 (61)	Pharmacologic	Arm 1: Diet + lovastatin 10-40 mg/d Period 1: Lovastatin 10 mg/d wk 0-7 Lovastatin 20 mg/d wk 8-15 Lovastatin 40 mg/d wk 16-24 Period 2: Lovastatin 40 mg/d wk 25-48 All subjects continued to receive diet instruction, monitoring, and evaluation throughout the study	65 (49)	Control Arm: Diet + placebo All subjects continued to receive diet instruction, monitoring, and evaluation throughout the study	**Primary:** Mean change in LDL-C [% (SE)] Mean change in TC [% (SE)] Mean change in apo B [g/L (SE)] [% (SE)] Mean change in TG [% (SE)] Mean change in HDL-C [% (SE)] Mean change in apo A-I [% (SE)] **Secondary:** Safety measures - growth and sexual development	**Primary:** **LOV Placebo** 10 mg -17(2) 1(1) 20 mg -24(1) 2(2) 40 mg 24w -27(2) -3(2) 40 mg 48 w -25(2) -4(2) 10 mg -13(1) 1(1) 20 mg -19(1) 2(1) 40 mg 24w -21(1) -2(1) 40 mg 48 w -20(2) -3(1) 40 mg 24w -23(2) -6(2) 40 mg 48 w -22(2) -6(3) No significant changes from B/L or difference between groups for any of these measures. **Secondary:** No differences between groups for ht,wt, testicular volume or Tanner stage. DHEAS level higher in **INT** group; no difference for any other hormone level.	**S** **S** **S** **S** **S** **S** **S** **S** **S** **S**	No significant differences for adverse events. No difference in hepatic function tests or CK levels during treatment.	Alpha tocopherol levels decreased significantly more with lovastatin than placebo. No difference for any other nutritional parameter. However, alpha tocopherol levels remained well within the accepted reference range.	In adolescent males with FH, lovastatin safely and effectively lowered TC, LDL-C and apoB levels.	Q10. In adolescent males with FH, lovastatin safely and effectively lowered TC, LDL-C and apoB levels.
10613408	Williams CL	Plant stanol ester and bran fiber in childhood: effects on lipids, stool weight and stool frequency in preschool children	1999	RCT (crossover)	None	Q13 (RF5, RF9)	USA	Community (other)	4 wk	13 wk Includes a 1 wk run-in period, a 2 wk washout period between treatments, and a 2 wk follow-up after the intervention	Evaluate the effects of plant stanol esters and bran fiber on lipids, stool weight and stool frequency in preschool children	21	Pediatric/ Young Adults	2-5 yr Exclusions: Baseline TC or TG > 300 mg%	Of subjects who completed the study: Mean age (SD): 3.58 yr (1.07) Males: Group 1: 3 Group 2: 5 White: Group 1: 6 Group 2: 8 Black: Group 1: 1 Group 2: 0 Hispanic: Group 1: 2 Group 2: 0 Other race: Group 1: 1 Group 2: 1	21 (19)	Dietary Supplements	Intervention 1: Plant stanols 3 servings of 8 g spread containing plant stanol ester as a substitute for usual spread. Each serving contained 1 g of plant stanol Intervention 2: Dietary fiber 1 serving/d Raisin Bran for a total of 5 g dietary fiber during the first 2 wk of intervention and 2 servings/d of Raisin Bran for a total of 10 g of dietary fiber for the next 2 wk	N/A	N/A	**Primary:** Change in mean TC [mg/dL] Change in mean LDL-C [mg/dL] Change in mean HDL-C [mg/dL] Change in mean TG [mg/dL]	**Primary:** **STANOL BRAN** -19.9(23.8) -6.1(23.9) -14.6(24.2) -3.3(21.5) -2.0(10.4) -0.1(9.0) -18.2(39.2) -17.7(37.1)	**S* **S** **NS** **NS**	Increased GI side effects with bran dietary supplementation	Consumption of iron, zinc, vitamin A and E increased significantly during the bran phase, and vitamin A and E increased during the plant stanol spread phase. Stool weight & number increased on the bran diet with no change on the plant stanol ester.	Total cholesterol and LDL-C are significantly decreased with use of a stanol-ester spread in a 4 week period. There were no significant changes with a bran fiber supplement.	Q10,13. Total cholesterol and LDL-C are significantly decreased with use of a stanol-ester spread in a 4 week period. There were no significant changes with a bran fiber supplement.
10753249	Tammi A	Plant stanol ester margarine lowers serum total and low-density lipoprotein cholesterol concentrations of healthy children: the STRIP project. Special Turku Coronary Risk Factors Intervention Project	2000	RCT (crossover)	None	Q13 (RF5)	Finland	Home	3 mo	7.5 mo Includes 6 wk washout period	Investigate cholesterol-lowering efficacy and safety of plant stanol ester margarine in healthy 6-year-old children already consuming a low-saturated-fat, low-cholesterol diet	81	Pediatric/ Young adults	6 yr STRIP project participants consuming low fat, low cholesterol diets Exclusions: Type I diabetes FH	Boys: 45	81(72)	Dietary Supplements	Intervention: Replaced 20g of daily dietary fat with plant stanol ester margarine Vitamins A and D were added to the plant sterol ester margarine	81 (72)	Control: Replaced 20g of daily dietary fat with control margarine Control margarine was rapeseed oil margarine with fatty acid content similar to that of the plant sterol ester margarine	**Primary:** Mean treatment effect on LDL-C[mmol/L (SE)] **Secondary:** Mean treatment effect on TC [mmol/L (SE)] Mean treatment effect on HDL-C [mmol/L (SE)] Mean treatment effect on TG [mmol/L (SE)]	**Primary:** - 0.20 (0.05) **Secondary:** - 0.23 (0.06) No significant effect No significant effect	**S** **S*** **NS** **NS**	Extensive analysis of serum plant sterol and cholesterol precursor sterol to cholesterol ratios where reported changes reflected decreased cholesterol absorption. Effects on vitamins were studied, but the preparation was supplemented with vitamins A and D. No changes in hematologic, creatinine, LDH and GGT indices. Complex analysis of a decrease in beta-carotene levels.		In healthy children, supplementation with a dietary plant stanol ester margarine resulted in an attributable 7.5% decrease in LDL levels and a 5.4% decrease in total cholesterol levels, with no adverse effects.	Q10,13. In healthy children, supplementation with a dietary plant stanol ester margarine resulted in an attributable 7.5% decrease in LDL levels and a 5.4% decrease in total cholesterol levels, with no adverse effects
10944645	Rask-Nissila L	Neurological development of 5-year-old children receiving a low-saturated fat, low-cholesterol diet since infancy: A randomized controlled trial	2000	RCT	None	Q13 (RF5, RF9)	Finland	Clinical	54 mo	54 mo	Analyze how parental counseling aimed at keeping children's diets low in saturated fat and cholesterol influences neurodevelopment during the first 5 yr of life	1062	Parental/ Family/ Caregiver	5 mo at recruitment, 7 mo at randomization	Equally representative of all socioeconomic classes	540 (225)	Behavioral	Arm 1: Individualized counseling + diet Counseling aimed at limiting fat intake to 30-35% of daily energy and maintaining a 1:1:1 ratio of SFA:MUFA:PUFA Parents advised to continue breastfeeding until 12 mo and to use skim milk thereafter Goal of reducing cholesterol intake to < 200 mg/d Parents taught to add soft margarine or vegetable oil to the daily food of infants 12-24 mo	522 (239)	Control Arm: Health education + diet Parents advised to continue breastfeeding until 12 mo with 1.9% fat cow's milk recommended thereafter	**Primary:** Neurologic development: SPEECH/LANGUAGE SKILLS GROSSMOTOR FUNCTION VISUAL MOTOR SKILLS Mean energy intake [kcal (SD)] Mean total fat intake [%E (SD)] Mean saturated fat intake [%E (SD)] Mean monounsaturated fat intake [%E (SD)] Mean polyunsaturated fat intake [%E (SD)] Mean cholesterol intake [mg (SD)] Mean TC [mmol/L (SD)] Mean HDL-C [mmol/L (SD)] Mean TG [mmol/L (SD)] Mean LDL-C [mmol/L (SD)]	**Primary:** RR of Failure: INT vs CON: 0.95(95%CI: 0.60, 1.49) INT vs CON: 0.95(95%CI: 0.58, 1.55) INT vs CON: 0.65(95%CI: 0.39, 1.08) INT vs CON: 1399+/-231 vs 1458+/-236 INT vs CON: 30.6+/-4.5 vs 33.4+/-4.4 INT vs CON: 11.7+/-2.3 vs 14.5+/-2.4 INT vs CON: 10.7+/-1.9 vs 11.0 +/-1.9 INT vs CON: 5.3+/-1.2 vs 4.8+/-1.2 INT vs CON: 164.2+/-60.1 vs 192.5+/-71.9 INT vs CON: 4.27+/-0.63 vs 4.41+/-0.74 Exact results not given INT vs CON: 0.68+/-0.22 vs 0.64+/-0.21 INT vs CON: 2.75+/-0.57 vs 2.88+/-0.64	**NS** **NS** **NS** **S*** **S**** **S**** **S** **S**** **S** **NS** **S** **S**	Normal growth; no AEs		In a RCT where a low fat/ low sat fat diet was implemented by individualized dietary counseling, intake of sat fats was markedly reduced, age-related increase in serum cholesterol & LDL-C was diminished and neurological development was at least as good as that of children in the control group with no identified areas of developmental dysfunction over a 5 y period.	Q13 (RF5,9) A low fat/ low sat fat diet can be implemented and maintained by individualized dietary counseling with markedly reduced intake of sat fats, diminished age-related increase in serum cholesterol & LDL-C and intact neurological development with no identified areas of developmental dysfunction over a 5 y period.

NHLBI Evidence Table: RF5-RCT

PMID	First Author	Title	Year	Study Type	CVD	RF by CQ	Country	Setting	Int Length	Total Study Duration	Main Study Objective	Total N	Target Population	Eligibility Criteria	Patient Characteristics	Int. n at Baseline (n at Final Follow-up)	Int Type	Specific Intervention	Control n at Baseline (n at Final Follow-up)	Specific Control	Outcomes Measured	Results/CI	Significance S (p<0.05 or non-overlapping CI); S* (p<0.01); S** (p<0.001); NS (p≥0.05 or overlapping CI)	Safety and Adverse Events	Additional findings	Summary	Main Reported Findings by Critical Question
11063474	Simell O	Special Turku Coronary Risk Factor Intervention Project for Babies (STRIP)	2000	RCT	None	Q10,Q11 (RF5, RF9) Q13 (RF5, RF8, RF9)	Finland	Clinical	30 mo	30 mo	Decrease exposure to known environmental atherosclerosis risk factors in children 7-36 mo of age through repeated, individualized counseling	1062	Parental/ Family/ Caregiver	5 mo of age at recruitment, 7 mo at randomization	Boys: 550 Mean midparental BMI at 7 mo visit [kg/m^2 (SD)]: Arm 1: 24.0 (2.7) Control Arm: 23.9 (2.7) Mean smokers at 7 mo visit, mothers [% (SD)]: Arm 1: 15% Control Arm: 19% Mean smokers at 7 mo visit, fathers [% (SD)]: Arm 1: 31% Control Arm: 34%	540 (426)	Behavioral	Arm 1: Intensive individualized counseling + diet Special attention was paid to dietary fat content and quality Promoted a fat intake of 30-35%E with a 1:1:1 intake ratio of SFA/MUFA/PUFA, a protein intake of 10-15%E, and CHO intake of 50-60%E Breast milk or formula was encouraged until 12 mo and then 0.5-0.6 L skim milk was recommended daily; patients were taught to add vegetable oil or soft margarine to milk	522 (417)	Control Arm: Basic health education + diet Breastfeeding was encouraged; at 12 mo, cow milk with ≥ 1.9% fat was recommended for daily use No suggestions on the use of fats were given and dietary issues were discussed only superficially	**Primary:** **DIET:** Mean cholesterol intake [mg/1000 kJ (SD)] Mean fat intake [%E (SD)] Mean energy intake [kJ (SD)] Polyunsaturated to Saturated fat ratio Unsaturated to saturated fat ratio Mean protein intake [%E (SD)] Mean CHO intake [%E (SD)] **GROWTH:** Mean relative weight [(SD)] Mean relative height [SD] **SERUM LIPIDS:** Mean TC [mmol/L (SD)] Mean HDL-C [mmol/L (SD)] Mean apo A-I [g/L (SD)] Mean apo B [g/L (SD)]	**Primary:** **13 mo,24 mo & 36 mo results:** Consistently lower in INT group Consistently lower in INT group No difference between groups Consistently higher in INT group Consistently higher in INT group Consistently higher in INT group Consistently higher in INT group No difference between groups No difference between groups Consistently lower in INT group Consistently lower in INT group Consistently lower in INT group Consistently lower in INT group	**S** at each determination** **S** at each determination** **NS** **S** at each determination** **S** at each determination** **S* to S** at serial determinations** **S* to S** at serial determinations** **NS** **NS** **S** in boys, p=.089 in girls** **S** in boys, p=S* in girls** **S* in boys & girls** **S* in boys, NS in girls**	None reported		A low fat, low cholesterol & decreased saturated fat diet instituted in infancy can be sustained X 3 y with repeated individualized dietary counseling. Serum cholesterol and HDL concentrations were consistently lower in the intervention group with TC & LDL-C levels significantly lower in males. The intervention had no effect on growth.	Q11, Q13, A low fat, low cholesterol & decreased saturated fat diet instituted in infancy can be sustained for 3 yrs with repeated individualized dietary counseling. Q10. Serum cholesterol and HDL concentrations were consistently lower in the intervention group with TC & LDL-C levels significantly lower in males.
11063475	Lauer RM	Efficacy and safety of lowering dietary intake of total fat, saturated fat, and cholesterol in children with elevated LDL cholesterol: the Dietary Intervention Study in Children	2000	RCT	None	Q6 (RF8, RF9) Q11 (RF5, RF8, RF9)	USA	Clinical	3 yr	3 yr	Assess the efficacy and safety of lowering dietary intake of total fat, saturated fat, and cholesterol to decrease LDL-C concentrations in children	663	Parental/ Family/ Caregiver	Age range: Boys: 8 yr 7 mo to 10 yr 10 mo Girls: 7 yr 10 mo to 10 yr 1 mo TC ≥ 175 mg/dL (approx. 75th age- and sex-specific percentile) Average of 2 screenings showing LDL-C > 80th percentile and < 98th percentile for age and sex Exclusions: Medical condition or medication that might affect growth or blood cholesterol	Mean age: Boys: 9.7 yr Girls: 9.0 yr Boys: 362 Higher proportion of patients with household income < $20,000 in Arm 1	334 (NR)	Behavioral	Arm 1: Diet (INT) Encouraged adherence to a diet providing 28%E from total fat, < 8%E from saturated fat, ≤ 9%E from polyunsaturated fat, and < 0.018 mg/kJ/d cholesterol (not to exceed 150 mg/d) Personalized program developed based on the participant's current eating patterns Included group and individualized sessions led by nutritionists, behaviorists, and health educators	329 (NR)	Control Arm: Usual care (UC) Families informed about child's blood cholesterol concentration and given publicly available educational information Provided 3 yr lipid results for families to share with their regular physicians	**Primary:** Mean LDL-C [mg/dL (SD)] Mean TC [mg/dL (SD)] Mean HDL-C [mg/dL (SD)] Mean TG [mg/dL (SD)] **Secondary:** Serum retinol [umol/L] Red cell folate [nmol/L of rbc] Serum ferritin [ug/L] Serum zinc [umol/L] Serum albumen [g/L] Mean height [cm (SD)] Mean weight [kg (SD)] Mean BMI [kg/m2 (SD)] Mean DBP [mmHg] Sum of skinfold thickness [mm]	**Primary:** **B/L 1y 3y** INT 130.6(12.2) 122.6(18.2) 115.3(18.7) UC 130.5(11.6) 127.2(19.4) 118.6(19.4) INT 200.0(14.6) 191.4(20.9) 183.3(21.5) UC 200.0(14.6) 197.4(21.4) 186.4(22.3) No difference between groups at any time No difference between groups at at any time **Secondary:** Slightly lower in UC at 1y, no difference at 3y No change and no difference between groups for any of these measures at any time	**S* between groups at 1y, S at 3 y** **S* between groups at 1y, S at 3 y** **NS** **NS** **S at 1y; NS at 3y** **NS**	No concerns	Lower depression score in the intervention group	Lower intake of total and saturated fat significantly and safely reduced LDL-C and total cholesterol over 3 yr follow-up when initiated at 8 - 10 years of age in children with baseline LDL-C in the range of 80th - 95th percentile.	Q10,13 Lower intake of total and saturated fat significantly and safely reduced LDL-C and total cholesterol over 3 yr follow-up when initiated at 8 - 10 years of age in children with baseline LDL-C in the range of 80th - 95th percentile.
11158455	Obarzanek E	Long-term safety and efficacy of a cholesterol-lowering diet in children with elevated low-density lipoprotein cholesterol: seven-year results of the Dietary Intervention Study in Children (DISC)	2001	RCT	None	Q10 (RF5) Q11 (RF5, RF8, RF9) Q13 (RF8, RF9)	USA	Clinical	Mean length: 7.4 yr	Mean length: 7.4 yr	Test the long-term efficacy and safety of a cholesterol-lowering dietary intervention in children	663	Pediatric/ Young Adults	8-10 yr Average of 2 LDL-C measurements ≥ 80th (≥ 111.5 mg/dL for boys and ≥ 117.5 mg/dL for girls) and < 98th (≤ 164.5 mg/dL for boys and girls) age- and sex-specific percentiles of the Lipid Research Clinics population	Mean age (SD): 9.5 yr (0.72) Boys: Arm 1: 179 Control Arm: 183 White: 86.5% Parents with at least some college education: 53.3% Household income ≥ $50,000: 35.6% Household income < $20,000: Arm 1: 15.1% Control Arm: 5.9%	334 (295)	Behavioral	Arm 1: Dietary intervention DISC dietary recommendations, similar to the NCEP Step 2 diet, promoted adherence to a diet with 28%E from total fat, < 8%E from saturated fat, up to 9%E from polyunsaturated fat, and < 7.5 mg/1000 kcal cholesterol per day Intervention strategies, based on social learning theory and social action theory, consisted of group sessions and individual visits with nutritionists and behaviorists	329 (285)	Control Arm: Usual care Parents/guardians were informed their child's blood cholesterol was high and given educational publications on heart-healthy eating available to the public	**Primary:** % of energy intake from fat % of energy intake from saturated fat Cholesterol intake [mg/1000 kcal] Mean LDL-C [mg/dL] Mean TC [mg/dL] Mean HDL-C [mg/dL (SD)]; Mean HDL-C [mg/dL (SD)]; BMI[kg/m2] **Secondary:** Red cell folate, serum retinol and zinc. Sexual maturation BMI[kg/m2]	**Primary:** **DISC UC** B/L 33.4% 34.0% 1y 28.5% 31.4% 7y 28.5% 30.6% B/L 12.5% 12.7% 1y 9.8% 11.7% 7y 10.2% 11.3% B/L 118 114 1y 90 104 7y 99 103 B/L 130.6 130.6 1y 109.8 112.2 7y 114.1 115.9 B/L 200.0 200.0 1y 191.4 197.4 7y 179.4 180.1 No difference between groups for any of these measures. **Secondary:** No difference between groups for any of these measures.	**S**** **S*** **S*** **S**** **S*** **S*** **S**** **S*** **NS** **NS** **S*** **NS** **NS** **S**** **NS**	No adverse events in treatment group		Dietary fat and saturated intake can be safely and effectively lowered in actively growing children with elevated LDL-C. These changes persisted through 7 y of F/U. LDL-C levels were significantly decreased through 3 yrs of F/U but this did not persist at 7y F/U.	Q10. Dietary fat and saturated intake can be safely and effectively lowered in actively growing children with elevated LDL-C. These changes persisted through 7 y of F/U. LDL-C levels were significantly decreased through 3 yrs of F/U but this did not persist at 7y F/U.
11435511	Tammi A	Dietary plant sterols alter the serum plant sterol concentration but not the cholesterol precursor sterol concentrations in young children (the STRIP Study). Special Turku Coronary Risk Factor Intervention Project	2001	RCT	None	Q10, Q13 (RF5, RF9)	Finland	Clinical	6 mo	6 mo	Determine whether natural dietary plant sterols derived mainly from vegetable oil or margarine in early childhood affect serum concentrations of plant sterols and cholesterol precursor sterols	40	Parental/ Family/ Caregiver	7 mo Participants in the STRIP project	Males: Arm 1: 13 Control Arm: 12	20 (20)	Behavioral	Arm 1: Dietary counseling to promote high plant sterol diet 4 counseling sessions that promoted a diet low in saturated fat and cholesterol (at 7, 8, 10, and 13 mo of age) Diet of intervention children was rich in plant sterols due to replacement of milk fat with vegetable fat (10-15 g of vegetable oil or margarine)	20 (20)	Control Arm: Basic health education 2 health education sessions at well baby clinics (at 7 and 13 mo of age)	**Primary:** Serum campesterol [umol/L (SD)] Serum sitosterol [umol/L (SD)] Serum cholesterol [mmol/L (SD)] **Secondary:** Mean total fat intake [%E (SD)] Mean cholesterol intake [mg (SD)] Mean SFA intake [%E (SD)] Mean MUFA intake [%E (SD)] Mean PUFA intake [%E (SD)]	**Primary:** High plant diet: 10.3+/-3.6 Low plant diet: 5.9+/-1.5 High plant diet: 6.5+/02.0 Low plant diet: 4.5+/-1.0 High plant diet: 3.55+/-0.52 Low plant diet: 3.80+/-0.36 **Secondary:** By design, children on the high plant sterol diet had significantly lower intake of total fat, SFA & cholesterol and significantly higher intake of MUFA, PUFA and plant sterols.	**S**** **S**** **NS**	None		Moderate vegetable fat supplementation of children's daily diet led to high dietary intake of plant sterols. This was associated with high serum levels of campesterol & sitosterol but no increase in serum cholesterol or cholesterol precursor levels.	Q10,13. Moderate vegetable fat supplementation of children's daily diet led to high dietary intake of plant sterols. This was associated with high serum levels of campesterol & sitosterol but no increase in serum cholesterol or cholesterol precursor levels.
11782868	Bayley TM	Longer term effects of early dietary cholesterol level on synthesis and circulating cholesterol concentrations in human infants	2002	RCT (partial crossover)	None	Q13 (RF5)	USA	Clinical	Phase 1: 4 mo Phase 2: 12 mo	12 mo	Examine the response of cholesterol homeostasis to long-term dietary cholesterol supplementation	168	Pediatric/ Young Adults	1 wk Parents were both black or both white Exclusions: Family history of hypercholesterolemia or hypertriglyceridemia Evidence of cardiac, respiratory, hematologic, gastrointestinal, or other systemic disease	NR	NR	Dietary Supplements	Phase 1 (RCT) Arm 1: Regular cow's milk protein-based formula (0.85 mmol cholesterol/L) (RF) Arm 2: Regular cow's milk protein-based formula + cholesterol (3.44 mmol cholesterol/L) (RF+Ch) During Phase 1, Arms 1 and 2 were randomized Phase 2 (crossover RCT using different infants than Phase 1) Intervention 1: Regular cow's milk protein-based formula (0.85 mmol cholesterol/L) Intervention 2: Regular cow's milk protein-based formula + cholesterol (3.44 mmol cholesterol/L) During Phase 2, Intervention 1 and 2 groups were randomized At 6 mo, Intervention 1 and 2 groups crossed over; infants initially receiving Intervention 1 received Intervention 2 until 11 mo of age, while infants initially receiving Intervention 2 received Intervention 1 until 12 mo of age	NR	Phase 1: 32 breastfed infants served as a reference group (BF) Phase 2: 17 breastfed infants served as a reference group; at 11 or 12 mo of age (depending on group assignment), infants in all groups of Phase 2 received an additional 250 mg of cholesterol powder/d for 1 mo as part of a cholesterol challenge At any point during Phase 2 if mothers of breastfed decided to discontinue breastfeeding, infants were converted to Intervention 2	**Primary:** Total cholesterol [mg/dL(SEM)] LDL-C [mg/dL(SEM)] HDL-C [mg/dL(SEM)] TG [mg/dL(SEM)] **Secondary:** Cholesterol fractional synthetic rate [%/day(SEM)]	**Primary:** **RF RF+Ch BF** 4m 131(9) 148(7) 167(8) 11m 163(7) 150(4) 152(7) 12m 158(8) 167(5) 162(6) **RF RF+Ch BF** 4m 49(10) 68(8) 88(9) 11m 84(5) 77(4) 82(7) 12m 85(6) 97(9) 92(5) No significant differences between groups or within groups over time. **Secondary:** **RF RF+Ch BF** 4m 8.58(0.27) 8.29(0.37) 2.19(0.29) 11m 3.58(0.57) 2.71(0.56) 6.16(1.05) 12m 3.15(0.48) 3.79(0.48) 4.34(0.66)	**RF,RF+Ch vs BF: S** **NS between groups** **NS between groups** **RF, RF+Ch vs BF: S** **NS between groups** **NS between groups** **RF, RF+Ch vs BF: S** **RF, RF+Ch vs BF: S** **NS between groups**	Not reported	Cholesterol metabolism is profoundly reduced at 11mos of age vs 4 mos of age irrespective of early dietary cholesterol intake.	Early exposure to infant formula supplemented with cholesterol does not induce differences in central pool cholesterol synthesis rates, nor in plasma cholesterol levels.	Q10,13.Early exposure to infant formula supplemented with cholesterol does not induce differences in central pool cholesterol synthesis rates, nor in plasma cholesterol levels.
11782868	Bayley TM	Longer term effects of early dietary cholesterol level on synthesis and circulating cholesterol concentrations in human infants	2002															At 11 or 12 mo of age (depending on group assignment), infants in all groups of Phase 2 received an additional 250 mg of cholesterol powder/d for 1 mo as part of a cholesterol challenge; during the cholesterol challenge all formula infants received Intervention 2								
12032266	McCrindle BW	A randomized crossover trial of combination pharmacologic therapy in children with familial hyperlipidemia	2002	RCT (crossover)	None	Q10 (RF5)	Canada	Clinical	18 wk	44 wk Includes 8 wk washout period Patients instructed to stop lipid-lowering medications ≥ 8 wk before study	Determine whether a low-dose combination of a bile acid-binding resin (colestipol) with an hydroxymethylglutaryl CoA reductase inhibitor (pravastatin) would result in improved lipid-lowering compared with conventional therapy	40	Pediatric/ Young Adults	Followed for familial hyperlipidemia for 6 mo before consideration for recruitment 8-18 yr FH or premature atherosclerotic CVD in first-degree relatives Minimum fasting LDL-C of > 4.15 mM/L before enrollment Participation and compliance in a dietary counseling program for ≥ 6 mo Exclusions: Secondary cause noted for hyperlipidemia Extreme primary elevations of TG (> 8 mM/L)	Median age at initial regimen assignment (range): Intervention: 14 yr (10-18 yr) Control: 14 yr (9-18 yr) Male: 25 Father with hyperlipidemia: 24 Father with CV event: 12 Mother with hyperlipidemia: 14	40 (36)	Pharmacologic	Intervention: Colestipol 5 g/d + pravastatin 10 g/d (COMB) All patients maintained on American Heart Association step 2 diet	39 (35)	Control: Colestipol 10 g/d (Resin) All patients maintained on American Heart Association step 2 diet	**Primary:** Compliance[%(SD)] **Secondary:** Acceptability[%] Realtive change in cholesterol [% (SD)] Relative change in LDL-C [% (SD)] Relative change in HDL-C [% (SD)] Relative change in TG [% (SD)] Relative change in apo-A [% (SD)] Relative change in apo-B [% (SD)]	**Primary:** COMB: 62(27) vs Resin: 60(28) **Secondary:** COMB: 52-72% vs Resin: 9-17% COMB: -12.9(12.9) vs Resin: -7.3(10.3) COMB: -16.(8(15.8) vs Resin: -9.(13.4) No change in either group COMB: +8.3(50.9) vs Resin: +11.6(45.5) No change in either group COMB: -13.9(17.4) vs Resin: 10.2(16.9)	**NS** **Not reported** **S** **S** **NS** **NS** **NS** **NS**	0-3% in combined group and 6 to 21% in colestipol alone group. Side effects included constipation, bloating/gas, stomach ache, headache and muscle ache.	Insufficient sample size to detect statistical difference in primary endpoint. Major problems with compliance.	The combination of pravastatin with low dose bile acid resin was more effective in LDL lowering, more acceptable to the participants and associated with fewer side effects.	Q 10 (RF5) High LDL-C can be lowered with combination drug therapy (pravastatin plus bile acid sequestrant). The combination of pravastatin with low dose bile acid resin was more effective in LDL lowering, more acceptable to the participants and associated with fewer side effects.

NHLBI Evidence Table: RF5-RCT

PMID	First Author	Title	Year	Study Type	CVD	RF by CQ	Country	Setting	Int Length	Total Study Duration	Main Study Objective	Total N	Target Population	Eligibility Criteria	Patient Characteristics	Int. n at Baseline (n at Final Follow-up)	Int Type	Specific Intervention	Control n at Baseline (n at Final Follow-up)	Specific Control	Outcomes Measured	Results/CI	Significance S (p<0.05 or non-overlapping CI); S* (p<0.01); S** (p<0.001); NS (p≥0.05 or overlapping CI)	Safety and Adverse Events	Additional findings	Summary	Main Reported Findings by Critical Question
12145004	Amundsen AL	Plant sterol ester-enriched spread lowers plasma total and LDL cholesterol in children with familial hypercholesterolemia	2002	RCT (crossover)	None	Q10 (RF5) Q13 (RF9)	Norway	Clinical	8 wk	25 wk Includes 3 wk run-in period, 4 wk washout period, and another 2 wk run-in period	Study the effect of sterol ester-enriched spread on serum lipids, lipoproteins, carotenoids, fat-soluble vitamins, and physiologic variables in children	41	Pediatric/ Young Adults	7-12 yr Definite or possible heFH diagnosis ≥ 1 hypercholesterolemic parent	Mean age (SD): 10.5 yr (1.7) Boys: 19	41 (38)	Dietary Supplements	Intervention: Sterol ester-enriched spread + dietary information (INT) 20 g/d to be consumed at 3 separate intervals Spread consisted of 8.8% free plant sterols, of which ~50% was sitosterol Subjects and families were advised to reduce the intake of saturated fat and cholesterol and to increase the intake of unsaturated fat, fruit, and vegetables. In the middle of intervention they were asked to keep a 4 d weighed-food record	41 (38)	Control: Control spread + dietary information (CON) 20 g/d to be consumed at 3 separate intervals Spread consisted of 0.16% plant sterols Subjects and families were advised to reduce the intake of saturated fat and cholesterol and to increase the intake of unsaturated fat, fruit, and vegetables. In the middle of intervention they were asked to keep a 4 d weighed-food record	**Primary:** Difference in mean LDL-C [mmol/L (SD)] Difference in mean TC [mmol/L (SD)] Difference in mean HDL-C [mmol/L (SD)] Difference in mean TG [mmol/L (SD)] Difference in mean apoB [g/L(SD)] Difference in mean apoA1 [g/L(SD)]	**Primary:** INT vs CON: - 0.58 (1.12) INT vs CON: - 0.53(1.14) INT vs CON: + 0.034(0.27) INT vs CON: + 0.095(0.76) INT vs CON: - 0.095(0.24) INT vs CON: - 0.024(0.25)	S** S** NS NS NS S	Significant decreases in lycopene and beta-carotene and an increase in retinol noted with the stanol ester spread; however changes in beta-carotene and retinol not significant after adjustment for changes in lipid levels. No other potentially adverse effects noted.		Addition of a sterol spread significantly reduced LDL-C, TC and apoB in children with FH who were already consuming a low fat and low saturated fat diet with no adverse effects.	Q10,13. Addition of a sterol spread significantly reduced LDL-C, TC and apoB in children with FH who were already consuming a low fat and low saturated fat diet with no adverse effects.
12390953	de Jongh S	Efficacy and safety of statin therapy in children with familial hypercholesterolemia: a randomized, double-blind, placebo-controlled trial with simvastatin	2002	RCT	None	Q10 (RF5) Q13 (RF7)	Multiple countries	Clinical	48 wk	52 wk Includes 4 wk run-in period with diet and placebo	Evaluate LDL-C lowering efficacy, overall safety, and tolerability and the influence on growth and pubertal development of simvastatin	173	Pediatric/ Young Adults	10-17 yr HeFH 4.1 mmol/L ≤ LDL-C ≤ 10.3 mmol/L Exclusions: Homozygous FH Secondary hyperlipidemia	Mean age (SD): Arm 1: 14.4 yr (2.1) Control Arm: 14.0 yr (2.1) Boys: Arm 1: 63 Control Arm: 36	106 (83)	Pharmacologic	Arm 1: (SIM) Period 1: Simvastatin 10 mg/d wk 0-8 Simvastatin 20 mg/d wk 9-16 Simvastatin 40 mg/d wk 17-24 Period 2: Simvastatin 40 mg/d wk 25-48	69 (56)	Control Arm: Placebo (CON)	**Primary:** Mean change in TC [% (SD)] Mean change in LDL-C [% (SD)] Mean change in apoB [% (SD)] **Secondary:** Mean change in TG[% (SD)] Mean change in VLDL-C [% (SD)] Mean change in HDL-C [% (SD)] Mean change in apo A1 [% (SD)] hsCRP	**Primary:** SIM: 10 mg -23.9(8.5); CON:+2.3(9.4) SIM: 20 mg -26.3(10.3); CON:+ 0.2(10.2) SIM: 40 mg,wk 24 -28.3(13.4); CON: -0.7(9.5) SIM: 40 mg,wk 48 -30.9(11.5); CON: +0.8(9.6) SIM: 10 mg -31.4(10.5); CON:+1.8(10.7) SIM: 20 mg -34.7(12.3); CON:-1.7(13.4) SIM: 40 mg,wk 24 -38.4(16.0); CON:-1.2(11.0) SIM: 40 mg,wk 48 -40.7(39.2); CON: +0.3(10.3) SIM: 10 mg -28.8(8.8); CON:0.7(12.1) SIM: 20 mg -31.2(11.3); CON:-2.1(13.7) SIM: 40 mg,wk 24 -34 .1(13.5); CON:-2.7(13.6) SIM: 40 mg,wk 48 -34.2(14.0); CON: 0.1(11.5) **Secondary:** SIM: 10 mg -8.9; CON: 1.5 SIM: 20 mg -12.5; CON: 1.4 SIM: 40 mg,wk 24 -7.9; CON:-3.2 SIM: 40 mg,wk 48 -8.7;CON: 4.3 SIM: 10 mg -11.8; CON: 2.5 SIM: 20 mg -12.0; CON: 19.9 SIM: 40 mg,wk 24 -12.5; CON:13.8 SIM: 40 mg,wk 48 -20.7; CON: 4.5 No significant changes in any of these measures	S** S** S** S** S** S** S** S** S** S** S** S** S S NS S S S** S S**	6 adverse events in treatment, 3 in control. One child developed severe CK elevation when simvastatin was combined with erythromycin accidentally. There were no significant changes in growth or adrenal, gonadal or pituitary hormones except a small decrease in DHEAS at the highest dose of simvastatin.		Simvastatin treatment resulted in significant reductions in LDL-C, apoB and total cholesterol, less significant decreases in TG and VLDL and apo B. No adverse outcomes of significance occurred.	Q10. Simvastatin treatment resulted in significant reductions in LDL-C, apoB and total cholesterol, less significant decreases in TG and VLDL and apo B. No adverse outcomes of significance occurred.
12463311	Tammi A	Effects of gender, apolipoprotein E phenotype and cholesterol-lowering by plant stanol esters in children: the STRIP study. Special Turku Coronary Risk Factor Intervention Project	2002	RCT (crossover)	None	Q6 (RF2, RF5) Q13 (RF5)	Finland	Clinical	3 mo	7.5 mo Includes 6 wk washout period	Evaluate the effects of gender, apo E phenotype and cholesterol absorption and synthesis on the cholesterol-lowering effect of plant stanol esters in children	81	Pediatric/ Young Adults	6 yr Recruited from the STRIP project and had consumed a diet low in cholesterol and saturated fat for years	Boys: 45	81 (72)	Dietary Supplements	Intervention: Plant stanol ester margarine 20 g/d Replaced 20 g of daily dietary fat with plant stanol ester margarine, resulting in a plant stanol intake of 1.6 g/d	81 (72)	Control: Margarine 20 g/d Replaced 20 g of daily dietary fat with margarine without added plant stanols	**Primary:** Mean LDL-C change[% (SD)] Boys Girls ApoE4+ ApoE4- Mean campesterol chnage(%) Boys Girls ApoE4+ ApoE4- Mean lathosterol change(umol/mmolTCx100) Boys Girls ApoE4+ ApoE4- **Secondary:** Mean TC [mmol/L (SD)] Boys Girls ApoE4+ ApoE4-	**Primary:** LDL-C Boys Decreased 9.1% Girls Decreased 5.8% ApoE4+ Decr 8.4% ApoE4- Decr 7.6% Campesterol Boys Decreased 36.3% Girls Decreased 42.0% ApoE4+ Decr 46.2% ApoE4- Decr 36.6% Lathosterol Boys Increased 7.6% Girls Increased 19.5% ApoE4+ Incr 24.4% ApoE4- Incr 7.6% **Secondary:** TC: Boys Decreased 6.3% Girls Decreased 4.4 ApoE4+ Decr 5.8% ApoE4- Decr 5.5%	S** S* S* S* S** S** S** S** NS S** S** NS S* S* S* S*	Not reported	The interaction term treatment by gender by apoE was NS.	Plant sterol esters significantly decreased cholesterol absorption and increased cholesterol biosynthesis. This resulted in a significant net fall in total and LDL-C. These effects were present in both genders regardless of apoE4 phenotype.	Q10 (RF2,RF5) Plant sterols lowered LDL-C in both boys and girls regardless of apoE4 phenotype.
12463311	Tammi A	Effects of gender, apolipoprotein E phenotype and cholesterol-lowering by plant stanol esters in children: the STRIP study. Special Turku Coronary Risk Factor Intervention Project	2002																		Mean HDL-C [mmol/L (SD)] Boys Girls ApoE4+ ApoE4- Mean HDL-C/TC (% change) Boys Girls ApoE4+ ApoE4- Mean TG [mmol/L (SD)] Boys Girls ApoE4+ ApoE4- Sitosterol(umol/mmolTCx100) Boys Girls ApoE4+ ApoE4- Delta 8 cholestanol(umol/mmolTCx100) Boys Girls ApoE4+ ApoE4- Desmosterol(umol/mmolTCx100) Boys Girls ApoE4+ ApoE4-	HDL-C Boys No change Girls No change ApoE4+ No change ApoE4- No Change HDL-C/TC Boys Increased 6.7% Girls Increased3.7% ApoE4+ Incr 7.4% ApoE4- Incr 6.7% TG Boys Decreased 7.5% Girls Decreased 5.3% ApoE4+ Decr 3.9% ApoE4- Decr 8.8% Sitosterol (umol/mmolTCx100) Boys Girls ApoE4+ Decr 36.9% ApoE4- Decr 30.0% Delta 8 cholestanol Boys Increased 16.7% Girls Increased 20.7% ApoE4+ Incr 27.0% ApoE4- Incr 14.8% Desmosterol Boys Increased 10.6% Girls Increased 11.9% ApoE4+ Incr 20.9% ApoE4- Incr 7.6%	NS NS NS NS S* S S S* NS NS NS NS S** S** S** S** NS S S* NS S* S** S** S				
12505222	de Jongh S	Early statin therapy restores endothelial function in children with familial hypercholesterolemia	2002	RCT	FMD	Q2 (RF5) Q10 (RF5) Q12a (RF5)	Netherlands	Clinical	28 wk	28 wk	Determine whether simvastatin improves endothelial function in children with FH	50	Pediatric/ Young Adults	9-18 yr HeFH Exclusions: Smoking Concomitant conditions (e.g., serious illness, hypertension, diabetes mellitus) Current use of any vasoactive medications	Mean age (SD): Arm 1: 14.6 yr (2.0) Control Arm: 14.6 yr (2.5) Males: Arm 1: 15 Control Arm: 11	28 (NR)	Pharmacologic	Arm 1: Simvastatin 10-40 mg/d (INT) Dosage was doubled every 8 wk from 10 to 20 to 40 mg/d	22 (NR)	Control Arm: Placebo (FH CON) 19 healthy non-FH siblings served as an additional control group (Non FH CON)	**Primary:** Mean change in FMD [% (SD)] FMD[%(SD)] **Secondary:** Mean change in TC [mmol/L (SD)] Mean HDL-C [mmol/L (SD)] Mean LDL-C [mmol/L (SD)] Median TG [mmol/L (SD)]	**Primary:** INT: + 3.9%(4.3) vs. FH CON: +1.2%(3.9) INT: 15.6%(6.8); Non FH CON: 15.5%(5.4) **Secondary:** INT: -2.16(1.04) vs. FH CON: -0.05(1.17) No difference in either group INT: -2.13 (0.99) vs. FH CON: -0.05(1.06) INT: 0.19(0.37) vs. FH CON: 0.10(0.54) The absolute change of FMD was inversely correlated to change in TC and LDL(both, r=0.31)	**Primary:** S NS S** NS S** S S, S	No significant differences in liver enzymes or CK, no adverse events were reported.		With a significant improvement in LDL levels in children with FH on statin therapy, endothelial function assessed by FMD is normalized.	Q2,10,12a. With a significant improvement in LDL levels in children with FH on statin therapy, endothelial function assessed by FMD is normalized.
12756385	Ketomaki AM	Red cell and plasma plant sterols are related during consumption of plant stanol and sterol ester spreads in children with hypercholesterolemia	2003	RCT (crossover)	None	Q10 (RF5)	Finland	Don't know	5 wk	15 wk Includes 5 wk wash out period on an ad libtum home diet	Show whether the ratios of squalene and cholesterol precursor sterols to cholesterol and cholesterol and plant sterols to cholestanol change differently in plasma and especially in the red cells of hypercholesterolemic children during consumption of plant stanol and sterol ester spreads	23	Pediatric/ Young Adults	Children TC > 194 mg/dL TG < 176 mg/dL	Mean age (SEM): 6.8 yr (0.5) Boys: 10 Girls: 13 FH: 16		Dietary Supplements	Intervention: Low-fat plant stanol ester spread 2.0 g/d Patients were advised to replace 25 g of daily dietary fat with the spreads on pieces of bread Stanol spread consisted of 16% SFA, 56% MUFA, and 28% PUFA	23 (23)	Control: Low-fat plant sterol ester spread 2.0 g/d Patients were advised to replace 25 g of daily dietary fat with the spreads on pieces of bread Sterol spread consisted of 25% SFA, 25% MUFA, and 50% PUFA	**Primary:** Change in TC in plasma [%(SEM)] Change in TC in red cells[%(SEM)] Change in LDL-C in plasma [%(SEM)] Change in plasma to red cell sitosterol to cholesterol ratio[%(SEM)] Change in plasma to red cell campesterol to cholesterol ratio[%(SEM)] Change in plasma to red cell avenasterol to cholesterol ratio **Secondary:** Change in HDL-C in plasma [%(SEM)] Change in TG in plasma [%(SEM)]	**Primary:** Stanol: - 9(3) Sterol: -6(2) Stanol: - 1(2) Sterol: +4(2) Stanol: - 12(3) Sterol: - 9(3) Stanol: - 36(4) Sterol: + 52(6) Stanol: - 32(4) Sterol:+ 43(5) Stanol: - 30(3) Sterol: -10(2) **Secondary:** No sig. change in TG or HDL	S* from B/L S** from B/L NS NS S* from B/L S** from B/L S** from B/L; S** between groups S** from B/L S** from B/L;S** between groups S** from B/L S** from B/L; S** between groups S** from B/L NS	No adverse events but no specific data given		Total cholesterol and LDL-C decreased significantly with stanol and sterols, but this did not affect red blood cell cholesterol levels. The ratios of plasma & red cell sitosterol and campesterol decreased significantly with the plant stanol ester but increased significantly with the sterol ester spread.	Q10. Total cholesterol and LDL-C decreased significantly with stanol and sterols, but this did not affect red blood cell cholesterol levels. The ratios of plasma & red cell sitosterol and campesterol decreased significantly with the plant stanol ester but increased significantly with the sterol ester spread.

NHLBI Evidence Table: RF5-RCT

PMID	First Author	Title	Year	Study Type	CVD	RF by CQ	Country	Setting	Int Length	Total Study Duration	Main Study Objective	Total N	Target Population	Eligibility Criteria	Patient Characteristics	Int. n at Baseline (n at Final Follow-up)	Int Type	Specific Intervention	Control n at Baseline (n at Final Follow-up)	Specific Control	Outcomes Measured	Results/CI	Significance S (p<0.05 or non-overlapping CI); S* (p<0.01); S** (p<0.001); NS (p≥0.05 or overlapping CI)	Safety and Adverse Events	Additional findings	Summary	Main Reported Findings by Critical Question
12885748	Kaitosaari T	Effect of 7-year infancy-onset dietary intervention on serum lipoproteins and lipoprotein subclasses in healthy children in the prospective, randomized Special Turku Coronary Risk Factor Intervention Project for Children (STRIP) study	2003	RCT	None	Q6 (RF2, RF5, RF9) Q11 (RF5, RF9) Q13 (RF5, RF9)	Finland	Clinical	7 yr	7 yr	Determine how low-saturated-fat dietary intervention from infancy until 7 yr of age safely and effectively influence serum lipids	1062	Parental/ Family/ Caregiver	7 mo 7 yr Boys: 274	540 (315)	Behavioral	Arm 1: Dietary counseling + lifestyle counseling Counseling given twice a yr Since the age of 3, the recommended intakes comprised of protein 10-15%E, fat 30%E, and CHO 55-60%E	522 (255)	Control Arm: Basic health education Education provided at Finnish well-baby clinics; Control Arm received no detailed dietary counseling	**Primary:** Mean cholesterol [mmol/L (SD)] Mean saturated fat intake [%E] **Secondary:** Mean LDL-C [mmol/L] Mean non HDL-C [mmol/L (SD)] Mean HDL-C [mmol/L (SD)] Mean HDL/TC (%) Mean TG [mmol/L] Mean apo-I [g/L (SD)] Mean apo-B [g/L (SD)] Mean energy intake [kJ] Mean total fat intake [%E] P + M/S ratio Mean total CHO intake [%E] LDL (MP) particle size (Ang)	**Primary (M=male;F=female)** M: Decreased 5% F: No Change M: Decreased 2.1% F: Decreased 1.9% **Secondary:** M: Decreased 7% F: No Change M: Decreased % F: No change M: No change F: No change M: Increased 5% F: No change M: No change F: No change M: Decreased 9% F: No change M: No change F: No change M: Decreased 0.9% F: Decreased 1.4% M: Increased 0.3 F: Increased 0.2 M: No change F: Increased 1.0 M: Increased 4.1 (Ang) F: Decreased 2.1(Ang)	**S*** **NS** **S**** **S*** **NS** **NS** **NS** **NS** **S** **NS** **NS** **NS** **NS** **S*** **NS** **NS** **NS** **NS** **S*** **S*** **S**** **NS** **NS** **S** **NS**	Heights and weights not different between intervention and control, for both boys and girls		The intervention produced a significant decrease in saturated fat in both genders but only the boys had a significant fall in total and LDL-C and apoB. The girls had no significant lipid response to the diet, while the boys responded as expected. The dietary change was not associated with any detectable adverse events. In a subgroup the intervention boys had larger LDL particles than the control boys, an effect most likely due to the reduction in TG levels in this intervention subgroup.	Q6 (RF 2, RF5, RF 9) Low fat diet lowered TC, LDL-C and apoB in boys but not girls. Q11 (RF5 RF 9) The above effects were sustained over 7 years. Q13 (RF5 RF 9) Lowering a higher fat diet prevents increase in LDL-C
12885748	Kaitosaari T	Effect of 7-year infancy-onset dietary intervention on serum lipoproteins and lipoprotein subclasses in healthy children in the prospective, randomized Special Turku Coronary Risk Factor Intervention Project for Children (STRIP) study	2003																		LDL (ave) particle size(Ang) TG mmol/L (in subset) HDL 2 (mmol/L) HDL 3 (mmol/L) **NB. Same endpoints for girls**	M: Increased 3.7 (Ang) F: No change M: Decreased 19.4% F: Increased 4.3% M: No change F: No change	**NS** **NS** **S*** **NS** **NS** **NS** **NS** **NS**				
12912807	Engler MM	Antioxidant vitamins C and E improve endothelial function in children with hyperlipidemia: Endothelial Assessment of Risk from Lipids in Youth (EARLY) Trial	2003	RCT (crossover)	FMD	Q10 (RF5) Q12a (RF5)	USA	Clinical	6 wk	6 mo Includes 6 wk run-in period with NCEP-II diet and 6 wk washout period	Determine whether antioxidant vitamin therapy improves endothelial function and affects surrogate biomarkers for oxidative stress and inflammation in hyperlipidemic children	19 4 subjects were later excluded from the study due to noncompliance with vitamin therapy	Pediatric/ Young Adults	8-21 yr FH or familial combined hyperlipidemia (FCH) Exclusions: Systemic illness with or without secondary hyperlipidemia Current smoking	9-20 yr Males: 8 FH: 6 FCH: 9	15 (15)	Dietary Supplements	Intervention: Vitamin C 250 mg bid and vitamin E 200 IU bid + nutritional counseling Nutritional counseling incorporated dietary recommendations based on the food guide pyramid and NCEP-II guidelines	15 (15)	Control: Placebo + nutritional counseling Nutritional counseling incorporated dietary recommendations based on the food guide pyramid and NCEP-II guidelines	**Primary:** Mean FMD [% (SD)] **Secondary:** Mean LDL-C [mg/dL (SD)] Mean TC [mg/dL (SD)] Mean VLDL-C [mg/dL (SD)] Mean HDL-C [mg/dL (SD)] Mean TG [mg/dL (SD)] Lp(a) [nmol/L(SD)] F2 isoprostanes[ng/ml(SD)] OxLDL autoantibody titers OxLDL-E06 levels Mean CRP [mg2/dL2 (SD)] Urinary 8-OH-2-dG [ug/g creatinine(SD)] ADMA [uM(SD]	**Primary:** Significant increase on anti-oxidants + diet, no change with diet alone or placebo **Secondary:** Diet: 187+/-49 to 172+/-48 No significant change in any other lipid or biomarker measure with any condition.	**S** vs baseline** **S* vs baseline**	None reported		In hypercholesterolemic children, NCEP-II diet + antioxidants VitC & VitE X 6 mos significantly improved brachial artery endothelial function assessed by FMD; no FMD improvement was seen with diet alone despite an 8% decrease in LDL-C.	Q10,.Q12a. Moderate daily doses of VitC & VitE restore endothelial function in hypercholesterolemic children.
12915827	McCrindle BW	Efficacy and safety of atorvastatin in children and adolescents with familial hypercholesterolemia or severe hyperlipidemia: a multicenter, randomized, placebo-controlled trial	2003	RCT	None	Q10 (RF5)	USA, Canada, Europe, South Africa	Clinical	52 wk	56 wk Includes 4 wk run-in period with the NCEP step 1 diet	Determine the safety and efficacy of atorvastatin in children and adolescents with FH or severe hypercholesterolemia	187	Pediatric/ Young Adults	10-17 yr HeFH or severe hypercholesterolemia	Mean age (SD): Arm 1: 14.1 yr (2.0) Control Arm: 14.1 yr (2.2) Males: Arm 1: 95 Control Arm: 34 White: Arm 1: 131 Control Arm: 41 Black: Arm 1: 2 Control Arm: 1 Asian: Arm 1: 2 Control Arm: 1 Other race: Arm 1: 5 Control Arm:	Double-blind phase: 140 (136) Open-label phase: 133 (NR)	Pharmacologic	Arm 1: Diet + atorvastatin 10-20 mg/d Double-blind phase: Subjects started with 10 mg/d of atorvastatin; dosage was increased to 20 mg/d if LDL-C levels remained > 3.4 mmol/dL at wk 4 Open-label phase: At wk 26, all subjects received 10 mg/d for 26 wk	Double-blind phase: 47 (46) Open-label phase: 43 (NR)	Control Arm: Diet + placebo Double-blind phase: Subjects received placebo for 26 wk Open-label phase: At wk 26, all subjects received 10 mg/d of atorvastatin for 26 wk	**Primary:** LDL-C **Secondary** Total-C HDL-C TG ApoA-I ApoB	**Primary:** Decreased 39.6% **Secondary:** Decreased 31.4% Increased 2.8% Decreased 12.0% Increased 3.3% Decreased 34.0%	**S** **S** **S** **S** **S** **S****	Abdominal pain, accidental injury, fever, flu syndrome, headache, infection, and pharyngitis were not statistically significantly different between treatment and placebo. Treatment had no significant effect on sexual development (by Tanner staging). The Overall, the percentage of patients with clinical laboratory test abnormalities was similar in the two groups except for increased triglycerides in placebo group.	None	Treatment of children 10 to 17 years old with FH or marked hypercholesterolemia with atorvastatin for up to 52 weeks was efficacious and safe	Q10RF5 Atorvastatin lowers LDL and TG and increases HDL-C
12915827	McCrindle BW	Efficacy and safety of atorvastatin in children and adolescents with familial hypercholesterolemia or severe hyperlipidemia: a multicenter, randomized, placebo-controlled trial	2003																				In the treatment group there were 2 patients (1%) with elevated (>3X ULN) AST elevations and one patient with elevated (3X ULN) ALT (1%). One subject in treatment group discontinued because of severe depression.			
12971422	de Jongh S	Plant sterols lower LDL cholesterol without improving endothelial function in prepubertal children with familial hypercholesterolemia	2003	RCT (crossover)	FMD	Q10 (RF5) Q12a (RF5)	Netherlands	Home	4 wk	16-20 wk Includes 2 wk run-in period or a 6 wk run-in period for children who used plant sterol-enriched products and a 6 wk washout period	Evaluate the effect of plant sterols on cholesterol and vascular function in prepubertal children with FH	41	Pediatric/ Young Adults	5-12 yr FH Exclusions: Smoker Concomitant conditions (e.g., diabetes mellitus, hypertension)	Mean age (SD): 9.2 yr (1.6) Males: 20	41 (41) - note that there were an additional 20 non-FH controls	Dietary Supplements	Intervention: Low saturated fat, low cholesterol diet + plant sterol spread	41 (41)	Change in m	**Primary:** Mean absolute change in TC [%,(95%CI)] Mean absolute change in LDL-C[%,(95%CI)] FMD [%] **Secondary:** Mean absolute change in HDL-C [%,(95%CI)] Mean absolute change in TG [%,(95%CI)]	**Primary:** -0.79(-1.02,-0.60) -0.78(-1.00,-0.60) B/L: 7.2(3.4) to 7.7(4.1) **Secondary:** No change from B/L No change from B/L	**S** **S** **NS** **NS** **NS**	Not reported		LDL-C and total cholesterol were significantly reduced by plant sterols in a 4 week treatment period, but the reductions of cholesterol were not associated with an improvement in flow mediated dilation.	Q10. LDL-C and total cholesterol were significantly reduced by plant sterols in a 4 week treatment period, but the reductions of cholesterol were not associated with an improvement in flow mediated dilation.
15265847	Wiegman A	Efficacy and safety of statin therapy in children with familial hypercholesterolemia: a randomized controlled trial	2004	RCT	IMT	Q10 (RF5) Q12a (RF5)	Netherlands	Clinical	2 yr	2.25 yr Includes ≥ 3 mo run-in period with fat-restricted diet	Determine the 2 yr efficacy and safety of pravastatin therapy in children with FH	214	Pediatric/ Young Adults	8-18 yr 1 parent with FH 2 fasting samples with LDL-C ≥ 155 mg/dL and TG < 350 mg/dL after 3 mo on a fat-restricted diet No drug treatment for FH and no use of plant sterols Exclusions: Homozygous FH	Mean age (SD): Arm 1: 13.0 yr (3.0) Control Arm: 13.0 yr (2.9) Younger than 14 yr: Arm 1: 65 Control Arm: 63 Boys: Arm 1: 46% Control Arm: 47% Smokers: Arm 1: 11 Control Arm: 13	106 (104)	Pharmacologic	Arm 1: Pravastatin 20-40 mg/d + diet + physical activity (INT) Children < 14 yr of age received 20 mg Children ≥ 14 yr received 40 mg All children were instructed to continue a fat-restricted diet and to maintain habitual physical activity during the trial	108 (107)	Control Arm: Placebo + diet + physical activity (CON) All children were instructed to continue a fat-restricted diet and to maintain habitual physical activity during the trial	**Primary:** Change in mean carotid IMT [mm (SD)] **Secondary:** Change in mean TC [mg/dL (SD)] Change in mean LDL-C [mg/dL (SD)] Change in mean HDL-C [mg/dL (SD)] Change in median TG [mg/dL (IQR)]	**Primary:** INT: -0.010(0.048) vs. CON:+0.005(0.044) **Secondary:** INT: -56(43) vs. CON: +2(39) INT. -57(40) vs. CON: 0(36) No difference in either of these measures.	**INT: B/L vs Post: S; INT vs CON: S** **CON: B/L vs POST: NS** **S** **S** **NS**	No significant differences in safety labs, growth, Tanner staging or events.	No difference in change in physical characteristics, liver and muscle enzymes or hormones.	In a 2 yr trial of statin therapy in 8-18 yr old children with FH, there was a significant reduction in total cholesterol and LDL associated with significant regression of CIMT, despite residual elevated LDL levels.	Q10,13. In a 2 yr trial of statin therapy in 8-18 yr old children with FH, there was a significant reduction in total cholesterol and LDL associated with significant regression of CIMT, despite residual elevated LDL levels.
15624283	Engler MM	Docosahexaenoic acid restores endothelial function in children with hyperlipidemia: results from the EARLY study	2004	RCT (crossover)	FMD	Q10 (RF5) Q12a (RF5, RF7)	USA	Clinical	6 wk	24 wk Includes 6 wk run-in period on diet and 6 wk wash out phase	Determine whether the NCEP Step II diet or supplementation with DHA with the diet, affects endothelial function in children with FH or the phenotype of familial combined hyperlipidemia (FCH)	20	Pediatric/ Young Adults	8-21 yr FH or FCH Exclusions: Chronic systemic illness with or without secondary hyperlipidemia Current smoking	9-19 yr FH: 12 FCH: 8	20 (NR)	Dietary Supplements	Intervention: Dietary intervention + DHA 1.2 g/d (Diet + DHA) Nutritional conseling incorporated guidelines from the NCEP-II diet and food guide period and was provided at baseline, 2 wk, and every 6 wk for the duration of the study	20 (NR)	Control: Dietary intervention (Diet) Nutritional conseling incorporated guidelines from the NCEP-II diet and food guide period and was provided at baseline, 2 wk, and every 6 wk for the duration of the study	**Primary:** Flow Mediated Dilation (FMD) [%(SD)] **Secondary:** Mean TC [mg/dL (SD)] Mean LDL-C [mg/dL (SD)] Mean HDL-C [mg/dL (SD)] Mean TG [mg/dL (SD)] Mean VLDL-C [mg/dL (SD)] F2 isoprostanes[ng/ml(SD)] Mean CRP [mg2/dL2 (SD)] 8-OH-2-dG [ug/g creatinine(SD)] ADMA [uM(SD]	**Primary:** B/L: 5.9(2.3); Diet: 6.3(2.6); DHA + Diet: 7.9(2.9); Washout + diet: 6.5(2.7); Placebo + DHA: 6.8(2.4) **Secondary:** Diet: 282+/-85 to 263+/-79 Diet+DHA: 282+/-85 to 297+/-81 Diet: 213+/-89 to 201+/-82 Diet+ DHA: 213+/-89 to 229+/-85 Diet: 48+/-9 to 44+/-8 Diet + DHA: 48+/-9 to 51+/-13 No change with either intervention. No change with either intervention Decreased with diet - no other change No change with any of these 3 measures with any intervention .	**DHA + Diet vs B/L: S**; vs Diet: S*;** **vs Washout + diet: S**; vs Placebo + diet: S** **S* vs baseline** **S* vs diet** **NS vs baseline** **S** vs diet** **NS vs baseline** **S** vs diet** **S* vs baseline** **NS**	None reported		In hypercholesterolemic children, NCEP-II diet + DHA for 6 wks significantly improved brachial artery endothelial function assessed by FMD despite an increase in total and LDL cholesterol on DHA; no FMD improvement was seen with diet alone despite a significant decrease in TC and LDL-C.	Q10,Q12a. In hypercholesterolemic children, NCEP-II diet + DHA for 6 wks significantly improved brachial artery endothelial function assessed by FMD despite an increase in total and LDL cholesterol on DHA; no FMD improvement was seen with diet alone despite a significant decrease in TC and LDL-C.

NHLBI Evidence Table: RF5-RCT

PMID	First Author	Title	Year	Study Type	CVD	RF by CQ	Country	Setting	Int Length	Total Study Duration	Main Study Objective	Total N	Target Population	Eligibility Criteria	Patient Characteristics	Int. n at Baseline (n at Final Follow-up)	Int Type	Specific Intervention	Control n at Baseline (n at Final Follow-up)	Specific Control	Outcomes Measured	Results/CI	Significance S (p<0.05 or non-overlapping CI); S* (p<0.01); S** (p<0.001); NS (p≥0.05 or overlapping CI)	Safety and Adverse Events	Additional findings	Summary	Main Reported Findings by Critical Question
15781019	Engler MM	Effect of docosahexaenoic acid on lipoprotein subclasses in hyperlipidemic children (the EARLY study)	2005	RCT (crossover)	None	Q10 (RF5)	USA	Clinical	6 wk	6 mo Includes 6 wk run-in period and 6 wk washout period	Test the hypothesis that a dietary omega-3 fatty acid, DHA, improves the lipoprotein subclass profile of children who have hyperlipidemia	20	Pediatric/ Young Adults	8-21 yr FH or familial combined hyperlipidemia Exclusions: Chronic systemic disease, Secondary hyperlipidemia Smoker	Ages 9 to 19 years, Males: 11 FH: 11 Familial combined hyperlipidemia: 9	20 (20)	Dietary Supplements	Intervention: Low-fat diet + DHA 1.2 g/d; (NCEP+DHA) Placebo: Low-fat diet + identical amount of corn/soy oil (placebo) (NCEP+ Placebo)	20 (20)	Control: Low-fat diet (NCEP)	**Primary:** **HDL/LDL lipoprotein subclasses:** LDL1 [mg/dL (SD)] LDL2 [mg/dL (SD)] LDL3 [mg/dL (SD)] LDL4 [mg/dL (SD)] HDL2 [mg/dL (SD)] HDL3 [mg/dL (SD)] **Secondary:** Mean TC [mg/dL (SD)] Mean LDL-C [mg/dL (SD)] Mean VLDL-C [mg/dL (SD)] Mean HDL-C [mg/dL (SD)] Mean TG [mg/dL (SD)]	**Primary:** NCEP: 27(13), 62(54), 82(41), 12(13), 8.2(2.7), 33(5) NCEP+DHA: 53(46), 92(59), 41(24), 8(8), 10.0(3.8), 33(7) NCEP + Placebo: 28(14), 69(83), 80(35), 12(15), 8.8(3.1), 35(5) **Secondary:** No difference between B/L or Placebo for any of these parameters.	**S*, NCEP-DHA vs Placebo** **NS, NCEP-DHA vs Placebo** **S*, NCEP-DHA vs Placebo** **NS, NCEP-DHA vs Placebo** **S, NCEP-DHA vs Placebo** **NS, NCEP-DHA vs Placebo**	NR		Addition of docosahexaenoic acid to a low fat diet resulted in significantly greater levels of LDL1 and HDL2 at intervention endpoint for the DHA group, indicating large buoyant less atherogenic particles; and significantly lower levels of LDL3 at intervention endpoint for the DHA group, indicating fewer small, dense LDL atherogenic particles. Thus while the intervention did not change major lipoprotein levels, it did alter the subclasses in such a way as to imply a reduced atherogenic risk.	Q10,13. Addition of docosahexaenoic acid to a low fat diet resulted in significantly greater levels of LDL1 and HDL2 at intervention endpoint for the DHA group, indicating large buoyant less atherogenic particles; and significantly lower levels of LDL3 at intervention endpoint for the DHA group, indicating fewer small, dense LDL atherogenic particles. Thus while the intervention did not change major lipoprotein levels, it did alter the subclasses in such a way as to imply a reduced atherogenic risk.
15930221	Demmers TA	Effects of early cholesterol intake on cholesterol biosynthesis and plasma lipids among infants until 18 months of age	2005	RCT	None	Q11 (RF5, RF9) Q13 (RF5, RF9)	USA	Clinical	From patient enrollment until time of weaning	18 mo	Determine whether levels of dietary cholesterol in infancy induced changes in fractional synthesis rate and plasma lipid levels that persisted at 18 mo of age	34	Pediatric/ Young Adults	< 2 wk	NR	Arm 1: 16 (15) Arm 2: 18 (17)	Dietary Supplements	Arm 1: Prepared commercial formula + 40 mg cholesterol X 6 mos as exclusive food, weaned to whole milk at 12 mo (MCF) Arm 2: Prepared commercial formula as exclusive food X 6 mo, then weaned to whole milk at 12 mo (CF)	N/A	18 infants who were breastfed exclusively until weaned at 12 mo were used as a reference group (BF)	**Primary:** Mean average energy intake [kJ (SEM)] Mean average cholesterol intake [mg (SEM)] Mean TC [mmol/L (SEM)] Mean HDL-C [mmol/L (SEM)] Mean LDL-C [mmol/L (SEM)] Mean TG [mmol/L (SEM)]	**Primary:** At 4 m & 18 m, breast-fed (BF) grp had lower energy intake than both formula grps. At 18 m, no difference. At 4 mo, BF & 80mgF had higher chol intake than standard 40mgF. At 18 m, no difference. **AT 4 MONTHS:** BF: 4.07+/-0.15 vs MCF: 3.85+/-0.16 vs CF: 3.28+/-0.15 **AT 18 MONTHS:** No difference. **AT 4 MONTHS:** BF:1.09+/-0.06 vs MCF: 1.43+/-0.07 vs CF:1.15+/00.06 **AT 18 MONTHS:** No difference. **AT 4 MONTHS:** BF: 2.08+/-0.11 vs MCF: 1.56+/-0.12 vs CF:1.20+/-0.11 **AT 18 MONTHS**: No difference. **AT 4 MONTHS:** BF:3.81+/-0.16 vs MCF:2.76+/-0.17 vs CF:2.96+/-0.16 **AT 18 MONTHS:** No difference.	**At 4 m, BF vs either formula: S**** **At 18m, NS between groups** **At 4 m, NS between BF & MCF;** **S** between CF & BF & MCF.** **At 18 m, NS between groups.** **S** for CF vs BF;S* for MCF vs CF.** **NS between groups** **S* between groups** **NS** **S* for BF vs MCF,S** vs CF** **NS** **S** for BF vs MCF,p=S* vs CF.** **NS**	None		At 4 months of age as dietary cholesterol increased, there was decreased cholesterol synthesis and increasing plasma cholesterol levels. These differences did not persist post weaning regardless of cholesterol intake in infancy.	Q11, 13: At 4 months of age as dietary cholesterol increased, there was decreased cholesterol synthesis and increasing plasma cholesterol levels. These differences did not persist post weaning regardless of cholesterol intake in infancy.
15955465	Martino F	Effect of dietary supplementation with glucomannan on plasma total cholesterol and low density lipoprotein cholesterol in hypercholesterolemic children	2005	RCT	None	Q6 (RF2, RF5) Q10 (RF5)	Italy	Clinical	8 wk - note each sterol was studied for 4 weeks each with a 6 week washout in between	16 wk Includes 2 - 6 wk run-in with Step-One-Diet	Evaluate the effect of the adjunct of the hydrosoluble fiber glucomannan to a Step-One-Diet to reduce plasma cholesterol in hypercholesterolemic children	61	Pediatric/ Young Adults	≤ 14 yr Cholesterol > 95th percentile for age and sex in 2 different measurements No dietary treatments in the previous 3 mo Either 1 parent with TC > 6.2 mmol/L, or family amamnesis for CVD in 1st or 2nd degree relatives Exclusions: Any illness or d	Mean age (SD): Arm 1: 8 yr (3) Control Arm: 8 yr (3) Males: 25 FH: 19 Family combined hyperlipidemia: 3 Polygenic hypercholesterolemia: 18 All patient characteristics except sex pertain only to children who completed the study	NR (20)	Pharmacologic	Arm 1: Glucomannan 2-3 g/d + Step-One-Diet (DIET+G) Each glucomannan capsule contained 0.5 g of active glucomannan Children < 6 yr received 2 capsules at lunch and dinner; children > 6 yr received 3 capsules at lunch and dinner Step-One-Diet restricted average intake of saturated fatty acids to < 10% total calories, intake of total fat to < 30% total calories, and intake of cholesterol to < 300 mg/d	NR (20)	Control Arm: Step-One-Diet (DIET) Step-One-Diet restricted average intake of saturated fatty acids to < 10% total calories, intake of total fat to < 30% total calories, and intake of cholesterol to < 300 mg/d	**Primary:** Mean TC [mmol/L (SD, 95% CI)] Mean LDL-C [mmol/L (SD, 95% CI)] **Secondary:** Mean HDL-C [mmol/L (SD, 95% CI)] Mean TG [mmol/L (SD, 95% CI)]	**Primary:** DIET: 6.56(1.01) to 5.83(0.87) DIET+G: 6.29(1.05) to 5.15(0.90) DIET: 4.54(1.19) to 3.99(1.11) DIET+G: 4.46(1.23) to 3.40(1.09) **Secondary:** No difference between groups No difference between groups	**S between groups** **S between groups** **NS** **NS**	No	Decreases were greater in females.	The addition of glucomannan to a low fat, low saturated fat diet significantly decreased total & LDL-C in hypercholesterolemic children. There were no changes in any other lipid parameter.	Q10. The addition of glucomannan to a low fat, low saturated fat diet significantly decreased total and LDL-C in hypercholesterolemic children. There no changes in any other lipid parameter.
16140708	Clauss SB	Efficacy and safety of lovastatin therapy in adolescent girls with heterozygous familial hypercholesterolemia	2005	RCT	None	Q10 (RF5)	USA	Clinical	24 wk	28 wk Includes 4 wk run-in period with diet	Evaluate lipid-altering efficacy, safety, and tolerability of lovastatin treatment in adolescent girls with heFH	54	Pediatric/ Young Adults	10-17 yr (3 patients who had reached their 18th birthday < 6 mo before randomization were also allowed to enter the study) Girls HeFH BMI between 10th and 95th percentiles for age Exclusions: Homozygous FH Dyslipidemias (types I, III, IV, and V) Diabetes Known impairment of renal function Nephrotic syndrome	Mean age (SD): Arm 1: 15 yr (2) Control Arm: 15 yr (2) White: Arm 1: 28 Control Arm: 15 Nonwhite: Arm 1: 7 Control Arm: 4	35 (33)	Pharmacologic	Arm 1: Diet + lovastatin 20 mg/d wk 1-4 Diet + lovastatin 40 mg/d wk 5-24 Patients followed an American Heart Association Step I or similar diet	19 (18)	Control Arm: Diet + placebo Patients followed an American Heart Association Step I or similar diet	**Primary:** Change in mean LDL-C [% (SE)] Change in mean TC [% (SE)] Change in mean apo B [% (SE)] **Secondary:** Change in median TG [% (SE)] Change in mean HDL-C [% (SE)] Change in median VLDL-C [% (SE)] Change in mean apo A-1 [%(SE)]	**Primary: Lovastatin 20 mg/ 40 mg** 20 mg:-23.0%(3.3);40 mg:-26.8%(3.4);CON:+3.4%(3.8) 20 mg:-17.4%(2.4);40 mg:-21.8%(2.5);CON:+2.4%(2.9) 20 mg:-19.9%(3.6);40 mg:-23.2%(3.3);CON:+5.6(4.1) **Secondary:** 20 mg:-10.3%(6.1);40 mg: -22.7%(6.8);CON:-11(11.3) 20 mg:-4.8%(2.4);40 mg:+2.5%(2.5);CON:+2.4(2.7) 20 mg: -22.0%(10.4); 40 mg:-6.7%(12.4);CON: 0(15.8) 20 mg: 2.5%(3.1);40 mg:+3.3(3.5); CON: +1.8(3.5)	**Primary:** **S** vs CON at each dose level** **S** vs CON at each dose level** **S** vs CON at each dose level** **NS vs CON at each dose level** **NS vs CON at each dose level** **NS vs CON at each dose level** **NS vs CON at each dose level**	No adverse events in treatment group	Safety parameters met - no change in physiologic measures, anthropomorphic measures or hormone levels	Lovastatin was safe and effective in adolescents girls with FH in a 24 week trial with no changes in growth or hormone levels. There was no significant difference with a dose increase from 20 to 40 mg/d.	Q10. Lovastatin was safe and effective in adolescents girls with FH in a 24 week trial with no changes in growth or hormone levels. There was no significant difference with a dose increase from 20 to 40 mg/d.
16200842	Allen HF	Randomized controlled trial evaluating response to metformin versus standard therapy in the treatment of adolescents with polycystic ovary syndrome	2005	RCT	None	Q10 (RF8, RF12, RF14)	USA	Clinical	6 mo	6 mo	Evaluate the hypothesis that metformin will improve signs and symptoms of PCOS in adolescents as compared to oral contraceptive pills and have a a favorable effect on obesity	35	Pediatric/ Young Adults	Female Adolescents aged 12-21 yr Symptoms and signs suggesting PCOS Hyperandrogenemia (total testosterone > 60 ng/dL and free testosterone > 1.1 pg/mL) No evidence of androgen secreting tumor (no clitoromegaly, male body habitus, or total testosterone level > 200 ng/dL) Oligomenorrhea (< 6 menses in the previous 6 mo) Obesity (> 95th percentile BMI for age) Stimulated 17-hydoxyprogesterone < 300 ng/dL Hyperinsulinemic (fasting insulin level > 20 µU/mL)	Mean age: Arm 1: 15.3 yr Arm 2: 15.4 yr Caucasian Arm 1: 8 Arm 2: 7 Hispanic Arm 1: 7 Arm 2: 6 African American Arm 1: 0 Arm 2: 3 Patient characteristics available only for patients who completed the study	Arm 1: 17 (15) Arm 2: 18 (16)	Pharmacologic	Arm 1: Oral contraceptives Oral contraceptive therapy consisted of ethinyl estradiol/norgestimate (35 µg/0.25 mg) Arm 2: Metformin Patients received 500 mg metformin bid for 2 wk If well tolerated the dose was increased to 1 g bid for the remainder of the study	N/A	N/A	**Primary: 6 MONTH RESULTS** Mean free testosterone [% change (95% CI)] **Secondary:** Mean weight [% change (95% CI)] Mean BMI [% change (95% CI)] Mean fasting insulin [% change (95% CI)] Mean glucose/insulin ratio [% change (95% CI)] Mean TC [mg/dL (SE)] Mean LDL [mg/dL (SE)] Mean HDL [mg/dL (SE)] Mean TG [mg/dL (SE)]	**Primary:** MET: -22% (-36,-4)vs OCP: -14%(-39,-10) **Secondary:** MET: -1.6%(-4,-1) vs OCP: -2.3%(-4,0) MET: -1.7%(-5,-1) vs OCP: -3.6(-5,-2) MET: -17% (-50,+16) vs OCP:-28%(-45,-11) MET:+65%(15,116) vs OCP: +62% (30,93) MET: 163+/-5 to 169+/-8 vs OCP:184+/-13 to 212+/-21 MET: 98+/-4 to 100+/-7 vs OCP:118+/-12 to 133+/-19 MET: 41+/-1 to 44+/-4 vs OCP:40+/-2 to 51+/-3 MET:119+/-12 to 127+/-15 vs OCP:130+/-10 to 135+/-10	**S** for both** **S* for both** **S for both** **NS for MET, S* for OCP** **S for both** **S for both** **NS for MET, S for OCP** **NS for MET, S *for OCP** **NS for both**	None reported		In a 6 month period, adolescents with PCOS had equivalent and significant wt loss, reduction in testosterone levels & improvement in insulin sensitivity on both metformin and OCP. TC, LDL & HDL levels increased in both groups, more in the OCP group.	Q10. In a 6 month period, adolescents with PCOS had equivalent and significant wt loss, reduction in testosterone levels & improvement in insulin sensitivity on both metformin and OCP. TC, LDL & HDL levels increased in both groups, more in the OCP group.
16200842	Allen HF	Randomized controlled trial evaluating response to metformin versus standard therapy in the treatment of adolescents with polycystic ovary syndrome	2005											Not diabetic (fasting glucose level < 126 mg/dL) Exclusions: Reported current or past sexual activity Oral contraceptive use within previous 6 mo Positive urine pregnancy test Abnormal BUN, Cr, AST, or a positive personal or family history of thrombosis											
16330680	Raitakari OT	Endothelial function in healthy 11-year-old children after dietary intervention with onset in infancy: the Special Turku Coronary Risk Factor Intervention Project for children (STRIP)	2005	RCT	FMD	Q10,13 (RF5) Q14a (RF5)	Finland	Clinical	NR	10 yr 5 mo (until children were 11 yr)	Assess endothelial function in healthy 11-year-old children after dietary intervention with onset in infancy	1062	Pediatric/ Young Adults	5 mo at recruitment, 7 mo at randomization	NR	540 (179)	Behavioral	Arm 1: Dietary and lifestyle counseling (INT) Counseling provided 2 times per yr Diet designed to meet Nordic Dietary Recommendations	522 (190)	Control Arm: Basic health education (CON) Minimal amount of nutritional counseling after infancy	**Primary:** Mean maximum FMD [% (SD)] Mean maximum FMD adjusted for LDL[%] Mean serum cholesterol [mmol/L (SD)] Mean LDL-C [mmol/L (SD)] **Secondary:** Mean weight [kg (SD)] Mean BMI [kg/m2 (SD)] Mean HDL-C [mmol/L (SD)] Mean TG [mmol/L (SD)] Mean SBP [mmHg (SD)] Mean DBP [mmHg (SD)] Mean physical activity [% (SD)] Exposure to tobacco smoke [%]	**Primary:** Females: INT=8.84% vs CON=8.44%. Males: INT=9.62% vs CON=8.36%. FMD remained significantly higher in intervention boys even after adjusting for LDL levels at various time points. Males: INT: 4.37 vs. CON: 4.58mmol/L Females: No difference between groups INT: 2.64 vs. CON: 2.92mmol/L Females: No difference between groups **Secondary:** There were no differences regarding HDL and triglycerides, blood pressure, family risk, physical activity or tobacco smoke exposure.	**NS** **S*** **S** **NS** **S*** **NS**	Not reported.	Intervention children had significantly lower intake of saturated fat and higher polyunsaturated/ saturated fat ratios.	A dietary intervention that lowers saturated fat intake with a higher polyunsaturated/ saturated fat ratio beginning in infancy can have lasting effects on dietary composition. At 11 yrs of age, there was a significant reduction in total and LDL cholesterol levels in the intervention group, but only for boys. FMD, a measure of vascular health was also higher in in intervention boys but not in girls.	Q10,13,12a. A dietary intervention that lowers saturated fat intake with a higher polyunsaturated/ saturated fat ratio beginning in infancy can have lasting effects on dietary composition. At 11 yrs of age, there was a significant reduction in total and LDL cholesterol levels in the intervention group, but only for boys. FMD, a measure of vascular health was also higher in in intervention boys but not in girls.

NHLBI Evidence Table: RF5-RCT

PMID	First Author	Title	Year	Study Type	CVD	RF by CQ	Country	Setting	Int Length	Total Study Duration	Main Study Objective	Total N	Target Population	Eligibility Criteria	Patient Characteristics	Int. n at Baseline (n at Final Follow-up)	Int Type	Specific Intervention	Control n at Baseline (n at Final Follow-up)	Specific Control	Outcomes Measured	Results/CI	Significance S (p<0.05 or non-overlapping CI); S* (p<0.01); S** (p<0.001); NS (p≥0.05 or overlapping CI)	Safety and Adverse Events	Additional findings	Summary	Main Reported Findings by Critical Question
16647412	Jakulj L	Plant stanols do not restore endothelial function in pre-pubertal children with familial hypercholesterolemia despite reduction of low-density lipoprotein cholesterol levels	2006	RCT (crossover)	FMD	Q10 (RF5) Q12a (RF5) Q13 (RF4, RF8)	Netherlands	Clinical	4 wk	20 wk Includes 2 wk diet run-in period and 6 wk wash-out period 29 subjects started with an extended run-in period of 6 wk	Examine the effect of plant stanols on lipids and endothelial function in pre-pubertal children with FH	42	Pediatric/ Young Adults	7-12 yr FH	Mean age (SD): 9.8 yr (1.5) Males: 22 Clinical signs of hypercholesterolemia: 0 Smokers: 0	42 (41)	Dietary Supplements	Intervention: Plant stanol-enriched yogurt + low-saturated fat, low-cholesterol diet (STAN) Children consumed 1 500-mL jar of yogurt daily, containing 2.0 g of plant stanols Diet was compatible with the NCEP-II diet	42 (41)	Control: Placebo yogurt + low-saturated fat, low-cholesterol diet (PLAC) Children consumed 1 500-mL jar of yogurt daily Diet was compatible with the NCEP-II diet	**Primary:** Mean absolute change in LDL-C [%(CI)](SD)] Mean FMD [% (SD)] **Secondary:** Mean absolute change in TC[%(CI)] Mean absolute change in HDL-C[%(CI)] Mean absolute change in TG [%(CI)]	**Primary (STAN vs PLAC)** -0.48(CI:-0.69,0.27) STAN:10.5(5.1); PLAC:10.6(5.0) **Secondary** -0.53(CI:-0.79,0.28) No significant change No significant change	**S** **NS** **S** **NS** **NS**	None reported.	None	Plant stanols reduced LDL significantly and moderately but did not improve FMD.	Q10,12a (RF 5) Plant stanols reduced LDL-C but did not improve FMD
16682304	Rodenburg J	Oxidized low-density lipoprotein in children with familial hypercholesterolemia and unaffected siblings: effect of pravastatin	2006	RCT	IMT	Q10 (RF5) Q12a (RF7)	USA Netherlands	Clinical	2 yr	2 yr	Assess the role of oxidized phospholipids (OxPLs) in children with FH and the effect of pravastatin	214	Pediatric/ Young Adults	8-18 yr FH	Mean age (SD): Arm 1: 12.9 yr (3.0) Control Arm 1: 12.9 yr (2.9) Males: Arm 1: 48 (53%) Control Arm 1: 45 (51%) Regular smokers: 6.1%	NR (90)	Pharmacologic	Arm 1: Pravastatin + low fat diet + physical activity Children < 14 yr received 20 mg pravastatin daily Children ≥ 14 yr received 40 mg pravastatin daily Children were instructed to assume or continue a low-fat diet and to maintain habitual physical a	NR (88)	Control Arm 1: Placebo + low fat diet + physical activity Children were instructed to assume or continue a low-fat diet and to maintain habitual physical activity 80 non-FH siblings served as a reference group	**Primary:** OxLDL markers OxPL/apoB Autoantibodies to MDA-LDL IgG IgM Immune complexes Total IgG apoB-IC Total IgM apoB-IC IgG IC/apoB IgM IC/apoB Lipoproteins Mean apoB(mg/dL (SD) Mean Lp(a) lipoprotein (mg/dL SD) **Secondary:** Mean TC [mg/dL (SD)] Mean HDL-C [mg/dL (SD)] Mean LDL-C [mg/dL (SD)] Mean TG [mg/dL (SD)] Mean hs-CRP [mg/L (SD)] Mean carotid IMT [mm (SD)]	**Primary:** OxLDL markers Incr 48.7 vs 29.3% IgG No change IgM No change Decr 31.9 vs 12.2 % Decr 25.5 vs 13.2 % No change No change Lipoproteins Decr 18.7 vs 0.3 % Incr 21.9 vs 10.7 % **Secondary:** Decr 18.6 vs 0.2 % Incr 7.4 vs 1.0 % Decr 24.2 vs 0.4 % No change Not provided Not provided	**S*** **NS** **NS** **S**** **S**** **NS** **NS** **S**** **S** **S**** **NS (p 0.073)** **S**** **NS**	None reported.	None of the OxLDL markers, Lp(a) lipoprotein or hsCRP predicted the baseline or change in carotid IMT.	Compared with placebo, pravastatin decreased total and LDL-C, apoB, total IgG apoB-IC, and total IgM apoB-IC. In contrast, pravastatin increased OxPL/apoB and Lp(a) lipoproteins. The authors speculate that the latter two findings may represent a novel mechanism of mobilization and clearance of OxPL; however, neither of these two markers predicted baseline or change in carotid IMT.	Q10 (RF5) In children with FH, pravastatin significantly reduced TC, LDL-C and apoB and markers of oxidation and inflammation with no correlation with CIMT.
17218893	Barrett LA	Exercise and postprandial plasma triacylglycerol concentrations in healthy adolescent boys	2007	RCT	None	Q13 (RF5, RF11, RF14)	UK	Clinical	4 d	11 d Includes 7 d separation period	Investigate whether continuous-exercise and intermittent-games activity would reduce postprandial TG concentrations in adolescent boys	19	Pediatric/ Young Adults	Adolescent boys Recreationally active Not taking any drugs thought to affect lipid or carbohydrate metabolism	Mean age (SE): 15.4 yr (0.1)	Arm 1: 10 (10) Arm 2: 9 (9)	Behavioral	Arm 1: 2 d rest trial + 2 d continuous exercise trial (ContEx) Day 1 of rest trial included no exercise Day 1 of exercise trial included 15-min warm-up on treadmill and 4 blocks (approx. 15 min each) of uphill treadmill walking with 3 min rest between each block Arm 2: 2 d rest trial + 2 d intermittent games (IntEx) Day 1 of rest trial included no exercise Day 1 of exercise trial included intermittent-games activity, which consisted of 2-4 blocks of a modified version of the Loughborough intermittent shuttle test (LIST)	N/A	N/A	**Primary:** Mean fasting plasma TG [mmol/L (SE)] Mean postprandial plasma TG [mmol/L (SE) (6-h area under the curve)] **Secondary:** Mean HR [bpm (SE)] Mean maximum HR [% (SE)] % peak VO2 treadmill [% (SE)] Mean block time [min:sec (SE)] Blood lactate[mmol/-L-1(SE)] Mean fasting blood TC [mmol/L (SE)] Mean fasting plasma HDL-C [mmol/L (SE)] Mean fasting blood glucose [mmol/L (SE)]Mean HR [bpm (SE)] Mean fasting blood TC [mmol/L (SE)]	**Primary:** ContEx: Rest 1.09+/-0.12 ContEx: EX 0.93+/-0.08 IntEx: Rest 1.11+/-0.15 IntE: EX 0.92+/-0.12 ContEx: 7.26+/-0.82 vs Rest: 8.39+/-0.75 IntEx: 6.92+/-0.79 vs Rest: 9.38+/-1.25 **Secondary:** ContEx: 143+/-3 vs IntEx: 161+/-4 ContEx:73.7+/-1.4 vs IntEx: 80.3+/-1.7 ContEx: 58.9+/-7.1 vs IntEx: 68.8+/-2.3 ContEx:1 5+/-0 vs IntEx: 18.29+/-0.08 ContEx: 2.0+/-0.3 vs IntEx: 2.4+/-0.7 No difference between rest & exercise results for either group for TC, HDL, or glucose	**NS** **S** **S** **S*** **Not given** **Not given** **Not given** **Not given** **Not given** **NS**	None	IntEx was more strenuous than the ContEx protocol and TG reduction was greater with the former.	A single session of either continuous or intermittent exercise 16 h before an oral fat-tolerance test reduced post-prandial TG in a small group of adolescent males. Exercise appears to have a beneficial short term effect on serum TGs.	Q10: A single session of either continuous or intermittent exercise 16 h before an oral fat-tolerance test reduced post-prandial TG in a small group of adolescent males. Exercise appears to have a beneficial short term effect on serum TGs.
17218893	Barrett LA	Exercise and postprandial plasma triacylglycerol concentrations in healthy adolescent boys	2007															On day 2 of each trial in both arms, subjects consumed a test meal consisting of 1.25 g fat, 1.07 g CHO, 0.20 g protein and 67 kJ/kg body mass, then read, watched videos, or played computer games Trials were separated by minimum of 7 d and performed in randomized order			Mean fasting plasma HDL-C [mmol/L (SE)] Mean fasting plasma TG [mmol/L (SE)] Mean postprandial plasma TG [mmol/L (SE)] Mean fasting blood glucose [mmol/L (SE)] Mean postprandial blood glucose [mmol/L (SE)] Mean gross energy expenditure for walk [kJ/kg body mass (SE)]					
17698729	Niinikoski H	Impact of Repeated Dietary Counseling Between Infancy and 14 Years of Age on Dietary Intakes and Serum Lipids and Lipoproteins: The STRIP Study	2007	RCT	None	Q10 (RF5, RF9)	Finland	Clinical	13 yr 5 mo	13 yr 5 mo	Evaluate the effect of low-saturated fat, low-cholesterol dietary counseling on fat intake, growth, serum lipid values, and pubertal development in children and adolescents	1,062	Pediatric/ Young Adults	Children and adolescents	Randomized children from well baby clinics in Turku, Finland to a low fat low saturated fat diet beginning at 7 m of age through repeated, individualized diet counseling. Current report is 14 y F/U of this cohort.	540 (254)	Behavioral	Provision of dietary counseling by a nutritionist. Nutritionist provided dietary counseling to children and families starting at 7 months of age, beginning at 1-3 month intervals until age 2, at which point they received counseling twice a year until age 7 and once a year until age 14. Annual 4-day food records were also obtained.	522 (278)	Basic health education routinely given to children and families starting at 7 months of age until age 14 at Finnish well-baby clinics and through school health care. Children were seen biannually until age 7 and annually thereafter.	**Primary:** Results assessed at least annually from 7mo to 14 yrs of age: 24 hour diet records: Energy intake Total fat intake Saturated fat intake Protein intake Carbohydrate intake Physiologic measures: TC HDL-C TG LDL-C Apo A-I Apo B BMI	**Primary:** (1) INT children had lower fat & sat fat intake than CON throughout the study period. (2) INT group had higher protein and carb intake throughout the study period. (3) Energy intake of INT group was slightly lower than CON throughout the study period. (4) Girls had higher sat fat intake as % of total calories than did boys. (5) There were no diffferences in ht,wt or BMI throughout the study period. (6) There were no differences in pubertal progression between the 2 groups. (7) Age at menarche did not differ between groups. (8) Serum TC and LDL-C were lower in boys throughout the study period but did not differ between groups for females after 7 y of age. (9) There was no difference between groups for HDL-C levels in Ms or Fs; Apo B levels reflected LDL-C results and ApoA1 levels reflected HDL-C results. (10) TG levels were lower in Ms than Fs in both groups and were significantly lower in INT boys than CON. (11) TC decreased in both groups beginning at 7-9 y. (12) TC, LDL-C and HDL-C all decreased with puberty, more in Ms than Fs.	**S** for both. **S** for both. **S**** **S** **NS for all.** **NS for all.** **NS** **S** for boys; **NS for girls.** **NS** **S**	None		Saturated fat intake remained significantly lower throughout childhood and early adolescence in children who received repeated dietary counseling beginning at 7 m of age. There were no adverse effects noted on growth, development or sexual maturation. In boys, the lower fat intake was associated with 5% lower TC and LDL-C levels; this was only seen in girls until age 7. As in other studies, cholesterol and HDL-C levels decreased with puberty,. more in Ms than Fs.	Repeated dietary counseling beginning at 7 mo of age results in sustained lower saturated fat intake X 10 yrs in males and females with lower TC and LDL-C levels in males but not in females; there were no adverse effects on growth, development or sexual maturation.