Specific Care Question :

In children with elevated blood lipids should omega-3 fatty acid (n3 FA) supplementation versus no n-3 FA with outcomes of serum total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides?

Question Originator:

Katherine Collum, BSN, RN

Plain Language Summary From The Office of Evidence Based Practice: Summary:

Dietary fat plays two important roles in metabolism. First, it is a major source of energy for humans, and second it is necessary for the absorption of fat soluble vitamins. For healthy children the Daily Reference Intake (DRI) for total fat intake is not determined. However DRIs are determined for specific fats:

	Linoleic acid, omega-6 fatty acid (g/d)		α- linolenic acid, omega-3 fatty acid (g/d)	
Infant				
0-6 mo	4.4		0.5	
6-12 mo	4.6		0.5	
Child				
1-3 years	7		0.7	
4-8 years	10		0.9	
Adolescent	**Male**	**Female**	**Male**	**Female**
9-13 years	12	10	1.2	1.0
14-18 years	16	11	1.6	1.1

As you can see the DRI for healthy children of n-3 fat ranges from 0.5-1.6 gram per day, which is equivalent to 4.5-14 kcal from n-3 FA per day.
(*Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients)*, 2005) The American Heart Association states that dose > 3 g/d of n-3 fat should be monitored by a physician.

From this review, supplementation with n-3 fatty acids for > 2 months:

- Serum LDL level- statistically significant elevation -Standard Mean Difference (SMD) = 1.03 (0.23, 1.83)
- Serum total cholesterol -no significant change - SMD = 0.18 (-01.2, 0.49)
- Serum triglycerides – statistically significant decrease- SMD = -0.81 (-1.60, -0.02)
- Serum HDL cholesterol no significant change- SMD = 0.07 (-0.22, 0.36)

Based on low quality evidence a weak recommendation is made not to supplement with n3 fatty acids. The desirable effect of lowering serum triglycerides is balanced with the undesirable effect of elevating serum LDL. Other alternatives may be equally reasonable.

EBP Scholar's Responsible for Analyzing the Literature:
K. Collum, RN
L. Thompson, MS, RD, LD
J. Menown, BSN, RN, CPN
T. Tobin, MSOD, RRT, NPS
A. Melanson, OTD, OTR/L
J. McCollum, RN, CNOR

EBP Team Member Responsible for Reviewing, Synthesizing, and Developing this Literature:
N. Allen, MS, MLS, RD, LD, CNSC

Search Strategy and Results:
Search Strategy: ("Fatty Acids, Omega-3/therapeutic use"[Mesh] AND "Cholesterol"[Mesh]) OR "Lipoproteins, HDL"[Mesh]) OR "Lipoproteins, LDL"[Mesh]) OR "Triglycerides"[Mesh]) AND "Pediatrics"[Mesh]

Twelve studies were identified for this review. Seven studies were excluded. Major reason for exclusion is the population adults with various diseases. Five studies are included. For the included studies the major reason for decreasing the quality of the evidence is the difference in when follow- up laboratory values were obtained. Hooper 2004 is a Cochrane Metaanalysis and Systematic Review. It was analyzed using a separate GRADE Profile. The Outcomes are labeled "> 2 months" of supplementation but the actual time varied from 8- 12 weeks at follow up. The other major difference is the dose of n-3 fatty acids varied from 2.2-3.5 g in each study. Finally, for each outcome the maximum number of subjects is < 100 and does not meet the standard for precision which is > 400 subjects across included studies.

The outcomes for this synthesis are change in blood lipid levels after supplementation of n--3 fatty acids. The desired direction of change is as follows:

Outcome	Interpretation
Change in S. LDL Cholesterol	Negative change is better
Change in S. Total Cholesterol	Negative change is better
Change in S. Triglycerides	Negative change is better
Change in S. HDL Cholesterol	Positive change is better

Studies Included in this Review:

1. *Adler & Holub, 1997*
2. *Davidson et al., 1997*
3. *Hooper et al., 2004*
4. *Radack, Deck, & Huster, 1990*
5. *Swahn, von Schenck, & Olsson, 1998*

Studies Excluded From this Review:

Study ID	Reason for Exclusion
Bonanome et al., 1996	Subjects were adults with chronic renal failure. There was no randomization, allocation concealment, or blinding of participants or outcome assessors.
Eslick, Howe, Smith, Priest, & Bensoussan, 2012	Low quality systematic review/meta analysis, details on heterogeneity, study quality and defintition of clinicla significance are missing.
Jacobson, Glickstein, Rowe, & Soni, 2012	The data is not in a usable form.

Meyer, Hammervold, Rustan, & Howe, 2007	Subjects were adults on statins therapy who continued to have elevated triglycerides.
Montoya et al., 2002	Does not answer the question
Theobald, Chowienczyk, Whittall, Humphries, & Sanders, 2004	Low quality study, with many biases. Poor reporting of their methods.
Vandongen, Mori, Codde, Stanton, & Masarei, 1988	Treatment was dietary manipulation, not supplemental n--3 therapy Subjects were adults with diabetes Type 1. The supplement was eicosapentaen.oic acid

Method Used for Appraisal and Synthesis:
The Cochrane Collaborative computer program, Review Manager (RevMan 5.1.7) was used to synthesize the five included studies. The GRADE Working Group Program GRADEProfiler (GradePro) was used to GRADE the evidence.

Updated November 11 2013; December 20, 2013, Dec 24, 2013, Feb 13 2014

References:

Adler, A. J., & Holub, B. J. (1997). Effect of garlic and fish-oil supplementation on serum lipid and lipoprotein concentrations in hypercholesterolemic men. *Am J Clin Nutr, 65*(2), 445-450.

Bonanome, A., Biasia, F., De Luca, M., Munaretto, G., Biffanti, S., Pradella, M., & Pagnan, A. (1996). n-3 fatty acids do not enhance LDL susceptibility to oxidation in hypertriacylglycerolemic hemodialyzed subjects. *Am J Clin Nutr, 63*(2), 261-266.

Davidson, M. H., Maki, K. C., Kalkowski, J., Schaefer, E. J., Torri, S. A., & Drennan, K. B. (1997). Effects of docosahexaenoic acid on serum lipoproteins in patients with combined hyperlipidemia: a randomized, double-blind, placebo-controlled trial. *J Am Coll Nutr, 16*(3), 236-243.

Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). (2005). The National Academies Press.

Eslick, G. D., Howe, P. R., Smith, C., Priest, R., & Bensoussan, B. A. (2012). Benefits of fish oil supplementation in hyperlipidemia: a systematic review and meta-analysis (Structured abstract). *Databas of Abstracts or Reviews of Effects, 4*.

Hooper, L., Thompson, R. L., Harrison, R. A., Summerbell, C. D., Moore, H., Worthington, H. V., . . . Ebrahim, S. B. (2004). Omega 3 fatty acids for prevention and treatment of cardiovascular disease. *Cochrane Database Syst Rev*(4), CD003177. doi: 10.1002/14651858.CD003177.pub2

Jacobson, T. A., Glickstein, S. B., Rowe, J. D., & Soni, P. N. (2012). Effects of eicosapentaenoic acid and docosahexaenoic acid on low-density lipoprotein cholesterol and other lipids: a review. *J Clin Lipidol, 6*(1), 5-18. doi: 10.1016/j.jacl.2011.10.018 S1933-2874(11)00745-8 [pii]

Meyer, B. J., Hammervold, T., Rustan, A. C., & Howe, P. R. (2007). Dose-dependent effects of docosahexaenoic acid supplementation on blood lipids in statin-treated hyperlipidaemic subjects. *Lipids, 42*(2), 109-115. doi: 10.1007/s11745-006-3014-4

Montoya, M. T., Porres, A., Serrano, S., Fruchart, J. C., Mata, P., Gerique, J. A., & Castro, G. R. (2002). Fatty acid saturation of the diet and plasma lipid concentrations, lipoprotein particle concentrations, and cholesterol efflux capacity. *Am J Clin Nutr, 75*(3), 484-491.

Radack, K. L., Deck, C. C., & Huster, G. A. (1990). n-3 fatty acid effects on lipids, lipoproteins, and apolipoproteins at very low doses: results of a randomized controlled trial in hypertriglyceridemic subjects. *Am J Clin Nutr, 51*(4), 599-605.

Swahn, E., von Schenck, H., & Olsson, A. G. (1998). Omega-3 Ethyl Ester Concentrate Decreases Total Apolipoprotein CIII and Increases Antithrombin III in Postmyocardial Infarction Patients. *Clin Drug Investig, 15*(6), 473-482. doi: 150603 [pii]

Theobald, H. E., Chowienczyk, P. J., Whittall, R., Humphries, S. E., & Sanders, T. A. (2004). LDL cholesterol-raising effect of low-dose docosahexaenoic acid in middle-aged men and women. *Am J Clin Nutr, 79*(4), 558-563.

Vandongen, R., Mori, T. A., Codde, J. P., Stanton, K. G., & Masarei, J. R. (1988). Hypercholesterolaemic effect of fish oil in insulin-dependent diabetic patients. *Med J Aust, 148*(3), 141-143.

Eslick, G. D., Howe, P. R., Smith, C., Priest, R., & Bensoussan, B. A. (2012). Benefits of fish oil supplementation in hyperlipidemia: a systematic review and meta-analysis (Structured abstract). *Databas of Abstracts or Reviews of Effects, 4*.

Characteristics of Included Studies:

Tables:

Adler 1997

Methods	RCT of fish oil and/or garlic supplementation on serum lipids
Participants	46 men with total cholesterol >200 mg/dl
Interventions	1) 900 mg garlic placebo + 12 gm oil placebo 2) 900 mg garlic + 12 gm oil placebo 3) 900 gm garlic placebo + 12 gm fish oil (3.6 gm n-3 fatty acids) 4) 900 gm garlic + 12 gm fish oil (3.6 gm n-3 fatty acids)
Outcomes	Serum total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol
Notes	

Risk of Bias Table

Bias	Scholars' Judgment	Support for Judgment
Random sequence generation (selection bias)	Unclear risk	Study mentions randomization but gives no detail about how subjects were randomized.
Allocation concealment (selection bias)	Unclear risk	Method of concealment is not described.
Blinding of participants and personnel (performance bias)	Low risk	Blinding of participants and study personnel ensured.
Blinding of outcome assessment (detection bias)	Low risk	No blinding of outcome assessment, but the outcome measurement is unlikely to be influenced by lack of blinding.
Incomplete outcome data (attrition bias)	Low risk	Missing outcome data balanced; similar reasons for missing data
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgment of low or high risk
Other bias	Unclear risk	

Davidson 1997

Methods	RCT
Participants	27 adult volunteers with combined hyperlipidemia (CHL)

Interventions	Initial 6-week period for dietary stabilization on an NCEP Step I diet. 3 randomly assigned groups: 1 - placebo (12 vegetable oil capsules) 2 - 1.25 g DHA/day (6 DHA and 6 placebo capsules) 3 - 2.5 g DHA/day (12 DHA capsules)
Outcomes	Change in LDL-C, change in HDL-C, and change in triglycerides.
Notes	Summary: dietary supplementation with an algae-derived DHA oil (both low and high dose) was associated with a 17-21% reduction in serum triglycerides among subjects with CHL. Increases in LDL-C were only significant at the higher dose.

Risk of Bias Table

Bias	Scholars' Judgment	Support for Judgment
Random sequence generation (selection bias)	Low risk	Stated randomization, but did not describe how it was achieved
Allocation concealment (selection bias)	High risk	Not described
Blinding of participants and personnel (performance bias)	Low risk	Note: personnel were blinded but blinding of participants may have been disturbed by side effects of burping ("fish burps" would distinguish treatment from placebo)
Blinding of outcome assessment (detection bias)	Low risk	Blinding not describe, but unlikely to have an effect on outcome if lab personnel were not blinded.
Incomplete outcome data (attrition bias)	Low risk	One subject withdrew for personal reasons. Analysis was per-protocol due to timing of withdrawal (week 1)
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Other bias	Low risk	

Radack 1990

Methods	RCT
Participants	25 adults with hypertriglyceridemia
Interventions	1 placebo group received olive oil 1 experimental group received 2.2g/d fish oil 1 experimental group received 1.1g/d fish oil
Outcomes	Total triglycerides Total cholesterol

	HDL cholesterol LDL cholesterol
Notes	Very small, clinically tolerable amounts of n-3 fatty acids in subjects with hypertriglyceridemia had minor hypertriglyceridemic effects while causing significant increases in LDL cholesterol.

Risk of Bias Table

Bias	Scholars' Judgment	Support for Judgment
Random sequence generation (selection bias)	Low risk	Computer-generated randomization
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias)	Low risk	Stabilization period was single-blind, treatment period was double-blind.
Blinding of outcome assessment (detection bias)	Low risk	Laboratory data was concealed from researchers until after study was complete.
Incomplete outcome data (attrition bias)	Low risk	4 subjects left in early stages (1 during stabilization, 3 during the beginning of the treatment period). 3 because of personal conflicts and 1 due to intolerance of olive oil. Their data was not included in the analysis. This should not have significantly affected results.
Selective reporting (reporting bias)	Low risk	All outcomes were reported on.
Other bias	Unclear risk	

Swahn 1998

Methods	Randomized w/computerized random numbers to receive in a double-blinded study
Participants	53 patients completed study, (42 men, 11 women) Exclusion criteria of patients with ongoing plasma lipid-lowering treatment, or other serious diseases that could influence interpretations of results were included. All patients were on medication with beta blockers, an low dose aspirin and this treatment remained throughout study
Interventions	Each participant received 2 g of Omega 3 or 2 g of corn oil. all tablets were identical in shape and color, (all were made by Norsk Hydor AS Research in Norway.) Study period was 12 weeks
Outcomes	All pts received clinical and lab assessments prior to study and after the 12 week study post labs were also drawn, BP was also taken supine after resting for 5 min.

Notes	22 excluded b/c they normalized lipid values with dietary changes. All lab analyses were run simultaneously. all participants were recruited from the Department of Cardiology at Linkopuing University Hospital

Risk of Bias Table

Bias	Scholars' Judgment	Support for Judgment
Random sequence generation (selection bias)	Low risk	Computerized random numbers to receive in a double-blinded study
Allocation concealment (selection bias)	Low risk	
Blinding of participants and personnel (performance bias)	Low risk	Double- blinded study
Blinding of outcome assessment (detection bias)	Unclear risk	
Incomplete outcome data (attrition bias)	Low risk	
Selective reporting (reporting bias)	Low risk	Both primary and secondary outcomes reported
Other bias	Low risk	

Date: 2013-12-24
Question: Should 2-3.5 gm n--3 fatty acids supplement vs. placebo be used for children with altered lipid profiles?
Bibliography: Alder 1997, Davidson 1997, Radak, 1990, Swahn 1998

Quality Assessment Alder 1997, Davidson 1997, Radak, 1990, Swahn 1998,							No of Patients		Effect		Quality	Importance
No of Studies	**Design**	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other Considerations**	**2-3.5 gm n--3 Fatty Acids Supplement**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Total Cholesterol > 2 months (follow-up >2 months; measured with: change in total cholesterol level; Better indicated by lower values)												
4	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	serious[2]	none	84	84	-	SMD 0.16 higher (0.26 lower to 0.58 higher)	LOW	CRITICAL
LDL Cholesterol >2 months (measured with: change in LDL level; Better indicated by lower values)												
4	randomized trials	no serious risk of bias	serious[1,3]	no serious indirectness	serious[2]	none	93	92	-	SMD 1.41 higher (0.24 to 2.58 higher)	LOW	CRITICAL
HDL Cholesterol Week > 2 months (measured with: change in HDL level; Better indicated by higher values)												
4	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	serious	none	93	92	-	SMD 0.01 higher (0.39 lower to 0.37 higher)	LOW	CRITICAL
Triglycerides > 2 months (measured with: serum triglycerides; Better indicated by lower values)												
4	randomized trials	no serious risk of bias	serious[1,3]	no serious indirectness	serious	none	55	54	-	SMD 0.81 lower (1.6 to 0.02 lower)	LOW	CRITICAL

[1] The studies varied on the included population; all were adults, no pediatric studies are included. The adults ranged from healthy adults to adults with various forms of hyperlipidemia. The dose of the fatty acid ranged from 2 g- 3.5 m per day.
[2] The number of subjects in the included studies is low. Aggregated, the number of subjects in the included studies does not approach 400 - that is the minimum number to detect a difference using a usual alpha and beta and effect size of 0.2 (small effect).
[3] The I2 statistic is > 50%

Date Jan 21 2014
Question: Should a low dose (0.4 -2.4 g per day) fish n-3 oil vs. placebo be used for children with altered lipid profiles?

Quality Assessment Hooper 2004							No of Patients		Effect		Quality	Importance
No of Studies	**Design**	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other Considerations**	**0.4 -2.4 g fish n-3 per day (low dose)**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Total Cholesterol > 2 months (follow-up >2 months; measured with: change in total cholesterol level; range of scores: 5.87-6.83; Better indicated by lower values)												
4	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	serious[2]	none	984	959	-	MD 0.11 higher (0 to 0.21 higher)	LOW	CRITICAL
Triglycerides > 2 months (measured with: serum triglycerides mg/dL; range of scores: 0.82-2.26; Better indicated by lower values)												
3	randomized trials	no serious risk of bias	serious[1,2]	no serious indirectness	serious[2]	none	116	112	-	MD 0.28 lower (0.52 to 0.04 lower)	LOW	CRITICAL
HDL Cholesterol > 2 months (measured with: change in HDL level; range of scores: 1.04-1.45; Better indicated by higher values)												
4	randomized trials	serious[3]	serious[1]	no serious indirectness	no serious imprecision	none	983	959	-	MD 0.01 higher (0.02 lower to 0.03 higher)	LOW	CRITICAL
LDL Cholesterol >2 months (measured with: change in LDL level; Better indicated by lower values)												
2	randomized trials	no serious risk of bias	serious[1,4]	no serious indirectness	serious[2]	none	104	100	-	MD 0.26 higher (0.05 lower to 0.57 higher)	LOW	CRITICAL

[1] The studies varied on the included population; all were adults, no pediatric studies are included. The adults ranged from healthy adults to adults with various forms of hyperlipidemia. The dose of the fatty acid ranged from 0.4-2.4 gm per day.
[2] The number of subjects in the included studies is low. Aggregated, the number of subjects in the included studies does not approach 400 - that is the minimum number to detect a difference using a usual alpha & beta and effect size of 0.2 (small effect)
[3] Blinding of providers is not assured in the included studies

Date: Jan 21 2014
Question: Should a medium dose (2-4.4gm) fish n-3 per day vs. placebo be used for children with altered lipid profiles?

Quality Assessment Hooper 2004							No of Patients		Effect		Quality	Importance
No of Studies	**Design**	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other Considerations**	**2-4.4gm fish n-3 per day (medium dose)**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Total Cholesterol > 2 months (follow-up >2 months; measured with: change in total cholesterol level; range of scores: 5.3-8.4; Better indicated by lower values)												
5	randomized trials	serious[1]	serious[2]	no serious indirectness	serious[3]	none	413	382	-	MD 0.08 higher (0.09 lower to 0.25 higher)	VERY LOW	CRITICAL
Triglycerides > 2 months (follow-up 2 months; measured with: serum triglycerides mg/dL; range of scores: 0.79-2.43; Better indicated by lower values)												
4	randomized trials	very serious[1]	serious[2,4]	no serious indirectness	serious[3]	none	376	345	-	MD 0.28 lower (0.71 lower to 0.16 higher)	VERY LOW	CRITICAL
HDL Cholesterol > 2 months (follow-up 2 months; measured with: change in HDL level; range of scores: 0.96-1.69; Better indicated by higher values)												
5	randomized trials	serious[1]	serious[2]	no serious indirectness	serious	none	413	382	-	MD 0.08 higher (0.04 to 0.12 higher)[5]	VERY LOW	CRITICAL
LDL Cholesterol >2 months (measured with: change in LDL level; Better indicated by lower values)												
3	randomized trials	serious[1]	serious[2]	no serious indirectness	serious[3]	none	362	331	-	MD 0.06 higher (0.11 lower to 0.23 higher)	VERY LOW	CRITICAL

[1] all but one study assessed as being medium to high risk of bias.
[2] The studies varied on the included population; all were adults, not pediatric studies are included. The adults ranged from healthy adults to adults with various forms of hyperlipidemia. The dose of the fatty acid ranged from 2 g- 3.5 m per day.
[3] The number of subjects in the included studies is low.
[4] Benefit driven by one study (Eritsland 1996) that did not blind participants or personnel, that may not have influenced outcome of a laboratory value. Blood lipid levels was a secondary outcome.

Date: Jan 21 2014
Question: Should a (high dose (> or = 4.5 g of fish n-3 per day) vs. placebo be used for children with altered lipid profiles?

Quality Assessment Hooper 2004							No of Patients		Effect		Quality	Importance
No of Studies	**Design**	**Risk of Bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other Considerations**	**High Dose**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Total Cholesterol > 2 months (follow-up 2 months; range of scores: 5.2-6.3; Better indicated by lower values)												
7	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	no serious imprecision	none	560	542	-	MD 0.04 lower (0.21 lower to 0.12 higher)	MODERATE	CRITICAL
Triglycerides > 2 months (range of scores: 1.42-5.07; Better indicated by lower values)												
6	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	no serious imprecision	none	542	527	-	MD 0.61 lower (0.88 lower to 0.35 higher)	MODERATE	CRITICAL
HDL Cholesterol > 2 months (follow-up 2 months; range of scores: 0.93-1.55; Better indicated by higher values)												
7	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	no serious imprecision	none	556	541	-	MD 0.01 lower (0.07 lower to 0.05 higher)	MODERATE	CRITICAL
LDL Cholesterol > 2 months (follow-up 2 months; range of scores: 3.03-4.24; Better indicated by lower values)												
6	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	no serious imprecision	none	357	341	-	MD 0.15 higher (0.01 to 0.29 higher)	MODERATE	CRITICAL

[1] Included studies are all adult studies, no pediatric subjects

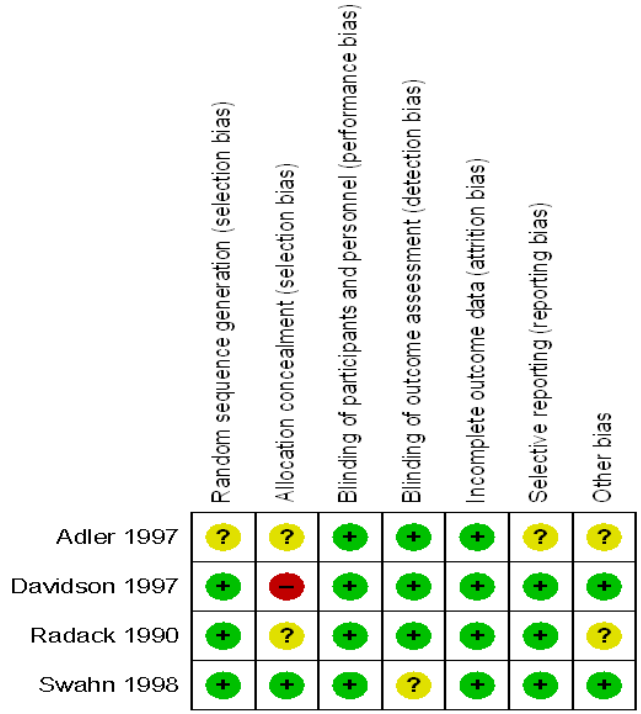

Figure 1. Risk of bias summary: review Scholars' judgments about each risk of bias item for each included study.

Study or Subgroup	Omega 3 FA Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Radack 1990	-0.54	1.1183	10	-0.63	2.177	8	24.7%	0.05 [-0.88, 0.98]	1990
Adler 1997	1.46	0.23	10	1.94	0.51	11	24.5%	-1.15 [-2.08, -0.21]	1997
Davidson 1997	-17.6	6.1	9	3.5	11.7	8	19.1%	-2.19 [-3.46, -0.92]	1997
Swahn 1998	2.53	0.94	26	2.98	1.25	27	31.8%	-0.40 [-0.94, 0.14]	1998
Total (95% CI)			**55**			**54**	**100.0%**	**-0.81 [-1.60, -0.02]**	

Heterogeneity: Tau² = 0.44; Chi² = 9.70, df = 3 (P = 0.02); I² = 69%
Test for overall effect: Z = 2.01 (P = 0.04)

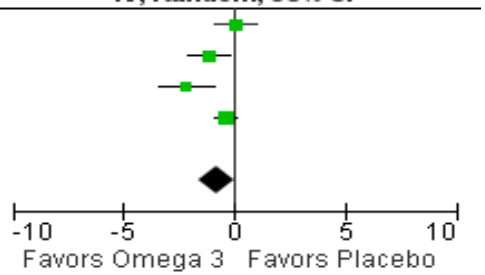

Figure 2. 2.2 gm – 3.5 gm N--3 FA Supplementation vs. Placebo, Outcome: Serum Triglycerides at > 2 Months of Supplementation

Study or Subgroup	Omega 3 FA Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Radack 1990	0.53	0.7968	10	-0.16	0.8493	8	18.3%	0.80 [-0.17, 1.78]	1990
Adler 1997	6.51	0.38	10	6.49	0.31	11	23.7%	0.06 [-0.80, 0.91]	1997
Swahn 1998	5.97	0.91	26	5.97	0.9	27	58.0%	0.00 [-0.54, 0.54]	1998
Total (95% CI)			**46**			**46**	**100.0%**	**0.16 [-0.26, 0.58]**	

Heterogeneity: Tau² = 0.00; Chi² = 2.05, df = 2 (P = 0.36); I² = 3%
Test for overall effect: Z = 0.74 (P = 0.46)

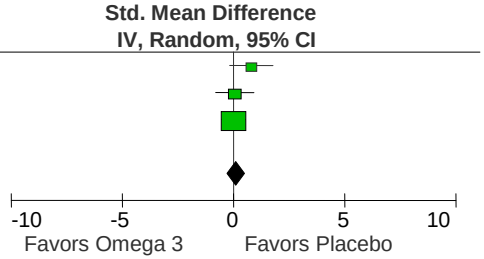

Figure 3. 2.2 gm – 3.5 gm N--3 FA Supplementation vs. Placebo, Outcome: Serum Total Cholesterol at > 2 Months of Supplementation

Study or Subgroup	Omega 3 FA Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Radack 1990	0.93	0.8248	10	-0.44	2.5956	8	26.3%	0.71 [-0.25, 1.68]	1990
Davidson 1997	13.6	2.3	9	-2.4	4.7	8	17.7%	4.19 [2.32, 6.06]	1997
Adler 1997	4.81	0.4	10	4.26	0.31	11	26.1%	1.49 [0.49, 2.48]	1997
Swahn 1998	4.13	0.76	26	3.87	0.82	27	30.0%	0.32 [-0.22, 0.87]	1998
Total (95% CI)			**55**			**54**	**100.0%**	**1.41 [0.24, 2.58]**	

Heterogeneity: Tau² = 1.11; Chi² = 17.48, df = 3 (P = 0.0006); I² = 83%
Test for overall effect: Z = 2.36 (P = 0.02)

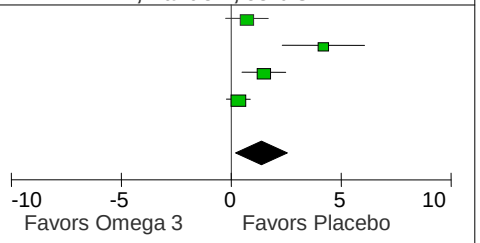

Figure 4. 2.2 gm – 3.5 gm N--3 FA supplementation vs. Placebo, Outcome: Serum LDL cholesterol at > 2 months of supplementation

Study or Subgroup	Omega 3 FA Mean	SD	Total	Placebo Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI	Year
Radack 1990	0.03	0.5452	10	0.04	0.1555	8	16.5%	-0.02 [-0.95, 0.91]	1990
Adler 1997	1.21	0.11	10	1.26	0.11	11	18.9%	-0.44 [-1.31, 0.43]	1997
Davidson 1997	6.2	2.3	9	5.6	2.6	8	15.6%	0.23 [-0.72, 1.19]	1997
Swahn 1998	0.92	0.26	26	0.9	0.25	27	49.1%	0.08 [-0.46, 0.62]	1998
Total (95% CI)			**55**			**54**	**100.0%**	**-0.01 [-0.39, 0.37]**	

Heterogeneity: Tau² = 0.00; Chi² = 1.27, df = 3 (P = 0.74); I² = 0%
Test for overall effect: Z = 0.06 (P = 0.95)

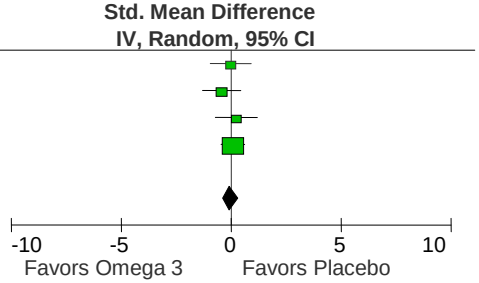

Figure 5. 2.2 gm – 3.5 gm N--3 FA Supplementation vs. Placebo, Outcome: Serum HDL Cholesterol at > 2 Months of Supplementation