Appendix A. Methodologic Approach

A.1 Preliminary Research Questions
A.2 Technical Expert Panel
A.3 Search Strategies
A.4 Inclusion/Exclusion Criteria
A.5 Evidence Grading System
A.6 External Peer Reviewer

A.1 Preliminary Research Questions

Table A.1.1. Preliminary research questions.

GENERAL QUESTIONS: Questions posed for all three participating EPCs, for years 1 and 2.
1. What is the evidence that variable clinical effects may reflect differences in: • Serving size (fish vs. dietary supplement); • Source (fish, food, plant) vs. dietary supplement (fish oil, plant oil); • Specific type(s) of omega-3 fatty acids (docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and alpha-linolenic acid (ALA), fish, fish oil), or the ratio of omega-6/omega-3 fatty acids used; • Manufacturer (different purity, presence of other potentially active agents)? 2. What is the evidence for adverse events, side effects, or counter-indications associated with omega-3 fatty acids (DHA, EPA, DPA, ALA, fish oil, fish)? 3. What is the evidence that omega-3 fatty acids are associated with adverse events in specific subpopulations such as diabetics? 4. What are the mean and median intakes of DHA, EPA, DPA, ALA, fish, fish oil, omega-6, omega-6/omega-3 ratio in the US population? 5. What is the evidence that omega-3 fatty acids influence overall energy balance? 6. What is the evidence that accurate interpretation of the results of clinical studies is dependent on knowing the absolute fatty acid content of the baseline data, the relative fatty acid content of the baseline diet, or the tissue ratios of fatty acids (omega-6/omega-3) during the investigative period?
DISEASE-SPECIFIC QUESTIONS: questions posed to the SCEPC for Year 1 of the project:
Immune-Mediated Diseases
1. What is the evidence that in adults or children with type I diabetes, omega-3 fatty acids increase insulin sensitivity? 2. What is the evidence that in adults or children with rheumatoid arthritis, omega-3 fatty acids decrease pain or the number of swollen joints? 3. What is the evidence that omega-3 fatty acids help maintain bone mineral status? 4. What is the evidence that in adults or children with inflammatory bowel disease (ulcerative colitis and Chrohn's disease), omega-3 fatty acids lower leukotriene B4 or prostaglandin E2 levels? 5. What is the evidence that in adults or children with systemic lupus erythematosis, omega-3 fatty acids prolong longevity?
Gastrointestinal/Renal
1. What is the evidence for the efficacy of omega-3 fatty acids in treatment of Crohn's disease, ulcerative colitis, renal inflammation, and glomerulosclerosis? 2. What is the evidence for the efficacy of omega-3 fatty acids in treatment of the hypertriglyceridemia of type II diabetes, insulin resistance, or the metabolic syndrome? 3. What is the evidence that omega-3 fatty acids influence the regulation of gene expression in the progression/prevention of obesity, and intestinal and liver diseases?

A.2 Technical Expert Panel

The members of our technical expert panels are listed in Table A.2.1. We conducted our TEP meetings via teleconference. We held a conference call with the rheumatoid arthritis, systemic lupus erythematosis, and bone density TEP on February 7, 2003; the renal/diabetes TEP on February 12, 2003; and the gastrointestinal TEP on February 12, 2003. Dr. Rosaly Correa-de-Araujo, the Task Order Officer, and Jacqueline Besteman, Director of the Evidence-Based Practice Center Program, represented AHRQ on these calls; Dr. Anne Thurn, Director of the Evidence-Based Review Program, represented ODS; and Dr. Paul Shekelle, Director of the SCEPC, Dr. Catherine MacLean, the Task Order Director, and Rena Hasenfeld, the Project Manager, represented the SCEPC. The key comments and recommendations of each TEP are summarized in Table A.2.2. The TEP continued to advise the SCEPC throughout the project via mail, fax, e-mail, and phone calls.

Table A.2.1 Technical expert panel members.

Rheumatoid Arthritis, Systemic Lupus Erythematosis, and Bone Density TEP		
Name	**Area of Expertise**	**Institution**
Judith Ashley, PhD, MSPH, RD	Omega-3 Fatty Acids	University of Nevada School of Medicine
William S. Harris, PhD	Omega-3 Fatty Acids	University of Missouri-Kansas City School of Medicine
Robert P. Heaney, MD	Bone	Creighton University
David A. Isenberg, MD	SLE	University College London Medical School
Joel Kremer, MD	Rheumatoid Arthritis	The Center for Rheumatology
Bruce A. Watkins, PhD	Omega-3 Fatty Acids	Purdue University
Josiah F. Wedgwood, MD, PhD	Rheumatoid Arthritis	National Institute of Allergy and Infectious Diseases
Renal Disease and Diabetes TEP		
Name	**Area of Expertise**	**Institution**
Judith Ashley, PhD, MSPH, RD	Omega-3 Fatty Acids	University of Nevada School of Medicine
Mayer B. Davidson, MD	Diabetes	Charles R. Drew University of Medicine and Science
James V. Donadio, MD	Renal Diseases	Mayo Medical School
William S. Harris, PhD	Omega-3 Fatty Acids	University of Missouri-Kansas City School of Medicine
Michael D. Jensen, MD	Diabetes	Mayo Medical School
William F. Keane, MD	Renal Diseases	Merck and Co., Inc.
Catherine Meyers, MD	Renal Diseases	NIDDK, Division of Kidney, Urologic & Hematologic Diseases
Gastrointestinal Diseases TEP		
Name	**Area of Expertise**	**Institution**
Judith Ashley, PhD, MSPH, RD	Omega-3 Fatty Acids	University of Nevada School of Medicine
Andrea Belluzzi, MD	Irritable Bowel Disease	S Orsola Hospital, Bologna, Italy
Frank Hamilton, MD	Irritable Bowel Disease	NIDDK, Division of Digestive Diseases & Nutrition
William S. Harris, PhD	Omega-3 Fatty Acids	University of Missouri-Kansas City School of Medicine
Stephen James, MD	Inflammatory Bowel Disease	NIDDK, Division of Digestive Diseases & Nutrition
Michael Ken May, PhD	Inflammatory Bowel Disease	NIDDK, Division of Digestive Diseases & Nutrition
William F. Stenson, MD	Inflammatory Bowel Disease	Washington University

Table A.2.2. Key TEP comments and recommendations.

Rheumatoid Arthritis, Systemic Lupus Erythematosis, and Bone Density TEP
1. What is the evidence that in adults or children with rheumatoid arthritis, omega-3 fatty acids decrease pain or the number of swollen joints?
• Restrict the search to randomized control trials.
• Include children with juvenile rheumatoid arthritis for now.
• If possible, the outcome measures should include: disease activity, damage, and patient perception (i.e. patient global assessment).

2. What is the evidence that omega-3 fatty acids help maintain bone mineral status?
• Include both randomized controlled trials and observational studies.
• The populations of interest are older women and women with osteoporosis.
• Outcomes for randomized controlled trials will likely be measures of bone density and biologic markers.
• Outcomes for observational studies are more likely to include fracture rates.
• There is a need to adjust for ethnicity in the analyses because bone shape may affect the • rate of fractures.
• In studies that report t-scores, there is a need to note the standard used to compute the t-score; WHO and NHANES are two different standards that may be used.
3. What is the evidence that in adults or children with systemic lupus erythematosus, omega-3 fatty acids prolong longevity?
• Restrict the study to randomized controlled trials.
• Longevity is not the correct outcome to assess.
• Recommended outcomes for assessment include disease activity, damage, and patient perception (i.e. patient global assessment).
General Comments
• Note reported side effects of omega-3 fatty acids when reviewing the literature.
Renal Disease and Diabetes TEP
1. What is the evidence for the efficacy of omega-3 fatty acids in treatment of hypertriglyceridemia of type II diabetes, insulin resistance, or the metabolic syndrome?
• The question should be re-worded in the following way: What is the evidence in adults or children for the efficacy of omega-3 fatty acids in treatment of hyperlipedemia in a) type II diabetes, or b) insulin resistance/the metabolic syndrome?
• Do not to limit the review to hypertriglyceridemia; collect data on other lipids, as well.
• The question pertains specifically to the effect of omega-3 fatty acids on lipids in two different clinical syndromes: type II DM and the insulin resistance/metabolic syndrome.
• The question pertains to both adults and children.
2. What is the evidence that in adults or children with type I diabetes, omega-3 fatty acids increase insulin sensitivity?
• Since insulin resistance is not a feature of type I diabetes, the questions should be re-worded in the following way: What is the evidence in adults and children for an effect of omega-3 fatty acids on insulin sensitivity in a) type II diabetes, or b) the metabolic syndrome?
3. What is the evidence for the efficacy of omega-3 fatty acids in treatment of renal inflammation and glomerulosclerosis?
• There was no consensus on how “renal inflammation” and “glomerulosclerosis” should be defined.
• There was no consensus about whether to assess the effect of omega-3 fatty acids on the progression of renal disease.
• Randomized controlled trials should be examined to determine whether sufficient evidence exists to assess the effect of omega-3 fatty acids on renal inflammation and/or the progression of renal acute or chronic renal insufficiency.
• The question may be re-worded after the literature review has been completed.

Table A.2.2. Key TEP comments and recommendations (continued).

Gastrointestinal Diseases TEP
1. What is the evidence for the efficacy of omega-3 fatty acids in treatment of Crohn's disease and ulcerative colitis?
• There are so few studies on the efficacy of omega-3 fatty acids in treating inflammatory bowel disease that it may be necessary to do a qualitative rather than a quantitative review of the literature.
• Efficacy is not uniformly defined in IBD. However, a recent NIH conference addressed defining efficacy in Crohn's disease.
• There are many potential confounders/effect modifiers for IBD, especially for Crohn's disease, including disease characteristics (severity, presence or absence of fistulas in Crohn's), medication use, and population characteristics.
2. What is the evidence that in adults or children with inflammatory bowel disease (ulcerative colitis and Crohn's disease), omega-3 fatty acids lower leukotriene B4 or prostaglandin E2 levels?
• A review of the effect of omega-3 fatty acids on leukotriene B4 or prostaglandin E2 should not be included in the report since neither is a measure of prevention or efficacy in IBD.
• There are no studies of the effects of omega-3 fatty acids on IBD in children.
General Comments
• Take note of the omega-3 preparation. • Abstract and report side effects.

A.3 Search Strategies

Table A.3.1. Core search strategy.

1. exp fatty acids, omega-3/
2. fatty acids, essential/
3. Dietary Fats, Unsaturated/
4. linolenic acids/
5. exp fish oils/
6. (n 3 fatty acid$ or omega 3).tw.
7. docosahexa?noic.tw,hw,rw.
8. eicosapenta?noic.tw,hw,rw.
9. alpha linolenic.tw,hw,rw.
10. (linolenate or cervonic or timnodonic).tw,hw,rw.
11. menhaden oil$.tw,hw,rw.
12. (mediterranean adj diet$).tw.
13. ((flax or flaxseed or flax seed or linseed or rape seed or rapeseed or canola or soy or soybean or walnut or mustard seed) adj2 oil$).tw.
14. (walnut$ or butternut$ or soybean$ or pumpkin seed$).tw.
15. (fish adj2 oil$).tw.
16. (cod liver oil$ or marine oil$ or marine fat$).tw.
17. (salmon or mackerel or herring or tuna or halibut or seal or seaweed or anchov$).tw.
18. (fish consumption or fish intake or (fish adj2 diet$)).tw.
19. diet$ fatty acid$.tw.
20. or/1-19
21. dietary fats/
22. (randomized controlled trial or clinical trial or controlled clinical trial or evaluation studies or multicenter study).pt.
23. random$.tw.
24. exp clinical trials/ or evaluation studies/
25. follow-up studies/ or prospective studies/
26. or/22-25
27. 21 and 26
28. (Ropufa or MaxEPA or Omacor or Efamed or ResQ or Epagis or Almarin or Coromega).tw.
29. (omega 3 or n 3).mp.
30. (polyunsaturated fat$ or pufa or dha or epa or long chain or longchain or lc$).mp.
31. 29 and 30
32. 20 or 27 or 28 or 31

Table A.3.2. Literature searches by disease category.

Diabetes
1. exp fatty acids, omega-3/
2. fatty acids, essential/
3. Dietary Fats, Unsaturated/
4. linolenic acids/
5. exp fish oils/
6. (n 3 fatty acid$ or omega 3).tw.
7. docosahexa?noic.tw,hw,rw.
8. eicosapenta?noic.tw,hw,rw.
9. alpha linolenic.tw,hw,rw.
10. (linolenate or cervonic or timnodonic).tw,hw,rw.
11. menhaden oil$.tw,hw,rw.
12. (mediterranean adj diet$).tw.
13. ((flax or flaxseed or flax seed or linseed or rape seed or rapeseed or canola or soy or soybean or walnut or mustard seed) adj2 oil$).tw.
14. (walnut$ or butternut$ or soybean$ or pumpkin seed$).tw.
15. (fish adj2 oil$).tw.
16. (cod liver oil$ or marine oil$ or marine fat$).tw.
17. (salmon or mackerel or herring or tuna or halibut or seal or seaweed or anchov$).tw.
18. (fish consumption or fish intake or (fish adj2 diet$)).tw.
19. diet$ fatty acid$.tw.
20. or/1-19
21. dietary fats/
22. (randomized controlled trial or clinical trial or controlled clinical trial or evaluation studies or multicenter study).pt.
23. random$.tw.
24. exp clinical trials/ or evaluation studies/
25. follow-up studies/ or prospective studies/
26. or/22-25
27. 21 and 26
28. (Ropufa or MaxEPA or Omacor or Efamed or ResQ or Epagis or Almarin or Coromega).tw.
29. (omega 3 or n 3).mp.
30. (polyunsaturated fat$ or pufa or dha or epa or long chain or longchain or lc$).mp.
31. 29 and 30
32. 20 or 27 or 28 or 31
33. hyperinsulin?emia.tw.
34. hyperinsulinemia/
35. exp diabetes mellitus/
36. diabetes.tw.
37. insulin.tw.
38. metabolic syndrome$.tw.
39. exp insulin resistance/
40. or/33-39
41. 32 and 40
42. 41 and human/

Table A.3.2. Literature searches by disease category (continued).

Inflammatory Bowel Disease and Renal Disease
1. exp fatty acids, omega-3/
2. fatty acids, essential/
3. Dietary Fats, Unsaturated/
4. linolenic acids/
5. exp fish oils/
6. (n 3 fatty acid$ or omega 3).tw.
7. docosahexa?noic.tw,hw,rw.
8. eicosapenta?noic.tw,hw,rw.
9. alpha linolenic.tw,hw,rw.
10. (linolenate or cervonic or timnodonic).tw,hw,rw.
11. menhaden oil$.tw,hw,rw.
12. (mediterranean adj diet$).tw.
13. ((flax or flaxseed or flax seed or linseed or rape seed or rapeseed or canola or soy or soybean or walnut or mustard seed) adj2 oil$).tw.
14. (walnut$ or butternut$ or soybean$ or pumpkin seed$).tw.
15. (fish adj2 oil$).tw.
16. (cod liver oil$ or marine oil$ or marine fat$).tw.
17. (salmon or mackerel or herring or tuna or halibut or seal or seaweed or anchov$).tw.
18. (fish consumption or fish intake or (fish adj2 diet$)).tw.
19. diet$ fatty acid$.tw.
20. or/1-19
21. dietary fats/
22. (randomized controlled trial or clinical trial or controlled clinical trial or evaluation studies or multicenter study).pt.
23. random$.tw.
24. exp clinical trials/ or evaluation studies/
25. follow-up studies/ or prospective studies/
26. or/22-25
27. 21 and 26
28. (Ropufa or MaxEPA or Omacor or Efamed or ResQ or Epagis or Almarin or Coromega).tw.
29. (omega 3 or n 3).mp.
30. (polyunsaturated fat$ or pufa or dha or epa or long chain or longchain or lc$).mp.
31. 29 and 30
32. 20 or 27 or 28 or 31
33. exp inflammatory bowel diseases/
34. inflammatory bowel.tw.
35. (hemorrhagic proctocolitis or ulcerative proctocolitis).tw.
36. (hemorrhagic rectocolitis or ulcerative rectocolitis).tw.
37. (ileocolitis or ileitis or enteritis or crohn$ or pancolitis or proctitis or colitis).tw.
38. exp nephritis/
39. ((renal or kidney) and inflammation).tw.
40. (glomerulo$ or nephritis or nephropath$).tw.
41. or/33-40
42. 32 and 41
43. 42 and human/

Table A.3.2. Literature searches by disease category (continued).

Rheumatoid Arthritis
1. exp fatty acids, omega-3/
2. fatty acids, essential/
3. Dietary Fats, Unsaturated/
4. linolenic acids/
5. exp fish oils/
6. (n 3 fatty acid$ or omega 3).tw.
7. docosahexa?noic.tw,hw,rw.
8. eicosapenta?noic.tw,hw,rw.
9. alpha linolenic.tw,hw,rw.
10. (linolenate or cervonic or timnodonic).tw,hw,rw.
11. menhaden oil$.tw,hw,rw.
12. (mediterranean adj diet$).tw.
13. ((flax or flaxseed or flax seed or linseed or rape seed or rapeseed or canola or soy or soybean or walnut or mustard seed) adj2 oil$).tw.
14. (walnut$ or butternut$ or soybean$ or pumpkin seed$).tw.
15. (fish adj2 oil$).tw.
16. (cod liver oil$ or marine oil$ or marine fat$).tw.
17. (salmon or mackerel or herring or tuna or halibut or seal or seaweed or anchov$).tw.
18. (fish consumption or fish intake or (fish adj2 diet$)).tw.
19. diet$ fatty acid$.tw.
20. or/1-19
21. dietary fats/
22. (randomized controlled trial or clinical trial or controlled clinical trial or evaluation studies or multicenter study).pt.
23. random$.tw.
24. exp clinical trials/ or evaluation studies/
25. follow-up studies/ or prospective studies/
26. or/22-25
27. 21 and 26
28. (Ropufa or MaxEPA or Omacor or Efamed or ResQ or Epagis or Almarin or Coromega).tw.
29. (omega 3 or n 3).mp.
30. (polyunsaturated fat$ or pufa or dha or epa or long chain or longchain or lc$).mp.
31. 29 and 30
32. 20 or 27 or 28 or 31
33. exp arthritis, rheumatoid/
34. (rheumat$ adj2 arthritis).tw.
35. stills diseas$.tw.
36. caplans syndrome$.tw.
37. feltys syndrome$.tw.
38. rheumatoid nodule$.tw.
39. sjogrens syndrome$.tw.
40. ankylosing spondylitis.tw.
41. rheumat$.tw.
42. or/33-41
43. 32 and 42
44. limit 43 to human

Table A.3.2. Literature searches by disease category (continued).

Systemic Lupus Erythematosus
1. exp fatty acids, omega-3/
2. fatty acids, essential/
3. Dietary Fats, Unsaturated/
4. linolenic acids/
5. exp fish oils/
6. (n 3 fatty acid$ or omega 3).tw.
7. docosahexa?noic.tw,hw,rw.
8. eicosapenta?noic.tw,hw,rw.
9. alpha linolenic.tw,hw,rw.
10. (linolenate or cervonic or timnodonic).tw,hw,rw.
11. menhaden oil$.tw,hw,rw.
12. (mediterranean adj diet$).tw.
13. ((flax or flaxseed or flax seed or linseed or rape seed or rapeseed or canola or soy or soybean or walnut or mustard seed) adj2 oil$).tw.
14. (walnut$ or butternut$ or soybean$ or pumpkin seed$).tw.
15. (fish adj2 oil$).tw.
16. (cod liver oil$ or marine oil$ or marine fat$).tw.
17. (salmon or mackerel or herring or tuna or halibut or seal or seaweed or anchov$).tw.
18. (fish consumption or fish intake or (fish adj2 diet$)).tw.
19. diet$ fatty acid$.tw.
20. or/1-19
21. dietary fats/
22. (randomized controlled trial or clinical trial or controlled clinical trial or evaluation studies or multicenter study).pt.
23. random$.tw.
24. exp clinical trials/ or evaluation studies/
25. follow-up studies/ or prospective studies/
26. or/22-25
27. 21 and 26
28. (Ropufa or MaxEPA or Omacor or Efamed or ResQ or Epagis or Almarin or Coromega).tw.
29. (omega 3 or n 3).mp.
30. (polyunsaturated fat$ or pufa or dha or epa or long chain or longchain or lc$).mp.
31. 29 and 30
32. 20 or 27 or 28 or 31
33. exp Lupus Erythematosus, Systemic/
34. (lupus glomerulonephritis or lupus nephritis).tw.
35. (libman-sacks or lupus erythematosus disseminatus or systemic lupus erythematosus).tw.
36. (lupus vasculitis or lupus meningoencephalitis or central nervous system systemic lupus).tw.
37. or/33-36
38. 32 and 37
39. limit 38 to human

Table A.3.2. Literature searches by disease category (continued).

Bone Density/Osteoporosis
1. exp fatty acids, omega-3/
2. fatty acids, essential/
3. Dietary Fats, Unsaturated/
4. linolenic acids/
5. exp fish oils/
6. (n 3 fatty acid$ or omega 3).tw.
7. docosahexa?noic.tw,hw,rw.
8. eicosapenta?noic.tw,hw,rw.
9. alpha linolenic.tw,hw,rw.
10. (linolenate or cervonic or timnodonic).tw,hw,rw.
11. menhaden oil$.tw,hw,rw.
12. (mediterranean adj diet$).tw.
13. ((flax or flaxseed or flax seed or linseed or rape seed or rapeseed or canola or soy or soybean or walnut or mustard seed) adj2 oil$).tw.
14. (walnut$ or butternut$ or soybean$ or pumpkin seed$).tw.
15. (fish adj2 oil$).tw.
16. (cod liver oil$ or marine oil$ or marine fat$).tw.
17. (salmon or mackerel or herring or tuna or halibut or seal or seaweed or anchov$).tw.
18. (fish consumption or fish intake or (fish adj2 diet$)).tw.
19. diet$ fatty acid$.tw.
20. or/1-19
21. dietary fats/
22. (randomized controlled trial or clinical trial or controlled clinical trial or evaluation studies or multicenter study).pt.
23. random$.tw.
24. exp clinical trials/ or evaluation studies/
25. follow-up studies/ or prospective studies/
26. or/22-25
27. 21 and 26
28. (Ropufa or MaxEPA or Omacor or Efamed or ResQ or Epagis or Almarin or Coromega).tw.
29. (omega 3 or n 3).mp.
30. (polyunsaturated fat$ or pufa or dha or epa or long chain or longchain or lc$).mp.
31. 29 and 30
32. 20 or 27 or 28 or 31
33. bone density/
34. (bone mineral or bone densit$ or bone mass).tw.
35. exp Bone Demineralization, Pathologic/
36. Bone Demineral$.tw.
37. exp Bone Resorption/
38. (bone loss$ or bone resportion).tw.
39. exp Densitometry/
40. or/33-39
41. 32 and 40
42. limit 41 to human

Table A.3.3. Industry experts that were contacted for data about efficacy of omega-3 fatty acids.

Name	Affiliation
Ian Newton	Roche Vitamins
Herb Wool, PhD	BASF Corporation
Annette Dickinson	Council for Responsible Nutrition

Figure A.3.1. Letter sent to industry experts.

Date

Name
Address
City, State, Zip Code

Dear XXX,

I am writing on behalf of the Evidence Based Practice Centers at RAND, New England Medical Center and the University of Ottawa. We are conducting a systematic review of the efficacy and toxicity of omega-3 fatty acids in the prevention and treatment of a number of different diseases/conditions. This review is being conducted under a contract from the Agency for Healthcare Research and Quality (AHRQ).

We are contacting you to see if there is any evidence, including unpublished evidence, that you want considered. Our focus is on clinical trials of omega-3 fatty acids in humans, so animal and chemical studies are not necessary.

The specific questions that all the EPCs will address are detailed in the attachment to this letter.

Please contact me with any information that you might have.

Best regards,

Catherine MacLean, M.D., Ph.D.
RAND1700 Main Street, M 23-C
Santa Monica, CA 90407-2138
Voice: 310 393-0411, x6364
Fax: 310-451-6930

A.4 Inclusion/Exclusion Criteria

Table A.4.1. Inclusion/Exclusion Criteria at Screening Stage.*

Assessed the effect of omega-3 fatty acids on arthritis (including rheumatoid arthritis and juvenile rheumatoid arthritis), bone mineral metabolism, diabetes, IBD, lupus, or renal disease
Presented research on human subjects
Reported the results of randomized or controlled clinical trials or cohort/case control studies;† we accepted observational studies for bone mineral status only.
For cross-over studies, reported outcomes for each arm before the cross-over at the end of the first phase of treatment‡

*Language was not a barrier to inclusion; † We defined a randomized controlled trial (RCT) as one in which the participants were assigned to one of two (or more) study groups using a process of random allocation (e.g., random number generation, coin flips); we defined a controlled clinical trial (CCT) as one in which participants were either: (1) assigned to one of two (or more) study groups using a quasi-random allocation method (e.g., alternation, date of birth, patient identifier), or (2) possibly assigned to one of two (or more) study groups using a process of random or quasi-random allocation; ‡ We did not use data from the end of the study period in studies with a cross-over design because as a result of this design, the treatment and placebo groups from these studies are not comparable to the treatment and placebo groups of the non-cross-over randomized controlled trials with which they would be pooled in a meta-analysis. For example, one half of the placebo group in a cross-over trial will have been exposed to treatment with omega-3 fatty acids prior to placebo and hence the measured effect could be biased by earlier treatment with Omega-3 fatty acids.

A.5 Evidence Grading System

Table A.5.1. Summary Score for Methodologic Quality.

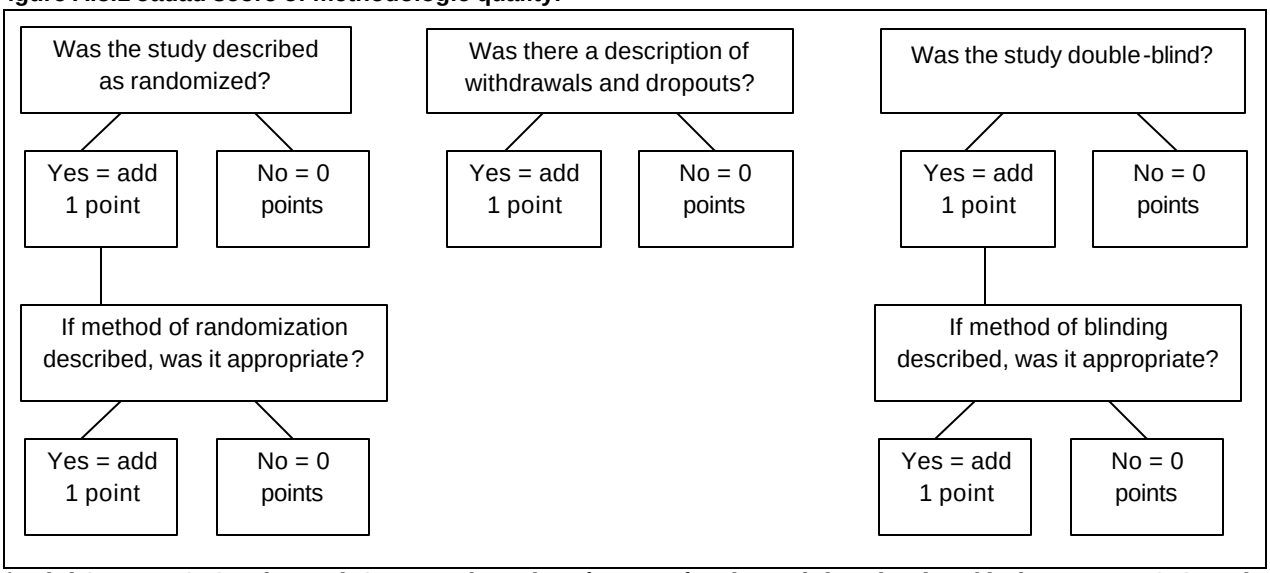
Summary Score	Jadad Score	Concealment of Allocation
A	5	Performed
B	5	Not performed, or Not reported
	3 or 4	Performed, Not performed, or Not reported
	0,1, or 2	Performed
C	0, 1, or 2	Not performed or not reported

Even though a study may focus on a specific target population, limited study size, eligibility criteria and patient recruitment process may result in a narrow population sample that is of limited applicability, even to the target population. To capture this parameter, we categorize studies into the applicability scale described in Table A.5.1.

Table A.5.2 Applicability ratings.

Applicability		**Health state**
I	Sample is representative of the U.S. population.	A General population. Typical healthy people similar to Americans without known cardiovascular diseases.
II	Sample is representative of a relevant sub-group of the target population, but not the entire population. For example, a study that is restricted to women or a fish oil study in Japan where the background diet is very different from that of the US would fall into this category.	B Diseased population. Subjects with any of the following: inflammatory bowel disease, rheumatoid arthritis, renal disease, systemic lupus erythematosus or osteoporosis.
III	Sample is representative of a narrow subgroup of subjects only, and not well applicable to other subgroups. For example, a study of oldest old men or a study of a population on highly controlled diet.	

Figure A.5.1 Jadad score of methodologic quality.*



***** Jadad A, Moore A, Carrol D, et al. Assessing the quality of reports of randomized clinical trials: Is blinding necessary? Control Clin Trials. 1996;17:1-12.

Table A.6.1. Peer Reviewers.

Peer Reviewer	Area of Expertise	Affiliation
Richard Glassock, MD	nephrology	UCLA
David Heber, MD	nutrition	UCLA
Ted Kraegen, PhD	diabetes, nutrition	Garvan Research Institute, Sydney
Kenneth Saag, MD, MPH	osteoporosis, SLE	University of Alabama
Walter Willett, MD	epidemiology, nutrition	Harvard University
Robert Zurier, MD	rheumatoid arthritis, omega-3 fatty acids	University of Massachusetts Medical School

Appendix B. Coding/Data Abstraction Forms

B.2 Literature Screener Form
B.3 Quality review form

Omega 3 Screening Form
Final Version

1. Article ID: _____
2. First Author: _____
   (Last name of first author)
3. Reviewer: _____

4. Research intervention topic: **(circle one)**
   - Omega 3 or synonymous topic 1
   - Unclear, no English abstract..... 8
     (If unclear, skip to question 8 on language)
   - None of the above ..... 9 **(STOP)**

5. Condition(s)/Subject(s) studied: **(check all that apply)**
   - Arthritis (RA, JRA).....❒
   - Bone mineral metabolism .....❒
   - Diabetes.....❒
   - IBD.....❒
   - Lupus .....❒
   - Renal.....❒
     (If any of the above conditions are checked, ignore stop codes for the following conditions listed below)
   - Other conditions:
     - Asthma .....❒ **(STOP)**
     - Cancer.....❒ **(STOP)**
     - CVD.....❒ **(STOP)**
     - Child/maternal health .....❒ **(STOP)**
     - Cognitive function .....❒ **(STOP)**
     - Eye health.....❒ **(STOP)**
     - Mental health .....❒ **(STOP)**
     - Neurological disease.....❒ **(STOP)**
     - Organ transplant.....❒ **(STOP)**
     - None of the above .....❒ **(STOP)**

6. Study population: **(check all that apply)**
   - Human.....❒
   - Animal .....❒ **(STOP)**
   - Unclear.....❒ **(STOP)**
   - Other (specify:_____)...❒ **(STOP)**

7. Study design: ..... **(circle one)**
   - Descriptive (historical, editorial, etc.) ..... 1 **(STOP)**
   - Review/ meta-analysis ..... 2 **(STOP)**
   - Randomized clinical trial 3
   - Controlled clinical trial..... 4
   - Cohort /Case control..... 5
     (For cohort/case control, if condition not Bone, then STOP)
   - Case Series/Case Report ..... 6 **(STOP)**
   - Other (specify:_____)..... 8 **(STOP)**

8. Language of article: **(circle one)**
   - English 1
   - German..... 2
   - French..... 3
   - Italian..... 4
   - Danish..... 5
   - Other (specify:_____)..... 8

9. Do you think this article might be a duplicate or include the same data as another study?
   - Yes..... 1
   - No..... 2

Notes:

RAND EPC, Omega-3 Project
Quality Review Form

Article ID:_____ Reviewer:_____

First Author: _____
(Last Name Only)

Study Number: ___of____Description:_____
(Enter '1of 1' if only one) (if more than one study)

1. Is there a difference in Omega-3 content between arms: (CIRCLE ONE)

Yes 1
No 2 (STOP)
Unclear 8 (STOP)

2. Design: (CIRCLE ONE)

RCT 1
CCT 2
Cohort or Case Control (Bone only) 3
Other design..... 4 (STOP)
(STOP IF COHORT/CASE CONTROL AND NOT BONE OR IF OTHER DESIGN)

3. Does the disease meet the appropriate criteria?
Is/are the outcome(s) of interest reported? (CHECK ALL THAT APPLY)
NOTE: for conditions to continue, both criteria and outcomes must be met.

	CRITERIA	OUTCOME(S)
RA	❑	❑
SLE	❑	❑
Bone Mineral Density	❑	❑
Type I Diabetes	❑	❑
Type II Diabetes	❑	❑
Metabolic Syndrome	❑	❑

NOTE: for each condition to continue only one criteria must be met.

Crohn's Disease ..... ❑
Ulcerative colitis ..... ❑
Renal inflammation ..... ❑
Glomerulosclerosis ..... ❑
IgA Nephropathy..... ❑
Chronic renal disease..... ❑
Study does not report required components ..... ❑ (STOP)
(SEE THE CODE SHEET FOR APPROPRIATE CRITERIA AND OUTCOMES OF INTEREST.)

4. Is the study described as randomized? (CIRCLE ONE)

Yes 1
No 2

5. If the study was randomized, was method of randomization appropriate? (CIRCLE ONE)

Yes 1
No 2
Method not described 8
Not applicable (not randomized) 9

6. Is the study described as: (CIRCLE ONE)

Double blind 1
Single blind, patient 2
Single blind, outcome assessment 3
Open 4
Blinding not described 8
Not applicable 9

7. If reported, was the method of double blinding appropriate? (CIRCLE ONE)

Yes 1
No 2
Double blinding method not described 8
Not applicable 9

8. If study was randomized, did the method of randomization provide
for concealment of allocation? (CIRCLE ONE)

Yes 1
No 2
Concealment not described.....8
Not applicable (not randomized) 9

9. Are withdrawals (W) and dropouts (D) described? (CIRCLE ONE)

Yes, reason described for **all** W and D 1

Yes, reason described for **some** W and D..... 2

Not described..... 8

Not applicable 9

10. Is this a cross-over study design? (CIRCLE ONE)

Yes 1

No..... 2

Not described 8

11. Does the study population represent (CHECK ALL THAT APPLY)

	Healthy	Diseased
Typical people	❑....	❑
Atypical people (in terms of diet, SES, other factors)	❑....	❑
Narrow, atypical people (including highly controlled diet)	❑....	❑
Cannot categorize (incomplete data)	❑....	❑

12. What was the number of sites involved in the study?

(ENTER NUMBER OF 99 IF NOT REPORTED)

___ ___

13. In what country was the study conducted? (CHECK ALL THAT APPLY)

US ❑

UK ❑

Japan ❑

China ❑

Italy ❑

Netherlands ❑

Canada ❑

Other (enter code) .....❑

____ ____, ____ ____, ____ ____, ____ ____

Not specified.....❑

14. Are data reported separately for or primarily on over 75% of any of the following populations? (CHECK ALL THAT APPLY)

Children (0-12) ..... ❑

Adolescents (13-17)..... ❑

Older Adults (=65) ..... ❑

Other (Enter code: ____ ____, ____ ____, ____ ____) . ❑

None of the above ..... ❑

15. What was the racial/ethnic breakdown in percent of the population studied?

Caucasian.....____ ____ ____%

African Ancestry.....____ ____ ____%

Hispanic .....____ ____ ____%

Asian.....____ ____ ____%

Native American.....____ ____ ____%

Eskimo/Inuit .....____ ____ ____%

Other (enter code):

____ ____.....____ ____ ____%

____ ____.....____ ____ ____%

____ ____.....____ ____ ____%

____ ____.....____ ____ ____%

Should TOTAL..._1__ _0__ _0__

Not described.....❑

16. What was the percent of male participants?
(ENTER NUMBER OF 999)

___ ___ ___ %

17. What was reported for the following questions regarding subjects ages? (Enter number 99 for not reported)

Mean Age.....____ ____

Median Age .....____ ____

Age Range.....____ ____ to ___ ____

18. What types of covariates are described? (CHECK ALL THAT APPLY)

Renal insufficiency..... ❑
Proteinuria/ nephrotic ..... ❑
Steroid use (daily) ..... ❑
Other..... ❑
(Enter code: ____ ____, ____ ____, ____ ___, ____ ____)

None described ..... ❑

19. What were the study's inclusion criteria? (Enter code 99 for not reported)

Enter code: ____ ____, ____ ____, ____ ___, ____ ____

____ ____, ____ ____, ____ ___, ____ ____

20. What were the study's exclusion criteria? (Enter code 99 for not reported)

Enter code: ____ ____, ____ ____, ____ ___, ____ ____

____ ____, ____ ____, ____ ___, ____ ____

21. Was there a measure of disease severity reported? (CIRCLE ONE)

Yes..... 1
No..... 2
If "yes", what was that measurement(s)?

Enter code: ____ ____, ____ ____, ____ ___, ____ ____

____ ____, ____ ____, ____ ___, ____ ____

Interventions

22. Enter sample size and intervention data for each arm beginning with placebo or control, then in order of first mention:

Arm	Sample size	Arm Type Intervention	Components	Total Dose	Units	Is omega 3 quantified?	Duration of treatment	Units	Co-intervention(s)
1	_____ N ENTERING _____ N COMPLETING	_____ ARM TYPE _____ INTERVENTION	_____ _____ _____ _____ _____ _____	_____	_____	ALA.....❑ DHA.....❑ EPA.....❑ DPA.....❑ Not Reported..❑	_____	_____	_____ _____ _____ _____ _____ _____
2	_____ N ENTERING _____ N COMPLETING	_____ ARM TYPE _____ INTERVENTION	_____ _____ _____ _____ _____ _____	_____	_____	ALA.....❑ DHA.....❑ EPA.....❑ DPA.....❑ Not Reported..❑	_____	_____	_____ _____ _____ _____ _____ _____
3	_____ N ENTERING _____ N COMPLETING	_____ ARM TYPE _____ INTERVENTION	_____ _____ _____ _____ _____ _____	_____	_____	ALA.....❑ DHA.....❑ EPA.....❑ DPA.....❑ Not Reported..❑	_____	_____	_____ _____ _____ _____ _____ _____
4	_____ N ENTERING _____ N COMPLETING	_____ ARM TYPE _____ INTERVENTION	_____ _____ _____ _____ _____ _____	_____	_____	ALA.....❑ DHA.....❑ EPA.....❑ DPA.....❑ Not Reported..❑	_____	_____	_____ _____ _____ _____ _____ _____
5	_____ N ENTERING _____ N COMPLETING	_____ ARM TYPE _____ INTERVENTION	_____ _____ _____ _____ _____ _____	_____	_____	ALA.....❑ DHA.....❑ EPA.....❑ DPA.....❑ Not Reported..❑	_____	_____	_____ _____ _____ _____ _____ _____
	Enter a number for N entering and N completing or enter 9999 if not reported.	Enter Code	Enter code(s)	Enter # or 999 for not reported	Enter a number 1. g 2. mg 3. oz 4. kcal 5. other	Enter a number 1.Yes 2.No 8.ND 9.NA	Enter a number 998. ND 999. NA	Enter a number ***1.Hour*** ***2.Day*** ***3.Week*** ***4.Month*** ***5.Year*** ***8.ND*** ***9.NA***	Enter code(s)

Interventions (continued)

22. Enter sample size and intervention data for each arm :

Arm	Sample size	Arm Type Intervention	Components	Total Dose	Units	Is omega 3 quantified?	Duration of treatment	Units	Co-intervention(s)
6	_____ N ENTERING _____ N COMPLETING	_____ ARM TYPE _____ INTERVENTION	_____ _____ _____ _____ _____ _____	_____	_____	ALA.....❑ DHA.....❑ EPA.....❑ DPA.....❑ Not Reported..❑	_____	_____	_____ _____ _____ _____ _____ _____
7	_____ N ENTERING _____ N COMPLETING	_____ ARM TYPE _____ INTERVENTION	_____ _____ _____ _____ _____ _____	_____	_____	ALA.....❑ DHA.....❑ EPA.....❑ DPA.....❑ Not Reported..❑	_____	_____	_____ _____ _____ _____ _____ _____
8	_____ N ENTERING _____ N COMPLETING	_____ ARM TYPE _____ INTERVENTION	_____ _____ _____ _____ _____ _____	_____	_____	ALA.....❑ DHA.....❑ EPA.....❑ DPA.....❑ Not Reported..❑	_____	_____	_____ _____ _____ _____ _____ _____
9	_____ N ENTERING _____ N COMPLETING	_____ ARM TYPE _____ INTERVENTION	_____ _____ _____ _____ _____ _____	_____	_____	ALA.....❑ DHA.....❑ EPA.....❑ DPA.....❑ Not Reported..❑	_____	_____	_____ _____ _____ _____ _____ _____
10	_____ N ENTERING _____ N COMPLETING	_____ ARM TYPE _____ INTERVENTION	_____ _____ _____ _____ _____ _____	_____	_____	ALA.....❑ DHA.....❑ EPA.....❑ DPA.....❑ Not Reported..❑	_____	_____	_____ _____ _____ _____ _____ _____
	Enter a number for N entering and N completing or enter 9999 if not reported.	Enter Code	Enter code(s)	Enter # or 999 for not reported	Enter a number 1. g 2. mg 3. oz 4. kcal 5. other	Enter a number 1.Yes 2.No 8.ND 9.NA	Enter a number 998. ND 999. NA	Enter a number ***1.Hour*** ***2.Day*** ***3.Week*** ***4.Month*** ***5.Year*** ***8.ND*** ***9.NA***	Enter code(s)

Outcomes

23. Type of outcomes measured:

Enter the code for each outcome measured:
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____

Evaluation

24. When, relative to the start of the intervention, were outcomes reported?

Enter the number and letters in the appropriate box

	Number	Unit
1st follow-up		
2nd follow-up		
3rd follow-up		
4th follow-up		
5th follow-up		
6th follow-up		
Additional follow-ups		

1. Hour
2. Day
3. Week
4. Month
5. Year
8. ND
9. NA

Adverse Events

25. Were any adverse events mentioned?

Enter the code for each adverse event or 99 if not reported:
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____
_____ _____

Appendix C. Evidence Tables

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome.

First Author, Year	Study Characteristics	Study design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Alekseeva, 2000[65]	Sample size: 60 Age (mean/range): 58 / 39-65 Race: NR % male: NR # sites: 1 Location: Russia	Design: RCT Duration: 4 wk	Inclusion: Controlled diabetes/Hyperlipidemia/Age Exclusion:NR	Covariates: Duration of diabetes/Obesity: BMI=27, kg=72.7, lbs=160/Hyperlipidemia/Hypertension	1	Low calorie diet
					2	Linseed oil 18 g/d X 4 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Alekseeva, 2000[65]	Total cholesterol (mg/dl at week 4) Arm 1 mean=251.35 Arm 2 mean=253.67 Mean difference=2.32 (-24.97, 29.60) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Triglyceride (mg/dl at week 4) Arm 1 mean=260.18 Arm 2 mean=313.27 Mean difference=53.10 (-33.55, 139.74) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. HDL: NR LDL: NR Fasting blood glucose (mg/dl at week 4) Arm 1 mean=176.58 Arm 2 mean=185.59 Mean difference=9.01 (-24.30, 42.32) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. HbA1c: NR	Quality: Jadad: 2 Concealment of allocation:NR Applicability: NR Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Annuzzi, 1991[57]	Sample size: 8 Age (mean/range): 51/45-57 Race: NR % male: 100 # sites: 1 Location: Italy	Design: RXT Duration: 4 wk X-over: week 8 Run-in: None Wash-out: None	Inclusion: Hyperlipidemia/ WHO diabetes criteria Exclusion: Lipid lowering drug use	Covariates: Hypoglycemic treatment/Duration of diabetes/Hb A1c/Obesity: BMI=27, kg=72.7, lbs=160 [Cathy: would just make this into a list as follows, but would have the bullets start further over to the left] Covariates: • Hypoglycemic treatment • Duration of diabetes/Hb A1c • Obesity: BMI=27, kg=72.7, lbs=160	1	Olive oil 10 g/d x 2 wk
					2	Max EPA (fish oil) 10 g/d x 2 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Annuzzi, 1991[57]	Total cholesterol (mg/dl at month 0.5) Arm 1 mean=177.61 Arm 2 mean=183.78 Mean difference=6.18 (-21.65, 34.00) Reported testing: Article reports no significant difference between Arm 1 and Arm 2 by using Wilcoxon's signed rank test. Triglyceride (mg/dl at month 0.5) Arm 1 mean=204.43 Arm 2 mean=171.68 Mean difference=-32.74 (-84.26, 18.77) Reported testing: Article reports significant difference (p<0.05) between Arm 1 and Arm 2 by using Wilcoxon's signed rank test. HDL (mg/dl at month 0.5) Arm 1 mean=22.78 Arm 2 mean=22.78 Mean difference=0.00 (-3.21, 3.21) Reported testing: Article reports no significant difference between Arm 1 and Arm 2 by using Wilcoxon's signed rank test. LDL (mg/dl at month 0.5) Arm 1 mean=109.65 Arm 2 mean=132.82 Mean difference=23.17 (-9.22, 55.56) Reported testing: Article reports significant difference (p<0.025) between Arm 1 and Arm 2 by using Wilcoxon's signed rank test. Fasting blood glucose (mg/dl at month 0.5) Arm 1 mean=153.15 Arm 2 mean=145.22 Mean difference=-7.93 (-66.18, 50.32) Reported testing: Article reports no significant difference between Arm 1 and Arm 2 by using Wilcoxon's signed rank test. HbA1c: NR	Quality: Jadad: 2 Concealment of allocation: ND Applicability: IIB Funding source: hospital and industry

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Axelrod, 1994[75]	Sample size: 20 Age (mean/range): 57 / NR Race: Caucasian, Black % male: NR # sites: 1 Location: US	Design: RCT Duration: 12 wk	Inclusion: Age/Controlled diabetes/No weight change in previous 2 or 3 mo./Hb A1c < 9.5% or 10.5%/Hb=13 for men, HB=12 for women/Retinopathy Exclusion: Steroids use/NSAIDs use/Reliable adherence/Bleeding disorder/ASA use/Not moderate or high fish intake/Proliferative retinopathy/Intraocular hemorrhage	Covariates: Hypoglycemic treatment/Duration of diabetes/Hb A1c/Obesity: BMI=27, kg=72.7, lbs=160	1	Safflower oil 5 g/d X 6 wk
					2	Super EPA (fish oil) 5 g/d X 6 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Axelrod, 1994[75]	Total cholesterol (mg/dl at week 6): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates at follow-up not reported. Reported testing: No significant effect (p=0.129) for fish oil (arm 2) using analysis of covariance. LDL (mg/dl at week 6): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates at follow-up not reported. Reported testing: No significant effect for fish oil (arm 2) using analysis of covariance. HDL (mg/dl at week 6): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates at follow-up not reported. Reported testing: No significant effect for fish oil (arm 2) using analysis of covariance. Triglycerides (mg/dl at week 6): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates at follow-up not reported. Reported testing: Significant (p=0.027) reduction in triglycerides for fish oil using analysis of covariance. HgA1c (% at week 6): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates at follow-up not reported. Reported testing: Significant (p=0.009) increase in HgA1c for fish oil using analysis of covariance. Fasting blood glucose (mg/dl at week 6): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates at follow-up not reported. Reported testing: No significant effect for fish oil (arm 2) using analysis of covariance.	Quality: Jadad: 4 Concealment of allocation:Yes Applicability: IB Funding source: private, non-industry, hospital

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Boberg, 1992[76]	Sample size: 14 Age (mean/range): 65 / 55-75 Race: NR % male: 86 # sites: 1 Location: Sweden	Design: RXT Duration: 16 wk X-over: week 8 Run-in: None Wash-out: None	Inclusion: Diet treatment=1 yr Exclusion: Lipid lowering drug use	Covariates: Hypoglycemic treatment/Duration of diabetes/Hb A1c/Obesity: BMI=27, kg=72.7, lbs=160	1	Olive oil 10 g/d X 8wk
					2	Max EPA (fish oil) 10 g/d X 8wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Boberg, 1992[76]	Total cholesterol (mg/dl at week 8): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between groups using analysis of covariance. LDL (mg/dl at week 8): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Significant (p<0.001) increase in LDL for for fish oil (arm 2) relative to olive oil (arm 1) using analysis of covariance. HDL (mg/dl at week 8): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: : No significant difference between groups using analysis of covariance. Triglycerides (mg/dl at week 8): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Significant (p< 0.001) reduction in triglycerides for fish oil (arm 2) relative to olive oil (arm 1) using analysis of covariance. HgA1c (% at week 8): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: : No significant difference between groups using analysis of covariance. Fasting blood glucose (mg/dl at week 8): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: : No significant difference between groups using analysis of covariance.	Quality: Jadad: 3 Concealment of allocation:NR Applicability: IIB Funding source: Government, private, non-industry

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Borkman, 1989[77]	Sample size: 10 Age (mean/range): 57 / 43-64 Race: NR % male: 70 # sites: 1 Location: Australia	Design: RXT Duration: 12 wk X-over: week 9 Run-in: 3 wk Washout: 3 wk	Inclusion: NR Exclusion: NR	Covariates: Duration of diabetes/Obesity: BMI=27, kg=72.7, lbs=160/Hypertension	1	Safflower oil 10 g/d X 3 wk
					2	Max EPA (fish oil) 10 g/d X 3 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Borkman, 1989[77]	Total cholesterol (mg/dl at week 6): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Testing between arms not reported. LDL (mg/dl at week 6): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Testing between arms not reported. HDL (mg/dl at week 6): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Testing between arms not reported. Triglycerides (mg/dl at week 6): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Testing between arms not reported. HgA1c: NR Fasting blood glucose (mg/dl at week 6): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Testing between arms not reported.	Quality: Jadad: 1 Concealment of allocation:NR Applicability: IB Funding source: Government, hospital

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Chan, 2002[58]	Sample size: 52 Age (mean/range): 53 / NR Race: NR % male: 100 # sites: 1 Location: Australia	Design: RCT Duration: 6 wk	Inclusion: Hyperlipidemia/No weight change in previous 2 or 3 mo Exclusion: Lipid lowering drug use/Baseline serum creatinine>0.40 mmol/l or >120 mmol/L/Not moderate or high fish intake/Diabetes/Thyroid abnormalities/Liver disease/Alcohol use	Covariates: Hypertension/Obesity: BMI=27, kg=72.7, lbs=160.	1	Placebo/control Dosage/duration not collected
					2	Atorvastatin Dosage/duration not collected
					3	Omacor 4 g for 6 wk
					4	Omacor plus Atorvastatin 4 g for 6 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Chan, 2002[58]	Total cholesterol (mg/dl at month 1.5) Arm 1 mean=223.94 Arm 3 mean=212.36 Mean difference=-11.58 (-36.35, 13.19) Arm 2 mean=139.00 Arm 4 mean=150.58 Mean difference=11.58 (-9.59, 32.76) Reported testing: Article reports significant Atorvastatin main effect (p=0.001) and nonsignificant Fish main effect based on general linear model. Triglyceride (mg/dl at month 1.5) Arm 1 mean=256.64 Arm 3 mean=132.74 Mean difference=-123.89 (-366.93, 119.14) Arm 2 mean=123.89 Arm 4 mean=106.20 Mean difference=-17.70 (-52.99, 17.59) Reported testing: Article reports significant Atorvastatin main effect (p=0.002) and Fish main effect (p=0.002) based on general linear model. HDL (mg/dl at month 1.5) Arm 1 mean=39.38 Arm 3 mean=38.61 Mean difference=-0.77 (-6.33, 4.78) Arm 2 mean=40.15 Arm 4 mean=48.26 Mean difference=8.11 (0.63, 15.59) Reported testing: Article reports significant Atorvastatin main effect (p=0.007) and Fish main effect (p=0.041) based on general linear model. LDL (mg/dl at month 1.5) Arm 1 mean=147.88 Arm 3 mean=142.09 Mean difference=-5.79 (-20.88, 9.29) Arm 2 mean=71.04 Arm 4 mean=83.01 Mean difference=11.97 (-4.51, 28.45) Reported testing: Article reports significant Atorvastatin main effect (p=0.001) and nonsignificant Fish main effect based on general linear model. Fasting blood glucose: NR HbA1c: NR	Quality: Jadad: 3 Concealment of allocation:NR Applicability: IIB Funding source: Government, industry,

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Connor, 1993[78]	Sample size: 16 Age (mean/range): 59 / 46-72 Race: NR % male: 81 # sites: 1 Location: US	Design: RXT Duration: 15 mo X-over: month 9 Run-in: 3 mo Washout: None	Inclusion: Hyperlipidemia Exclusion: NR	Covariates: Hypoglycemic treatment/Obesity: BMI=27, kg=72.7, lbs=160.	1	Olive oil 15 g/d X 6 mo
					2	Promega (fish oil) 15 g/d X 6 mo

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Connor, 1993[78]	Total cholesterol (mg/dl at month 9): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between arms using Wilcoxian signed rank test. LDL (mg/dl at month 9): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Significant (p=0.0003) difference favoring olive oil (arm 1) using Wilcoxian signed rank test. HDL (mg/dl at month 9): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between arms using Wilcoxian signed rank test. Triglycerides (mg/dl at month 9): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Significant (p=0.0004) difference favoring fish oil (arm 2) using Wilcoxian signed rank test. HgA1c (% at month 9) Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between arms using Wilcoxian signed rank test. Fasting blood glucose (mg/dl at month 9): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between arms using Wilcoxian signed rank test.	Quality: Jadad: 2 Concealment of allocation:NR Applicability: IIIB Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Dunstan, 1998[59]	Sample size: 48 Age (mean/range): 53 / NR Race: NR % male: 76 # sites: 1 Location: Australia	Design: RCT Duration: 8 wk	Inclusion: Age/Nonsmoker/Hyperlipidemia/Sedentary Exclusion: Lipid lowering drug use/Not moderate or high fish intake/Proliferative retinopathy/Alcohol use/Liver disease/ReNRI disease/Neuropathy/Cardiovascular disease	Covariates: Hypoglycemic treatment/Duration of diabetes/Obesity: BMI=27, kg=72.7, lbs=160/Hb A1c	1	Low-fat and low-sodium diet X 8 wk
					2	Low-fat and low-sodium diet X 8 wk
					3	Fish Approximately 3.6 g/d of omega-3 fatty acids/d X 8 wk
					4	Fish Approximately 3.6 g/d of omega-3 fatty acids/d X 8 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source

Dunstan, 1998[59]	Total cholesterol (mg/dl at month 2) Arm 1 mean=204.63 Arm 3 mean=185.33 Mean difference=-19.31 (-46.67, 8.06) Arm 2 mean=173.75 Arm 4 mean=181.47 Mean difference=7.72 (-19.28, 34.73) Reported testing: Article reports no significant differences based on a generalized linear model or a multiple regression model. Triglyceride (mg/dl at month 2) Arm 1 mean=247.79 Arm 3 mean=132.74 Mean difference=-115.04 (-195.84, -34.24) Arm 2 mean=168.14 Arm 4 mean=115.04 Mean difference=-53.1 (-132.84, 26.65) Reported testing: Article reports significant results for a generalized linear model and a multiple regression model. HDL (mg/dl at month 2) Arm 1 mean=29.73 Arm 3 mean=34.36 Mean difference=4.63 (-3.90, 13.16) Arm 2 mean=30.50 Arm 4 mean=30.89 Mean difference=0.39 (-8.03, 8.80) Reported testing: Article reports no significant differences based on a generalized linear model or a multiple regression model. LDL (mg/dl at month 2) Arm 1 mean=127.41 Arm 3 mean=132.43 Mean difference=5.02 (-21.44, 31.48) Arm 3 mean=108.10 Arm 4 mean=127.41 Mean difference=19.31 (-6.81, 45.42) Reported testing: Article reports no significant differences based on a generalized linear model or a multiple regression model. Fasting blood glucose (mg/dl at month 2) Arm 1 mean=167.57 Arm 3 mean=176.58 Mean difference=9.01 (-33.00, 51.02) Arm 2 mean=165.77 Arm 4 mean=169.37 Mean difference=3.60 (-37.85, 45.06) Reported testing: Article reports significant results for a generalized linear model and a multiple regression model. HbA1c: NR	Quality: Jadad: 2 Concealment of allocation: NR Applicability: IIB Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Fasching, 1996[79]	Sample size: 10 Age (mean/range): 61 / NR Race: NR % male: 40 # sites: 1 Location: Australia	Design: RXT Duration: 20 wk X-over: week 18 Run-in: 8 wk Wash-out: 8 wk	Inclusion: Hyperlipidemia/Controlled diabetes/WHO diabetes criteria Exclusion: Lipid lowering drug use	Covariates: Duration of diabetes/Obesity: BMI=27, kg=72.7, lbs=160.	1	Gemfibrozil 4 mmol/d x 2 wk
					2	EPAX 5000 (fish oil) 22 mol/d x 2 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Fasching, 1996[79]	Total cholesterol: (at week 10): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Significant (p=.05) difference between groups, test not specified. LDL: (at week 10): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Significant (p<.02) difference between groups, test not specified. HDL: (at week 10): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between groups, test not specified. Triglycerides: (at week 10): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Significant (p<.05) difference between groups, test not specified. HgA1c: (at week 10): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between groups, test not specified. Fasting blood glucose: (at week 10): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between groups, test not specified.	Quality: Jadad: 2 Concealment of allocation: NR Applicability: IB Funding source: Government, hospital

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Goh, 1997[80]	Sample size: 28 Age (mean/range): 58 / NR Race: NR % male: NR # sites: 1 Location: Canada	Design: RXT Duration: 9 mo X-over: month 6 Run-in: 3 mo Wash-out: None	Inclusion: Controlled diabetes/Hb A1c < 9.5% or 10.5% Exclusion: Lipid lowering drug use	Covariates: Hb A1c .	1	Linseed oil Variable dose x 3 mo
					2	Fish oil Variable dose x 3 mo

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Goh, 1997[80]	Total cholesterol (mg/dl at month 3): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between arms by ANOVA. LDL (mg/dl at month 9): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Significant (p=0.0003) difference favoring olive oil (arm 1) using Wilcoxian signed rank test. HDL (mg/dl at month 3): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between arms by ANOVA. Triglycerides (mg/dl at month 3): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Significant (p=0.05) difference favoring fish oil (arm 2) by ANOVA. HgA1c (% at month 3) Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between arms using Wilcoxian signed rank test. HgA1c: NR Fasting blood glucose: NR	Quality: Jadad: 2 Concealment of allocation: NR Applicability: NR Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Hendra, 1990[60]	Sample size: 80 Age (mean/range): 56 / NR Race: Caucasian, Black, Asian % male: 69 # sites: 1 Location: UK	Design: RCT Duration: 1.5 mo	Inclusion: Controlled diabetes/Hyperlipidemia Exclusion: PregNRncy/lactating/Cardiovascular disease	Covariates: Duration of diabetes/Hypertension/Hypoglycemic treatment/Obesity: BMI=27, kg=72.7, lbs=160	1	Placebo/control Dosage/duration not collected
					2	Max EPA (fish oil) 10 g for 6 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Hendra, 1990[60]	Total cholesterol (mg/dl at month 1.5) Arm 1 mean=239.38 Arm 2 mean=227.80 Mean difference=-11.58 (-30.89, 7.72) Reported testing: Article reports no significant differences (p=0.7) for changes between Arm 1 and Arm 2 with unpaired Student's t tests. Triglyceride (mg/dl at month 1.5) Arm 1 mean=194.69 Arm 2 mean=150.44 Mean difference=-44.25 (-89.80, 1.31) Reported testing: Article reports significant differences (p<0.001) for changes between Arm 1 and Arm 2 with unpaired Student's t tests. HDL (mg/dl at month 1.5) Arm 1 mean=46.33 Arm 2 mean=38.61 Mean difference=-7.72 (-14.68, -0.76) Reported testing: Article reports no significant differences (p=0.6) for changes between Arm 1 and Arm 2 with unpaired Student's t tests. LDL (mg/dl at month 1.5) Arm 1 mean=162.16 Arm 2 mean=158.30 Mean difference=-3.86 (-22.97, 15.25) Reported testing: Article reports no significant differences (p=0.085) for changes between Arm 1 and Arm 2 with unpaired Student's t tests. Fasting blood glucose (mg/dl at month 1.5) Arm 1 mean=203.60 Arm 2 mean=225.23 Mean difference=21.62 (-18.06, 61.30) Reported testing: Article reports no significant differences (p=0.17) for changes between Arm 1 and Arm 2 with unpaired Student's t tests. HbA1c: NR	Quality: Jadad: 3 Concealment of allocation: NR Applicability: IB Funding source: industry, hospital

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Hermans [74]	Sample size: 20 Age (mean/range): 46 / NR Race: NR % male: NR # sites: 1 Location: Belgium	Design: RCT Duration: 2 mo	Inclusion: Diabetic nephropathy Exclusion: NR	Covariates: Hypoglycemic treatment/Hb A1c/Hypertension	1	Placebo/control NR Dosage NR x 2 mo
					2	Fish oil 9 g/d x 2 mo

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Hermans [74]	Total cholesterol: NR LDL: NR HDL: NR Triglyceride: (at month 2) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported. Reported testing: Testing between groups not reported. HgA1c: (at month 2) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported. Reported testing: Testing between groups not reported. Fasting blood glucose: NR	Quality: Jadad: 2 Concealment of allocation: NR Applicability: NR Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Jensen, 1989[81]	Sample size: 18 Age (mean/range): 37 / 22-47 Race: NR % male: 78 # sites: 1 Location: Denmark	Design: RXT Duration: 28 wk X-over: week 20 Run-in: 4 wk Wash-out: 8 wk	Inclusion: Proteinuria/Retinopathy Exclusion: NR	Covariates: Duration of diabetes/Hypoglycemic treatment	1	Olive oil 21 ml/d x 8 wk
					2	Cod-liver oil (Eskisol) 21 ml/d x 8 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Jensen, 1989[81]	Total cholesterol: (at week 10) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: Testing between groups was not significant; either Wilcoxon test for paired differences or paired Student's t-test used. LDL: (at week 10) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: Significant (p<.05) difference between groups; either Wilcoxon test for paired differences or paired Student's t-test used. HDL: (at week 10) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: Testing between groups was not significant; either Wilcoxon test for paired differences or paired Student's t-test used. Triglycerides: (at week 10) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: Significant (p<.05) difference between groups favoring cod-liver oil; either Wilcoxon test for paired differences or paired Student's t-test used. Change in HgA1c(at week 10) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: Statisticaltesting between groups was not reported	Quality Jadad: 2 Concealment of allocation: NR Applicability: IIB Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Luo, 1998[82]	Sample size: NR Age (mean/range): 54 / NR Race: NR % male: 10 # sites: 1 Location: Portugal	Design: RXT Duration: 6 mo X-over: month 2 Run-in: None Wash-out: 2 mo	Inclusion: Hb A1c < 9.5% or 10.5%/Fasting blood glucose Exclusion: ReNRI disease/Thyroid abnormalities/Liver disease/Lipid lowering drug use/GI disorders	Covariates: Duration of diabetes/Hb A1c/Obesity: BMI=27, kg=72.7, lbs=160/Hypoglycemic treatment	1	Sunflower oil 6g/d x 2 mo
					2	Fish oil 6 g/d x 2 mo

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Luo, 1998[82]	Total cholesterol: (at month 2) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: No treatment effect by ANOVA. LDL: (at month 2) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: No treatment effect by ANOVA. HDL: (at month 2) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: No treatment effect by ANOVA. Triglycerides: (at month 2) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: Significant (p<.05) treatment effect for arm 2 (fish oil) by ANOVA. HgA1c: (at month 2) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: No treatment effect by ANOVA. Fasting blood glucose: (at month 2) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: No treatment effect by ANOVA.	Quality: Jadad: 2 Concealment of allocation: Yes Applicability: IIB Funding source: Government, industry

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Maffettone, 1996[73]	Sample size: 16 Age (mean/range): 56 / NR Race: NR % male: 40 # sites: NR Location: Italy	Design: RCT Duration: 6 mo	Inclusion: Diabetes type II > 2 years/ elevated triglycerides/age 40-75 Exclusion: End organ failure/coagulopathy/anticoagulants	Covariates: NR	1	Placebo/control Dosage/duration not collected
					2	Fish oil 2 g for 6 mo

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Maffettone, 1996[73]	Total cholesterol: NR Triglyceride: NR HDL (mg/dl at month 6) Arm 1 mean=36.68 Arm 2 mean=34.36 MD =-2.32 (-10.69, 6.06) Reported testing: Article reports no significant differences (p>0.05) for changes between Arm 1 and Arm 2. LDL (mg/dl at month 6) Arm 1 mean=127.41 Arm 2 mean=127.02 Mean difference=-0.39 (-47.32, 46.55) Reported testing: Article reports no significant differences (p>0.05) for changes between Arm 1 and Arm 2. Fasting blood glucose: NR HbA1c: NR	Quality: Jadad: 3 Concealment of allocation: NR Applicability: IIB Funding source: NR

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
McGrath, 1996[83]	Sample size: 23 Age (mean/range): 53 / 44-61 Race: NR % male: 87 # sites: 1 Location: UK	Design: RXT Duration: 18 wk X-over: week 6 Run-in: None Wash-out: 6 wk	Inclusion: NR Exclusion: Cardiovascular disease/Hypertension/ReNRI disease/Lipid lowering drug use/Antihypertensive meds/Cardiovascular drugs	Covariates: Obesity: BMI=27, kg=72.7, lbs=160/Hypoglycemic treatment/Duration of diabetes/Hb A1c	1	Olive oil 10g/d x 6 wk
					2	Max EPA (fish oil) 10 g/d x 6 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
McGrath, 1996[83]	Total cholesterol: (at week 6) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: No treatment effect by ANOVA. LDL: (at week 6) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: No treatment effect by ANOVA. HDL: (at week 6) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: No treatment effect by ANOVA. Triglycerides: (at week 6) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: No treatment effect by ANOVA. HgA1c: (at week 6) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: No treatment effect by ANOVA. Fasting blood glucose: (at week 6) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: No treatment effect by ANOVA.	Quality: Jadad: 3 Concealment of allocation: NR Applicability: IIB Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Meshcheriakova, 2001[66]	Sample size: 120 Age (mean/range): 55 / 39-65 Race: NR % male: NR # sites: 1 Location: Russia	Design: RCT Duration: 4 wk	Inclusion: Controlled diabetes/Hyperlipedemia/Age Exclusion: NR	Covariates: Duration of diabetes/Obesity: BMI=27, kg=72.7, lbs=160/Hb A1c	1	Low-fat and low-sodium diet
					2	Eiconol 8 g for 4 wk
					3	Linseed oil 18 g for 4 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Meshcheriakova, 2001[66]	Total cholesterol (mg/dl at week 4) Arm 1 mean=244.40 Arm 2 and Arm 3 (combined) mean=249.03 Mean difference=4.63 (-15.75, 25.01) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. LDL: NR HDL: NR Triglyceride (mg/dl at week 4) Arm 1 mean=283.19 Arm 2 and Arm 3 (combined) mean=247.79 Mean difference=-35.40 (-88.83, 18.03) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. HgA1c: NR Fasting blood glucose: NR	Quality: Jadad: 1 Concealment of allocation: NR Applicability: NR Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Morgan, 1995[61]	Sample size: 40 Age (mean/range): 54 / NR Race: Caucasian, Black, Hispanic % male: 45 # sites: 1 Location: US	Design: RCT Duration: 3.0 mo	Inclusion: Hyperlipedemia/Controlled diabetes Exclusion: NR	Covariates: Hb A1c/Hypoglycemic treatment/Duration of diabetes	1	Placebo/control Dosage/duration not collected
					2	Placebo/control Dosage/duration not collected
					3	Fish oil 9 g for 12 wk
					4	Fish oil 18 g for 12 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Morgan, 1995[61]	Total cholesterol (mg/dl at month 3) Arm 1 mean=263.71 Arm 2 mean=250.58 Mean difference=-13.13 (-37.43, 11.18) Reported testing: Article reports no significant differences (p>0.05). Triglyceride (mg/dl at month 3) Arm 1 mean=760.17 Arm 2 mean=413.27 Mean difference=-346.90 (-656.00, -37.81) Reported testing: Article reports significant differences (p=0.0001) between Arm 1 and Arm 2. HDL (mg/dl at month 3) Arm 1 mean=35.91 Arm 2 mean=38.61 Mean difference=2.70 (-6.18, 11.58) Reported testing: Article reports no significant differences (p>0.05). LDL (mg/dl at month 3) Arm 1 mean=149.42 Arm 2 mean=157.53 Mean difference=8.11 (-19.46, 35.67) Reported testing: Article reports no significant differences (p>0.05). Fasting blood glucose (mg/dl at month 3) Arm 1 mean=223.42 Arm 2 mean=209.01 Mean difference=-14.41 (-52.95, 24.12) Reported testing: Article reports no significant differences (p>0.05). HbA1c (% at month 3) Arm 1 mean=7.80 Arm 2 mean=7.70 Mean difference=-0.10 (-1.25, 1.05) Reported testing: Article reports no significant differences (p>0.05).	Quality: Jadad: 2 Concealment of allocation: NR Applicability: IB Funding source: Hospital, industry

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Morgan,[67]	Sample size: 25 Age (mean/range): 54 / 41-64 Race: Caucasian, Black, Hispanic % male: 40 # sites: 1 Location: US	Design: RCT Duration: 5.3 mo	Inclusion: Age/Hyperlipidemia Exclusion: Cardiovascular disease/Liver disease/PregNRncy/lactating/ReNRl disease/Thyroid abnormalities/Alcohol use/Cardiovascular drugs/Hormone replacement treatment	Covariates: Hypoglycemic treatment/Duration of diabetes/Obesity: BMI=27, kg=72.7, lbs=160/Hyperlipidemia	1	Placebo/control Dosage/duration not collected
					2	Placebo/control Dosage/duration not collected
					3	Fish oil 18 g for 12 wk
					4	Fish oil 9 g for 12 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes, Results	Quality . Applicability Funding Source
Morgan,[67]	Total cholesterol (mg/dl at week 12) Arm 1 (Low dosage placebo) mean=282.00 Arm 3 (Low dosage fish oil) mean=245.00 Mean difference=-37.00 (-96.98, 22.98) Arm 2 (High dosage placebo) mean=249.00 Arm 4 (High dosage fish oil) mean=273.00 Mean difference=24.00 (-5.75, 53.75) Reported testing: Article reports no significant differences (p>0.05). Triglyceride (mg/dl at week 12) Arm 1 (Low dosage placebo) mean=311.00 Arm 2 (Low dosage fish oil) mean=195.00 Mean difference=-116.00 (-267.44, 35.44) Arm 1 (High dosage placebo) mean=204.00 Arm 2 (High dosage fish oil) mean=197.00 Mean difference=-7.00 (-110.19, 96.19) HDL (mg/dl at week 12) Arm 1 (Low dosage placebo) mean=23.00 Arm 3 (Low dosage fish oil) mean=32.00 Mean difference=9.00 (-3.49, 21.49) Arm 2 (High dosage placebo) mean=37.00 Arm 4 (High dosage fish oil) mean=46.00 Mean difference=9.00 (-13.03, 31.03) Reported testing: Article reports no significant differences (p>0.05). LDL (mg/dl at week 12) Arm 1 (Low dosage placebo) mean=157.00 Arm 3 (Low dosage fish oil) mean=165.00 Mean difference=8.00 (-52.53, 68.53) Arm 2 (High dosage placebo) mean=134.00 Arm 4 (High dosage fish oil) mean=157.00 Mean difference=23.00 (-31.39, 77.39) Reported testing: Article reports no significant differences (p>0.05). Fasting blood glucose (mg/dl at week 12) Arm 1 (Low dosage placebo) mean=252.00 Arm 2 (Low dosage fish oil) mean=211.00 Mean difference=-41.00 (-114.16, 32.16) Arm 1 (High dosage placebo) mean=226.00 Arm 2 (High dosage fish oil) mean=209.00 Mean difference=-17.00 (-89.43, 55.43) Reported testing: Article reports no significant differences (p>0.05). HbA1c (% at week 12) Arm 1 (Low dosage placebo) mean=8.80 Arm 2 (Low dosage fish oil) mean=7.50 Mean difference=-1.30 (-3.42, 0.82) Arm 1 (High dosage placebo) mean=7.30 Arm 2 (High dosage fish oil) mean=8.00 Mean difference=0.70 (-0.68, 2.08) Reported testing: Article reports no significant differences (p>0.05).	Quality: Jadad: 4 Concealment of allocation: Yes Applicability: IB Funding source: NR

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Patti, 1999[68]	Sample size: 1006 Age (mean/range): 57 / NR Race: NR % male: 44 # sites: 1 Location: Italy	Design: RCT Duration: 6.0 mo	Inclusion: Age/WHO diabetes criteria/Disease > 1 year/Controlled diabetes/No weight change in previous 2 or 3 mo/Hyperlipidemia/Diet treatment=1 yr/Postmenopausal women ± hormone replacement Exclusion: Lipid lowering drug use/Antiplatelet or anticoagulation/Liver disease/ReNRl disease/Bleeding disorder/Proliferative retinopathy/Intraocular hemorrhage	Covariates: Hb A1c/Obesity: BMI=27, kg=72.7, lbs=160/Hypoglycemic treatment/Duration of diabetes	1	Placebo/control Dosage/duration not collected
					2	Fish oil Variable dose for 6 mo

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Patti, 1999[68]	Total cholesterol (mg/dl at month 6) Arm 1 mean=239.77 Arm 2 mean=220.46 Mean difference=-19.31 (-57.98, 19.37) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Triglyceride (mg/dl at month 6) Arm 1 mean=277.88 Arm 2 mean=258.41 Mean difference=-19.47 (-89.24, 50.30) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. HDL (mg/dl at month 6) Arm 1 mean=36.68 Arm 2 mean=34.36 Mean difference=-2.32 (-10.78, 6.14) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. LDL: NR Fasting blood glucose (mg/dl at month 6) Arm 1 mean=185.59 Arm 2 mean=196.40 Mean difference=10.81 (-28.67, 50.29) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. HbA1c (% at month 6) Arm 1 mean=7.70 Arm 2 mean=8.30 Mean difference=0.60 (-0.79, 1.99) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2.	Quality: Jadad: 2 Concealment of allocation: NR Applicability: IB Funding source: Government, industry

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Pelikanova, 1993[62]	Sample size: 20 Age (mean/range): 52 / 40-60 Race: NR % male: 100 # sites: 1 Location: Czech Republic	Design: RCT Duration: 0.8 mo	Inclusion: Age/Hyperlipidemia/Controlled diabetes Exclusion: NR	Covariates: Hb A1c/Obesity: BMI=27, kg=72.7, lbs=160/Malabsortion	1	Placebo/control Dosage/duration not collected
					2	Fish oil 15 ml for 3 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Pelikanova, 1993[62]	Total cholesterol (mg/dl at week 3) Arm 1 mean=236.68 Arm 2 mean=255.60 Mean difference=18.92 (-12.96, 50.80) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Triglyceride (mg/dl at week 3) Arm 1 mean=168.14 Arm 2 mean=131.86 Mean difference=-36.28 (-101.90, 29.33) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. HDL: NR LDL: NR. Fasting blood glucose: NR HbA1c (% at week 3) Arm 1 mean=7.50 Arm 2 mean=8.40 Mean difference=0.90 (0.02, 1.78) Reported testing: Article reports no significant differences between Arm 1 and Arm 2.	Quality: Jadad: 1 Concealment of allocation: NR Applicability: IIB Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Petersen, 2002[63]	Sample size: 42 Age (mean/range): 63 / 33-85 Race: NR % male: 62 # sites: 1 Location: Denmark	Design: RCT Duration: 2.0 mo	Inclusion: Disease > 1 year/Hyperlipidemia/Diabetes onset at 30 years up/Not postmenopausal or hormone replacement Exclusion: Lipid lowering drug use/No fish or fish supplement/Alcohol use	Covariates: Hypoglycemic treatment/Duration of diabetes/Hb A1c/Hypertension	1	Placebo/control Dosage/duration not collected
					2	Futura 1000 (fish oil) 4 g for 8 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Petersen, 2002[63]	Total cholesterol (mg/dl at month 2) Arm 1 mean=209.65 Arm 2 mean=226.64 Mean difference=16.99 (-5.97, 39.95) Reported testing: Article reports no significant differences (p=0.162) between Arm 1 and Arm 2. Triglyceride (mg/dl at month 2) Arm 1 mean=240.71 Arm 2 mean=160.18 Mean difference=-80.53 (-175.69, 14.63) Reported testing: Article reports no significant differences (p=0.105) between Arm 1 and Arm 2. HDL (mg/dl at month 2) Arm 1 mean=42.86 Arm 2 mean=49.42 Mean difference=6.56 (0.13, 13.00) Reported testing: Article reports no significant differences (p=0.062) between Arm 1 and Arm 2. LDL (mg/dl at month 0.5) Arm 1 mean=110.81 Arm 2 mean=132.43 Mean difference=21.62 (2.79, 40.45) Reported testing: Article reports significant differences (p=0.031) between Arm 1 and Arm 2. Fasting blood glucose: (at month 0.5) Arm 1: point estimate not reported. Arm 2: point estimate not reported. Meta-analysis: Not included; point estimates not reported. Reported testing: Article reports 'no significant changes.' HgA1c: (at month 0.5) Arm 1: point estimate not reported. Arm 2: point estimate not reported. Meta-analysis: Not included; point estimates not reported. Reported testing: Article reports 'no significant changes.	Quality: Jadad: 3 Concealment of allocation: NR Applicability: IB Funding source: government, industry

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Puhakainen, 1995[86]	Sample size: 9 Age (mean/range): 53 / NR Race: NR % male: 44 # sites: 1 Location: Finland	Design: RXT Duration: 12 wk X-over: week 6 Run-in: None Wash-out: None	Inclusion: NR Exclusion: Cardiovascular disease	Covariates: Duration of diabetes/Hb A1c/Obesity: BMI=27, kg=72.7, lbs=160/Hypoglycemic treatment	1	Corn and olive oils 12 g/d x 6 wk
					2	Max EPA (fish oil) 12 g/d x 6 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Puhakainen, 1995[86]	Total cholesterol: (at week 6) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: No difference between groups by paired Student's t test . LDL: (at week 6) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: No difference between groups by paired Student's t test. HDL: (at week 6) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: No difference between groups by paired Student's t test. Triglycerides: (at week 6) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: Significant (p<.05) difference between groups favoring fish oil by Student's t test. HgA1c: (at week 6) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: Reported testing: No difference between groups by paired Student's t test. Fasting blood glucose: (at week 6) Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported before crossover. Reported testing: Reported testing: No difference between groups by paired Student's t test.	Quality: Jadad: 2 Concealment of allocation: NR Applicability: IB Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Rivellese, 1996[69]	Sample size: 904 Age (mean/range): 57 / NR Race: NR % male: 44 # sites: 1 Location: Italy	Design: RCT Duration: 6 mo	Inclusion: WHO diabetes criteria/Controlled diabetes/Diet treatment=1 yr/No weight change in previous 2 or 3 mo/Hyperlipidemia/Age/Postmenopausal women ± hormone replacement/Disease > 1 year Exclusion: Intraocular hemorrhage/Liver disease/ReNRI disease/Bleeding disorder/Proliferative retinopathy/Antiplatelet or anticoagulation/Lipid lowering drug use	Covariates: Hypoglycemic treatment/Duration of diabetes/Hb A1c/Obesity: BMI=27, kg=72.7, lbs=160	1	Olive oil Variable dose x 6 mo
					2	Fish oil Variable dose x 6 mo

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Rivellese, 1996[69]	Total cholesterol: (mmol/l at month 6) Arm 1= point estimate not reported Arm 2= 5.7 mmol/l Meta-analysis: Not included; point estimate for Arm 1 not reported. Reported testing: Testing between arms was not reported. LDL (mg/dl at month 6) Arm 1 mean=127.41 Arm 2 mean=127.02 Mean difference=-0.39 (-47.31, 46.54) Reported testing: Article reports no significant differences (p>0.05) for changes between Arm 1 and Arm 2. HDL: (mmol/l at month 6) Arm 1= 0.25 Arm 2= 0.19 Meta-analysis: Not included. Reported testing: No significant difference between groups using paired Student's t test. Triglycerides: Not reported Note: triglyceride contend of specific lipoproteins was reported, but not total serum triglycerides. HgA1c: (%at month 6) Arm 1 = 6.9 Arm 2 = 8.3 Meta-analysis: Not included. Reported testing: No difference between groups by paired Student's t test. Fasting blood glucose: (mmol/l at month 6) Arm 1 = 10.3 Arm 2 = 10.9 Meta-analysis: Not included. Reported testing: No difference between groups by paired Student's t test.	Quality: Jadad: 2 Concealment of allocation: NR Applicability: IB Funding source: Government, industry

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Sarkkinen, 1996[70]	Sample size: 31 Age (mean/range): 56 / NR Race: NR % male: 59 # sites: 1 Location: Finland	Design: RCT Duration: 2.0 mo	Inclusion: WHO diabetes criteria/WHO impaired glucose tolerance criteria Exclusion: NR	Covariates: NR	1	Sunflower oil Dosage/duration not collected
					2	Rapeseed (LEAR) oil Dosage/duration NR

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Sarkkinen, 1996[70]	Total cholesterol (mg/dl at month 2) Arm 1 mean=232.82 Arm 2 mean=215.06 Mean difference=-17.76 (-45.21, 9.69) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Triglyceride (mg/dl at month 2) Arm 1 mean=151.33 Arm 2 mean=128.32 Mean difference=-23.01 (-80.05, 34.03) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. HDL (mg/dl at month 2) Arm 1 mean=49.03 Arm 2 mean=45.94 Mean difference=-3.09 (-9.84, 3.67) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. LDL (mg/dl at month 2) Arm 1 mean=151.74 Arm 2 mean=141.70 Mean difference=-10.04 (-37.38, 17.30) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Fasting blood glucose: (mg/dl at month 2) Arm 1 = point estimate not reported. Arm 2 = point estimate not reported. Meta-analysis: Not included; point estimates not reported. Reported testing: No significant difference between Arm 1 and Arm 2 using Students t test. HgA1c: NR	Quality: Jadad: 1 Concealment of allocation: NR Applicability: IB Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Schectman, 1988[87]	Sample size: 13 Age (mean/range): 52 / 29-66 Race: NR % male: 69 # sites: 1 Location: US	Design: RXT Duration: 15 wk X-over: week 11 Run-in: 3 wk Wash-out: 4 wk	Inclusion: Hyperlipidemia/Diet treatment=1 yr/Controlled diabetes Exclusion: Liver disease/ReNRI disease/Thyroid abnormalities/Diabetes/Lipid lowering drug use/No fish or fish supplement	Covariates: Obesity: BMI=27, kg=72.7, lbs=160/Hyperlipidemia/Hypoglycemic treatment/Hypertension	1	Safflower oil 12g/d x 4 wk
					2	Max EPA (fish oil) 12 g/d x 4 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Schectman, 1988[87]	Total cholesterol: (at week 7) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates before cross over not reported. Reported testing: A tendency towards an increase with fish oil by ANOVA (p<0.05). LDL: (at week 7) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates before cross over not reported. Reported testing: A tendency towards an increase with fish oil by ANOVA (p<0.05). HDL: (at week 7) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates before cross over not reported. Reported testing: No significant treatment effect by ANOVA. Change in Triglycerides: (at week 7) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates before cross over not reported. Reported testing: A tendency towards an increase with fish oil by ANOVA (p<0.05). Fasting blood glucose: (at week 7) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates before cross over not reported. Reported testing: A tendency towards an increase with fish oil by ANOVA (p<0.05). HgA1c. (at week 7) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates before cross over not reported. Reported testing: No significant treatment effect by ANOVA.	Quality: Jadad: 2 Concealment of allocation: NR Applicability: IB Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Schwab, 1998[88]	Sample size: 31 Age (mean/range): 56 / 47-64 Race: NR % male: 59 # sites: 1 Location: Finland	Design: RCT Duration: 8 wk	Inclusion: WHO diabetes criteria/WHO impaired glucose tolerance criteria Exclusion: NR	Covariates: Obesity: BMI=27, kg=72.7, lbs=160/Hypertension	1	Sunflower oil Dosage NR x 8 wk
					2	Rapeseed (LEAR) oil Dosage NR x 8 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Schwab, 1998[88]	Total cholesterol: (at week 8) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates before cross over not reported. Reported testing: No significant difference between groups by paired Student's t test. LDL: (at week 8) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates before cross over not reported. Reported testing: No significant difference between groups by paired Student's t test. HDL: (at week 8) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates before cross over not reported. Reported testing: No significant difference between groups by paired Student's t test. Change in Triglycerides: (at week 8) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates before cross over not reported. Reported testing: No significant difference between groups by paired Student's t test. Fasting blood glucose: NR HgA1c. NR	Quality: Jadad: 1 Concealment of allocation: NR Applicability: IB Funding source: Government, non-industry, private

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Shimizu, 1995[56]	Sample size: 45 Age (mean/range): 63 / NR Race: NR % male: 49 # sites: 1 Location: Japan	Design: RCT Duration: 12 mo	Inclusion: Normal BUN/Normal serum creatinine Exclusion: NR	Covariates: Hypertension/Hypoglycemic treatment/Duration of diabetes	1	Placebo/control Dosage/duration not collected
					2	EPA-E 900 mg for 12 hr

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Shimizu, 1995[56]	Total cholesterol (mg/dl at month 12) Arm 1 mean=191.00 Arm 2 mean=203.40 Mean difference=12.40 (-2.30, 27.10) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Triglyceride (mg/dl at month 12) Arm 1 mean=162.00 Arm 2 mean=192.40 Mean difference=30.40 (-23.37, 84.17) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. HDL (mg/dl at month 12) Arm 1 mean=50.00 Arm 2 mean=55.80 Mean difference=5.80 (-2.70, 14.30) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. LDL: NR Fasting blood glucose: NR HbA1c (% at month 12) Arm 1 mean=7.76 Arm 2 mean=7.82 Mean difference=0.06(-8.44, 8.56) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2.	Quality: Jadad: 1 Concealment of allocation: NR Applicability: IB Funding source: unclear

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Sirtori, 1997[89]	Sample size: 935 Age (mean/range): 59 / NR Race: NR % male: 62 # sites: 63 Location: Italy	Design: RCT Duration: 6 mo	Inclusion: Age/Hyperlipidemia/Disease > 1 year/Controlled diabetes Exclusion: ReNRl disease/Lipid lowering drug use/Cardiovascular disease/Reliable adherence/Alcohol use/Cardiovascular drugs/Insulin treatment/Obesity	Covariates: Obesity: BMI=27, kg=72.7, lbs=160 .	1	Olive oil Variable dose x 6 mo
					2	Esapent (fish oil) Variable dose x 6 mo

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Sirtori, 1997[89]	Total cholesterol: (at month 6) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates not reported; graphical data only. Reported testing: No difference between arms by ANOVA. LDL: (at month 6) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates not reported; graphical data only. Reported testing: Significant (p<.048) difference between arms with higher LDL in fish oil arm by ANOVA. HDL: (at month 6) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates not reported; graphical data only. Reported testing: No difference between arms by ANOVA. Change in Triglycerides: (at month 6) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates not reported; graphical data only. Reported testing: Significant (p<.0001) difference between arms with lower triglyceride in fish oil arm by ANOVA. Fasting blood glucose: : (at month 6) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates not reported; graphical data only. Reported testing: No difference between arms by ANOVA. HgA1c. : (at month 6) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates not reported; graphical data only. Reported testing: No difference between arms by ANOVA.	Quality: Jadad: 4 Concealment of allocation: NR Applicability: IB Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Sirtori, 1998[64]	Sample size: 935 Age (mean/range): 59 / NR Race: NR % male: 62 # sites: 63 Location: Italy	Design: RCT Duration: 12 mo	Inclusion: Hyperlipidemia/Age/Disease > 1 year/Controlled diabetes Exclusion: Lipid lowering drug use/Reliable adherence/ReNRI disease/Alcohol use/Cardiovascular disease/Cardiovascular drugs/Insulin treatment/Obesity	Covariates: Obesity: BMI=27, kg=72.7, lbs=160	1	Olive oil Variable dose x 12 mo
					2	Esapent (fish oil) Variable dose for 12 mo

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Sirtori, 1998[64]	Total cholesterol (change from graph data mg/dl at month 6): Arm 1: +0.5 Arm 2: -1.0 Meta-analysis: Not included; point estimates not reported; graphical data only. Reported testing: No significant difference between groups using repeated measures ANOVA. LDL(change mg/dl at month 6) : Arm 1: point estimate not reported Arm 2: +8.16 Meta-analysis: Not included; point estimates not reported; graphical data only. Reported testing: Borderline significant (p=0.046) between fish oil (Arm 1) and olive oil (Arm 2) using repeated measures ANOVA. HDL (% change mg/dl at month 6): Arm 1: + 5% Arm 2: + 5% Meta-analysis: Not included; point estimates not reported. Reported testing: No significant difference between groups using repeated measures ANOVA. Triglycerides(change from graph data mg/dl at month 6): Arm 1: -20 Arm 2: -62 Meta-analysis: Not included; point estimates not reported; graphical data only. Reported testing: Significant (P<0.0001) difference between fish oil (Arm 1) and olive oil (Arm 2) using repeated measures ANOVA. Fasting blood glucose (mg/dl at month 6) Arm 1 mean=142.90 Arm 2 mean=147.20 Mean difference=4.30 (-2.82, 11.42) Reported testing: Article reports no significant differences (p>0.05) between Arm 1 and Arm 2. HbA1c (% at month 6) Arm 1 mean=6.88 Arm 2 mean=7.05 Mean difference=0.17 (-0.12, 0.46) Reported testing: Article reports no significant differences (p>0.05) between Arm 1 and Arm 2.	Quality: Jadad: 3 Concealment of allocation: NR Applicability: IB Comments: Meta-analysis performed on HgA1c and fasting blood glucose. Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Vandongen, 1988[90]	Sample size: 22 Age (mean/range): 32 / 20-41 Race: NR % male: 100 # sites: 1 Location: Australia	Design: CCT Duration: 9 wk	Inclusion: Hyperlipidemia/Age Exclusion: NR	Covariates: Duration of diabetes/Obesity: BMI=27, kg=72.7, lbs=160/Hypoglycemic treatment	1	Usual diet X 3 wk
					2	Max EPA (fish oil) 15 g/d x 3 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Vandongen, 1988[90]	Total cholesterol (at week 9): Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported. Reported testing: Testing between groups not reported. HDL (at week 9): Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported. Reported testing: Testing between groups not reported. LDL (at week 9): Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported. Reported testing: Testing between groups not reported. Triglycerides (at week 9): Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported. Reported testing: Testing between groups not reported. HgA1c (at week 9): Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported. Reported testing: Testing between groups not reported. Fasting blood glucose (at week 9): Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported. Reported testing: Testing between groups not reported.	Quality: Jadad: 0 Concealment of allocation: NR Applicability: IIB Funding source: government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Vessby, 1990[91]	Sample size: 14 Age (mean/range): NR / 39-72 Race: NR % male: 79 # sites: 1 Location: Sweden	Design: RXT Duration: 16 wk X-over: week 8 Run-in: None Wash-out: None	Inclusion: Diet treatment=1 yr/Controlled diabetes Exclusion: Lipid lowering drug use	Covariates: NR	1	Olive oil 10 g/d x 8 wk
					2	Max EPA (fish oil) 10 g/d x 8 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Vessby, 1990[91]	Total cholesterol (at week 8): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between arms using analysis of variance. LDL(at week 8): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between arms using analysis of variance. HDL(at week 8): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between arms using analysis of variance. Triglycerides(at week 8): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between arms using analysis of variance. HgA1c(at week 8): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: No significant difference between arms using analysis of variance. Fasting blood glucose(at week 8): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-analysis: Not performed; point estimates before cross-over not reported. Reported testing: Significant (p=0.007) difference between fish oil (Arm 1) and olive oil (Arm 2) using analysis of variance.	Quality: Jadad: 3 Concealment of allocation: NR Applicability: IIB Funding source: Government, non-industry, private

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Westerveld, 1993[71]	Sample size: 24 Age (mean/range): 57 / 37-71 Race: NR % male: 63 # sites: 1 Location: Netherlands	Design: RCT Duration: 8 wk	Inclusion: WHO diabetes criteria/Clinically stable/Diet treatment=1 yr Exclusion: Cardiovascular disease/Lipid lowering drug use/No fish or fish supplement/GI disorders/Liver disease/ReNRI disease/Bleeding disorder/Antiplatelet or anticoagulation	Covariates: Duration of diabetes/Hypoglycemic treatment/Hb A1c/Obesity: BMI=27, kg=72.7, lbs=160	1	Olive oil 1656 mg/d x 8 wk
					2	EPA-E 1800 mg/d x 8 wk
					3	EPA-E 900 mg/d x 8 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Westerveld, 1993[71]	Total cholesterol (at week 8): Arm 1= point estimate not reported Arm 2= point estimate not reported Arm 3= point estim ate not reported Meta-analysis: Not performed; point estimates not reported. Reported testing: No significant difference between arms using repeated measures ANOVA. LDL (at week 8): Arm 1= point estimate not reported Arm 2= point estimate not reported Arm 3= point estimate not reported Meta-analysis: Not performed; point estimates not reported. Reported testing: No significant difference between arms using repeated measures ANOVA. HDL(at week 8): Arm 1= point estimate not reported Arm 2= point estimate not reported Arm 3= point estimate not reported Meta-analysis: Not performed; point estimates not reported. Reported testing: No significant difference between arms using repeated measures ANOVA. Triglyceride (at week 8): Arm 1= point estimate not reported Arm 2= point estimate not reported Arm 3= point estimate not reported Meta-analysis: Not performed; point estimates not reported. Reported testing: No significant difference between arms using repeated measures ANOVA. HbA1c (% at month 2) Arm 1 mean=9.30 Arm 2 and Arm 3 (combined) mean=8.00 Mean difference=-1.30 (-3.55, 0.95) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2 and Arm 3. Fasting blood glucose (at week 8): Arm 1= point estimate not reported Arm 2= point estimate not reported Arm 3= point estimate not reported Meta-analysis: Not performed; point estimates not reported. Reported testing: No significant difference between arms using repeated measures ANOVA.	Quality: Jadad: 4 Concealment of allocation: NR Applicability: IB Funding source: Government

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Woodman, 2002[72]	Sample size: 51 Age (mean/range): 61 / NR Race: NR % male: 77 # sites: 1 Location: Australia	Design: RCT Duration: 1.5 mo	Inclusion: Hyperlipidemia/Age/Hb A1c < 9.5% or 10.5%/Controlled diabetes/Nonsmoker/Clinically stable/Fasting blood glucose/Not on insulin treatment Exclusion: NSAIDs use/Liver disease/ReNRI disease/Cardiovascular disease/Not moderate or high fish intake/Microproteinuria/Neuropathy/Smoking	Covariates: Duration of diabetes/Hb A1c/Obesity: BMI=27, kg=72.7, lbs=160/ 0	1	Placebo/control Dosage/duration not collected
					2	EPA 4 g for 6 wk
					3	DHA 4 g for 6 wk

Table C.1. Evidence table of clinical effect of omega-3 fatty acids in type II diabetes or metabolic syndrome (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Woodman, 2002[72]	Total cholesterol (mg/dl at week 6) Arm 1 mean=177.99 Arm 2 and Arm 3 (combined) mean=173.24 Mean difference=-4.75 (-22.48, 12.97) Reported testing: Article reports no significant EPA effect (p>0.05) and DHA effect (p>0.05) without adjusting baseline value by using the Bonferroni method. Triglyceride (mg/dl at week 6) Arm 1 mean=148.67 Arm 2 and Arm 3 (combined) mean=109.15 Mean difference=-39.52 (-68.98, -10.06) Reported testing: Article reports significant EPA effect (p<0.05) and DHA effect (p<0.05) without adjusting baseline value by using the Bonferroni method. HDL (mg/dl at week 6) Arm 1 mean=41.31 Arm 2 and Arm 3 (combined) mean=43.33 Mean difference=2.02 (-4.44, 8.48) Reported testing: Article reports no significant EPA effect (p>0.05) and DHA effect (p>0.05) without adjusting baseline value by using the Bonferroni method. LDL (mg/dl at week 6) Arm 1 mean=106.95 Arm 2 and Arm 3 (combined) mean=107.45 Mean difference=0.50 (-13.80, 14.79) Reported testing: Article reports no significant EPA effect (p>0.05) and DHA effect (p>0.05) without adjusting baseline value by using the Bonferroni method. Fasting blood glucose (mg/dl at week 6) Arm 1 mean=136.04 Arm 2 and Arm 3 (combined) mean=155.85 Mean difference=19.81 (2.25, 37.37) Reported testing: Article reports significant EPA effect (p=0.002) and DHA effect (p=0.002) after adjustment for baseline value by using the Bonferroni method. HbA1c (% at week 6) Arm 1 mean=7.04 Arm 2 and Arm 3 (combined) mean=7.27 Mean difference=0.23 (-0.28, 0.75) Reported testing: Article reports no significant EPA effect (p>0.05) and DHA effect (p>0.05) after adjustment for baseline value by using the Bonferroni method.	Quality: Jadad: 3 Concealment of allocation: NR Applicability: IIB Funding source: Government

Table C.2. Evidence table of clinical effect of omega-3 fatty acids in inflammatory bowel disease.

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Almallah YZ, 1998[44]	Sample size: 18 Age (mean/range): NA / 29-72 Race: NA % male: 50 # sites: NA Location: UK	Design: RCT Duration: 6 mo	Inclusion: Biopsy-proven ulcerative colitis/Distal disease Exclusion: Steroid treatment/Pregnancy/ Immune disorder	Covariates: Sulphasalazine or mesalazine (SASP)/Rectal steroids	1	Sunflower oil 15 ml/d x 6 mo
					2	Fish oil 15 ml/d x 6 mo

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Almallah YZ, 1998[44]	Clinical score (change at month 6): Arm 1= -2 Arm 2 = -5 Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported. Sigmoidoscopic score (change at month 6): Arm 1= -5 Arm 2 = -9 Meta-anlysis: Not done; too few studies to pool. Reported testing: Significant (p = 0.013) effect for fish oil (Arm 2) relative to sunflower oil (Arm 1) using Mann-Whitney U test. Histological score (change at month 6): Arm 1= -2 Arm 2 = -4 Meta-anlysis: Not done; too few studies to pool. Reported testing: Significant (p = 0.016) effect for fish oil (Arm 2) relative to sunflower oil (Arm 1) using Mann-Whitney U test. Induced remission(rate at month 6): Arm 1= point estimate not reported Arm 2 = 100% Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported. Relapse: NA Immunosupressive requirement (# of patients at month 6, prednisolone enemata/oral corticosteroids): Arm 1 = 4/3 Arm 2 = 2/0 Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported.	Quality: Jadad: 2 Concealment of allocation: Yes Applicability: IB Funding source: Hospital

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Aslan A, 1992[46]	Sample size: 11 Age (mean/range): 63 / 31-74 Race: NR % male: 100 # sites: 1 Location: US	Design: RXT Duration: 3 mo X-over: month 3 Run-in: None Wash-out: 2 mo	Inclusion: Mild to moderate IBD with min 10 cm/Biopsy-proven ulcerative colitis Exclusion: NR	Covariates: Sulphasalazine or mesalazine (SASP)/Rectal steroids	1 2	Oleic, palmitic, and linoleic acids 15 cap/d x 3 mo Max EPA (fish oil) 15 cap/d x 3 mo

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Aslan A, 1992[46]	Clinical score (change at month 3): Arm 1= point estimate before cross-over not reported Arm 2 = point estimate before cross-over not reported Meta-anlysis: Not done; too few studies to pool. Reported testing: Significant ($p < 0.05$) effect for fish oil (Arm 2) relative to oleic, palmitic, and linoleic acids (Arm 1) using paired univariate Student's t test. Sigmoidoscopic score: NA Histological score (change at month 3): Arm 1= point estimate before cross-over not reported Arm 2 = point estimate before cross-over not reported Meta-anlysis: Not done; too few studies to pool. Reported testing: No significant difference between groups using paired univariate Student's t test. Induced remission: NA Relapse: NA Immunosupressive requirement: NA	Quality: Jadad: 5 Concealment of allocation: NR Applicability: IIIB Funding source: NR

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Belluzzi A, 1996[54]	Sample size: 78 Age (mean/range): NA / 18-67 Race: NA % male: 50 # sites: NA Location: Italy	Design: RCT Duration: 12 mo	Inclusion: Remission of Crohn's disease/Elevated serum markers of inflammation Exclusion: Steroid treatment/Previous cytotoxic or immunosuppressive drug treatment/Pregnancy/lactating/Age between 18 and 75 years old/ Previous bowel resection of more than 1 m/ Previous sulphasalazine or mesalazine treatment	Covariates: Previous surgery	1 2	Miglyol 812 15 g/d x 12 mo Fish oil, enteric coated 15 g/d x 12 mo

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Belluzzi A, 1996[54]	Clinical score: NA Sigmoidoscopic score: NA Histological score: NA Induced remission: NA Relapse (# of relapse at month 12) Arm 1 =27 Arm 2 =11 risk ratio=0.41 (0.24, 0.70) Reported testing: Article reports significant difference (p<0.001) between Arm 1 and Arm 2. Immunosupressive requirement: NA	Quality: Jadad: 5 Concealment of allocation: NA Applicability: IB Funding source: Industry

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Greenfield SM, 1993[42]	Sample size: 43 Age (mean/range): 54 / NA Race: NA % male: 70 # sites: NA Location: UK	Design: RCT Duration: 9 mo	Inclusion: Ulcerative colitis, Disease > 1 year/Clinically stable/Prednisone or prednisolone treatment < 10 mg/day Exclusion: NA	Covariates: Sulphasalazine or mesalazine treatment (SASP)/Rectal steroids	1 2 3	Olive oil Variable dose x 6 mo Max EPA (fish oil) Variable dose x 6 mo Super evening primrose oil (Borage and evening primrose oils) Variable dose x 6 mo

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Greenfield SM, 1993[42]	Clinical score: NA Sigmoidoscopic score (change at month 9): Arm 1= point estimate not reported Arm 2 = point estimate not reported Arm 3 = point estimate not reported Meta-anlysis: Not done; too few studies to pool. Reported testing: No significant difference between groups using Mann-Whitney U test. Histological score(change at month 9): Arm 1= point estimate not reported Arm 2 = point estimate not reported Arm 3 = point estimate not reported Meta-anlysis: Not done; too few studies to pool. Reported testing: No significant difference between groups using Mann-Whitney U test Induced remission: NA Relapse(rate at month 9): Arm 1= point estimate not reported Arm 2 = point estimate not reported Arm 3 = point estimate not reported Meta-anlysis: This study was excluded from the meta-analysis of relapse because data was not reported separately by arm/group. The data was reported as number of patients in remission at entry. Reported testing: No significant difference between groups using Mann-Whitney U test Immunosuppressive requirement: NA	Quality: Jadad: 2 Concealment of allocation: NA Applicability: IB Funding source: NR

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Hawthorne A, 1992[95]	Sample size: 96 Age (mean/range): 47 / 17-77 Race: NA % male: 55 # sites: 2 Location: UK	Design: RCT Duration: 14 mo	Inclusion: Biopsy-proven ulcerative colitis/ two or more relapses in the previous 3 years Exclusion: Prednisolone > 20 mg/Likely to require surgery or deteriorating	Covariates: Sulphasalazine or mesalazine treatment (SASP)	1	Olive oil 20 ml/d x 12 mo
					2	Hi EPA (Fish oil) 20 ml/d x 12 mo

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Hawthorne A, 1992[95]	Clinical score: NA Sigmoidoscopic score: NA Histological score: NA Induced remission (rate at month 12): Arm 1= 63% Arm 2 = 54% Meta-anlysis: Not done; too few studies to pool. Reported testing: No significant effect (p = 0.44) for fish oil (Arm 2) relative to olive oil (Arm 1) using log rank analysis and Kaplan Meier method. [I think it's just Kaplan Meier] Relapse(rate at month 12): Arm 1= 48% Arm 2 = 42% Meta-anlysis: This study was excluded from the meta-analysis of relapse because the population was the same as another study that was included in the MA.[41] Reported testing: No significant effect (p = 0.54) for fish oil (Arm 2) relative to olive oil (Arm 1) using log rank analysis and Kaplan Meier method. I think it's just Kaplan Meier] Immunosuppressive requirement: (median prednisolone dose, mg at month 1, month 2) Arm 1: 6/5 Arm 2: 1/0 Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported.	Quality: Jadad: 3 Concealment of allocation: Yes Applicability: IIIB Funding source: Industry and Private, non-industry

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Hawthorne A[41]	Sample size: 96 Age (mean/range): 47 / 17-77 Race: NA % male: 55 # sites: 2 Location: UK	Design: RCT Duration: 12 mo	Inclusion: Biopsy-proven ulcerative colitis / two or more relapses in the previous 3 years Exclusion: Prednisolone > 20 mg/Likely to require surgery or deteriorating	Covariates: Sulphasalazine or mesalazine treatment (SASP)	1	Olive oil 20 ml/d x 12 mo
					2	Hi EPA (Fish oil) 20 ml/d x 12 mo

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Hawthorne A[41]	Clinical score: NA Sigmoidoscopic score: NA Histological score: NA Induced remission(rate at month 12): Arm 1: 70% Arm 2: 61% Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported. Relapse (# of relapse at month 12) Arm 1 =11 Arm 2 =15 risk ratio=1.32 (0.71, 2.46) Reported testing: Article reports no significant difference between Arm 1 and Arm 2 by survival analysis. Immunosuppressive requirement: NA	Quality: Jadad: 3 Concealment of allocation: Yes Applicability: IIIB Funding source: Industry and Private, non-industry

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Loeschke K, 1996[39]	Sample size: 64 Age (mean/range): 40 / NA Race: NA % male: 52 # sites: 2 Location: Germany	Design: RCT Duration: 24 mo	Inclusion: Biopsy-proven ulcerative colitis/ At least 1 relapse in the last 2 years/Gomes clinical score (IBD) below 8 Exclusion: Steroid treatment/Pregnancy/Cytotoxic or immunosuppressive drug treatment/Questionable adherence	Covariates: 5-ASA/Sulphasalazine or mesalazine treatment (SASP)	1 2	Corn oil 6 ml/d x 24 mo Fish oil 5 g/d x 24 mo

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Loeschke K, 1996[39]	Clinical score(change from graph data at month 24): Arm 1: +0.7 Arm 2: + 0.2 Meta-anlysis: Not done; too few studies to pool. Reported testing: No significant difference between groups using two-way analysis of variance. Sigmoidoscopic score: NA Histological score (at month 24): Arm 1= point estimate not reported Arm 2= point estimate not reported Meta-anlysis: Not done; too few studies to pool. Reported testing: No significant difference between groups using Mann-Whiney U test. Induced remission: NA Relapse (# of relapse at month 24) Arm 1 =18 Arm 2 =18 risk ratio=1.06 (0.69, 1.64) Reported testing: Article reports no significant difference between Arm 1 and Arm 2 by chi-square test. Immunosuppressive requirement: NA	Quality: Jadad: 5 Concealment of allocation: NA Applicability: IB Funding source: Industry

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Lorenz R, 1989[52]	Sample size: 39 Age (mean/range): 37 / 21-71 Race: NA % male: 41 # sites: 1 Location: Germany	Design: RXT Duration: 7 mo X-over: month 3 Run-in: None Wash-out: 1 mo	Inclusion: Biopsy-proven Crohn's disease or ulcerative colitis Exclusion: Pregnancy/Pending surgery, abscesses or severe bleeding/Questionable adherence/Prednisone>8 mg/day/Inactive disease	Covariates: Sulphasalazine or mesalazine treatment (SASP)/Flagyl	1 2	Olive oil 11 ml/d x 3 mo Max EPA (fish oil) 11 ml/d x 3 mo
Lorenz-Meyer H, 1996[55]	Sample size: 204 Age (mean/range): 31 / 17-65 Race: NA % male: 33 # sites: 23 Location: Germany	Design: RCT Duration: 12 mo	Inclusion: Biopsy-proven Crohn's disease/Active disease/Steroid treatment Exclusion: Questionable adherence/Pregnancy/Cytotoxic or immunosuppressive drug treatment/NSAID treatment/Sulphasalazine or mesalazine treatment/Total parenteral nutrition (TPN)/Short bowel syndrome/Steatorrhea	Covariates: Fistula	1 2 3	Corn oil 6 g/d x 12 mo Low-carbohydate diet Dosage NA x 12 mo Fish oil 6 g/d x 12 mo

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Lorenz R, 1989[52]	Clinical score(change from graph data at month 3): Arm 1= -12 Crohn's Disease Activity Index -2 Ulcerative Colitis Activity Index Arm 2 = -3 Crohn's Disease Activity Index -2 Ulcerative Colitis Activity Index Meta-anlysis: Not done; too few studies to pool. Reported testing: No significant difference between groups using… Sigmoidoscopic score (change at month 3): Arm 1= point estimate before cross-over not reported Arm 2 = point estimate before cross-over not reported Meta-anlysis: Not done; too few studies to pool. Reported testing: Significant ($p < 0.05$) effect for fish oil (Arm 2) relative to olive oil (Arm 1) using… Histological score: NA Induced remission: NA Relapse: NA Immunosuppressive requirement: NA	Quality: Jadad: 5 Concealment of allocation: Yes Applicability: IB Funding source: Unclear
Lorenz-Meyer H, 1996[55]	Clinical score: NA Sigmoidoscopic score: NA Histological score: NA Induced remission: NA Relapse (# of relapse at month 12) Arm 1 =36 Arm 3 =40 risk ratio=1.03 (0.77, 1.39) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 3. Immunosuppressive requirement: NA	Quality: Jadad: 3 Concealment of allocation: NA Applicability: IB Funding source: NA

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Mantzaris GJ, 1996[40]	Sample size: 50 Age (mean/range): 36 / 17-65 Race: NA % male: 48 # sites: NA Location: Greece	Design: RCT Duration: 12 mo	Inclusion: Remission of biopsy-proven ulcerative colitis/Mesalazine treatment Exclusion: NA	Covariates: Sulphasalazine or mesalazine treatment (SASP)	1 2	Olive oil 20 ml/d x 12 mo Max EPA (fish oil) 20 ml/d x 12 mo

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Mantzaris GJ, 1996[40]	Clinical score: NA Sigmoidoscopic score: NA Histological score: NA Induced remission: NA Relapse (# of relapse at month 12) Arm 1 =5 Arm 2 =6 risk ratio=0.98 (0.36, 2.70) Reported testing: Article reports no significant difference (p>0.1) between Arm 1 and Arm 2 by chi-square test. Immunosuppressive requirement: NA	Quality: Jadad: 2 Concealment of allocation: NA Applicability: IB Comments: This study is included in the meta-analysis of relapse. Funding source: NA

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Middleton SJ, 2002[43]	Sample size: 63 Age (mean/range): 42 / 18-66 Race: NA % male: 50 # sites: 1 Location: UK	Design: RCT Duration: 12 mo	Inclusion: Age between 18 and 70 years old/Biopsy-proven ulcerative colitis in remission Exclusion: Serious liver disease/Malignant disease/Pregnancy/lactating/ Antiplatelet or anticoagulating treatment/Epilepsy/Lithium or phenothiazine/Serious renal disease	Covariates: Smoking/Sulphasalazine or mesalazine treatment (SASP)/5-ASA	1 2	Sunflower oil 6 cap/d x 12 mo GLA+ EPA+DHA 6 cap/d x 12 mo

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Middleton SJ, 2002[43]	Clinical score: NA Sigmoidoscopic score (at month 12): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-anlysis: Not done; too few studies to pool. Reported testing: No significant difference between groups using proportional Cox hazard regression. Histological score: NA Induced remission: NA Relapse (rate at month 12, extrapolated from graph): Arm 1= 38% Arm 2 = 55% Meta-anlysis: Not included in MA; point estimates not reported. Reported testing: No significant difference between groups using proportional Cox hazard regression. Immunosuppressive requirement: NA	Quality: Jadad: 3 Concealment of allocation: NR Applicability: IB Funding source: NR

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Stenson WF, 1992[53]	Sample size: 24 Age (mean/range): 42 / 25-62 Race: NA % male: 56 # sites: 4 Location: US	Design: RXT Duration: 9 mo X-over: month 4 Run-in: None Wash-out: 1 mo	Inclusion: Ulcerative colitis Active disease Exclusion: NA	Covariates: Rectal steroids/Sulphasalazine or mesalazine treatment (SASP)	1 2	Vegetable oil 18 cap/d x 4 mo Max EPA (fish oil) 18 cap/d x 4 mo

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Stenson WF, 1992[53]	Clinical score (change at month 4): Arm 1= point estimate before cross-over not reported Arm 2 = point estimate before cross-over not reported Meta-anlysis: Not done; too few studies to pool. Reported testing: Significant (P < 0.14) effect for fish oil (Arm 2) relative to vegetable oil (Arm 1) using rank-sign test. Sigmoidoscopic score (change at month 4): Arm 1= point estimate before cross-over not reported Arm 2 = point estimate before cross-over not reported Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported. Histological score(change at month 4): Arm 1= point estimate before cross-over not reported Arm 2 = point estimate before cross-over not reported Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported. Induced remission: NA Relapse: NA Immunosuppressive requirement (mean prednisolone dose 8 in mg at month 4) Arm 1: 12.9 Arm 2: 6.1 Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported.	Quality: Jadad: 2 Concealment of allocation: NA Applicability: NA Funding source: Government and Private, non-industry

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Varghese TJ, 2000[94]	Sample size: 51 Age (mean/range): NA / NA Race: NA % male: 99 # sites: NA Location: UK	Design: RCT Duration: 6 mo	Inclusion: Ulcerative colitis and extensive disease Exclusion: Cytotoxic or immunosuppressive drug treatment	Covariates: NA	1 2	Sunflower oil Dosage NA x 12 mo Omega-3 EFAs 6 mg/d x 6 mo

Table C.2. Evidence table of clinical effect and association of omega-3 fatty acids with inflammatory bowel disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Varghese TJ, 2000[94]	Clinical score (change at month 6): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-anlysis: Not done; too few studies to pool. Reported testing: Significant (p = 0.001) effect for Omega-3 EFAs (Arm 2) relative to sunflower oil (Arm 1). Sigmoidoscopic score (change at month 6): Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-anlysis: Not done; too few studies to pool. Reported testing: Significant (p = 0.054) effect for Omega-3 EFAs (Arm 2) relative to sunflower oil (Arm 1). Histological score: NA Induced remission: NA Relapse: NA Immunosuppressive requirement: NA	Quality: Jadad: 2 Concealment of allocation: NA Applicability: NA Funding source: NA

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Adam O, 2003[26]	Sample size: NA Age (mean/range): 57 / NA Race: NA % male: 7 # sites: NA Location: Germany	Design: RXT Duration: 8 mo X-over: month 5 Run-in: None Wash-out: 2 mo	Inclusion: >= 6 tender joints/>= 3 swollen joints/ AND one or both : morning stiffness >= 30 min/ elevated ESR or CRP Exclusion: Prednisone > 10 mg/d/GI disorders/Alcohol use/Metabolic disease/Known allergies	Covariates: Diet	1	Western diet Corn oil capsules 1g/10 kg body weight/day X 3 mo
					2	Placebo/control Modified lacto- vegetarian diet Corn oil capsules 1g/10 kg body weight/day X 3 mo
					3	Western diet Menhaden oil 1g/10 kg body weight/day X 3 mo
					4	Modified lacto-vegetarian diet Menhaden oil 1g/10 kg body weight/day X 3 mo

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability) Funding Source
Adam O, 2003[26]	Pain (cm on VAS at month 3) Arms 1, 2, 3, 4 = point estimate not reported Meta-analysis: Not included, point estimates not reported. Reported testing: Testing between placebo (arms 1 and 2) and fish oil (arms 3 and 4) not reported. Swollen joints (number at month 3): Arms 1, 2, 3, 4 = point estimate not reported Meta-analysis: Not included, point estimates not reported. Reported testing: Testing between placebo (arms 1 and 2) and fish oil (arms 3 and 4) not reported. Acute phase reactant: NA Patient global assessment (at month 3): Arms 1, 2, 3, 4 = point estimate not reported Meta-analysis: Not included, point estimates not reported. Reported testing: Testing between placebo (arms 1 and 2) and fish oil (arms 3 and 4) not reported. Radiographic damage: NA NSAID consumption (at month 3): Arms 1, 2, 3, 4 = point estimate not reported Meta-analysis: Not performed, too few studies to pool. Reported testing: Testing between placebo (arms 1 and 2) and fish oil (arms 3 and 4) not reported. Steroid consumption (at month 3): Arms 1, 2, 3, 4 = point estimate not reported Meta-analysis: : Not performed, too few studies to pool. Reported testing: Testing between placebo (arms 1 and 2) and fish oil (arms 3 and 4) not reported. DMARD consumption: NA	Quality: Jadad: 3 Concealment of allocation: NR Applicability: IIB Funding source: Government

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Alpigiani M, 1996[27]	Sample size: 32 Age (mean/range): 14 / NA Race: NA % male: 44 # sites: 1 Location: Italy	Design: Duration: 6 mo	Inclusion: Juvenile chronic arthritis/Age 4-13 Exclusion: NA	Covariates: NA	1	Diet
					2	Cod-liver oil (Eskisol) 5 g/d x 6 mo

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	
Alpigiani M, 1996[27]	Pain: NA Swollen joints: NA Acute phase reactant: (change at month 6, CRP, mg%): Arm 1: -0.05 Arm 2: -0.28 Meta-analysis: Not included; point estimates not reported. Reported testing: Significant (p=.009) difference between arms by ANOVA. Patient global assessment: NA Radiographic damage: NA NSAID consumption: NA Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 1 Concealment of allocation: NR Applicability: IIB Funding source: NA

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Belch JF, 1988[28]	Sample size: 49 Age (mean/range): 49 / 28-74 Race: NA % male: 12 # sites: NA Location: UK	Design: RCT Duration: 15 mo	Inclusion: NSAIDs use/No DMARDs Exclusion: NA	Covariates: Evening primrose oil	1	Placebo: Liquid paraffin capsules 12/d x 12 months
					2	Fish oil (240 mg EPA) plus evening primrose oil (540 mg GLA) daily x 12 mo
					3	Evening primrose oil (540 mg GLA) daily x 12 mo

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Belch JF, 1988[28]	Pain (cm on VAS at month 12) Arms 1, 2, 3 = point estimate not reported Meta-analysis: Not included, point estimates not reported. Reported testing: No difference between groups using Mann-Whitney U test. Swollen joints (number at month 3): Arms 1, 2, 3 = point estimate not reported Meta-analysis: Not included, point estimates not reported. Reported testing: No difference between groups using Mann-Whitney U test. Acute phase reactant: (CRP and ESR at month 12) Arms 1, 2, 3 = point estimate not reported Meta-analysis: Not included, point estimates not reported. Reported testing: No difference in CRP or ESR between groups using Mann-Whitney U test. Patient global assessment: NA Radiographic damage: NA NSAID consumption (at month 15): Arm 1: Reduced in 33% of subjects Arm 2: Reduced in 80% of subjects Arm 3: Reduced in 73% of subjects Meta-analysis: Not performed, too few studies to pool. Reported testing: Testing between groups not reported. Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 4 Concealment of allocation: NR Applicability: IIB Comments: Meta-analysis not performed because of insufficient statistics; study only reported data in graph. Funding source: Private, non-industry

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Cleland LG, 1988[16]	Sample size: 60 Age (mean/range): 51 / 22-74 Race: NA % male: 30 # sites: NA Location: Australia	Design: RCT Duration: 3 mo	Inclusion: NA Exclusion: NA	Covariates: NSAIDs/DMARDs	1	Olive oil 18 g/d x 3 mo
					2	Max EPA (fish oil) 18 g/d x 3 mo

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Cleland LG, 1988[16]	Pain (Analogue pain scale at month 3) Arm 1 =7.1 Arm 2 =7 effect size=-0.02(-0.60, 0.56) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Swollen joints (# of swollen joint at month 3) Arm 1 =3.5 Arm 2 =3.6 effect size=0.04(-0.54, 0.62) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Acute phase reactant: (ESR at month 12) Arms 1, 2 = point estimate not reported Meta-analysis: Not included, point estimates not reported. Reported testing: No significant change within group by Student's t test; testing between groups not reported. Patient global assessment: (at month 12) Arms 1, 2 = point estimate not reported Meta-analysis: Not included, point estimates not reported. Reported testing: No significant change within group; testing between groups not reported. Radiographic damage: NA NSAID consumption NA Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 3 Concealment of allocation: NR Applicability: IB Funding source: Government; Private, non-industry; Hospital

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Geusens P, 1994[17]	Sample size: 90 Age (mean/range): 57 / NA Race: NA % male: 22 # sites: NA Location: Belgium	Design: RCT Duration: 12 mo	Inclusion: Active disease Exclusion: NA	Covariates: NSAIDs/DMARDs	1	Olive oil capsules 6 g/d x 12 mo
					2	Fish oil 3 g x 12 mo plus olive oil 3 g/d x 12 mo
					3	Fish oil 6 g/d x 12 mo

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability) Funding Source
Geusens P, 1994[17]	Pain (0-4 scale at month 3) Arm 1 =1.97 Arm 2 and Arm 3 (combined) =1.89 effect size=-0.04(-0.57, 0.50) Reported testing: Article reports no significant differences (p>0.05) of the changes between Arm 2 or Arm 3 and Arm 1. Swollen joint:s NA Acute phase reactant: NA Radiographic damage:NA NSAID consumption: consumption of NSAIDs and DMARDs combined reported, see below. Steroid consumption: NA DMARD consumption: consumption of NSAIDs and DMARDs combined reported, see below. Patient global assessment (0-10cm visual analog scale at month 3) Arm 1 =5.68 Arm 2 and Arm 3 (combined) =4.53 effect size=-1.38(-1.97, -0.79) Reported testing: Article reports significant differences (p<0.01) of the changes between Arm 3 and Arm1 by Mann-Whitney test. NSAID and/or DMARD consumption: (% with dose reduction at month 12) Arm 1 = 15 Arm 2 = 29 Arm 3 = 47 Meta-analysis: Not done, too few studies to pool. Reported testing: Significant (p<.05) difference between arms 3 (high dose fish oil) and arm 1 (placebo) using chi-square test.	Quality: Jadad: 3 Concealment of allocation: NR Applicability: IB Funding source: ND

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Hansen G, 1996[29]	Sample size: 109 Age (mean/range): 57 / NA Race: NA % male: 26 # sites: NA Location: Denmark	Design: RCT Duration: 6.0 mo	Inclusion: Increased morning stiffness/Increased sed rate/>= 3 swollen joints Exclusion: Underweight/Severe disorders	Covariates: NSAIDs	1	Normal diet
					2	Fish 114 g for 6 mo

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability) Funding Source
Hansen G, 1996[29]	Pain: (change on VAS at month 6) Arm 1 = 0.2 Arm 2 = -0.2 Meta-analysis: Not included, point estimates not reported. Reported testing: Significant (p=0.01) difference between arms using Wilcoxons unpaired rank test. Swollen joints: (change on 1-3 scale at month 6) Arm 1 = -1 Arm 2 = -3 Meta-analysis: Not included, point estimates not reported. Reported testing: Significant (p=0.01) difference between arms using Wilcoxons unpaired rank test. Acute phase reactant: (change, ESR, mm/hr at month 6) Arm 1 = 0 Arm 2 = 1 Meta-analysis: Not included, point estimates not reported. Reported testing: No significant difference between arms using Wilcoxons unpaired rank test. Patient global assessment: NA Radiographic damage: (Change, Larsen score at month 6) Arm 1 = 4 Arm 2 = 3 Meta-analysis: Not included, point estimates not reported. Reported testing: No significant difference between arms using Wilcoxons unpaired rank test. NSAID consumption: Arm 1 = point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not performed, too few studies to pool. Reported testing: Testing between groups not reported. Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 1 Concealment of allocation: NR Applicability: IB Funding source: ND

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Kjeldsen-Kragh J, 1992[30]	Sample size: 79 Age (mean/range): 57 / 23-73 Race: NA % male: 24 # sites: 7 Location: Russia	Design: RCT Duration: 4.0 mo	Inclusion: >= 6 tender joints/>= 3 swollen joints/Increased sed rate/Increased morning stiffness/Prednisone or prednisolone = 10 mg/Functional class/Stable medication Exclusion: NA	Covariates: Naproxen	1	Corn oil 7g/d X 16 weeks Naproxen 750 mg/d x 10 weeks then reduction to 0 mg/d by week 13 continued through week 16.
					2	K-85 (fish oil) 750 mg for 16 wk Naproxen 750 mg/d X 16 weeks
					3	K-85 (fish oil) 750 mg for 16 wk Naproxen 750 mg/d x 10 weeks then reduction to 0mg/d by week 13 continued through week 16.

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Kjeldsen-Kragh J, 1992[30]	Pain: (VAS at week 16) Arms 1, 2, 3: point estimates not reported. Meta-analysis: Not included, point estimates not reported. Reported testing: Testing between groups not reported. Swollen joints: (number at month 16) Arms 1, 2, 3: point estimates not reported. Meta-analysis: Not included, point estimates not reported. Reported testing: Testing between groups not reported. Acute phase reactant: NA Patient global assessment: (at week 16) Arms 1, 2, 3: point estimates not reported. Meta-analysis: Not included, point estimates not reported. Reported testing: Testing between groups not reported. Radiographic damage: NA NSAID consumption: NA Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 3 Concealment of allocation: NR Applicability: IB Funding source: Private, non-industry

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Kremer J, 1990[19]	Sample size: 64 Age (mean/range): 58 / 22-81 Race: NA % male: 33 # sites: 1 Location: US	Design: RCT Duration: 9 mo	Inclusion: >= 6 tender joints/Increased sed rate/Increased morning stiffness/Stable medication/>= 3 swollen joints Exclusion: NA	Covariates: NSAIDs/DMARDs	1	Olive oil capsules 9/d X 24 weeks
					2	Fish oil capsules X 24 weeks (27 mg/kg/d EPA, 18 mg/kg/d DHA)
					3	Fish oilcapsules X 24 weeks (54 mg/kg/d EPA, 36 mg/kg/d DHA)

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Kremer J, 1990[19]	Pain (0-4 five point scale at week 12) Arm 1 =1.60 Arm 2 and Arm3 (combined) =1.51 effect size=-0.04(-0.69, 0.61) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2 and Arm 3. Swollen joints (# of swollen joint at week 12) Arm 1 =13.50 Arm 2 and Arm3 (combined) =10.96 effect size=-0.63(-1.30, 0.03) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2 and Arm 3. Acute phase reactant: (ESR at week 24 and at week 36) Arms 1,2,3 = point estimates not reported. Meta-analysis: Not included, point estimates not reported. Reported testing: No significant difference in any arm using Student's t-test; testing between groups not reported. Patient global assessment (0-4 five point scale at week 12) Arm 1 =1.8 Arm 2 and Arm3 (combined) =1.69 effect size=-0.13(-0.78, 0.52) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2 and Arm 3. Radiographic damage: NA NSAID consumption: NA Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 2 Concealment of allocation: NR Applicability: IB Funding source: NA

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Kremer J, 1995[31]	Sample size: 66 Age (mean/range): 58 / NA Race: NA % male: 45 # sites: 3 Location: US	Design: RCT Duration: 6.5 mo	Inclusion: >= 6 tender joints/>= 3 swollen joints/Increased morning stiffness/Increased sed rate Exclusion: NA	Covariates: DMARDs/NSAIDs	1	Corn oil, 9 capsules/d X 26 or 30 wk. Diclofenac, 75 mg BID X first 18 or 22 wk
					2	Menhaden oil (130 mg/kg/d of omega-3) X 26 or 30 wk, then corn oil until week 48. Diclofenac, 75 mg BID X first 18 or 22 wk

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Kremer J, 1995[31]	Pain: (0-4 scale, mean change at week 18 or 22) Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included because point estimates not reported. Reported testing: Not reported for this outcome. Tender joints: (number, change at week 18 or 22) Arm 1= point estimate not reported Arm 2 = -5.3 Meta-analysis: Not included because point estimate not reported for control group. Reported testing: Testing between groups not reported. Swollen joints: (number at week 18 or 22) Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included because point estimates not reported. Reported testing: Not reported for this outcome. Acute phase reactant: NA Patient global assessment: (mean change at week 18 or 22) Arm 1= point estimate not reported Arm 2 = -0.38 Meta-analysis: Not included because point estimate not reported for control group. Reported testing: Testing between groups not reported. Radiographic damage: NA NSAID consumption: Defined in study protocol Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 2 Concealment of allocation: NR Applicability: IB Funding source: NR

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Kremer J, 1985[18]	Sample size: 52 Age (mean/range): 56 / NA Race: NA % male: 32 # sites: NA Location: US	Design: RCT Duration: 3 mo	Inclusion: Increased sed rate/>= 6 tender joints/>= 3 swollen joints/Increased morning stiffness Exclusion: Reliable adherence	Covariates: NSAIDs/DMARDs	1	Parafin placebo capsules 10/day X 12 weeks Diet with polyunsaturated fat: saturated fat ratio=1:4.
					2	Max EPA (fish oil) capsules 10/d X 12 wk Diet with polyunsaturated fat: saturated fat ratio=1.4:1.

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Kremer J, 1985[18]	Pain (1-5 five point scale at week 12) Arm 1 =2.8 Arm 2 =2.5 effect size=-0.13(-0.78, 0.51) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Swollen joints (# of swollen joint at week 12) Arm 1 =13.5 Arm 2 =13.4 effect size=-0.02(-0.66, 0.63) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Acute phase reactant Arm 1 =34.9 Arm 2 =24.2 effect size=-0.44(-1.10, 0.21) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Patient global assessment (1-5 five point scale at week 12) Arm 1 =2.9 Arm 2 =2.7 effect size=-0.24(-0.89, 0.41) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Radiographic damage: NA NSAID consumption: NA Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 4 Concealment of allocation: NR Applicability: IB Funding source: NA

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Lau CS, 1995[38]	Sample size: 45 Age (mean/range): NA / 27-69 Race: NA % male: 29 # sites: 1 Location: UK	Design: RCT Duration: 6 mo	Inclusion: NSAIDs use/Clinically stable/No DMARDs Exclusion: NA	Covariates: NSAIDs	1	Air-filled placebo capsules 10/day X 6 mo
					2	Max EPA (fish oil) 10/day X 6 mo

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability) Funding Source
Lau CS, 1995[38]	Pain: (at month 6) Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported. Reported testing: No statistically significant change within or between groups by ANOVA. Swollen joints: (at month 6) Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported. Reported testing: No statistically significant change within or between groups by ANOVA. Acute phase reactant: (ESR at month 6) Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported. Reported testing: No statistically significant change within or between groups by ANOVA. Patient global assessment: NA Radiographic damage: NA NSAID consumption: NA Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 2 Concealment of allocation: NR Applicability: IB Funding source: ND

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Lau CS, 1993[32]	Sample size: 64 Age (mean/range): 51 / 26-73 Race: NA % male: 30 # sites: 1 Location: Scotland	Design: RCT Duration: 15 mo	Inclusion: NSAIDs use/Clinically stable/No DMARDs Exclusion: NA	Covariates: NSAIDs	1	Air-filled placebo capsules 10/day X 12 mo
					2	Max EPA (fish oil) capsules 10/day X 12 mo

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability) Funding Source
Lau CS, 1993[32]	Pain: (VAS at month 6) Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported. Reported testing: No statistically significant change between groups by Wilcoxon rank sum test. Swollen joints: NA Acute phase reactant: (ESR at month 6) Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not included; point estimates not reported. Reported testing: No statistically significant change within or between groups by ANOVA. Patient global assessment: NA Radiographic damage: NA NSAID consumption: (% requiring at month 15) Arm 1 = 86 Arm 2 = 45 Meta-analysis: Not performed, too few studies to pool. Reported testing: No statistically significant change within or between groups by ANOVA. Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 3 Concealment of allocation: NR Applicability: IIB Funding source: Industry

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Magaro M, 1988[21]	Sample size: 20 Age (mean/range): NA / 25-45 Race: NA % male: NA # sites: NA Location: Italy	Design: RCT Duration: 1.5 mo	Inclusion: Increased sed rate/>= 6 tender joints/>= 3 swollen joints/Increased morning stiffness/NSAIDs use/No DMARDs Exclusion: Diabetes/Obesity	Covariates: NSAIDs	1	Usual diet
					2	Max EPA (fish oil) 9 g/d x 45 days Usual diet

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Magaro M, 1988[21]	Patient assess pain (cm at day 45) Arm 1 =4.20 Arm 2 =4.80 effect size=0.41 (-0.48, 1.29) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Swollen joints: NA Acute phase reactant (mm/1st hour at day 45) Arm 1 =66.00 Arm 2 =59.50 effect size=-0.16 (-1.04, 0.72) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Patient global assessment: NA Radiographic damage: NA NSAID consumption: NA Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 1 Concealment of allocation: NR Applicability: IIB Funding source: ND

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Magalish T, 2002[20]	Sample size: 112 Age (mean/range): NA / 17-77 Race: NA % male: 26 # sites: 2 Location: Russia	Design: CCT Duration: 10 d	Inclusion: Age Exclusion: NA	Covariates: Duration of diabetes	1	Phonopheresis with hydrocortisone cream q/d X 10 d
					2	Phonopheresis with omega-3 fatty acids q/d 10 d

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Magalish T, 2002[20]	Pain: (unspecified measure at day 10) Arm 1 = 0.7 Arm 2 = 0.6 Meta-analysis: Not included; measure not defined. Reported testing: Testing between groups not reported. Swollen joints (# of swollen joint at month 0.3) Arm 1 =0.7 Arm 2 =0.6 effect size=-0.02(-0.66, 0.63) Reported testing: Unable to translate. Acute phase reactant: NA Patient global assessment: NA Radiographic damage: NA NSAID consumption: NA Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 0 Concealment of allocation: NR Applicability: IIB Funding source: NR

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Nielsen G, 1992[22]	Sample size: 57 Age (mean/range): NA / 33-78 Race: NA % male: NA # sites: 3 Location: Denmark	Design: RCT Duration: 3.0 mo	Inclusion: Increased sed rate/>= 6 tender joints/>= 3 swollen joints/Increased morning stiffness Exclusion: No current change in meds	Covariates: NSAIDs/DMARDs	1	Control capsules (n-6 fatty acids) 6/day X 12 weeks
					2	Pikasol (fish oil) capsules 6/d X 12 weeks

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Nielsen G, 1992[22]	Pain (Visual pain score at week 12) Arm 1 =136 Arm 2 =104 effect size=-0.85 (-1.42, -0.27) Reported testing: Article reports significant differences (p=0.002) between Arm 1 and Arm 2. Swollen joints (0-2 three point index scale at wee 12) Arm 1 =8 Arm 2 =8 effect size=0.00 (-0.55, 0.55) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Acute phase reactant (mm/hour at week 12) Arm 1 =33 Arm 2 =34 effect size=0.06 (-0.49, 0.61) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Patient global assessment: NA Radiographic damage: NA NSAID consumption: (at week 12) Arms 1, 2 = point estimate not reported Meta-analysis: Not performed, too few studies to pool. Reported testing: No difference within group, testing between groups not reported. Steroid consumption: (at week 12) Arms 1, 2 = point estimate not reported Meta-analysis: Not performed, too few studies to pool. Reported testing: No difference within group, testing between groups not reported. DMARD consumption(at week 12) Arms 1, 2 = point estimate not reported Meta-analysis: Not performed, too few studies to pool. Reported testing: No difference within group, testing between groups not reported.	Quality: Jadad: 4 Concealment of allocation: NR Applicability: NR Comments: Meta-analysis performed on patient assessment of pain, acute phase reactant, and swollen joints. Funding source: Private, non-industry

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Nordstrom D, 1995[23]	Sample size: 22 Age (mean/range): 52 / 34-72 Race: NA % male: NA # sites: 1 Location: Finland	Design: RCT Duration: 3 mo	Inclusion: NA Exclusion: NA	Covariates: NSAIDs/DMARDs	1	Safflower oil 30 g/day X 3 mo
					2	Flaxseed oil 30 g/day X 3 mo

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Nordstrom D, 1995[23]	Pain (Visual analogue scale at month 3) Arm 1 =4.60 Arm 2 =4.00 effect size=-0.21 (-1.04, 0.63) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Swollen Joints (Kaarela'sjoint score index at month 3) Arm 1 =9.50 Arm 2 =9.10 effect size=-0.06 (-0.90, 0.77) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Acute phase reactant (mm/hour at month 3) Arm 1 =32.50 Arm 2 =35.70 effect size=0.13 (-0.71, 0.96) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Patient global assessment (five-scale at month 3) Arm 1 =2.70 Arm 2 =2.90 effect size=0.26 (-0.58, 1.10) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Radiographic damage: NA NSAID consumption: NA Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 3 Concealment of allocation: NR Applicability: NR Funding source: Government; Private, non-industry

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Skoldstam L, 1992[25]	Sample size: 46 Age (mean/range): 57 / 28-73 Race: NA % male: 26 # sites: NA Location: Sweden	Design: RCT Duration: 6 mo	Inclusion: Clinically stable/Stable medication/Increased sed rate/Increased morning stiffness/>= 6 tender joints/>= 3 swollen joints Exclusion: NA	Covariates: NSAIDs/DMARDs	1	Control oil (maize, olive and peppermint oil) capsules 10 g/day X 6 mo
					2	Max EPA (fish oil) 10 g/day X 6 mo

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Skoldstam L, 1992[25]	Pain (0-3 VAS at month 3) Arm 1 mean=1.28 Arm 2 mean=136 effect size=0.11 (-0.49, 0.71) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Swollen joints: NA Acute phase reactant (mm/hour at month 3) Arm 1 =39 Arm 2 =40 effect size=0.04 (-0.55, 0.64) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Patient global assessment (0-3 scale at month 3) Arm 1 =1.11 Arm 2 =1.20 effect size=0.04 (-0.56, 0.63) Reported testing: Article did not report statistical results comparing Arm 1 and Arm 2. Radiographic damage: NA NSAID consumption: NA Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 3 Concealment of allocation: NR Applicability: IB Funding source: Government

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Tulleken J, 1990[24]	Sample size: 28 Age (mean/range): 55 / 29-68 Race: NA % male: 11 # sites: NA Location: Italy	Design: RCT Duration: 3 mo	Inclusion: Stable medication Exclusion: NA	Covariates: NSAIDs/DMARDs	1	Coconut oil capsules 4 TID X 3 mo
					2	Fish oil capsules 4 TID (6 g/day) X 3 mo

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Tulleken J, 1990[24]	Pain (10 cm VAS at month 3) Arm 1 =3.8 Arm 2 =2.4 effect size=-0.72 (-1.50, 0.06) Reported testing: Article reports no significant differences (p>0.05) between Arm 1 and Arm 2. Swollen joints ((# of swollen joint at month 3) Arm 1 =4 Arm 2 =3 effect size=-0.26(-1.02, 0.50) Reported testing: Article reports no significant differences (p>0.05) between Arm 1 and Arm 2. Acute phase reactant (mm/hour at month 3) Arm 1 =53 Arm 2 =21 effect size=-1.82 (-2.71, -0.92) Reported testing: Article reports no significant differences (p>0.05) between Arm 1 and Arm 2. Patient global assessment: NA Radiographic damage: NA NSAID consumption: NA Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 4 Concealment of allocation: Yes Applicability: IIB Comments: Meta-analysis performed on patient assessment of pain, swollen joints, and acute phase reactant. Funding source: Private, non-industry

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage Duration
Tulleken J, 1988[34]	Sample size: NA Age (mean/range): NA / NA Race: NA % male: NA # sites: NA Location: Netherlands	Design: RXT Duration: 24 X-over: week 13 Run-in: NR Wash-out: NR	Inclusion: Active RA Exclusion: NR	Covariates: NSAIDs/DMARDs	1	Coconut oil capsules 12/day X 3 mo
					2	Fish oil capsules 12/day X 3 mo

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Tulleken J, 1988[34]	Pain: NA Swollen joints: (at month 3) Arms 1, 2 = point estimates not reported Meta-analysis: Not included; point estimates not reported. Reported testing: Significant difference between arms favoring fish oil, test not stated. Acute phase reactant: (CRP, mg/dl, at month 3) Arms 1, 2 = point estimates not reported before cross-over Meta-analysis: Not included; point estimates not reported. Reported testing: No significant difference between arms , test not stated. Patient global assessment: NA Radiographic damage: NA NSAID consumption: NA Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 2 Concealment of allocation: NR Applicability: NR Funding source: ND

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage Duration
van der Tempel H, 1990[33]	Sample size: NA Age (mean/range): 53 / NA Race: NA % male: 44 # sites: NA Location: Netherlands	Design: RXT Duration: 36 wk X-over: week 13 Run-in: 12 wk Wash-out: None	Inclusion: NR Exclusion: NR	Covariates: NSAIDs/DMARDs	1	Coconut oil capsules 12/day X 12 wk
					2	Fish oil capsules 12/day X 12 wk

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis.

First Author, Year	Outcomes Results	Quality Applicability Funding Source
van der Tempel H, 1990[33]	Pain:(VAS, cm at week 12) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates not reported before cross-over. Reported testing: No significant differences between arms using t-test. Swollen joints: (at week 12) Arms 1, 2 = point estimates not reported. Meta-analysis: Not included; point estimates not reported before cross-over. Reported testing: Significant differences between favoring fish oil using t-test. Acute phase reactant: (CRP, mg/dl, at month 3) Arms 1, 2 = point estimates not reported before cross-over Meta-analysis: Not included; point estimates not reported. Reported testing: No significant differences between arms using t-test. Patient global assessment: NA Radiographic damage: NA NSAID consumption: NA Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 4 Concealment of allocation: NR Applicability: IB Comments: Meta-analysis not performed because data was not reported by arm separately. Funding source: Private, non-industry

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Volker D, 2000[35]	Sample size: 50 Age (mean/range): 57 / NA Race: NA % male: NA # sites: NA Location: Australia	Design: RCT Duration: 15 wk	Inclusion: Stable medication/Active disease/Diet<10g n-6 fatty acids Exclusion: NA	Covariates: NSAIDs/DMARDs	1	Corn (50%)/olive oil (50%) soft gel capsules 40 mg/kg body weight/day x 15 wk
					2	Pikasol (fish oil) capsules 40 mg/kg body weight/day x15 wk

Table C.3. Evidence table of clinical effect of omega-3 fatty acids in rheumatoid arthritis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Volker D, 2000[35]	Pain: (percent change at week 15) Arm 1 = -8.6 Arm 2 = -10.0 Meta-analysis: Not included; data reported as percent change. Reported testing: No significant differnce between goups by MANOVA. Swollen joints: (percent change at week 15) Arm 1 = -16.6 Arm 2 = -36.7 Meta-analysis: Not included; data reported as percent change. Reported testing: No significant differnce between goups by MANOVA. Acute phase reactant: (ESR, percent change at week 15) Arm 1 = -31.9 Arm 2 = -6.2 Meta-analysis: Not included; data reported as percent change. Reported testing: No significant differnce between goups by MANOVA. Patient global assessment: NA Radiographic damage: NA NSAID consumption: NA Steroid consumption: NA DMARD consumption: NA	Quality: Jadad: 3 Concealment of allocation: NR Applicability: NR Funding source: Industry, private non-industry

Table C.4. Evidence table of clinical effect of omega-3 fatty acids in renal disease.

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Covariates	Arm	Interventions Dosage/Duration
Bennett WM, 1989[100]	Sample size: 37 Age (mean/range) 39 / NA Race NA % male : 57 # sites: NA Location: Australia	Design: RCT Duration: 24 mo	Inclusion Biopsy-proven Ig A nephropathy Exclusion: Baseline serum creatinine>0.40 mmol/l or = 0.12 mmol/l without active disease	Covariates: Renal/Proteinuria/ Nephrotic Renal impairment: scr > 0.12 mm/l	1	No treatment x 24 mo
					2	Max EPA (fish oil) 10 g/d x 24 mo

Table C.4. Evidence table of clinical effect of omega-3 fatty acids in renal disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Bennett WM, 1989[100]	Serum creatinine (change mmol/l at month 24): Arm 1= Subjects with baseline > 0.12 mmol/l = 0.22; Subjects with baseline <0.12 mmol/l, but with active disease = 0.01 Arm 2 = Subjects with baseline >0.12 mmol/l = 0.19; Subjects with baseline <0.12 mmol/l, but with active disease = 0.07 ± .06 Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported. Creatinine clearance (change ml/min at month 24): Arm 1= -21 Arm 2 = -23 Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported. ESRD (rate at month 24): Arm 1= 10% Arm 2 = 12% Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported. Graft thrombosis: NA Mortality: NA Immunosuppressive requirement: NA	Quality: Jadad: 2 Concealment of allocation: NA Applicability: IIB Funding source: NA

Table C.4. Evidence table of clinical effect of omega-3 fatty acids in renal disease (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Covariates	Arm	Interventions Dosage/Duration
Clark WFP, 1993[99]	Sample size: 21 Age (mean/range) 39 / 22-66 Race: NA % male: 19 # sites: NA Location: Canada	Design: RXT Duration: 13 mo X-over: month 5 Run-in: None Wash-out: 3 mo	Inclusion: Lupus nephritis Exclusion: NA	Covariates: NSAIDs/DMARDs	1	Olive oil 15 cap/d x 12 mo
					2	Max EPA (fish oil) 15 cap/d x 12 mo
De Fijter CW, 1995[103]	Sample size: NA Age (mean/range) NA / NA Race: NA % male: NA # sites: NA Location: Netherlands	Design: RXT Duration: 27 mo X-over: month 12 Run-in: None Wash-out: 3 mo	Inclusion: Dialysis/Start of erythropoietin/ Exclusion: NA	Covariates: Hypertension	1	Corn oil 3 g/d x 5 mo
					2	EPA-B (fish oil) 3 g/d x 5 mo

Table C.4. Evidence table of clinical effect of omega-3 fatty acids in renal disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Clark WFP, 1993[99]	Serum creatinine (µmol/L at month 12): Arm 1= point estimate before cross-over not reported Arm 2 = point estimate before cross-over not reported Meta-analysis: Not done; too few studies to pool. Reported testing: No significant (p = 0.60) effect for fish oil (Arm 2) relative to olive oil (Arm 1). Creatinine clearance (ml/min/1.73 m^2 at at month 12): Arm 1= 78 Arm 2 = 75 Meta-anlysis: Not done; too few studies to pool. Reported testing: No significant difference between groups. ESRD: NA Graft thrombosis: NA Mortality: NA Immunosuppressive requirement: NA	Quality: Jadad: 3 Concealment of allocation: NA Applicability: IIIB Funding source: Private, non industry
De Fijter CW, 1995[103]	Serum creatinine: NA Creatinine clearance: NA ESRD: NA Graft thrombosis (rate at month 5): Arm 1= 0% Arm 2 = 0% Meta-analysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported. Mortality: NA Immunosuppressive requirement: NA	Quality: Jadad: 3 Concealment of allocation: NA Applicability: NA Funding source: NA

Table C.4. Evidence table of clinical effect of omega-3 fatty acids in renal disease (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Covariates	Arm	Interventions Dosage/Duration
Donadio JV, 1994[98]	Sample size: 106 Age (mean/range): 37 / NA Race: Caucasian % male: 74 # sites: 21 Location: US	Design: RCT Duration: 60 mo	Inclusion: Biopsy-proven Ig A nephropathy /Proteinuria/Serum creatinine increased by 25%/Creatinine <3.0 mg/dl/Expected survival of 2 or more years Exclusion: SLE/ Chronic liver disease/Pregnancy/lactating/ Antiglomerular basement membrane glomerulonephritis	Covariates: Renal/Proteinuria/Nephrotic	1	Olive oil 12 g/d x 24 mo
					2	Max EPA (fish oil) 12 g/d x 12 mo Menhaden oil (fish oil) 12 g/d x 12 mo

Table C.4. Evidence table of clinical effect of omega-3 fatty acids in renal disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Donadio JV, 1994[98]	Serum creatinine (Annual median change mg/dl at month 24): Arm 1= 0.14 Arm 2 = 0.03 Meta-anlysis: Not done; too few studies to pool. Reported testing: Significant (P = 0.001) effect for fish oil (Arm 2) relative to olive oil (Arm 1) using rank-sum test. Creatinine clearance(Annual median change ml/min/1.73 m^2 at at month 24): Arm 1= -7.1 Arm 2 = -0.3 Meta-anlysis: Not done; too few studies to pool. Reported testing: Significant (P = 0.009) effect for fish oil (Arm 2) relative to olive oil (Arm 1) using rank-sum test. ESRD (rate at month 60): Arm 1= 28% Arm 2 = 7% Meta-anlysis: Not done; too few studies to pool. Reported testing: Significant effect for fish oil (Arm 2) relative to olive oil (Arm 1) using rank-sum test and Kaplan-Meier analysis. Graft thrombosis: NA Mortality(rate at month 60): Arm 1= 1% Arm 2 = 2% Meta-anlysis: Meta-analysis not performed on renal studies due to insufficient statistics. Reported testing: No significant effect for fish oil (Arm 2) relative to olive oil (Arm 1) using rank-sum test and Kaplan-Meier analysis. Immunosuppressive requirement: NA	Quality: Jadad: 4 Concealment of allocation: NR Applicability: IIB Funding source: Hospital and Industry

Table C.4. Evidence table of clinical effect of omega-3 fatty acids in renal disease (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Covariates	Arm	Interventions Dosage/Duration
Donadio JV, 2001[104]	Sample size: 73 Age (mean/range): 46 / NA Race: Caucasian % male: 83 # sites: 14 Location: US	Design: RCT Duration: 60 mo	Inclusion: Biopsy-proven Ig A nephropathy /Age/Serum creatinine 1.5-4.9 mg/dl Exclusion: NA	Covariates: Previous meds tx/ Hypertension	1	Omacor 4 g/d x 24 mo
					2	Omacor 8 g/d x 24 mo

Table C.4. Evidence table of clinical effect of omega-3 fatty acids in renal disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Donadio JV, 2001[104]	Serum creatinine (annual median change, mg/dl at month 60): Arm 1= 0.08 Arm 2 = 0.10 Meta-anlysis: Not done; too few studies to pool. Reported testing: No significant (P = 0.51) effect for high dose Omacor (Arm 2) relative to low dose Omacor(Arm 1) using rank-sum test. Creatinine clearance: NA ESRD ((rate at month 36): Arm 1= 27% Arm 2 = 24% Meta-anlysis: Not done; too few studies to pool. Reported testing: No significant (P = 0.56) effect for high dose Omacor (Arm 2) relative to low dose Omacor(Arm 1) using rank-sum test. Graft thrombosis: NA Mortality (rate at month 36): Arm 1= 0% Arm 2 = 0% Meta-anlysis: Not done; too few studies to pool. Reported testing: No significant effect for high dose Omacor (Arm 2) relative to low dose Omacor(Arm 1) using rank-sum test. Immunosuppressive requirement: NA	Quality: Jadad: 2 Concealment of allocation: NA Applicability: IIB Funding source: Hospital and Industry

Table C.4. Evidence table of clinical effect of omega-3 fatty acids in renal disease (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Covariates	Arm	Interventions Dosage/Duration
Gentile MG, 1993[106]	Sample size: NA Age (mean/range): 45 / 15-60 Race: NA % male: 45 # sites: 1 Location: Italy	Design: RXT Duration: 9 mo X-over: month 4 Run-in: 2 mo Wash-out: None	Inclusion: Biopsy-proven glomerular disease/Proteinuria/ Hyperlipidemia Exclusion: Steroid treatment/Cytotoxic treatment/NSAID treatment/Lipid lowering drug treatment	Covariates: soy diet	1	Soy diet alone Dosage NA x 2 mo
					2	Soy diet Dosage NA x 2 mo Fish oil 5 g/d x 2 mo

Table C.4. Evidence table of clinical effect of omega-3 fatty acids in renal disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Gentile MG, 1993[106]	Serum creatinine (mg/dl at month 2): Arm 1= point estimate before cross-over not reported Arm 2 = point estimate before cross-over not reported Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported. Creatinine clearance(ml/min atb month 2): Arm 1= point estimate before cross-over not reported Arm 2 = point estimate before cross-over not reported Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported. ESRD: NA Graft thrombosis: NA Mortality: NA Immunosuppressive requirement: NA	Quality: Jadad: 2 Concealment of allocation: NA Applicability: IB Funding source: Government

Table C.4. Evidence table of clinical effect of omega-3 fatty acids in renal disease (continued).

First Author Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Covariates	Arm	Interventions Dosage/Duration
Pettersson EE, 1994[101]	Sample size: 34 Age (mean/range): 41 / 22-68 Race: NA % male: 78 # sites: NA Location: Sweden	Design: RCT Duration: 6 mo	Inclusion : Biopsy-proven Ig A nephropathy /Proteinuria Exclusion: SLE/Steroid treatment /Cytotoxic or immunosuppressive drug treatment/NSAID treatment /Diabetes/Malignant disease/Heart failure/Rapidly progressive renal insufficiency/Uncontrolled hypertension	Covariates: Proteinuria/ nephrotic	1	Corn oil 6g/d x 6 mo
					2	K-85 (fish oil) 6g/d x 6 mo

Table C.4. Evidence table of clinical effect of omega-3 fatty acids in renal disease (continued).

First Author, Year	Outcomes Results	Quality Applicability) Funding Source
Pettersson EE, 1994[101]	Serum creatinine(change µmol/l at month 6): Arm 1= 1 Arm 2 = 8 Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported. Creatinine clearance (change ml/min at month 6): Arm 1= 0 Arm 2 = 12 Meta-anlysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported. ESRD: NA Graft thrombosis: NA Mortality: NA Immunosuppressive requirement: NA	Quality: Jadad: 4 Concealment of allocation: NA Applicability: IIB Funding source: NA

Table C.4. Evidence table of clinical effect of omega-3 fatty acids in renal disease (continued).

First Author Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Covariates	Arm	Interventions Dosage/Duration
Schmitz PG, 2002[102]	Sample size: 24 Age (mean/range): 53 / NA Race: Black % male: 46 # sites: 1 Location: US	Design: RCT Duration: 12 mo	Inclusion: Initiation of hemodialysis with PTFE graft/Hemodialysis with new placement of PTFE graft Exclusion: Pregnancy/lactating/Surgical revision of graft/History of GI bleeding/Chronic anticoagulation treatment/ Malignant hypertension/Terminal of life-threatening diseases	Covariates: Hyperlipidemia/ Hypertension/ Diabetes/Venous output resistance	1	Corn oil 4g/d x 12 mo
					2	Fish oil 4g/d x 12 mo

Table C.4. Evidence table of clinical effect of omega-3 fatty acids in renal disease (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Schmitz PG, 2002[102]	Serum creatinine: NA Creatinine clearance: NA ESRD:NA Graft thrombosis(rate at 12 mo): Arm 1= 75% Arm 2 = 25% Meta-analysis: Not done; too few studies to pool. Reported testing: Testing between arms not reported. Patency (rate at 12 mo): Arm 1= 15% Arm 2 = 76% Meta-analysis: Not done; too few studies to pool. Reported testing: Significant ($p < .03$) effect for fish oil (Arm 2) relative to corn oil (Arm 1) using Mantel-Cox test. Mortality: NA Immunosuppressive requirement: NA	Quality: Jadad: 4 Concealment of allocation: NA Applicability: IIB Funding source: Private, non-industry and Government

Table C.5. Evidence table of clinical effects of omega-3 fatty acids in systemic lupus erythematosus.

First Author, Year	Study Characteristics	Study design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Clark WF, 1993[99]	Sample size: 26 Age (mean/range): 39 / 22-66 Race: NA % male: 19 \# sites: NA Location: Canada	Design: RXT Duration: 24 mo X-over: month 13 Run-in: None Wash-out: 10 wk	Inclusion: Lupus nephritis Exclusion: NA	Covariates: NSAIDs/DMARDs	1 2	Olive oil capsules 15/d x 12 mo Max EPA (fish oil) 15/d x 12 mo
Walton AJ, 1991[107]	Sample size: 27 Age (mean/range): NA / 21-68 Race: NA % male: 7 \# sites: 1 Location: UK	Design: RXT Duration: 34 wk X-over: week 22 Run-in: 2 wk Wash-out: 8 wk	Inclusion: Established SLE	Covariates: NA	1 2	Olive oil 20g/d x 12 wk Max EPA (fish oil) 20g/d x 12 wk

Table C.5. Evidence table of clinical effects of omega-3 fatty acids in systemic lupus erythematosus (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Clark WF, 1993[99]	Disease activity: (SLEDAI score at month 12) Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not done; too few studies to pool. **Reported testing: No change in SLEDAI scores for either arm, statistical test used and comparison between arms for this outcome not explicitly stated.** Disease activity: (anti-ds-DNA Ab level at month 12) Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not done; too few studies to pool. Reported testing: No treatment (p=0.71), time (p=0.25), order (p=0.35) or carry-over effect (p=0.92); statistical test used not stated. Damage: NA Patient perception: NA	Quality: Jadad: 3 Concealment of allocation: NA Applicability: IIIB Funding source: Private, non-industry
Walton AJ, 1991[107]	Disease Activity: (Unspecified individualized responses defined a priori and based on change in clinical and laboratory parameters at month 6) Arm 1: 4/17 useful/ideal status 13/17 static/worse status Arm 2: 14/17 useful/ideal status 3/17 static/worse status Meta-analysis: Not done; too few studies to pool. Reported testing: Testing between groups not reported. Damage: NA Patient perception: NA	Quality: Jadad: 3 Concealment of allocation: Yes Applicability: IIB Funding source: government; private, non-industry

Table C.5. Evidence table of clinical effects of omega-3 fatty acids in systemic lupus erythematosus (continued).

First Author, Year	Study Characteristics	Study design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Westberg G, 1990[108]	Sample size: 20 Age (mean/range): 44 / 31-64 Race: NA % male: 12 # sites: 2 Location: Australia	Design: RXT Duration: 21 mo X-over: month 12 Run-in: 3 mo Wash-out: 3 mo	Inclusion: Stable medication Exclusion: Inactive disease	Covariates: DMARDs, steroid use	1 2	Placebo/control Dosage/duration not collected Max EPA (fish oil) Variable dose for 6 mo

Table C.5. Evidence table of clinical effects of omega-3 fatty acids in systemic lupus erythematosus (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Westberg G, 1990[108]	Disease activity: (Author's own instrument, at 6 mo) Arm 1= point estimates not reported. Arm 2 = point estimates not reported. Meta-analysis: Not done; too few studies to pool. Reported testing: No significant difference between groups using Student's t-test. Disease activity: (anti-DNA Ab level at month 6) Arm 1= point estimate not reported Arm 2 = point estimate not reported Meta-analysis: Not done; too few studies to pool. Reported testing No significant difference between groups using Student's t-test. Damage: NA Patient Perception: NA	Quality: Jadad: 5 Concealment of allocation Yes Applicability: IIB Funding source: NA

Table C.6. Evidence table of clinical effect of omega-3 fatty acids in bone mineral density/osteoporosis.

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Bassey EJ, 2000[109] Study A	Sample size: 64 Age (mean/range): 35 / 25-40 Race: NA % male: 0 # sites: 1 Location: UK	Design: RCT Duration: 12 mo	Inclusion: Age/Pre-menopausal Exclusion: Health problems/BMI>36, <18/BMD outside 2SD of norms/Confounding drug therapy/Pregnancy/Lactating/ Dietary supplements/Irregular menses	Covariates: Weight/Age/Dietary Calcium	1 2	Calcium 1g/d x 12 mo Efacal (Ca, Primrose oil, Fish oil) Ca 1 g/d x 12 mo Evening primrose oil 4 g/d x 12 mo Fish oil 440 g/d x 12 mo
Bassey EJ, 2000[109] Study B	Sample Size: 57 Age (mean/range): 57/50-65 race: NA % male: 0 # sites: 1 Location: UK	Design: RCT Duration: 12 mo	Inclusion: Age/Postmenopausal Exclusion: Health problems/ BMI >36, <18/BMD outside 2SD of norms/Confounding drug therapy/Dietary supplements/ within 1 yr of menopause/Hormone levels outside of normal postmenopausal range/hormone replacement therapy	Covariates: Weight/Age/Dietary Calcium	1 2	Calcium 1g/d x 12 mo Efacal (Ca, Primrose oil, Fish oil) Ca 1 g/d x 12 mo Evening primrose oil 4 g/d x 12 mo Fish oil 440 g/d x 12 mo

Table C.6. Evidence table of clinical effect of omega-3 fatty acids in bone mineral density/osteoporosis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Bassey EJ, 2000[109] Study A	Bone mineral density: (change at month 12, g/cm^2) Arm 1= 0.011 Arm 2 = 0.008 Meta-analysis: Not done; too few studies to pool. Reported testing: Significant (p<.001) difference between groups using paired Student's t-test. Fractures: NA	Quality: Jadad: 2 Concealment of allocation: Yes Applicability: IA Funding source: Industry
Bassey EJ, 2000[109] Study B	Bone mineral density: (change at month 12, g/cm^2) Arm 1= -0.013 Arm 2 = -0.008 Meta-analysis: Not done; too few studies to pool. Reported testing: Significant (p<.001) difference between groups using paired Student's t-test. Fractures: NA	Quality: Jadad: 2 Concealment of allocation: Yes Applicability: IA Funding source: Industry

Table C.6. Evidence table of clinical effect of omega-3 fatty acids in bone mineral density/osteoporosis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Kruger MC, 1998[110]	Sample size: 66 starting Age (mean/range): 80 / NA Race: NA % male: 0 # sites: NA Location: South Africa	Design: RCT Duration: 18 mo	Inclusion: Osteoporosis confirmation by BMD Exclusion: Metabolic bone disease/ Diabetes/Renal failure	Covariates: Weight/Age	1	Coconut oil 6 g/d X 18 mo
					2	Fish oil 6 g/d X 18 mo
					2	EPA 2g x 12 mo plus HMGCoA reductace inhibitor

Table C.6. Evidence table of clinical effect of omega-3 fatty acids in bone mineral density/osteoporosis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Kruger MC, 1998[110]	Bone mineral density: (lumbar spine, g/cm ^{2} at month 18) Arm 1= 0.979 Arm 2 = 1.053 Meta-analysis: Not done; too few studies to pool. Reported testing: Testing between groups not reported. Bone mineral density: (femoral neck, g/cm ^{2} at month 18) Arm 1= 0.709 Arm 2 = 0.774 Meta-analysis: Not done; too few studies to pool. Reported testing: Testing between groups not reported. Fractures: (cumulative number at month 18) Arm 1= 0 Arm 2 = 0 Meta-analysis: Not done; too few studies to pool. Reported testing: Testing between groups not reported.	Quality: Jadad: 2 Concealment of allocation: NA Applicability: IIIB Funding source: Industry

Table C.6. Evidence table of clinical effect of omega-3 fatty acids in bone mineral density/osteoporosis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Terano T, 2001[111]	Sample size: 33 Age (mean/range): 58 / NA Race: NA % male: 0 # sites: NA Location: Japan	Design: RCT Duration: 12 mo	Inclusion: Hyperlipidemia Exclusion: NA	Covariates: Hyperlipidemia/Age/ Weight	1	HMGCoA reductase inhibitor

Table C.6. Evidence table of clinical effect of omega-3 fatty acids in bone mineral density/osteoporosis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Terano T, 2001[111]	Bone mineral density: (speed of sound, %, at month 12) Arm 1= 98.6 Arm 2 = 99.3 Meta-analysis: Not done; too few studies to pool. Reported testing: Testing between groups not reported. Bone mineral density: (transmission index, %, at month 12) Arm 1= 99.4 Arm 2 = 101 Meta-analysis: Not done; too few studies to pool. Reported testing: Testing between groups not reported. Bone mineral density: (osteosono assessment index, %, at month 12) Arm 1= 99.4 Arm 2 = 99.3 Meta-analysis: Not done; too few studies to pool. Reported testing: Testing between groups not reported. Fractures: NA	Quality: Jadad: 1 Concealment of allocation: NR Applicability: Not described Funding source: NR

Table C.6. Evidence table of clinical effect of omega-3 fatty acids in bone mineral density/osteoporosis (continued).

First Author, Year	Study Characteristics	Study Design Duration	Eligibility Criteria	Concurrent Disease Condition Medication	Arm	Interventions Dosage/Duration
Tsuchida K, 1999[112]	Sample size: 995 Age (mean/range): 45 / 40-49 Race: Asian % male: 0 # sites: 18 Location: Japan	Design: Cohort Duration: NA	Inclusion: Age Exclusion: Medical treatment/Ovalectomy	Covariates: Weight/Age/Dietary Calcium/Menstrual cycle	1	Fish -0-1 portions/week
					2	Fish 2-5 portions/week
					3	Fish 6-7 portions/week
					4	Soybean 0-1 portions/week
					5	Soybean 2-5 portions/week
					6	Soybean 6-7 portions/week

Table C.6. Evidence table of clinical effect of omega-3 fatty acids in bone mineral density/osteoporosis (continued).

First Author, Year	Outcomes Results	Quality Applicability Funding Source
Tsuchida K, 1999[112]	Bone mineral density: There was no association between fish intake and BMD of the 2nd metacarpal bone. Soybean intake was associated with a significant (p=.03 by ANOVA) gradient in BMD of 2nd metacarpal independent of age, height, weight and weekly calcium intake. Those with 2 or more portions were significantly higher than 0-1 portions. Fractures: NA	Quality Jadad: NA Concealment of allocation: NA Applicability: IA Funding source: NR