



Should I take fish oil?

Fish oil supplements are a billion dollar industry and many patients take them for health conditions such as osteoarthritis, memory loss and heart disease. Fish oil contains omega-3 fatty acids with DHA and EPA being the key long chain polyunsaturated fatty acids known to have an effect on neural membrane phospholipids, to have antiplatelet and lipid lowering properties as well as anti-inflammatory effects.

Fish Oil for Mental Health & Cognitive Function

BIPOLAR DISORDER

Strong Recommendation For: Based on the evidence below we recommend fish oil supplements for **adult patients with bipolar disorder** in addition to their standard medication (lithium, psychotropic or mood stabilisers). There was a small-moderate improvement in depression scores for bipolar patients taking 1.0-1.5g of fish oil per day in addition to their standard medication but this effect does not occur with mania scores.

Outcome (Timeframe)	Study results and measurements	Certainty in effect estimates (Quality of evidence)	Absolute effect estimates Placebo plus standard treatment vs Fish oil (1g-1.5g of mixed EPA and DHA) plus standard treatment	Summary
Bipolar depression score (Follow up 4 - 16 weeks)	Measured by: Depression scales High score = better Based on data from 291 patients in 5 studies	High quality evidence with low risk of bias	Difference: SMD 0.34 higher (CI 95% 0.04 higher - 0.64 higher)	Fish oil in addition to bipolar medication can moderately improve depression symptoms in patients with bipolar disorder (NB: an SMD of 0.34 is equivalent to a small-moderate effect)
Bipolar mania score (Follow up 4 - 16 weeks)	Measured by: Mania scales (Standardized Mean Difference) Scale: - High better Based on data from 291 patients in 5 studies	High quality evidence with low risk of bias	Difference: SMD 0.2 higher (CI 95% 0.37 lower - 0.43 higher)	Fish oil in addition to standard bipolar medication makes little or no difference on mania scores

References

[1] J S, D M, I S Omega-3 for bipolar disorder: meta-analyses of use in mania and bipolar depression.. The Journal of clinical psychiatry 2012;73(1):81-6-null

MEMORY LOSS

Weak Recommendation For: Based on the evidence below we recommend fish oil >1g daily in **adults with mild memory complaints**. There is evidence of a small beneficial effect on episodic memory (compared with placebo) that should be balanced against the practical consequences of taking fish oil such as cost and adverse effects.

Outcome Timeframe	Study results and measurements	Certainty in effect estimates (Quality of evidence)	Absolute effect estimates Placebo Fish oil (DHA/EPA) >1.0g daily	Summary
Episodic Memory* (Follow up 4 - 6 months)	Measured by: Neuropsychological tests including immediate and delayed word list recall, word recognition, story recall, picture recall, the Rey Complex Figure Test, CANTAB PAL, and verbal recognition memory. Scale: - High better Based on data from 3369 patients in 18 studies	High certainty due to low risk of bias	Difference: SMD 0.23 higher (CI 95% null lower - null lower)	Fish Oil Supplements >1g daily over 4-6 months may have a small beneficial effect in adults with mild memory complaints (NB: SMD values of 0.2 are considered to have a small effect)

*Where episodic memory is defined as “memory for personally experienced events that occur at a specific place and time and is measured by memory of stories, word lists, or figures

References

[3] Yurko-Mauro K, Alexander DD, Van Elswyk ME Docosahexaenoic Acid and Adult Memory: A Systematic Review and Meta-Analysis. PLOS ONE 2015/03/18;10(3):e0120391-null

Fish Oil for Cardiovascular Disease

Weak Recommendation Against: Based on the evidence below we make a weak recommendation against fish oil supplementation for the prevention of heart attacks and strokes. In these studies on men and women aged 49-70 years of age taking fish oil supplements (0.24-3.4g daily) compared with no supplements or placebo over 1-6 years there was no effect on overall mortality, cardiac death, sudden death, heart attacks or strokes. The studies included primary and secondary prevention and implantable cardioverter-defibrillator patients.

Outcome (Timeframe)	Study results and measurements	Certainty in effect estimates (Quality of evidence)	Absolute effect estimates		Summary
			No supplements or placebo	Omega-3 supplementation	
All-cause mortality (Follow up: 1 - 6.2 years)	Relative risk: 0.96 (CI 95% 0.91 - 1.02) Based on data from 63279 patients in 17 studies	Moderate risk of bias	102 per 1000	98 per 1000	Fish oil supplementation has little or no effect on all-cause mortality (95% CI crosses 1.0)
Cardiac death (Follow up: 1 - 6.2 years)	Relative risk: 0.91 (CI 95% 0.89 - 1.02) Based on data from 34492 patients in 14 studies	Moderate risk of bias	79 per 1000	72 per 1000	Fish oil supplementation has little or no effect on cardiac death (95% CI crosses 1.0)
Sudden death (Follow up: 1 - 6.2 years)	Relative risk: 0.87 (CI 95% 0.75 - 1.01) Based on data from 41751 patients in 8 studies	Moderate risk of bias	26 per 1000	23 per 1000	Fish oil supplementation has little or no effect on sudden death (95% CI crosses 1.0)
Myocardial infarction (Follow up: 1 - 6.2 years)	Relative risk: 0.89 (CI 95% 0.76 - 1.04) Based on data from 53805 patients in 14 studies	Moderate risk of bias	33 per 1000	32 per 1000	Fish oil supplementation has little or no effect on myocardial infarction (95% CI crosses 1.0)
Stroke (Follow up: 1 - 6.2 years)	Relative risk: 1.05 (CI 95% 0.93 - 1.18) Based on data from 52589 patients in 9 studies	Moderate risk of bias	28 per 1000	29 per 1000	Fish oil supplementation has little or no effect on stroke (95% CI crosses 1.0)

References

[2] EC R, EE N, E B, MS K, MS E Association between omega-3 fatty acid supplementation and risk of major cardiovascular disease events: A systematic review and meta-analysis. JAMA 2012/09/12;308(10):1024-1033

Fish Oil for Knee Osteoarthritis

Weak Recommendation For: Based on the evidence below we make a weak recommendation for low dose fish oil supplementation for the treatment of pain and function in **patients with knee osteoarthritis**. In these studies on men and women, with a mean age of 61, there is a greater difference from the baseline for both the pain and function score when the patients are given a low dose fish oil (0.45g) than compared to a high dose fish oil (4.5g).

Outcome Timeframe	Study results and measurements	Certainty in effect estimates (Quality of evidence)	Absolute effect estimates		Summary
			Baseline	Follow-up	
High dose - change in Pain score 2 years	Measured by: WOMAC* Pain Score Scale: 0-50 Lower better Based on data from 101 patients in 1 studies	High quality evidence with low risk of bias	16.0 (Mean)	13.5 (Mean)	Small reduction in the pain score from baseline at 2 years
Low dose - change in Pain score 2 years	Measured by: WOMAC Pain Score Scale: 0-50 Lower better Based on data from 101 patients in 1 studies	High quality evidence with low risk of bias	15.0 (Mean)	8.0 (Mean)	Significant reduction in the pain score from baseline at 2 years
High dose - change in Function score 2 years	Measured by: WOMAC Function Score Scale: 0-170 Lower better Based on data from 101 patients in 1 studies	High quality evidence with low risk of bias	54.0 (Mean)	42.0 (Mean)	Significant reduction in the function score from baseline at 2 years
Low dose - change in Function score 2 years	Measured by: WOMAC Function Score Scale: 0-170 Lower better Based on data from 101 patients in 1 studies	High quality evidence with low risk of bias	49.0 (Mean)	32.0 (Mean)	Significant reduction in the function score from baseline at 2 years

Outcome	Study results and measurements	Certainty in effect estimates (Quality of evidence)	Absolute effect estimates		Summary
			Low dose fish oil (0.45g omega-3 fatty acids)	High dose fish oil (4.5g omega-3 fatty acids)	
Withdrawal from therapy	Relative risk: 1.88 (CI 95% 1.12 - 3.16) Based on data from 101 patients in 1 studies Follow up 2 years	High quality evidence with low risk of bias	168 per 1000	316 per 1000	The high dose group has a higher rate of withdrawals
			Difference: 148 more per 1000 (CI 95% 20 more - 363 more)		

Percentage of participants with Adverse events	Low-dose fish oil	High-dose fish oil
Infection (respiratory, other)	65.3%	70.3%
Gastrointestinal	61.4%	66.3%
Cardiovascular	15.8%	17.8%

References

[4] Hill CL, March LM, Aitken D, Lester SE, Battersby R, Hynes K, Fedorova T, Proudman SM, James M, Cleland LG, Jones G Fish oil in knee osteoarthritis: a randomised clinical trial of low dose versus high dose. *Annals of the rheumatic diseases* 2016;75(1):23-9-null

*WOMAC: Western Ontario and McMaster Universities Arthritis Index pain score – The pain score uses a numerical rating scale of 0-50 and the function score uses a 0-170 scale.

Practical consequences



Medication routine

How much fish oil should I take for bipolar?

Fish oil (1g-1.5g of mixed EPA and DHA) plus standard treatment

For most fish oil supplements you will need to take at least 4 tablets/capsules per day (although does of active ingredients varies between brands).



Food and drinks

Can I get the same dose of fish oil through diet?

Fish oil (1g-1.5g of mixed EPA and DHA) plus standard treatment

The best way to meet a 1g per daily quota through diet would be to consume approximately 600g to 900g of oily fish (e.g. salmon, tuna, sardines) per week with skin on. A small can of tuna/salmon is around 130g.



Adverse effects, interactions and antidote

Does fish oil interact with other medication?

Fish oil (1g-1.5g of mixed EPA and DHA) plus standard treatment

Fish oil in doses of 3g or more may interact with anticoagulants with an increased bleeding risk. Doses of 1g-1.5g appear to be safe.



Adverse effects, interactions and antidote

Are there any side effects from fish oil?

Fish oil (1g-1.5g of mixed EPA and DHA) plus standard treatment

High doses of fish oil greater than 3g may increase LDL cholesterol levels and bleeding times. The most common side effect is nausea and a fishy after-taste which may occur in as many as 6-7 out of 10 people.



Costs and access

How much does 1.0-1.5g fish oil cost per day?

Fish oil (1g-1.5g of mixed EPA and DHA) plus standard treatment

The cost of fish oil tablets vary from 0.05 to 0.40AUD per tablet/capsule. That could be from \$0.20 to \$1.60 per day.