Supplementary Online Content


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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Excluded Studies and Reasons

Case report (n=2)


Lack of adequate control (n=15)


**Meta-analysis (n=2)**


Downloaded From: https://jamanetwork.com/ by a Non-Human Traffic (NHT) User on 12/08/2019
Not human clinical trial (n=5)


Not human clinical trial in the part of anxiety study (n=1)


Not related to omega 3 supplement effect on anxiety (n=38)


29. Sanchez-Villegas A, Henriquez P, Figueiras A, Ortuno F, Lahortiga F, Martinez-


61. Nieminen LR, Makino KK, Mehta N, Virkkunen M, Kim HY, Hibbeln JR.


**Not simply treat with omega-3 related product (n=3)**


**Protocol but no result of studies (n=2)**


**Review article (n=7)**


The same sample source from Buydens-Branchey, L. (2008) (n=1)


The same sample source from Nishi, D. (2013) (n=1)


The same sample source from Matsuoka, Y. (2015) (n=1)


Database study but not clinical trials (n=1)

79. Adams J, Sibbritt D, Lui CW, Broom A, Wardle J. {Omega}-3 fatty acid


No detailed information about changes of anxiety symptoms despite of our request of detailed data (n=6)


### eTable. Study Design and Jadad Scores of Recruited Studies

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>Study design</th>
<th>Diagnosis</th>
<th>Jadad Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watanabe, N. (2018)</td>
<td>Double-blind randomized placebo controlled</td>
<td>Junior nurses work in hospital</td>
<td>1 2 1 4</td>
</tr>
<tr>
<td>Bellino, S. (2014)</td>
<td>Randomized controlled</td>
<td>Borderline personality disorders</td>
<td>1 0 1 2</td>
</tr>
<tr>
<td>Pomponi, M. (2014)</td>
<td>Double-blind randomized placebo controlled</td>
<td>Parkinson's Disease</td>
<td>2 1 1 4</td>
</tr>
<tr>
<td>Widenhorn-Muller, K. (2014)</td>
<td>Double-blind randomized placebo controlled</td>
<td>Children with ADHD</td>
<td>2 1 1 4</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Participants</td>
<td>Outcome Areas</td>
</tr>
<tr>
<td>-------</td>
<td>--------</td>
<td>--------------</td>
<td>---------------</td>
</tr>
<tr>
<td>Sauder, K.A. (2013)</td>
<td>Double-blind randomized placebo control cross-over</td>
<td>Healthy, nonsmoking men and postmenopausal women with moderate hypertriglyceridemia</td>
<td>1 1 1 3</td>
</tr>
<tr>
<td>Sohrabi, N. (2013)</td>
<td>Double-blind randomized placebo controlled</td>
<td>Healthy women with premenstrual syndrome</td>
<td>1 2 1 4</td>
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<tr>
<td>Gabbay, V. (2012)</td>
<td>Double-blind randomized placebo controlled</td>
<td>Tourette syndrome</td>
<td>1 2 1 4</td>
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<tr>
<td>Kiecolt-Glaser, J.K. (2011)</td>
<td>Double-blind randomized placebo controlled</td>
<td>Generally healthy subjects</td>
<td>2 1 1 4</td>
</tr>
<tr>
<td>Rogers, P.J. (2008)</td>
<td>Double-blind randomized placebo controlled</td>
<td>Mild to severe depression</td>
<td>1 2 1 4</td>
</tr>
<tr>
<td>van de Rest, O. (2008)</td>
<td>Double-blind randomized placebo controlled</td>
<td>Elderly volunteers</td>
<td>2 2 1 5</td>
</tr>
<tr>
<td>Yehuda, S. (2005)</td>
<td>Case-placebo control trial</td>
<td>Undergraduate college students with test anxiety</td>
<td>0 1 1 2</td>
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</table>
eFigure 1. Whole Flowchart of Current Meta-Analysis

Identification

PubMed: (omega 3 OR eicosapentaenoic acid OR EPA OR DHA OR docosahexaenoic acid) AND (anxiety OR anxiety disorder OR generalized anxiety disorder OR agoraphobia OR panic disorder OR post-traumatic stress disorder)
Limits: N/A
Date: 2018/03/04

Embase: (omega 3 OR eicosapentaenic acid OR EPA OR DHA OR docosahexaenic acid) AND (anxiety OR anxiety disorder OR generalized anxiety disorder OR agoraphobia OR panic disorder OR post-traumatic stress disorder)
Limits: N/A
Date: 2018/03/04

ProQuest: (omega 3 OR eicosapentaenic acid OR EPA OR DHA OR docosahexaenic acid) AND (anxiety OR anxiety disorder OR generalized anxiety disorder OR agoraphobia OR panic disorder OR post-traumatic stress disorder)
Limits: N/A
Date: 2018/03/04

ScienceDirect: (omega 3 OR eicosapentaenic acid OR EPA OR DHA OR docosahexaenic acid) AND (anxiety OR anxiety disorder OR generalized anxiety disorder OR agoraphobia OR panic disorder OR post-traumatic stress disorder)
Limits: N/A
Date: 2018/03/04

Cochrane Library: (omega 3 OR eicosapentaenic acid OR EPA OR DHA OR docosahexaenic acid) AND (anxiety OR anxiety disorder OR generalized anxiety disorder OR agoraphobia OR panic disorder OR post-traumatic stress disorder)
Limits: N/A
Date: 2018/03/04

ClinicalKey: (omega 3 OR eicosapentaenic acid OR EPA OR DHA OR docosahexaenic acid) AND (anxiety OR anxiety disorder OR generalized anxiety disorder OR agoraphobia OR panic disorder OR post-traumatic stress disorder)
Limits: N/A
Date: 2018/03/04

Web of Science: (omega 3 OR eicosapentaenic acid OR EPA OR DHA OR docosahexaenic acid) AND (anxiety OR anxiety disorder OR generalized anxiety disorder OR agoraphobia OR panic disorder OR post-traumatic stress disorder)
Limits: N/A
Date: 2018/03/04

ClinicalTrials.gov: (omega 3 OR eicosapentaenic acid OR EPA OR DHA OR docosahexaenic acid) AND (anxiety OR anxiety disorder OR generalized anxiety disorder OR agoraphobia OR panic disorder OR post-traumatic stress disorder)
Limits: N/A
Date: 2018/03/04

Screen

Removal duplication (n=2141)

Excluded articles which not discussed this topic, case reports/series, not humane clinical trials (n=2037)

Screen for eligibility (n=104)

Not meet the inclusion criteria (n=85)

Recruited studies (n=19)

**eFigure 2.** Funnel Plot of Changes in Anxiety Symptoms in Patients With and Without n-3 PUFA Treatment

![Funnel Plot of Standard Error by Hedges's g](image-url)
### eFigure 3. Subgroup MA of Anxiolytic Effect Based Upon Placebo Controlled or Non–Placebo Controlled Design

<table>
<thead>
<tr>
<th>Compared to</th>
<th>Study name</th>
<th>Sample size</th>
<th>Statistics for each study</th>
<th>Hedges' g and 95% CI</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Non-placebo</td>
<td>Ballito, S. (2014)</td>
<td>18 16</td>
<td>0.172 0.457 0.331 61</td>
<td>13.78</td>
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<tr>
<td></td>
<td>Niho, D. (2013)</td>
<td>86 86</td>
<td>0.390 0.052 0.583 41</td>
<td>66.31</td>
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<tr>
<td></td>
<td>Haberka, M. (2013)</td>
<td>26 26</td>
<td>0.610 0.062 1.158 63</td>
<td>19.91</td>
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</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td>0.399 0.154 0.643 &lt; 0.01</td>
<td>160.00</td>
<td></td>
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<tr>
<td>Placebo</td>
<td>Sauder, K.A. (2013)</td>
<td>52 26</td>
<td>-0.296 -0.769 0.178 22</td>
<td>6.41</td>
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<tr>
<td></td>
<td>van de Rest, O. (2006)</td>
<td>196 106</td>
<td>-0.214 -0.450 0.023 68</td>
<td>7.05</td>
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<tr>
<td></td>
<td>Freund-Levi, Y. (2000)</td>
<td>36 24</td>
<td>-0.149 -0.659 0.362 57</td>
<td>6.27</td>
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<td></td>
<td>Cohen, L.B. (2014)</td>
<td>177 178</td>
<td>-0.136 -0.347 0.069 19</td>
<td>7.10</td>
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<tr>
<td></td>
<td>Matsumoto, Y. (2015)</td>
<td>53 57</td>
<td>-0.107 -0.479 0.294 57</td>
<td>6.71</td>
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<tr>
<td></td>
<td>Corra, C. (2017)</td>
<td>79 81</td>
<td>-0.077 -0.365 0.232 63</td>
<td>6.38</td>
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<tr>
<td></td>
<td>Widenhorn-Muller, K. (2014)</td>
<td>46 49</td>
<td>0.081 -0.318 0.481 69</td>
<td>6.63</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fux, M. (2004)</td>
<td>6 5</td>
<td>0.165 -0.522 1.252 77</td>
<td>4.18</td>
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<tr>
<td></td>
<td>Rogers, P.J. (2008)</td>
<td>109 109</td>
<td>0.200 -0.065 0.465 14</td>
<td>6.99</td>
<td></td>
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<tr>
<td></td>
<td>Watanabe, N. (2010)</td>
<td>40 40</td>
<td>0.217 -0.219 0.562 53</td>
<td>5.52</td>
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<tr>
<td></td>
<td>Gebbay, V. (2012)</td>
<td>17 16</td>
<td>0.306 -0.364 0.976 37</td>
<td>5.89</td>
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<tr>
<td></td>
<td>Pomponi, M. (2014)</td>
<td>12 12</td>
<td>0.477 -0.308 1.281 23</td>
<td>5.26</td>
<td></td>
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<tr>
<td></td>
<td>Kiecolt-Glaser, J.K. (2011)</td>
<td>34 34</td>
<td>0.607 0.126 1.086 01</td>
<td>6.37</td>
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<tr>
<td></td>
<td>Buydens-Branchez, L. (2009)</td>
<td>11 11</td>
<td>1.010 0.153 1.958 02</td>
<td>4.96</td>
<td></td>
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<tr>
<td></td>
<td>Yehuda, S. (2005)</td>
<td>80 38</td>
<td>1.056 1.220 2.079 &lt; 0.001</td>
<td>6.54</td>
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<tr>
<td></td>
<td>Sokrab, N. (2013)</td>
<td>63 61</td>
<td>2.459 1.594 3.323 &lt; 0.001</td>
<td>6.42</td>
<td></td>
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<tr>
<td>Overall</td>
<td></td>
<td></td>
<td>0.372 0.032 0.712 .03</td>
<td>160.00</td>
<td></td>
</tr>
</tbody>
</table>

Subgroup meta-analysis of the anxiolytic effect by n-3 PUFAs based upon placebo-control or non-placebo-control. There was significantly better improvement in anxiety symptoms in patients treated with n-3 PUFAs compared with controls in subgroups of both placebo controls (k = 16, Hedges' g = 0.372, 95% CI = 0.032 to 0.712, p = 0.032) and non-placebo-control (k = 3, Hedges' g = 0.399, 95% CI = 0.154 to 0.643, p = 0.001)