

# The Role of Omega-3 Polyunsaturated Fatty Acids in Chronic Obstructive Pulmonary Disease (COPD) Comorbid Mood Disorders

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## ABSTRACT

**Background:** Chronic obstructive pulmonary disease (COPD) often comorbid mood disorders, including depression and anxiety. Inflammation is a shared mechanism in depression and COPD. Omega-3 polyunsaturated fatty acids (n-3 PUFAs) play a vital role in regulating inflammatory responses and help improve mood symptoms. To our knowledge, there has been no review on the role of n-3 PUFAs in COPD comorbid mood disorders.

**Methods:** To identify eligible studies for this review, a computerized search was performed for all publications available up to 16th of June 2022 with the key words “COPD, depression, anxiety”, “depression, anxiety, COPD, inflammation”, “depression, anxiety, n-3 PUFA”, and “COPD, n-3 PUFA.”

**Result:** Depression and anxiety are reported to be the two most common mood disorders comorbid with COPD. The anti-inflammatory roles of n-3 PUFAs have been well documented. We retrieved 10 trials on n-3 PUFAs and COPD with varying primary and secondary outcomes including: exercise performance, dyspnea, physical activity level, body composition, inflammation markers, biochemical parameters, lung endothelial function, brachial artery flow-mediated dilation, and health-related quality of life. None of the trials had anxiety or depression as primary or secondary outcome. Only 1 trial considered anxiety and depression as exploratory outcomes. In the study, COPD patients supplemented with leucine, vitamin D, and n-3 PUFAs had lower depressive symptoms than those in the placebo group at the endpoint. N-3 PUFAs may play a role in COPD comorbid mood disorders putatively *via* their ability to modulate inflammatory processes and inhibit Kynurenine pathway.

**Conclusion:** There are promising potentials of n-3 PUFAs in managing comorbid mood disorders in COPD, especially via modulating the inflammatory mechanisms.

## BACKGROUND

•Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide.

•Depression and anxiety in COPD result in poor clinical outcomes and reduced quality of life.

•Inflammation characterizes anxiety and depression and is believed to play a major role in the development of comorbid anxiety and depression in COPD.

•Omega-3 polyunsaturated fatty acids (n-3 PUFAs) play a vital role in regulating inflammatory responses and have been used to improve mood symptoms.

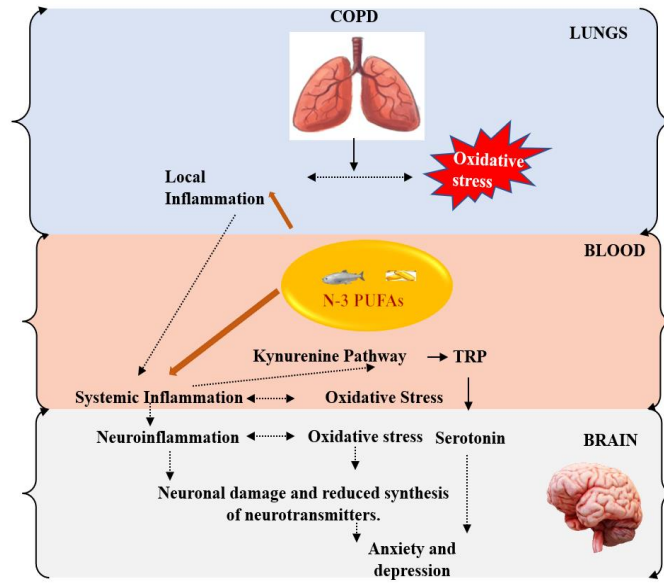
•To our knowledge, there has been no review on the role of n-3 PUFAs in COPD comorbid mood disorders.

## METHODS

We conducted a literature search to identify eligible studies for this review, a computerized search was performed for all publications available up to 16th of June 2022 through PubMed, Web of Science, Cochrane, Embase, and Google search, with the keywords “COPD, depression, anxiety”, “depression, anxiety, COPD, inflammation”, “depression, anxiety, n-3 PUFA”, and “COPD, n-3 PUFA.”

## RESULTS

- Depression and anxiety are reported to be the two most common mood disorders comorbid with COPD.
- Elevated levels of activated leukocytes, C-reactive protein (CRP), fibrinogen, Interferon (IFN)- $\gamma$ , IFN- $\alpha$ , interleukin (IL)-1 $\beta$ , IL-2, IL-6, IL-18, tumor necrosis factor (TNF)- $\alpha$ , and TNF- $\alpha$  receptors in anxiety, depression, and COPD were reported.
- The positive effects of n-3 PUFAs on anxiety and depression have been well documented in several studies.



**Figure 1:** Summary of the potential roles of n-3 PUFAs in managing comorbid anxiety and depression in COPD. N-3 PUFAs can play a role in managing comorbid mood disorders in COPD via the modulation of inflammatory processes and inhibition of Kynurenine pathway. N-3 PUFAs: Omega-3 polyunsaturated fatty acids, COPD: Chronic obstructive pulmonary disease, TRP: Tryptophan.

**Table 1:** Summary of n-3 PUFAs trials in COPD

Authors and year	Design	Intervention type	Outcomes
Zhang and Zou, 2015	RCT	N-3 PUFAs and energy	Biochemical parameters and inflammatory markers.
van de Boel et al., 2017	RCT	leucine, vitamin D, and n-3 PUFAs+ Exercise training	<b>Primary:</b> Quadriceps muscle strength <b>Secondary:</b> Body composition, cycle endurance time, inspiratory muscle strength, daily steps, habitual dietary intake, fasting plasma levels of vitamin D, branched-chain amino acids and fatty acid profile. <b>Exploratory:</b> 6 min walk distance 6MWD and mood assessment.
van Beers et al., 2020	RCT	leucine, vitamin D, and n-3 PUFAs + Exercise training	<b>Primary:</b> Quadriceps muscle strength <b>Secondary:</b> Body composition, cycle endurance time, inspiratory muscle strength, daily steps, habitual dietary intake, fasting plasma levels of vitamin D, branched-chain amino acids and fatty acid profile.
Thomashow et al., 2014	RCT	High-dose n-3 PUFAs	<b>Primary:</b> Change in flow-mediated dilation of the brachial artery. <b>Secondary:</b> Peripheral arterial tonometry, CD31+ and CD62E+ endothelial microparticles, pulmonary function, 6MWD, oxygen saturation, and the SGRQ
Sugawara et al., 2010	RCT	N-3 PUFAs + vitamin A + Low intensity exercise	Lung function, maximum inspiratory and expiratory muscle force, the CRQ, 6MWD, and the Borg scale and inflammatory markers.
Ogasawara et al., 2018	RCT	EPA-enriched supplement	<b>Primary:</b> Changes lean body mass index and skeletal body mass index. <b>Secondary:</b> Change of body mass index, step counts per day, dyspnea, quality of life, and biochemical parameters.
Kim et al., 2020	RCT	high-dose fish oil	<b>Primary:</b> Percentage change in brachial artery flow-mediated dilation. <b>Secondary:</b> Peripheral arterial tonometry, endothelial microparticles, 6MWD, respiratory symptoms, and pulmonary function.
Gurgun et al., 2011	RCT	Nutrition supplementation including n-3 PUFAs and dietary counselling	Perceived dyspnea, 6MWD, quality of life, and body composition.
Calder et al., 2018	RCT	Energy + N-3 PUFAs + 25-hydroxy-vitamin D3	<b>Primary:</b> Adverse events and changes in vital signs, laboratory parameters, and concomitant medications. <b>Secondary:</b> Changes in weight, body composition, exercise tolerance, metabolic biomarkers, and systemic inflammation
Broekhuizen et al., 2005	RCT	N-3 PUFAs + Other n-3 fatty acids	Body composition, functional capacity, and inflammatory markers

Note: RCT: Randomized controlled trial, n-3 PUFAs: Omega-3 polyunsaturated fatty acids, EPA: Eicosapentaenoic acid, 6MWD: 6-minute walking distance, CRQ: Chronic respiratory disease questionnaire, SGRQ: St. Georges Respiratory Questionnaire.

## CONCLUSION AND RECOMMENDATION

COPD has been associated with depression and anxiety. Both COPD and depression have been associated with inflammation. Further studies are warranted to investigate the role of anti-inflammation agents, such as n-3 PUFAs, in COPD comorbid depression and anxiety.

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