Table S1 The specific search strategies

	Search Strategy
#1	Pulmonary Disease, Chronic Obstructive[MeSH Terms] OR Chronic Obstructive Lung Disease[Title/Abstract] OR Chronic Obstructive Pulmonary Diseases[Title/Abstract] OR COAD[Title/Abstract] OR COPD[Title/Abstract] OR Chronic Obstructive Airway Disease[Title/Abstract] OR Chronic Obstructive Pulmonary Disease[Title/Abstract] OR Chronic Airflow Obstructions[Title/Abstract] OR Chronic Airflow Obstruction[Title/Abstract]
#2	Polyunsaturated Fatty Acids[Title/Abstract] OR Polyunsaturated Fatty Acid[Title/Abstract]
#3	Fatty Acids, Omega-3[MeSH Terms] OR Omega-3 Fatty Acid[Title/Abstract] OR Omega 3 Fatty Acid[Title/Abstract] OR Omega-3 Fatty Acids[Title/Abstract] OR n-3 Oil[Title/Abstract] OR n 3 Oil[Title/Abstract] OR n3 Oil[Title/Abstract] OR n-3 Fatty Acids[Title/Abstract] OR n 3 Fatty Acids[Title/Abstract] OR Omega 3 Fatty Acids[Title/Abstract] OR n-3 PUFA[Title/Abstract] OR n 3 PUFA[Title/Abstract] OR n3 Fatty Acid[Title/Abstract] OR n3 PUFA[Title/Abstract] OR n3 Polyunsaturated Fatty Acid[Title/Abstract] OR n3 Oils[Title/Abstract] OR n-3 Oils[Title/Abstract] OR n 3 Oils[Title/Abstract] OR N-3 Fatty Acid[Title/Abstract] OR N 3 Fatty Acid[Title/Abstract] OR n-3 Polyunsaturated Fatty Acid[Title/Abstract] OR n 3 Polyunsaturated Fatty Acid[Title/Abstract]
#4	Linolenic Acids[MeSH]
#5	Docosahexaenoic Acids[MeSH Terms] OR Docosahexenoic Acids[Title/Abstract] OR Docosahexaenoic Acid[Title/Abstract] OR Docosahexaenoic Acid All-Z Isomer[Title/Abstract] OR Docosahexaenoic Acid Dimer All-Z Isomer[Title/Abstract] OR Docosahexaenoate[Title/Abstract] OR DHA[Title/Abstract]
#6	Eicosapentaenoic Acid[MeSH Terms] OR Eicosapentanoic Acid[Title/Abstract] OR omega-3-Eicosapentaenoic Acid[Title/Abstract] OR omega 3 Eicosapentaenoic Acid[Title/Abstract] OR Timnodonic Acid[Title/Abstract] OR Icosapent[Title/Abstract] OR 5,8,11,14,17-Icosapentaenoic Acid[Title/Abstract] OR EPA[Title/Abstract] OR 5,8,11,14,17-Eicosapentaenoic Acid[Title/Abstract]
#7	Fatty Acids, Omega-6[MeSH Terms] OR Omega-6 Fatty Acid[Title/Abstract] OR Omega 6 Fatty Acid[Title/Abstract] OR Omega-6 Fatty Acids[Title/Abstract] OR Omega 6 Fatty Acids[Title/Abstract] OR N-6 Fatty Acid[Title/Abstract] OR N 6 Fatty Acid[Title/Abstract] OR N-6 Fatty Acids[Title/Abstract] OR N 6 Fatty Acids[Title/Abstract]
#8	gamma-Linolenic Acid[MeSH Terms] OR gamma Linolenic Acid[Title/Abstract] OR Gamolenic Acid[Title/Abstract]
#9	Arachidonic Acids[MeSH Terms] OR Eicosatetraenoic Acids[Title/Abstract]
#10	Linoleic Acids[MeSH Terms] OR Acids Linoleic[Title/Abstract]
#11	fish oils[MeSH Terms] OR Fish Oil[Title/Abstract] OR Fish Liver Oils[Title/Abstract]
#12	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
#13	#1 AND #12

Table S2 The risk of bias for case-control studies by the Newcastle-Ottawa scale (NOS) De Castro J, et al. 2007

Study type	Case-control study	
Participants	Patients with COPD recruited during a moderate-to-severe exacerbation and 15 healthy male and female volunteers as controls. Sample size: 30 Mean age in years: 64.00±6.38 Gender: NA Location: Spain	
Outcomes	Main study outcome: analyze and compare the phospholipid and fatty acid composition of total lipids from erythrocytes or platelets of COPD and asthma patients. Available outcomes: fatty acid composition of total lipids from erythrocytes in control subjects and COPD and asthma patients.	
Risk of bias		
Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	1	healthy male and female volunteers as controls, whose age, body weight, blood lipids, blood pressure and BMI were equivalent to those of the patient groups.
Definition of Controls(Selection)	1	healthy male and female volunteers
Comparability of cases and controls on the basis of the design or analysis(Comparability)	2	study controls for age, body weight, blood lipids, blood pressure and BMI and other factors
Ascertainment of exposure(Exposure)	1	laboratory examination
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	1	the same no response rate

Novgorodtseva TP, et al. 2013

Study type	Case-control study	
Participants	COPD patients (stable stage) / healthy subjects Sample size: 25 Age: 23-57 Gender: - Location: Russia	
Outcomes	Main study outcome: the fatty acid composition of the membranes of the red blood cells in patients with chronic bronchitis and stable chronic obstructive pulmonary disease. Available outcomes: Fatty acid composition of erythrocyte membranes in patients with COPD.	
Risk of bias		
Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	1	healthy subjects
Definition of Controls(Selection)	1	ex-smokers or nonsmokers without respiratory infection within at least the last 4 weeks.
Comparability of cases and controls on the basis of the design or analysis(Comparability)	1	study controls for basic illness.
Ascertainment of exposure(Exposure)	1	secure record (laboratory examination)
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	non respondents described

Wada H, et al. 2012

Study type	Case-control study	
Participants	Eighteen COPD patients (10 patients with stage I/II disease and 8 with stage III/IV) and 20 age-matched controls were enrolled. Sample size: 38 Mean age in years: 70.29±9.22 Gender: - Location: Japan	
Outcomes	Main study outcome: comparison of plasma total free fatty acid levels between COPD patients and control group Available outcomes: plasma levels of each composition of FFA in COPD patients and control group.	
Risk of bias		
Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	1	age-matched controls
Definition of Controls(Selection)	1	age-matched
Comparability of cases and controls on the basis of the design or analysis(Comparability)	1	study controls for Age.
Ascertainment of exposure(Exposure)	1	secure record (Laboratory examination)
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	non respondents described

Chambaneau A, et al. 2016

Study type	Case-control study	
Participants	cases of COPD from medical wards and control subjects without COPD. Sample size: 40 Mean age in years: 65.20±5.67 Gender: - Location: France	
Outcomes	Main study outcome: investigate whether nutritional factors could explain membership of a group of COPD patients. Available outcomes: Comparison of the food intakes between COPD group and control group.	
Risk of bias		
Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	1	matched control subject
Definition of Controls(Selection)	1	without COPD
Comparability of cases and controls on the basis of the design or analysis(Comparability)	2	study controls for Age, gender and occupation
Ascertainment of exposure(Exposure)	1	secure record
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	non respondents described

Ahmadi A, et al. 2012

Study type	Case-control study
Participants	age between55-75 years and having COPD diagnosis as the primary limiting illness within the past four years and matched control subject. Sample size: 201 Age: 55-75 Gender: - Location: Iran
Outcomes	Main study outcome: evaluated the nutritional status in COPD patients and compared it with healthy control groups. Available outcomes: Mean intake of macro-nutrients in COPD patient and control group.

Risk of bias

Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	1	matched Controls
Definition of Controls(Selection)	1	their health was confirmed by physicians.
Comparability of cases and controls on the basis of the design or analysis(Comparability)	2	study controls for age and gender.
Ascertainment of exposure(Exposure)	1	secure record
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	non respondents described

Hirayama F, et al. 2010

Study type	Case-control study
Participants	patients were referred by respiratory physicians from the outpatient departments of six hospitals and matched control subject. Sample size: 618 Mean age in years: 65.84±6.10 Gender: 516males/102females Location: Japan
Outcomes	Main study outcome: evaluate the effects of these two types of dietary nutrients on lung function, breathlessness and the prevalence of COPD. Available outcomes: Comparison of between case and control groups.

Risk of bias

Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	1	community controls
Definition of Controls(Selection)	1	age-matched
Comparability of cases and controls on the basis of the design or analysis(Comparability)	1	study controls for age and gender.
Ascertainment of exposure(Exposure)	1	secure record
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	non respondents described

Denisenko YK, et al. 2022

Study type	Case-control study
Participants	Diagnosed as COPD patients of different levels and healthy subjects. Sample size:169 Mean age in years: 56.88±4.39 Gender: 133males/36females Location: Russia
Outcomes	Main study outcome: investigate the modification of the fatty acid composition of leukocyte membranes in patients with COPD of various severity. Available outcomes: Fatty acid composition of leukocyte membrane and serum level of eicosanoids in patients with COPD.

Risk of bias

Bias	Authors' judgment	Support for judgment
Is the case definition adequate(Selection)	1	yes, with independent validation
Representativeness of the cases(Selection)	1	consecutive or obviously representative series of cases
Selection of Controls(Selection)	1	community controls
Definition of Controls(Selection)	1	healthy subjects
Comparability of cases and controls on the basis of the design or analysis(Comparability)	1	study controls for smoking and basic illness.
Ascertainment of exposure(Exposure)	1	secure record (laboratory examination)
Same method of ascertainment for cases and controls(Exposure)	1	yes
Non-Response rate(Exposure)	0	non respondents described

Table S3 The risk of bias for cohort studies by the Newcastle-Ottawa scale (NOS)

Varraso R, et al. 2015

Study type	Cohort study	
Participants	121701 female nurses 30–55 y old who were living in 11 US States and 51529 male US health professionals aged 40–75 y. Sample size: 120175 Mean age in years: 51.66±8.44 Gender: 46947males/73288females Location: America	
Outcomes	Main study outcome: Investigate relations of fish and PUFA intakes with risk of COPD. Available outcomes: Association between the cumulative average of fatty acids and newly diagnosed COPD.	
Risk of bias		
Bias	**Authors' judgment**	**Support for judgment**
Representativeness of the exposed cohort (**Selection**)	1	truly representative of US health professionals.
Selection of the non exposed cohort (**Selection**)	1	Excluding participants who reported a diagnosed asthma or COPD at baseline
Ascertainment of exposure (**Selection**)	1	doctor-diagnosed chronic bronchitis or emphysema and report of a diagnostic test at diagnosis.
Demonstration that outcome of interest was not present at start of study (**Selection**)	1	yes
Comparability of cohorts on the basis of the design or analysis (**Comparability**)	1	study controls for Age, smoking, pack-years of smoking, pack-years squared of smoking, secondhand tobacco exposure, race-ethnicity, physician visit, US region, spouse's highest educational attainment, menopausal status, BMI, physical activity, multivitamin use, energy intake, and modified prudent and Western dietary patterns and

		other factors
Assessment of outcome (**Outcome**)	1	independent blind assessment (medical records)
Was follow up long enough for outcomes to occur (**Outcome**)	1	yes (6 years)
Adequacy of follow up of cohorts (**Outcome**)	0	no description provided for the lost contact person.

Table S4 The risk of bias for cross-sectional studies based on the AHRQ tool

Study	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Total score	Quality
McKeever TM, et al. (2008)	Y	N	Y	Y	N	Y	Y	Y	N	Y	N	7	M
Shahar E, et al. (1999)	Y	N	Y	N	Y	Y	N	Y	N	Y	N	6	M
Shahar E, et al. (1994)	Y	N	Y	N	Y	Y	N	Y	N	Y	N	6	M
Kim KS, et al. (2023)	Y	N	Y	N	Y	Y	N	Y	N	Y	N	6	M

Note: Y, yes; N, no; U, unclear; H, high quality; M, medium quality; L, low quality.

Item 1: Define the source of information (survey, record review).

Item 2: List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications.

Item 3: Indicate time period used for identifying patients.

Item 4: Indicate whether or not subjects were consecutive if not population-based.

Item 5: Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants.

Item 6: Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements).

Item 7: Explain any patient exclusions from analysis.

Item 8: Describe how confounding was assessed and/or controlled.

Item 9: If applicable, explain how missing data were handled in the analysis.

Item 10: Summarize patient response rates and completeness of data collection.

Item 11: Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained.

Table S5 Summary of Findings (SoF) with the GRADE system (observational studies)

The level of dietary PUFA intake or Plasma PUFA in people with COPD compared with healthy controls.			
Population: Subjects with COPD vs. healthy controls.			
Settings: Six studies were conducted in Europe, three studies were conducted in Asia and three studies were conducted in North America.			
Cases: Subjects with COPD.			
Controls: Healthy controls.			
Outcomes	*SMD/OR* (95% *CI*)[a]	No of participants (studies)	Quality of the evidence Comments (GRADE)
Dietary PUFA intake levels	-0.80(-1.28,-0.31)	9699 (4 case-control/cross sectional studies)	⊕⊕⊕ MODERATE [b]
Plasma PUFA levels	-0.09(-1.42,1.24)	262 (4 case-control studies)	⊕⊕⊕ MODERATE [b]
Risk of COPD	1.06(0.94,1.19)	154762 (6 cohort/case-control studies/cross sectional studies)	⊕⊕⊕ MODERATE [b]
GRADE working group grades of evidence. High quality: We are very confident that the true effect lies close to that of the estimate of the effect. Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect. Abbreviations: SMD, standard mean deviation; OR, odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; PUFA, polyunsaturated fatty acids. [a] Results for dietary PUFA intake levels or circulating relative PUFA levels of subjects with COPD compared with controls. [b] Upgraded by one level because PUFA levels was associated with COPD and all the results of the included studies were almost identical.			

GRADE, Grading of Recommendations Assessment, Development and Evaluation system;

⊕, quality of evidence.

Table S6 The risk of bias in randomized controlled trials

Engelen MPKJ, et al. 2022

Methods	RCT, (ω-3 PUFA vs. placebo) 4 weeks Summary risk of bias: low
Participants	Clinically stable patients with a diagnosis of COPD (grades II–IV) N: 12 intervention, 10 control Mean age in years (SD): 70.70(7.85) intervention, 67.58(7.48) control Gender: 6 males/6females intervention, 7 males /3 females control Location: America
Interventions	Type: supplement (edible pearls) Comparison: EPA + DHA supplementation vs. olive oil Intervention: Participants in intervention group received 3.5 g EPA + DHA per day. Control: 7 g olive oil. Compliance: Normal-weight participants with moderate to severe COPD (n=32) received daily for 4 week, according to a randomized double-blind placebo controlled 3-group design, a high dose (3.5 g, n=10) of EPA + DHA, a low dose (2.0 g, n=10) of EPA + DHA, or placebo (olive oil, n=12) via gel capsules. Length of intervention: 4 weeks
Outcomes	Main study outcome: further refine nutritional supplementation in COPD to enhance protein gain and ultimately restore progressive muscle wasting and dysfunction in these patients. Available outcomes: Clinical characteristics and body composition of the COPD groups at the end of the 4-week intervention in response to the low compared with high EPA + DHA supplementation as compared with placebo.
Notes	The score of intervention group and control group, the beginning and the end of the intervention group were compared.

Risk of bias

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	This was a randomized clinical trial.
Allocation concealment (selection bias)	Low risk	This was a double-blinded clinical trial randomized by a statistician.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	double-blinded
Blinding of outcome	Low risk	Participants of the study, project

assessment (detection bias) All outcomes		executives and clinic's personnel were completely unaware of (blinded) control and intervention groups.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Participant flow well described.
Selective reporting (reporting bias)	Low risk	Approved by the local institutional review boards at University of Arkansas Medical Sciences and Texas A&M University.
Other bias	Low risk	No commercial company involved, and no conflict of interest.

Kim JS, et al. 2021

Methods	RCT (Omega-3 Fatty Acid vs. placebo) 6 months Summary risk of bias: low
Participants	participants were former smokers with at least a 10 pack-year history who were older than 40 years of age, had post-bronchodilator forced expiratory volume in 1 second (FEV1) to forced vital capacity (FVC) ratio < 65% predicted, and were on a stable medical regimen for 30 days prior to enrollment. N: 20 intervention, 20 control Mean age in years (SD): 67.50 (6.50) intervention, 66.20 (7.50) control Gender: 10 males/10 females intervention, 12 males /8 females control Location: America
Interventions	Type: supplement (capsule) Comparison: EPA+DHA vs. control Intervention: supplemented with 3g/d EPA+DHA for 6 months. Control: 3 soft gel capsules of placebo (corn oil) Compliance: In order to minimize gastrointestinal effects when starting high-dose n-3 PUFA, all participants were instructed to take 1 capsule daily for 1 week, then 2 capsules daily for 1 week, followed by 3 capsules daily for the remainder of the study. At each follow up visit, compliance with treatment was assessed (see the online supplement for a full description).

	Length of intervention: 6 months
Outcomes	Main study outcome: evaluate the efficacy and safety of n-3 PUFA supplementation among former smokers with stable COPD, hypothesizing that randomization to n-3 PUFAs would improve endothelial function as measured by FMD and other measures of endothelial health. Available outcomes: Primary and Secondary Efficacy End Point.
Notes	The score of intervention group and control group, the beginning and the end of the intervention group were compared.

Risk of bias

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Low risk	All participants, investigators and study personnel were blinded to treatment assignment..
Blinding of participants and personnel (performance bias) All outcomes	Low risk	double-blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not described.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Participant flow well described.
Selective reporting (reporting bias)	Low risk	registration of clinical trials: NCT00835289
Other bias	Low risk	No commercial company involved, and no conflict of interest.

Aslani MR, et al. 2020

Methods	RCT (conjugated linoleic acid vs. placebo) 6 weeks Summary risk of bias: low
Participants	All patients receive regular medical care and pain management. N: 40 intervention, 42 control Mean age in years (SD): 63.82(10.58) intervention, 61.55(10.81) control Gender: 40 males intervention, 42 males control

	Location: Iran.	
Interventions	Comparison: conjugated linoleic acid vs. control Intervention: supplemented with 3.2g/d conjugated linoleic acid for 6 weeks. Control: the same amount of placebo Length of intervention: 6 weeks.	
Outcomes	Main study outcome: investigate the preventive effect of six-week treatment of conjugated linoleic acid supplementation on the modulation of the serum concentrations of IL-6 and SIRT1, exercise tolerance and pulmonary function test in patients with COPD. Available outcomes: Percent change in different parameters after treatment period relative to baseline values.	
Notes	The score of intervention group and control group, the beginning and the end of the intervention group were compared.	
Risk of bias		
Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Low risk	containers containing placebo and intervention capsules were coded with the letters A and B and the interviewers and patients were not aware of the contents of the containers.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	double-blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Not described.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Participant flow well described.
Selective reporting (reporting bias)	Low risk	The clinical registration number was IRCT2015080823559N1.
Other bias	Low risk	No commercial company involved, and no conflict of interest.

Ogasawara T, et al. 2018

Methods	RCT, (eicosapentaenoic acid vs. placebo) Summary risk of bias: unclear
Participants	Clinically diagnosed as COPD according to the GOLD criteria and hospitalized for exacerbation of COPD or pneumonia. N: 24 intervention, 21 control Mean age in years (SD): 77.40(9.70) intervention, 79.10(7.00) control Gender: 21 males/3 females intervention, 20 males/1 female control Location: Japan
Interventions	Type: supplement (capsule) Comparison: eicosapentaenoic acid vs. control Intervention: 1 g/day of EPA-enriched oral nutrition supplementation (ONS) (EPA group) Control: EPA-free ONS of similar energy (control group) Compliance: Patients were asked to consume one pack or one can per day of the ONSs. Total energy, including the ONS, was aimed at 30e35 kcal/kg per day in both groups. The consumption rates of hospital food and ONS were recorded, after which total energy intake was calculated. Length of intervention: -
Outcomes	Main study outcome: evaluate whether supplementation of eicosapentaenoic acid prevents depletion of LBM and muscle mass in hospitalized patients with exacerbation of COPD. Available outcomes: Nutritional and inflammatory markers, serum lipids, and plasma EPA at the study baseline and discharge.
Notes	The score of intervention group and control group, the beginning and the end of the intervention group were compared.

Risk of bias

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	randomized clinical trial
Allocation concealment (selection bias)	Low risk	The random assignment was generated by a computerized program.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described

Incomplete outcome data (attrition bias) All outcomes	Low risk	Participant flow well described.
Selective reporting (reporting bias)	Unclear risk	The clinical registration number was UMIN000015805.
Other bias	Low risk	No commercial company involved, and no conflict of interest.

Fulton AS, et al. 2017

Methods	RCT, (Long-chain omega-3 polyunsaturated fatty acids vs. corn oil (placebo)) 16 weeks Summary risk of bias: unclear
Participants	Eligible participants were adults aged 18 years or over with a clinical and spirometric diagnosis of COPD. N: 6 intervention, 6 control Age: 68.50 intervention, 70.50 control Gender: 3 males/3 females intervention, 4 males/2 female control Location: Australia
Interventions	Type: supplement (capsule) Comparison: Long-chain omega-3 polyunsaturated fatty acids vs. control Intervention: six 1-g capsules of fish oil (3.6 g LCn-3PUFA) daily Control: corn oil (placebo) Compliance: Participants were required to take six 1-g capsules orally per day for 16 weeks. Length of intervention: 16 weeks
Outcomes	Main study outcome: determine the feasibility of undertaking a randomised controlled trial of Long-chain omega-3 polyunsaturated fatty acids supplementation in adults with COPD. Available outcomes: The effect of supplementing long-chain omega-3 polyunsaturated fatty acids in COPD patients.
Notes	The score of intervention group and control group, the beginning and the end of the intervention group were compared.

Risk of bias

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Low risk	randomized clinical trial
Allocation concealment	Low risk	random assignment

(selection bias)		
Blinding of participants and personnel (performance bias) All outcomes	Low risk	double-blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Participant flow well described
Incomplete outcome data (attrition bias) All outcomes	High risk	Obviously not used
Selective reporting (reporting bias)	Low risk	registration of clinical trials: ACTRN12612000158864
Other bias	Unclear risk	Not described

Ghobadi H, et al. 2016

Methods	RCT, (conjugated linoleic acid vs. placebo) 6 weeks Summary risk of bias: low
Participants	COPD patients aged 40-80. N: 45 intervention, 45 control Mean age in years (SD): 63.60(10.94) intervention, 61.64(10.60) control Gender: 45 males intervention, 45 males control Location: Iran
Interventions	Type: supplement (capsule) Comparison: conjugated linoleic acid vs. control Intervention: 3.2 grams of conjugated linoleic acid per day Control: placebo Compliance: The patients' nutritional intake levels were assessed using a 24-hour dietary recall 3 days a week (2 weekdays and 1 weekend day) at the beginning, at the 4th week, and at the 6th week of the study (nine times in total). The content of the nutrients (macronutrients and micronutrients) and the energy intake of the patients were measured and analyzed by the Nutritionist IV software. A standard form was used to determine the appetite score of the participants at the beginning, at the fourth week, and at the sixth week of the study. Length of intervention: 6 weeks
Outcomes	Main study outcome: the effect of CLA supplementation on the nutritional status of COPD patients.

Notes	The score of intervention group and control group, the beginning and the end of the intervention group were compared.

Risk of bias

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Low risk	random assignment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	double-blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All other study staff was blind to the randomization status.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Participant flow well described.
Selective reporting (reporting bias)	Low risk	registration of clinical trials: IRCT2015080823559N1
Other bias	Unclear risk	Not described

Broekhuizen R, et al. 2005

Methods	RCT, (Polyunsaturated fatty acids vs. placebo) 8 weeks Summary risk of bias: low
Participants	Dutch patients with clinically stable GOLD stage II–IV COPD consecutively admitted to an inpatient pulmonary rehabilitation centre during the years 2000–2002. N: 38 intervention, 42 control Mean age in years (SD): 64.00(10.00) intervention, 62.00(8.00) control Gender: 27 males/11 females intervention, 30 males/42 females control Location: Nether-lands
Interventions	Type: supplement (capsule) Comparison: Polyunsaturated fatty acids vs. control Intervention: 9 grams of polyunsaturated fatty acids per day. Control: placebo Compliance: All capsules were enriched with 3.5 mg/g vitamin E to stabilise the oil and to serve as an antioxidant. The patients who

	were depleted or suffering from recent weight loss (n = 48, 24 in PUFA group and 24 in placebo group) also received 36 daily liquid nutritional supplements (RespiforH 375 ml total) containing 3.4 g PUFA (2.85 g linoleic acid (LA: 18:2n-6) and 0.6 g a-linolenic acid (ALA: 18:3n-3)). Length of intervention: 8 weeks
Outcomes	Main study outcome: investigate the effect of PUFA modulation on systemic inflammation, reversal of muscle wasting, and functional status in COPD. Available outcomes: Difference in body composition and peripheral muscle function before and after PUFA or placebo intervention during an 8 week rehabilitation program.
Notes	The score of intervention group and control group, the beginning and the end of the intervention group were compared.

Risk of bias

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Low risk	random assignment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	double-blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All other study staff was blind to the randomization status.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Participant flow well described.
Selective reporting (reporting bias)	Low risk	The ethical review board of the University Hospital Maastricht approved the study and all patients gave their written informed consent.
Other bias	Low risk	No commercial company involved, and no conflict of interest.

Table S7 The Summary of Findings (SoF) with GRADE system (PUFAs supplementation for patients with COPD)

PUFA supplementation for patients with COPD			
Population: Subjects with COPD			
Settings: Three RCTs were conducted in Asia, two RCTs were conducted in North America, one RCT were conducted in Oceania, one RCT were conducted in Europe.			
Intervention: PUFA			
Comparison: placebo (similar capsule without PUFA)			
Outcomes	SMD (95% CI) [a]	No. of participants (studies)	Quality of the evidence Comments (GRADE)
6MWD (m)	-0.075(-1.394,1.243)	120 (3RCTs)	⊕⊕⊕⊖ MODERATE [b]
FEV1 (%pred)	0.589(-0.427,1.605)	128 (3RCTs)	⊕⊕⊕⊖ MODERATE [b]
FEV1/FVC (%)	0.256(-0.655,1.167)	128 (3RCTs)	⊕⊕⊕⊖ MODERATE [b]
DLCO (mL/ (min·mmHg))	-0.632(-2.334,1.070)	46 (2RCTs)	⊕⊕⊕⊖ MODERATE [b]
DLCO/VA ratio	-0.089(-0.673,0.494)	46 (2RCTs)	⊕⊕⊕⊖ MODERATE [b]
FVC (L)	-0.210(-0.970,0.550)	128 (3RCTs)	⊕⊕⊕⊖ MODERATE [b]
CRP (mg/dL)	-0.171(-0.497,0.156)	147 (3RCTs)	⊕⊕⊕⊖ MODERATE [b]
IL-6 (pg/mL)	-0.285(-0.901,0.332)	162 (2RCTs)	⊕⊕⊕⊖ MODERATE [b]
HDL (mg/dL)	0.015(-0.457,0.488)	70 (2RCTs)	⊕⊕⊕⊖ MODERATE [b]
LDL (mg/dL)	0.632(0.147,1.117)	70 (2RCTs)	⊕⊕⊕⊖ MODERATE [b]
TG (mg/dL)	0.262(-0.213,0.737)	70 (2RCTs)	⊕⊕⊕⊖ MODERATE [b]
mMRC	0.094(-0.334,0.523)	84 (2RCTs)	⊕⊕⊕⊖ MODERATE [b]
BMI (kg/m^2)	-0.027(-0.342,0.324)	157 (3RCTs)	⊕⊕⊕⊖ MODERATE [b]
weight (kg)	0.208(-0.094,0.509)	170 (2RCTs)	⊕⊕⊕⊖ MODERATE [b]
GRADE working group grades of evidence. High quality: We are very confident that the true effect lies close to that of the estimate of the effect. Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.			

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Abbreviations: SMD, standard mean deviation; CI, confidence interval; COPD, chronic obstructive pulmonary disease; PUFA, polyunsaturated fatty acids; 6MWD, 6-minutes walk distance; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; DLCO, diffusing capacity of the lungs for carbon monoxide; VA, alveolar volume; CRP, C-reaction protein; IL-6, interleukin-6; HDL, high density lipoprotein; LDL, low density lipoprotein; TG, triglyceride; mMRC, modified Medical Research Council; BMI, body mass index.

[a] Results for physical endurance, lung function, inflammatory biomarker, lipid composition, dyspnea assessment and nutritional condition in subjects with COPD (PUFA *vs* placebo).

[b] Downgraded by one level due to limited numbers of original studies, and results may be inaccurate.

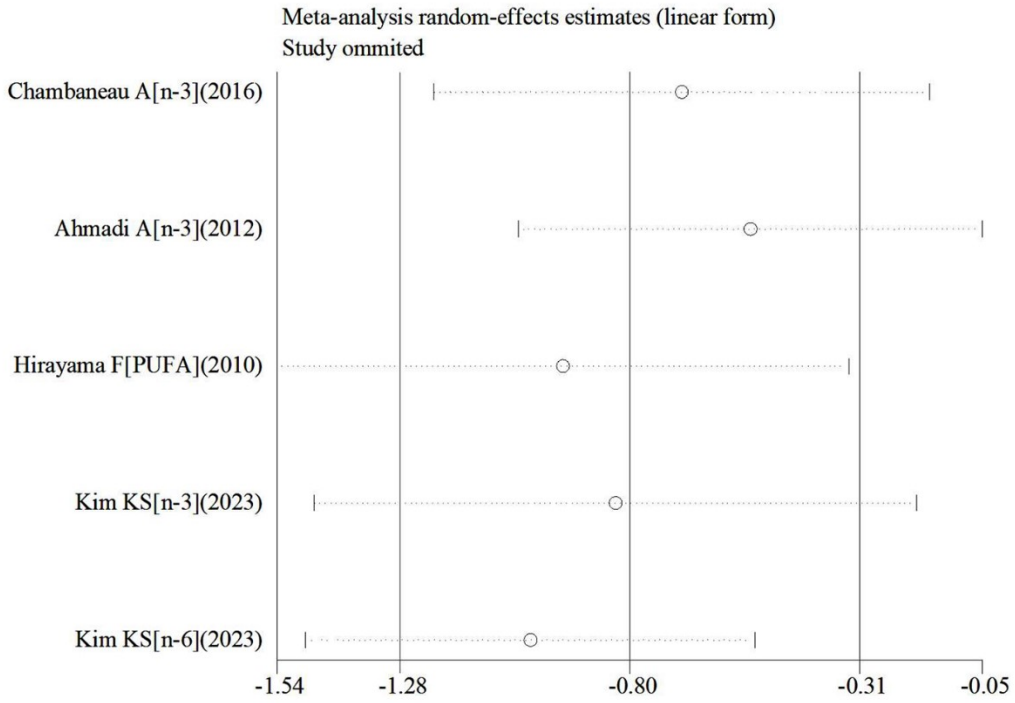

Figure S1 Sensitivity analysis for the dietary PUFAs intake with COPD patients vs. controls

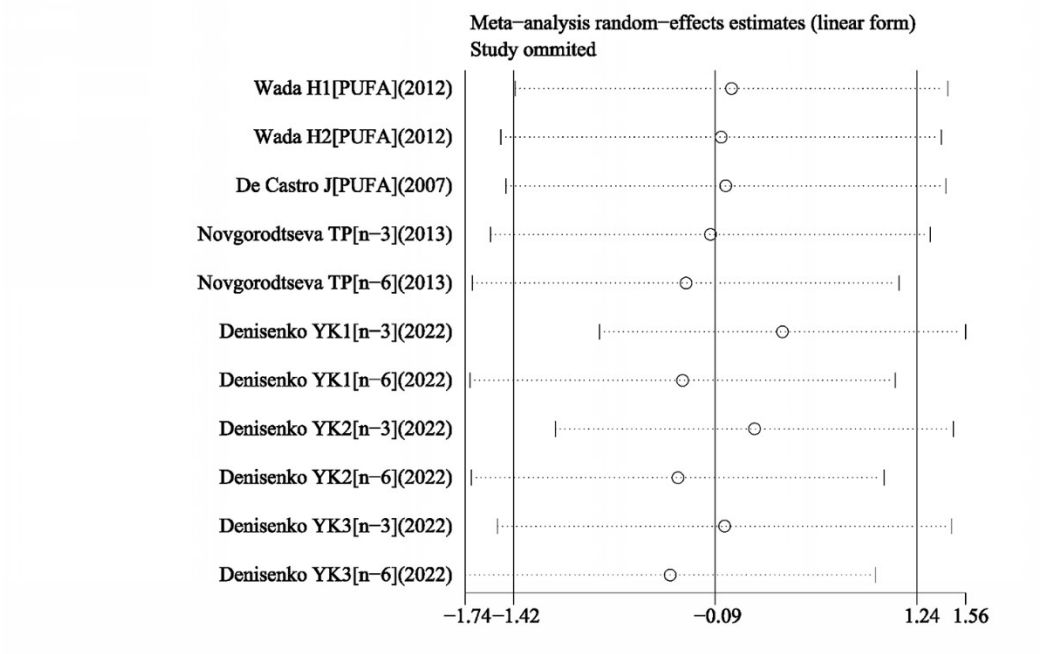

Figure S2 Sensitivity analysis for the plasma PUFAs levels with COPD patients vs. controls

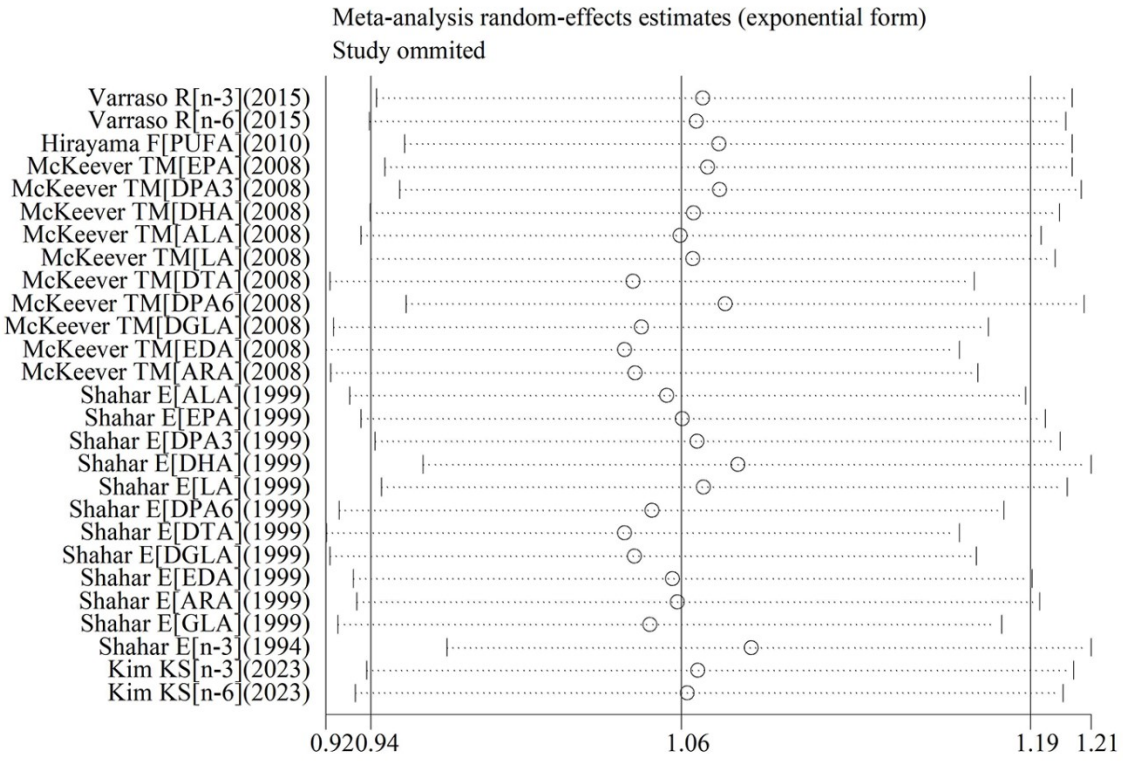

Figure S3 Sensitivity analysis for the COPD risk in subjects with higher PUFAs vs. control groups