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The Impact of Omega-3 on Improving Sleep Quality: A Systematic Review of Current Clinical Research

Camila Bernardes[1,2,#*], Igor Malheiros Assad[2,3,#], Vitor Yukio Yonekura[2,#], Marilia Ribeiro de Azevedo Aguiar[2,4], Stalin Canizares[2], Luis Rivera-Quinto[2,5], María Lucía Sequeira[2], Lukas Rudzevicius[2,6], Aline Aparecida Lacerda Gruber[2], Agustin Perez-Londono[2,7], Ahmad G. A. Khater[2,8], Dongwoo Nam[2,9], Franja Dugar[2,10], Maria Isabel Bojorquez Ortiz[2,11], Vanesa Scholl[2,12], Yinxue Linsey Zhao[2,13]

[1]D'Or Institute for Research and Education (IDOR), Botafogo, Rio de Janeiro, Brazil; [2]Principles and Practice of Clinical Research (PPCR) Course, Executive and Continuing Professional Education, Harvard T.H. Chan School of Public Health, Boston, USA; [3]Department of Medicine, Universidade Federal de São Paulo, São Paulo, Brazil; [4]Department of Internal Medicine, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil; [5]Johns Hopkins Bloomberg School of Public Health; [6]Klinikum Chemnitz gGmbH, Klinik für Neurochirurgie, Chemnitz; [7]Division of Urologic Surgery, Beth Israel Deaconess Medical Center; [8]Faculty of Oral and Dental Medicine, Egyptian Russian University, Cairo, Egypt; [9]Department of Acupuncture & Moxibustion, College of Korean Medicine, Kyung Hee University, Seoul, Korea; [10]University Hospital Basel, Switzerland; [11]Universidad Francisco Marroquín, Guatemala; [12]Molecular Biology Laboratory, Conciencia Clinic, Neuquen, Argentina; [13]University of Pennsylvania, United States.

Abstract

Introduction: *Omega-3 fatty acids are known to improve cardiovascular and metabolic outcomes. While studies have suggested that omega-3 may also enhance sleep quality and regulate melatonin, the data on its efficacy for individuals with poor sleep quality or related disorders must be more consistent. We aim to pave the way for future investigations, ultimately contributing to the clinical management of sleep health.*

Methods: *87 articles were retrieved from MEDLINE and Cochrane databases through a systematic search strategy, and 19 articles from 2002 to 2022 were included. Inclusion criteria encompassed randomized controlled trials (RCTs) and observational studies focused on the impact omega-3 on outcomes related to sleep clinical parameters. Exclusion criteria included preclinical studies and literature reviews.*

Results: *The review identified 19 eligible studies, consisting of 9 RCTs and ten observational studies. The results displayed a complex relationship between omega-3 supplementation and sleep quality, with some studies suggesting positive effects, particularly in specific subpopulations. In contrast, others showed no significant impact or even negative effects on sleep. Among the RCTs, 7 showed positive and promising results in favor of omega-3 supplementation for sleep quality, while 1 RCT indicated the need for further studies, and 1 RCT suggested no benefit of omega-3 on sleep quality. Among observational studies, 7 reported positive and promising outcomes with omega-3 supplementation, 2 indicated no benefit in improving sleep quality, and 1 suggested further studies.*

Conclusion: *Based on the available data, our systematic review found that omega-3 improved sleep quality in 74% of the included clinical research; however, such evidence still needs to be conclusive due to high heterogeneity among study designs. Therefore, well-designed clinical studies are required to confirm this conclusion.*

Introduction

Due to their clinical benefits, Long-chain polyunsaturated fatty acids (LC-PUFA), namely omega-3, constitute a field of scientific interest. A potential application of omega-3 is in the realm of sleep conditions. Improving sleep patterns minimizes the risk of cardiovascular disease (Bertisch et al., 2018) and dysglycemia (Kay et al., 2016) and improves cogni-

*Corresponding author: camila.faria-2023@ppcr.org
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tive function, alertness, and attention (Lee et al., 2015; Louca et al., 2014). Studies have also highlighted that LC-PUFA enhances melatonin regulation and helps sustain the structure of the neuronal membrane (Catalá, 2010; Zhang et al., 1998). Thus, investigators have analyzed the potential benefits of omega-3 supplementation on sleep clinical parameters.

Nonetheless, there is conflicting data on how omega-3 can benefit populations suffering from poor sleep quality or correlated disorders. Daily physiological cycles, which are fundamental for the body's normal function, are regulated by sleep and circadian rhythm. (Vasey et al., 2021). Sleep can be divided into NREM and REM sleep, and NREM can be further divided into three stages - N1, N2, and N3. The cues the body follows to synchronize its rhythm are called zeitgeber, and there are two types: photic and nonphotic. Omega-3 is believed to act as a nonphotic zeitgeber by raising melatonin levels, a known endogenous synchronizer (Checa-Ros & D'Marco, 2022). Moreover, omega-3 has been shown to protect the glymphatic system, which is essential to clean the brain from neurotoxins (Ren et al., 2017).

In this mini-review, our objective is to comprehend the current evidence in the literature regarding the impact of omega-3 on sleep. Furthermore, we aim to pave the way for future investigations, ultimately contributing to the clinical management of sleep health.

Materials and Methods

This study follows the PRISMA guidelines for reporting systematic reviews (Liberati et al., 2009).

Eligibility Criteria

The inclusion criteria were: (1) RCT or observational studies (cohort, cross-sectional studies, surveys, and unspecified studies); (2) oral ingestion of omega-3 through regular diet or supplementation or assessment of LC-PUFA plasma levels; and (3) sleep quality or clinical parameters primary outcomes. The exclusion criteria were (1) literature reviews, (2) preclinical studies, and (3) gray literature. Our population included patients regardless of baseline covariates.

Information Sources and Selection process

This mini-review examined studies published from the date of incorporation on databases up to September 1st, 2023, within the publication interval of 2002 to 2022. The search strategy is specified in Table 1.

Four reviewers independently screened the titles and abstracts of papers obtained after running the search strategy on MEDLINE (PubMed) and Cochrane Library. Publications that fulfilled the inclusion criteria were included for screening. Articles selected after two rounds of screening were included for data extraction and quality assessment.

Data Collection and Items

A standardized data extraction process was designed to retrieve information from each article, including authorship, country, year of publication, study design, number of participants and baseline characteristics, measurement tools of the intervention and control, primary and secondary outcomes, and corresponding results. For randomized clinical trials (RCT), parameters such as sampling method, randomization strategy, blinding procedure, and sample size calculation were also evaluated. The extracted information was transcribed into an Excel spreadsheet and verified by four additional authors. The final version deleted duplicates, and a PRISMA flow diagram was performed in Figure 1.

Risk of Bias Assessment

Paired reviewers assessed the risk of bias of included RCTs using the revised version of the Cochrane Risk of Bias (RoB 2.0) Tool (Higgins et al., 2016) and the observational studies using the Risk Of Bias In Non-randomized Studies - of Exposure (ROBINS-E) tool (Higgins et al., 2023).

Results

Study Selection

Our study identified 87 articles (66 from MEDLINE and 21 from Cochrane). All RCTs retrieved from Cochrane were duplicates. Out of the 66 records screened, 27 were found to be eligible for more detailed review. Of the 27 studies, three were excluded due to wrong exposure/intervention, four due to wrong outcome, and one due to wrong design. Only 19 studies were included in the final review. Study characteristics

Nine RCTs were included (Table 2). We had no restrictions on participants' characteristics, resulting in a varied population, including neonates, children, young adults, and pregnant women. All studies used convenience sampling methods. Interventions included omega-3 as external dietary supplements containing either DHA or EPA - the two most important forms of omega-3 fatty acids - except one in which authors decided to administer omega-3 through fish intake. Matched placebo compounds were used to allow proper blinding in some of the studies with

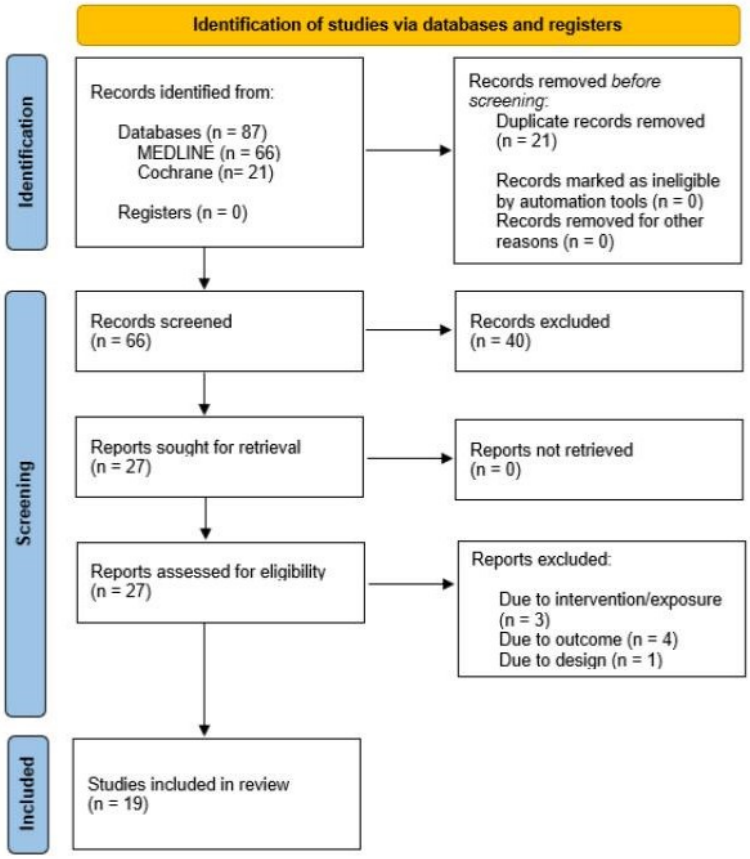

Figure 1: *PRISMA flow diagram.*

	#3 #1 AND #2
PubMed (n= 66)	#1 "Fatty Acids, Omega-3"[Mesh]
	#2 "Sleep"[Mesh] OR "Sleep Medicine Specialty"[Mesh] OR "Sleep Phase Chronotherapy"[Mesh] OR "Sleep Wake Disorders"[Mesh] OR "Sleep Apnea Syndromes"[Mesh] OR "Sleep Aids, Pharmaceutical"[Mesh] OR "Polysomnography"[Mesh]
	#10 #9 AND #8
	#1 Mesh Descriptor: [Sleep] explode all trees
	#2 Mesh Descriptor: [Sleep Medicine Specialty] explode all trees
	#3 Mesh Descriptor: [Sleep Phase Chronotherapy] explode all trees
Cochrane Library (n= 21)	#4 Mesh Descriptor: [Sleep Wake Disorders] explode all trees
	#5 Mesh Descriptor: [Sleep Apnea Syndrome] explode all trees
	#6 Mesh Descriptor: [Sleep Aids, Pharmaceutical] explode all trees
	#7 Mesh Descriptor: [Polysomnography] explode all trees
	#8 Mesh Descriptor: [Fatty acids, Omega 3] explode all trees
	#9 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7

Table 1: *Search strategies.*

inactive compounds, except one that assessed the supplement's effect on sleep and pruritus and administered an active standard treatment. The remaining placebo elements included corn oil or refined olive oil. The duration of the RCTs varied from 12 weeks to 12 months, and the frequency of administration varied among them. Five studies used objective sleep measures, such as actigraphy, pressure-sensitive mattresses, and Sleep State Test. Four used questionnaires, such as the Child Sleep Habits Questionnaire, Brief Infant Sleep Questionnaire, and sleep diaries, to gather subjective data on sleep patterns. One of the studies assessed infant sleep patterns after the mother consumed a DHA-containing diet – all the other studies measured sleep patterns from the supplemented participants.

The studies which corresponded to observational designs (Table 3) included cohort studies (n = 2), cross-sectional studies (n = 4), surveys (n = 1) and unspecified studies (n = 3). They mainly assessed the dietary patterns using subjective sleep quality scales, including self-reported questionnaires, previously diagnosed sleep disorders, and other objective scales, including the apnea-hypopnea index or objective evaluations, such as those provided by actigraphy. All participants in these studies were over 18 years old except for two studies in which pregnant women were the subjects of the intervention, and the outcome was evaluated in the neonate, demonstrating an adverse effect of the supplement on their future sleep pattern (Sugimori et al., 2022, Cheruku et al., 2022). Many studies proved no retrospective significance between the intervention and improving sleep quality (Zhang et al., 2022; Titus et al., 2017). One of them even found omega three's statistically significant negative effect on sleep disorders (Lui et al., 2021). The remaining studies showed an overall positive association between omega-3 and sleep behavior (Jansen et al., 2020; Murphy et al., 2021; Christian et al., 2016; Jackson et al., 2020; Liu et al., 2022).

Risk of Bias in Studies

According to Cochrane's RoB 2.0, five clinical trials have a low risk of bias, one has some concerns about the risk of bias, and three have a high risk of bias. Studies by (Judge et al., 2012), (Hansen et al., 2014), and (Montgomery et al., 2014) raised some bias concerns as no information about allocation concealment was reported. Also, the studies by (Judge et al., 2012, Hansen et al., 2014 and Pantan et al., 2021) were assessed as having some bias concerns since we could not find any protocols to compare them with the reported results. Furthermore, the studies by (Hansen et al., 2014) and (Montgomery et al., 2014) did not report any information about the blinding process, raising some concerns of bias in the second domain (Bias due to deviations from the intended interventions); additionally, not all participants completed the study of (Hansen et al., 2014) and handled such attrition using an "As treated analysis," which raised further concerns in the third domain (Bias due to missing outcome data).

According to the ROBINS-E, two observational studies have a low risk of bias, six studies have some concerns about discrimination, and two studies have a high risk of bias. All studies, except for (Christian et al., 2016) and (Jansen et al., 2020), have some bias ranging from some concerns (six studies) to very high (one study) in the fifth domain due to inappropriate handling of missing data. The studies by (Christian et al., 2016), (Luo et al., 2021), (Murphy et al., 2021), (Sugimori et al., 2022), and (Zhang et al., 2022) were assessed as some concerns of bias in the third domain due to inappropriate selection of participants into research. The studies by (Luo et al., 2021), (Cheruku et al., 2022), (Liu et al., 2022), and (Zhang et al., 2022) assessed some concerns of bias and (Murphy et al., 2021) as a high-risk in the sixth domain due to discrimination arising from the outcome measurement. Figures 2 and 3 summarize the risk of bias assessment.

Results of Individual Studies and Syntheses

A positive association between omega three and most sleep parameters analyzed was observed in most studies, as shown in Tables 2 and Table 3. However, we observed a negative relationship between the supplement and total sleep disturbance score in the pediatric population. When analyzing neonates, differences between the supplements and placebo were insignificant except in specific subgroups, including males. The remaining adult population shows overall homogeneous results. Judge et al. showed significant differences in sleep quality, including arousals, compared to placebo (on D1 (P=0.006) and D2 (P=0.011). Other studies in similar populations showed similar results regarding sleep quality in subjective (Heydarbaki et al., 2021; Yokoi et al., 2022) and objective study parameters (Patan et al., 2021). Nevertheless, other authors have observed discrepancies among the objective parameters, like actigraphy, used to assess sleep patterns after similar interventions (Hansen et al., 2014), as seen in Table 2.

Figure 2: *Risk of bias assessment for randomized controlled trials*

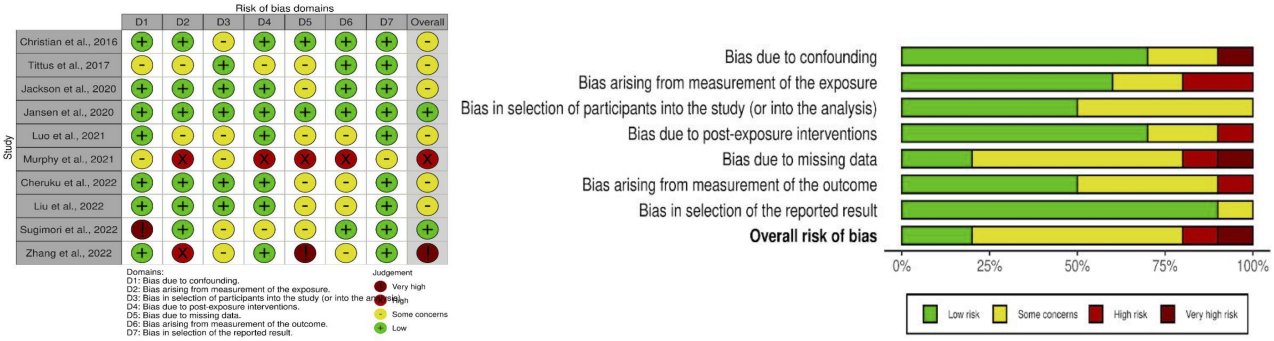

Figure 3: *Risk of bias assessment for observational studies.*

Study Country	Participants		Setting		Intervention	Control	Regimen	Follow-up	Outcome measurement	Results	Conclusions	Funding
	Population	Age	Sample size	Design (location)								
Judge et al., 2012 USA	Healthy pregnant women at 20-week gestation	(18 - 35) 24 years	48	RCT-Pa (Large urban hospital and affiliated private physicians)	Cereal-based functional food (92 kcal) containing 300 mg DHA.	Placebo	(5 d/week)	14 to 16 weeks	Infant sleep/wake states were measured on postnatal days 1 (D1) and 2 (D2) using a pressure sensitive mattress recording respiration and body movements.	Compared to placebo, the DHA intervention significantly reduced arousals in quiet sleep on D1 (P=0.006) and D2 (P=0.011), and arousals in active sleep on D1 (P=0.012).	The infant sleep organization has benefited from DHA-containing functional diet.	Funded by Government/University grant.
Hansen et al., 2014 Norway	Male adults	21-60	95	RCT-Pa (Secure forensic inpatient facility)	Salmon fish (portion size 150-300 g)	meat (e.g., chicken, pork, beef) meals	(3d/week)	6 months	Sleep latency, sleep efficiency, actual wake time, total sleep time, measured by actigraphy, HRV, measured by *Actiheart*, vitamin D status and EPA+DHA, measured in serum.	* Increase in sleep latency in the Control group (p = 0.04; d = 0.60). * Sleep efficiency significantly decreased in both groups (Control group p < 0.001; d = 0.91 and Fish group, p = 0.01; d = 0.36). * Fish group reported better daily functioning than the Control group during post-test (p = 0.03; d = 0.65).	Fish consumption seemed to have a positive impact on both sleep and daily functioning.	Funded by Government/University grant.
Hall et al., 2013 UK	Male and female	45-70	367	RCT	n-PUFA at 3 doses: 0.45 g/day, 0.9 g/day, 1.8 g/day	Placebo (olive oil)	Different groups that received different doses daily	12 months	Heart interbeat interval, and time and frequency domain heart rate variability.	Omega-3 supplementation was associated with increased periods of very low heart frequencies and increased variability in heart rate during sleep.	Further studies warranted for prognostic meaning in the general population.	Funded by Food/ Pharmaceutical companies.
Montgomery et al., 2014 UK	Healthy children	(7 - 9) years	362	RCT-Pa (Mainstream UK schools)	algal DHA supplementation (600 mg day1)	Placebo (corn/soybean oil)	Three 500-mg capsules/day	16 weeks	*Subjective sleep; measured by Child Sleep Habits Questionnaire (CSHQ). *Objective Sleep; measured by actigraphy and sleep diaries.	*Subjective sleep improved slightly but not significantly in both groups for all CSHQ subscales except one (sleep duration). *Actigraphy findings revealed that children receiving active treatment experienced an increase in total sleep time of 58 minutes compared to controls, which significantly reduced wake episodes.	Based on parents-reporting, higher DHA levels in the blood may be associated to better child sleep.	Funded by Food/ Pharmaceutical companies.
Jahangard et al., 2018 Iran	Male and female who suffered with major depression	18-65	50	RCT	Omega-3 PUFA 1 g/day + Sertralin	Sertralin	Sertralin and Omega-3 PUFA daily	12 weeks	Insomnia Severity Index (ISI), Anxiety Sensitivity Index-3, Intolerance of Uncertainty Scale, Emotionale Kompetenz-Fragebogen inventory, Montgomery-Asberg Depression Rating Scale, Beck Depression Inventory.	Patients with major depressive disorders and treated with adjuvant omega-3 improved symptoms of depression, sleep, anxiety traits and above at higher rates than with sertraline alone.	Omega -3 improved sleep on patients suffering from depression.	Not funded.
Boone et al., 2019 USA	Infants who who were born at less than 35 completed weeks' gestation	(10 - 16) months	377	RCT-Pa (Nationwide Children'sHos pital)	DHA (200mg) + AA (200mg) supplementation	Placebo (400mg corn oil)	400 mg/day	180 days	*Depressive symptomatology, measured by caregivers-reported questionnaire (Center for Epidemiologic Studies Depression Scale). *Child's sleep, measured by caregivers-reported questionnaire (Brief Infant Sleep Questionnaire).	There were statistically significant differences between DHA+AA and placebo groups for the entire cohort as well as for the binary sleep characteristics (nighttime waking episodes, falling asleep while being held or rocked, short sleep duration, or caregiver-reported sleep problems).	DHA+AA supplementation had no beneficial impact on child sleep.	Funded by Government/University grant.
Heydarbaki et al., 2021 Iran	Adult hemodialysis patients with uremic pruritus	61.34 years	52	RCT-CO (Dialysis Center at a Medical University)	Omega-3 (1g) + Cetirizine (5g)	Cetirizine (5g)	Mode A: omega-3 [3 times/day] + cetirizine [3 d/week] Mode B: cetirizine [3 d/week]	6 weeks	*Sleep quality, measured by the Pittsburgh Sleep Quality Index (PSQI). *Itching severity, measured by the Yosipovitch Itch Questionnaire.	Sleep quality improved in both interventions (sleep score<5), but more significantly with omega-3 + cetirizine.	Omega-3 supplement has a beneficial effect in improving the sleep quality in hemodialysis patients.	Not funded.
Patan et al., 2021 UK	Healthy adults who habitually consumed low amounts of oily fish	(25 - 49) years	84	RCT-Pa (NR)	G1: DHA-rich (900 mg DHA) G2: EPA-rich (360mg DHA + 900mg EPA)	Placebo [1 g refined olive oil]	One capsule/day	26 weeks	*Subjective sleep, measured by the LSEQ questionnaire. *Objective Sleep; measured by actigraphy and sleep diaries.	Actigraphy results revealed that participants receiving DHA-rich oil experienced improvements in sleep efficiency (p = 0.030) and latency (p = 0.026) compared to placebo; however, they felt less energetic (p = 0.041) and rested (p = 0.017) compared to the placebo, and they felt less ready to perform (p = 0.075) compared to those getting EPA-rich oil.	Supplements containing n-3 PUFAs (especially DHA) have a beneficial effect in improving sleep quality through increasing sleep efficiency and decreasing sleep latency in healthy normal sleepers.	Funded by Food/ Pharmaceutical companies.
Yokoi-Shimizu et al., 2022 Japan	Healthy adults aged _ 45 years with poor sleep quality	(46 – 58) years	66	RCT-Pa	Six 480 mg capsules of DHA/EPA containing refined fish oil (DHA: 576 mg; EPA: 284 mg)	Placebo [corn oil without DHA and EPA]	Six capsules/ day	12 weeks	* Subjective sleep quality, measured by OSA-MA, POMS2. * Objective sleep, measured by Sleep State Test.	* Score of factor III (frequent dreaming) was significantly higher than that in the placebo group (p = 0.043). * POMS2, no significantly different between the two groups. * Sleep efficiency score was significantly higher than that in the placebo group (p = 0.018).	DHA/EPA supplementation can improve sleep quality in middle- and old-aged adults with poor sleep quality.	Funded by Nippon Suisan Kaisha, Ltd.

RCT, Randomized Clinical Trial; **Pa,** Parallel design; **CO**, cross-over design; **DHA,** docosahexaenoic acid; **EPA,** Eicosa Pentaenoic Acid; **AA,** Arachidonic Acid; **OSA-MA,** Oguri-Shirakawa-Azumi sleep inventory MA version; **POMS2,** Profile of Mood States 2nd version; **HRV,** Heart Rate Variability

Table 2: *Main characteristics of included clinical trials.*

Study	Participants		Setting		Exposure / Comparator	Outcome measurement	Results/Conclusions
Country	Population	Age	Sample size	Study design			
Zhang Y 2012 USA	Men and women from longitudinal Coronary Artery Risk Development in Young Adults	25 ± 3.6 years	3,964	Cohort Study	Intake of long-chain omega-3 polyunsaturated fatty acids (LCω3PUFA)	Self-reported measures of sleep quality	No significant associations between the intake of long-chain omega-3 polyunsaturated fatty acids (LCω3PUFA) and either sleep quality or sleep duration.
Sugimori et al., 2022 Japan	Pregnant women in the first trimester	25 – 36 years	87,337	Cohort Study	Dietary consumption of fish and total n-3 PUFAs was determined using the Food Frequency Questionnaire (FFQ) in mid-late pregnancy	Mothers were asked on the FFQ to indicate if their infants slept on the previous day, by drawing lines through boxes indicating 30-min intervals from 12:00 to 12:00 am the next day.	Low fish intake during pregnancy may increase the risk of infants sleeping less than lower limit of the recommended sleep duration of 11 hours at 1 year of age (adjusted odds ratio < 0.001)
Jansen et al., 2020 USA	Adolescents with low- to middle-income	14.2 ±2.1 years	405	Cross-sectional Study	Categorized DHA and AA plasma concentrations into quartiles (Q1–Q4; Q4 = highest fatty acids).	Sleep midpoint and duration were assessed with 7-d wrist actigraphy.	Higher plasma DHA was linearly associated with longer sleep duration on the weekends (95% CI: 7, 57; P trend = 0.005) and with earlier sleep timing during weekdays and weekends. The largest difference was a 0.75-h (45-min) later sleep midpoint in Q2 compared with Q4 (95% CI: 0.36, 1.14).
Tittus et al., 2017 Germany	NR	28 – 92 years	315	Cross-sectional Study	Fish oil supplement.	Apnea-hypopnea index	No correlation between omega-3 index and severity of OSA [fish oil supplement analysis with p = 0.10 and in the fish meals per month analysis with p-value = 0.68].
Luo et al., 2021 USA	Civilian non-institutionalized US population	Over 18 years	18,31	Cross-sectional Study	Dietary ω-3 and ω-6 fatty acids consumption was assessed by two 24 h dietary recall interviews.	Parameter evaluating sleep disorder and duration was defined according to the self-reported doctor-diagnosis.	ω-6 consumption and the ω-6:ω-3 ratio are positively associated with the risk of sleep disorders (odds ratio 1.30 (CI: 1.04-1.62) and 1.36 (CI: 1.08-1.70) respectively), while the negative association between ω-3 fatty acids and sleep disorders may exist only in men (OR: 0.68 with CI95% of 0.49-0.95)
Murphy et al., 2021 USA	Civilian non-institutionalized US population	Over 18 years	1314	Cross-sectional Study	Serum LC omega-3 fatty acid levels	Sleep duration, difficulty falling asleep, sleep disorder	Positive association between omega-3 fatty acid levels and healthy sleep.
Cheruku et al., 2022 USA	Women at parturition	24 – 29 years	17	Observational Study	Maternal venous blood samples were collected at delivery and maternal plasma phospholipid fatty acid concentrations were measured. Maternal plasma phospholipid DHA concentrations were categorized into high DHA (> 3.0% by weight of total fatty acids) and low DHA (≤ 3.0% by weight of total fatty acids) groups.	Newborn sleep recordings were obtained using a pressure-sensitive pad under the infants' bedding on postpartum day 1 (P1) and day 2 (P2). Sleep states assessment included quiet sleep (QS), active sleep (AS), sleep-wake transition, wakefulness, and time spent out of the crib, as percentages of total sleep time.	Infants born to mothers with higher plasma phospholipid DHA had significantly lower ratios of AS to QS, less AS, and less sleep-wake transition. Maternal ratios of n-6 to n-3 fatty acids were associated with different sleep states in infants. Quiet sleep 0.06; active sleep 0.004 transition 0,12; wakefulness 0,06
Christian et al., 2016 USA	Pregnant women in the 2nd trimester with lower socioeconomic backgrounds	24 years	135	Observational Study	Measurement of Red Blood Cell polyunsaturated fatty acids (PUFA). PUFA included DHA, EPA and AAA.	Sleep quality was measured by PSQI as a continuous variable.	A linear regression showed longer sleep duration (p = 0.019), and better sleep efficiency (p = 0.047). Only DHA was statistically significant.
Jackson et al., 2020 England	University staff and students	25 – 44 years	21	Observational Study	No restriction in meals or sleep behavior	EPA and DHA were measured in plasma samples collected every two hours from 22:00 until 22:00 the following day, with all meals being provided at conventional times with no restrictions or additional supplementation and normal sleep patterns.	A significant diurnal variation in the pooled plasma concentrations of both fatty acids was detected. The timing of the peak concentration of DHA was 17:43 with a corresponding nadir at 05:43.
Liu et al., 2022 USA	Civilian non-institutionalized US population	Over 18 years	17,771	Survey	Dietary intake of ALA (α-linolenic acid) was obtained through two 24 h dietary recalls	Sleep duration was based on the respondents' answers to the following question: "How much sleep do you usually get at night on weekdays or workdays?" They were further divided into very short (<5 h), short (5–7 h), normal (7–9 h), and long (≥9 h) sleep duration	Compared with the first tertile, the ORs of very short sleep and the corresponding 95% CIs for the second and the third tertile of dietary ALA intake in males were 0.618 (0.612, 0.624) and 0.544 (0.538, 0.551), respectively, and in females were 0.575 (0.612, 0.624) and 0.432 (0.427, 0.437). The risk of a very short sleep duration was negatively related to the dietary intake of ALA

Table 3: *Main characteristics of included observational studies.*

Discussion

This review investigated the effect of omega-3 supplementation on sleep by summarizing the results in the literature. Nineteen studies, among RCT and observational studies, were analyzed with diverse outcomes. Thirteen studies demonstrated positive results for Omega-3 on sleep, 8 RCTs, and five observational studies. The other six studies indicate no or even a negative effect.

In RCT studies, five used objective and subjective sleep measures to gather information on sleep patterns. Five studies employed a placebo-controlled and blinded design, which could have helped reduce the placebo effect and ensure more objective results, even more so considering some of the measures were self-reported.

Studies involved participants of different ages, including one that evaluated infants in the first 48 postnatal hours, two that included children, three that included adults, and one that considered older adults. Further studies are necessary to corroborate specific subpopulations with appropriate omega-3 targets.

Regarding interventions, five studies administered DHA, while one combined DHA and EPA supplementation. A different research administered a combination of DHA and arachidonic acid (AA), an omega-6 fatty acid. A contrasting approach was used in one of the studies since investigators studied the effects of consuming fatty fish, a natural source of omega-3.

(Judge et al., 2012) suggests DHA intake during pregnancy might benefit infant sleep patterns. (Montgomery et al., 2014) in children aged 7-9 years, DHA supplementation did not significantly affect subjective sleep measures but showed a positive effect on objective criteria in a small subgroup. (Boone et al., 2019) also showed positive results while analyzing since they concluded toddlers born preterm did not show significant differences in sleep patterns overall with DHA and AA supplementation, but there were improvements in specific subgroups. These subgroups involved male children and children of caregivers with depressive symptoms in the intervention group. In (Heydarbaki et al., 2021), omega-3 supplementation improved sleep quality in hemodialysis patients. In the study by (Patan et al., 2021), DHA-rich oil improved sleep efficiency and reduced sleep latency in healthy adults (although participants reported feeling less energetic). (Yokoi-Shimizu et al., 2022) Also, positive results were found in older adults since DHA and EPA supplementation improved sleep quality in these individuals. This improvement might be explained again by the effect omega-3 in increasing the melatonin level in those patients and be particularly important in the elderly since melatonin levels decrease with age (Godfrey et al., 2022). In (Hansen et al.'s 2014) study – which did not use supplementation - fish consumption positively impacted sleep and daily functioning in male forensic patients.

The study designs took into account confounders such as age. (Kay et al., 2016) carried out the trials with matching age, sex, and race. The statistical analyses adjusted for age differences using linear regression (Ebbesson S.O. et al., 2005) or propensity scores (Bertisch et al., 2018). Normality was attested using Kolmogorov Smirnov or Shapiro Wilks test if parametric methods were used. Other studies used non-parametric methods to compare baseline characteristics, including age, sex, and race. However, the statistical power should have been reported. Differences in baseline characteristics explain mixed results. However, positive effects of omega-3 supplementation on sleep quality, especially in specific subgroups, were found. The significant heterogeneity of response to supplementation, especially in the pediatric population, could be explained by the difference in outcome measurements, as the answer was assessed using self-reported outcomes via questionnaires, diaries, or objective measures that could limit the results' pooling and generalizability.

Limitations we found in our mini-review include the heterogeneous population and outcomes measurements, jeopardizing statistical analysis of the results. Future research could benefit from focusing on omega-3 regimens and specific population strata that could take more advantage of supplementation, such as those with a low omega-3 index. Future research on omega-3 impact on sleep quality should be designed as RCTs focused on determining efficacious regimens and exploring population groups that possibly benefited from the intervention.

Conclusion

This literature review corroborates that the impact of omega-3 on sleep still needs to be conclusive despite several findings pointing towards the clinical benefits of optimized ingestion of this compound. Therefore, additional studies are warranted to investigate benefits further, clarify beneficiary populations, and recommend regimens for potential clinical application.

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Conflicts of Interest

The authors declare no conflict of interest.

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