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Posted Date: 13 January 2026

doi: 10.20944/preprints202601.0891.v1

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Can Krill Oil Help Knee Osteoarthritis? A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Abstract

Background. Knee osteoarthritis is a prevalent degenerative joint disease associated with pain, functional limitation, and reduced quality of life. Krill oil, a marine-derived source of omega-3 fatty acids with antioxidant properties, has been explored as a potential adjunctive intervention. This systematic review and meta-analysis evaluated the efficacy and safety of krill oil supplementation in knee osteoarthritis. **Methods.** A systematic review and meta-analysis of randomized controlled trials was conducted using multiple electronic databases. Adults with clinically or radiographically diagnosed knee osteoarthritis were included. Outcomes included knee pain, physical function, stiffness, biomarkers, and adverse events. Meta-analyses were performed using a random-effects model. **Results.** Three randomized controlled trials involving 597 participants were included. Krill oil supplementation showed numerical improvements and favorable trends in WOMAC-assessed pain, stiffness, and physical function, but these effects did not consistently reach statistical significance. No significant differences were observed for Visual Analog Scale–assessed pain or systemic biomarkers. Adverse event rates were comparable between groups and were predominantly mild gastrointestinal symptoms. **Conclusion.** Krill oil has been investigated as a potential adjunctive approach for knee osteoarthritis, with limited evidence suggesting possible short-term benefits in patient-reported outcomes.

Keywords: Krill oil; knee osteoarthritis; omega-3 fatty acids; WOMAC; randomized controlled trials; systematic review; meta-analysis; safety

1. Introduction

Knee osteoarthritis (OA) is a prevalent degenerative joint disorder and a leading cause of chronic pain, functional limitation, and disability worldwide [1–4]. Recent global estimates indicate that osteoarthritis affects more than 650 million individuals aged 40 years and older, with the knee being the most commonly involved joint [5,6]. The burden of Knee OA continues to increase due to population ageing, rising obesity rates, and longer life expectancy, resulting in substantial socioeconomic and healthcare impacts [5,7].

Current management of Knee OA primarily focuses on symptom relief rather than disease modification. Pharmacological treatments such as nonsteroidal anti-inflammatory drugs and corticosteroids may reduce pain in the short term but do not halt disease progression and are associated with gastrointestinal, renal, and cardiovascular adverse effects when used long term [8–

 doi:10.20944/preprints202601.0891.v1

12]. These limitations have driven interest in adjunctive and non-pharmacological interventions that may offer symptom improvement with a more favourable safety profile [4,9].

Marine-derived omega-3 fatty acids have been widely investigated for their anti-inflammatory properties and potential benefits in musculoskeletal disorders [13–17]. Krill oil, derived from Antarctic krill (*Euphausia superba*), represents a distinct source of omega-3 fatty acids in which eicosapentaenoic acid and docosahexaenoic acid are predominantly bound to phospholipids, potentially enhancing bioavailability compared with conventional fish oil [18–22]. In addition, krill oil contains astaxanthin, a potent antioxidant that may mitigate oxidative stress, a key contributor to osteoarthritis pathophysiology [23–25].

Several randomized controlled trials have evaluated krill oil supplementation in knee pain [26–28] and knee osteoarthritis [19,29,30], but their findings have been inconsistent. Moreover, previous systematic reviews and meta-analyses have reported conflicting conclusions, partly due to heterogeneous study populations and inclusion of non-specific knee pain conditions rather than clinically defined Knee OA [31,32]. Therefore, an updated and focused systematic review and meta-analysis restricted to randomized controlled trials enrolling patients with clinically diagnosed knee osteoarthritis is warranted to clarify the efficacy and safety of krill oil supplementation in this population.

2. Materials and Methods

This systematic review and meta-analysis of randomized controlled trials (RCTs) was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [33]. The study protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD420251012831.

2.1. Eligibility Criteria

Studies were eligible if they met the following criteria: (1) population: adults (≥18 years) with clinically or radiographically diagnosed knee osteoarthritis; (2) intervention: oral krill oil supplementation at any dose or duration; (3) comparison: placebo, no intervention, or standard care; (4) primary outcome: knee pain; and (5) secondary outcomes: physical function, stiffness, high-sensitivity C-reactive protein (hs-CRP), lipid profile parameters, and adverse events. Only randomized controlled trials were included. No restrictions were applied with respect to language or publication status.

2.2. Information Sources and Search Strategy

A comprehensive literature search was conducted in PubMed, the Cochrane Library, Scopus, Google Scholar, ScienceDirect, ProQuest, and EBSCOhost from inception to November 28, 2025. Additional searches were performed in ClinicalTrials.gov and the World Health Organization International Clinical Trials Registry Platform (ICTRP) to identify unpublished or ongoing trials. The search strategy combined Medical Subject Headings (MeSH) and free-text terms related to “knee osteoarthritis” and “krill oil”. The full search strategy for all databases is provided in Supplementary Table S1.

2.3. Study Selection and Data Extraction

Two reviewers independently screened titles, abstracts, and full-text articles to determine eligibility. Disagreements were resolved through discussion, with consultation of a third reviewer when necessary. Data extraction was performed independently using a standardized data collection form. Extracted data included study characteristics, country, sample size, participant demographics, diagnostic criteria, intervention dose and duration, comparator, outcome measures, and reported results.

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2.4. Outcomes

The primary outcome was change in knee pain from baseline, assessed using validated pain scales (Huskisson). Secondary outcomes included changes in physical function and stiffness, inflammatory biomarkers (hs-CRP), lipid profile parameters, and the incidence of adverse events. Functional outcomes were assessed using disease-specific instruments validated for osteoarthritis populations [34]. Planned subgroup or sensitivity analyses based on krill oil dosage or treatment duration were not conducted due to the limited number of eligible studies.

2.5. Risk of Bias Assessment

The risk of bias of included studies was assessed independently by two reviewers using the Cochrane Risk of Bias 2.0 tool [35], which evaluates bias across five domains: the randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of the reported result. Any disagreements were resolved by consensus.

2.6. Statistical Analysis

Meta-analyses were performed using Review Manager (RevMan) version 5.4. Continuous outcomes were pooled using mean differences (MD) or standardized mean differences (SMD), as appropriate, while dichotomous outcomes were summarized using risk ratios (RR), each with corresponding 95% confidence intervals (CIs). A random-effects model was applied to account for anticipated clinical and methodological heterogeneity [36]. Statistical heterogeneity was assessed using the I^2 statistic [37], with values greater than 50% indicating substantial heterogeneity. Formal assessment of publication bias was not performed due to the small number of included studies.

3. Results

This section may be divided by subheadings. It should provide a concise and precise description of the experimental results, their interpretation as well as the experimental conclusions that can be drawn.

3.1. Study Selection and Characteristics

The study selection process is illustrated in Figure 1. Following a comprehensive literature search and screening process, three randomized controlled trials met the predefined eligibility criteria and were included in the final meta-analysis [19,29,30]. The included studies were conducted in Australia and South Korea and collectively enrolled a total of 597 participants. Of these, 267 participants received krill oil supplementation, while 330 participants were allocated to placebo groups.

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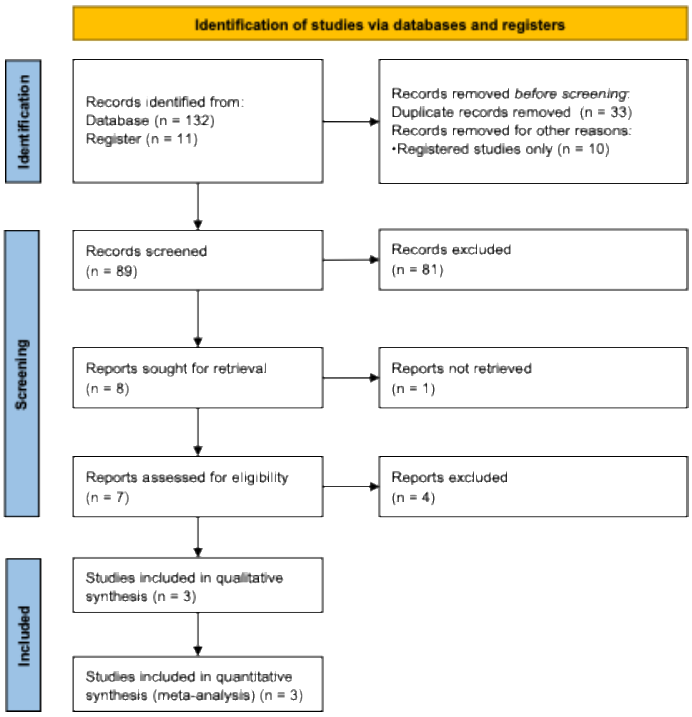

Figure 1. PRISMA flow diagram of study screening and selection.

The daily dose of krill oil ranged from 1 to 4 g, and treatment durations varied between 12 and 24 weeks [19,29,30]. In two trials, krill oil was administered in combination with additional active components, including astaxanthin and hyaluronic acid [19,29]. Control groups received placebo capsules containing mixed vegetable oils or other inert substances matched in appearance. Detailed characteristics of the included studies are summarized in Table 1.

Table 1. Characteristics of included studies.

Study	Location	Study Design	Inclusion Criteria	Treatment		Duration
				Intervention	Control	
Laslett et al., 2024	Australia	RCT double blind	Patients aged ≥40 yr with ACR criteria for osteoarthritis of the knee, significant knee pain and synovial inflammation	Krill Oil (2 g in two soft gels) supplying 350 mg of omega-3 and 12 mg/g of omega 6, daily	Placebo (two soft gels of vegetable oils), daily	24 weeks
Hill et al., 2023	South Korea	RCT double blind	Korean men and women between 30 and 75 yr of age with mild knee osteoarthritis	Krill Oil (321 mg) with astaxanthin (2 mg) and Hyaluronic acid (30 mg), one capsule daily	Placebo (containing pal, olive, soybean oil and beeswax), one capsule daily	12 weeks
Stonehouse et al., 2022	Australia	RCT double blind	Healthy adults (n = 235, 40–65 yr, BMI > 18.5 to < 35 kg/m²) with a clinical diagnosis of mild-to-moderate knee OA, regular knee pain	Krill Oil (4 g in four soft gelatine capsules) providing a total of 0.6 g/d EPA+0.28 g DHA and 0.45 g astaxanthin, daily	Placebo (4 g in four capsules of vegetable oils), daily	24 weeks

Abbreviations: RCT, randomized controlled trial; ACR, American College of Rheumatology; OA, osteoarthritis; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; BMI, body mass index.
Note: Krill oil formulations and dosages varied across studies, and intervention duration ranged from 12 to 24 weeks.

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3.2. Risk of Bias Assessment

The risk of bias of the included randomized controlled trials was assessed using the Cochrane Risk of Bias 2.0 tool. Overall, all three studies were judged to have some concerns regarding risk of bias [19,29,30]. Uncertainty was primarily related to the randomization process, as methods for sequence generation and allocation concealment were not fully described in some trials. Bias due to deviations from intended interventions, missing outcome data, and outcome measurement was generally assessed as low. Concerns regarding selective reporting were noted for some secondary outcomes. A detailed summary of the risk of bias assessment across all domains is presented in Supplementary Figure S1.

3.3. Study Selection and Characteristics

Knee pain was the primary outcome and was assessed using both the Visual Analog Scale (VAS) and the WOMAC pain subscale. Two randomized controlled trials reported VAS pain outcomes [19,30]. Pooled analysis showed no statistically significant difference between krill oil supplementation and placebo (mean difference [MD] −4.78; 95% confidence interval [CI] −15.06 to 5.50; Figure 2), with substantial heterogeneity observed across studies.

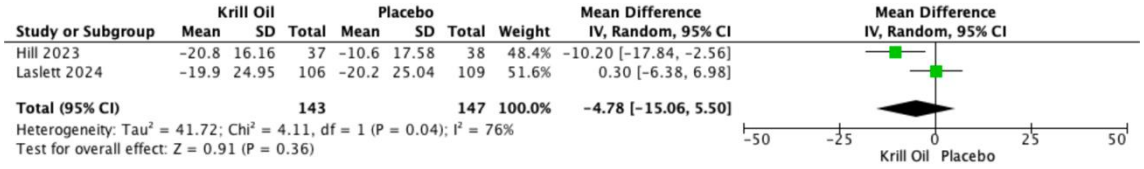

Figure 2. Forest Plot of Pain-VAS.

All three trials reported WOMAC pain outcomes [19,29,30]. Meta-analysis demonstrated a reduction in WOMAC-assessed knee pain favoring krill oil supplementation; however, this effect did not reach statistical significance (MD −13.03; 95% CI −28.22 to 2.16; Figure 3). Considerable heterogeneity was observed among studies.

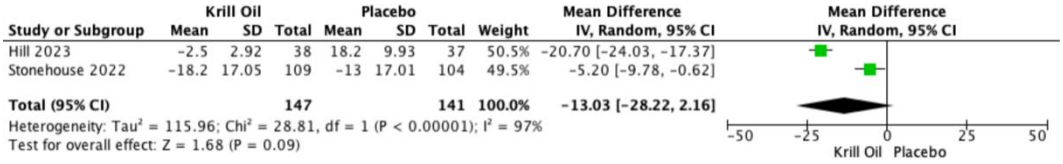

Figure 3. Forest Plot of WOMAC Knee Pain.

Pooled analyses also showed reductions in WOMAC-assessed joint stiffness (MD −2.60; 95% CI −7.68 to 2.48; Figure 4) and physical function (MD 1.79; 95% CI −18.05 to 21.63; Figure 5). These differences were not statistically significant, and substantial heterogeneity was observed for both outcomes.

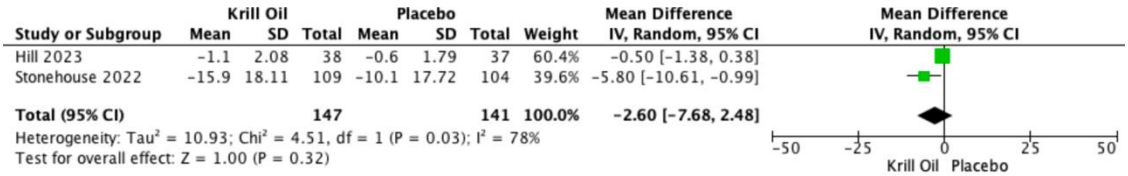

Figure 4. Forest Plot of WOMAC Knee Stiffness.

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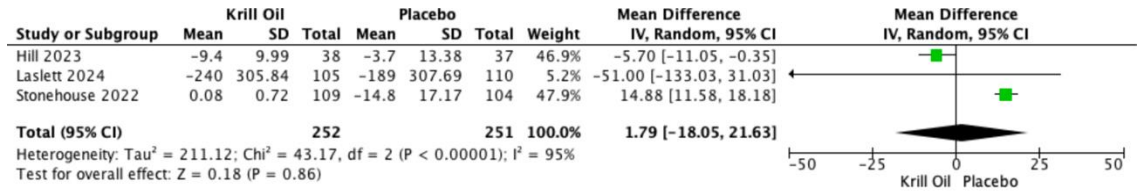

Figure 5. Forest Plot of WOMAC Knee Function.

3.4. Study Selection and Characteristics

Two studies reported outcomes related to inflammatory and cardiometabolic biomarkers, including high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides, and high-sensitivity C-reactive protein (hs-CRP) [19,29]. Pooled analyses demonstrated no statistically significant differences between krill oil supplementation and placebo for any of these biomarkers. Effect estimates were generally close to the null, and heterogeneity across studies ranged from low to moderate. Forest plots for these secondary outcomes are presented in Supplementary Figures S2–S5.

3.5. Study Selection and Characteristics

All included randomized controlled trials reported adverse events associated with krill oil supplementation [19,29,30]. Pooled analysis of overall adverse events showed no statistically significant difference between the krill oil and placebo groups (odds ratio [OR] 1.23; 95% confidence interval [CI] 0.52 to 2.89), with no observed heterogeneity (I^2 = 0%). Analysis of gastrointestinal adverse events also demonstrated no statistically significant difference between groups (OR 0.75; 95% CI 0.51 to 1.09), with low heterogeneity (I^2 = 29%). Reported adverse events were predominantly mild gastrointestinal symptoms, such as bloating or dyspepsia. No serious adverse events attributable to krill oil were reported across the included studies. Forest plots summarizing overall and gastrointestinal adverse events are presented in Supplementary Figures S6 and S7.

4. Discussion

This systematic review and meta-analysis suggests that krill oil supplementation has been investigated as a potential adjunctive intervention for knee osteoarthritis, with overall trends toward improvement in patient-reported outcomes [19,29,30]. In contrast, pain assessed using the Visual Analog Scale did not show a statistically significant reduction, which is consistent with findings from individual randomized controlled trials reporting VAS outcomes [19,30]. Across studies, physical function outcomes showed numerically favorable trends, although these did not reach statistical significance, suggesting that any potential effects may be modest and variable [19,31,32].

The discrepancy between WOMAC- and VAS-based pain outcomes may reflect differences in measurement sensitivity, construct validity, or timing of assessment, as well as limited statistical power due to the small number of trials reporting VAS outcomes [31,32,34,38]. WOMAC is a multidimensional, disease-specific instrument that captures pain in functional contexts, whereas VAS represents a unidimensional measure of pain intensity, which may be less sensitive to change in chronic conditions such as knee osteoarthritis [32,34]. These methodological differences may partially explain why numerical reductions were observed for WOMAC-based outcomes but not consistently reflected in VAS-assessed pain.

Our findings partially align with those of previous meta-analyses. Pimentel et al. [31], reported that krill oil supplementation did not significantly improve knee pain or stiffness but demonstrated a small benefit in physical function, while Meng et al.[32], reported statistically significant improvements in WOMAC-based outcomes but not in VAS-measured pain, the present study was restricted to randomized controlled trials enrolling patients with clinically defined knee osteoarthritis and excluded heterogeneous knee pain populations, which may have included individuals without structural joint disease. This stricter inclusion criterion may have reduced clinical heterogeneity and

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improved the interpretability of pooled estimates, albeit at the cost of a smaller number of eligible studies.[3,6]

The observed clinical effects are biologically plausible. Krill oil contains phospholipid-bound omega-3 fatty acids, including eicosapentaenoic acid and docosahexaenoic acid, which are known to modulate inflammatory pathways by reducing the synthesis of pro-inflammatory eicosanoids and promoting the production of specialized pro-resolving mediators [13,14,23]. In addition, krill oil contains astaxanthin, a potent antioxidant that may mitigate oxidative stress, a key contributor to cartilage degradation and synovial inflammation in osteoarthritis [24,25,28]. Despite these mechanistic pathways, no significant changes were observed in systemic inflammatory biomarkers or lipid profiles in the included trials, suggesting that the symptomatic benefits of krill oil may be mediated primarily through localized joint-level effects rather than systemic anti-inflammatory activity [18,19,21,32].

Methodological heterogeneity across the included trials may also have contributed to variability in effect estimates. Differences in analytical approaches, supplement formulations, and dosages were evident, with some trials employing intention-to-treat analyses and others relying on per-protocol analyses, which may overestimate treatment effects for subjective outcomes such as pain and function [29,30,36,37]. In addition, two trials used multi-component formulations containing astaxanthin or hyaluronic acid, which may have augmented observed effects and limited direct comparability across studies [19,29]. The presence of substantial heterogeneity and consistent 'some concerns' risk of bias across included trials further limits the certainty of the pooled estimates.

Across all included trials, krill oil supplementation was generally well tolerated, with no statistically significant difference in adverse event rates compared with placebo [19,29,31,32]. Reported adverse events were predominantly mild gastrointestinal symptoms, and no serious adverse events attributable to krill oil were reported, suggesting a favourable short-term safety profile [18,28].

Taken together, these findings suggest that krill oil may represent a safe adjunctive option for symptom management in knee osteoarthritis [8,9]. These findings should not be interpreted as evidence for routine clinical use. However, the limited number of eligible trials and relatively short follow-up durations preclude definitive conclusions regarding long-term efficacy. Further large-scale, high-quality randomized controlled trials with standardized formulations, consistent analytical frameworks, and longer follow-up periods are warranted to confirm these findings and clarify the long-term role of krill oil in knee osteoarthritis management.

5. Conclusions

This systematic review and meta-analysis indicates that krill oil supplementation has been explored as a potential adjunctive intervention for knee osteoarthritis. The available evidence suggests numerical improvements and favorable trends in WOMAC-based patient-reported outcomes, although these effects did not consistently reach statistical significance. No clear benefits were observed for Visual Analog Scale–assessed pain or systemic biomarkers, and krill oil appeared to be well tolerated in the short term. Given the limited number of trials and short follow-up durations, further high-quality randomized controlled trials are required to clarify its clinical effectiveness and long-term role in knee osteoarthritis management.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org.

Author Contributions: Conceptualization, A.H.; methodology, A.H. and S.C.A.N.; formal analysis, A.H. and Y.R.H.S.; investigation, S.C.A.N., Y.R.H.S., and F.R.; resources, S.C.A.N. and Y.R.H.S.; data curation, A.H. and S.C.A.N.; writing—original draft preparation, A.H. and S.C.A.N.; writing—review and editing, A.H., S.C.A.N., H.D.S., Y.R.H.S., F.R., M.M.M., and R.P.S.; visualization, M.M.M. and H.D.S.; supervision, A.H.; project administration, Y.R.H.S., H.D.S. and R.P.S.; validation, A.H. and S.C.A.N.

 doi:10.20944/preprints202601.0891.v1

All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable, as this study is a systematic review and meta-analysis of published data and did not involve direct interaction with human participants.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data supporting the findings of this study are available within the article and its supplementary materials. No new data were created or analyzed in this study.

Acknowledgments: The authors would like to thank all researchers whose work was included in this systematic review.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

The following abbreviations are used in this manuscript:

OA	Osteoarthritis
RCT	Randomized controlled trial
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROSPER	International Prospective Register of Systematic Reviews
O	
VAS	Visual Analog Scale
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index
EPA	Eicosapentaenoic acid
DHA	Docosahexaenoic acid
BMI	Body mass index
hs-CRP	High-sensitivity C-reactive protein
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
MD	Mean difference
SMD	Standardized mean difference
RR	Risk ratio
OR	Odds ratio
CI	Confidence interval
I^2	Inconsistency index

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