REVIEW

Are There Benefits from the Use of Fish Oil Supplements in Athletes? A Systematic Review

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ABSTRACT

Despite almost 25 y of fish oil supplementation (FS) research in athletes and widespread use by the athletic community, no systematic reviews of FS in athletes have been conducted. The objectives of this systematic review are to: *1*) provide a summary of the effect of FS on the athlete's physiology, health, and performance; *2*) report on the quality of the evidence; *3*) document any side effects as reported in the athlete research; *4*) discuss any risks associated with FS use; and *5*) provide guidance for FS use and highlight gaps for future research. Electronic databases (PubMed, Embase, Web of Science, Google Scholar) were searched up until April 2019. Only randomized placebo-controlled trials (RCTs) in athletes, assessing the effect of FS on a health, physiological/biochemical, or performance variable were included. Of the 137 papers identified through searches, 32 met inclusion criteria for final analysis. Athletes varied in classification from recreational to elite, and from Olympic to professional sports. Mean age for participants was 24.9 ± 4.5 y, with 70% of RCTs in males. We report consistent effects for FS on reaction time, mood, cardiovascular dynamics in cyclists, skeletal muscle recovery, the proinflammatory cytokine TNF-α, and postexercise NO responses. No clear effects on endurance performance, lung function, muscle force, or training adaptation were evident. Methodological quality, applying the PEDro scale, ranged from 6 to a maximum of 11, with only 4 RCTs reporting effect sizes. Few negative outcomes were reported. We report various effects for FS on the athlete's physiology; the most consistent findings were on the central nervous system, cardiovascular system, proinflammatory cytokines, and skeletal muscle. We provide recommendations for future research and discuss the potential risks with FS use. *Adv Nutr* 2020;11:1300–1314.

Keywords: performance, injury, inflammation, mood state, recovery, DHA, EPA, exercise

Introduction

The effects of fish oil supplementation (FS) on athlete health and performance have been researched for the past ∼25 y. The early research focused on the potential of FS to modify the inflammatory response to exercise. However, subsequent studies have investigated the effects of FS on metabolism, the immune response, and the respiratory and cardiovascular, musculoskeletal, or central and peripheral nervous systems, with most recent research exploring the effect of FS on neuronal injury.

DHA (22:6n–3) and EPA (20:5n–3) are the long-chain polyunsaturated ω-3 (n–3) fatty acids present in FS. They are natural constituents of seafood including algae, crustaceans, and fish, and to a much a lesser extent in dairy and meat (the diet of the animal influencing the n–3 fatty acid content). In addition to both dietary intake (e.g., eating fish) and FS changing n–3 fatty acid status, endurance training is known to alter skeletal muscle membrane composition, leading to changes in the muscle phospholipids including increasing DHA content and decreasing the n–6:n–3 fatty acid ratio (1, 2). By virtue of training, athletes can acquire a "superior" n–3 fatty acid status compared with the nonathlete and therefore have less need to use supplements. For example, endurance training alters muscle DHA content significantly (1). Therefore, dietary requirements for the specific long-chain n–3 fatty acids can differ in athletes, both collectively in terms of recovery and performance effects, or individually

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Abbreviations used: EIB, exercise-induced bronchoconstriction; FS, fish oil supplementation; PBMC, peripheral blood mononuclear cell; RCT, randomized placebo-controlled trial; SPM, specialized proresolving mediator; URTI, upper respiratory tract illness.

for the respective fatty acids. EPA and DHA have been reported to have differential effects on the antioxidant systems and anabolic-catabolic pathways in skeletal muscle (3, 4). Moreover, EPA has inhibitory effects on cyclooxygenase-2 expression, and metabolism of arachidonic acid (an n–6 fatty acid) (5). Furthermore, EPA is the precursor for 3-series prostanoids and 5-series leukotrienes (eicosanoids), whereas DHA is the precursor for protectins and maresins, with both fatty acids producing the anti-inflammatory and proresolving, aptly named, resolvins (5).

Case studies have demonstrated that elite athletes use FS (6, 7). A review focusing on nutritional recovery strategies in team sports athletes concluded there was emerging evidence for n–3 fatty acid supplementation (the studies referenced used FS) to support recovery in season (8). However, the American College of Sports Medicine position statement on nutrition and athletic performance (9), although comprehensive, provides no statement or guidance on the use of FS (9). According to the International Olympic Committee's recent consensus statement on dietary supplements, there is "limited support" for FS in modifying inflammation and reducing upper respiratory tract infections, and although low risk, it is "unclear if FS should be pursued by athletes" (10). A lack of consensus for FS in athletes is evident within the literature.

FS use constitutes a billion-dollar industry, in which growth has been exponential, with the fish oil market expected to reach USD 5 billion by 2025 if trends continue (11). Concerns have been raised, however, over the quality of some fish oil products (12, 13). Furthermore, FS products are marketed by sports nutrition manufacturers specifically for the athlete, varying in formulation, and it is well recognized that nutritional supplements are not without risk for the athlete (10). To our knowledge no systematic review of FS in athletes has been conducted to date, despite numerous publications, including many narrative reviews. A systematic review of the evidence is warranted. In this review we will focus specifically on FS (EPA and DHA) in relation to the athlete. The aims of this systematic review are to: *1*) provide a summary of the effect of FS on the health and performance of athletes; *2*) report on the quality of the evidence; *3*) document any side effects as reported in the athlete research; *4*) discuss any risks associated with FS; and *5*) provide guidance for FS use and highlight gaps for future research.

Methods

Search strategy

The Preferred Reporting for Systematic Reviews and Meta-analysis protocols (PRISMA) checklist was followed. **Figure 1** summarizes the study selection process. Electronic searches were performed up until April 2019 with no date restrictions in PubMed, Embase, Web of Science, and Google Scholar using the search terms "athlete" and "omega-3," and "athlete" and "fish oil" with the terms being included in the study title, abstract, and/or keywords. To ensure the search strategy captured all relevant studies, searches within the electronic databases were conducted under each of the following specific terms—cognition, performance, injury, recovery, adaptation, skeletal muscle, muscle soreness, endurance, strength—and the following methods were applied to the searches: in PubMed, MESH headings were used and combined, whereas in Embase, Emtree was used with the expansion of the subject search term with the subject added to query builder. Reference lists of individual study publications and reviews were consulted for additional studies. The publication abstracts and titles were screened individually to ensure removal of studies not meeting the inclusion/exclusion criteria. If there was any doubt over article inclusion or exclusion, the article was obtained in full for clarification. The remaining publications were obtained in full, with each author independently reviewing the screened articles according to the inclusion and exclusion criteria.

Eligibility criteria for studies

Only publications written in the English language were included. Due to the plethora of research papers on FS, we focused on studies in which the research participants were characterized as male or female *athletes*, whether recreational, well-trained, or elite athletes. We chose not to include research on healthy physically active individuals and extrapolate such findings to athletes, *1*) due to the known effects of training on increasing muscle phospholipid n–3 fatty acid content (1); *2*) to summarize the evidence for practitioners in sport settings; and *3*) to identify gaps in the literature as they pertain to the athlete. Only randomized placebo-controlled trials (RCTs), assessing the effect of FS on health, and/or physiological/biochemical or performance variables were included. For example, studies that did not include a matched control or placebo group were excluded (6, 7, 14–16), as were nonrandomized trials (17). Publications that failed to report fully the methodology and statistical approach were excluded (18, 19), as were studies where the participants were not classified as athletes (i.e., recreationally or physically active, or resistance trained were excluded) (20–30). Figure 1 summarizes the studies excluded. To ensure we captured a broad spectrum of FS studies, no restrictions were imposed on sport, sex of participants, fish oil dose, duration of FS, whether supplements were EPA or DHA only, or lack of reporting of dietary or blood n–3 fatty acid status, or whether FS was combined with other ingredients (e.g., antioxidants). The latter point is relevant because these are the products that make it to market and are used by athletes. We chose to extract and tabulate separately both the statistically significant and nonsignificant findings, given the wide range of outcomes and variables assessed (**Tables 1**–**4**).

Assessment of study quality and risk of bias

Studies were rated using the Physiotherapy Evidence Database (PEDro) scale (https://www.pedro.org.au/english/downloads/pedro-scale/), an 11-point validated scale for the assessment of RCTs. Any differences of opinion regarding the rating of study quality were resolved between authors.

TABLE 1 Summary of studies of fish oil supplementation (FS) in athletes relating to oxidative stress[1]

Author	Sport	Athlete status	Sex and sample size	Biomarkers affected by FS	Dosing period, wk	Active treatment, mg/d	ω-3 biomarker response to FS	No effect for FS[2]
Żebroswka et al. (31)	Cycling	Competitive	Male participants $n = 13$	↑NO at rest and postexercise	3	1320 EPA 880 DHA	Not measured	Endothelium independent vasodilatation, peak power, TGs, LDL and HDL cholesterol, total cholesterol, HR, SBP, DBP, glycerol, TAS, PWV
Filaire et al. (32)	Judo	Elite	Male participants $n = 20$	↓TGs, ↑MDA at rest only, ↑MDA, Rmax, CDmax post-ex, ↑NO post-ex	6	600 EPA 400 DHA	Not measured	GPx
Filaire et al. (33)	Judo	Elite	Male participants $n = 28$	↑MDA, Rmax, CDmax at rest, and ↓post-ex	6	600 EPA 400 DHA Vitamin C, vitamin E, β-carotene	Not measured	
Filaire et al. (33)	Judo	Elite	Male participants $n = 28$	↑MDA, Rmax, CDmax at rest and post-ex, ↑NO post-ex	6	600 EPA 400 DHA	Not measured	
McAnulty et al. (34)	Cycling	Competitive	Male and female participants $n = 48$	↑F2-isoprostane post-ex	6	2000 EPA 400 DHA	↑Plasma DHA (55.8%), EPA (61.5%)	
McAnulty et al. (34)	Cycling	Competitive	Male and female participants $n = 48$	Prevented F2-isoprostane ↑post-ex	6	2000 EPA 400 DHA Vitamins, minerals, antxs	↑Plasma DHA (95.3%), EPA (77.8%)	
McAnulty et al. (35)	Cycling	Competitive	Male and female participants $n = 39$	Prevented F2-isoprostane ↑post-ex	2	220 EPA 180 DHA Vitamin C, EGCG, quercetin, B vitamins	Not measured	ORAC, ferric-reducing ability of plasma
Martorell et al. (36)	Soccer	Semiprofessional	Male participants $n = 15$	↑RBC SOD and GRd activity, ↓GPx	5 d/wk for 8 wk	1140 DHA CHO, proteins, almonds	↑RBC DHA (26.4%)	RBC MDA, carbonyl index, nitrotryosine, CAT
Ghiasvand et al. (19)	Basketball	Well-trained	Male participants $n = 34$	Resting: ↑MDA	6	2000 EPA	Not measured	No change TNF-α

[1] CAT, catalase; CDmax, maximum amount of conjugated dienes; CHO, ; DBP, diastolic blood pressure; EGCG, epigallocatechin 3-gallate; GPx, glutathione peroxidase; GRd, glutathione reductase; HR, heart rate; MDA, malondialdehyde; ORAC, oxygen radical absorption capacity; post-ex, ; PWV, pulse wave velocity; Rmax, maximum rate of oxidation during the propagating chain reaction; SBP, systolic blood pressure; SOD, superoxide dismutase; TAS, ; TG, triglyceride.
[2] All nonsignificant findings for the effects of FS.

TABLE 2 Summary of studies of fish oil supplementation (FS) in athletes relating to immunity and inflammation[1]

Author	Sport	Athlete status	Sex and sample size	Biomarkers affected by FS	Dosing period, wk	Active treatment, mg/d	ω-3 biomarker response to FS	No effect for FS[2]
Andrade et al. (37)	Swimmers	Elite	Male participants $n = 20$	Resting: ↑PBMC, ↓plasma PGE_2, ↓IFN-γ	6	950 EPA 500 DHA	↑Plasma total ω-3 fatty acids (45.4%), EPA (196%), DHA (96%)	PBMC TNF-α, IL-2, IL-4, cortisol, insulin
Delfan et al. (38)	Paddlers	Elite	Male participants $n = 22$	Resting PBMCs: ↓TNF-α, ↓IL-1β, ↑IL-6, ↑IL-10, ↓IFN-γ	4	2400 EPA 1200 DHA	Not measured	IL-4, Th1/Th2 ratio
Santos et al. (39)	Marathon	Competitive	Male participants $n = 21$	Resting: ↑lymphocyte proliferation; ↓IL-2, ↓TNF-α, ↓IL-10 Postrace: ↑lymphocyte proliferation	8.5	300 EPA 1500 DHA	Not measured	Lymphocyte death. Postrace lymphocyte: IL-2, IL-4, TNF-α, IL-10
Nieman et al. (40)	Cyclists	Competitive	Male and female participants $n = 23$		6	2000 EPA 400 DHA	↑Plasma EPA (311%), DHA (40%)	Total blood leukocytes, CK, CRP, ratio sIgA:protein, myeloperoxidase, IL-6, IL-8, IL-1Ra, endurance performance
Da Boit et al. (41)	Athletic, nonspecific	Recreational	Male and female participants $n = 30$	↓Total number of symptom days	16	550 EPA 550 DHA Whey protein, vitamin D	Not measured	URTI incidence, severity and duration of URTI, visits to medical doctor, sIgA conc. and secretion rate
Capó et al. (42, 43)	Soccer	Semiprofessional	Male participants $n = 15$	↓Post-ex MIP1-α. Post-ex LPS-stimulated PBMCs: ↓TNF-α, ↓IL-6, ↓TLR-4 protein concentrations ↑PBMCs UCP-3, ↓GPx	5 d/wk for 8 wk	1140 DHA CHO, proteins, almonds	↑RBC DHA (36%)	Oxidative damage in PBMCs, ROS production by PBMCs. Resting and postexercise plasma: IL-2, IL-4, IL-6, IL-8, IL-10, VEGF, IFN-γ, TNF-α, IL-1α, IL-1β, TNF-β, EGF, IL-5, IL-15, MCP-1, GMCSF
Capó et al. (44)	Soccer	Semiprofessional	Male participants $n = 15$	Resting: neutrophil gene expression (IL-8, NFκB); ↑neutrophil total MPO, ↑neutrophil total CAT activity	5 d/wk for 8 wk	1140 DHA CHO, proteins, almonds	↑RBC DHA (36%)	Neutrophils: nitrate, nitrite; NO; MPO, TNF-α, gene expression (COX2, TNF-α, MPO)
Nieman et al. (45)	Cyclists	Competitive	Male and female participants $n = 39$	Resting: serum ↓CRP, plasma IL-6, total leukocytes, ↓granulocyte oxidative burst	24 d	400 EPA 400 DHA EGCG, quercetin	Not measured	Plasma IL-10, IL-1Ra, TNF-α, CK, MCP, MPO, sIgA protein, HSP-70
Ghiasvand et al. (19)	Basketball	Well-trained	Male participants $n = 34$	Resting: ↓IL-6, ↑GPx	6	2000 EPA Vitamin E +/−	Not measured	No change GPx in EPA-only group

[1] CAT, catalase; CHO, carbohydrate; CK, creatine kinase; COX, cycloxygenase; CRP, C-reactive protein; EGCG, epigallocatechin 3-gallate; EGF, epidermal growth factor; GMCSF, granulocyte macrophage colony-stimulating factor; GPx, glutathione peroxidase; HSP, heat-shock protein; MCP, monocyte chemotactic protein; MIP, macrophage inflammatory protein; MPO, myeloperoxidase; PBMC, peripheral blood mononuclear cell; ROS, reactive oxygen species; sIgA, salivary immunoglobulin A; TG, triglyceride; Th1/2; T helper cell 1/2; TLR, toll-like receptor; UCP, mitochondrial uncoupling protein; URTI, upper respiratory tract illness; VEGF, vascular endothelial growth factor.

[2] All nonsignificant findings for the effects of FS.

TABLE 3 Summary of studies of fish oil supplementation (FS) in athletes relating to recovery and injury[1]

Author	Sport	Athlete status	Sex and sample size	Mood and cognition and skill	Cardiovascular and respiratory	Skeletal/muscle	Biomarkers	Physical performance	Dosing period, wk	Active treatment, mg/d	ω-3 biomarker response to FS	No effect for FS[2]
Jakeman et al. (46)	Athletes	Recreational	Male participants $n = 27$					>Recovery of CMJ	<1	7500 EPA 500 DHA	Not measured	Muscle soreness, CK, IL-6
Lewis et al. (47)	Summer Olympic sports	Competitive	Male participants $n = 31$					↓Fatigue (% drop Wingate power), ↑VL EMG	3	375 EPA 510 DHA Vitamin D	Plasma EPA↑ (65.8%), DHA no change	MVC, squat jump, CMJ, back squat, push-ups, endurance performance (time trial)
Black et al. (48)	Rugby	Professional-elite	Male participants $n = 20$	↓Fatigue, ↑sleep quality		↓Muscle soreness		↑Mean CMJ peak force	5	1102 EPA 1102 DHA Whey PRO, CHO, vitamin D	Plasma ω-3 fatty acids(240%)↑	
Philpott et al. (49)	Soccer	Competitive	Male participants $n = 30$			Muscle soreness ↓	↓CK conc.		6	1102 EPA 1102 DHA Whey PRO, CHO, vitamin D	Blood ω-3 fatty acids↑ (58%)	CRP, MVC, soccer passing test, yo-yo level 2 test
Gravina et al. (50)	Soccer	Competitive	Male and female participants $n = 26$					↑Anaerobic endurance (enhanced training effect)	4	4900 EPA 1400 DHA	Blood ω-3 fatty acids↑ (100%)	Respiratory function (FEV1, FVC), MVC, 20-m sprints, vertical jump height, yo-yo level 1 test
Raastad et al. (51)	Soccer	Professional-elite	Male participants $n = 28$				↓TGs		10	1600 EPA 1004 DHA	Plasma EPA (175%), DHA (40%) ↑	$\dot{V}O_2$max, running speed at anaerobic threshold, run time to exhaustion
Buckley et al. (52)	Aussie Rules	Professional-elite	Male participants $n = 25$		↓DBP, ↓sub-max exercise HR		↓TGs		5	360 EPA 1560 DHA	RBC EPA (116%) DHA (100%), ↑total n−3 (74%)	Run time to exhaustion, $\dot{V}O_2$/running economy
Oliver et al. (53)	American football	Competitive	Male participants $n = 81$				↓NFL		27	2000–6000 DHA	↑Plasma DHA (98–99.9%), dose dependent	
Mavrogenis et al. (54)	All sports	Recreational	Male participants $n = 31$	↓Pain				↑Activity	32 d	3000 EPA 2112 DHA Vitamins and minerals, GLA	Not measured	

[1] CHO, carbohydrate; CK, creatine kinase; CMJ, counter movement jump; CRP, C-reactive protein; DBP, diastolic blood pressure; EMG, electromyography recording from vastus lateralis; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; GLA, γ-linolenic acid; HR, heart rate; MVC, maximum voluntary contraction; NFL, neurofilament light; PRO,; TG, triglyceride; VL, vastus lateralis; $\dot{V}O_2$max, maximum oxygen uptake.

[2] All nonsignificant findings for the effects of FS.

TABLE 4 Summary of studies of fish oil supplementation (FS) in athletes relating to cardiovascular performance, cognition and mood, and respiratory function[1]

Author	Sport	Athlete status	Sex and sample size	Mood, cognition, and skill	Immune and inflammation	Cardiovascular and respiratory	Skeletal/muscle	Biomarkers	Physical performance	Dosing period, wk	Active treatment, mg/d	ω-3 biomarker response to FS	No effect for FS[2]
Raastad et al. (51)	Soccer	Professional-elite	Male participants $n = 28$				↓TGs			10	1600 EPA 1004 DHA	↑Plasma EPA (175%), DHA (40%)	$\dot{V}O_2$max, running speed at anaerobic threshold, run time to exhaustion
Buckley et al. (52)	Aussie Rules	Professional-elite	Male participants $n = 25$		↓DBP, ↓sub-max exercise HR		↓TGs			5	360 EPA 1560 DHA	↑RBC EPA (116%) DHA (100%), total n–3 (74%)	Run time to exhaustion, $\dot{V}O_2$/running economy
Hingley et al. (55)	Runners and cyclists	Well-trained, recreational	Male participants $n = 26$			↓Sub-max $\dot{V}O_2$ during 5-min cycling time trial				8	140 EPA 560 DHA	↑OM3I: 4.5% to 6%	Endurance performance (time-trial), Wingate, MVC
Peoples et al. (56)	Cyclists	Competitive	Male participants $n = 16$			↓Exercise HR, ↑cycling economy (↓sub-max $\dot{V}O_2$) ↑$\dot{V}O_2$max (+5%), FMD (%)				8	800 EPA 2400 DHA	↑RBC DHA (41.4%), total n–3 (24.3%),	
Żebroswka et al. (31)	Cyclists	Competitive	Male participants $n = 13$					↑NO at rest, postexercise, ↑glucose and FFA at rest		3	1320 EPA 880 DHA	Not measured	Endothelium independent vasodilatation, peak power, TGs, LDL and HDL cholesterol, total cholesterol, HR, SBP, DBP, glycerol, TAS, BM, PWV
Fontani et al. (57)	Athletics	Recreational	Male and female participants $n = 33$	↑Vigor, attention, ↓reaction time, anger, anxiety, depression				↓Homocysteine		5	1600 EPA 800 DHA	↓AA/EPA	
Fontani et al. (58)	Karate	Competitive	Male and female participants $n = 18$	↑POMS, ↓reaction time						3	4800 EPA 2400 DHA Policosanol	Not measured	
Guzmán et al. (59)	Soccer	Professional-elite	Female participants $n = 34$	↓Complex reaction time						4	3500 DHA	Not measured	
Black et al. (48)	Rugby	Professional-elite	Male participants $n = 20$	↓Fatigue, ↑sleep quality			↓Muscle soreness		↑Mean CMJ peak force	5	1102 EPA 1102 DHA Whey PRO, CHO, vitamin D	↑Plasma ω-3 fatty acids (240%)	
Mickleborough et al. (60)	Endurance sports	Competitive	Male and female participants $n = 20$		↓Urinary LTE4 and ↓9α11β-PGF_2; ↓plasma LTB4, TNF-α, IL-1β	Improved lung function (FEV1)				3	3200 EPA 2200 DHA	↑Neutrophil EPA (1206%), but no change DHA	
Tartibian et al. (61)	Wrestling	Recreational	Male participants $n = 40$			↑FEV1, ↑FVC, ↑VC, ↑MVV, ↑FEF25–75, ↑FIV1				12	180 EPA 120 DHA	Not measured	FEV1% and FIV1%
Gravina et al. (50)	Soccer	Competitive	Male and female participants $n = 26$						↑Anaerobic endurance	4	4900 EPA 1400 DHA	↑Blood ω-3 fatty acids (100%)	Respiratory function (FEV1, FVC), MVC, 20-m sprints, vertical jump height, yo-yo level 1 test

[1] AA,; BM,; CHO, carbohydrate; CMJ, counter movement jump; DBP, diastolic blood pressure; FEF, forced expiratory flow from 25% to 75%; FEV1, forced expiratory volume in 1 s; FFA, free fatty acid; FIV1, forced inspiratory volume in 1 s; FMD, flow mediated dilation; FVC, forced vital capacity; HR, heart rate; LT, leukotriene; MVC, ; MVV, maximal voluntary ventilation; OM3I, ω-3 index; POMS, profile of mood states; PRO, protein; PWV, pulse wave velocity; SBP, systolic blood pressure; TAS, total antioxidant status; TG, triglyceride; VC, vital capacity; $\dot{V}O_2$, oxygen uptake; $\dot{V}O_2$max, maximal oxygen uptake; 9α,11β-PGF_2, prostaglandin metabolite.

[2] All nonsignificant findings for the effects of FS.

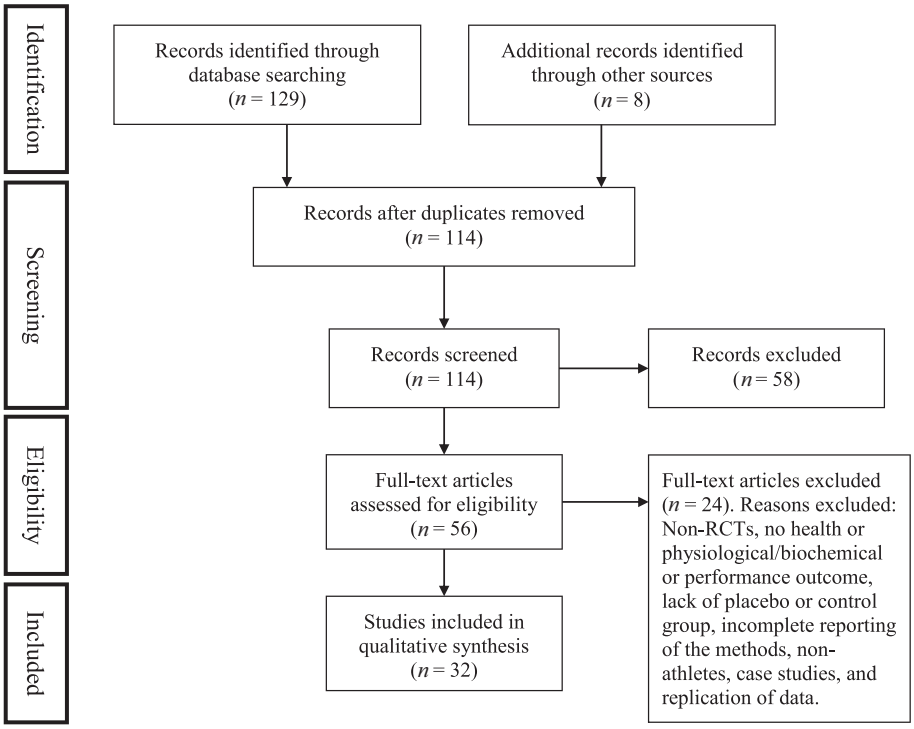

FIGURE 1 Flow diagram of study selection criteria. RCT, randomized controlled trial.

Data synthesis and extraction

A meta-analysis was not conducted due to the heterogeneity across studies and the variety of outcomes reported. Data extraction captured information relating to: *1*) study design (e.g., randomized, placebo-controlled trial); *2*) sample characteristics (e.g., age, sample size, sex, sport, athlete status); *3*) health and performance variables (e.g., mood, cognition and skill, cardiovascular and respiratory, skeletal muscle, immune and inflammation, biomarkers, physical performance); *4*) fish oil dose and dosing period; *5*) additions to the fish oil (e.g., vitamin D, vitamin E, etc.); *6*) measurement of n–3 fatty acid biomarkers (e.g., plasma EPA and DHA); and *7*) nonsignificant effects and findings.

Results

Study selection and sports

We identified a total of 137 papers using our search strategy, of which 32 RCTs (level of evidence 1B) met the inclusion criteria (Figure 1). The mean sample size of included studies was 27 participants (range: 15–81 participants).

The 32 RCTs were grouped into the following areas (some studies represented twice): oxidative stress only ($n = 5$); immunity, inflammation, and oxidative stress ($n = 10$); muscle recovery ($n = 5$); team sports and training adaptation ($n = 5$); cardiovascular physiology ($n = 5$); cognition and mood state ($n = 4$); respiratory health ($n = 2$); and injury related ($n = 2$) (Tables 1–4). Only significant findings are reported in the results and discussed. However, Tables 1–4 provide a summary of both the significant and nonsignificant findings.

Subject characteristics

The majority of investigations ($n = 22$) studied men only. Nine RCTs included participants of both sexes, and one RCT included women only. The mean age for participants in the FS and placebo groups across the RCTs was 24.9 ± 4.5 y; 1 RCT failed to report the age of the participants (53). Athletes varied in classification, from recreational (e.g., non-competitive) to elite (referring to a professional or national-level competitive standard) and from a range of summer Olympic sports (e.g., judo, swimming, cycling, marathon) and professional sports (i.e., American football, soccer, rugby, Australian Rules football, and basketball) (Tables 1–4).

Methodological quality and risk of bias

The methodological quality of the RCTs, applying the PEDro scale (maximum score obtainable 11), ranged from a score of 6 (2 studies) to a maximum of 11 (1 study), with an average score of 9. Of the 32 RCTs included, 25 (75%) were double-blind in design, 7 (20%) were single-blind, and 3 incorporated a crossover design with a wash-out period ranging from 2 wk to 35 d (31, 57, 60). A major methodological flaw affecting 28 of the 32 RCTs (88%), was that the size of the treatment effect (i.e., effect sizes) was not reported. Sponsorship and research funding by the fish oil industry was clearly reported in 7 RCTs.

Seventeen studies (53%) measured various biomarkers of n–3 fatty acid status to confirm compliance with the FS. Only 1 RCT ensured subjects were matched at baseline for n–3 fatty acid status, thus reducing the potential confounding effect of different baseline status on outcome (50).

Main findings

The findings were analyzed and grouped in relation to the main outcomes assessed. Inflammation was the most frequently studied variable in athletes (19, 37–45), with doses of EPA ranging from 300 to 2400 mg/d, and of DHA from 400 to 1500 mg/d. For the majority of pro- and anti-inflammatory mediators measured, the effects were inconsistent: for example, despite the variation in the timing of blood sampling and source of the cytokines, IL-6 (measured at rest) showed a reduction in 4 RCTs (19, 42, 43, 45) and an increase in 1 RCT (38), with no effect at rest or postexercise in 3 RCTs (40, 42, 43). However, there was evidence in 4 of the 5 RCTs for an effect of FS on attenuating the production of TNF-α by peripheral blood mononuclear cells (PBMCs) in ex vivo culture (38, 39, 42, 43). Only 1 RCT reported on upper respiratory tract illness (URTI), via an illness log and questionnaire, in which a moderate dose of fish oil reduced the total number of symptom days, but not the number of URTI episodes, symptom severity score, or URTI duration; however, the FS included vitamin D, whey protein, and 100 kcal more energy than the control group condition (41).

Muscle recovery and team sport training adaptations were examined across 7 RCTs (Table 3). Four RCTs reported positive effects on measures of recovery (e.g., muscle soreness, counter movement jump, creatine kinase activity) (46–49), a single RCT noted a positive effect on anaerobic endurance in soccer players but not on a battery of other physiological measures (50), whereas 2 RCTs reported no effect on physiological adaptations and performance (51, 52). Overall effects were consistent for muscle recovery, but inconsistent for training adaptation and performance outcomes in team sport athletes. The RCT with the largest change in plasma n–3 fatty acids (240%) with FS did observe effects on subjective and objective measures of recovery in professional rugby players (48). The 2 RCTs using the same FS in a recovery product formulation (i.e., administered posttraining with whey protein), reported positive effects on muscle recovery (48, 49).

Positive effects of EPA and DHA at various doses were observed on cardiovascular and oxygen kinetics in all studies of cyclists [cycling efficiency, maximum oxygen uptake ($\dot{V}O_2$max)] (31, 55, 56) but there were no improvements in endurance performance [e.g., time trial (55)]; see Table 4. An effect on endurance was not observed in the 2 RCTs of individuals involved in team sports (51, 52), or in athletes from 4 summer Olympic sports (47).

Three RCTs with various doses of EPA and DHA showed that FS increased biomarkers of lipid peroxidation (i.e., malondialdehyde, F_2-isoprostanes) at rest (19, 32, 33), and 4 RCTs reported this postexercise (32–35) (Table 1). Two RCTs showed the postexercise effect for FS on increasing F_2-isoprostanes was prevented with the addition of various antioxidants (33, 34). Antioxidant enzyme activity (i.e., superoxide dismutase, glutathione peroxidase, glutathione reductase) was increased with FS in 3 RCTs (19, 36, 44), and decreased in 2 RCTs (42, 43). Finally, 3 RCTs showed an effect on increasing NO postexercise (31–33) (Table 1).

Of the studies assessing cognitive variables, a positive effect on reaction time and mood state was seen across all RCTs where measured ($n = 4$), regardless of sport and ability, that is, professional rugby (48), soccer (59), athletics (57), and karate (58) (Table 4).

Few studies have examined injury risk. A positive effect for DHA was observed on biomarkers of neuronal injury (53), and a single RCT incorporating high doses of both EPA and DHA showed an effect on tendinopathy pain and subsequent activity level (54) (Table 3). Three RCTs explored the effect of FS on respiratory function (Table 4), 1 of which examined the effect of FS on exercise-induced bronchoconstriction (EIB) (60). The RCT reporting positive findings in EIB was of the highest methodological quality score (11 out of 11). In healthy athletes, a positive effect for FS on lung function was identified in 1 RCT in wrestlers (61), but this was not corroborated when examined in soccer players (50).

Adverse effects and product analysis

Of the included RCTs, only 1 reported on adverse effects with FS (DHA use only), citing poor palatability, gastrointestinal distress, and nausea in a small number of participants (~10%) (53). Three RCTs reported the laboratory analysis of the FS and thus verification of the product contents (52, 53, 56), with analysis independent of the manufacturer in just 2 studies (52, 53). No RCTs reported on FS analysis confirming the absence of traces of banned substances in the batches studied, which is relevant for the elite athlete participants.

Discussion

Summary of key findings

We present to our knowledge, the first systematic review of FS in athletes. We report evidence from a number of RCTs for an impact of FS upon the athlete's physiology. The most consistently reported findings to date relate to skeletal muscle recovery, postexercise NO response, biomarkers of lipid peroxidation, TNF-α production by immune cells, and cardiovascular dynamics in cyclists. Inflammation was the most studied variable in athletes, with FS modifying various inflammatory markers at rest and postexercise (via immune cell activation), with a consistent effect on attenuating the production of TNF-α by PBMCs. No effects on endurance performance, muscle force, or training adaptation were evident across sports. Few negative outcomes were reported. Where relevant, we will contextualize findings from studies in athletes with the inclusion of research published in nonathletes and conclude with recommendations for future research and guidance for practitioners in sport.

Cardiovascular and performance effects in endurance athletes

DHA is preferentially increased in skeletal muscle phospholipids in response to training (2), whereas both EPA and DHA are incorporated into mitochondrial phospholipids with FS (62). We found evidence for a consistent effect of FS on advantageously modifying cardiovascular physiology and whole-body oxygen consumption in athletes. A mechanism for this effect could be related to the capacity for DHA and EPA to moderate sympathetic activation of blood vessels and blood flow, via the expression and activation of endothelial NO synthase and production of NO (63). Indeed, 3 RCTs reported an effect for FS on increasing NO. Nevertheless, effects for FS on aerobic performance were not evident. Furthermore, the positive findings extended only to controlled laboratory studies in cyclists. Indeed, FS consistently showed no effect on tests of endurance undertaken in competitive and professional team sport athletes. It is possible that greater intra- and intersubject variability for performance tests could have confounded the findings. Finally, a recently published review article on the effects of FS on performance (encompassing both sedentary and athletic populations) was in agreement with our findings; an effect for FS in endurance-based athletes on oxygen efficiency, but no clear effects on performance (64).

Muscle recovery and adaptation

The research into muscle recovery in athletes has been focused on a greater dose of EPA compared with DHA administered, with 1 study showing that EPA, but not DHA, stimulates muscle protein synthesis in the presence of leucine and inhibits muscle protein breakdown in muscle cell culture (4). We identified 7 RCTs investigating muscle recovery and training adaptation, in which differences in FS formulations and types of sport participation could account for divergent findings. For example, the positive effects on muscle soreness (i.e., perceived), damage (i.e., creatine kinase activity), and recovery (i.e., counter movement jump peak force) were evident in professional rugby and competitive soccer players when administered over several weeks, in which the FS also included vitamin D and whey protein (48, 49). This was notwithstanding the fact that the control groups in both studies received matched timed protein and carbohydrate intakes. In addition, the 3-wk FS study in Olympic athletes showing an effect on fatigue (i.e., percentage drop in Wingate power), also included vitamin D (47). It is conceivable that the strongest effects for FS on accelerating muscle recovery can be most evident when administered alongside other nutrients known to impact on skeletal muscle remodeling (i.e., vitamin D, whey protein) as part of a recovery drink. The strength of the evidence for FS on enhancing adaptations to training in team sport athletes is very weak, with 3 RCTs reporting no effect on performance (49, 51, 52), and just 1 observing an effect for FS on increasing anaerobic capacity over 4 wk of training (50). An effect of FS on muscle force (maximal voluntary contraction) was absent across all RCTs. Three separate RCTs of recreational, competitive, and professional athletes reported an effect for FS on neuromuscular performance measures, for example, muscle activation, Wingate power, counter movement jumps (46–48). Further research is needed to clarify the effect of FS on the neuromuscular system, and whether EPA is more effective for enhancing muscle recovery in vivo, given the effects on muscle recovery that were seen using a 1:1 ratio of EPA and DHA.

Respiratory function

EIB causes narrowing of the airways leading to decrements in pulmonary function and is well known to adversely affect elite athlete performance. Inflammation is part of the pathophysiology of EIB, and as such FS has been tested as a nonpharmacological therapeutic treatment option. FS reduced the postexercise decline in forced expiratory volume, systemic inflammation, and bronchodilator use in elite athletes (60). However, the evidence for an effect of FS on modifying lung function in healthy athletes without EIB is weak, with only 1 RCT showing benefit after 12 wk of FS (61). In short, FS may reduce airway inflammation in elite athletes with EIB and can be considered as an adjunctive nonpharmacological low-risk treatment option; clearly, further research is needed to better understand the effects of FS on respiratory function. However, the absence of EIB is likely to limit the potential application of FS on respiratory function.

Inflammation and immunity

For the healthy athlete, the evidence summarized in Table 2 suggests that FS can modify the PBMC inflammatory response, when assessed through changes in cytokines, for example, TNF-α (37–39, 42, 43). However, we acknowledge the conflicting evidence with regard to immunomodulation in athletes; with differences in study design (e.g., pre- compared with postexercise sampling), training and immune function status, n–3 fatty acid dose, measures of immunity, and the underlying fatty acid status affecting the consistency of study outcomes (19, 37–40, 42–44, 65). In contrast to our findings, a systematic review published in 2012 reported that moderate n–3 fatty acid consumption (900–2000 mg/d) does not lead to changes in inflammatory biomarkers in healthy nonathletes (66), suggesting a differential effect between trained and untrained individuals. The biological material sampled and thus the source of the cytokines [e.g., plasma compared with in vitro (ex vivo) assessments of immune cell function], the timing (at rest compared with postexercise), and dose of n–3 fatty acids are critical factors in determining consistency of study outcomes with regard to inflammation. Finally, complicating the findings, using modest doses (400 mg/d EPA and DHA) combined with polyphenols such as green tea and quercetin and administered during an intensified period of training, Nieman et al. (45) showed an anti-inflammatory effect (i.e., a reduction in high sensitivity C-reactive protein and IL-6 compared with placebo) both at rest and postexercise (45). Because antioxidant supplements

can modify adaptive responses to exercise (67), caution should be applied to their use.

We did not find any convincing evidence that FS provided protection from illness. Of the 10 RCTs exploring the effects of FS on immune and inflammatory variables in athletes, only 1 RCT included data on infectious symptoms and illness (41). FS in combination with 10 μg vitamin D-3 and 8 g whey protein reduced the number of illness symptom days. Further research is needed to corroborate these findings.

Cognition

We observed consistent findings for an effect of FS on aspects of cognition and mood state in athletes, namely reaction time, using combinations of EPA and DHA (48, 57–59). Improvements in reaction times related to working memory and episodic memory using DHA (68), and complex reaction times with EPA (69) have also been reported in healthy male and female nonathletes. Furthermore, higher RBC DHA concentrations are associated with improved working memory performance and are predictive of baseline performance (70). Thus FS, with an emphasis on DHA, could be anticipated to improve mood states and cognitive performance in athletes; mental tasks requiring more complex cortical processing are likely to benefit the most, as could athletes with poor n–3 fatty acid status prior to FS (e.g., low RBC DHA, bottom quartile ω-3 fatty acid index). Mechanisms by which FS might modify brain function and therefore mood (e.g., vigor and fatigue), include the increased incorporation of DHA into neuronal membranes leading to alterations in membrane fluidity and speed of signal transduction and neurotransmission (71), and via neuroprotective and antidepressant-like effects in the face of a physiological stress as observed with FS in rodents (72). Decreased n–3 fatty acid status has been reported in chronic fatigue patients compared with healthy controls (73).

Injury

Tendinopathy.

FS as a means of treating tendinopathy in athletes in conjunction with pharmacological therapy has been previously proposed (74). We identified 1 positive clinical trial in athletes, which reported a reduction in pain with FS compared with the placebo (99% compared with 31%; $P < 0.001$), and greater increases in voluntary sporting activity (54). Two FS trials in nonathletes have been published and are discussed (75): in contrast to the findings of Mavrogenis et al. (54) in athletes, Røe et al. (75) using the same FS supplement found no effect for the FS compared with placebo when administered to patients ($n = 55$) with unilateral epicondylitis (i.e., tennis elbow) over several months. Neither study assessed the participants' underlying n–3 fatty acid status. In a recent multicenter clinical trial ($n = 73$), Sanford et al. (76), recruiting patients with unilateral shoulder pain, found no significant difference between FS (EPA 1530 mg/d plus DHA 1035 mg/d) compared with placebo in the primary outcome measure (the Oxford shoulder score). However, the FS group experienced a more rapid improvement from baseline to 3 mo, and a modest effect ($P < 0.05$) on shoulder pain and disability, flexion, and abduction at 3, but not 2, 6, or 12 mo, and strength at 12 mo. More patients in the placebo group were using analgesic medication ($P = 0.02$). Moreover, a significant relation between increasing plasma EPA and DHA and reduction in pain was reported. An effect of DHA and EPA on tendinopathy might result from alterations in the formation of specialized proresolving mediators (SPMs) leading to alterations in pain and inflammatory signaling. For example, in arthritis patients taking FS, plasma SPMs were negatively correlated with erythrocyte sedimentation rate, and synovial fluid resolvin E2 was negatively associated with pain score (77). Thus, at present the evidence for an effect of FS is inconclusive; however, in lieu of the above and the reported minimal side effects, FS could provide a nonpharmacological, low-risk means of supporting tendinopathy rehabilitation in athletes, exerting a modest effect dependent on dose and n–3 fatty acid status.

Concussion and head trauma.

We identified only 1 publication in American football (53), a sport well recognized for having a high incidence of concussions (78). The RCT was designed to test the effects of DHA (3 different DHA dosing strategies) on neuronal injury across a playing season in National Collegiate Athletic Association Division 1 American football players ($n = 81$). The authors demonstrated that FS (DHA only) attenuated the rise in neurofilament light (a biochemical marker of axonal injury that is observed to rise across the playing season in American football players). Caution should be exercised with regard to dosing strategies for DHA, given that the lowest dose used (2000 mg/d) was the most effective. Further work in other sports that present with a high incidence of concussion is clearly warranted.

Surgery and rehabilitation.

FS is sometimes prescribed to elite athletes following surgery (7) and, despite the emerging role of resolvins, protectins, and maresins in inflammatory control and resolution, no RCTs have examined the effects of FS on wound healing in athletes postsurgery. Of relevance, FS (1660 mg/d EPA and 1100 mg/d DHA) administered to healthy young subjects failed to enhance wound closure at any of the time points examined after initiation of the wound compared with placebo (79). Research in healthy animals corroborates these findings, with FS and linseed (a source of plant n–3 fatty acids but not EPA and DHA) delaying the percentage wound closure and re-epithelialization compared with controls at 14 d postwound (80). In contrast, obese diseased and therefore "inflamed" animals display enhanced wound healing with an n–3 fatty acid–rich "high-fat" diet compared with controls, and with diets rich in n–6 fatty acids and saturated fat (81). Given the lack of supportive scientific evidence in athletes or indeed healthy young participants, caution is advised over the use of FS in otherwise healthy athletes recovering from acute surgery or an acute traumatic injury (with the exception of neuronal injury and the use of DHA and the correction of any underlying n–3 fatty acid deficiency). The decision

whether to use FS for rehabilitation purposes is further complicated by the findings of recent experimental research using a nonsurgical unilateral limb immobilization approach (no actual injury or wound and therefore no activation of an immune inflammatory response). FS prevented muscle disuse atrophy in nonathletes, preserving both muscle mass and mitochondrial respiration (82, 83).

Bone health.

Bone stress injuries are common injuries sustained by athletes (84), and interventions that can mitigate the risk are warranted. There have been no RCTs in athletes that examined the effects of FS on bone metabolism, or bone mineral density. However, the National Aeronautics and Space Administration agency conducted a series of research studies from cell culture to human interventions in association with bed rest and space flight, to assess the potential for FS to ameliorate bone loss, with an effect for n–3 fatty acids (85). Those astronauts who ate more n–3 fatty acid–rich fish experienced less decline in bone mineral density as a result of short-duration space flight. Moreover, a higher intake of n–3 fatty acids (i.e., fish intake) was associated with reduced bone resorption (measured via N-telopeptide) with bed rest in nonathletes (85). In conclusion, a higher fish intake and better n–3 fatty acid status can serve to protect against bone loss. Speculatively this might also allow attainment of a higher bone mineral density for the athlete. However, research in athletes would clearly be needed to support this hypothesis.

Adverse effects of FS

Only 1 RCT reported adverse effects of FS, in which the athletes' complaints were mild and affected a small proportion (∼10%). Thus, given the wide range of FS used, doses administered, and time frames, FS appears to be safe in athletes. The most commonly stated concerns with regard to the use of chronic high doses of FS are: *1*) increased oxidative stress, driven by oxidation of the polyunsaturated fats in FS; *2*) a hypocoagulant effect; *3*) exposure to heavy metals and toxins concentrated in the oils; and *4*) mild gastrointestinal side effects such as nausea. Each area will be briefly discussed below. Table 1 provides a summary of the RCTs measuring the effect of FS on oxidative stress in athletes, with or without added nutrients. Based on these studies in athletes, FS use increases lipid peroxidation at rest and postexercise compared with a placebo or control (32, 33); however, the increase in oxidative stress postexercise is prevented when FS is consumed with antioxidant nutrients, for example, polyphenols and/or vitamins (33–35). In addition, 3 RCTs reported an effect for FS on increasing NO postexercise (31–33). It should be noted that well-designed human studies examining the effect of FS on intracellular antioxidant enzymes and systems, have found that ∼3 wk of FS increases the expression and activity of antioxidant enzymes (86). Others have reported differential effects for the fatty acids, EPA and DHA, on muscle antioxidant enzymes (3).

Anecdotally, athletes sometimes consume supplements in excess of recommendations, in accordance with the "more is better" mantra. Excessive FS doses over a prolonged period of time can pose an increased risk of bleeding. For example, an amateur athlete consuming 20 g/d of n–3 fats from supplements presented with a duodenal ulcer and bleeding (87). A recent systematic review including 52 publications incorporating data on both healthy and surgical patients, concluded that FS reduces platelet aggregation in healthy subjects; however, in RCTs there is no increased risk of bleeding during or after surgery with FS (88). The European Food Safety Authority (89) scientific opinion states, "Long-term supplemental intakes of EPA and DHA combined up to about 5g day^{-1} do not appear to increase the risk of spontaneous bleeding episodes or bleeding complications, or affect glucose homeostasis, immune function or lipid peroxidation, provided the oxidative stability of the n–3 long chain polyunsaturated fatty acids is guaranteed." Athletes should be educated to avoid excessively high doses of FS. Overall, we are not aware of any RCTs in which FS exerted a negative outcome on performance or recovery. Furthermore, mild gastrointestinal side effects (belching, nausea, fishy taste) in the studies reviewed were rare occurrences.

Quality of FS products

Only 2 studies sought independent laboratory analysis of the FS used, which is somewhat concerning given that 9 studies were conducted in elite athletes, and a further 2 in semiprofessional athletes. A number of studies from different countries have raised concerns over both the quantity and the quality of the fatty acids contained within various commercial products (12, 13, 90). For example, in the United States, Kleiner et al. (12) found that >70% of the supplements analyzed (47 FS products were selected) did not contain the amounts of EPA and DHA stated on the product label. Moreover, a study in New Zealand identified just 3 of 32 supplements contained quantities of EPA and DHA that were ≥100% of the label content. Two-thirds contained <69% of label-claimed content (13). Of greater concern is the finding that 83% of supplements exceeded concentrations of peroxide markers, with 50% exceeding recommended total oxidation values calculated (13). Only 3 supplements met international recommendations. Such results are not without controversy, however, with the analytical methods in the latter study (13) receiving criticism from industry scientists (91). In fact, in an industry-sponsored study, all 10 fish oil products met international guidelines (91). In summary, care needs to be taken when recommending FS products for athletes, and ideally the products should be analyzed not only from an antidoping perspective, but also for the presence and concentration of heavy metals, dioxins, and polychlorinated biphenyls.

Study Limitations and Bias

Only randomized placebo-controlled trials were included in the review to minimize selection bias associated with the nonrandomization of participants. However, our initial

search strategy captured 6 nonrandomized and/or non–placebo-controlled studies in athletes (14, 15, 17, 50, 65, 92), which could offer further insight into this field albeit without the same scientific rigor. We included both single (20%) and double-blind (80%) studies, however, and thus there is a risk of bias due to the lack of blinding of researchers in the single-blind studies. Removing the 7 single-blind studies (31, 33, 37, 39, 41, 51, 58) does not change the conclusions, but it weakens the strength of the findings for inflammation because 2 single-blind studies reported on TNF-α (37, 39), and 2 on postexercise NO (31, 33).

With regard to the specific FS characteristics, some included additional nutrients, as stated in Tables 1–4. Such studies were not excluded from the review. In fact, by including studies with additional nutrients (e.g., antioxidants), an effect for antioxidants on attenuating lipid peroxidation was observed. Furthermore, FS sold into the marketplace contains various antioxidants (i.e., α-tocopherol or carotenoids) in order to reduce oxidation of the fatty acids, ensuring greater product stability, and to prolong the product's shelf life. The inclusion of such studies gives the review ecological validity.

Conclusion

We provide a summary on FS research in athletes (Tables 1–4), which demonstrates broadly positive effects and serves as a resource for practitioners. Indeed, FS exerts positive effects on cognition, cardiovascular dynamics in cyclists, and muscle recovery. FS also attenuates proinflammatory cell responses and can increase lipid peroxidation and postexercise NO. An effect for FS on endurance exercise performance was absent across all studies. We are not aware of any RCTs that have demonstrated a negative effect of FS on performance, and the reported side effects with FS use are mild. Many of the RCTs that report positive effects have used doses of FS that are achievable through the consumption of oily fish. It is recommended that future research on FS and n–3 fatty acid–rich diets should measure biomarkers of n–3 fatty acid status, to allow the proper investigation and understanding of the impact of n–3 fatty acid status and the dose–response on outcomes. Furthermore, FS research is needed in athletes to further understand the impact on neuromuscular performance, bone metabolism, rehabilitation from injury (e.g., surgical compared with nonsurgical outcomes including bone stress), EIB, risk of illness, and risk of sudden cardiac death in athletes (93) with high compared with low n–3 fatty acid status. Finally, future FS studies should include effect sizes and have the supplement analyzed for contaminants and the supplement contents verified independently from the manufacturer.

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