Effectiveness of Omega-3 supplements in the treatment of dry eye. A systematic review

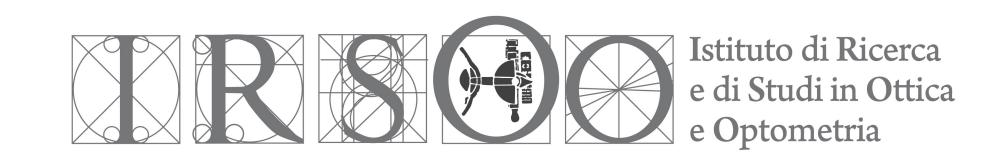


5th Optometry Conference of Central and South-Eastern Europe April 21st to 23rd 2023, Split, Dalmatia, Croatia Giulia Cenini¹, Sabrina Giometto² Irsoo – Vinci (FI)¹ **University of Pisa²**

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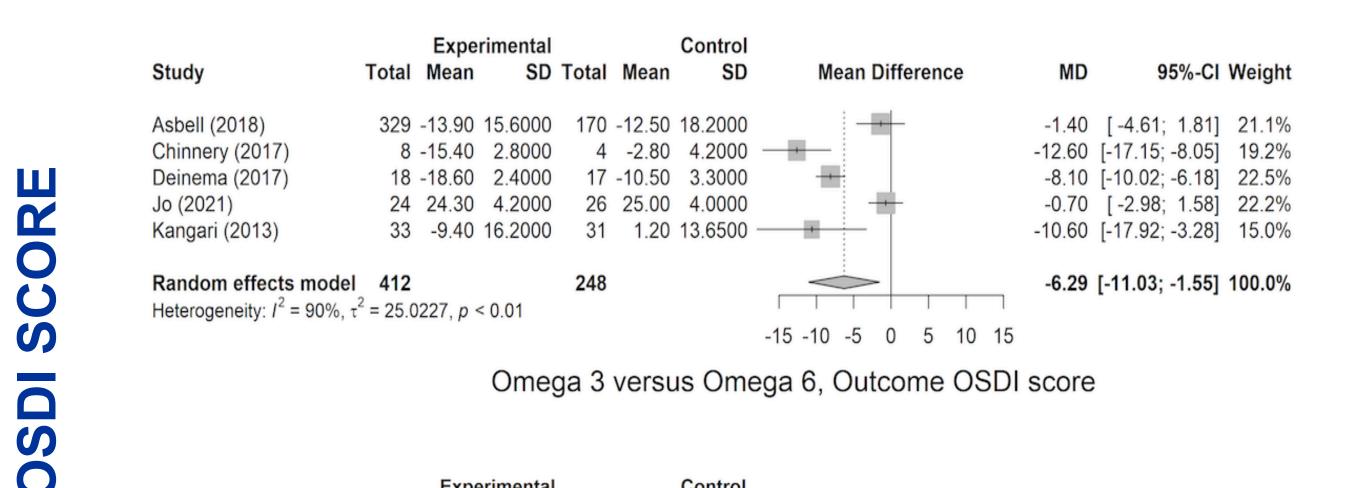
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Purpose

Dry eye syndrome (DES) is a multifactorial inflammatory disorder of the ocular surface, with an increasing incidence in the world, that significantly affects visual function, as well as quality of life.

The aim of this study is to critically evaluate the scientific evidence regarding the efficacy of oral supplementation with omega-3 fatty acids for the treatment of dry eye syndrome.



Omega 3 versus Placebo, Outcome OSDI score

Method

- The systematic search was conducted in June 2022 using the electronic databases PubMed and Cochrane Library, using the following terms: ((dry eye) OR (dry eye syndrome) OR (dry eye disease) OR (DED)) AND ((omega 3) OR (omega 3 fatty acid) OR (omega 3 fatty acids) OR (EPA) OR (DHA) OR (PUFA))
- **INCLUSION CRITERIA**: randomized controlled trials (RCTs) comparing oral omega-3 fatty acid supplementation with placebo in patients with mild to severe dry eye disease
- **OUTCOME MEASURES**: ocular surface disease index (OSDI), tear breakup time (TBUT), Schirmer test and osmolarity
- The pooled effect sizes were estimated using a random-effects model or a fixed-effects model depending on the level of heterogeneity. Heterogeneity was evaluated using Q and I² tests

RESULTS

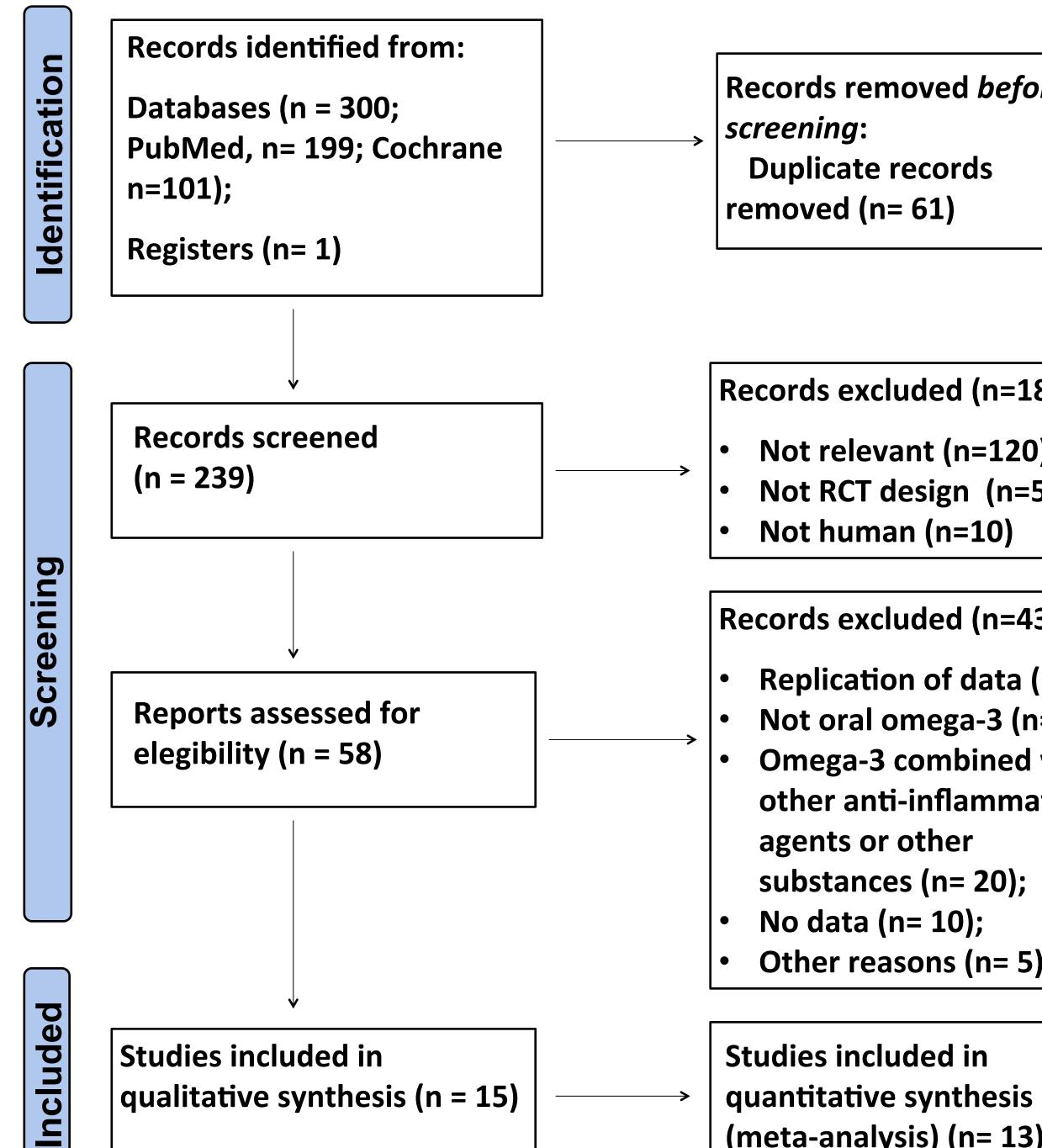
Identification of studies via databases and registers

U			Expe	rimental			Control							
_	Study	Total	Mean	SD	Total	Mean	SD	Mean I	Difference	Ð	MD	95%-CI	Weight	
	Epitropoulos (2016) NCT01107964			2.6000 20.6000			2.7000 34.0000					[-13.01; -10.99] [-32.65; 11.05]		
	Common effect model Heterogeneity: $I^2 = 0\%$, τ^2		= 0.91		64			¢			-12.00	[-13.01; -10.98]	100.0%	
								-30 -20 -10	0 10	20 30				

			0	mega	3 ver	sus P	lac	ebo, Outcom	e TBL	JT			
			Experimen			Control							
	Study	Total	Mean	SD Tota	l Mean	SD		Mean Differenc	е	MD	95%-CI	Weight	
	Asbell (2018) Bhargava (2015a) Bhargava (2016a) Bhargava (2016b) Deinema (2017) Jo (2021) Kangari (2013)	65		00 230 00 65 00 260 00 17 00 20	5 12.00 5 9.00 5 9.20 7 -2.80 5 5.08	1.6000 2.2000 2.0000 0.2000 1.3000 1.2800 2.3600			-	3.00 3.70 1.70 6.80 0.92	[-0.23; 0.43] [2.63; 3.37] [3.03; 4.37] [1.42; 1.98] [5.87; 7.73] [0.11; 1.73] [0.45; 2.69]	14.6% 14.6% 14.3% 14.6% 14.0% 14.2% 13.7%	
5	Random effects model Heterogeneity: $I^2 = 98\%$, τ^2		58, <i>p</i> < 0.01	811	I		∟ -6	5 -4 -2 0 2	4 6	2.53	[0.89; 4.17]	100.0%	
			O	nega	3 ver	sus O	me	ega 6, Outcor	ne TB	UT			
	Study	Total	Experimer Mean	ital SD Tota		Control SD		Mean Differenc	e	MD	95%-CI	Weight	
)	Bhargava (2013) Bhargava (2015b) Epitropoulos (2016) NCT01107964	240	2.54 2.34 3.30 1.60 3.50 0.50 1.90 2.90	000 25 000 5	6 0.30 1 1.20	0.1600 2.3000 0.5000 4.2000				3.00 2.30	[2.13; 2.69] [2.65; 3.35] [2.11; 2.49] [-2.21; 3.41]	30.1%	
	Random effects model Heterogeneity: $I^2 = 78\%$, τ^2	-		57	4		-3	-2 -1 0 1	2 3	2.51	[2.10; 2.92]	100.0%	

Omega 3 versus Placebo, Outcome Schirmer test

	Study	Experimental Total Mean SD	Control Total Mean SD	Mean Difference	MD 95%-CI Weight	
TEST	Asbell (2018) Bhargava (2015a) Bhargava (2016a) Bhargava (2016b) Kangari (2013)	3290.405.300022021.404.00006515.004.800025616.006.0000330.931.4300	1700.305.000023620.504.70006512.804.800026615.606.6000310.190.5700		0.10 [-0.84; 1.04] 14.9% 0.90 [0.10; 1.70] 20.9% - 2.20 [0.55; 3.85] 4.9% 0.40 [-0.68; 1.48] 11.4% 0.74 [0.21; 1.27] 47.9%	
HIRMER	Common effect mode Heterogeneity: $I^2 = 24\%$,	$\tau^2 < 0.0001, p = 0.26$		3 -2 -1 0 1 2 3 6, Outcome Schirm	0.71 [0.35; 1.08] 100.0% ner test	
HH	Study	Experimental Total Mean SD	Control Total Mean SD	Mean Difference	MD 95%-CI Weight	
SC	Bhargava (2013) Bhargava (2015b) Epitropoulos (2016) Wojtowicz (2011) NCT01107964 Random effects mode Heterogeneity: <i>I</i> ² = 86%,		254 0.14 0.3500 256 13.50 4.5000 51 1.30 1.0000 15 2.52 8.0500 13 0.30 6.6000 - 589		0.48 [0.35; 0.61] 30.7% 2.60 [1.82; 3.38] 27.4% 0.40 [0.04; 0.76] 30.0% 1.68 [-3.60; 6.96] 4.7% -1.80 [-5.87; 2.27] 7.1% 0.93 [-0.31; 2.17] 100.0%	
2		Om	ega 3 versus Pla	-4 -2 0 2 4 6 acebo, Outcome os	smolarità	
ARI	Study	Experiment Total Mean S	al Control D Total Mean SD		MD 95%-CI	Weight
JOL	Asbell (2018) Chinnery (2017) Deinema (2017)	329 -0.70 18.400 8 -22.60 5.700 18 -18.60 3.900	4 -8.00 2.8000		-4.30 [-7.60; -1.00] -14.60 [-19.41; -9.79] -17.10 [-19.86; -14.34]	33.8% 31.7% 34.5%
OSMOLARI	Random effects mode Heterogeneity: <i>I</i> ² = 94%,		191	-10 0 10	-11.98 [-19.78; -4.17]	100.0%



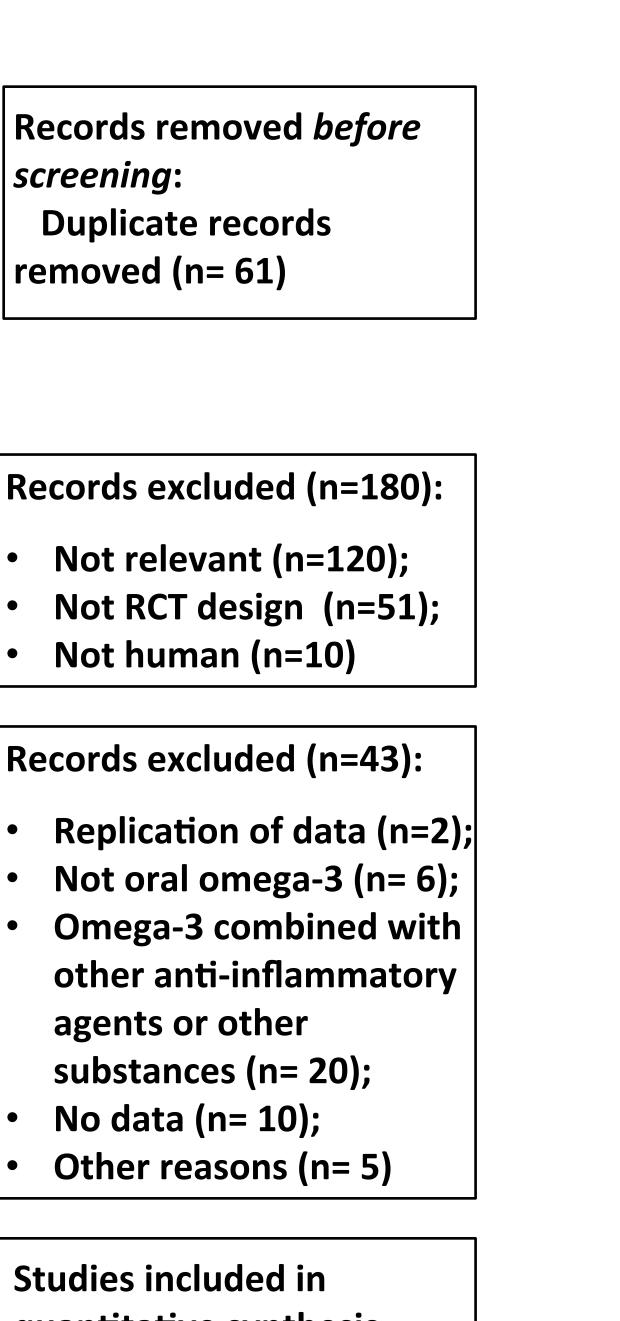


Figure 3. Meta-analysis of outcome measures.

Discussion

- The studies were divided into two subgroups according to the type of placebo used: olive oil and medium-chain triglycerides or oil largely containing omega-6 (corn and safflower oil)
- Estimation of the aggregated results shows that patients who received the treatment experience greater improvements than

(meta-analysis) (n= 13)

Figure 1. PRISMA Flow Chart

- Trials involved a total of 3069 participants from 6 countries with dry eye of variable severity and etiology (71% women)
- The mean age was 48.4 years (46.7 treatment group; 49.3 control) group)
- Follow-up ranged from one to 12 months
- All the studies were published between 2011 and 2021
- Most of the studies used a dosage of omega-3 greater than 1000 mg per day

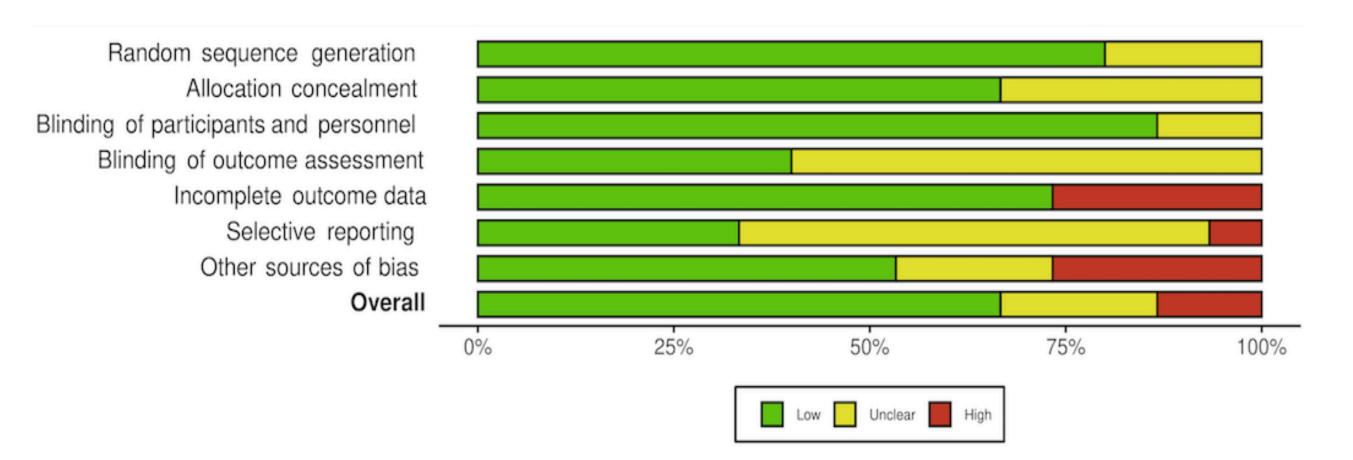


Figure 2. Qualitative results. Percentage of the risk of bias of the included studies using Cochrane Collaboration tool.

those who received placebo

Limitations

- High statistical heterogeneity of the studies
- Variations among dose and composition of treatment and placebo

Conclusions

Oral supplements of omega-3 fatty acids can contribute to reduce signs and symptoms of dry eye syndrome and may be an effective therapy in clinical practice.

It is recommended for future to use a placebo as neutral as possible.

Acknowledgments

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