

THE EFFECT OF OMEGA-3 FATTY ACIDS SUPPLEMENTATION ON PEDIATRIC PATIENTS WITH NON- ALCOHOLIC FATTY LIVER DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in children and several studies have investigated the potential role of omega-3 fatty acids supplementation as a treatment option.

AIM

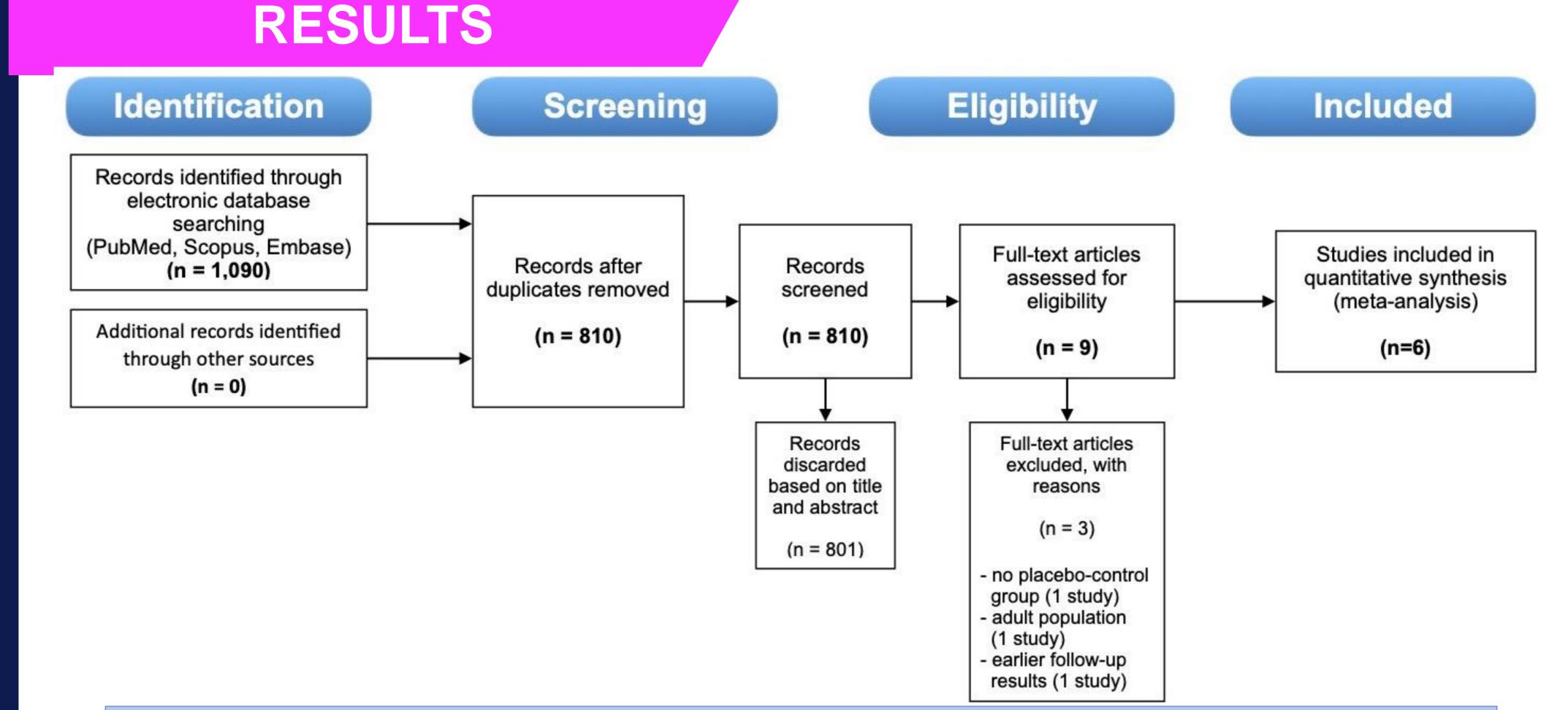
The aim of this study was to conduct a systematic review and meta-analysis in order to examine the effect of omega-3 fatty acids on the treatment of pediatric NAFLD.

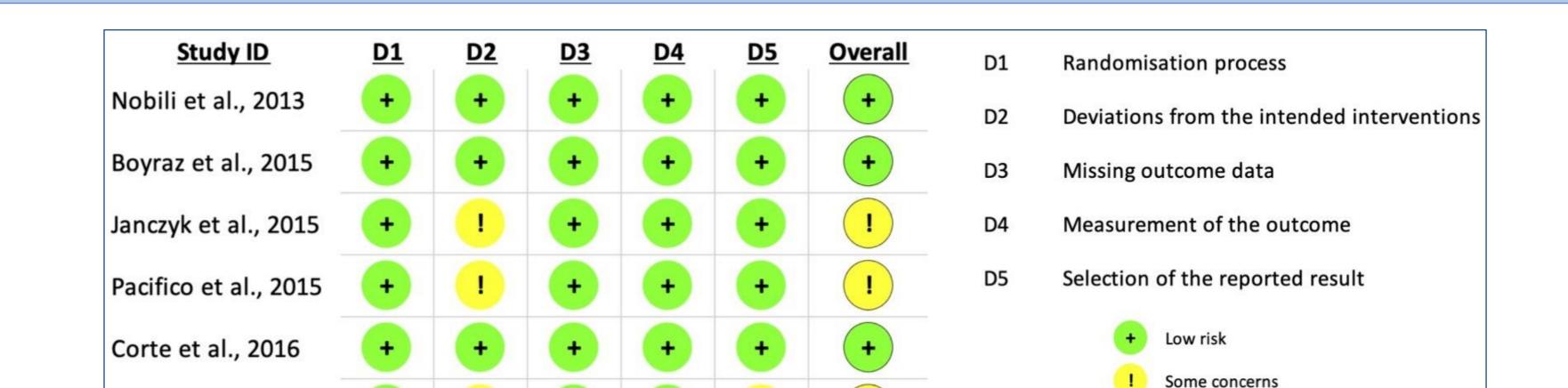
METHOD

- A systematic literature search was performed (PubMed, Scopus and Embase) till February randomised controlled examining n-3 FA versus placebo in children with NAFLD.
- Change in liver enzymes (ALT, AST) and liver steatosis improvement were considered as primary outcomes and change in GGT, lipids, blood glucose, HOMA-IR and Waist Circumference as **secondary outcomes**.
- Risk of bias assessment was conducted with the Cochrane risk-of-bias tool (RoB 2).
- A random-effects model was used to calculate the pooled Mean Difference (MD) for continuous outcomes or the pooled Odds Ratio for dichotomous outcomes with the accompanying 95% CI.

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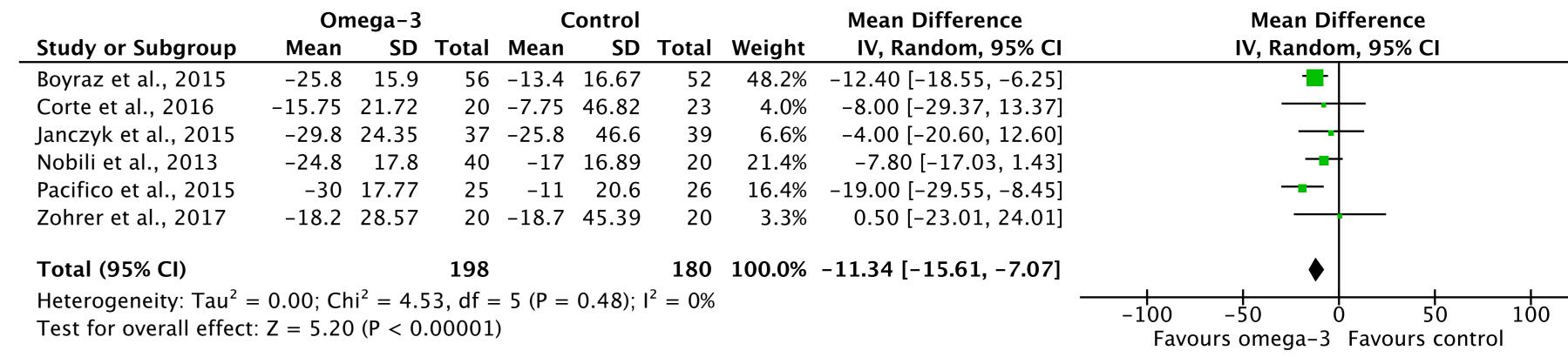




A flow diagram of the studies included in the Systematic Review and the main reasons for rejection during study selection

Quality Assessment of the included studies using Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2)

A total of 6 RCTs with 378 patients were finally included in the study. Treatment with omega-3 resulted in a statistically significant reduction in ALT (ALT IU/L: MD = -11.34, 95% CI: -15.61 to -7.07, p < 0.01; AST IU/L: MD = -4.72, 95% CI: -8.09 to -1.36, p = 0.006), as well as, a significant improvement in liver steatosis assessed by ultrasonography (OR: 0.31, 95% CI: 0.16 to 0.62, p = 0.001), when compared to placebo, in parallel with a significant decrease in weight (BMI kg/m²: MD = -1.15, 95% CI: -2.22 to -0.09, p = 0.03).



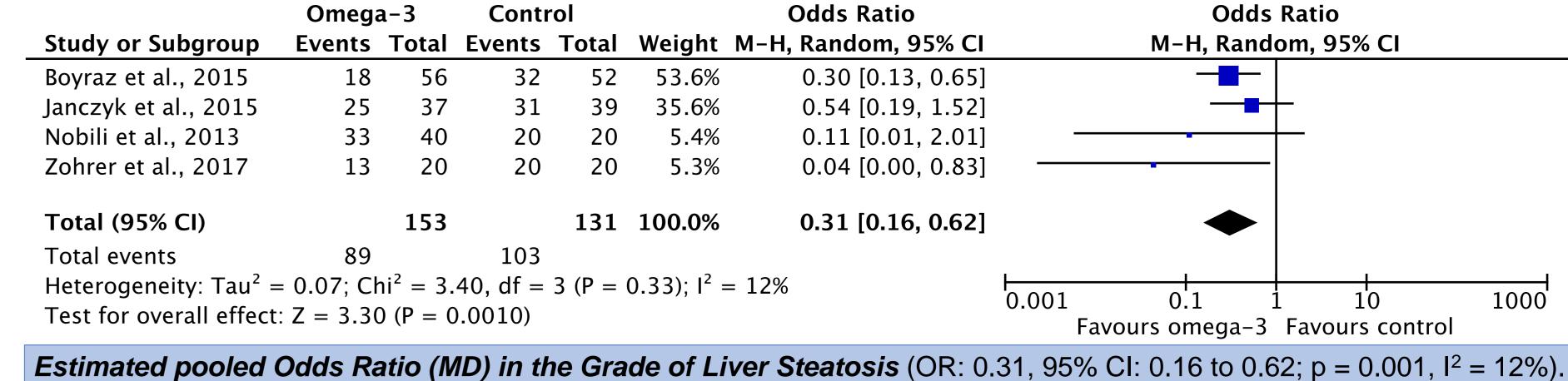
Estimated pooled Mean Difference (MD) in ALT (ALT IU/L: MD = -11.34, 95% CI: -15.61 to-7.07, p < 0.01, I² = 0%)

| | O | mega-3 | 3 | C | Control | | | Mean Difference | Mean Difference |
|-----------------------------------|-----------|-------------|--|----------|----------|-----------|--------|------------------------|--------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| Boyraz et al., 2015 | -13.5 | 11.56 | 56 | -10.1 | 9.85 | 52 | 69.3% | -3.40 [-7.44, 0.64] | |
| Corte et al., 2016 | -8.55 | 20.62 | 20 | 2 | 32.03 | 23 | 4.5% | -10.55 [-26.46, 5.36] | |
| Janczyk et al., 2015 | -14.4 | 13.36 | 37 | -7 | 18.82 | 39 | 21.2% | -7.40 [-14.71, -0.09] | |
| Zohrer et al., 2017 | -5 | 14.1 | 20 | 1.5 | 31.43 | 20 | 5.0% | -6.50 [-21.60, 8.60] | |
| Total (95% CI) | | | 133 | | | 134 | 100.0% | -4.72 [-8.09, -1.36] | • |
| Heterogeneity: Tau ² = | = 0.00; 0 | $Chi^2 = 1$ | .50, df | = 3 (P : | = 0.68); | $I^2 = 0$ | % | _ | -50 -25 0 25 50 |
| Test for overall effect | | | -50 -25 0 25 50 Favours omega-3 Favours control | | | | | | |

Estimated pooled Mean Difference (MD) in AST (AST IU/L: MD = -4.72 IU/L, 95% CI: -8.09 to -1.36, p = 0.006, I² = 0%)

| | On | nega- | 3 | C | ontrol | | | Mean Difference | Mean Difference |
|-----------------------------------|-----------|--------------------|--|-------|--------|-------|--------|-----------------------------|--------------------|
| Study or Subgroup | Mean | SD | Total | Mean | SD | Total | Weight | IV, Random, 95% CI | IV, Random, 95% CI |
| Boyraz et al., 2015 | -6 | 4.3 | 56 | -3.6 | 2.99 | 52 | 21.8% | -2.40 [-3.79, -1.01] | |
| Corte et al., 2016 | -3.84 | 3.87 | 20 | -0.37 | 5.53 | 23 | 10.1% | -3.47 [-6.30 , -0.64] | |
| Janczyk et al., 2015 | -0.7 | 1.39 | 37 | -0.33 | 1.28 | 39 | 31.1% | -0.37 [-0.97, 0.23] | |
| Nobili et al., 2013 | -0.45 | 2.71 | 40 | -0.26 | 3.77 | 20 | 16.9% | -0.19 [-2.04, 1.66] | |
| Pacifico et al., 2015 | -1.6 | 4.2 | 25 | -0.3 | 5.45 | 26 | 11.0% | -1.30 [-3.96, 1.36] | |
| Zohrer et al., 2017 | -0.1 | 4.51 | 20 | -0.2 | 5.25 | 20 | 9.1% | 0.10 [-2.93, 3.13] | |
| Total (95% CI) | | | 198 | | | 180 | 100.0% | -1.15 [-2.22, -0.09] | |
| Heterogeneity: Tau ² = | = 0.86; 0 | Chi ² = | | | | | | | |
| Test for overall effect | | | −10 −5 0 5 10 Favours omega−3 Favours control | | | | | | |

Estimated pooled Mean Difference (MD) in BMI (BMI kg/m²: MD = -1.15, 95% CI: -2.22 to -0.09, p = 0.03, $I^2 = 56\%$)



CONCLUSIONS

n-3 FA supplementation can improve liver function and liver steatosis in children with NAFLD. Further research is essential to determine their potential role in the treatment of pediatric NAFLD and their effect on liver histology.

REFERENCES

High risk

- Vajro P, et al. Diagnosis of nonalcoholic fatty liver disease in children and adolescents: position paper of the ESPGHAN Hepatology Committee. Journal of pediatric gastroenterology and nutrition. 2012;54(5):700-13.
- Chen LH, et al. Omega-3 fatty acids as a treatment for non-alcoholic fatty liver disease in children: A systematic review and meta-analysis of randomized controlled trials. Clinical Nutrition. 2018;37(2):516-21.
- Alkhouri N, et al. Designing Clinical Trials in Pediatric Nonalcoholic Steatohepatitis: Tips for Patient Selection and Appropriate Endpoints. Hepatol Commun. 2019;3(12):1563-70.
- Vos MB, et al. NASPGHAN Clinical Practice Guideline for the Diagnosis and Treatment of Nonalcoholic Fatty Liver Disease in Children: Recommendations from the Expert Committee on NAFLD (ECON) and the North American Society Email: mhourd@gapps.auth.gr of Pediatric Gastroenterology, Hepatology and N. JPGHAN 2017;64(2):319-34.

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