

# INPLASY

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## Comparative analysis of fish oil (FO)-derived omega-3 fatty acid enriched parenteral nutrition regimens versus standard non-FO-enriched parenteral nutrition regimens in hospitalized patients: Study protocol for a systematic review and meta-analysis

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## ADMINISTRATIVE INFORMATION

**Support** - B. Braun Melsungen AG, Germany.

**Review Stage at time of this submission** - Completed but not published.

**Conflicts of interest** - PS has received speaking honoraria from Nestle, Fresenius Kabi, Nutricia and Baxter and received grants from Nestle and ART MEDICAL. PC acts as an ad hoc consultant/advisor to Danone Nutricia Research, dsm-firmenich, Fresenius-Kabi, B. Braun Melsungen, Nestle, Baxter Healthcare and Abbott Nutrition, and has received speaking honoraria from dsm-firmenich, Fresenius-Kabi and Abbott Nutrition.

**INPLASY registration number:** INPLASY202630092

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 March 2026 and was last updated on 25 March 2026.

## INTRODUCTION

**Review question / Objective** The objective of this study is to conduct an updated systematic review and meta-analysis comparing the clinical efficacy and safety of FO-enriched PN regimens with standard non-FO-enriched PN regimens in parenterally nourished hospitalized patients in order to extend the results of previous analyses and determine whether certain formulations are more beneficial than others.

**Rationale** Parenteral nutrition in hospitalized patients has become an established procedure throughout the last decades. Intravenous lipid emulsions (ILEs) play a key role in PN regimens as they are characterized by a high energy density and low osmolarity. The usual composition of

those emulsions consists mainly of  $\omega$ -6 fatty acids enriched vegetable oils, e. g. soybean oil (SO). In the last years, fish oils, which are characterized by a high  $\omega$ -3 fatty acid content, have been added to some of the PN regimens as source for energy. So far, trials have explored whether FO-enriched PN regimens can modulate inflammatory over-response in sepsis patients and after major abdominal surgery, compared to the traditional lipid emulsions. A more recent meta-analysis by Pradelli et al. could show that  $\omega$ -3 fatty-acid enriched PN was beneficial in reducing risk of infection and sepsis by 40% and 56%, respectively, and in reducing length of both ICU and hospital stay by about 2 days. It was concluded that provision of  $\omega$ -3-enriched lipid emulsions should be preferred over standard lipid emulsions in patients with an indication for PN. So far, no publications have separately evaluated the effects of FO alone or added to other lipid

emulsions, or FO within different commercially available mixed emulsions.

**Condition being studied** Parenteral nutrition in hospitalized adult patients, including surgical and ICU patients.

## METHODS

**Search strategy** Systematic search in the databases MEDLINE (Pubmed interface), EMBASE (Elsevier interface), and the Cochrane Central Register of Controlled Trials (Wiley interface) in order to identify randomized controlled trials.

Key search terms include “parenteral nutrition”, “fish oil”, “omega-3”, “lipid” and “emulsion”. In addition to the search for the intervention compositions, different brand names used as search terms.

Search strategy adapted accordingly for each database. Each database searched separately.

**Participant or population** Hospitalized adult patients ( $\geq 18$  years of age) who are eligible for parenteral nutrition (either in the form of total parenteral nutrition or supplemental parenteral nutrition).

### Intervention

The following compositions of PN regimens are included as interventions:

FO (as an add-on to standard non-FO-enriched PN regimens)

Fish oil (FO) + soy oil (SO) + medium-chain triglycerides (MCT)

FO + SO + MCT + olive oil (OO).

**Comparator** Standard non-FO-enriched PN regimens.

**Study designs to be included** Randomized controlled trials (RCTs).

**Eligibility criteria** Contains data of at least one outcome of interest

Only scientific articles published in peer-reviewed journals, no letters, no comments, no conference abstracts, no reviews.

**Information sources** MEDLINE (Pubmed interface), EMBASE (Elsevier interface), and the Cochrane Central Register of Controlled Trials (Wiley interface).

**Main outcome(s)** • Mortality rate (When multiple mortality endpoints are reported in a trial, the data

are included in the following order of preference: 28-day mortality > hospital mortality > ICU mortality > other mortality)

- Infection rate
- Sepsis rate
- Length of stay (LOS) hospital
- LOS ICU
- Duration of mechanical ventilation
- ICU-free days until day 30
- ICU-free days until day 60
- Re-admissions up to day 30 (ICU and hospital)
- Re-admissions up to 6 months (ICU and hospital)
- Ventilation-free days until day 30
- Transfused blood units
- Oxygenation index
- Length of the PN support
- Hand grip strength
- Six-minute walk test
- Quality of life.

### Quality assessment / Risk of bias analysis

Cochrane risk-of-bias tool for randomized trials version 2 (RoB 2).

**Strategy of data synthesis** Systematic review with meta-analysis using Cochrane's Review Manager (RevMan).

### Subgroup analysis

- Categorization of patients (surgical vs. ICU)
- Acute Physiology And Chronic Health Evaluation (APACHE) II score in ICU patients (<15 vs.  $\geq 15$  vs. not reported)
- Duration of total PN (<6 days vs.  $\geq 6$  days)
- FO dosage per day (<0.15 g/kg body weight [BW]/day vs.  $\geq 0.15$  g/kg BW/day)
- Lipid dosage per day (<1 g/kg BW/day vs.  $\geq 1$  g/kg BW/day vs. not reported)
- Type of standard PN (SO vs. LCT/MCT vs. glucose 10% vs. OO vs. other)
- Age (<60 years vs.  $\geq 60$  years)
- Body Mass Index (<25 kg/m<sup>2</sup> vs.  $\geq 25$  kg/m<sup>2</sup> vs. not reported)
- Sex (female vs. male vs. not reported)
- Overall level of bias (low risk vs. some concerns vs. high risk)
- Publication year of the study (until and including 2010 vs. after 2010).

**Sensitivity analysis** None.

**Language restriction** None.

**Country(ies) involved** Israel, Germany, United Kingdom.

**Keywords** Parenteral nutrition; fish oil; omega-3; clinical outcome; meta-analysis.

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**Dissemination plans** Journal publication.

**Contributions of each author**

Author 1 - Pierre Singer - Supervision; Writing - review & editing.

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