SINPE
Società Italiana di Nutrizione Artificiale e Metabolismo
Membro della Federazione delle Società Italiane di Nutrizione (FeSIN)

**CLINICAL NUTRITION: shaping a better future of health care**
**Congresso Nazionale SINPE**
**27-29 novembre 2025**

# OMEGA-3 NELLA NUTRIZIONE PARENTERALE DEL PAZIENTE ADULTO E PEDIATRICO: EVIDENZE E PROSPETTIVE CLINICHE


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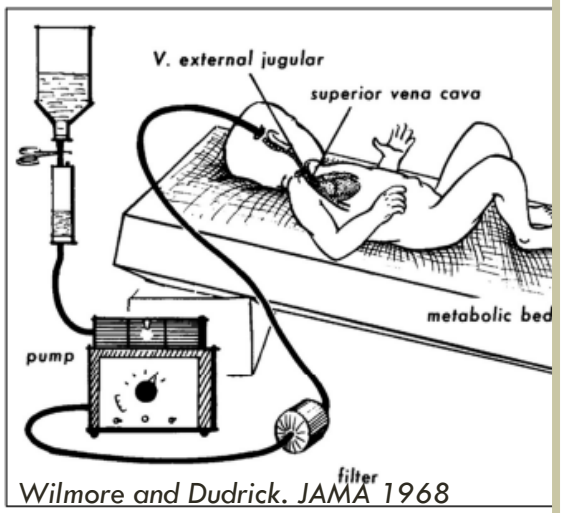
*Presidente Società Italiana di Nutrizione Artificiale e Metabolismo SINPE*

# LA NUTRIZIONE PARENTERALE… DOMICILIARE

## 1960

…an infant with small bowel atresia and fail
received PN for months **in the hospital** until i
that she would be dependent on PN for the r



*Wilmore and Dudrick. JAMA 1968*

## 1969

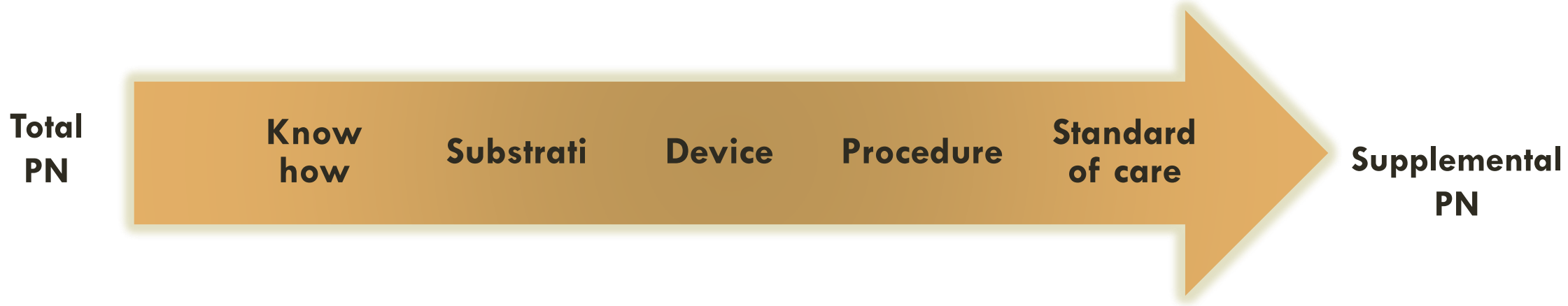
"Can intravenous feeding as the sole means of nutrition support growth in the child and restore weight loss in an adult? **An affirmative answer**".

Dudrick SJ, et al.AnnSurg.**1969**;169(6):974-984

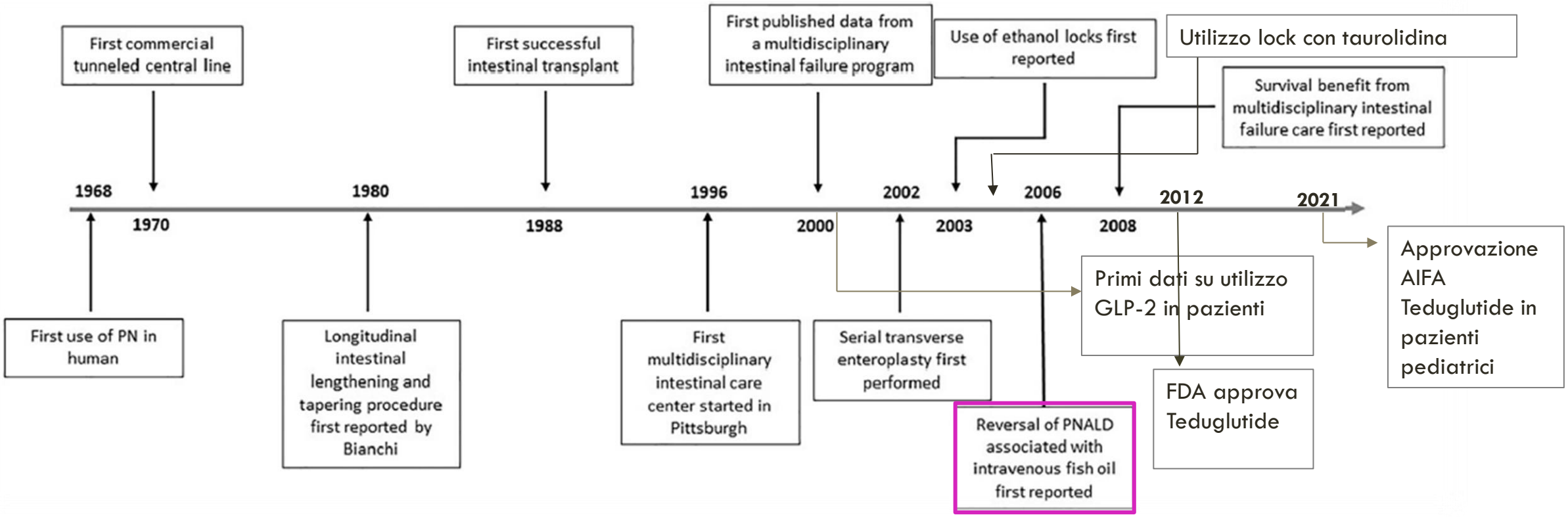
"***hyperalimentation team***" *initially consisting of an* ***interested group*** *of surgeons, pharmacists, and basic scientists.*

*What is needed: a* ***multidisciplinary approach*** *to nutrition support with a designated nurse, a team to ensure continuity, standardization of safe principles, and quality assurance, … addition of a dietitian, psychiatrist, and social worker.*

# L'EVOLUZIONE DELLA NP



# STORIA DELLA GESTIONE DELL'INSUFFICIENZA INTESTINALE




*P.J. Javid et al. / Seminars in Pediatric Surgery 27 (2018) 218–222*

EXPERIENCE & REASON

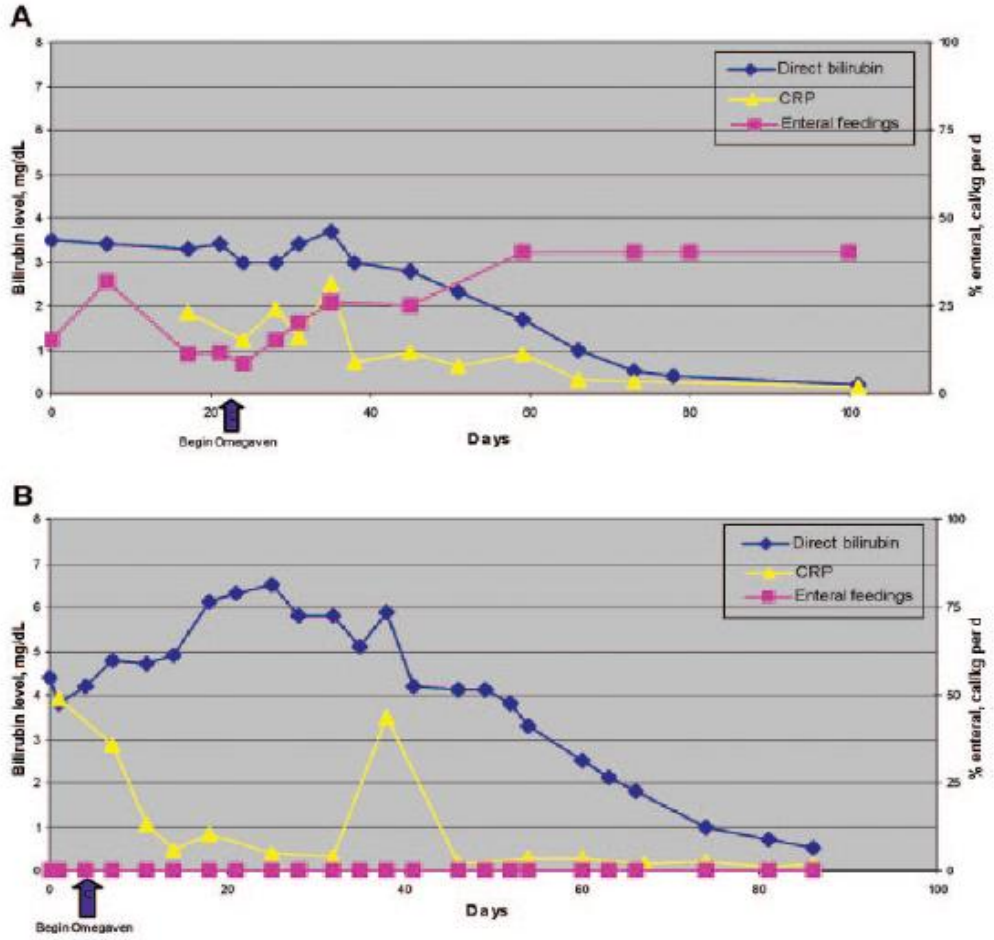
PEDIATRICS Volume 118, Number 1, July 2006

# Reversal of Parenteral Nutrition–Associated Liver Disease in Two Infants With Short Bowel Syndrome Using Parenteral Fish Oil: Implications for Future Management

Kathleen M. Gura, PharmD[a,b], Christopher P. Duggan, MD, MPH[b], Sharon B. Collier, MS, RD[b], Russell W. Jennings, MD[c], Judah Folkman, MD[c], Bruce R. Bistrian, MD[d], Mark Puder, MD, PhD[c]

## CONCLUSIONS

This brief report describes a new use of a fat emulsion consisting solely of fish oils to reverse severe PN cholestasis in 2 infants, one receiving >50% and a second receiving 100% of his energy intake parenterally. From historical data, neither patient would be expected to improve but instead would develop progressive liver disease. Both infants' cholestasis resolved within 8 weeks. This new therapy may offer a potential solution in the treatment or prevention of hepatotoxicity in PN-dependent patients and may provide an alternative therapy to avoid the morbidity, mortality, and the need for liver/small bowel transplantation in children and adults who are dependent on PN and provide the time necessary for bowel adaptation. A randomized, controlled trial is necessary to determine the efficacy of this new treatment.



... 2008

# Nostro caso clinico

Maschio, nato a 36 sett, peso neonatale 3165 g

Gastroschisi → anastomosi digiuno-colica (26 cm tenue su colon discendente, no VIC)

Sviluppo di colestasi, citolisi, cirrosi, ipersplenismo, deficit di sintesi, no varici.

A 6 mesi proposto Tx di fegato salvavita

Omegaven 0.5 g/kg x 3/sett per 3 sett e in seguito  Clinoleic 1 g/kg + Omegaven 0.2 g/kg x 5/sett

NP 70% + NE (elementare) 30%; decontaminazione

Progressiva regressione degli indici di colestasi (normalizzazione BD, GGT) INR 1.35, fibroscan 11kPa (fibrosi di grado moderato) – avvio NPD

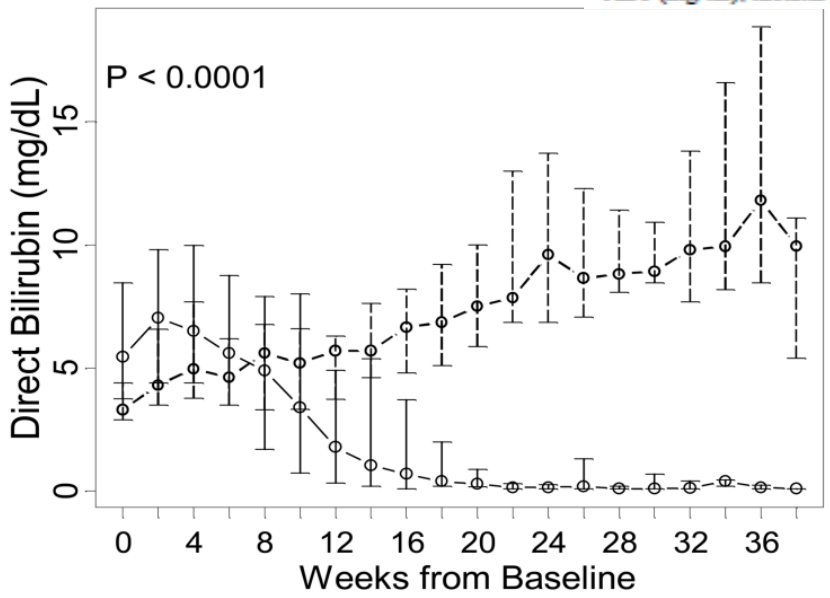
Rimozione dalla lista di trapianto in follow-up

# Il seguito…

*Ann Surg.* 2009 September ; 250(3): 395–402.

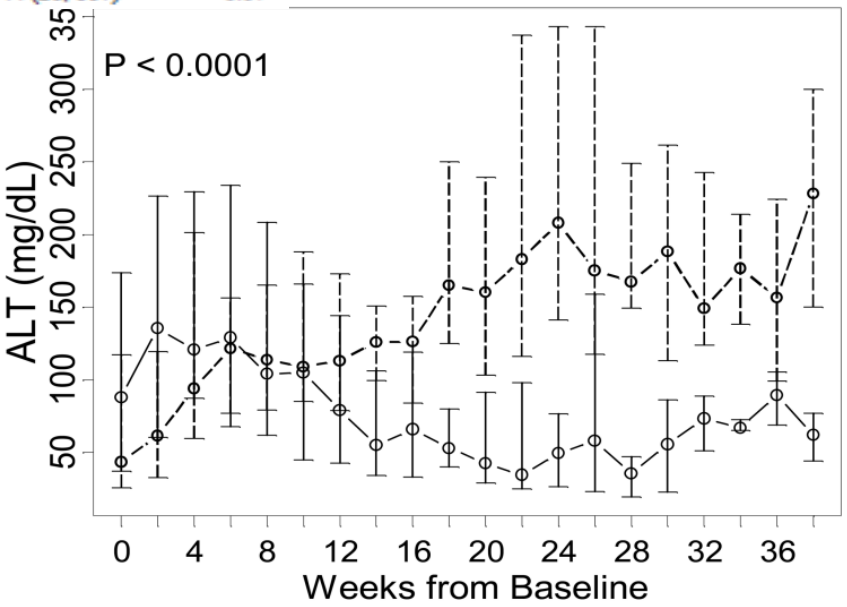
Omegaven (1 g/kg/die) vs Intralipid (dose standard) in neonati SBS con PNALD

| Variables | Fish Oil (N=42 ) | Soybean Oil (N=49 ) | P Value[†] |
|---|---|---|---|
| **Demographic and Medical History** | | | |
| Gender (male), *n (%)* | 28 (67%) | 31 (63%) | 0.73 |
| Age (weeks), *median (IQR)* | 12 (8, 25) | 7 (5,12) | 0.0002 |
| Birth weight (kg), *mean ± SD* | 1.6 ± 0.86 | 1.8 ± 0.98 | 0.29 |
| Gestational age (weeks), *mean ± SD* | 30 ± 5 | 32 ± 5 | 0.046 |
| Duration of PN prior to enrollment (days), *median (IQR)* | 63 (48, 118) | 40 (21, 74) | 0.008 |
| **Laboratory** | | | |
| Direct bilirubin (mg/dL), *median (IQR)* | 5.5 (3.7, 8.5) | 3.3 (2.9, 4.4) | 0.0003 |
| ALT (mg/dL), *median (IQR)* | 88 (37, 174) | 44 (26, 117) | 0.07 |




Risoluzione della colestasi in 19/42 bambini vs 2/49

Morte o trapianto di intestino 4/42 vs 17/49



# Emulsioni lipidiche composite con olio di pesce in HPN

## EFFICACIA + SICUREZZA

RCT

Goulet O et al. *JPEN J Parenter Enteral Nutr*. 2010;34(5):485-495

Tomsits E et al. *J Pediatr Gastroenterol Nutr*. 2010;51(4):514-521

Skouroliakou M et al. *Eur J Clin Nutr*. 2010;64(9):940-947

Rayyan M et al. *JPEN J Parenter Enteral Nutr*. 2012;36(1 suppl):81S-94S

| RISULTATI |
| --- |
| ↑ EPA e DHA nelle membrane cellulari |
| ↓ n-6 / n-3 |
| ↓ Bilirubina totale e diretta, ↓ γGT |
| ↑ Vitamina E |
| ↑ Total Antioxidant Capacity |
| Non differenze nella perossidazione lipidica |

# ESPGHAN Committee on Nutrition Position Paper. Intravenous Lipid Emulsions and Risk of Hepatotoxicity in Infants and Children: a Systematic Review and Meta-analysis

## CONCLUSIONS

The ESPGHAN Committee on Nutrition (CoN) concludes

- There is no evidence of a difference in bilirubin, conjugated bilirubin, AST, ALT, ALP, and GGT between short-term use of OO/SO and SO ILE in infants and children (level of evidence 2a).
- There is no evidence of a difference in bilirubin, conjugated bilirubin, AST, ALT, ALP, and GGT between short-term use of multicomponent FO-containing ILE and SO ILE in neonates (level of evidence 2a).
- The use of multicomponent FO-containing ILE may contribute to a decrease in total bilirubin levels in children with IF on prolonged PN (level of evidence 2b).
- Pure FO supply combined with a decrease or interruption of SO ILE may contribute to cholestasis recovery in children with PNALD (level of evidence 2b).

## RECOMMENDATIONS

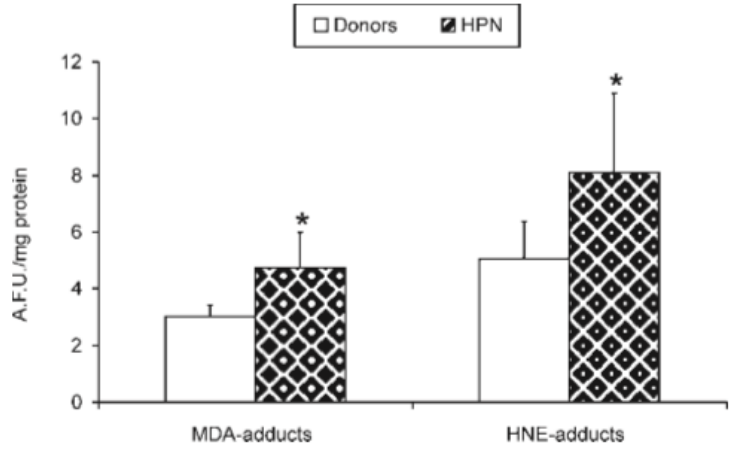
- Prevention and care of PNALD in children should not be focused exclusively on parenteral ILE intake.
- Because of their high phospholipid content, 10% ILE should no longer be used (GR B).
- Based on available evidence, the CoN cannot currently recommend the use of any specific ILE for short-term use in infants and children for the prevention and treatment of PNALD (GR B).
- For children in whom long-term use of PN is expected, it appears prudent to use multicomponent FO-containing ILE (GR C).
- The present evidence base is inadequate to determine the optimal strategy for intravenous lipid supply in both preterm and term infants and older children to prevent or treat liver complications.
- In particular, studies on both the prevention and treatment of PNALD should be conducted in high-risk infants and children who are likely to require long-term PN, and should also consider additional extrahepatic outcomes such as growth and cognition.

Journal of Pediatric Gastroenterology and Nutrition 2016;62(5):776–792

# NUTRIZIONE PARENTERALE PEDIATRICA DI LUNGA DURATA CONSEGUENZE A LIVELLO MOLECOLARE

**FABBISOGNO INFUSIONALE**

- ↑ **STRESS OSSIDATIVO (perossidazione lipidica)**
- ↑ **INFIAMMAZIONE**
- ↑ **FIBROSI EPATICA -> IFALD -> NUTRITIONAL FAILURE**

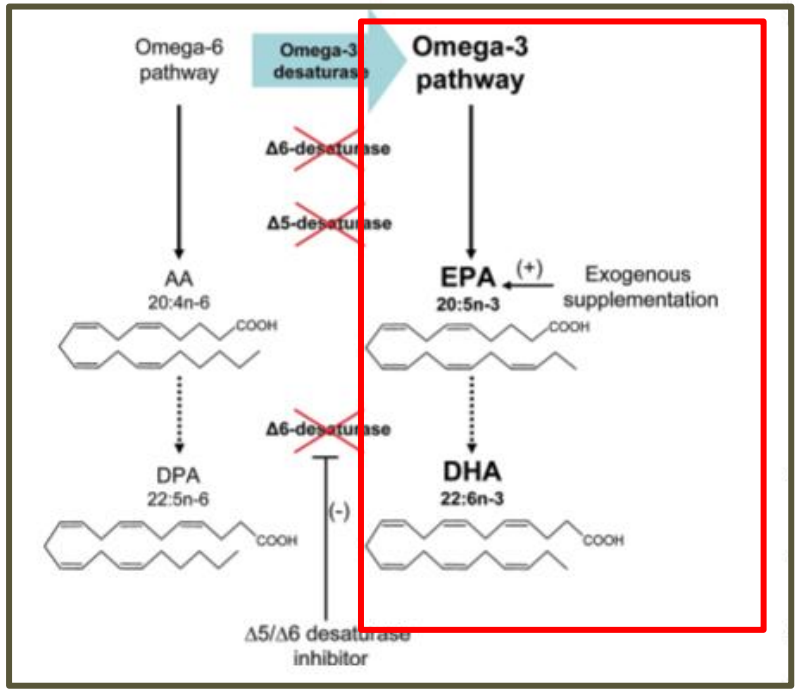



*Courtney C.M. et al. Pediatric intestinal failure-associated liver disease Curr. Opi Pediatr. 2017 Jun;29(3):363-3702017*

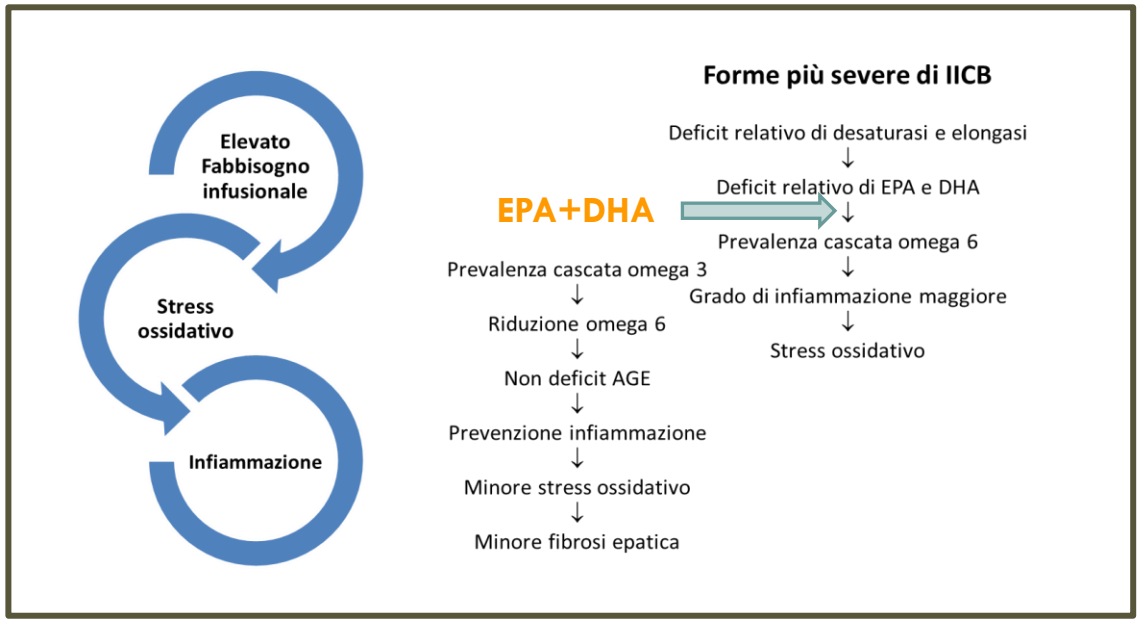
*Florence Lacaille et.al Intestinal Failure–Associated Liver Disease: A Position Paper of the ESPGHAN Working Group of Intestinal Failure and Intestinal Transplantation. JPGN " Volume 60, Number 2, February 2015*

*Massarenti P. et al. 4-Hydroxynonenal is Markedly Higher in Patients on a Standard Long-term Home Parenteral Nutrition. Free Radical Research, Volume 38 Number 1 (January 2004), pp. 73–80*

# DEFICIT RELATIVO DI EPA E DHA: IL MODELLO DELLA NASH NELLA PATOGENESI DELL'IFALD




*Lopez-Vicario C. et al. Molecular interplay between Δ5/Δ6 desaturases and long-chain fatty acids in the pathogenesis of non-alcoholic steatohepatitis; Gut 2014; 63:344–355.*




*Lezo A. et al. Plasma and red blood cell PUFAs in home parenteral nutrition paediatric patients – effects of lipid emulsions. Nutrients 2020; 12(12), 3748*

# THE LIPIDS IN PARENTERAL NUTRITION INTERNATIONAL SUMMIT

NOVEMBER 2–4, 2018, MIAMI, USA

| Statement Number | Consensus Statement | Expert Voting Results |
|---|---|---|
| 1 | We recognize that lipid emulsions are an integral part of PN. Originally, lipid emulsions were an energy-dense source of calories and provided essential FAs. | 100% agreement (16 agree, 0 do not agree, 0 do not wish to answer). |
| 2 | Subsequent generations of lipid emulsions include combinations of various lipid components, predominantly with the aim of improving the safety profile of ILEs. Each lipid has its own FA composition and biological effects, which may be more or less beneficial on, for example, pro- or anti-inflammatory, immune-stimulating or modulating properties. | 100% agreement (17 agree, 0 do not agree, 0 do not wish to answer). |
| 3 | An important component of modern, composite lipid emulsions is fish oil. The group recognizes that the biological effects of fish oil are increasingly characterized in preclinical studies (different models). The biological effects of fish oil can mainly be attributed to $\omega$-3 polyunsaturated FAs, especially EPA and DHA, and include anti-inflammatory and immunomodulatory and antioxidative properties. | 94% agreement (16 agree, 1 does not agree, 0 do not wish to answer). |
| 4 | In the view of the group, the latest findings regarding the role of specialized pro-resolution mediators (SPMs) in immune modulation adds considerably to our understanding of the biological characteristics of fish oil. Specialized pro-resolution mediators (SPMs) are a new class of mediators, which are produced directly from EPA and DHA, and are increasingly recognized as key mediators in the resolution of inflammation. | 94% agreement (16 agree, 0 do not agree, 1 does not wish to answer). |

DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; FA, fatty acid; ILE, intravenous lipid emulsion; PN, parenteral nutrition; SPM, specialized pro-resolution mediators.

*Martindale RG, et al. JPEN J Parenter Enteral Nutr. 2019*

Clinical Nutrition 42 (2023) 590–599

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

# Omega-3 fatty acids in parenteral nutrition — A systematic review with network meta-analysis on clinical outcomes☆

Lorenzo Pradelli [a, *], Konstantin Mayer [b], Stanislaw Klek [c], Martin D. Rosenthal [d], Massimiliano Povero [a], Axel R. Heller [e], Maurizio Muscaritoli [f]

Sepsis risk: 10 studies, 1627 participants.
Very highly credible reduction in sepsis risk:
- FO-ILEs versus SO-ILEs
- OO-ILEs vs SO-ILEs

Infection risk: 28 studies, 3081 participants.
Very highly credible reduction in infection risk with FO-ILEs vs:
- SO-ILEs
- MCT/SO-ILEs
- OO-ILEs

LOS: 28 studies with 3343 participants
substantial reduction in LOS was observed with:
- FO-ILEs versus SO-ILEs
- FO-ILEs versus MCT/SO-ILEs
- OO-ILEs versus SO-ILEs

In-hospital mortality: 31 studies, 2828 participants.
Very highly credible reduction in mortality with:
FO-ILEs vs SO-ILEs

*Heterogeneity between studies was very low for all the dichotomous outcomes*
*Inconsistency was low for mortality, infection risk and hospital LOS;*
*Heterogeneity and inconsistency were low for mortality and infection risk.*

Clinical Nutrition 42 (2023) 590–599

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Original article

# Omega-3 fatty acids in parenteral nutrition – A systematic revi with network meta-analysis on clinical outcomes☆

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NMA included 1651 publications, 47 RCTs → ranking of ILEs

FO-ILEs have the potential to confer ***meaningful clinical benefits*** for hospitalized patients receiving PN and ***should*** **be *standard of care*,** particularly in situations associated with a hypermetabolic and/or hyperinflammatory state e.g., in critical illness or post surgery.

→ anti-inflammatory
→ inflammation-resolution
→ immune-modulating

**EPA and DHA**

Probabilities of being the best intervention for each outcome according to the Surface Under the Cumulative RAnking (SUCRA) and median ranks with (90%) credibility intervals (CrI).

| **Infection risk** | **SUCRA** | **Median rank (90% CrI)** |
|---|---|---|
| FO-ILEs | 99.0% | 1 (1–1) |
| MCT/SO-ILEs | 47.6% | 2 (2–4) |
| OO-ILEs | 44.4% | 3 (2–4) |
| SO-ILEs | 9.1% | 4 (3–4) |
| **Sepsis risk** | **SUCRA** | **Median rank (90% CrI)** |
| FO-ILEs | 83.2% | 1 (1–3) |
| OO-ILEs | 60.8% | 2 (1–3) |
| MCT/SO -ILEs | 49.3% | 3 (1–4) |
| SO-ILEs | 6.7% | 4 (3–4) |
| **ICU LOS** | **SUCRA** | **Median rank (90% CrI)** |
| FO-ILEs | 77.2% | 1 (1–3) |
| OO-ILEs | 52.7% | 2 (1–4) |
| SO-ILEs | 39.9% | 3 (1–4) |
| MCT/SO -ILEs | 30.2% | 3 (1–4) |
| **Hospital LOS** | **SUCRA** | **Median rank (90% CrI)** |
| FO-ILEs | 93.2% | 1 (1–2) |
| OO-ILEs | 66.5% | 2 (1–4) |
| MCT/SO -ILEs | 27.6% | 3 (2–4) |
| SO-ILEs | 12.7% | 4 (3–4) |
| **In-hospital mortality** | **SUCRA** | **Median rank (90% CrI)** |
| FO-ILEs | 76.7% | 1 (1–3) |
| MCT/SO-ILEs | 55.8% | 2 (1–4) |
| OO-ILEs | 49.4% | 3 (1–4) |
| SO-ILEs | 18.1% | 4 (2–4) |

Clinical Nutrition 42 (2023) 1671–1689

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ESPEN Guideline

# ESPEN practical and partially revised guideline: Clinical nutrition in the intensive care unit

Pierre Singer [a, *], Annika Reintam Blaser [b, c], Mette M. Berger [d], Philip C. Calder [e], Michael Casaer [f], Michael Hiesmayr [g], Konstantin Mayer [h], Juan Carlos Montejo-Gonzalez [i], Claude Pichard [j], Jean-Charles Preiser [k], Wojciech Szczeklik [l], Arthur R.H. van Zanten [m], Stephan C. Bischoff [n]

37) Parenteral lipid emulsions enriched with EPA + DHA (0.1-0.2 g/kg/d) can be provided in patients receiving PN.
(R33, updated, Grade 0, strong consensus, 100%)

Several studies have shown the biological effects, clinical benefits, and safety of lipid emulsions with **reduced content of 18-carbon omega-6 FA**.

In critically ill ICU patients, fish oil was associated with:

- reductions in infections (RR 0.65, 95% CI 0.46e0.94),
- ICU LOS (2.14 days, 95% CI -3.89 to 0.40),
- hospital length of stay (3.98 days, 95% CI -6.90 to 1.06),
- reduction in 30-day mortality in all ICU patients (RR 0.90, 95% CI 0.69e1.16 = n.s.).

Cost-effectiveness analyses estimated that parenteral fish oil would **lower overall hospital costs** (compared with standard PN).

# EMULSIONI LIPIDICHE IN NP

**Table 2.** Typical Fatty Acid Compositions (% of Total) of Commercially Available Lipid Emulsions for Use in Parenteral Nutrition.

| | Pure SO[a] | SO/MCT-Oil Blend[b] | Restructured SO/MCT-Oil Blend[c] | Pure FO[d] | OO/SO Blend[e] | FO Blend 1[f] | FO Blend 2[g] |
|---|---|---|---|---|---|---|---|
| Lipid source | 100% SO | 50% SO, 50% MCT | 64% SO, 36% MCT | 100% FO | 20% SO, 80% OO | 40% SO, 50% MCT, 10% FO[j] | 30% SO, 30% MCT, 25% OO, 15% FO[c] |
| SFA | 15 | 58 | 46 | 21 | 14 | 49 | 37 |
| MUFA[h] | 24 | 11 | 14 | 23 | 64 | 14 | 33 |
| PUFA | 61 | 31 | 40 | 56 | 22 | 37 | 30 |
| n-3 PUFA: | 8 | 4 | 5 | 48 | 3 | 10 | 7 |
| ALA | 8 | 4 | 5 | 1 | 3 | 4 | 2 |
| EPA | – | – | – | 20 | – | 3.5 | 3 |
| DHA | – | – | – | 19 | – | 2.5 | 2 |
| n-6 PUFA[i] | 53 | 27 | 35 | 5 | 19 | 27 | 23 |

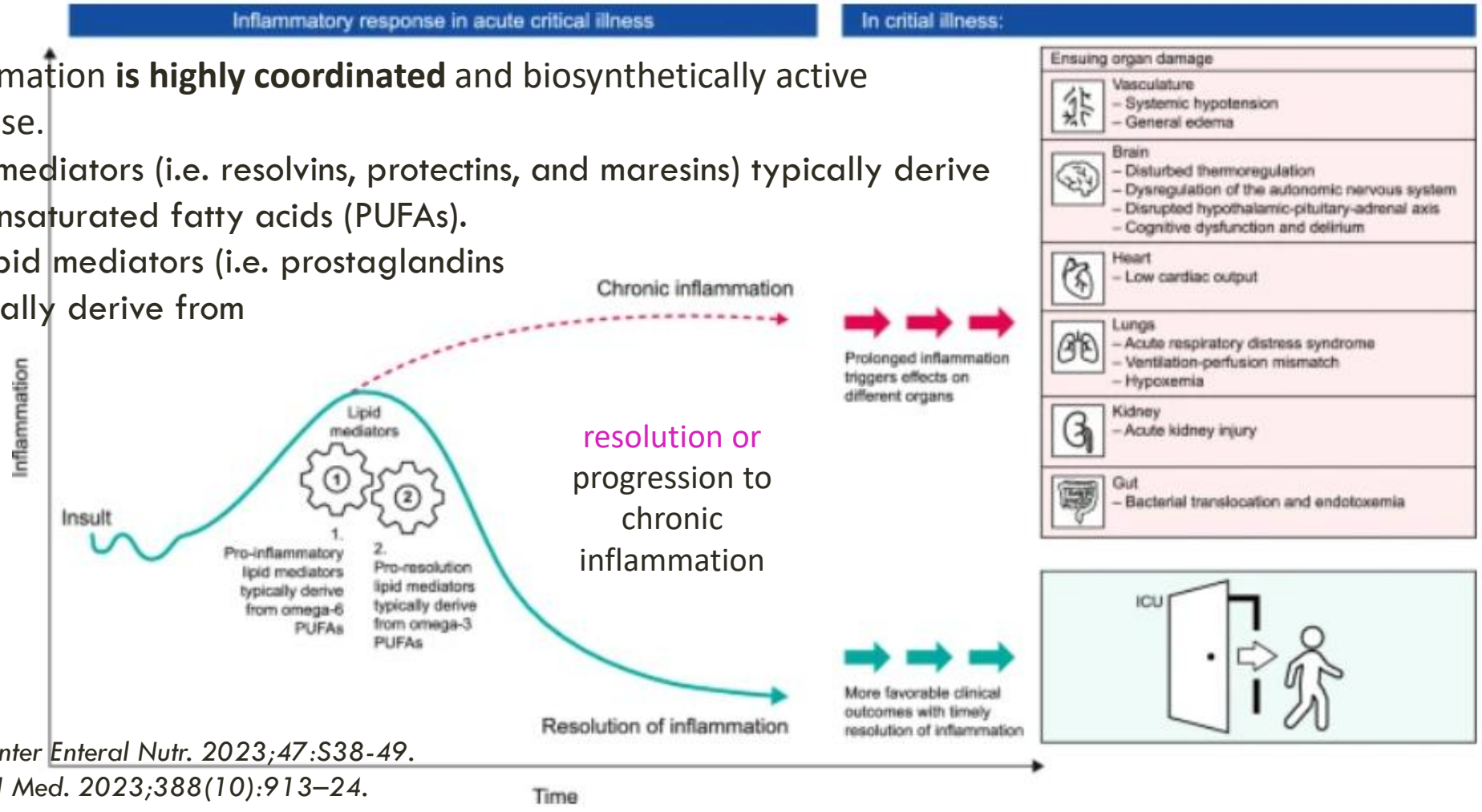
*Calder PC, Waitzberg DL, Klek S, Martindale RG. Lipids in parenteral nutrition: biological aspects. J Parenter Enter Nutr 2020;44(Suppl 1):S21-7.*

# INFLAMMATION AND OUTCOMES IN SURGICAL AND CRITICALLY ILL PATIENTS

Resolution of inflammation **is highly coordinated** and biosynthetically active programmed response.

**Pro-resolution** lipid mediators (i.e. resolvins, protectins, and maresins) typically derive from omega-3 polyunsaturated fatty acids (PUFAs).

**Pro-inflammatory** lipid mediators (i.e. prostaglandins or leukotrienes) typically derive from omega-6 PUFAs.





*Dresen E, et al. JPEN J Parenter Enteral Nutr. 2023;47:S38-49.*
*Herridge MS, et al. N Engl J Med. 2023;388(10):913–24.*
*Calder PC, et al. JPEN J Parenter Enteral Nutr. 2020;44:S21–7.*

*Review*

aspen | LEADING THE SCIENCE AND PRACTICE OF CLINICAL NUTRITION
American Society for Parenteral and Enteral Nutrition

# Lipids in Parenteral Nutrition: Biological Aspects

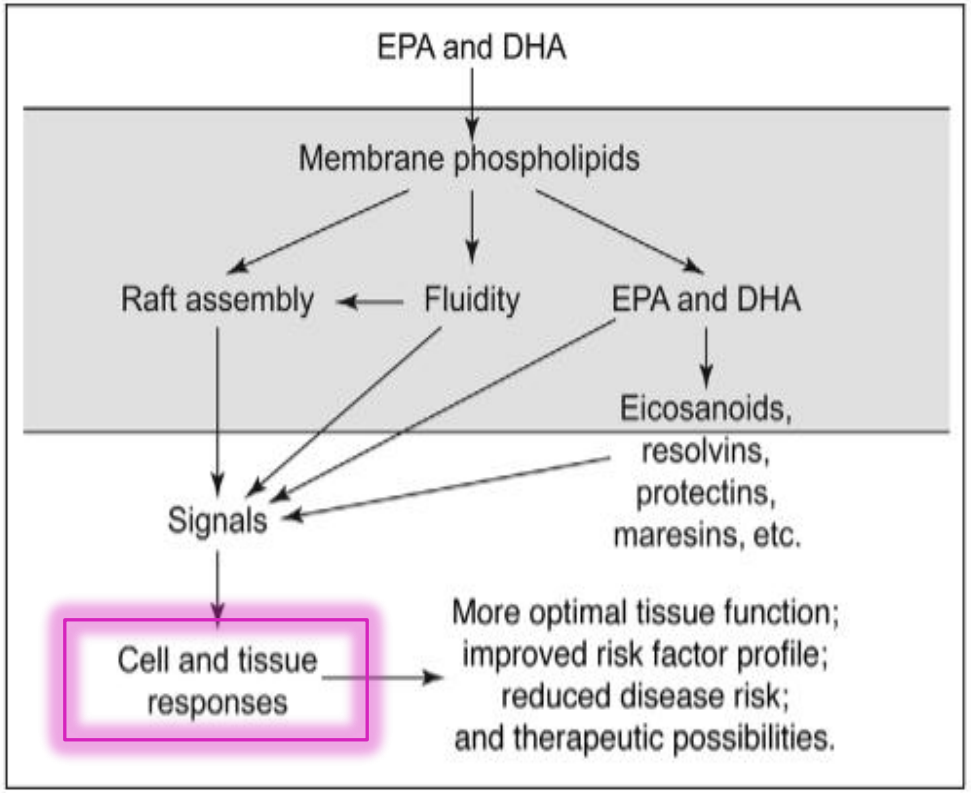
**Philip C. Calder, PhD[1,2]; Dan L. Waitzberg, MD, PhD[3]; Stanislaw Klek, MD, PhD[4]; and Robert G. Martindale, MD, PhD[5]**

Journal of Parenteral and Enteral Nutrition
Volume 44 Supplement 1
February 2020 S21–S27

DOI: 10.1002/jpen.1756
wileyonlinelibrary.com
WILEY

**Specialized Pro-resolving Mediators (SPMs)** has provided an additional molecular basis for the many health benefits attributed to the ω-3 fatty acids.

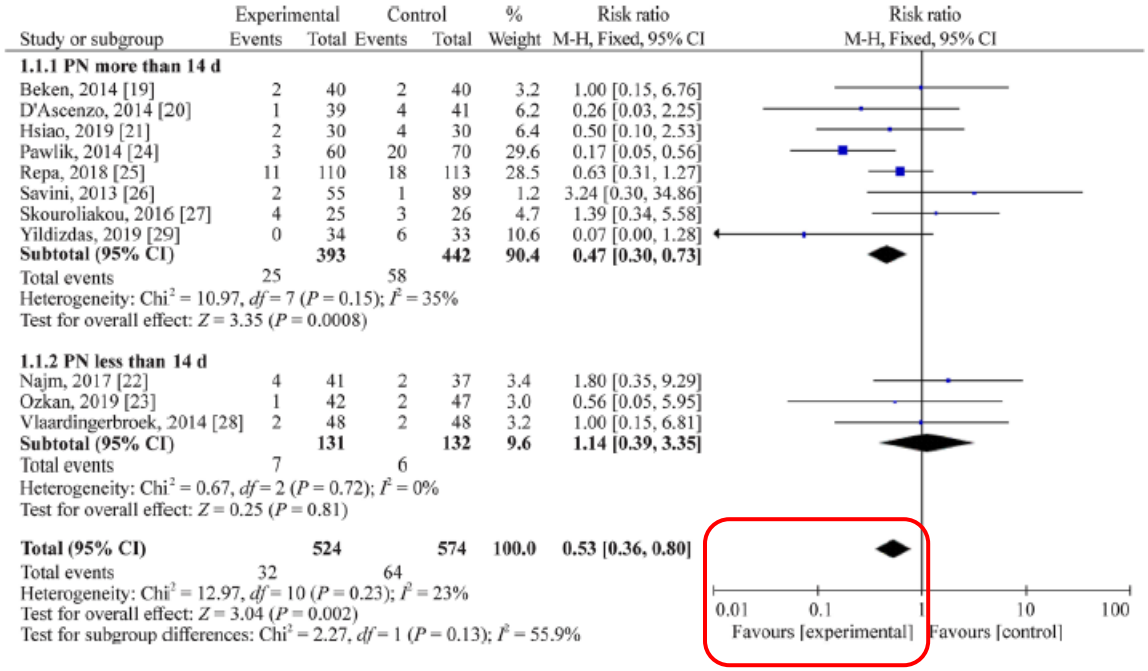
- Actively *terminate* the production of inflammatory mediators
- Directly stimulate *macrophage phagocytosis* of both apoptotic cells and bacteria,
- Promote egress of *phagocytes* from sites of inflammation,
- Regulate *polymorphonuclear neutrophil(PMN) apoptosis*,
- Promote *chemokine scavenging*,
- Stimulate *tissue repair and regeneration*.



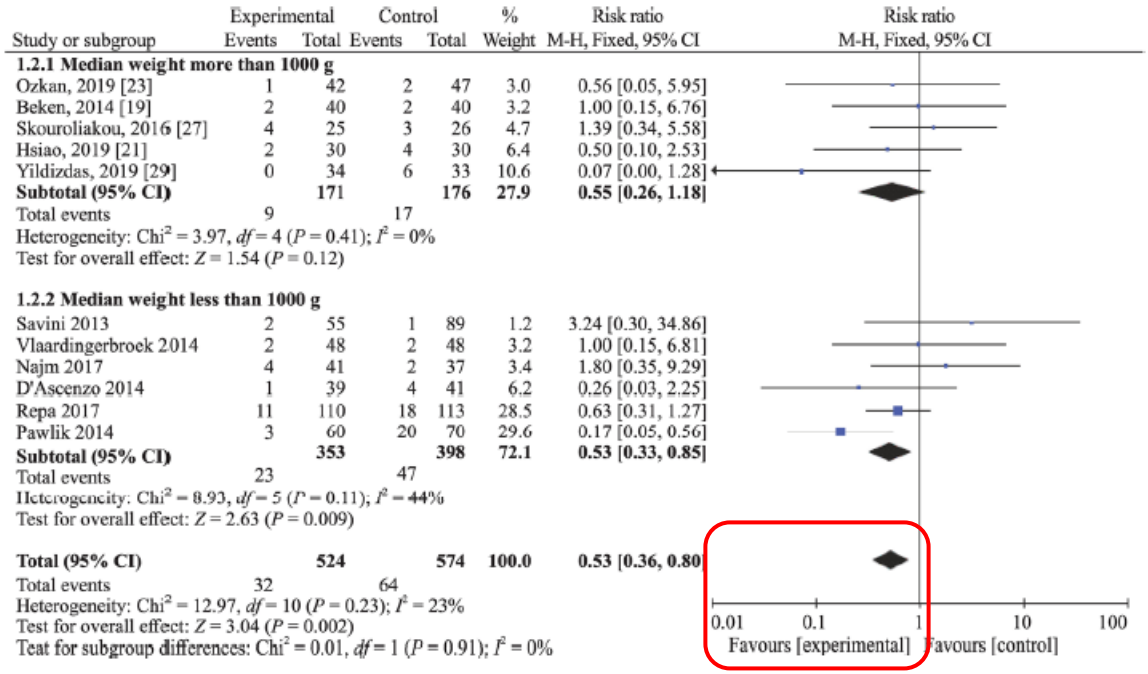
World Journal of Pediatrics (2022) 18:463–471
https://doi.org/10.1007/s12519-022-00536-2

META-ANALYSIS

# Fish oil-containing lipid emulsions prevention on parenteral nutrition-associated cholestasis in very low birth weight infants: a meta-analysis




Subgroup analysis based on parenteral nutrition duration.




Subgroup analysis based on birth weight

Clinical Nutrition 37 (2018) 2324–2336

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journal homepage: http://www.elsevier.com/locate/clnu

# ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Lipids

Alexandre Lapillonne [a, b, *], Nataša Fidler Mis [c], Olivier Goulet [d], Chris H.P. van den Akker [e], Jennifer Wu [f], Berthold Koletzko [g], the ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition [1]

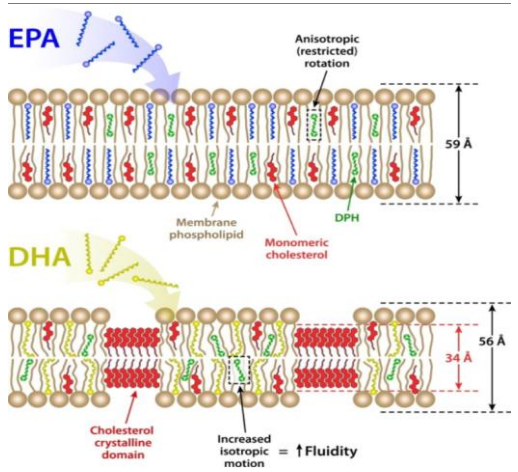
### 6.2. Prevention of intestinal failure associated liver disease

| | |
|---|---|
| R 4.7 | In preterm infants, newborns and older children on short term PN, pure soybean oil (SO) ILEs may provide less balanced nutrition than composite ILEs. For PN lasting longer than a few days, pure SO ILEs should no longer be used and composite ILEs with or without fish oil (FO) should be the first-choice treatment (LoE 1−, RG A, conditional recommendation for, strong consensus) |

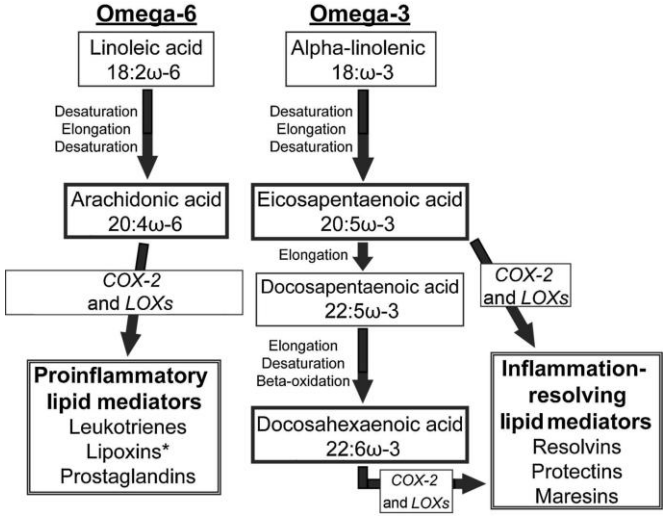
### 8.4. Management of intestinal failure associated liver disease

| | |
|---|---|
| R 4.18 | As part of measures to reverse IFALD in paediatric patients, a discontinuation of SO ILE, a reduction of other ILE dosage and/or the use of composite ILE with FO, should be considered along with the treatment and management of other risk factors (LoE 2+, RG B, strong recommendation for) |
| R 4.19 | The use of pure FO ILE is not recommended for general use in paediatric patients but may be used for short-term rescue treatment in patients with progression to severe IFALD, based on case reports. (LoE 3–4, GPP, conditional recommendation for, strong consensus) |

# PHYSIOLOGICAL EFFECTS AND ASSOCIATED HEALTH BENEFITS OF *N*-3 LC-PUFA




1. Cardioprotective, Antihypertensive, and Antithrombotic Effects
   - EPA and DHA partly replace AA in membrane phospholipids→ improve membrane structure, ligand/receptor binding, enzyme secretion, antigen presentation, activation of intracellular signaling pathways; delay platelet aggregation
2. Anticancer and Anti-Cachectic Effects and Inhibition of Tumor Growth
   - suppress the inflammatory milieu, decrease tumor micro-vessel density, regulation of cell cycle and apoptosis, regulate muscle protein breakdown/synthesis
3. Visual and Cognitive Development
4. Lipid Metabolism and Insulin Sensitivity
5. Inflammatory Disease
6. Immune function




*Klek S. Omega-3 fatty acids in modern parenteral nutrition: a review of the current evidence. J Clin Med 2016;5.*


Advocate a balanced approach: providing clinicians with **guidance based on evidence** to help choose nutritional Interventions…

… but simultaneously acknowledging the **desirability of additional, definitive evidence** regarding complex subjects in clinical nutrition

*Stoppe et al. Critical Care (2024) 28:271*

*Grazie dell'attenzione*