

Omega-3 fatty acids in clinical nutrition

Alastair Forbes

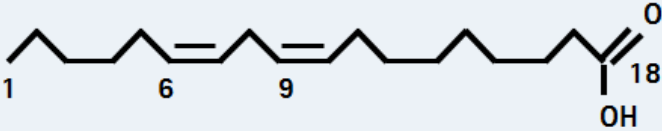
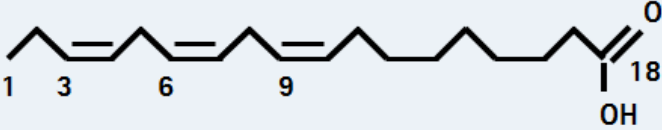
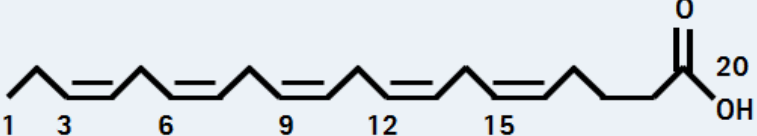
With thanks to Jon Shaffer, UK
and many ESPEN colleagues

Omega-3 fatty acids in clinical nutrition

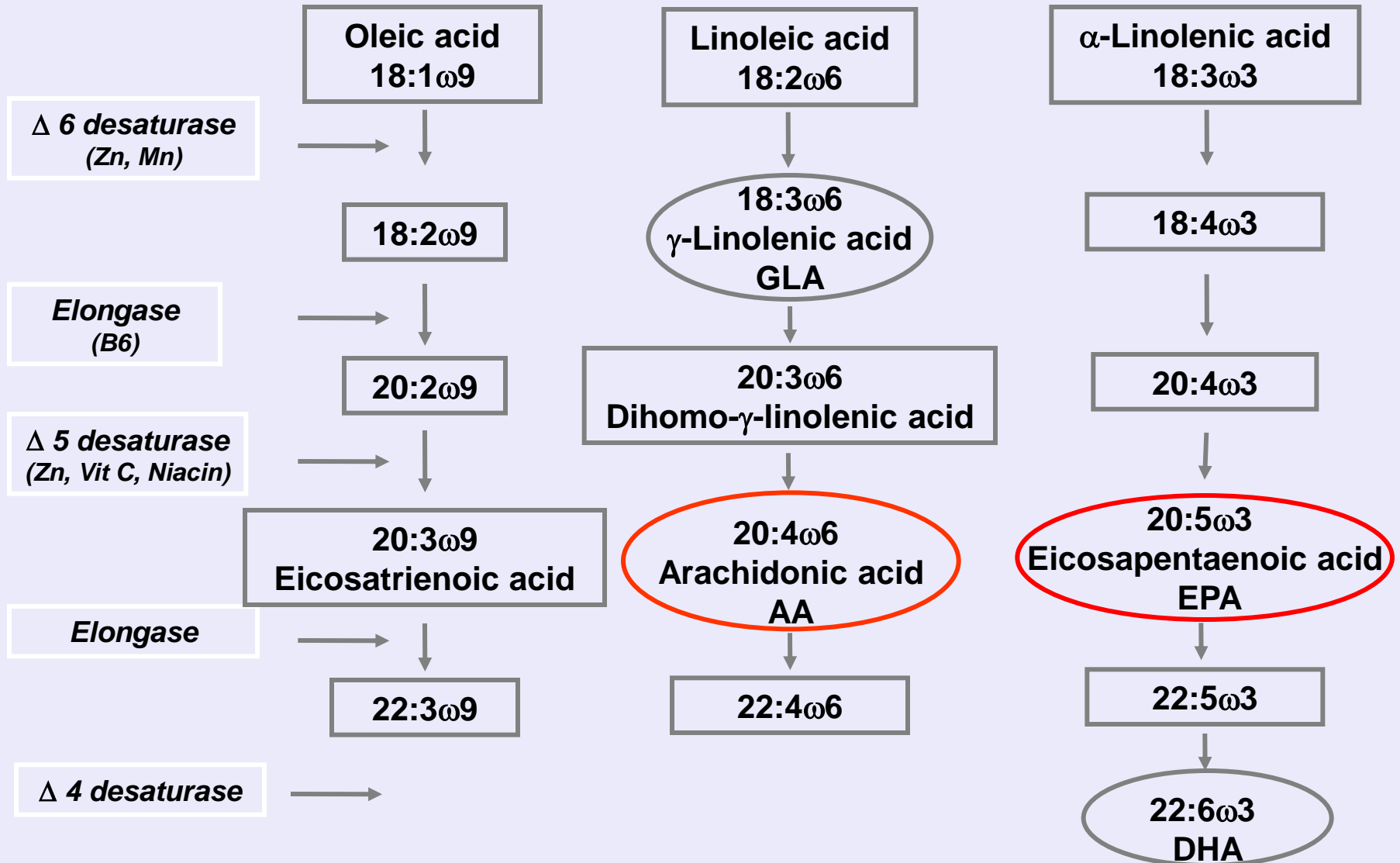
- Review of lipids in nutrition
- Why and how lipids in PN are changing
- Evidence: short- and long-term studies

Classification of unsaturated fatty acids

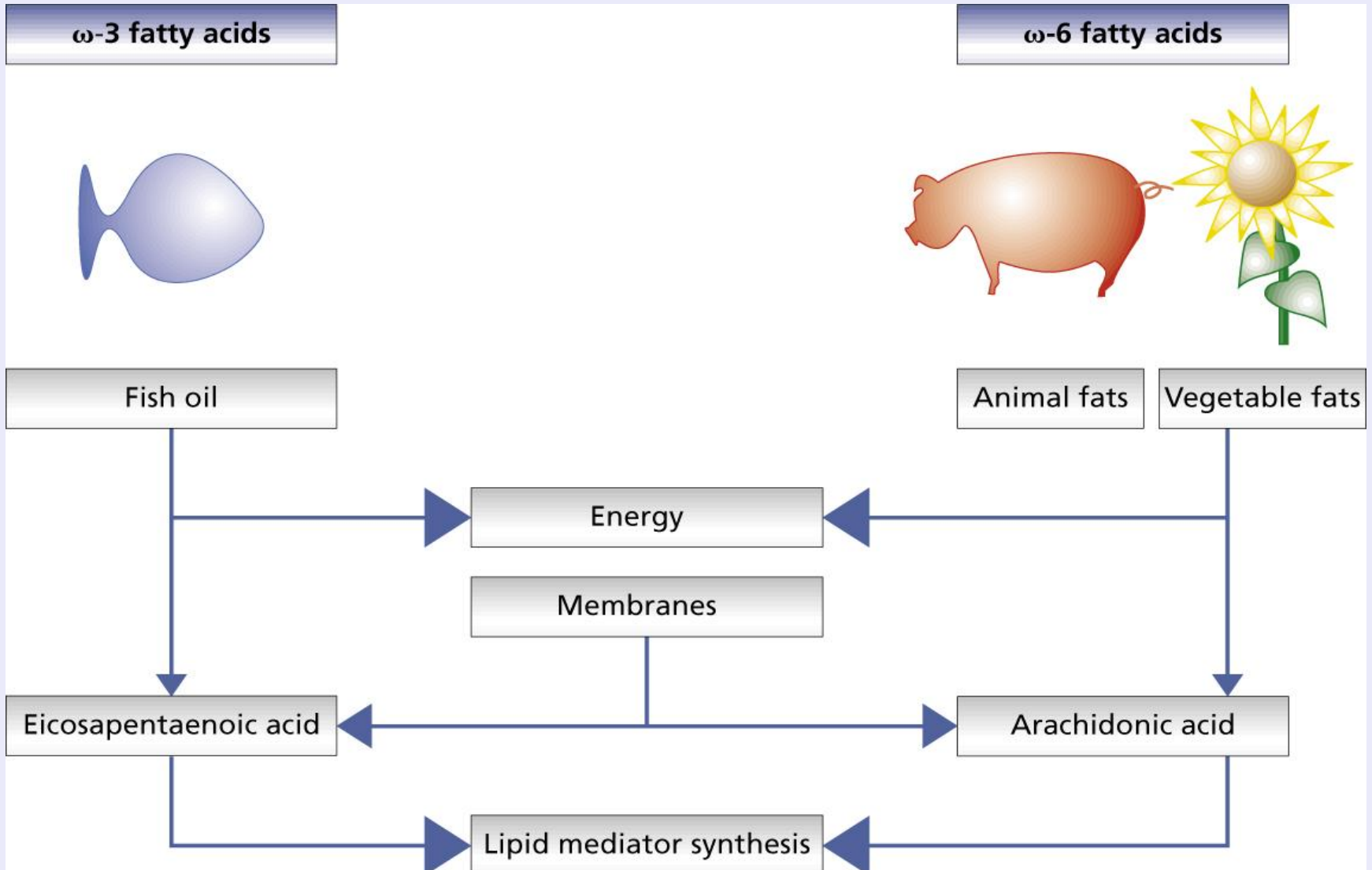
According to the position of the first double bond

	Structure	Abbreviation
Linoleic: n-6		$C_{18:2}, \omega-6$
α -linolenic: n-3		$C_{18:3}, \omega-3$
Eicosapenta-enoic: n-3		$C_{20:5}, \omega-3$

The unsaturated fatty acids



Nutritional sources of LCT



Lipid emulsions for PN

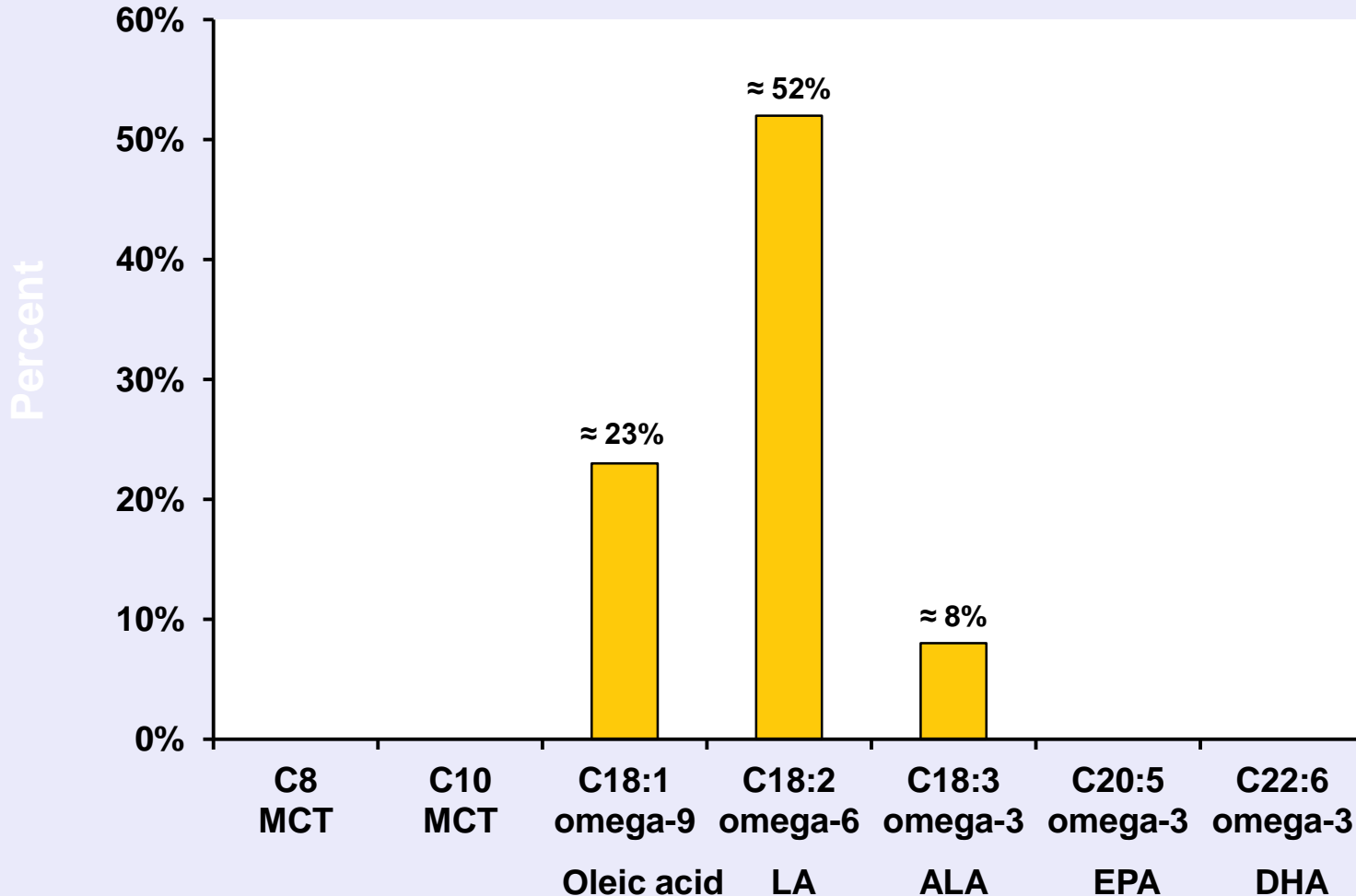
- Intralipid - Schuberth and Wretling (1957 German abstract, 1959 Swedish)
- Based on soya oil and egg yolk
- Full article 1963 (also in Swedish)
- Approved in Europe 1963
- Approved in USA 1977

Lipid emulsions for PN

- “First generation”
- Soybean derived – LCT
- Good toxicity profile
- Efficiently cleared from plasma
- Source of energy and essential fatty acids

Soya oil – composition

ω -6 to ω -3 ratio: 7:1



Possible consequences of excess n-6 fatty (linoleic) acids

- Unbalanced membrane fatty acid profile (excess n-6 PUFAs)
- Modified production of lipid mediators (prostaglandins, leukotrienes)
- Promotion of immunosuppression and systemic inflammatory reactions

Evolution of lipid emulsions

1980 onwards: new preparations

- MCT + soybean oil
- Olive oil + soybean oil
- Fish oil
- Combinations

Soybean oil

Reliable source of essential fatty acids

linoleic acid (ω -6 fatty acid)

α -linolenic acid (ω -3 fatty acid)



Essential fatty acids – requirements

Linoleic acid	1-10%	of energy provision
α -linolenic acid	0.5-2%	
PUFA intake	5-10%	

Linoleic acid	2-20g	per day
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Or perhaps 100-200ml 20% soya-based lipid per week in a patient on a lipid-free PN regimen

MCT

Medium-chain triglycerides

Derived from purified coconut or palm kernels



Benefits of MCT (iv)

- rapidly available energy source
- taken up into mitochondria by a carnitine independent pathway
- efficient elimination from the bloodstream
- better controlled triglyceride levels than with LCT

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- rapidly available energy source
- taken up into mitochondria by a carnitine independent pathway
- efficient elimination from the bloodstream
- better controlled triglyceride levels than with LCT
- lipid emulsions containing MCT \leq 50% are well tolerated in postoperative and critically ill patients

*Bach AC, Babayan VK. Am J Clin Nutr 1982;36:950-962
Chambrier C et al. Nutrition 1999;15:274-277
Lindgren BF et al. Clin Nutr 2001;20:43-48
Sandström R et al. JPEN 1995;19:381-386*

Olive oil

High content of MUFA: oleic acid (ω -9)

- low content of saturated fatty acids
- low content of ω -6 PUFA



Recommendations for olive oil

- Inclusion of olive oil has been recommended for immunonutrition
- Suggested that $\geq 10\%$ of energy requirements should be from oleic acid
- Evidence not strong – and note 23% in soya oil



Gaßmann B. Ernährungs-Umschau 2006

Simopoulos AP. Ann Nutr Metab 1999

Grimm H. Arch Surg 2001

Fürst P. Clin Nutr 2000

Fish oil

- Rich in the (very) long-chain ω -3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).
- Origins not from fish but fish food!



Source of “fish” oil

α -linolenic acid mainly from plants

essential in man

can also yield EPA/DHA but not much

EPA/DHA produced by marine plants

Human dietary EPA/DHA mainly from oily
fish & seafood

Biological effects of omega-3 fatty acids

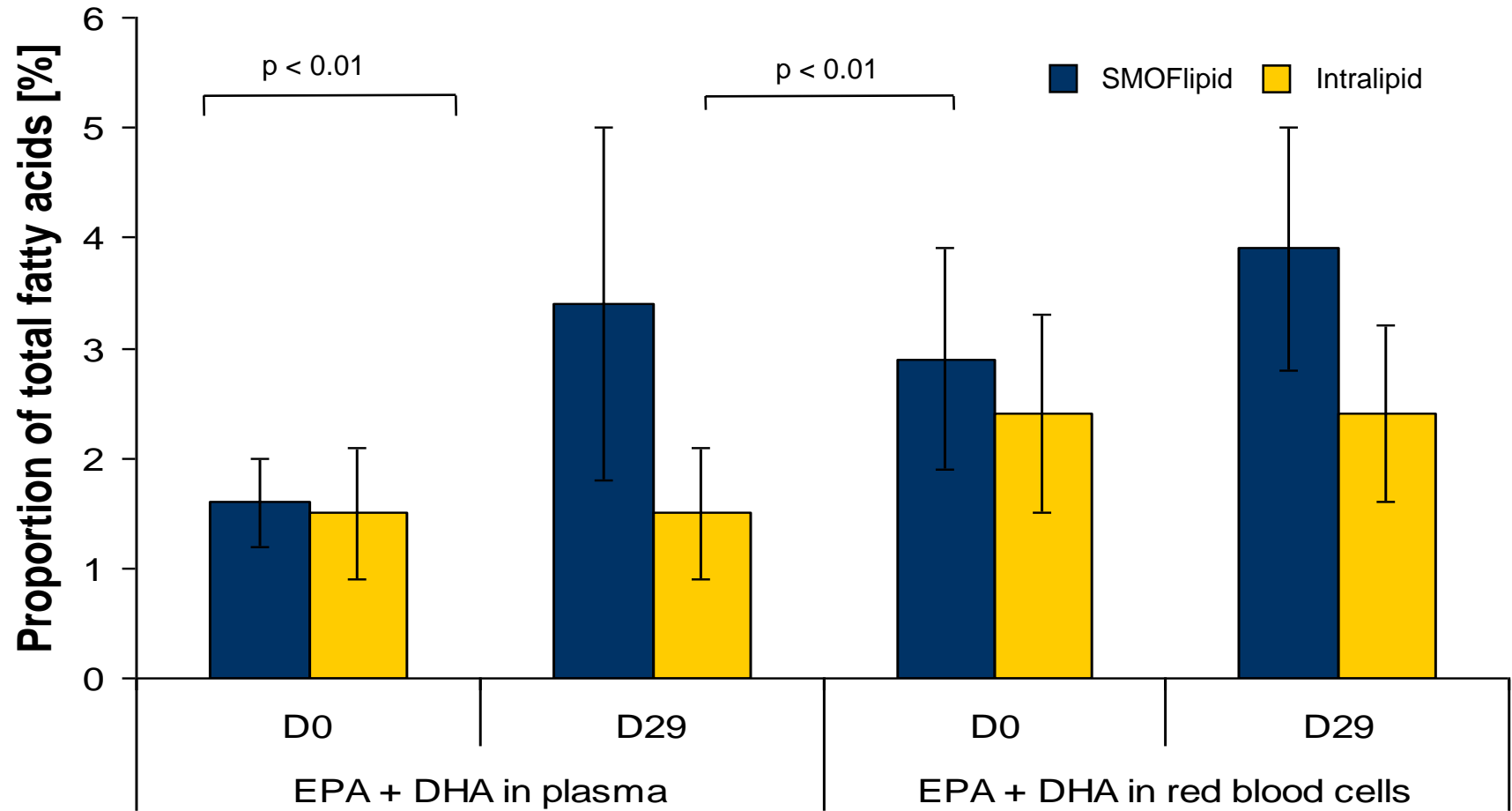
- Let cell membranes function properly
- Involved in gene function, especially genes of inflammation, as signallers
- Regulate production of eicosanoids (eg PGE2) (turn on inflammation) and resolvins (turn it off)
- Can have direct effects via EPA receptors
- Improve organ perfusion
- Improve maturation of central nervous system and retina in preterm infants

Comparison of oil source in selected lipid emulsions (g/100 ml)

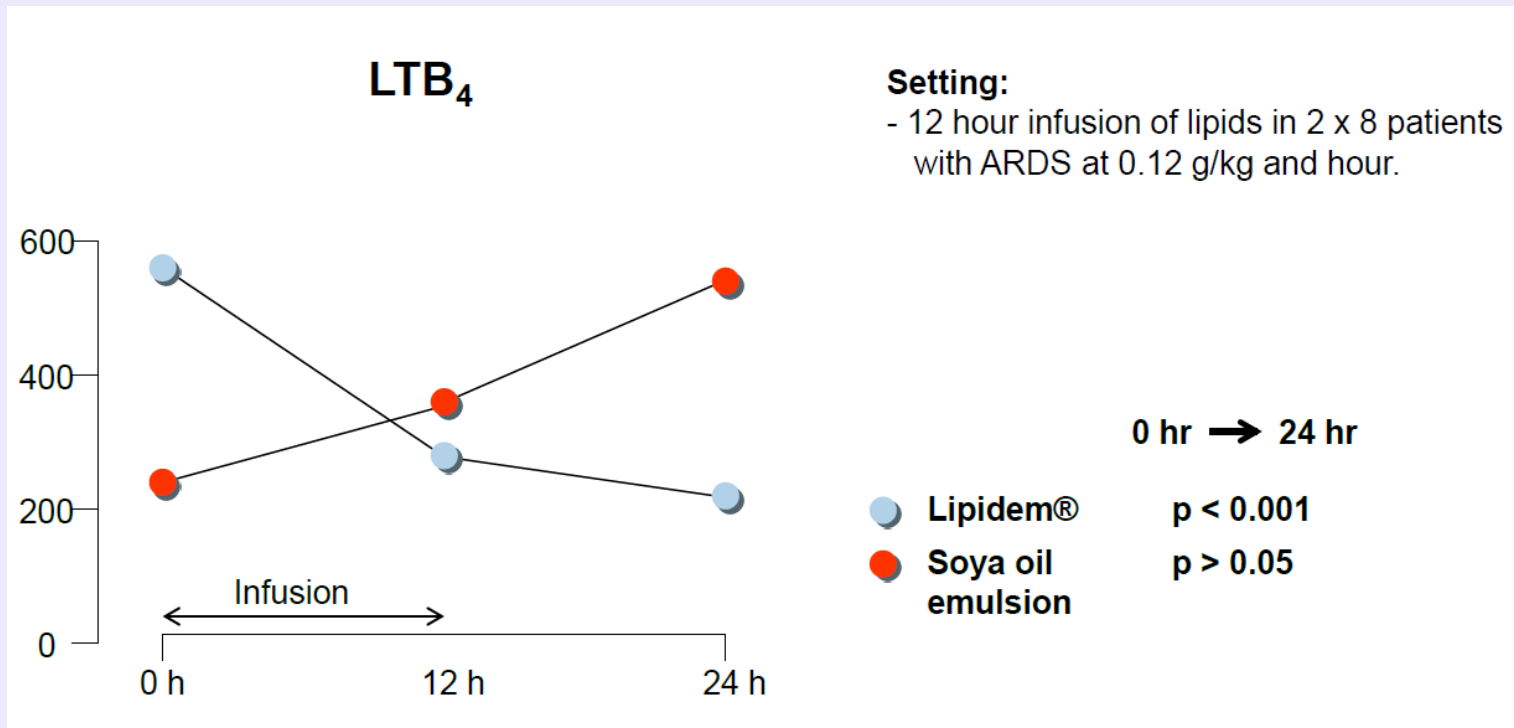
Product	Oil source			
	Soybean	MCT	Olive oil	Fish oil
• Intralipid 20%	20	0	0	0
• Ivelip 10%	10	0	0	0
• Lipofundin 20%	10	10	0	0
• ClinOleic 20%	4	0	16	0
• SMOF lipid	3	3	2.5	1.5
• Lipidem/Lipoplus	8	10	0	2
• Omegaven	0	0	0	10

**Does inclusion of fish oil make
any difference ?**

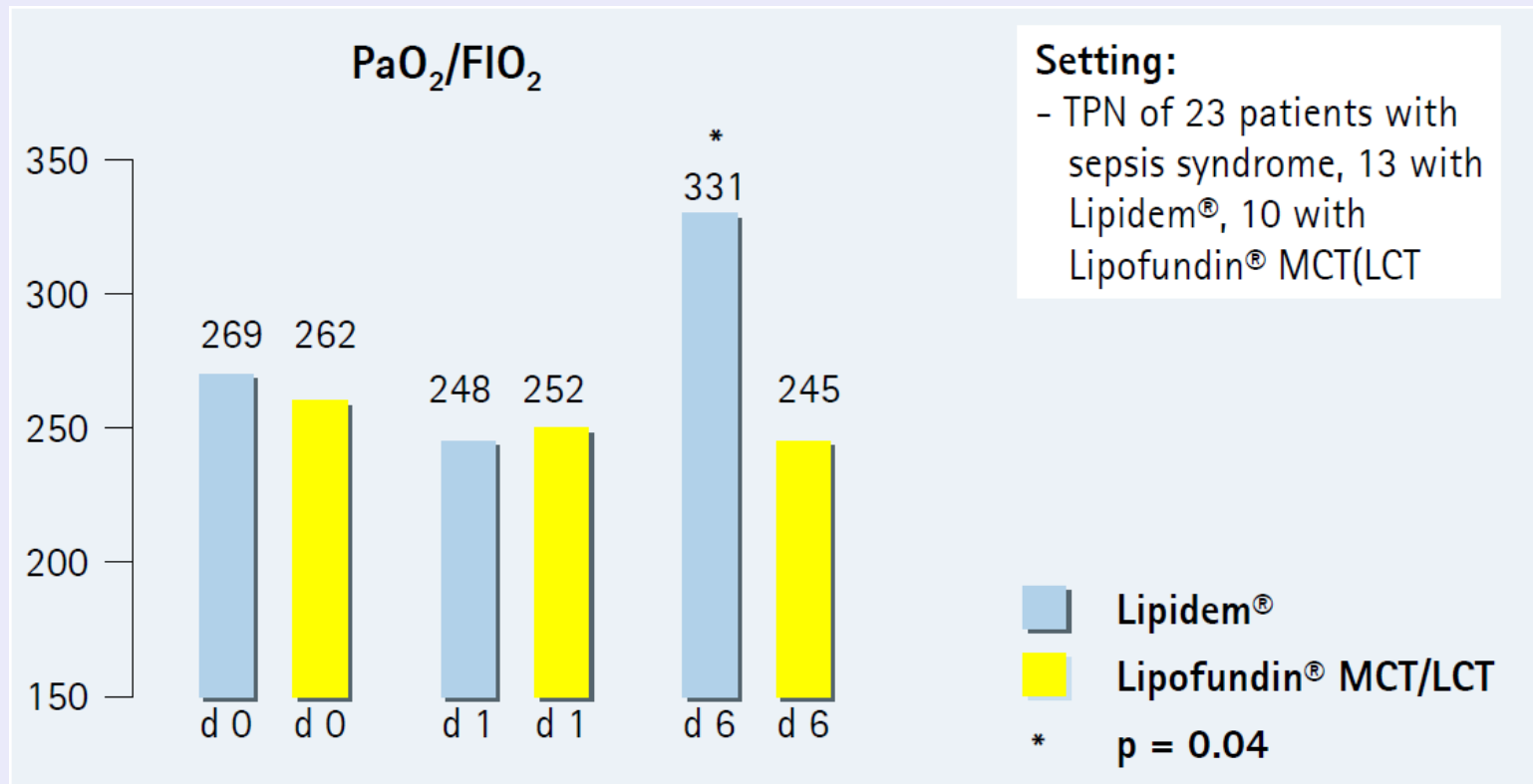
n-3 fatty acid status changes



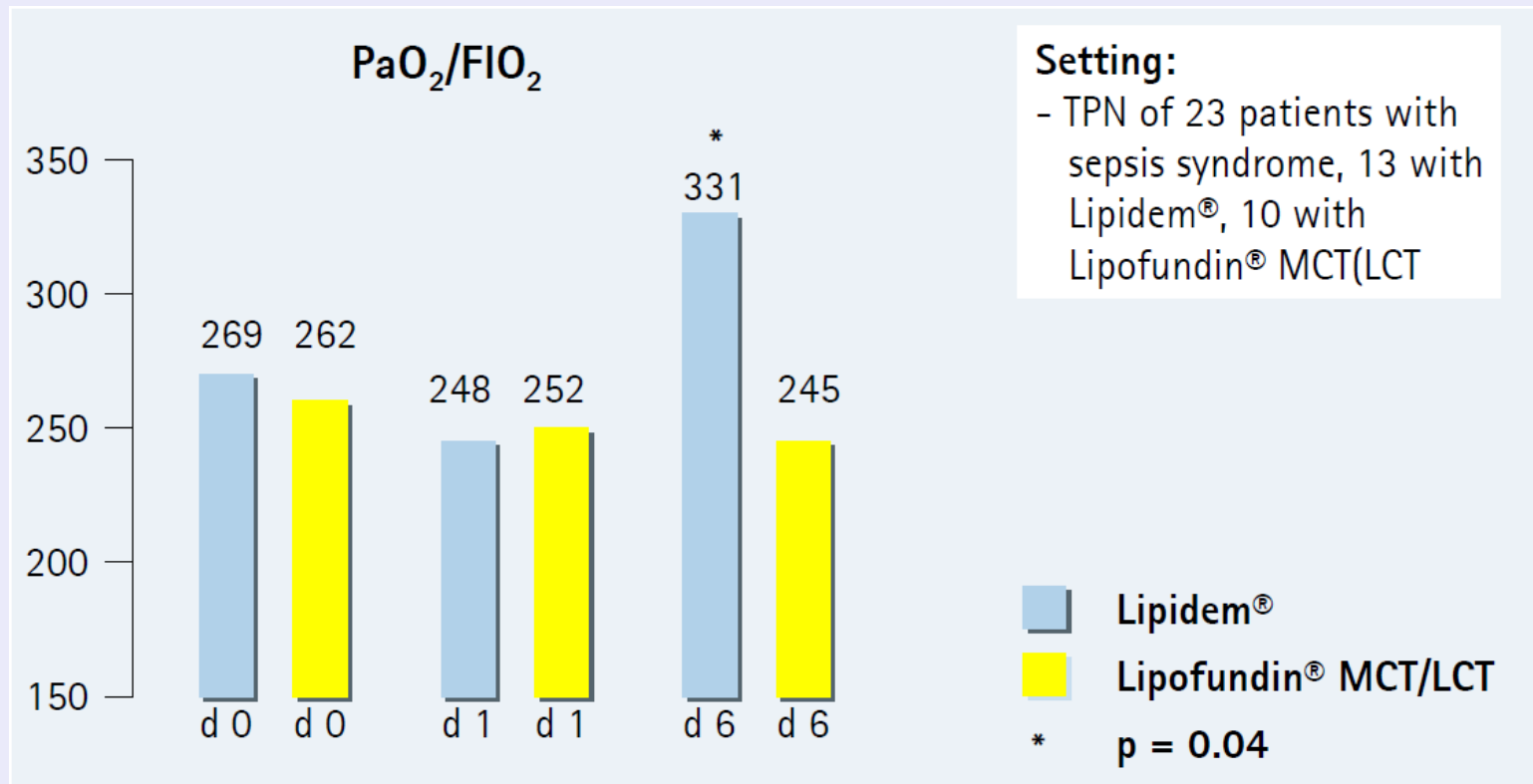
... which affects inflammatory mediators



... and pulmonary function



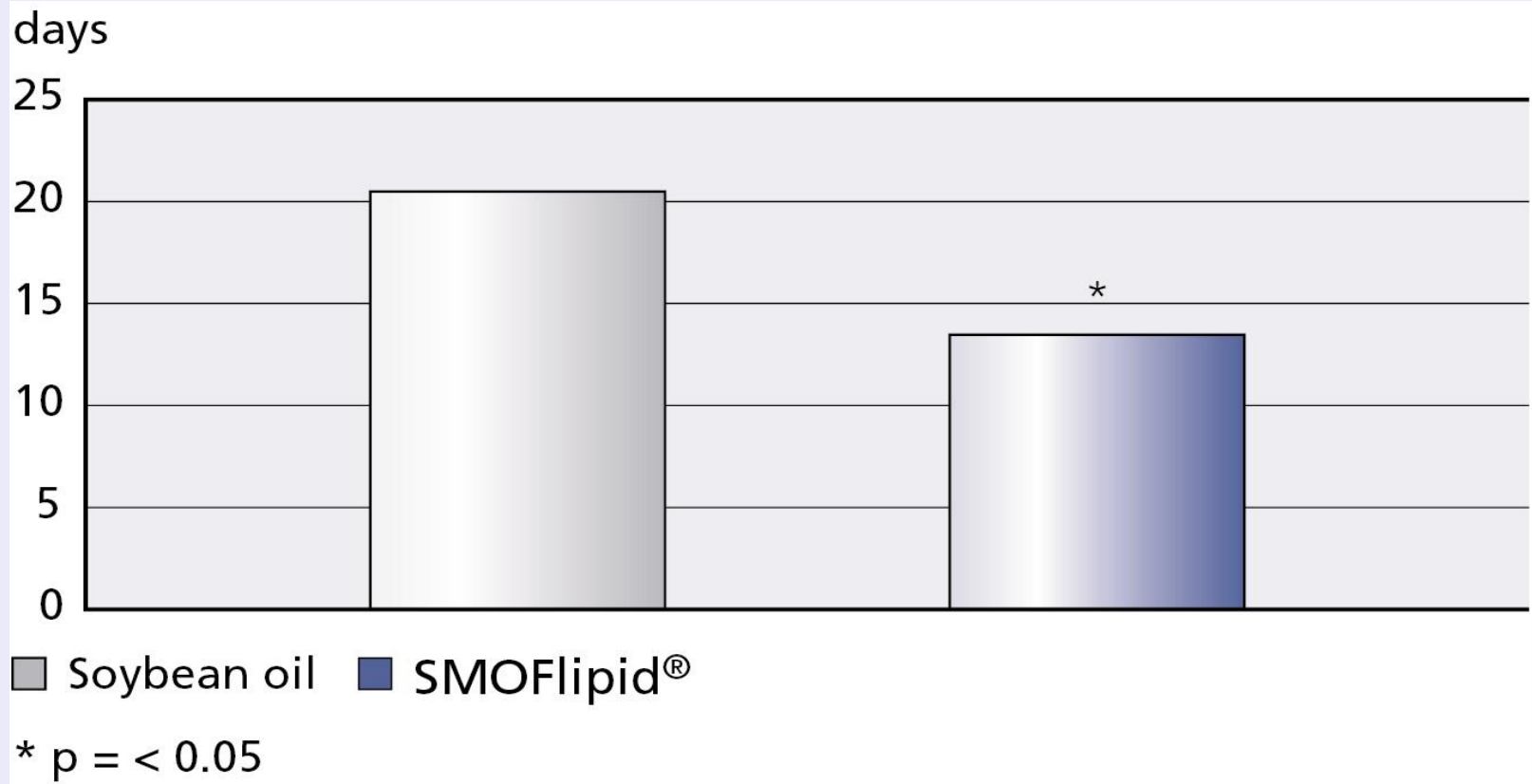
... and pulmonary function



... with shortened LoS – 55 vs 22d

**So fish oil makes you better
quicker**

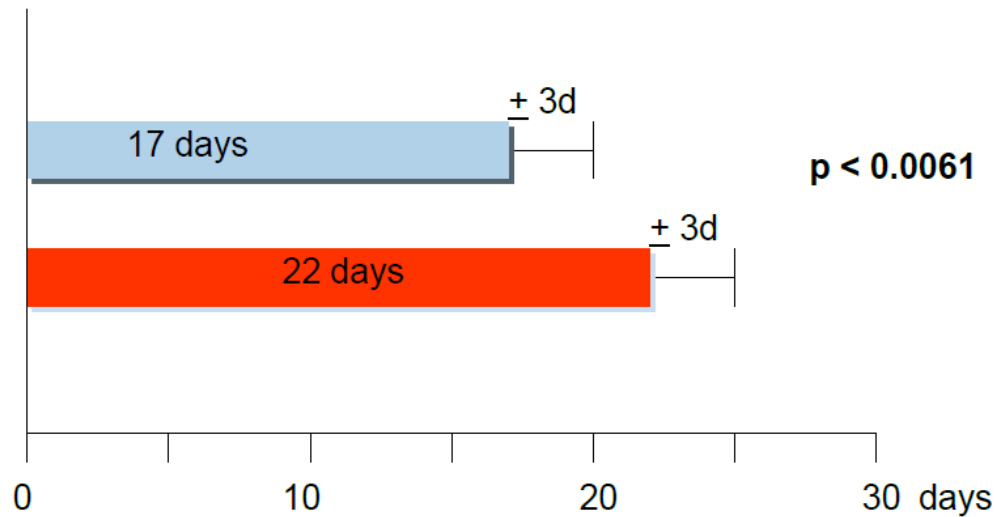
Length of hospital stay



Grimm et al EJM
2006

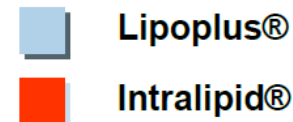
Length of hospital stay

Mean postoperative hospital stay



Setting:

- 256 patients with major abdominal surgery, 127 with Lipidem® (MLF), 129 with soya oil emulsion (LCT)



Wichmann, 2007

Not all fish oil studies are positive

Better outcomes in acute pancreatitis
less need for dialysis and LOS 27 vs 21d

Wang X '08

But ...

No effect on outcome
when given iv as treatment of inflammation

Friesecke S '08

T Grau - ESPEN 2013 - ICU

SO/MCT vs Lipofundin with FO
n=175; APACHE scores of 20 =

Infections in **37 vs 21%** (p=0.02)

No significant differences for other outcomes

Most infections if
septic on admission
worse still if more kcal given

Many iv fish oil studies

Clear need for meta-analysis

Fish oil meta-analyses

Pradelli L. Crit Care Med, 2012

favourable changes in inflammatory mediators

infection rates lower (non-ICU patients)

LOS reduced (by 9d in ICU patients; $p < 0.05$)

no other confirmed positive or negative outcomes

Palmer A. Crit Care Med, 2013

infection rate =

ICU LOS =

Hospital LOS lower with FO

Manzanares. 2013

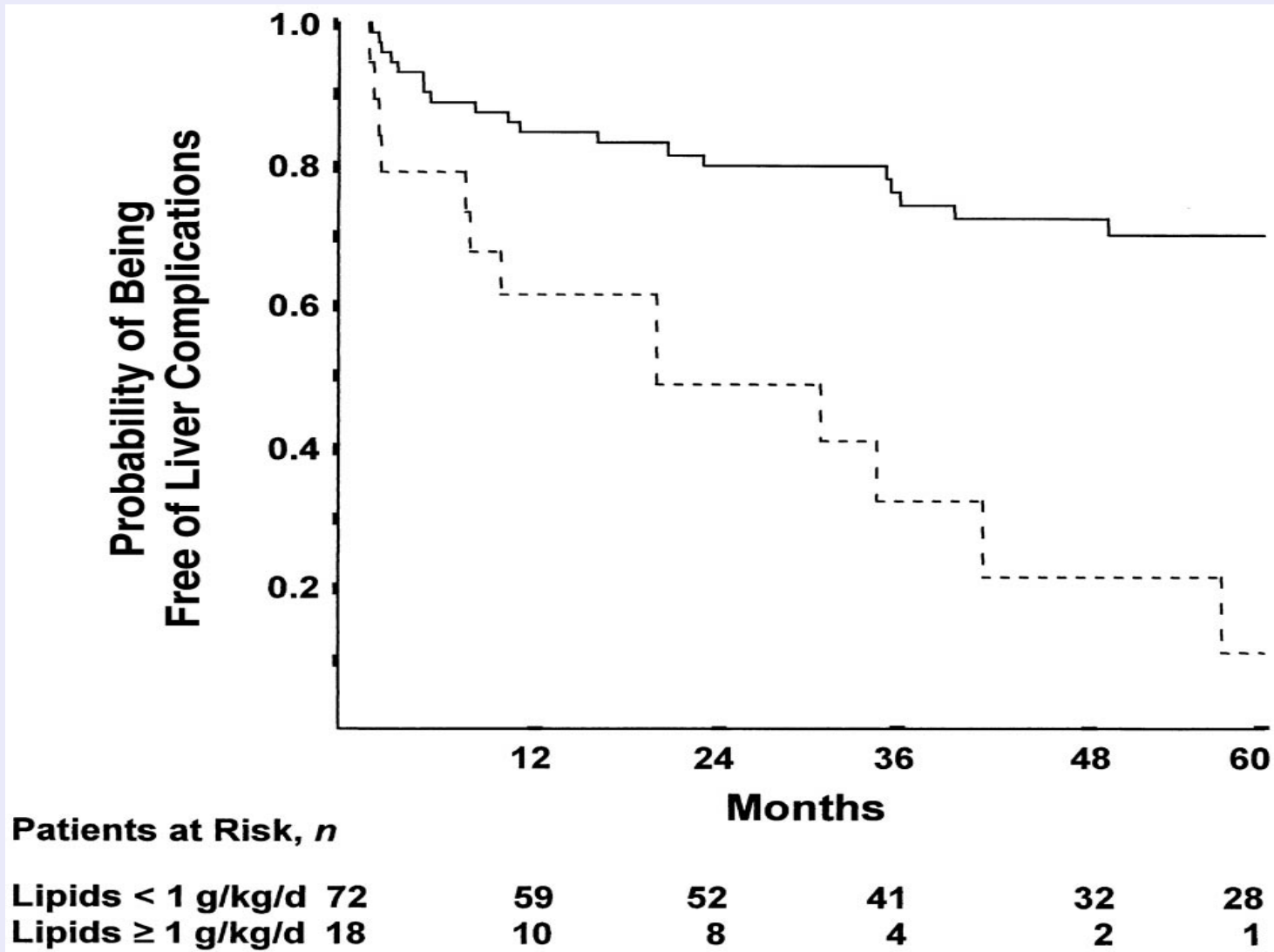
highly comparable results

Grau T. ESPEN 2013

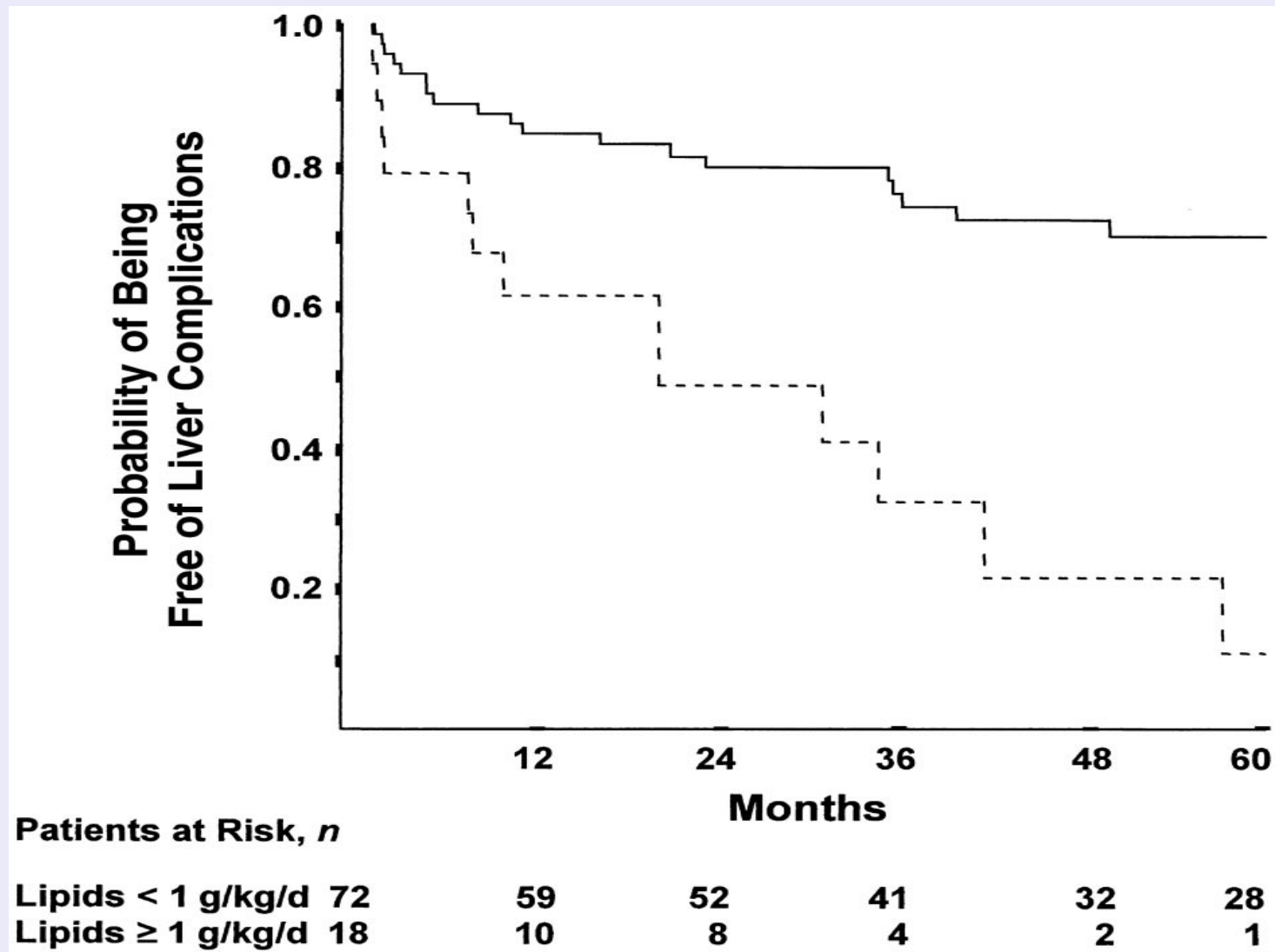
reduced ICU nosocomial infections – RR 0.56

Long term issues

Too much lipid is bad ?



Too much soy lipid is bad



Fish oil in neonates

Boston group

- Anecdotal review of babies referred with PN-associated jaundice
- “Rescued” with change to pure fish oil
- “Soy oil bad + pure fish oil good”
- Comparable evidence in adults

iv lipids with fish oil

Increasing consensus

- Reduces infection rates in critical care
- Reduces infection rates in peri-operative patients
- Reduces length of stay on ICU
- Reduces length of stay in hospital
- Reduces risk of long-term hepatic complications
- May reverse those already induced by soya lipid
- No adverse effects

Summary

- Intravenous lipid emulsions can now reflect biological profiles seen in healthy individuals assumed to be optimal
- Fish oil containing preparations have the potential to have positive effects
- These are not just an energy source and may actively prevent late toxicity
- A new standard of care?

