



# Dietetic evidence derived from Randomized Controlled Trials

**ROUNDTABLE** Research and Evidence-Based Practice: Gaps between  
recommendations and evidence.

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# Content

Dietetic evidence derived from Randomized Controlled Trials

in theory

in practice

1. from a patients' question to a research question
2. search for evidence
3. quality of output
4. evidence-based answer

**yes!**

**but....**

# in theory

- Methodology of RCT

Randomized  
Controlled  
Trial

&

Methodological  
checklists

- Methodology of dietetic evidence

5 steps to take

# in practice

## Case:

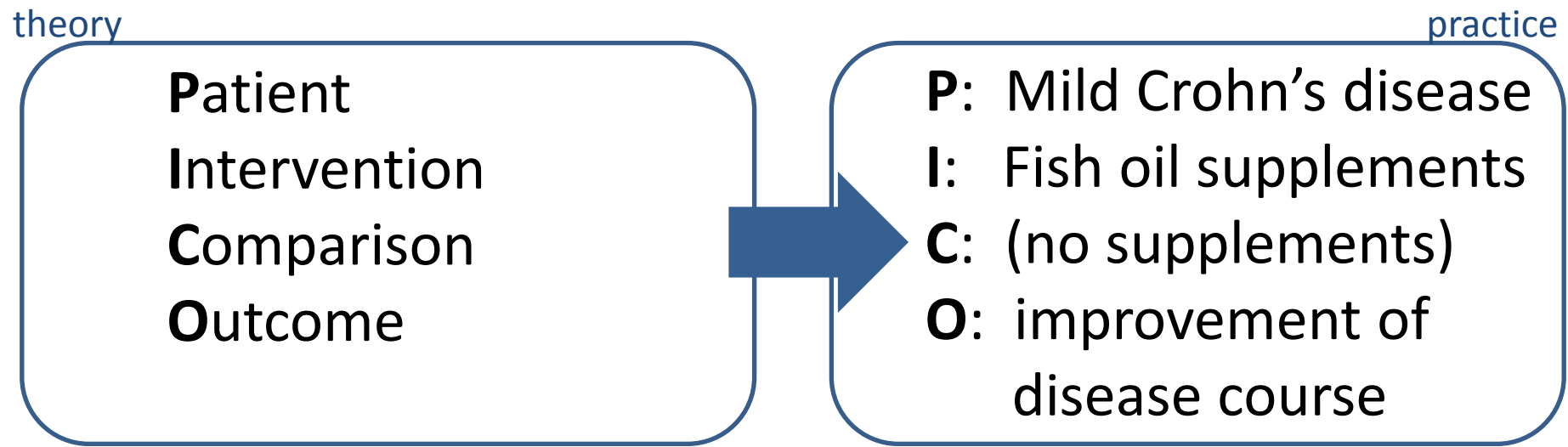
Female patient with Crohn's disease  
Age 32, diagnosis since 5 years, mild disease, oral 5-ASA therapy, good patients' compliance, interested in health & nutrition, no smoker

## Patients' question

A friend showed some interesting data on the treatment of CD with fish oil supplements. You know that such item is of special interest for me. Can this not be the solution for me? Can I replace or add such supplements to my current diet to control the disease? What would you recommend and why?

?

# 1. From a patients' question to a research question



Research question

Does the intake of fish oil supplements improve the disease course of patients with mild Crohn's disease?

## 2. Search for evidence

theory

practice

Keywords /  
MeSH terms

Synonyms/  
Combinations (and, or,  
not)

Databases

Crohn's disease - fish  
oil supplements -  
disease course

Crohn disease (IBD) -  
Omega 3 fatty acids –  
EPA DHA – remission

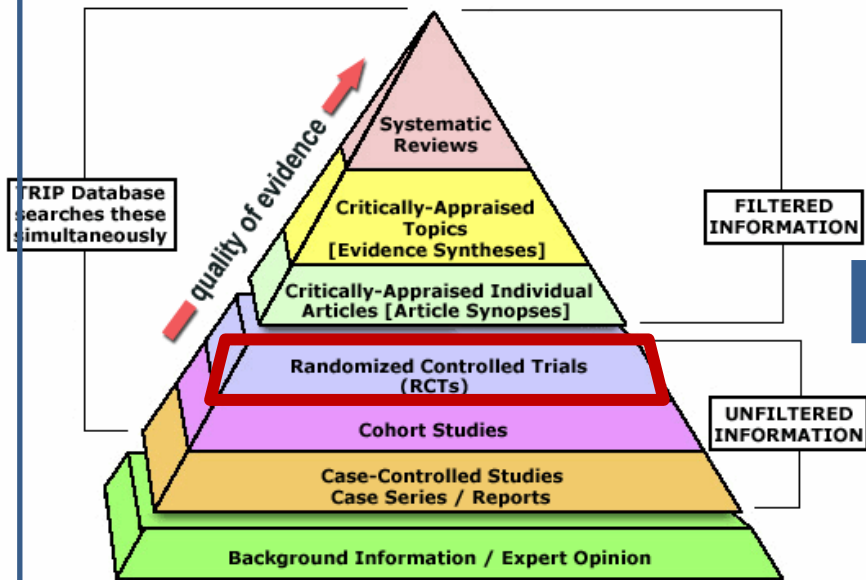
Medline (PubMed) -  
google scholar - ...

# 3. Quality of output

theory

practice

## Levels of evidence:



[http://www.google.nl/imgres?imgurl=http://www.ebmpyramid.org/images/pyramid.gif&imgrefurl=http://www.ebmpyramid.org/samples/complicated.html&usq=\\_\\_bv7R6p9fjL0GDMxNblznWdtzmU=&h=410&w=546&sz=27&hl=nl&start=9&zoom=1&tbnid=KW6kXbq5m8atTM:&tbnh=100&tbnw=133&ei=MRnqTuKyLshOula3bgO&prev=/search%3Fq%3Devidence%2Bpiram%2Bunfiltered%2Binformation%26%3Dnl%26sa%3Dn%26gbv%3D2%26tbnm%3D3ch&itbs=1](http://www.google.nl/imgres?imgurl=http://www.ebmpyramid.org/images/pyramid.gif&imgrefurl=http://www.ebmpyramid.org/samples/complicated.html&usq=__bv7R6p9fjL0GDMxNblznWdtzmU=&h=410&w=546&sz=27&hl=nl&start=9&zoom=1&tbnid=KW6kXbq5m8atTM:&tbnh=100&tbnw=133&ei=MRnqTuKyLshOula3bgO&prev=/search%3Fq%3Devidence%2Bpiram%2Bunfiltered%2Binformation%26%3Dnl%26sa%3Dn%26gbv%3D2%26tbnm%3D3ch&itbs=1)

## Omega-3 Free Fatty Acids for the Maintenance of Remission in Crohn Disease

### The EPIC Randomized Controlled Trials

Brian G. Feagan, MD  
 William J. Sandborn, MD  
 Ulrich Mittmann, MD  
 Simon Bar-Meir, MD  
 Geert D'Haens, MD, PhD  
 Marc Bradette, MD  
 Albert Cohen, MD  
 Chrystian Dallaire, MD  
 Perry P. Ponich, MD  
 W. D. McDonald, MD, PhD  
 M. B. Hebuterne, MD, PhD  
 J. F. Colombel, MD  
 M. K. Kivana, MD  
 M. Niv, MD  
 Sandro Ardizzone, MD  
 Olga Alexeeva, MD  
 Alaa Rostom, MD  
 Gediminas Kiudelis, MD  
 Johannes Spleiss, MSc  
 Denise Gilgen, PhD  
 Margaret K. Vandervoort, MSc  
 Cindy J. Wong, MSc  
 Guang Yong Zou, PhD  
 Allan Donner, PhD  
 Paul Rutgeerts, MD, PhD

**Context** Maintenance therapy for Crohn disease features the use of immunosuppressive drugs, which are associated with an increased risk of infection. Identification of safe and effective maintenance strategies is a priority.

**Objective** To determine whether the oral administration of omega-3 free fatty acids is more effective than placebo for prevention of relapse of Crohn disease.

**Design, Setting, and Patients** Two randomized, double-blind, placebo-controlled studies (Epanova Program in Crohn's Study 1 [EPIC-1] and EPIC-2) conducted between January 2003 and February 2007 at 98 centers in Canada, Europe, Israel, and the United States. Data from 363 and 375 patients with quiescent Crohn disease were evaluated in EPIC-1 and EPIC-2, respectively.

**Interventions** Patients with a Crohn's Disease Activity Index (CDAI) score of less than 150 were randomly assigned to receive either 4 g/d of omega-3 free fatty acids or placebo for up to 58 weeks. No other treatments for Crohn disease were permitted.

**Main Outcome Measure** Clinical relapse, as defined by a CDAI score of 150 points or greater and an increase of more than 70 points from the baseline value, or initiation of treatment for active Crohn disease.

**Results** For EPIC-1, 188 patients were assigned to receive omega-3 free fatty acids and 186 patients to receive placebo. Corresponding numbers for EPIC-2 were 189 and 190 patients, respectively. The rate of relapse at 1 year in EPIC-1 was 31.6% in patients who received omega-3 free fatty acids and 35.7% in those who received placebo (hazard ratio, 0.82; 95% confidence interval, 0.51-1.19;  $P=.30$ ). Corresponding values for EPIC-2 were 47.8% and 48.8% (hazard ratio, 0.90; 95% confidence interval, 0.67-1.21;  $P=.48$ ). Serious adverse events were uncommon and mostly related to Crohn disease.

**Conclusion** In these trials, treatment with omega-3 free fatty acids was not effective for the prevention of relapse in Crohn disease.

**Trial Registration** clinicaltrials.gov Identifiers: EPIC-1: NCT00613197, EPIC-2: NCT00074542

JAMA. 2008;299(14):1690-1697

www.jama.com

Figure 1. Immunosuppressive agents such as 5-aminosalicylic acid, corticosteroids, and thiopurines are anti-inflammatory. Omega-3 free fatty acids are anti-inflammatory.

JAMA. 2008;299(14):1690-1697

Methodological checklists

# 4. Evidence-based answer

theory

practice

## Characteristics of study population

**Table 1.** Baseline Characteristics of the Study Patients in EPIC-1 and EPIC-2<sup>a</sup>

Characteristic	EPIC-1			EPIC-2		
	Omega-3 Free Fatty Acids (n = 183)	Placebo (n = 180)	P Value	Omega-3 Free Fatty Acids (n = 187)	Placebo (n = 188)	P Value
Age, mean (SD), y	40.5 (15.2)	38.2 (13.1)	.12	38.5 (13.8)	40.0 (13.6)	.28
Male sex, No. (%)	88 (48.1)	74 (41.1)	.18	81 (43.3)	79 (42.0)	.80
Weight, mean (SD), kg	69.0 (13.2)	67.9 (13.8)	.42	69.8 (15.5)	68.4 (16.1)	.40
Current smoker, No. (%)	56 (30.6)	62 (34.4)	.43	47 (25.1)	70 (37.2)	.01
Remission induction therapy, No. (%)						
Oral 5-ASA or antibiotics	82 (44.8)	83 (46.1)				
Steroids, in remission 3-6 mo	57 (31.1)	57 (31.7)	.97			
Steroids, in remission >6-12 mo	36 (19.7)	32 (17.8)				
Immunosuppressives	8 (4.4)	8 (4.4)				
Prednisone				106 (56.7)	110 (58.5)	.72
Budesonide				81 (43.3)	78 (41.5)	
Harvey-Bradshaw index, mean (SD) <sup>b</sup>	2.3 (2.0)	2.3 (2.3)	.82	6.2 (4.2)	6.0 (3.6)	.58
Crohn's Disease Activity Index, mean (SD) <sup>c</sup>	79.6 (40.7)	75.4 (43.5)	.34	77.4 (44.8)	78.0 (41.6)	.90
Months since diagnosis						
Mean (SD)	85.7 (106.3)	82.7 (98.9)	.78	84.6 (94.0)	90.6 (108.5)	.57
Median (range)	42.0 (4-540)	42.5 (1-465)		51.0 (1-427)	42.0 (2-482)	
Previous surgery for Crohn disease, No. (%)	61 (33.3)	64 (35.6)	.66	56 (29.9)	67 (35.6)	.24
Crohn disease therapy prior 12 mo, No. (%)						
Oral 5-ASA therapy	142 (77.6)	141 (78.3)	.87	102 (54.5)	90 (47.9)	.20
Topical rectal therapy	9 (4.9)	8 (4.4)	.83	5 (2.7)	11 (5.9)	.13
Systemic corticosteroids	97 (53.0)	94 (52.2)	.88	39 (20.9)	36 (19.1)	.68
Immune-modifying agents	12 (6.6)	15 (8.3)	.52	13 (7.0)	13 (6.9)	.99
Immune modifiers/biologics	3 (1.6)	2 (1.1)	.67	4 (2.1)	3 (1.6)	.70
Antibiotic therapy	37 (20.2)	32 (17.8)	.55	23 (12.3)	25 (13.3)	.77

<sup>a</sup>Abbreviations: ASA, aminosalicylates; EPIC, Epanova Program in Crohn's Study.  
<sup>b</sup>Values for comparison of continuous outcomes were derived by the t test. Pearson  $\chi^2$  test was used to compare categorical variables.  
<sup>c</sup>Harvey-Bradshaw scores range from 0 to approximately 14. Higher scores indicate worse disease activity; scores of  $\geq 4$  are associated with clinical remission. Baseline score for EPIC-2 was assessed at the screening visit prior to steroid tapering.  
<sup>d</sup>Scores of  $\geq 150$  points are associated with quiescent disease, scores  $> 150$  points indicate active disease, and scores  $> 450$  points are seen with extremely severe disease.

## Fish oil supplement

4x1 g/d of 50-60% EPA and 15-25% DHA in a delayed-release soft gelatin capsule

## Results of this study

HR: 0.82; 95%CI, 0.57-1.19; p=0.30  
 HR: 0.90; 95%CI, 0.67-1.21; p=0.48

## Characteristics of patient

Female CD patient, age 32, diagnosis since 5 years, mild disease, oral 5ASA therapy

OK

## Fish oil supplement

Not specified by patient

## Results for all Crohn's disease patients?

+: large study population; intervention time; study design; HR and CI



# Dietetic evidence derived from RCT's: **yes!**

The outcome of RCT can result in dietetic evidence

Consultation of scientific literature results in the following answer:  
**no evidence so far to promote the intake of fish oil supplements as a part of the treatment of the disease, since no effect is observed**

*More than one example! What is your experience?*



# Dietetic evidence derived from RCT's: **but...**

RCT in Nutrition & Dietetics: **methodology** versus content

*Dietary approach versus medication, lifestyle habits, ...*

*Diet versus nutrients, supplements,...*

*More than one example! What is your experience?*



# Dietetic evidence derived from RCT's: but...

## RCT in Nutrition and Dietetics: **content** versus methodology

[Lancet](#), 2011; Oct 22;378(9801):1485-92. doi: 10.1016/S0140-6736(11)61344-5. Epub 2011 Sep 7.

**Primary care referral to a commercial provider for weight loss treatment versus standard care: a randomised controlled trial.**

Jebb SA<sup>1</sup>, Ahern AL, Olson AD, Aston LM, Holzapfel C, Stoll J, Amann-Gassner U, Simpson AE, Fuller NR, Pearson S, Lau NS, Mander AP, Hauner H, Caterson ID.

[Author information](#)

### Abstract

**BACKGROUND:** The increasing prevalence of overweight and obesity needs effective approaches for weight loss in primary care and community settings. We compared weight loss with standard treatment in primary care with that achieved after referral by the primary care team to a commercial provider in the community.

**METHODS:** In this parallel group, non-blinded, randomised controlled trial, 772 overweight and obese adults were recruited by primary care practices in Australia, Germany, and the UK. Participants were randomly assigned with a computer-generated simple randomisation sequence to receive either 12 months of standard care as defined by national treatment guidelines, or 12 months of free membership to a commercial programme (Weight Watchers), and followed up for 12 months. The primary outcome was weight change over 12 months. Analysis was by intention to treat (last observation carried forward [LOCF] and baseline observation carried forward [BOCF]) and in the population who completed the 12-month assessment. This trial is registered, number ISRCTN85485463.

**FINDINGS:** 377 participants were assigned to the commercial programme, of whom 230 (61%) completed the 12-month assessment; and 395 were assigned to standard care, of whom 214 (54%) completed the 12-month assessment. In all analyses, participants in the commercial programme group lost twice as much weight as did those in the standard care group. Mean weight change at 12 months was -5.06 kg (SE 0.31) for those in the commercial programme versus -2.25 kg (0.21) for those receiving standard care (adjusted difference -2.77 kg, 95% CI -3.50 to -2.03) with LOCF; -4.06 kg (0.31) versus -1.77 kg (0.19; adjusted difference -2.29 kg, -2.99 to -1.58) with BOCF; and -6.65 kg (0.43) versus -3.26 kg (0.33; adjusted difference -3.16 kg, -4.23 to -2.11) for those who completed the 12-month assessment. Participants reported no adverse events related to trial participation.

**INTERPRETATION:** Referral by a primary health-care professional to a commercial weight loss programme that provides regular weighing, advice about diet and physical activity, motivation, and group support can offer a clinically useful early intervention for weight management in overweight and obese people that can be delivered at large scale.

**FUNDING:** Weight Watchers International, through a grant to the UK Medical Research Council.

*More than one example! What is your experience?*

**DIETS – EFAD Conference 9-12 October 2014 Athens Greece**

# Dietetic evidence derived from RCT's: **but...**

One RCT versus RCT's, systematic reviews, meta-analysis, guidelines

## Levels of evidence!

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<b>DATABASE TOOLS</b> <ul style="list-style-type: none"><li>Save to My Profile</li><li>Recommend to Your Librarian</li></ul>	<b>Intervention Review</b> <b>Omega 3 fatty acids (fish oil) for maintenance of remission in Crohn's disease</b> Raffi Lev-Tzion <sup>1,*</sup> , Anne Marie Griffiths <sup>2</sup> , Oren Ledder <sup>1</sup> , Dan Turner <sup>1</sup>
<b>DATABASE MENU</b> <ul style="list-style-type: none"><li>Database Home</li></ul>	Database Title: <u>The Cochrane Library</u>
<b>FIND ARTICLES</b> <ul style="list-style-type: none"><li>A-Z</li><li>By Topic</li></ul>	Editorial Group: <a href="#">Cochrane Inflammatory Bowel Disease and Functional Bowel Disorders Group</a> Published Online: 28 FEB 2014 Assessed as up-to-date: 22 NOV 2013

### Authors' conclusions

Evidence from two large high quality studies suggests that omega 3 fatty acids are probably ineffective for maintenance of remission in CD. Omega 3 fatty acids appear to be safe although they may cause diarrhea and upper gastrointestinal tract symptoms.

*More than one example! What is your experience?*