Acido Linoleico

“Del efecto antiinflamatorio al riesgo cardiovascular”



Acidos Grasos

- Saturados: fuente animal (mantequilla, manteca, huevo)aceite de coco, aceite de palma, leche
- Monoinsaturados: Aceite de oliva
- Poli-Insaturados (PUFA): No escenciales y Esenciales
  - ✓ Omega 3
  - ✓ Omega 6

PUFA Omega 6

Grasas y ácidos grasos en nutrición humana
Consulta de expertos

10 - 14 de Noviembre de 2008

Ginebra

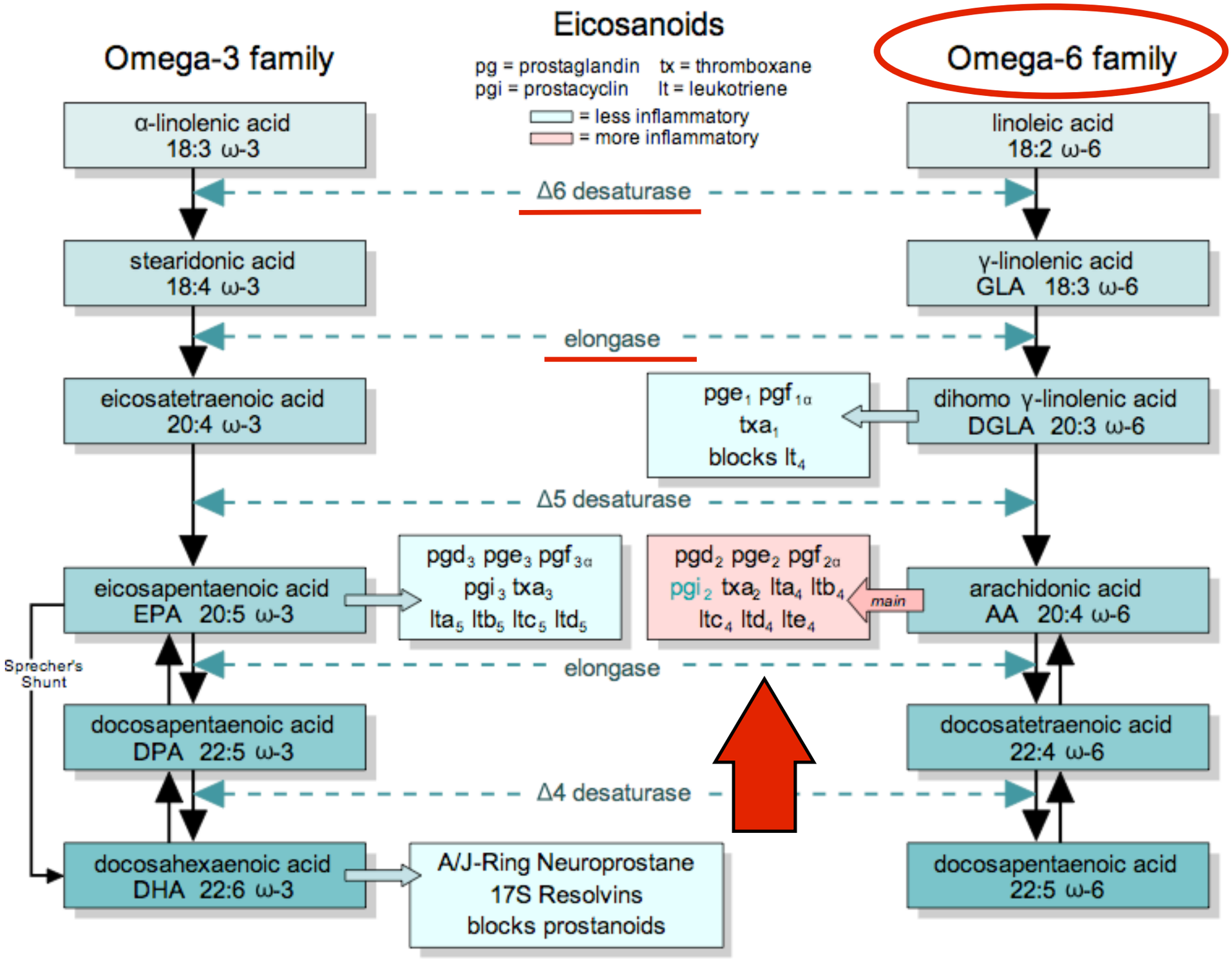
ESTUDIO FAO ALIMENTACIÓN Y NUTRICIÓN

91

PUFA n-6 importantes a nivel nutricional

Nombre común	Nombre sistemático	Abreviatura omega componente en cantidad mínima de tejidos animales	Fuentes principales
Ácido linoleico	ácido *cis*-9,*cis*-12 -octadecadienoico	18:2n-6 (LA)	la mayoría de aceites vegetales
Ácido γ-linolénico	ácido *cis*-6,*cis*-9,*cis*-12 -octadecatrienoico	18:3n-6 (GLA)	aceites de semillas de onagra, borraja y grosella negra
Ácido dihomo-γ-linolénico	ácido *cis*-8,*cis*-11,*cis*-14 -eicosatrienoico	20:3n-6 (DHGLA)	componente en cantidad mínima de tejidos animales
Ácido araquidónico	ácido *cis*-5,*cis*-8,*cis*-11, *cis*-14-eicosatetraenoico	20:4n-6 (AA)	grasas animales, hígado, lípidos del huevo, pescado
Ácido docosatetraenoico	ácido *cis*-7,*cis*-10,*cis*-13, *cis*-16-docosatetraenoico	22:4n-6	componente en cantidad mínima de tejidos animales
Ácido docosapentaenoico	ácido *cis*-4,*cis*-7,*cis*-10, *cis*-13, *cis*-16-docosapentaenoico	25:5n-6 (DPA)	componente en cantidad mínima de tejidos animales

Relación metabólica entre ambos grupos



Efecto antinflamatorio

Efecto pro inflamatorio

Enfermedad Arterial Coronaria y PUFA

- El consumo de AG PUFA disminuye la relación Col Total:HDL
- Siendo este "*tal vez*", el mejor predictor de riesgo cardiovascular

Lewington S, Whitlock G, Clarke R, Sherliker P, Emberson J, et al. (2007) Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. Lancet 370: 1829–1839.

Cuál es la evidencia respecto al Acido Linoleico y la Inflamación?

RESEARCH
Review

Effect of Dietary Linoleic Acid on Markers of Inflammation in Healthy Persons: A Systematic Review of Randomized Controlled Trials

Guy H. Johnson, PhD; Kevin Fritsche, PhD

ARTICLE INFORMATION

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n-6 fatty acids
Inflammation
C-reactive protein

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2212-2672/$36.00
doi: 10.1016/j.jand.2012.03.029

ABSTRACT

The majority of evidence suggests that n-6 polyunsaturated fatty acids, including linoleic acid (LA), reduce the risk of cardiovascular disease as reflected by current dietary recommendations. However, concern has been expressed that a high intake of dietary n-6 polyunsaturated fatty acid contributes to excess chronic inflammation, primarily by prompting the synthesis of proinflammatory eicosanoids derived from arachidonic acid and/or inhibiting the synthesis of anti-inflammatory eicosanoids from eicosapentaenoic and/or docosahexaenoic acids. A systematic review of randomized controlled trials that permitted the assessment of dietary LA on biologic markers of chronic inflammation among healthy noninfant populations was conducted to examine this concern. A search of the English- and non–English-language literature using MEDLINE, the Cochrane Controlled Trials Register, and EMBASE was conducted to identify relevant articles. Fifteen studies (eight parallel and seven crossover) met inclusion criteria. None of the studies reported significant findings for a wide variety of inflammatory markers, including C-reactive protein, fibrinogen, plasminogen activator inhibitor type 1, cytokines, soluble vascular adhesion molecules, or tumor necrosis factor-α. The only significant outcome measures reported for higher LA intakes were greater excretion of prostaglandin E2 and lower excretion of 2,3-dinor-thromboxane B_2 in one study and higher excretion of tetranorprostanedioic acid in another. However, the authors of those studies both observed that these effects were not an indication of increased inflammation. We conclude that virtually no evidence is available from randomized, controlled intervention studies among healthy, noninfant human beings to show that addition of LA to the diet increases the concentration of inflammatory markers.
J Acad Nutr Diet. 2012;112:1029-1041.

J Acad Nutr Diet. 2012;112:1029-1041.

Shadman *et al. Journal of Diabetes & Metabolic Disorders* 2013, **12**:42
http://www.jdmdonline.com/content/12/1/42



Journal of Diabetes & Metabolic Disorders

RESEARCH ARTICLE Open Access

Effect of conjugated linoleic acid and vitamin E on glycemic control, body composition, and inflammatory markers in overweight type2 diabetics

Zhaleh Shadman[1], Forough Azam Taleban[1], Navid Saadat[2] and Mehdi Hedayati[3*]

RESEARCH
Review

Effect of Dietary Linoleic Acid on Markers of Inflammation in Healthy Persons: A Systematic Review of Randomized Controlled Trials

Guy H. Johnson, PhD; Kevin Fritsche, PhD

We conclude that virtually no evidence is available from randomized, controlled intervention studies among healthy, noninfant human beings to show that addition of LA to the diet increases the concentration of inflammatory markers.

J Acad Nutr Diet. 2012;112:1029-1041.

Cuál es la evidencia respecto al Acido Linoleico y Enfermedad Arterial Coronaria?

OPEN ACCESS Freely available online

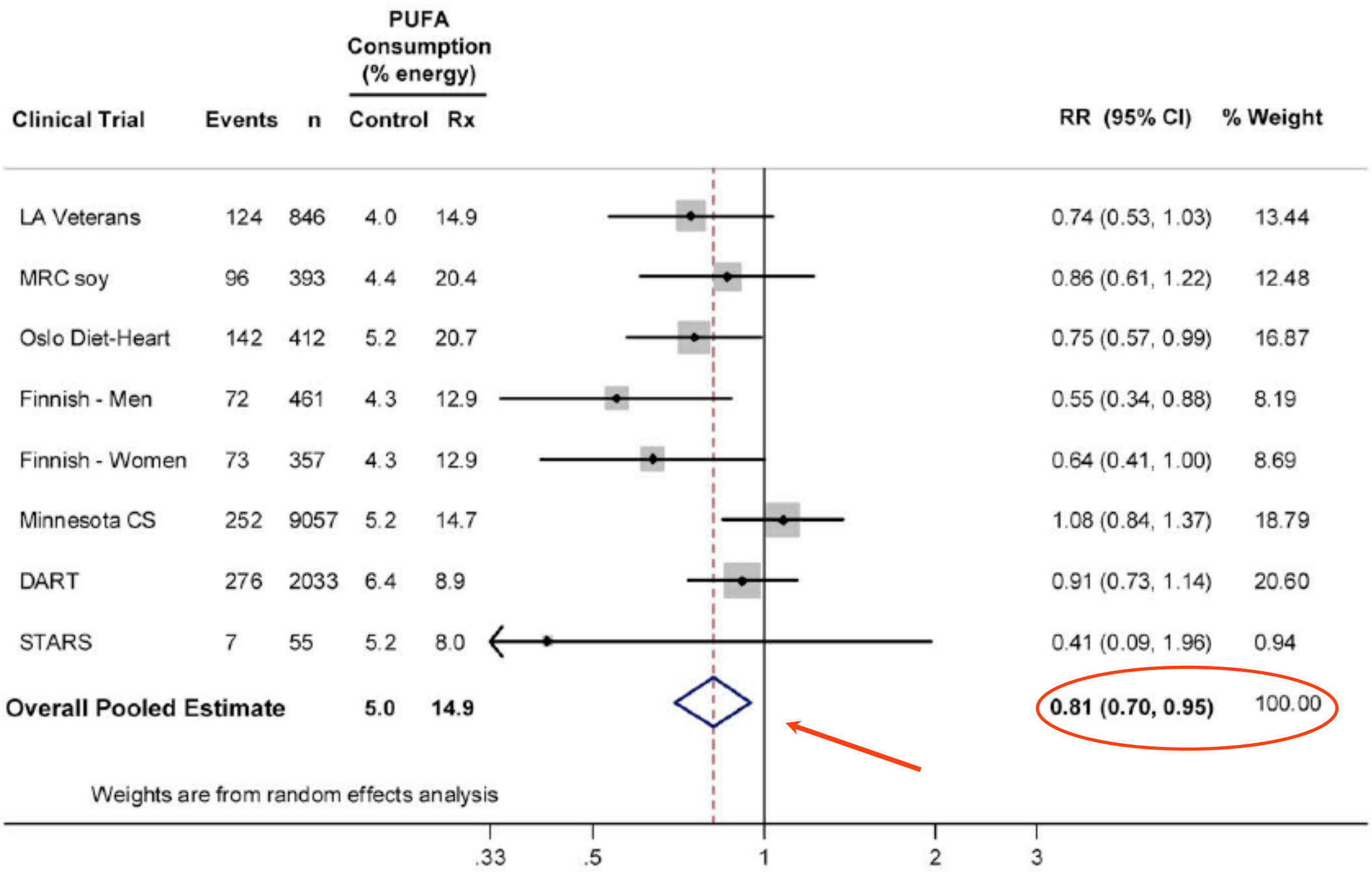
PLoS MEDICINE

Effects on Coronary Heart Disease of Increasing Polyunsaturated Fat in Place of Saturated Fat: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Dariush Mozaffarian[1,2,3]*, Renata Micha[2], Sarah Wallace[2]

1 Division of Cardiovascular Medicine and Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, United States of America, **2** Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, United States of America, **3** Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts, United States of America

March 2010 | Volume 7 | Issue 3


Clinical Trial
Events
n
PUFA Consumption (% energy)
Control
Rx
RR (95% CI)
% Weight
LA Veterans 124 846 4.0 14.9 0.74 (0.53, 1.03) 13.44
MRC soy 96 393 4.4 20.4 0.86 (0.61, 1.22) 12.48
Oslo Diet-Heart 142 412 5.2 20.7 0.75 (0.57, 0.99) 16.87
Finnish - Men 72 461 4.3 12.9 0.55 (0.34, 0.88) 8.19
Finnish - Women 73 357 4.3 12.9 0.64 (0.41, 1.00) 8.69
Minnesota CS 252 9057 5.2 14.7 1.08 (0.84, 1.37) 18.79
DART 276 2033 6.4 8.9 0.91 (0.73, 1.14) 20.60
STARS 7 55 5.2 8.0 0.41 (0.09, 1.96) 0.94
Overall Pooled Estimate 5.0 14.9 0.81 (0.70, 0.95) 100.00
Weights are from random effects analysis
.33
.5
1
2
3

British Journal of Nutrition

British Journal of Nutrition / Volume 104 / Issue 11 / , pp 1586-1600
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DOI: http://dx.doi.org/10.1017/S0007114510004010 (About DOI), Published online: 01 December 2010

Systematic Review

n-6 Fatty acid-specific and mixed polyunsaturate dietary interventions have different effects on CHD risk: a meta-analysis of randomised controlled trials

Christopher E. Ramsden[a1] [c1], Joseph R. Hibbeln[a1], Sharon F. Majchrzak[a1] and John M. Davis[a2]

[a1] Section on Nutritional Neurosciences, Laboratory of Membrane Biochemistry and Biophysics, NIAAA, NIH, Bethesda, MD, USA

[a2] Department of Psychiatry, School of Medicine, University of Illinois, Chicago, IL, USA

De Goede J, Geleijnse JM, Boer JM, *et al.* Linoleic acid intake, plasma cholesterol and 10-year incidence of CHD in 20 000 middle-aged men and women in the Netherlands. Br J Nutr 2011; 107:1070–1076.

In this population-based study of 20 069 Dutch men and women, no different ratio of total to HDL-cholesterol or a different CHD incidence were seen with a 5% difference in linoleic acid or carbohydrate intake.

BMJ

BMJ 2013;346:e8707 doi: 10.1136/bmj.e8707 (Published 5 February 2013)

RESEARCH

Use of dietary linoleic acid for secondary prevention of coronary heart disease and death: evaluation of recovered data from the Sydney Diet Heart Study and updated meta-analysis


OPEN ACCESS

Christopher E Ramsden *clinical investigator*[1 2], Daisy Zamora *epidemiologist*[2], Boonseng Leelarthaepin *retired, original study investigator*[3], Sharon F Majchrzak-Hong *research chemist*[1], Keturah R Faurot *epidemiology doctoral candidate*[2], Chirayath M Suchindran *senior biostatistician*[4], Amit Ringel *guest researcher*[1], John M Davis *professor*[5], Joseph R Hibbeln *senior clinical investigator*[1]

All cause

Cumulative death rate

0.25
0.20
0.15
0.10
0.05
0

Intervention
Control

Hazard ratio 1.62 (95% CI 1.00 to 2.64), P=0.05

No at risk (deaths)

Cardiovascular disease

Cumulative death rate

0.25
0.20
0.15
0.10
0.05
0

Hazard ratio 1.70 (95% CI 1.03 to 2.80), P=0.04

No at risk (deaths)

Coronary heart disease

Cumulative death rate

0.25
0.20
0.15
0.10
0.05
0

Hazard ratio 1.74 (95% CI 1.04 to 2.92), P=0.04

0 1 2 3 4 5

Follow-up (years)

No at risk (deaths)



En Conclusión...

- Se requiere de más evidencia clínica para sustentar el efecto del ACIDO LINOLEICO sobre el estado inflamatorio del paciente y el riesgo cardiovascular
- Cuál sería el rango de ingesta recomendado y cómo debe de ser la relación Omega6/Omega3
- Realmente aplica para los ancianos???

Pura Vida!!!



- Relación con CA es controversial

➡Mama, colon y próstata resultados neg

Zock PL, Katan MB. Linoleic acid intake and cancer risk: a review and meta-analysis. Am J Clin Nutr. 1998;68:142–53.

➡Alguna evidencia en cuanto a la relación omega6/omega3 (CA próstata)

Williams CD, Whitley BM, Hoyo C, Grant DJ, Iraggi JD, Newman KA, Gerber L, Taylor LA, McKeever MG, Freedland SJ. A high ratio of dietary n-6/n-3 polyunsaturated fatty acids is associated with increased risk of prostate cancer. Nutr Res. 2011;31:1–8.

Dieta

- Alto consumo de pescado y linasa = OMEGA 3
- Bajo consumo de aceites ricos en Omega 6 y grasas trans
- Consumo de acidos grasos saturados en forma moderada pero sin oxidar!!!
- Restricción de CHO *refinado

PUFA Omega 3

Grasas y ácidos grasos en nutrición humana
Consulta de expertos

10 - 14 de Noviembre de 2008

Ginebra

ESTUDIO FAO ALIMENTACIÓN Y NUTRICIÓN

91

PUFA n-3 importantes a nivel nutricional

Nombre común	Nombre sistemático	Abreviatura omega	Fuentes principales
Ácido α-linolénico	ácido *cis*-9,*cis*-12-*cis*-15 -octadecatrienoico	18:3n-3 (ALA)	aceites de lino, perilla, canola y soja
Ácido estearidónico	ácido *cis*-6,*cis*-9,*cis*-12,*cis*-15-octadecatetraenoico	18:4n-3 (SDA)	aceites de pescado, aceite de soja modificado genéticamente, aceite de semilla de grosella negra y aceite de cáñamo
	ácido *cis*-8,*cis*-11,*cis*-14,*cis*-17-eicosatetraenoico	20:4n-3	componente en cantidad mínima de tejidos animales
Ácido eicosapentaenoico	ácido *cis*-5, *cis*-8,*cis*-11,*cis*-14,*cis*-17-eicosapentaenoico	20:5n-3 (EPA)	pescado, especialmente el azul (salmón, arenque, anchoa, eperlano y caballa)
Ácido docosapentaenoico	ácido *cis*-7,*cis*-10,*cis*-13, *cis*-16, *cis*-19 -docosapentaenoico	22:5n-3 (n-3 DPA)	pescado, especialmente el azul (salmón, arenque, anchoa, eperlano y caballa)
Ácido docosahexaenoico	ácido *cis*-4,*cis*-7,*cis*-10, *cis*-13,*cis*-16,*cis*-19 -docosahexaenoico	22:6n-3 (DHA)	pescado, especialmente el azul (salmón, arenque, anchoa, eperlano y caballa)

Acido Linoleíco

Acciones fisiológicas de los eicosanoides derivados del ácido araquidónico

Eicosanoide	Acción fisiológica
PGE_2	Proinflamatoria, proagregatoria, reprime la respuesta inmunitaria, promueve el crecimiento y la proliferación celular, la vasodilatación y la broncoconstricción. Antiinflamatoria leve (inhibe la 5-LOX y así disminuye la formación de la serie 4 del LT, produce la 15-LOX que promueve la formación de lipoxinas antiinflamatorias).
PGI_2	Antiinflamatoria, inhibe la agregación plaquetaria y es un potente vasodilatador.
TXA_2	Potente agregante plaquetario y potente vasoconstrictor.
PGD_2	Inhibe la agregación plaquetaria, vasodilatación, produce sueño.
$PGF_{2\alpha}$	Induce la contracción del músculo liso y del útero.
LTB_4	Proinflamatoria, produce agregación de neutrófilos y quimiotaxis de neutrófilos y de eosinófilos.
LTC_4	Proinflamatoria, promueve la permeabilidad de las células endoteliales, contrae las células del músculo liso y estrecha las vías respiratorias periféricas.
LTD_4	Contrae las células del músculo y estrecha las vías respiratorias periféricas.
12-HETE	Quimiotaxis de neutrófilos, estimula la secreción de insulina inducida por la glucosa.
15-HETE	Inhibe las lipooxigenasas 5 y 12.
Lipoxina A	Genera aniones superóxido, quimiotaxis.
Lipoxina B	Inhibe la actividad de los linfocitos NK (citolíticos naturales).

British Journal of Nutrition (2012), **108**, 1300–1306
doi:10.1017/S0007114511006726
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α-Linolenic acid, linoleic acid and heart failure in women

Emily B. Levitan[1]*, Alicja Wolk[2], Niclas Håkansson[2] and Murray A. Mittleman[3,4]

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[2]*Division of Nutritional Epidemiology, Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden*
[3]*Cardiovascular Epidemiology Research Unit, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, MA, USA*
[4]*Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA*

(Submitted 6 June 2011 – Final revision received 7 November 2011 – Accepted 8 November 2011 – First published online 15 December 2011)

- Múltiples estudios con resultados contradictorios:
  - Algunos logran demostrar una relación de aumento de ECV en relación a alta concentración de Ac Linoleico, especialemente si Omega 6>>> Omega 3

Después de una amplia revisión bibliográfica se puede concluir que...

- Trans-PUFA son AG con > evidencia R CV

Atherosclerosis. 2013 Sep;230(1):140-7.

N Engl J Med 2006;354:1601-13.

- Evidencia insuf AG Saturados↑ R CV

Altern Med Rev. 2007; 12: 228-45

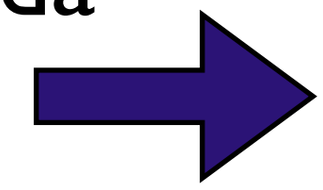
Lipids. 2010; 45: 893-905

Otro aspecto importante....

Less fat generally means more carbohydrate

- CHO (REFINADOS) ⟶ Colesterol y AG

Esto no es nada nuevo



Dreon DM, Fernstrom HA, Campos H, Blanche P, Williams PT, Krauss RM. Change in dietary saturated fat intake is correlated with change in mass of large low-density-lipoprotein particles in men. Am J Clin Nutr. 1998;67:828–36.

Nelson GJ, Schmidt PC, Kelley DS. Low-fat diets do not lower plasma cholesterol levels in healthy men compared to high-fat diets with similar fatty acid composition at constant caloric intake. Lipids. 1995;30: 969–76.

Turley ML, Skeaff CM, Mann JI, Cox B. The effect of a low-fat, high-carbohydrate diet on serum high density lipoprotein cholesterol and triglyceride. Eur J Clin Nutr. 1998;52:728–32.

- Los alimentos procesados “ FAT FREE” o bajos en grasa tienen alto contenido en azúcares para hacerlos gustosos Ej. Fructosa

Concluyendo...

- Se requiere MAS evidencia en cuanto al rol del Acido Linoleico y su efecto antinflamatorio vs riesgo CV

BIOCHEMICAL PHARMACOLOGY 77 (2009) 937–946

American Society for Nutrition. Adv. Nutr. 4: 311–312, 2013;