UNIVERSITY OF COPENHAGEN

Dairy matrix effects on T2 diabetes and cardiometabolic health?

Arne Astrup
Head of department, professor, MD, DMSc.

Department of Nutrition, Exercise and Sports
University of Copenhagen

DIETARY GUIDELINES 2015-2020

efsa European Food Safety Authority

Key Recommendations

Consume a healthy eating pattern that accounts for all foods and beverages within an appropriate calorie level.

A healthy eating pattern includes:[2]

- A variety of vegetables from all of the subgroups—dark green, red and orange, legumes (beans and peas), starchy, and other
- Fruits, especially whole fruits
- Grains, at least half of which are whole grains
- Fat-free or low-fat dairy, including milk, yogurt, cheese, and/or fortified soy beverages
- A variety of protein foods, including seafood, lean meats and poultry, eggs, legumes (beans and peas), and nuts, seeds, and soy products
- Oils

A healthy eating pattern limits:

- Saturated fats and *trans* fats, added sugars, and sodium

Key Recommendations that are quantitative are provided for several components of the diet that should be limited. These components are of particular public health concern in the United States, and the specified limits can help individuals achieve healthy eating patterns within calorie limits:

- Consume less than 10 percent of calories per day from added sugars[3]

EFSA: As low as possible

- Consume less than 2,300 milligrams (mg) per day of sodium[5]
- If alcohol is consumed, it should be consumed in moderation—up to one drink per day for women and up to two drinks per day for men—and only by adults of legal drinking age.[6]

“People don’t want to hear the truth because they don’t want their illusions destroyed.”

Friedrich Nietzsche

The lipid hypothesis and CHD

SATURATED FAT

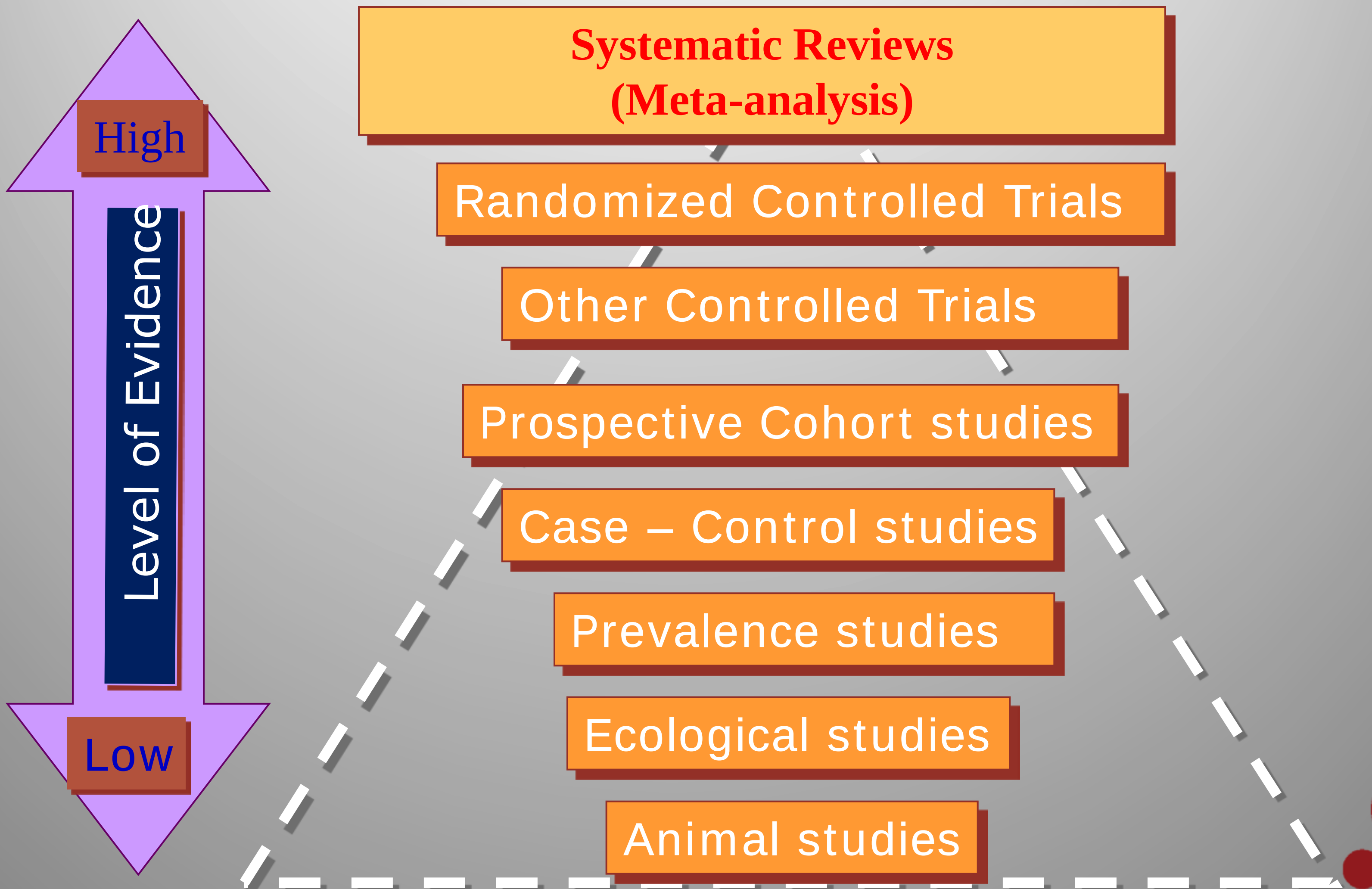
HIGH BLOOD CHOLESTEROL

?

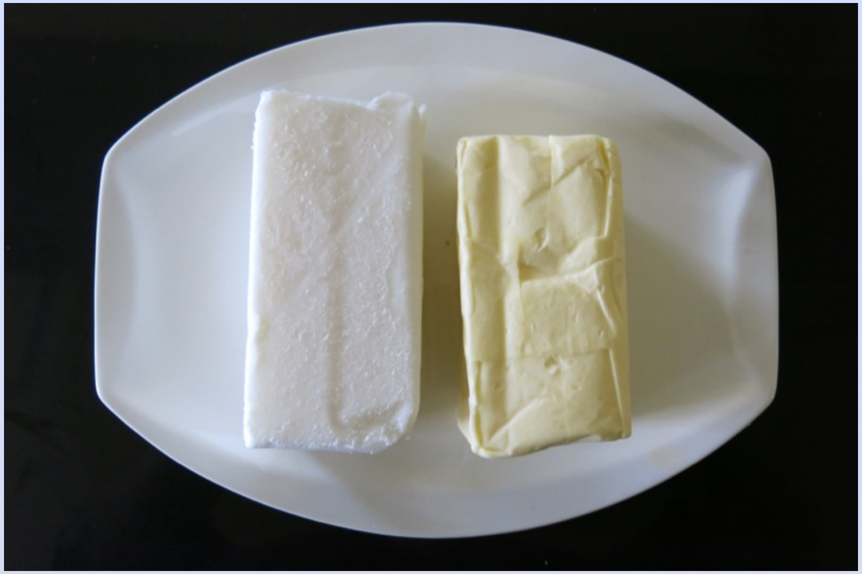
ATHEROSCLEROSIS

CHD

Hierarchy in Scientific Evidence



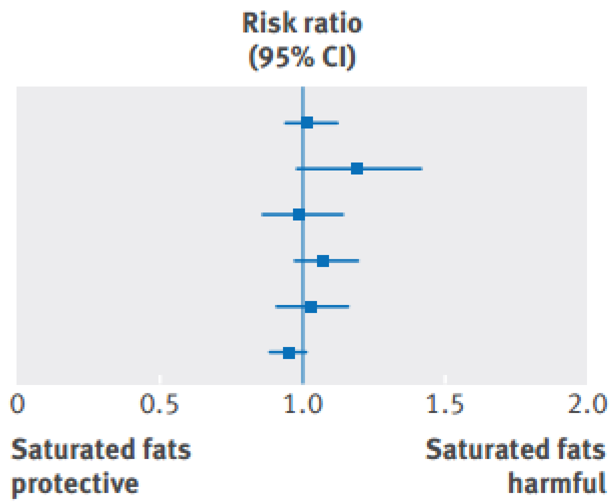
Saturated fat intake and CVD risk
-the most recent evidence



Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies

Russell J de Souza,[1,2,3,4] Andrew Mente,[1,2,5] Adriana Maroleanu,[2] Adrian I Cozma,[3,4] Vanessa Ha,[1,3,4] Teruko Kishibe,[6] Elizabeth Uleryk,[7] Patrick Budylowski,[4] Holger Schünemann,[1,8] Joseph Beyene,[1,2] Sonia S Anand[1,2,5,8]

Outcome	No of studies /comparisons	No of events /participants	Relative risk (95% CI)	P	P_{het}	I^2 (%)
All cause mortality	5/7	14 090/99 906	0.99 (0.91 to 1.09)	0.91	0.17	33
CHD mortality	11/15	2970/101 712	1.15 (0.97 to 1.36)	0.10	<0.001	70
CVD mortality	3/5	3792/90 501	0.97 (0.84 to 1.12)	0.69	0.29	19
CHD total	12/17	6383/267 416	1.06 (0.95 to 1.17)	0.29	0.02	47
Ischemic stroke	12/15	6226/339 090	1.02 (0.90 to 1.15)	0.79	0.002	59
Type 2 diabetes	8/8	8739/237 454	0.95 (0.88 to 1.03)	0.20	0.61	0



BMJ 2015;351:h3978 | doi:10.1136/bmj.h3

Similar conclusion in a previous meta-analysis of prospective cohort studies and CVD. (Siri-Tarino et al.,Am J Clin Nutr 2010;91:535–46)

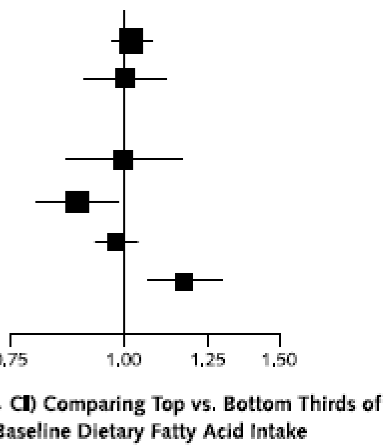
Association of Dietary, Circulating, and Supplement Fatty Acids With Coronary Risk

A Systematic Review and Meta-analysis

Rajiv Chowdhury, MD, PhD; Samantha Warnakula, MPhil*; Setor Kunutsor, MD, MSt*; Francesca Crowe, PhD; Heather A. Ward, PhD; Laura Johnson, PhD; Oscar H. Franco, MD, PhD; Adam S. Butterworth, PhD; Nita G. Forouhi, MRCP, PhD; Simon G. Thompson, FMedSci; Kay-Tee Khaw, FMedSci; Dariush Mozaffarian, MD, DrPH; John Danesh, FRCP*; and Emanuele Di Angelantonio, MD, PhD*

Figure 1. RRs for coronary outcomes in prospective cohort studies of dietary fatty acid intake.

Fatty Acid Intake	Studies, *n*	Participants, *n*	Events, *n*	RR (95% CI)*
Total saturated fatty acids	20	276 763	10 155	1.03 (0.98–1.07)
Total monounsaturated fatty acids	9	144 219	6031	1.00 (0.91–1.10)
Total ω-3 fatty acids				
α-Linolenic	7	157 258	7431	0.99 (0.86–1.14)
Total long-chain ω-3	16	422 786	9089	0.87 (0.78–0.97)
Total ω-6 fatty acids	8	206 376	8155	0.98 (0.90–1.06)
Total trans fatty acids	5	155 270	4662	1.16 (1.06–1.27)



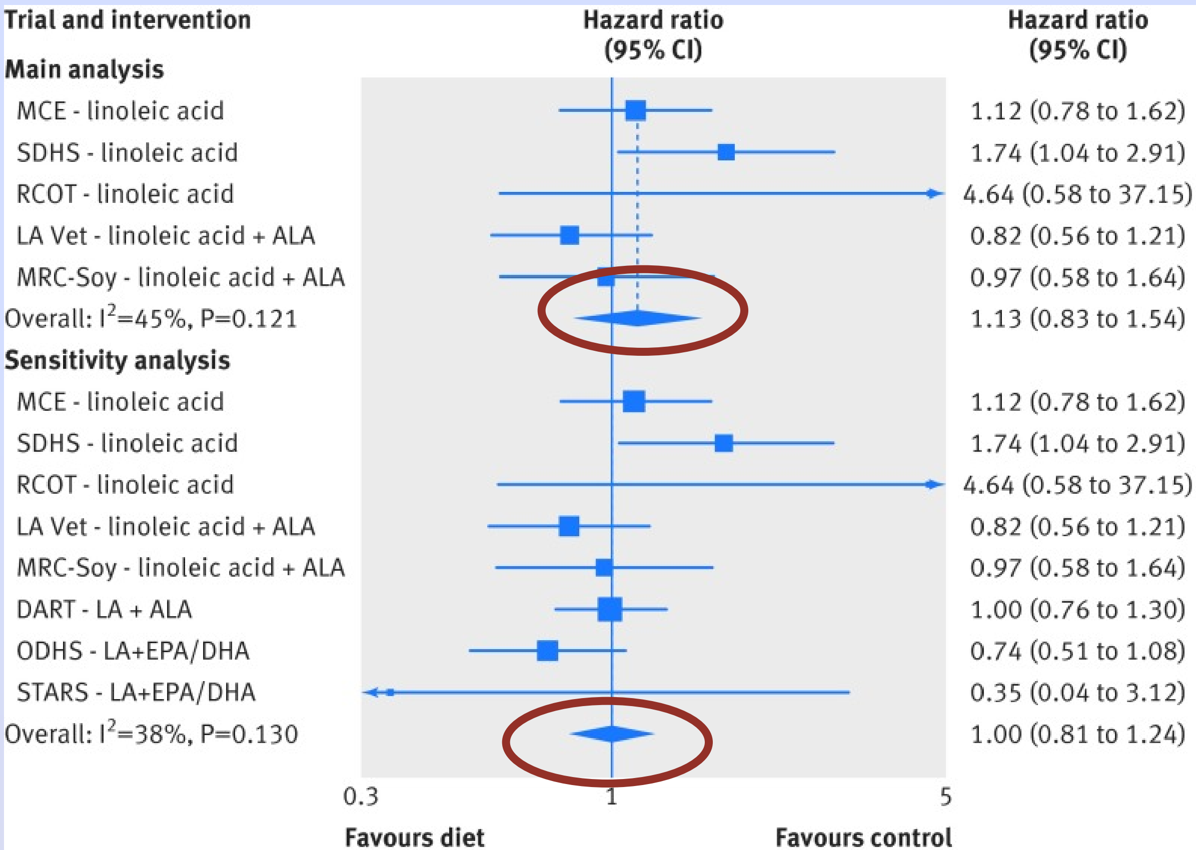
Size of the data marker is proportional to the inverse of the variance of the RR. RR = relative risk.
* Pooled estimate based on random-effects meta-analysis. Corresponding forest plots, I^2 estimates, and pooled RRs based on fixed-effects meta-analysis are provided in Supplement 1, available at www.annals.org.

Randomized controlled trials:

Saturated fat versus PUFA

Re-evaluation of the traditional diet-heart hypothesis: analysis of recovered data from Minnesota Coronary Experiment (1968-73)

Christopher E Ramsden,[1,2] Daisy Zamora,[3] Sharon Majchrzak-Hong,[1] Keturah R Faurot,[2] Steven K Broste,[4] Robert P Frantz,[5] John M Davis,[3,6] Amit Ringel,[1] Chirayath M Suchindran,[7] Joseph R Hibbeln[1]



Meta-analysis for **mortality from coronary heart disease** in trials testing replacement of saturated fat with vegetable oils rich in linoleic acid. Main analysis: trials provided replacement foods (vegetable oils) and were not confounded by any concomitant interventions.

thebmj | *BMJ* 2016;353:i1246 | doi: 10.1136/bmj.i1246

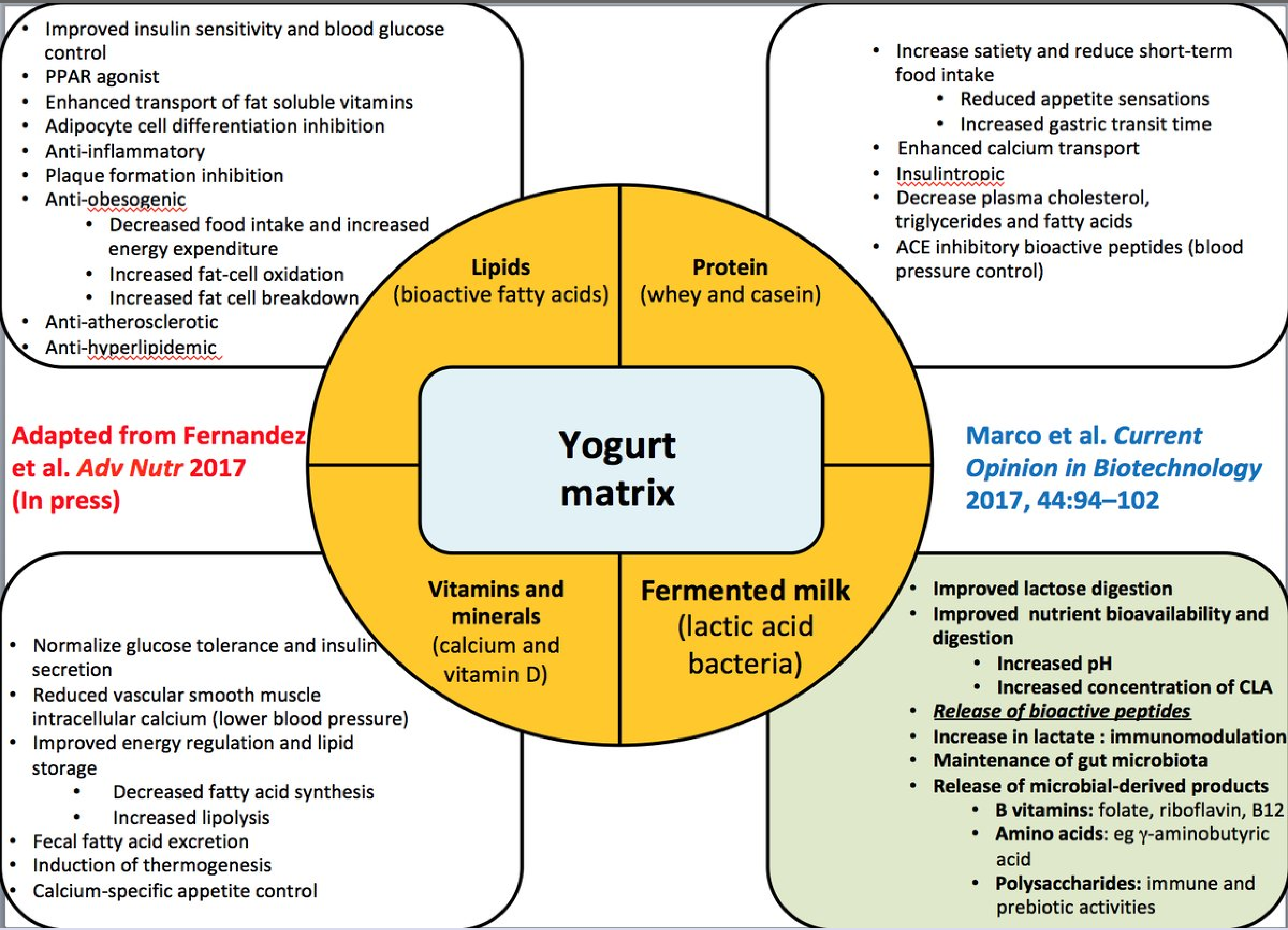
Can we predict the health effects of foods based on the information on the label ?

Or just by the content of saturated fat ?



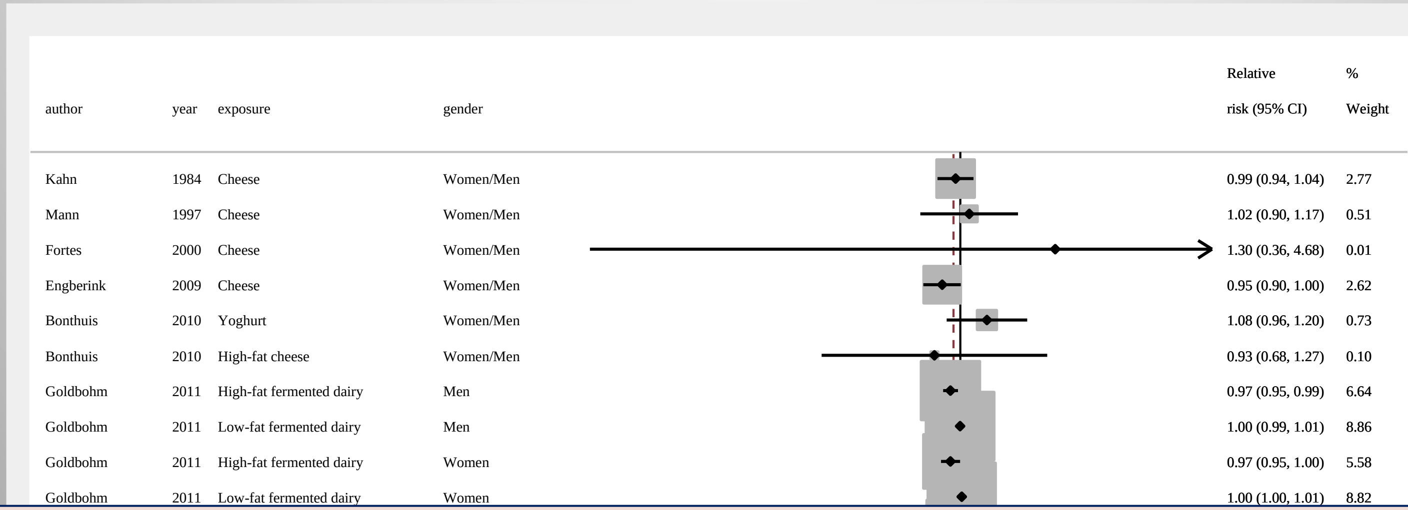



From simgle nutrients to whole foods: the importance of the food matrix


• Improved insulin sensitivity and blood glucose control
• PPAR agonist
• Enhanced transport of fat soluble vitamins
• Adipocyte cell differentiation inhibition
• Anti-inflammatory
• Plaque formation inhibition
• Anti-obesogenic
• Decreased food intake and increased energy expenditure
• Increased fat-cell oxidation
• Increased fat cell breakdown
• Anti-atherosclerotic
• Anti-hyperlipidemic
• Increase satiety and reduce short-term food intake
• Reduced appetite sensations
• Increased gastric transit time
• Enhanced calcium transport
• Insulintropic
• Decrease plasma cholesterol, triglycerides and fatty acids
• ACE inhibitory bioactive peptides (blood pressure control)
Lipids
(bioactive fatty acids)
Protein
(whey and casein)
Adapted from Fernandez et al. Adv Nutr 2017 (In press)
Yogurt matrix
Marco et al. Current Opinion in Biotechnology 2017, 44:94–102
Vitamins and minerals
(calcium and vitamin D)
Fermented milk
(lactic acid bacteria)
• Normalize glucose tolerance and insulin secretion
• Reduced vascular smooth muscle intracellular calcium (lower blood pressure)
• Improved energy regulation and lipid storage
• Decreased fatty acid synthesis
• Increased lipolysis
• Fecal fatty acid excretion
• Induction of thermogenesis
• Calcium-specific appetite control
• Improved lactose digestion
• Improved nutrient bioavailability and digestion
• Increased pH
• Increased concentration of CLA
• Release of bioactive peptides
• Increase in lactate : immunomodulation
• Maintenance of gut microbiota
• Release of microbial-derived products
• B vitamins: folate, riboflavin, B12
• Amino acids: eg γ-aminobutyric acid
• Polysaccharides: immune and prebiotic activities

Current evidence does not support a positive association between intake of dairy products and risk of cardiovascular disease (i.e., stroke and coronary heart disease) and type 2 diabetes. In contrast, fermented dairy products, such as cheese and yogurt, generally show inverse associations. *2*) Intervention studies have indicated that the metabolic effects of whole dairy may be different than those of single dairy constituents when considering the effects on body weight, cardiometabolic disease risk, and bone health. *3*) Different dairy products seem to be distinctly linked to health effects and disease risk markers. *4*) Different dairy structures and common processing methods may enhance interactions between nutrients in the dairy matrix, which may modify the metabolic effects of dairy consumption. *5*) In conclusion, the nutritional values of dairy products should not be considered equivalent to their nutrient contents but, rather, be considered on the basis of the biofunctionality of the nutrients within dairy food structures. *6*) Further research on the

Updated meta-analysis of fermented dairy and CVD and mortality



Total 29 cohort studies are available for meta-analysis. Inverse associations were found between total fermented (included sour milk products, yogurt or cheese) with mortality (RR 0.98, 95% CI: 0.97-0.99; I^2=94.4%) and risk of CVD (RR 0.98, 95% CI: 0.97-0.99; I^2=87.5%). Also stratified analysis of total fermented dairy of cheese shown a lower 2% lower risk of CVD (RR 0.98, 95% CI: 0.95-1.00; I^2=82.6%). No associations were found for total dairy, high-fat/ low-fat dairy or milk with the health outcomes.

Guo J, Astrup A, Lovegrove JA, et al. Milk and dairy consumption and risk of cardiovascular diseases and all-cause mortality: dose-response meta-analysis of prospective cohort studies. Eur J Epidemiol 2017;32:269-87.

Dairy and body weight regulation

International Journal of Obesity (2012) 1 - 9

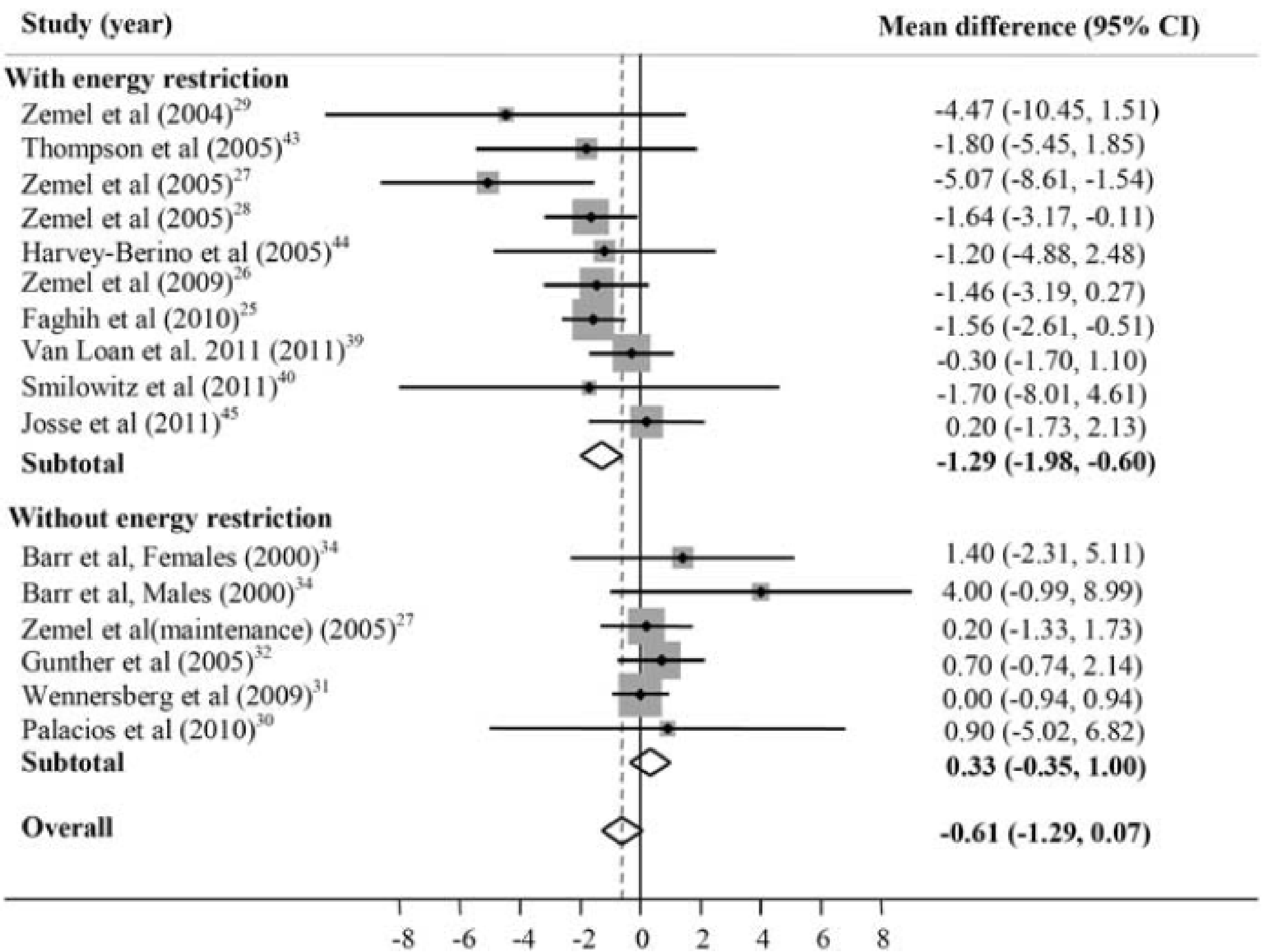
www.nature.com/ijo

ORIGINAL ARTICLE

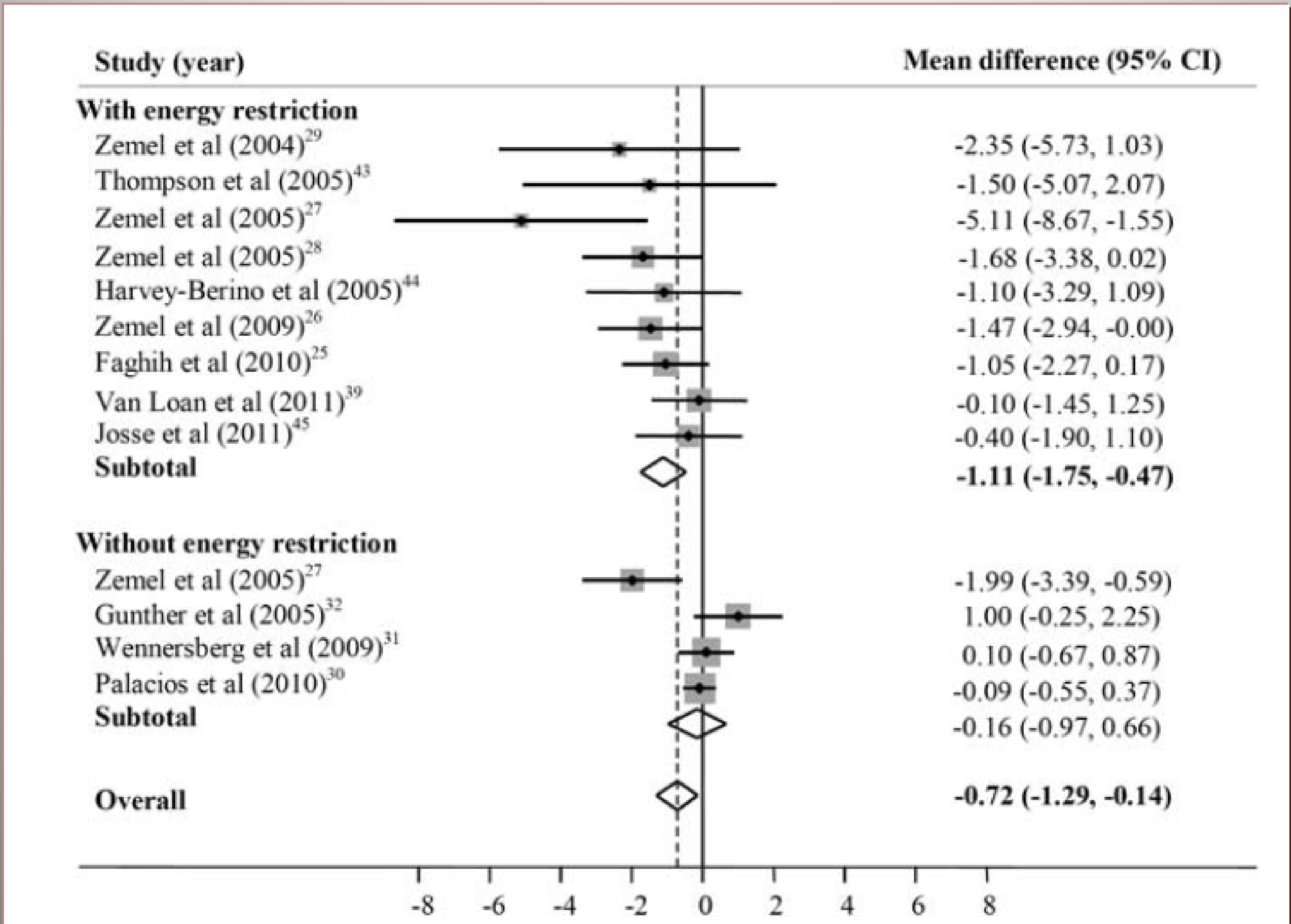
Effect of dairy consumption on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials

AS Abargouei[1,2], M Janghorbani[3], M Salehi-Marzijarani[3] and A Esmaillzadeh[1,2]

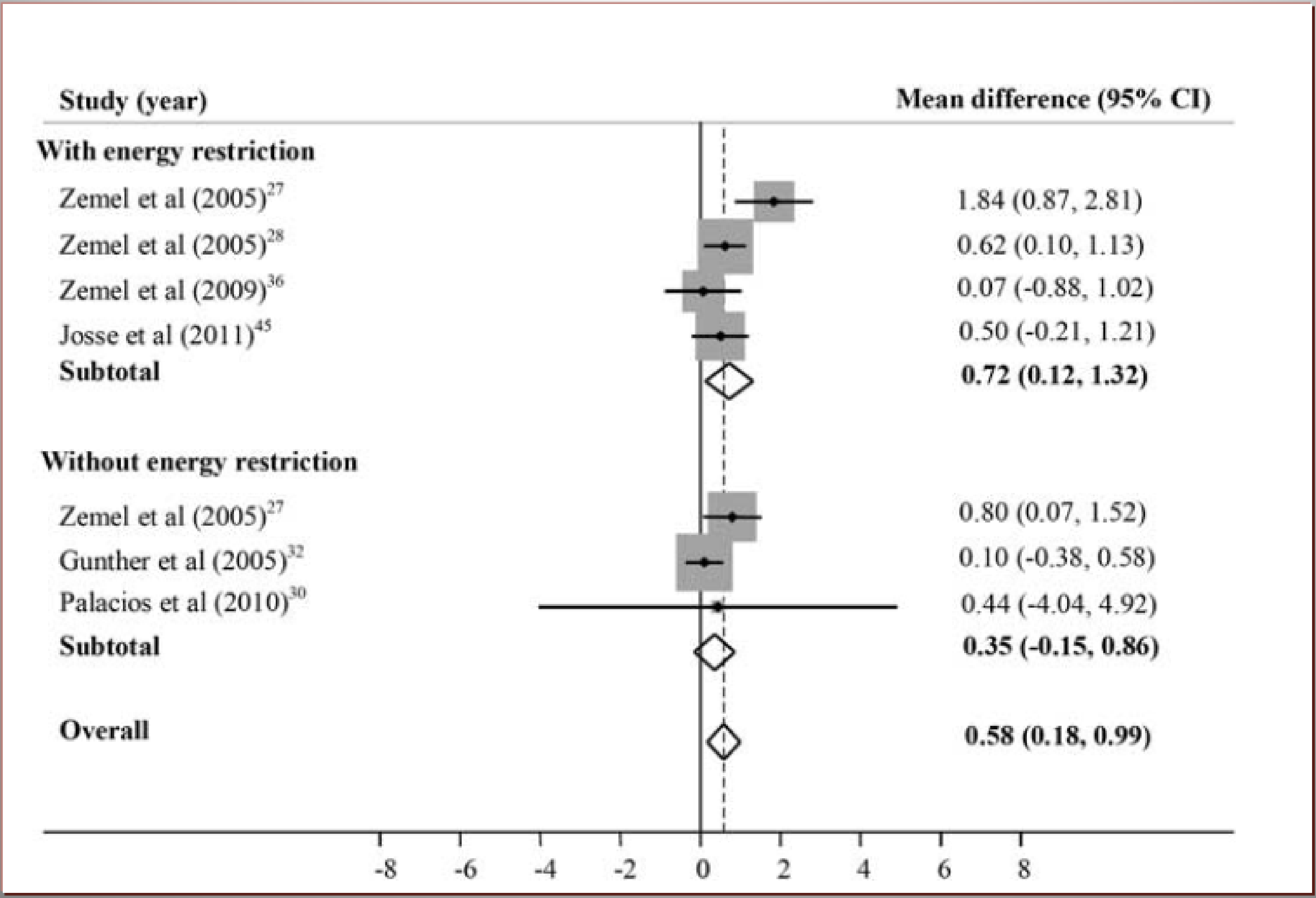
Effect of high vs low dairy on weight loss



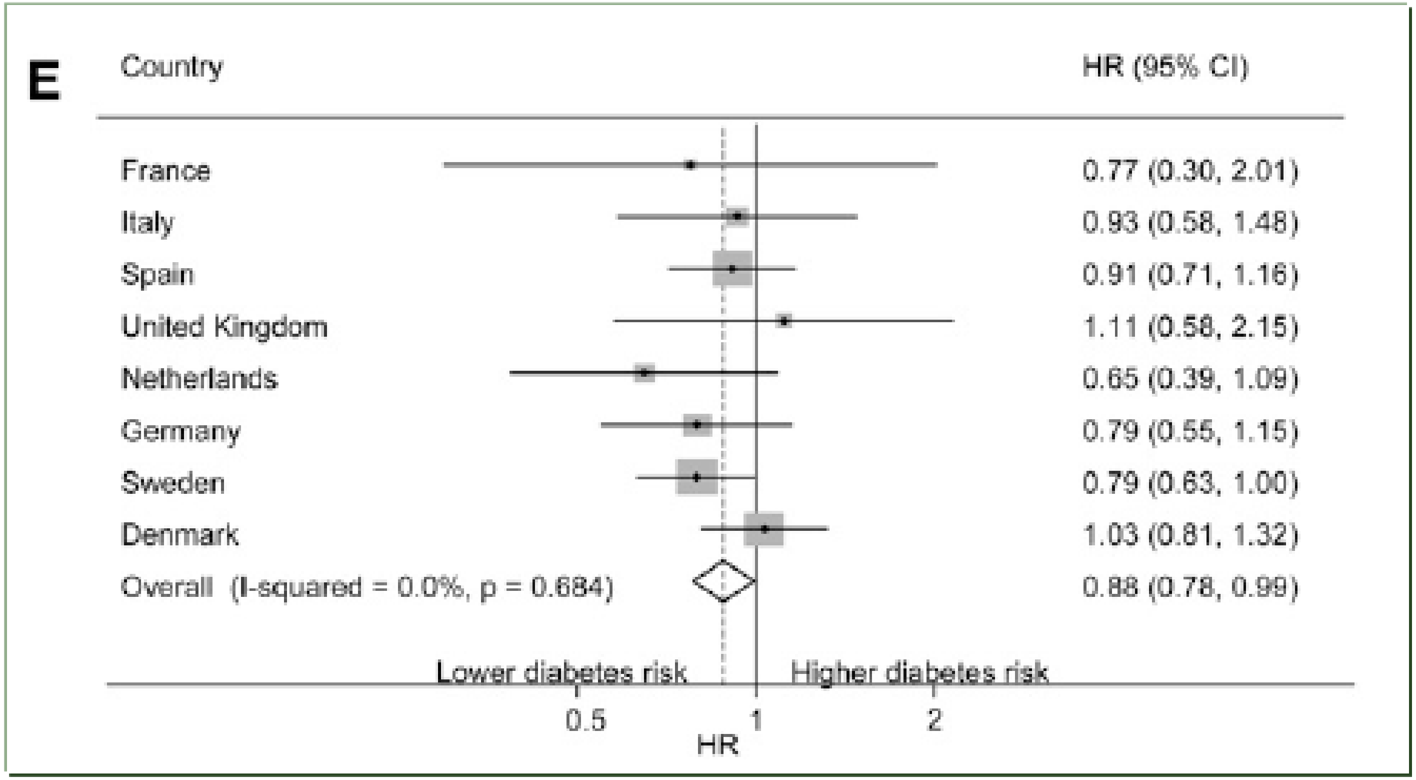
Effect of high vs low dairy on fat loss



Effect of high vs low dairy on fat free mass



Cheese intake lowers diabetes risk



Clinical Trial: DASH vs. full-fat dairy DASH on blood pressure and lipids and lipoproteins

The DASH (Dietary Approaches to Stop Hypertension) diet is rich in fruit, vegetables, and low-fat dairy foods

DASH significantly lowers blood pressure but has mixed effects on blood lipids

- Improves LDL cholesterol but worsens other CVD risk factors such as triglycerides and HDL cholesterol

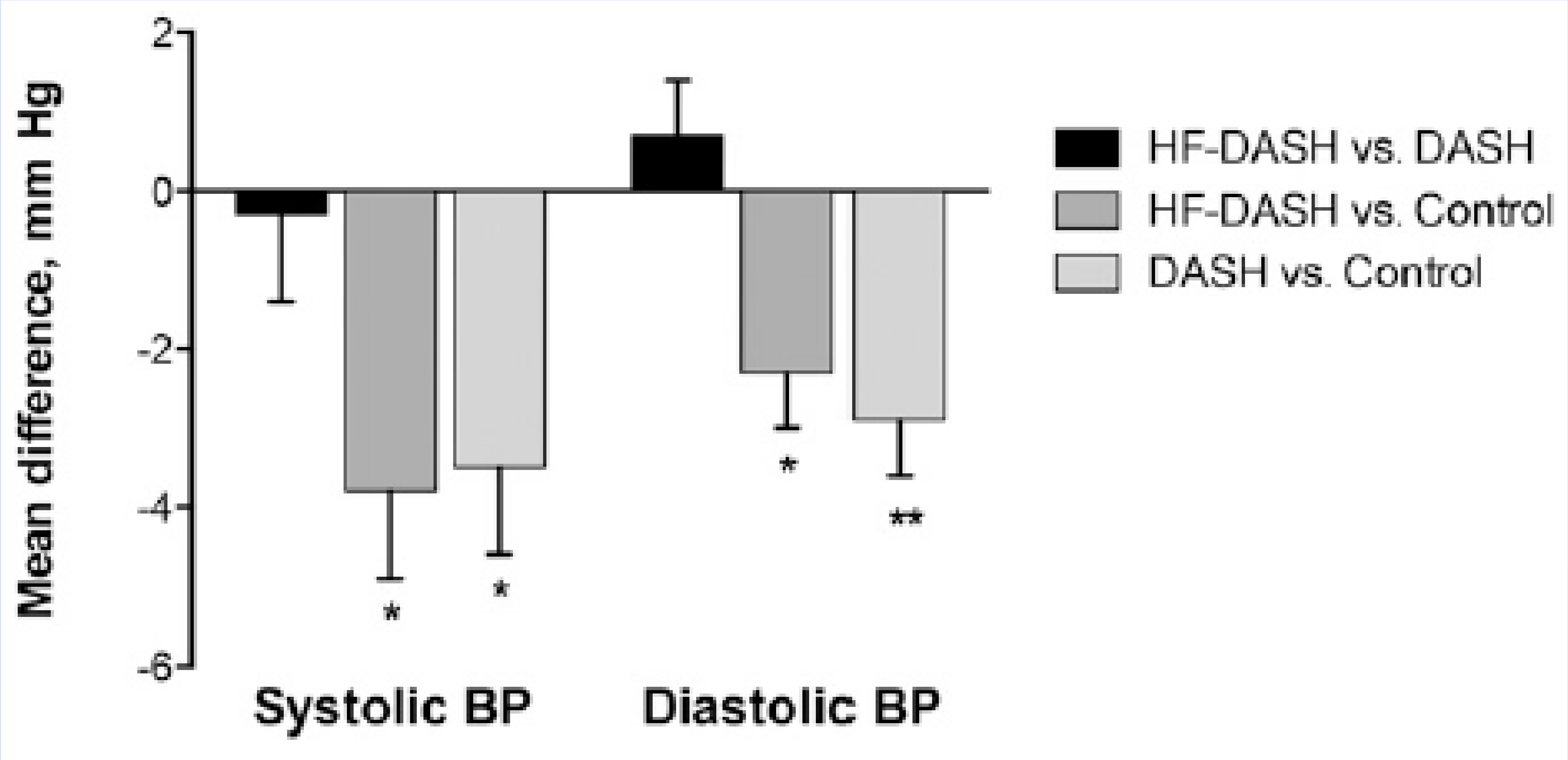
This study was designed to test the effects of substituting full-fat for low-fat dairy foods in the DASH diet

- Replacing sugars, mostly from fruit juices, which constituted 59% of total fruit intake in the DASH, to whole milk, cheese, and yogurt

The full-fat dairy DASH diet contained 14% of calories from saturated fat, provided mainly by dairy, whereas the low-fat DASH contained 8% of calories from saturated fat

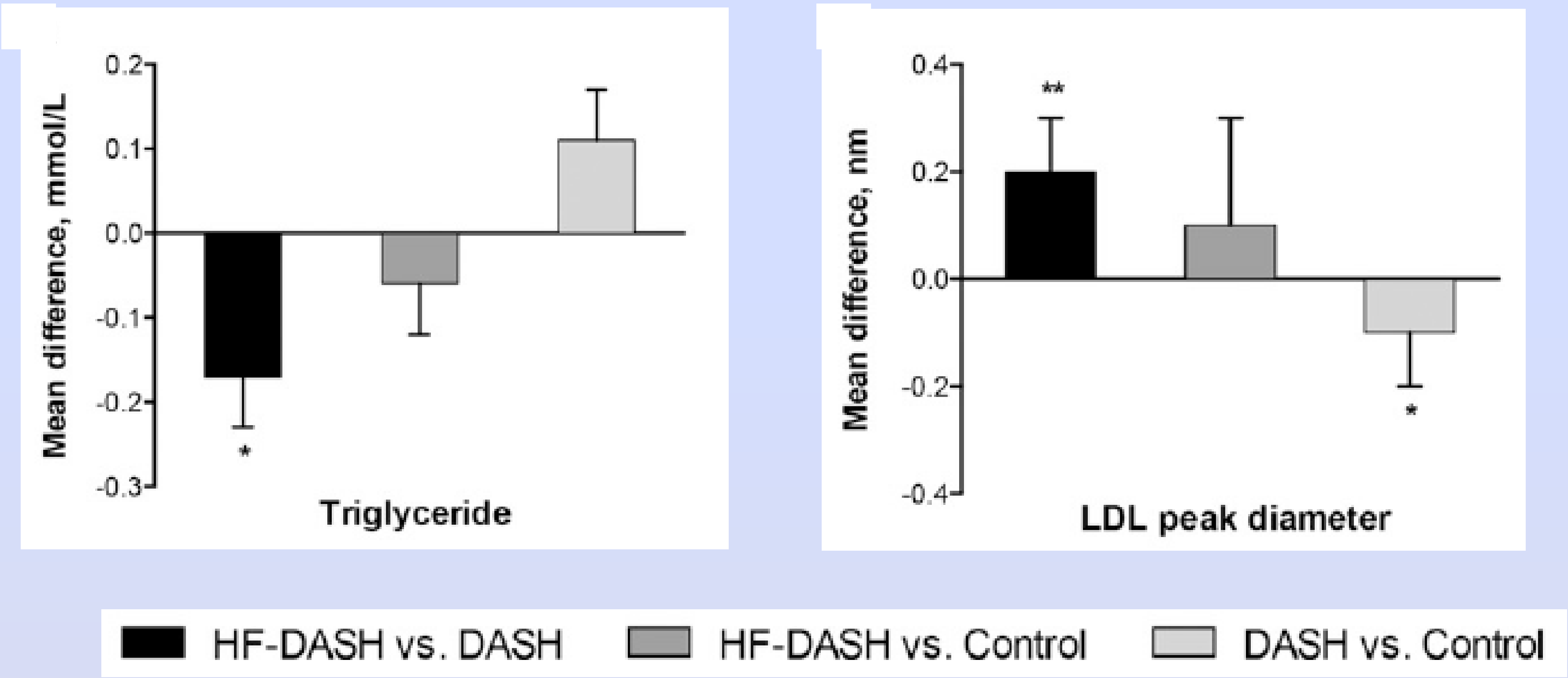
Chiu et al. AJCN 2016

Full-fat dairy DASH and standard DASH confer the same blood pressure benefit



Chiu et al. AJCN 2016

Full-fat dairy DASH resulted in better overall lipid profile than standard DASH



Chiu et al. AJCN 2016

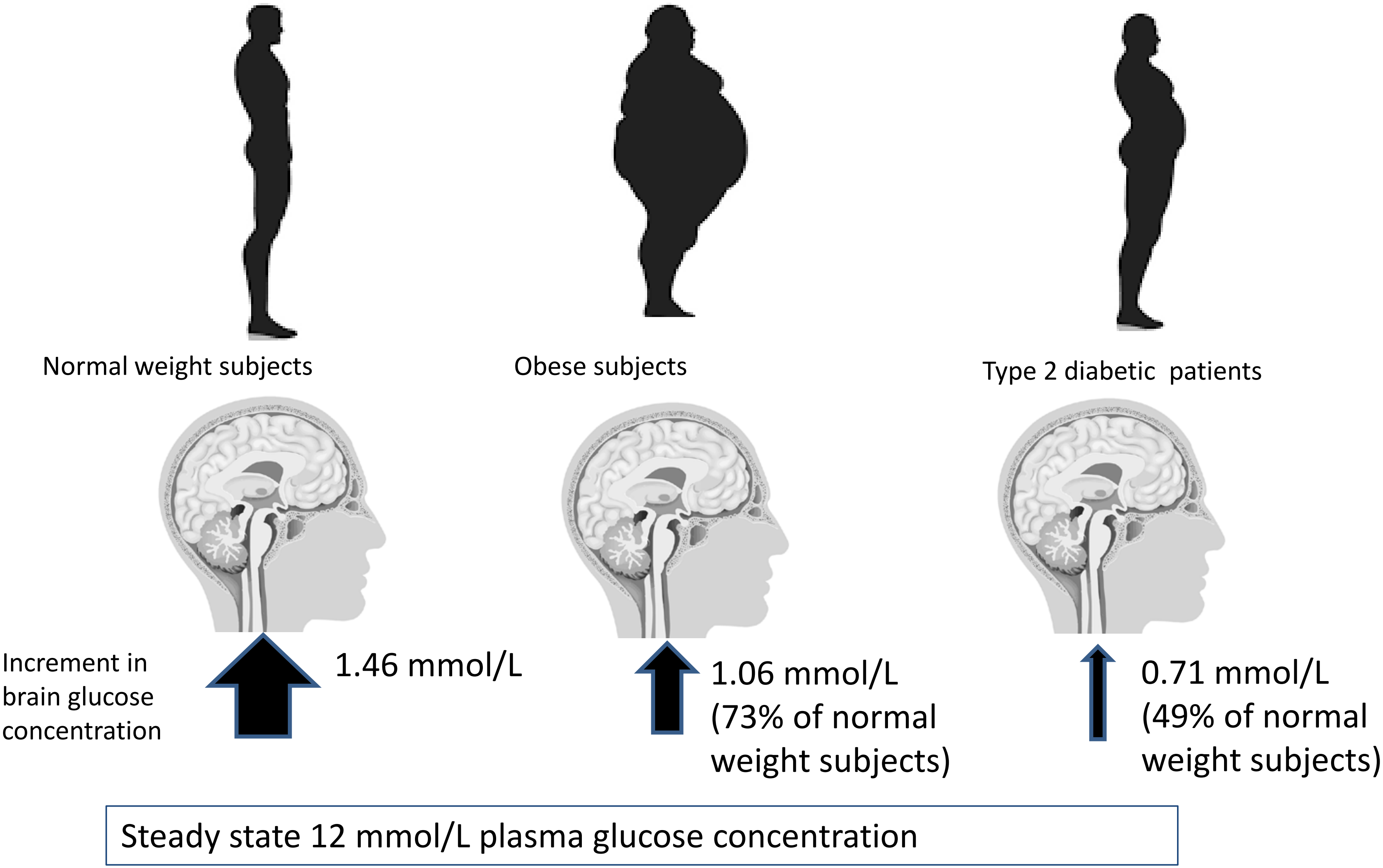
DASH vs. full-fat dairy DASH on blood pressure and lipids and lipoproteins

Despite a higher saturated fat content (14% vs. 8%) full-fat dairy DASH resulted in a better overall lipid profile than standard DASH

- LDL cholesterol was not different between full-fat dairy DASH and standard DASH
- Full-fat dairy DASH improved LDL particle size compared to standard DASH
- HDL cholesterol worsened on standard DASH
- Full-fat dairy DASH improved plasma triglycerides compared to standard DASH

These findings indicate that full-fat dairy foods could be incorporated in the DASH dietary pattern without impairing its positive healthy effects on blood pressure, and is perhaps superior in terms of blood lipid profile

Chiu et al. AJCN 2016



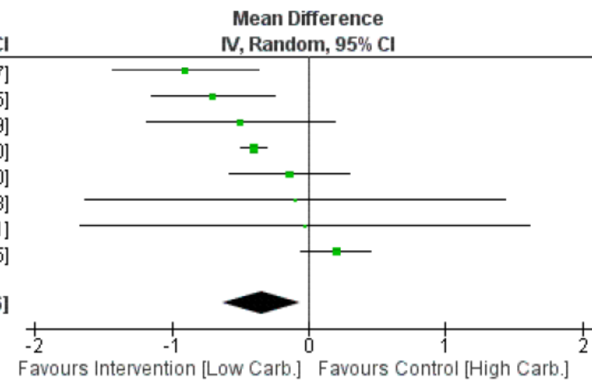
Normal weight, obese and type 2 diabetic participants underwent 1H MR spectroscopy scanning to measure change in intracerebral glucose levels during a 2-hour hyperglycemic clamp (glucose ~220 mg/dl). The change in intracerebral glucose in the lean subjects is used as a reference (100%), and it is was lower in the overweight and the diabetic after controlling for age and sex. Modified from Hwang et al

A Systematic Review and meta-analysis of Dietary Carbohydrate Restriction in Patients with Type 2 Diabetes

Ole Snorgaard, Grith Møller Poulsen, Henning Keinke Andersen and Arne Astrup

Study or Subgroup	Intervention [Low Carb.] Mean	SD	Total	Control [High Carb.] Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Risk of Bias A	B	C	D	E	F	G
Saslow 2014	6	0.3	15	6.9	1.1	18	12.9%	-0.90 [-1.43, -0.37]	+	+	−	+	+	+	?
Tay 2014	-2.6	1	46	-1.9	1.2	47	14.7%	-0.70 [-1.15, -0.25]	+	+	−	+	+	?	?
Yamada 2014	7	0.7	12	7.5	1	12	9.9%	-0.50 [-1.19, 0.19]	?	?	−	?	+	+	+
Iqbal 2010	-0.5	0.2	28	-0.1	0.2	40	22.3%	-0.40 [-0.50, -0.30]	+	?	+	+	−	+	+
Davis 2012	-0.29	0.92	44	-0.15	1.1	40	15.0%	-0.14 [-0.58, 0.30]	+	+	?	?	?	+	?
Guldbrand 2012	7.1	3.1	30	7.2	3	31	3.1%	-0.10 [-1.63, 1.43]	+	?	−	?	+	+	+
Larsen 2011	-0.52	4.15	53	-0.49	4.15	46	2.7%	-0.03 [-1.67, 1.61]	+	?	?	?	+	+	+
Krebs 2012	7.9	1.3	173	7.7	1.1	174	19.4%	0.20 [-0.05, 0.45]	+	+	?	+	?	+	+
Total (95% CI)			**401**			**408**	**100.0%**	**-0.34 [-0.63, -0.06]**							

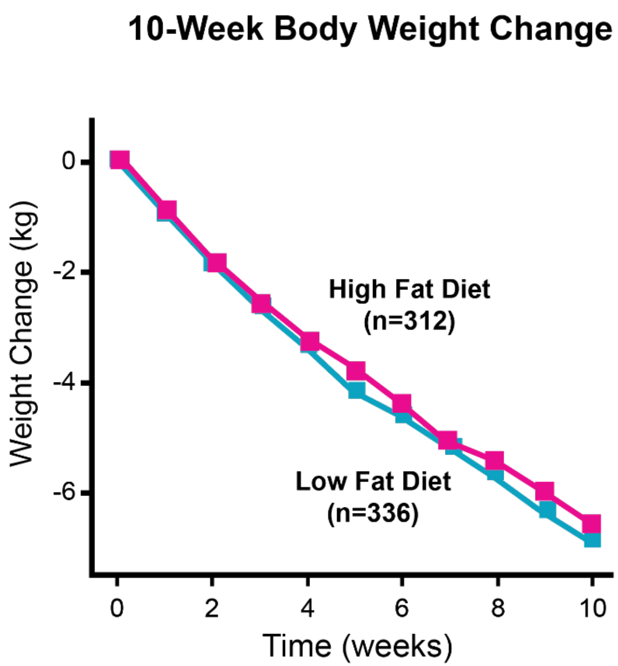
Heterogeneity: Tau² = 0.09; Chi² = 26.90, df = 7 (P = 0.0003); I² = 74%
Test for overall effect: Z = 2.34 (P = 0.02)

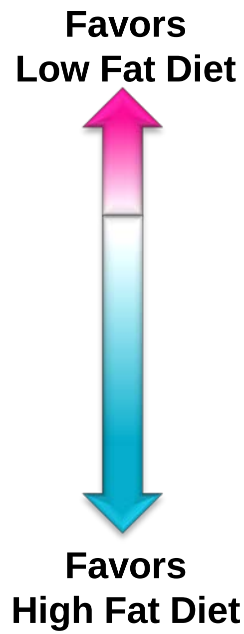


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

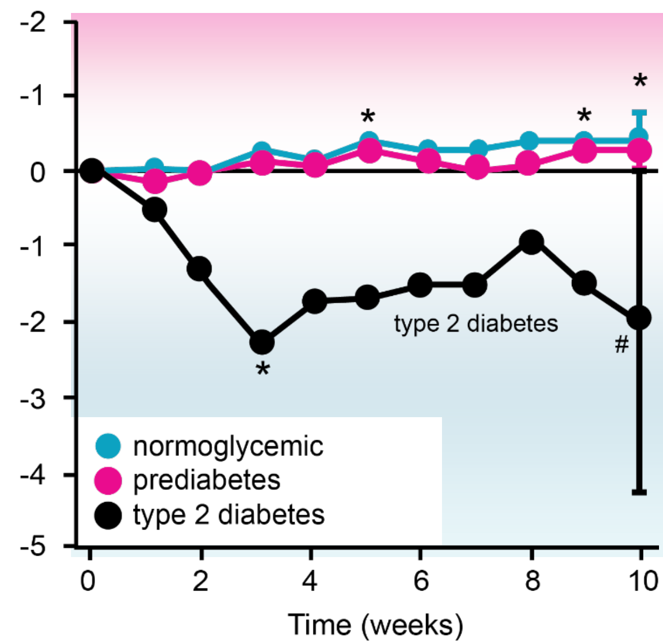
Within the first year of intervention, LCD was followed by a 0.34 %-point lower [95% CI: 0.06, 0.63] HbA1c compared to HCD. A greater reduction in carbohydrate restriction was associated with greater reduction in HbA1c (R = -0.85, P<0.01).

Normoglycemic Subjects Lost More Weight On A Low-Fat Diet. Subjects w/T2D More Responsive To a High-Fat Diet





Variable: Fasting Plasma Glucose



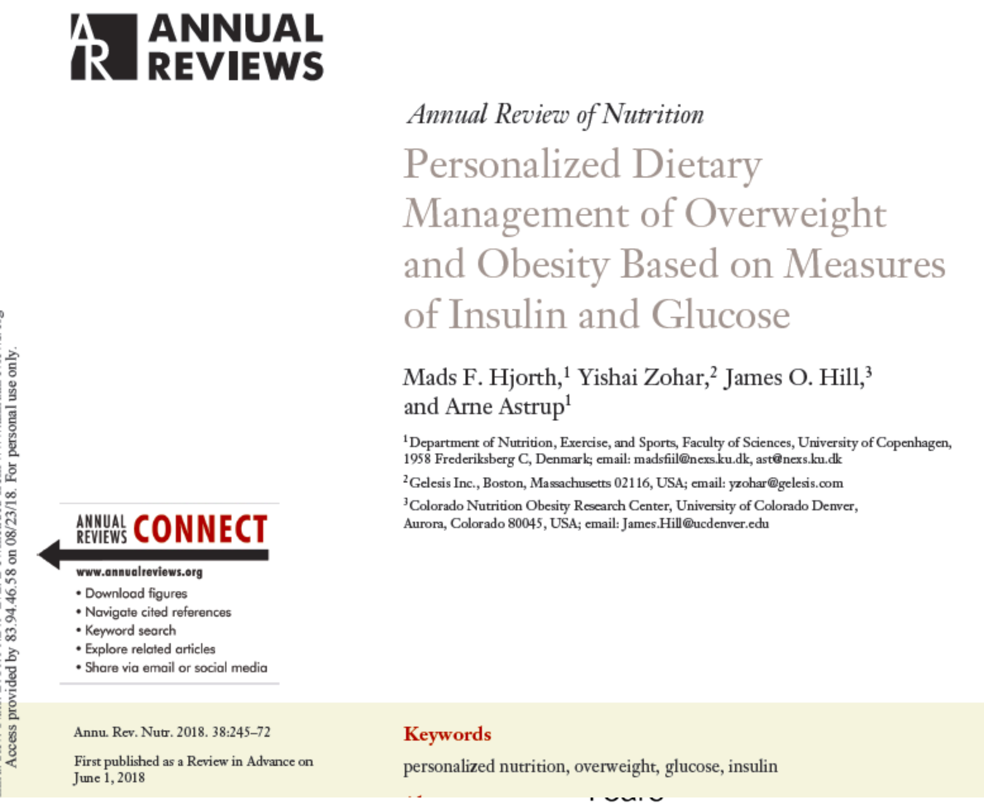
*$P < 0.05$ from zero
#$P < 0.05$ between glycemic groups


AJCN. First published ahead of print July 5, 2017 as doi: 10.3945/ajcn.117.155200.

Pretreatment fasting plasma glucose and insulin modify dietary weight loss success: results from 3 randomized clinical trials

Mads F Hjorth,[1] Christian Ritz,[1] Ellen E Blaak,[4] Wim HM Saris,[4] Dominique Langin,[5–8] Sanne Kellebjerg Poulsen,[1,9] Thomas Meinert Larsen,[1] Thorkild IA Sørensen,[2,3,10] Yishai Zohar,[11] and Arne Astrup[1]

PREDIMED 2017: Subjects With Elevated Fasting Glucose Lost Significantly More Weight on *Ad Libitum*, High Fat Diets



ANNUAL REVIEWS

Annual Review of Nutrition

Personalized Dietary Management of Overweight and Obesity Based on Measures of Insulin and Glucose

Mads F. Hjorth,[1] Yishai Zohar,[2] James O. Hill,[3] and Arne Astrup[1]

[1]Department of Nutrition, Exercise, and Sports, Faculty of Sciences, University of Copenhagen, 1958 Frederiksberg C, Denmark; email: madsfiil@nexs.ku.dk, ast@nexs.ku.dk

[2]Gelesis Inc., Boston, Massachusetts 02116, USA; email: yzohar@gelesis.com

[3]Colorado Nutrition Obesity Research Center, University of Colorado Denver, Aurora, Colorado 80045, USA; email: James.Hill@ucdenver.edu

Annu. Rev. Nutr. 2018. 38:245–72

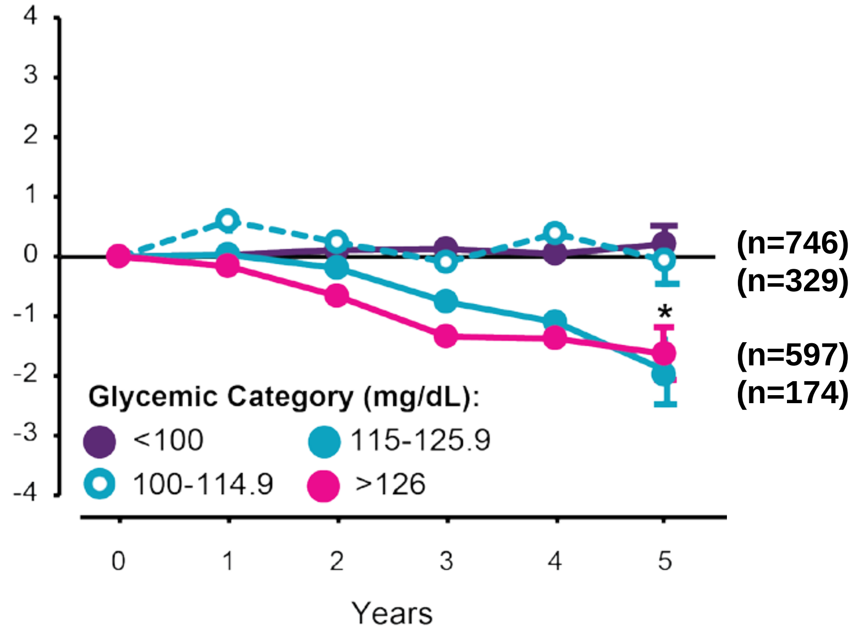
First published as a Review in Advance on June 1, 2018

Keywords

personalized nutrition, overweight, glucose, insulin

NEW ANALYSIS

Ad Libitum, High Fat Mediterranean Diets (2017)



food & nutrition research

Co-Action Publishing

REVIEW ARTICLE

Milk and dairy products: good or bad for human health? An assessment of the totality of scientific evidence

Tanja Kongerslev Thorning[1], Anne Raben[1], Tine Tholstrup[1], Sabita S. Soedamah-Muthu[2], Ian Givens[3] and Arne Astrup[1]*

[1]Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, Copenhagen, Denmark; [2]Division of Human Nutrition, Wageningen University, Wageningen, The Netherlands; [3]Centre for Food, Nutrition and Health, University of Reading, Reading, UK

Abstract

Background: There is scepticism about health effects of dairy products in the public, which is reflected in an increasing intake of plant-based drinks, for example, from soy, rice, almond, or oat.

Objective: This review aimed to assess the scientific evidence mainly from meta-analyses of observational

Received: 7 June 2016; Revised: 4 October 2016; Accepted: 21 October 2016; Published: 22 November 2016

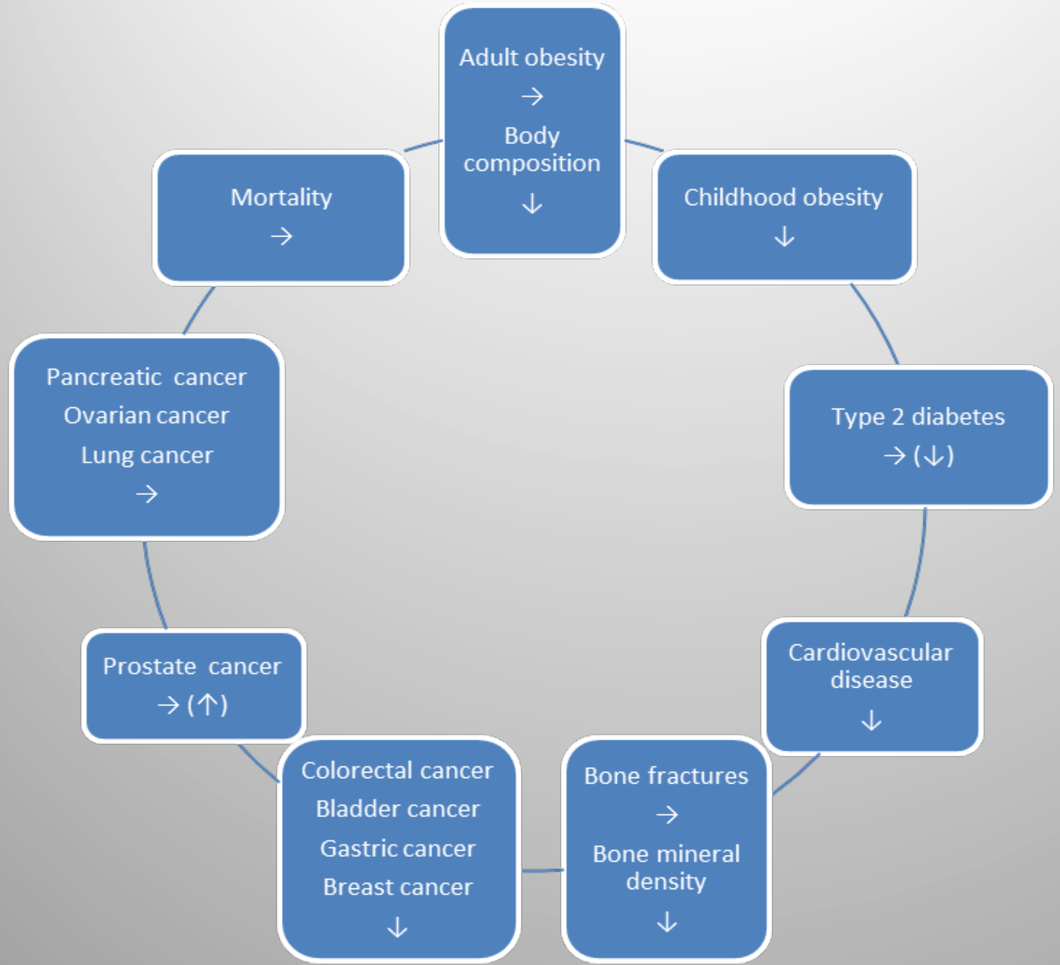


Figure 1. Overall effect/association between dairy (**<u>cheese and yogurt</u>**) intake and health outcomes. ↓favorable effect/association; ↑adverse effect/association; → no effect/association.

Conclusions

- The totality of evidence i.e. meta-analyses of both observational studies and RCT's cannot find any harmful effects of dairy on body fat, metabolic syndrome, type 2 diabetes, or CVD.
- Yogurt and cheese does not exert the detrimental effects on blood lipids and blood pressure as previously predicted by its sodium and saturated fat content.
- Dairy, in particular full-fat, exerts beneficial effects on LDL-cholesterol, blood pressure and postprandial triglycerides as compared to butter.
- Meta-analysis of observational studies support that full fat yogurt and cheese (and perhaps other fermented dairy) may protect from CVD and type 2 diabetes.
- The effects of yogurt and cheese on body composition, diabetes and CVD risks can be attributed to the food matrix with nutrients i.e. protein, calcium, SCFA from fermentation, and perhaps peptides, phospholipids.
- Whereas the low-fat version might by helpful for non-diabetic overweight and obese individuals, the full-fat versions are optimal for type 2 diabetics.
- A diet including yogurt and cheese should be recommended for all to prevent and manage type 2 diabetes and cardiovascular disease.

Evidence based information ?