UNIVERSITY OF COPENHAGEN

Metabolic Health – The impact of the dairy matrix

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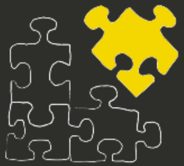
DIETARY GUIDELINES 2015-2020

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:

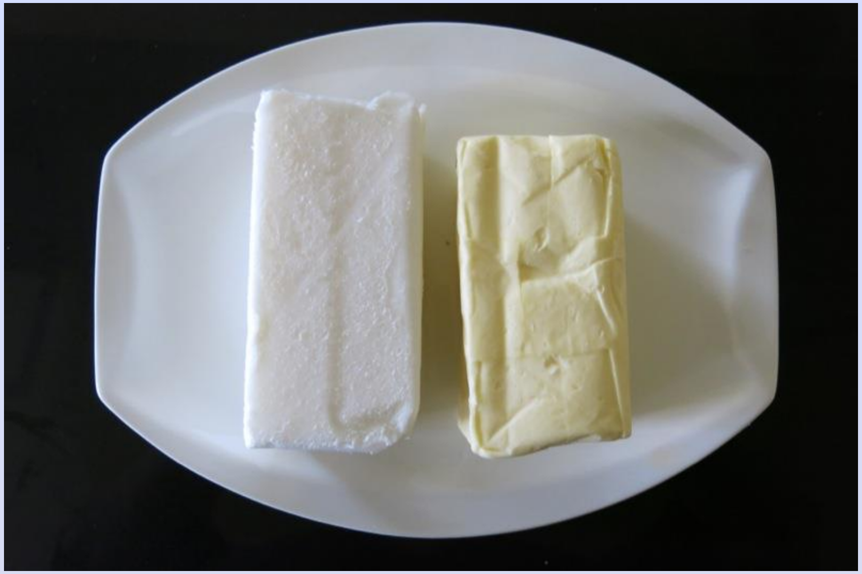
- Consume less than 10 percent of calories per day from added sugars[3]

EFSA: As low as possible

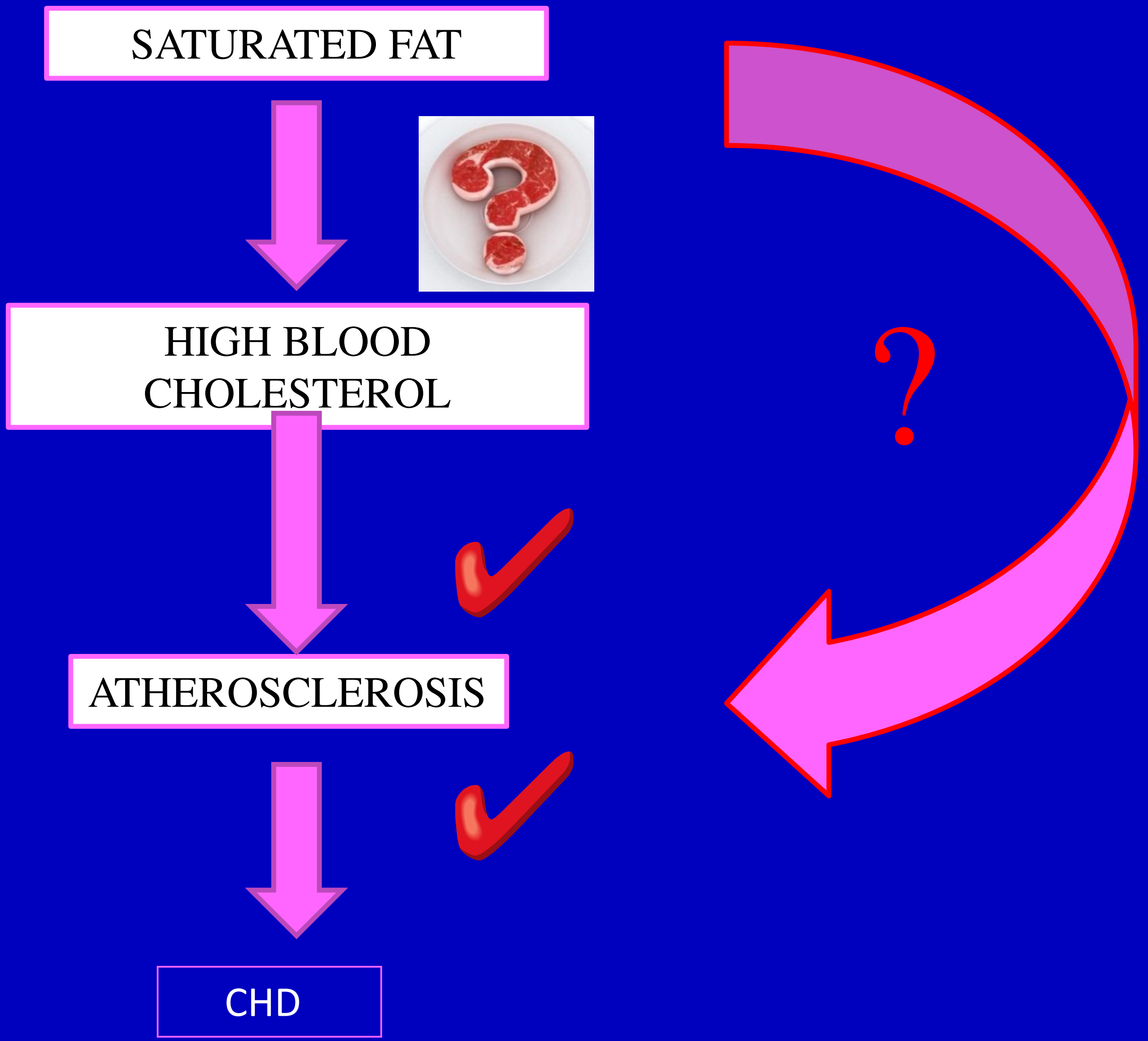
- Consume less than 2,300 milligrams (mg) per day of sodium[5]
- If alcohol is consumed, it should be consumed in moderation—up to one drink per day for women and up to two drinks per day for men—and only by adults of legal drinking age.[6]

Saturated fat intake and CVD risk

-the most recent evidence



The lipid hypothesis and CHD



Hierarchy in Scientific Evidence

High

Level of Evidence

Low

- **Systematic Reviews (Meta-analysis)**
- Randomized Controlled Trials
- Other Controlled Trials
- Prospective Cohort studies
- Case – Control studies
- Prevalence studies
- Ecological studies
- Animal studies

thebmj

BMJ 2019;366:l4137 doi: 10.1136/bmj.l4137 (Published 3 July 2019)

ANALYSIS

Check for updates

WHO draft guidelines on dietary saturated and trans fatty acids: time for a new approach?

The 2018 WHO draft guidance on fatty acids fails to consider the importance of the food matrix, argue **Arne Astrup and colleagues**

Arne Astrup *head of department*[1], Hanne CS Bertram *professor*[2], Jean-Philippe Bonjour *honorary professor of medicine*[3], Lisette CP de Groot *professor*[4], Marcia C de Oliveira Otto *assistant professor*[5], Emma L Feeney *assistant professor*[6], Manohar L Garg *director*[7], Ian Givens *professor and director*[8], Frans J Kok *emeritus professor of nutrition and health*[4], Ronald M Krauss *senior scientist and Dolores Jordan endowed chair*[9], Benoît Lamarche *chair of nutrition*[10], Jean-Michel Lecerf *head of department*[11], Philippe Legrand *professor*[12], Michelle McKinley *reader*[13], Renata Micha *associate professor*[14], Marie-Caroline Michalski *research director*[15], Dariush Mozaffarian *dean*[14], Sabita S Soedamah-Muthu *associate professor*[16]

The WHO evidence: Cochrane analysis that only included data from 15 RCTs

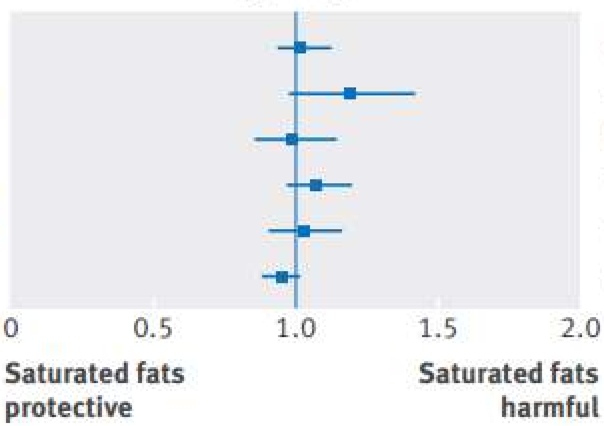
- An association between reducing SFA intake and a reduction in the composite end-point of cardiovascular events [RR 0.83 (0.72 to 0.96)].
- However, the study showed no significant association between reducing SFA and total mortality (RR) 0.97, 95% CI 0.90 to 1.05) or
- CVD mortality (RR 0.95, 95% CI 0.80 to 1.12), or
- Fatal and non-fatal myocardial infarction (RR 0.90, 95% CI 0.80 to 1.01) or
- Non-fatal myocardial infarction (RR 0.95, 95% CI 0.80 to 1.13), or
- Stroke (RR 1.00, 95% CI 0.89 to 1.12), or
- CHD events (RR 0.87, 95% CI 0.74 to 1.03), or
- CHD mortality (RR 0.98, 95% CI 0.84 to 1.15)

BMJ 2019;366:l4137 doi: 10.1136/bmj.l4137 (Published 3 July 2019)

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	Risk ratio (95% CI)	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)

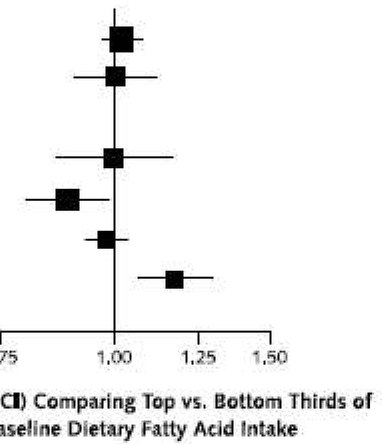
Association of Dietary, Circulating, and Supplement Fatty Acids With Coronary Risk

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.

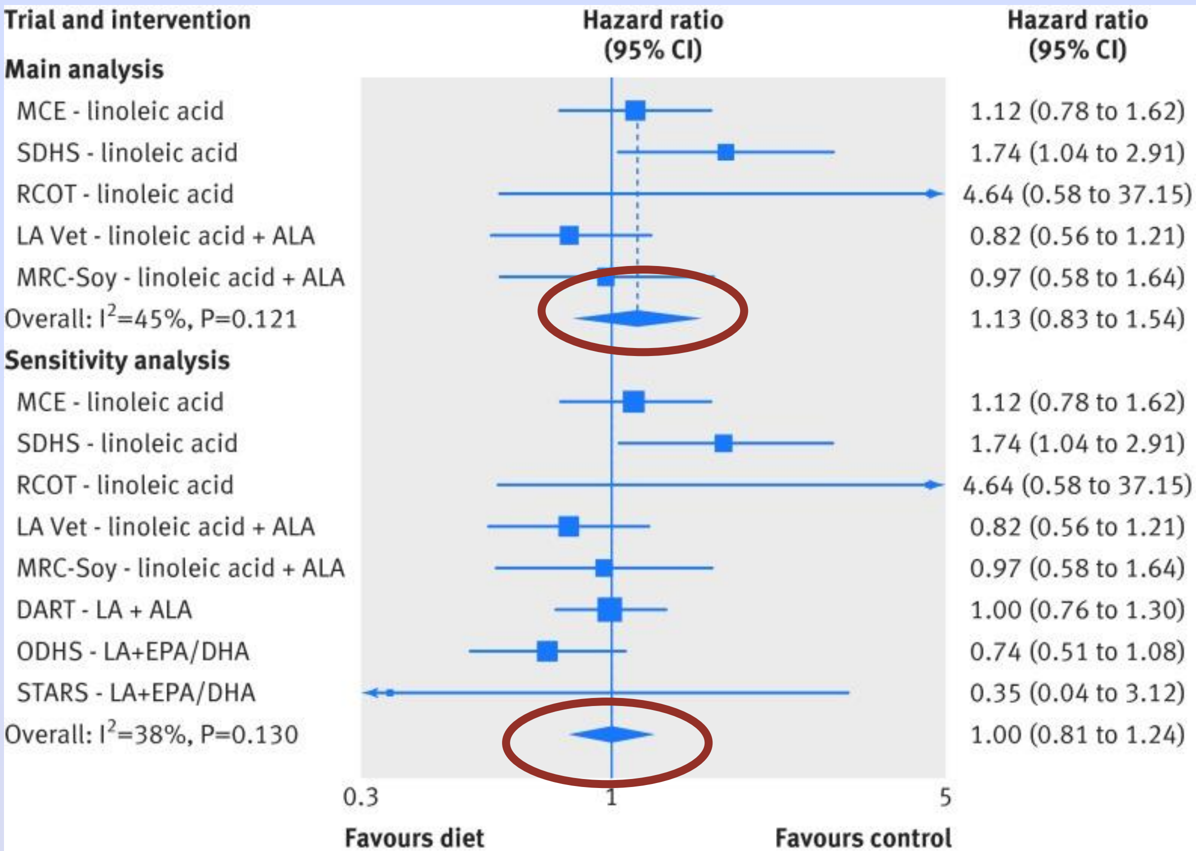
Ann Intern Med. 2014;160:398-406

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]



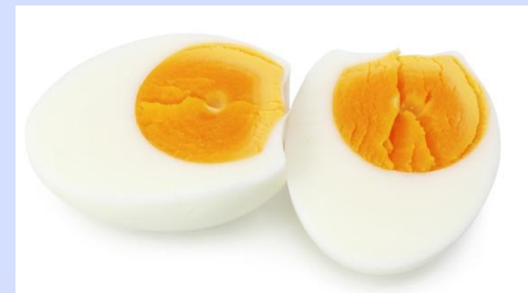
Meta-analysis for **mortality from coronary heart disease** in trials testing replacement of saturated fat with vegetable oils rich in linoleic acid. Main analysis: trials provided replacement foods (vegetable oils) and were not confounded by any concomitant interventions.

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

Pure fats for cooking ?

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

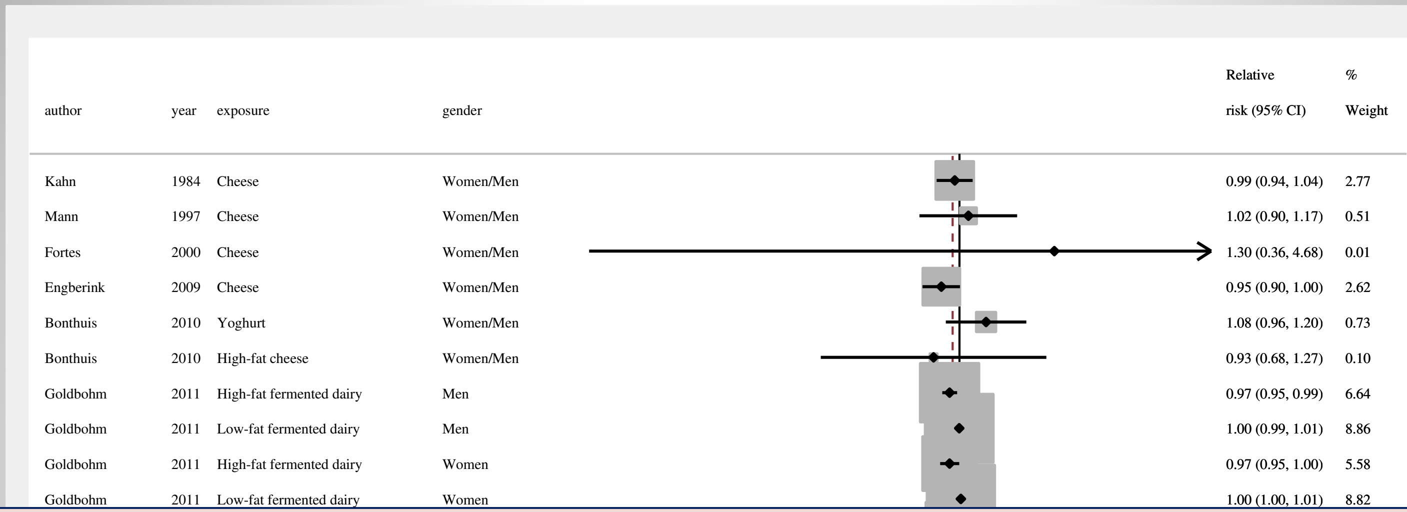
Or just by the content of saturated fat ?



BMJ 2019;366:l4137 doi: 10.1136/bmj.l4137 (Published 3 July 2019)

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

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

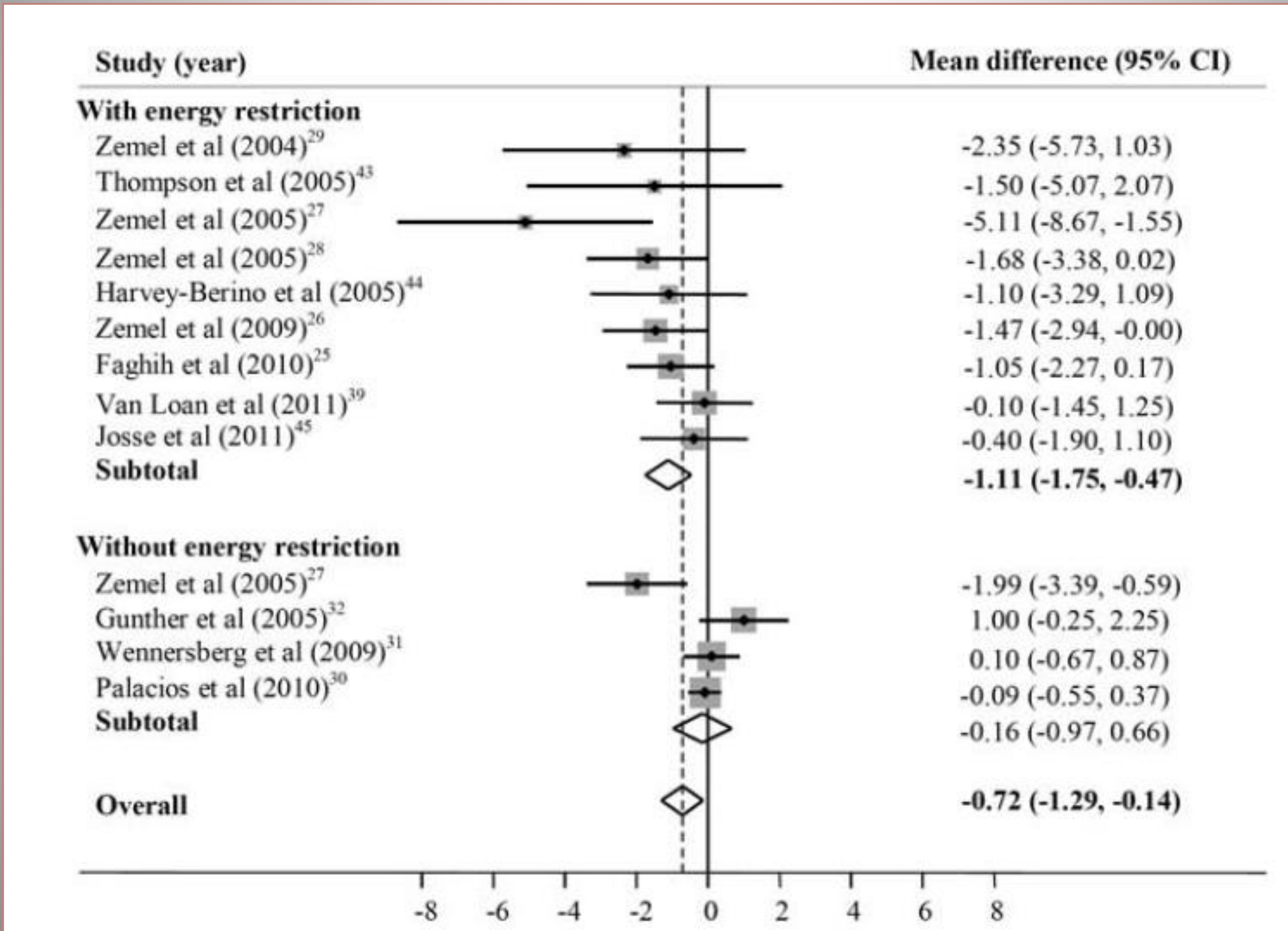
www.nature.com/ijo

ORIGINAL ARTICLE

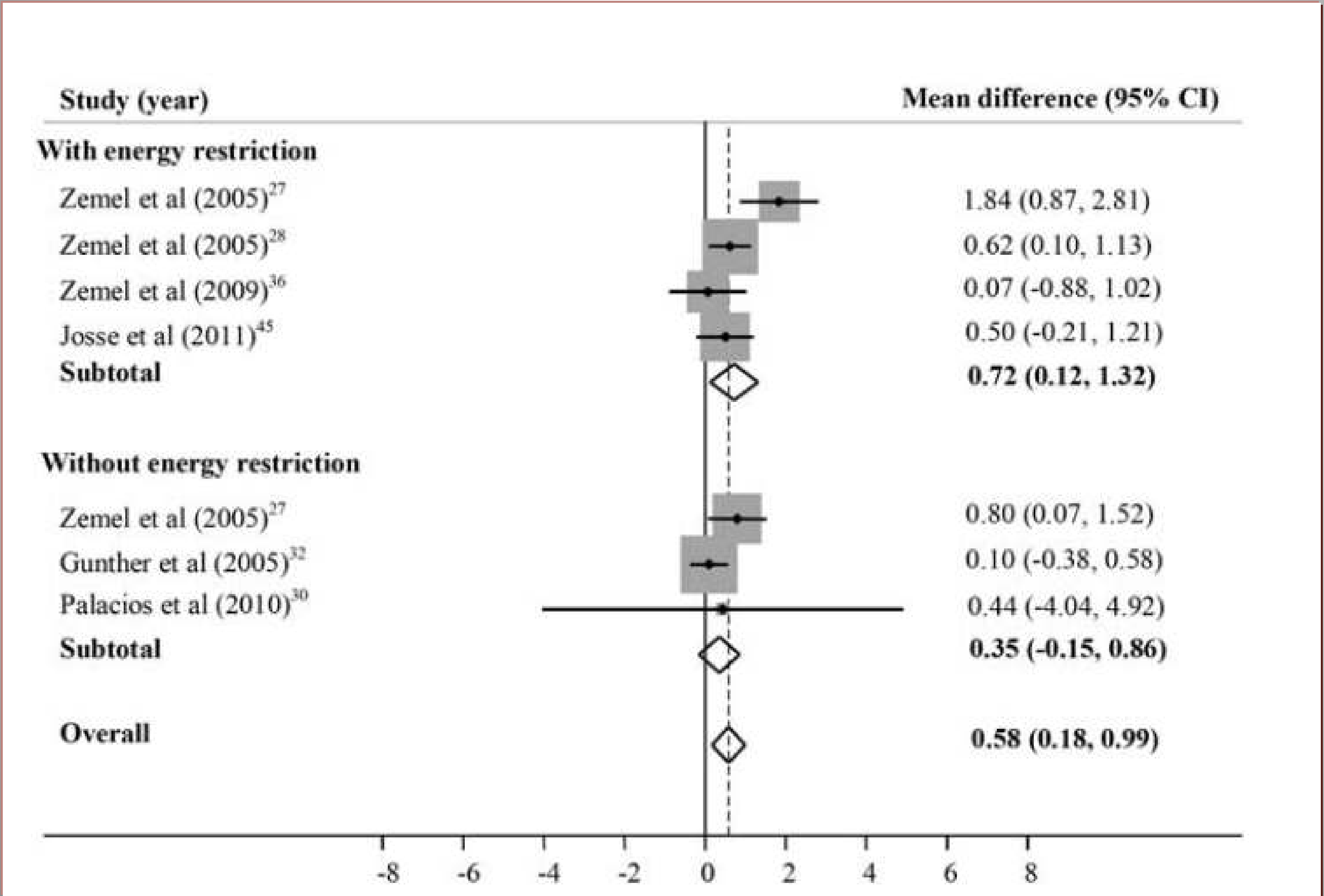
Effect of dairy consumption on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials

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

Effect of high vs low dairy on fat loss

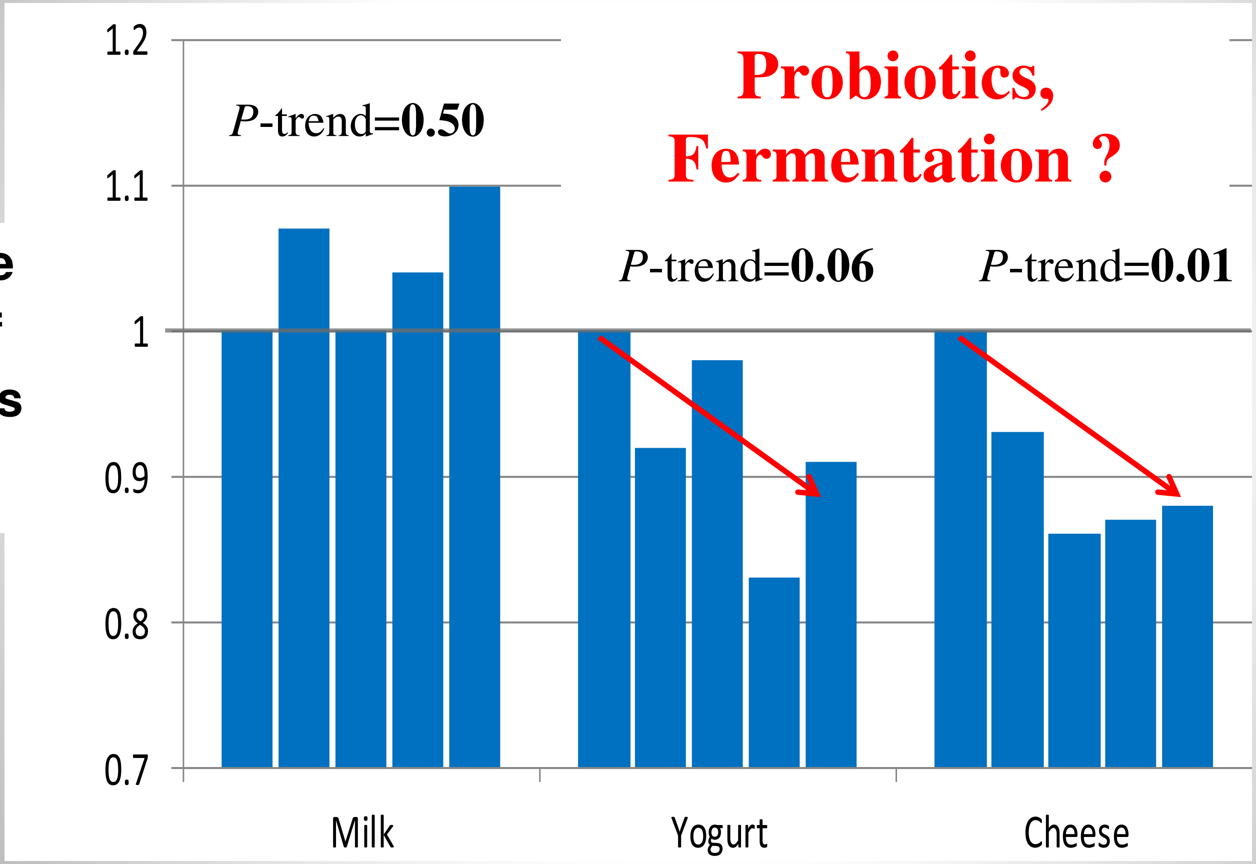


Effect of high vs low dairy on **fat free mass**



Dairy Foods and Risk of Diabetes

340,234 Europeans, 8 countries, 12,403 cases



Relative Risk of Diabetes

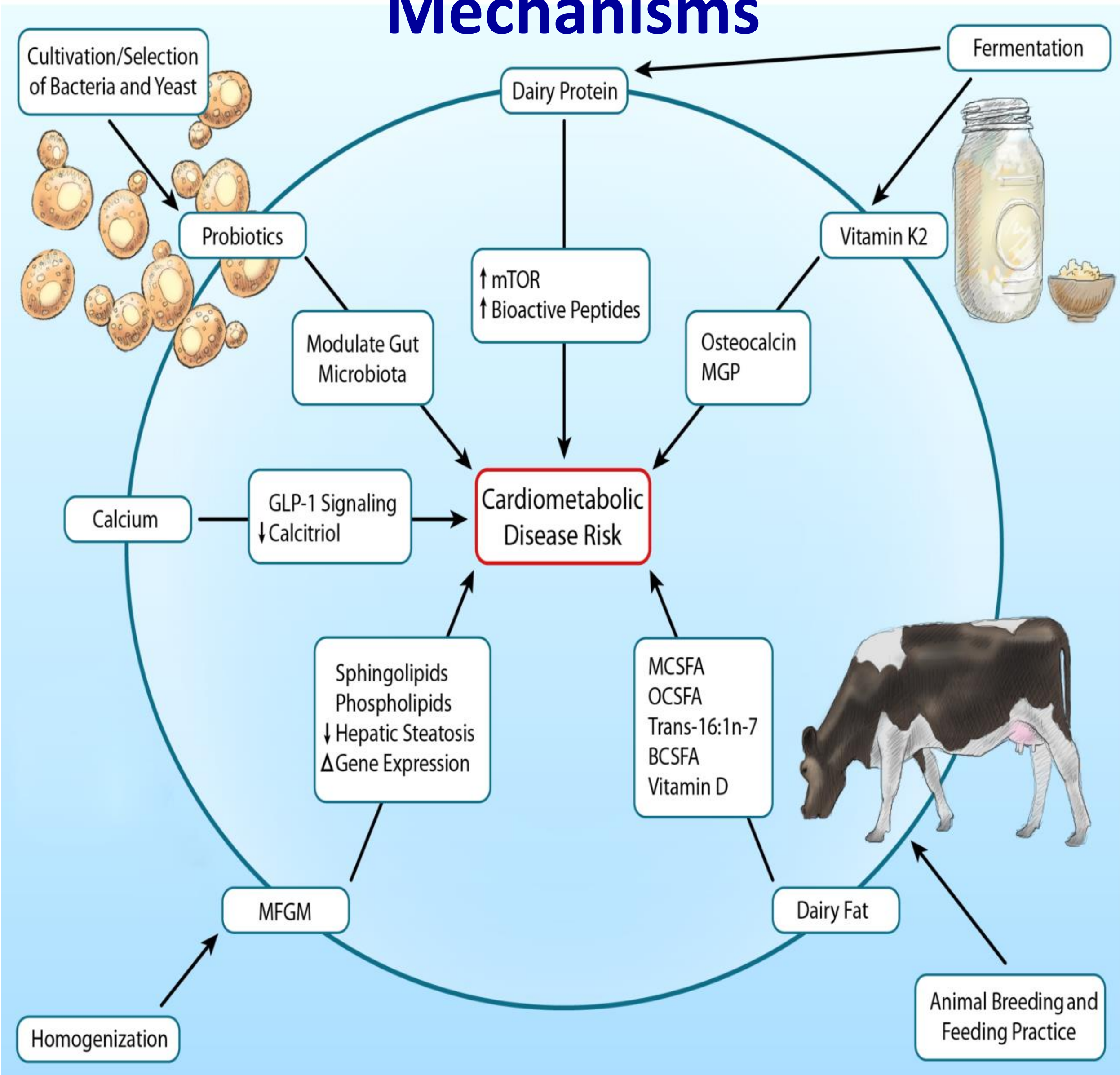
Quintiles of Consumption

Sluijis et al., AJCN
2012

Effects of cheese on CVD risk factors & Mechanisms

The cheese food matrix and mechanisms

Dairy & Cardiometabolic Health: Potential Mechanisms

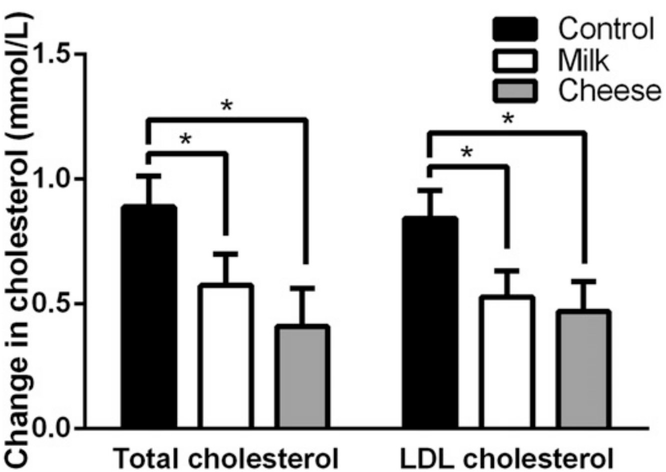


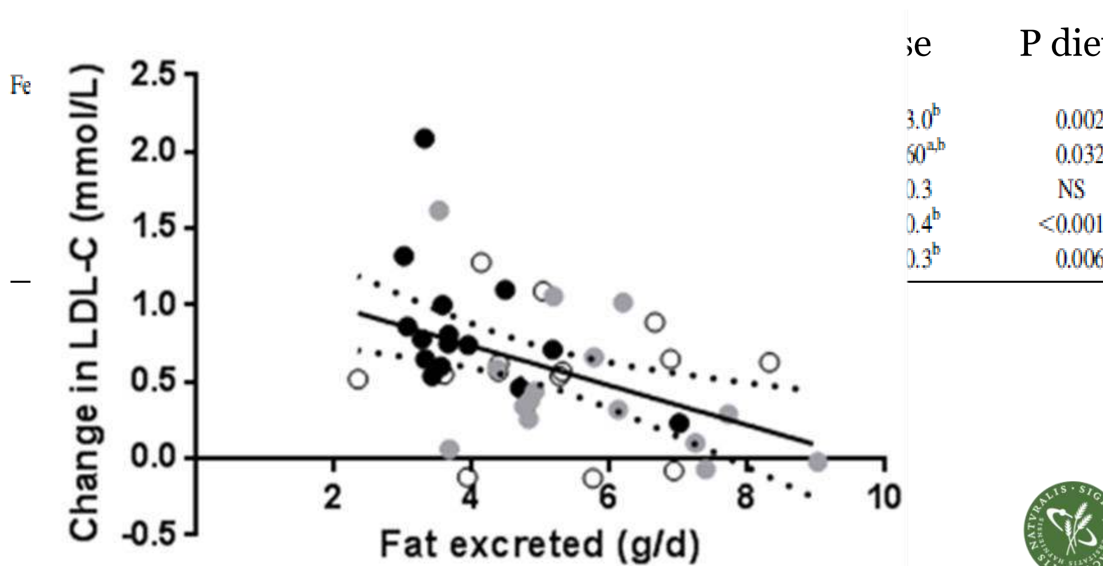
Mozaffarian & Wu, Circulation Res 2018

Calcium in cheese and lipid metabolism

Effect of dairy calcium from cheese and milk on fecal fat excretion, blood lipids, and appetite in young men[1–3]

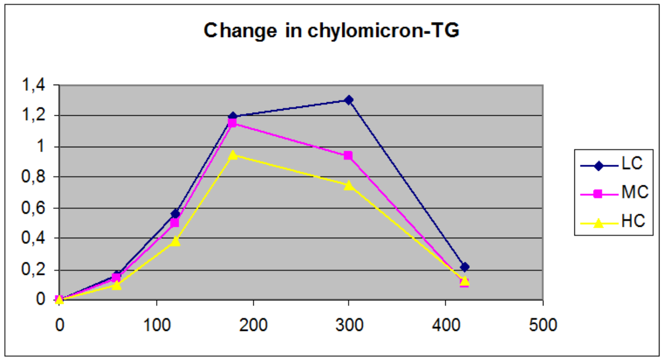
Karina V Soerensen, Tanja K Thorning, Arne Astrup, Mette Kristensen, and Janne K Lorenzen





Suggested mechanisms

- Reduction in fat digestibility/absorption by calcium

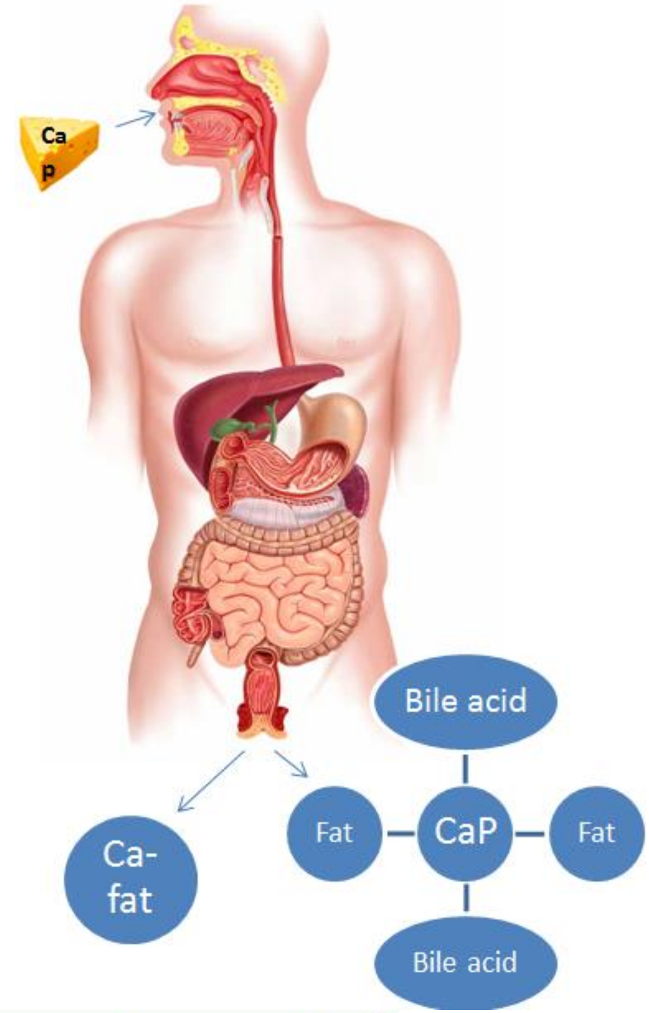


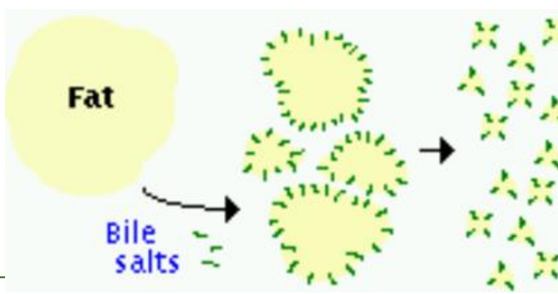
Lorenzen JK, Astrup A. Am. J. Clin. Nutr. (2007)

- Precipitation of calcium and fatty acids in insoluble fatty acid soaps

- Precipitation of calcium and phosphate in amorphous calcium phosphate

- Possibly also increased fecal excretion of bile acids





Metabolomics investigation to shed light on cheese as a possible brick in the French paradox puzzle

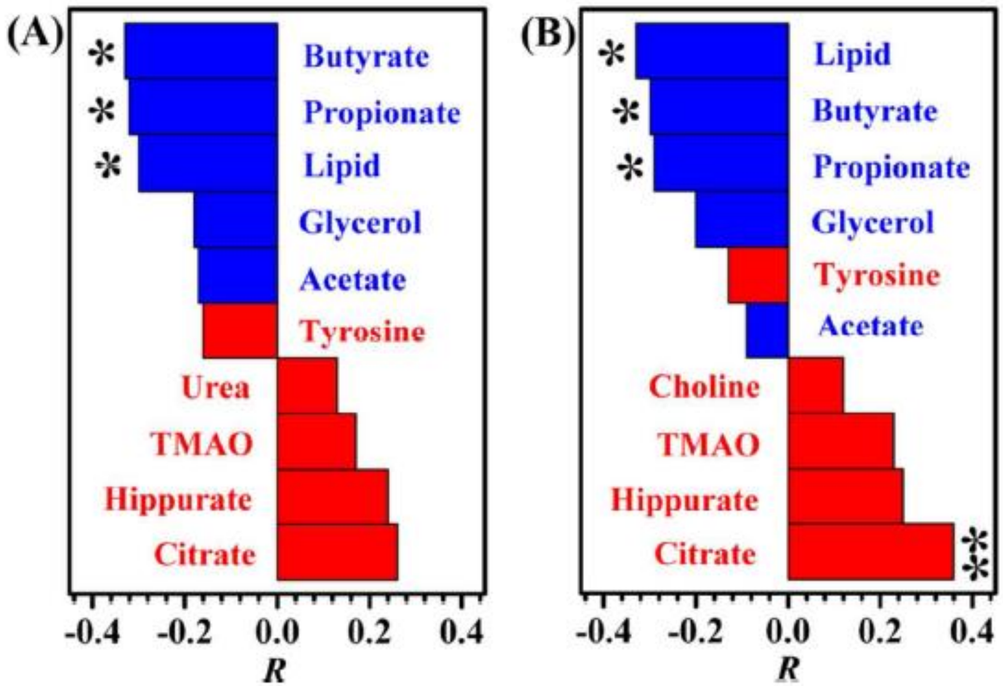


Figure 6. Top 10 metabolites correlated with the diet-induced increases in (A) total and (B) LDL cholesterol based on Pearson correlation coefficients. Red and blue bar represents urinary and fecal metabolites, respectively. *, $P < 0.05$; **, $P < 0.01$.

Effect of vegetarian and vegan diet on whole body BMD

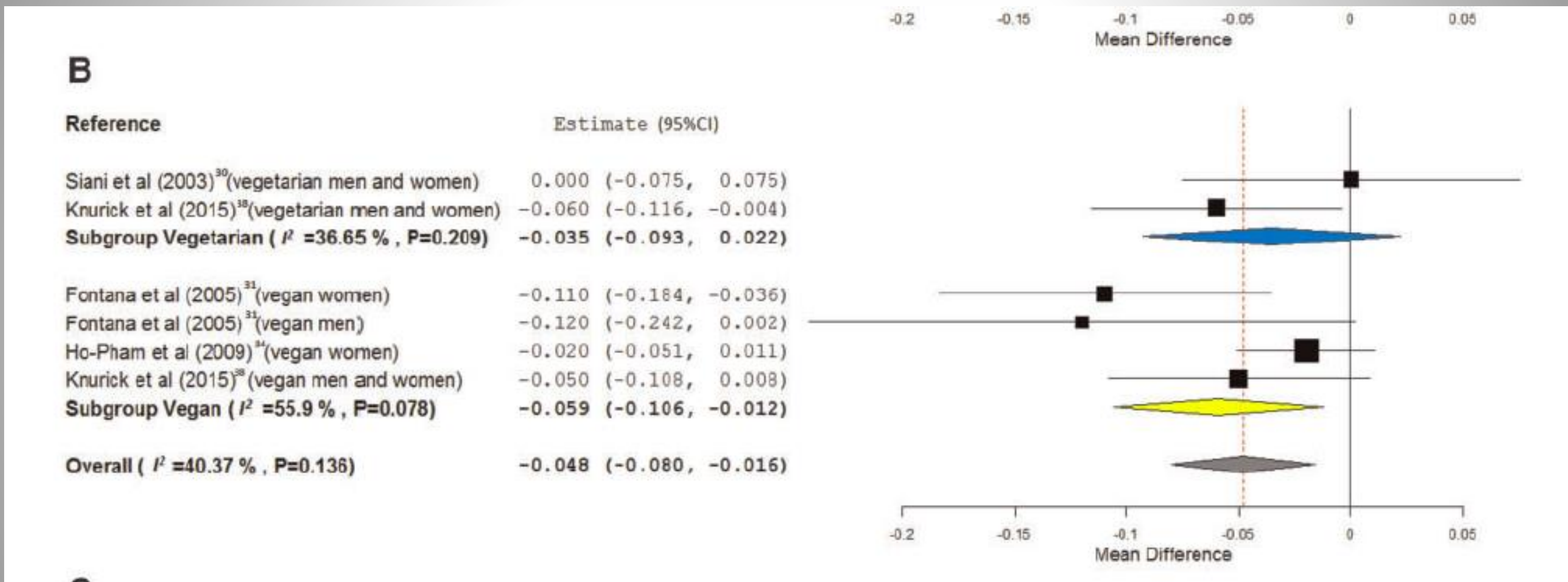
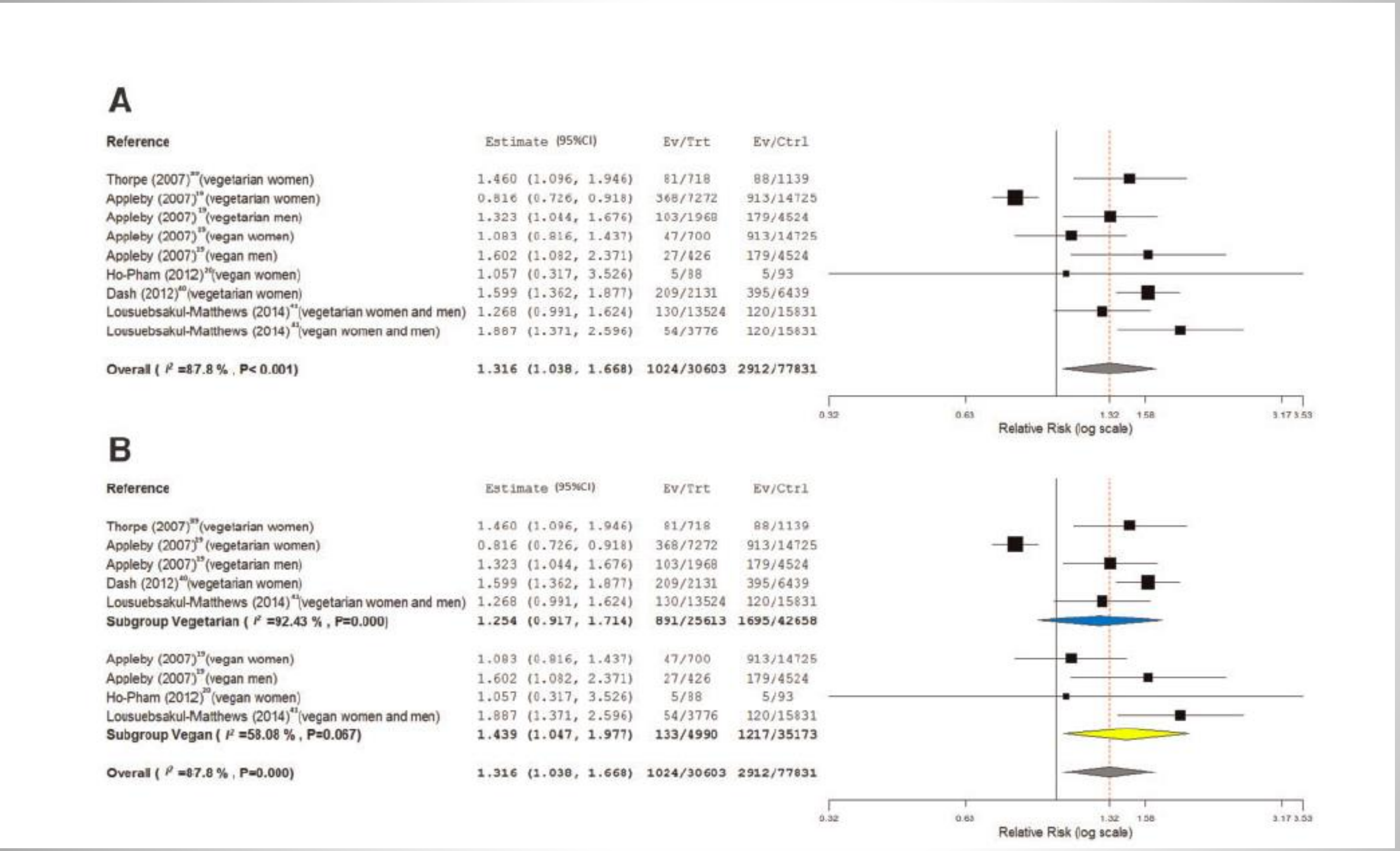


Figure 4 **Random-effects meta-analysis of the effects of vegetarian and vegan diets on bone mineral density (BMD) on the whole body (WB).** (a) BMD differences between vegetarians/vegans and omnivores. (b) Subgroup analyses by diet (vegetarians vs vegans). (c)

Effect of vegetarian and vegan diet on fractures

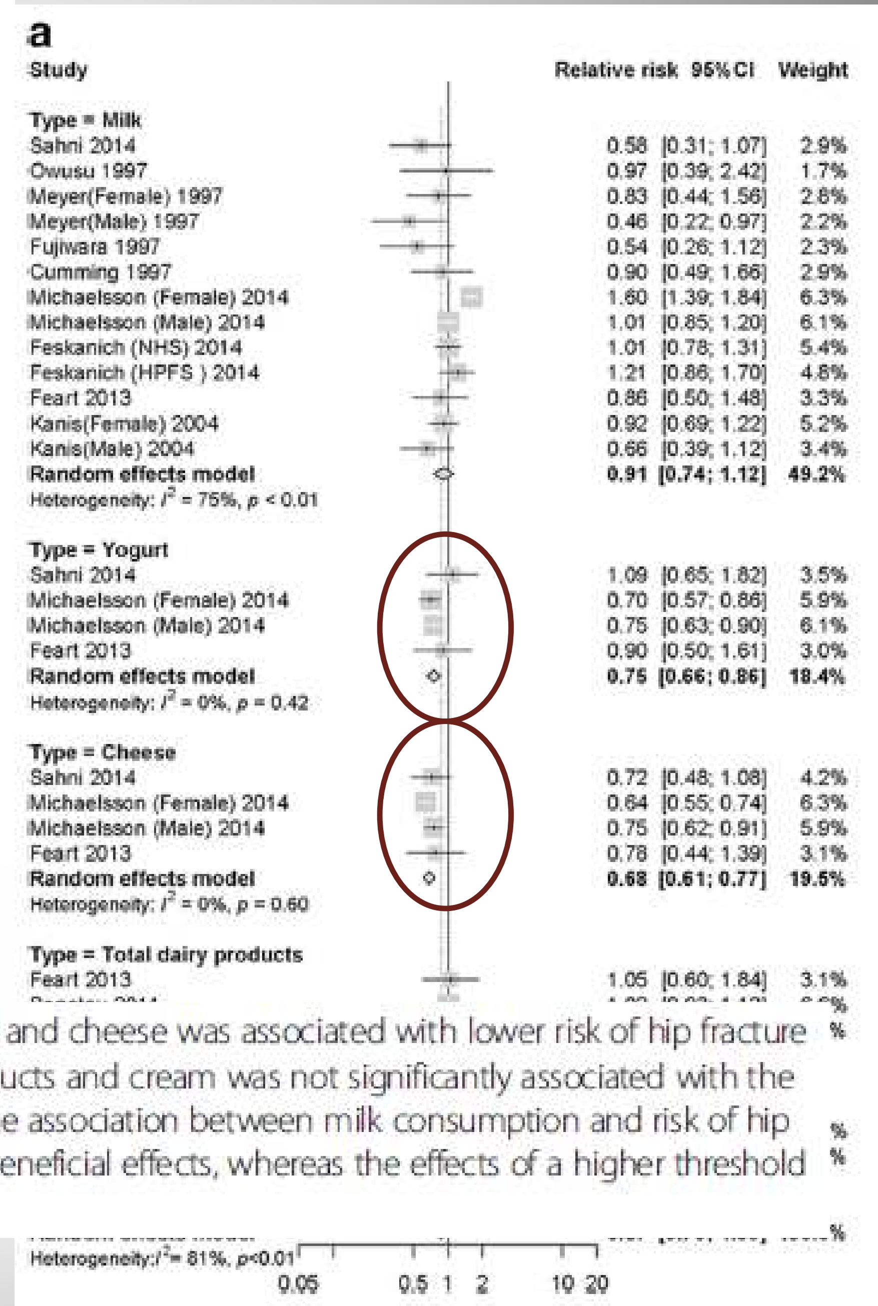


Random effects meta-analysis of the effects of vegetarian and vegan diets on fracture rates.

Bian *et al. BMC Public Health* (2018) 18:165
DOI 10.1186/s12889-018-5041-5
BMC Public Health
RESEARCH ARTICLE Open Access

Dairy product consumption and risk of hip fracture: a systematic review and meta-analysis

Shanshan Bian[1†], Jingmin Hu[1†], Kai Zhang[1], Yunguo Wang[2], Miaohui Yu[3] and Jie Ma[3*]



Conclusions: Our findings indicate that consumption of yogurt and cheese was associated with lower risk of hip fracture in cohort studies. However, the consumption of total dairy products and cream was not significantly associated with the risk of hip fracture. There was insufficient evidence to deduce the association between milk consumption and risk of hip fracture. A lower threshold of 200 g/day milk intake may have beneficial effects, whereas the effects of a higher threshold of milk intake are unclear.

Yogurt matrix

Lipids (bioactive fatty acids)

- 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

Protein (whey and casein)

- 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)

Adapted from Fernandez et al. *Adv Nutr* 2017 (In press)

Marco et al. *Current Opinion in Biotechnology* 2017, 44:94–102

Vitamins and minerals (calcium and vitamin D)

- 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

Fermented milk (lactic acid bacteria)

- **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

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 dairy, particularly yogurt and cheese should be recommended for all to prevent and manage type 2 diabetes and cardiovascular disease.

"People don't want to hear the truth because they don't want their illusions destroyed."

Friedrich Nietzsche

Back-up slides

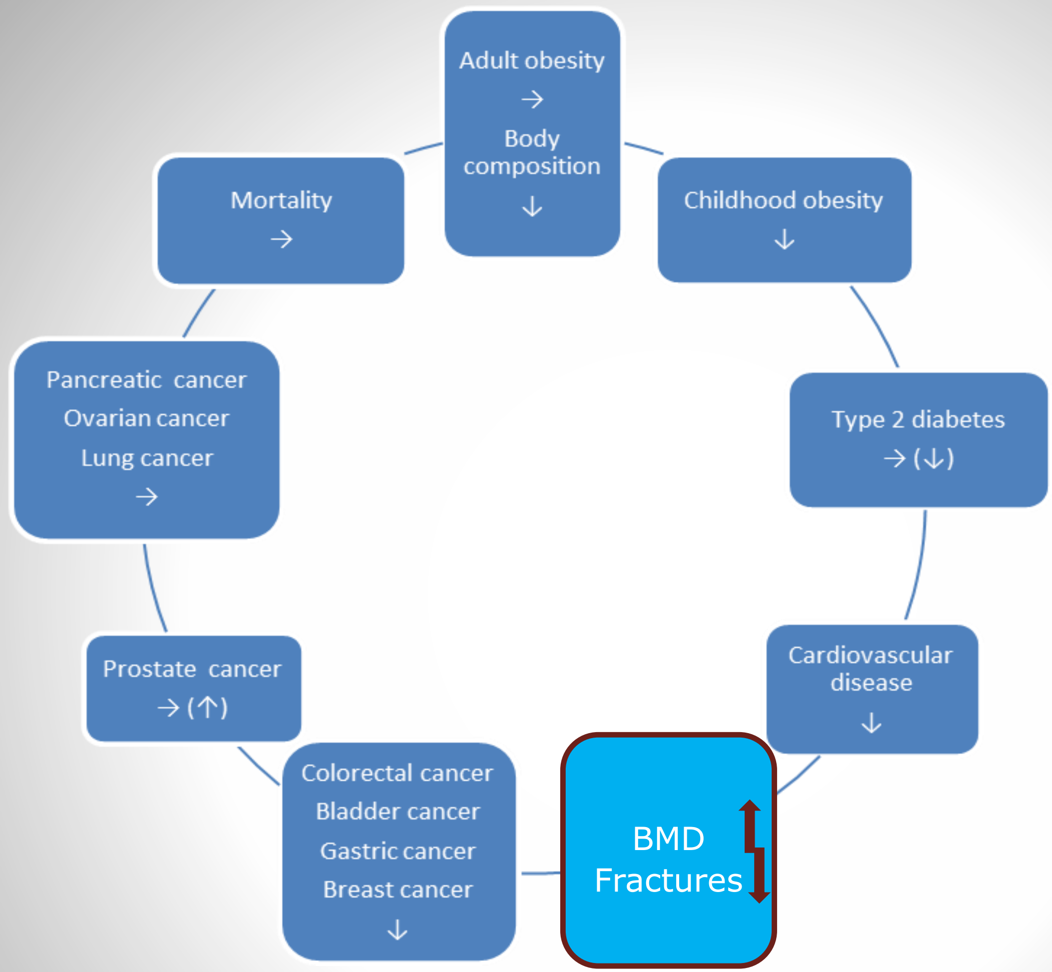


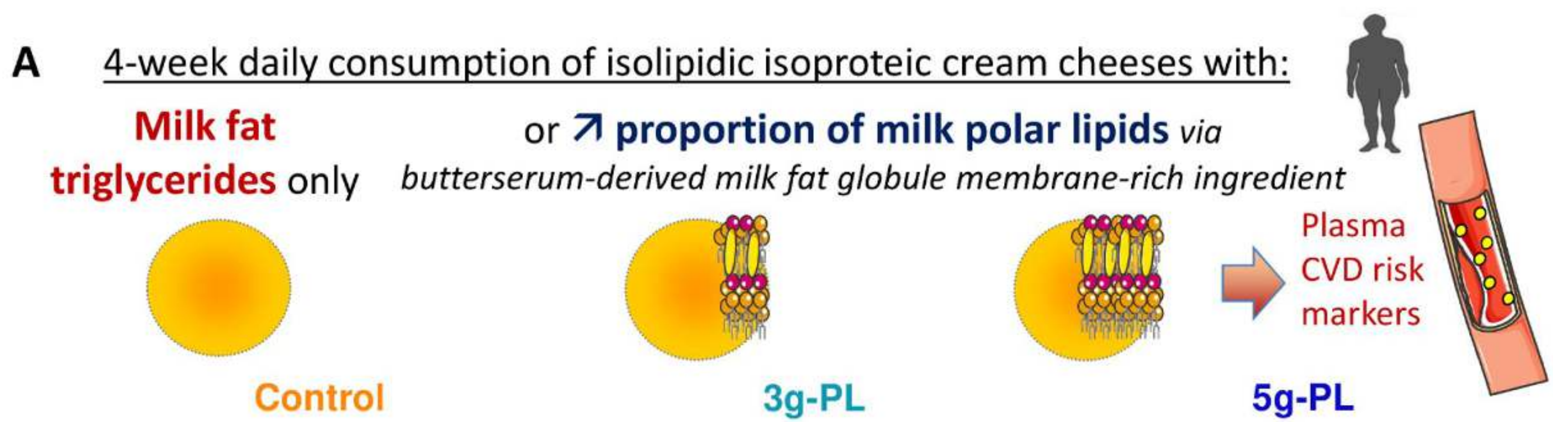
Figure 1. Overall effect/association between dairy (**cheese and yogurt**) intake and health outcomes. ↓favorable effect/association; ↑adverse effect/association; → no effect/association.

Nutrition

ORIGINAL ARTICLE

Milk polar lipids reduce lipid cardiovascular risk factors in overweight postmenopausal women: towards a gut sphingomyelin-cholesterol interplay

Cécile Vors,[1,2] Laurie Joumard-Cubizolles,[3] Manon Lecomte,[1] Emmanuel Combe,[1] Lemlih Ouchchane,[4,5] Jocelyne Drai,[1,6] Ketsia Raynal,[7] Florent Joffre,[8] Laure Meiller,[1,2] Mélanie Le Barz,[1] Patrice Gaborit,[7] Aurélie Caille,[9] Monique Sothier,[2] Carla Domingues-Faria,[3] Adeline Blot,[9] Aurélie Wauquier,[10] Emilie Blond,[1,6] Valérie Sauvinet,[1,2] Geneviève Gésan-Guiziou,[11] Jean-Pierre Bodin,[12] Philippe Moulin,[1,13] David Cheillan,[1,14] Hubert Vidal,[1] Béatrice Morio,[1] Eddy Cotte,[15,16] Françoise Morel-Laporte,[9] Martine Laville,[1,2] Annick Bernalier-Donadille,[10] Stéphanie Lambert-Porcheron,[2,17] Corinne Malpuech-Brugère,[3] Marie-Caroline Michalski[1,2]



Vors C, *et al*. *Gut* 2019;**0**:1–15. doi:10.1136/gutjnl-2018-318155

BMJ

The relevance of dairy matrix for bone health

Lead Article

Veganism, vegetarianism, bone mineral density, and fracture risk: a systematic review and meta-analysis

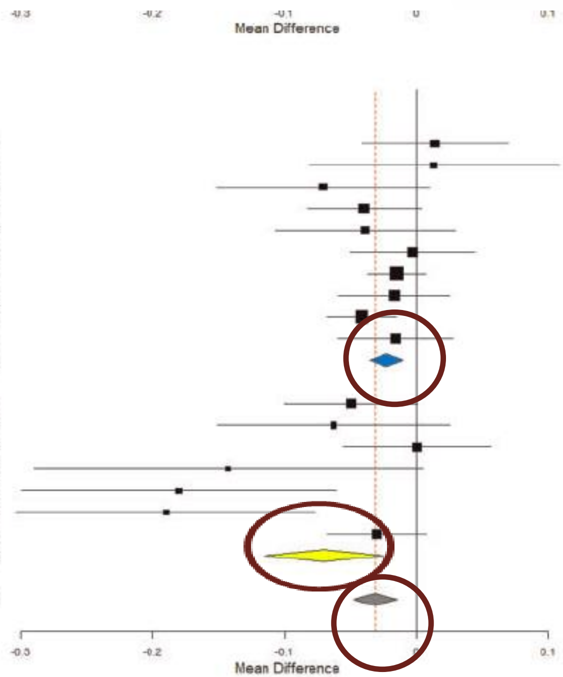
Isabel Iguacel*, María L. Miguel-Berges*, Alejandro Gómez-Bruton, Luis A. Moreno, and Cristina Julián

Context: *The numbers of vegans and vegetarians have increased in the last decades. However, the impact of these diets on bone health is still under debate.* ***Objective:*** *This systematic review and meta-analysis sought to study the impact of vegetarian and vegan diets on bone mineral density (BMD) and fracture risk.* ***Data***

Random-effects meta-analysis of the effects of vegetarian and vegan diets on bone mineral density (BMD) at the lumbar spine (LS).

B

Reference	Estimate (95%CI)
Lloyd et al (1991) (vegetarian women)	0.014 (-0.041, 0.069)
Tesar et al (1992) (vegetarian women)	0.013 (-0.082, 0.108)
Barr et al (1998) (vegetarian women)	-0.071 (-0.152, 0.010)
Lau et al (1998) (vegetarian women)	-0.040 (-0.083, 0.003)
Outila et al (2000) (vegetarian women)	-0.039 (-0.107, 0.029)
Kim et al (2007) (vegetarian women)	-0.003 (-0.050, 0.044)
Wang et al (2008) (vegetarian women)	-0.015 (-0.037, 0.007)
Krivosikova et al (2009) (vegetarian women)	-0.017 (-0.059, 0.025)
Yin-Ming et al (2010) (vegetarian women)	-0.042 (-0.068, -0.016)
Kaur et al (2013) (vegetarian women)	-0.016 (-0.060, 0.028)
Subgroup Vegetarian (I^2 =0 % , P=0.553)	**-0.023 (-0.035, -0.010)**
Chiu et al (1997) (vegan women)	-0.050 (-0.100, 0.000)
Barr et al (1998) (vegan women)	-0.063 (-0.152, 0.026)
Lau et al (1998) (vegan women)	0.000 (-0.056, 0.056)
Outila et al (2000) (vegan women)	-0.143 (-0.290, 0.004)
Fontana et al (2005) (vegan women)	-0.180 (-0.299, -0.061)
Fontana et al (2005) (vegan men)	-0.190 (-0.304, -0.076)
Ho-Pham et al (2009) (vegan women)	-0.030 (-0.068, 0.008)
Subgroup Vegan (I^2 =62.83 % , P=0.013)	**-0.070 (-0.116, -0.025)**
Overall (I^2 =41.04 % , P=0.040)	**-0.032 (-0.048, -0.015)**



Vegetarians and vegans, Only vegetarians, Only vegans, Overall results.

Osteoporos Int
https://doi.org/10.1007/s00198-017-4285-8

CrossMark

ORIGINAL ARTICLE

Milk and other dairy foods and risk of hip fracture in men and women

D. Feskanich[1] · H. E. Meyer[2,3] · T. T. Fung[4] · H. A. Bischoff-Ferrari[5] · W. C. Willett[1,6]

- Each serving of milk per day was associated with a significant 8% lower risk of hip fracture in men and women combined (RR = 0.92, 95% confidence interval (CI) 0.87 to 0.97).
- A suggestive inverse association was found for cheese in women only (RR = 0.91, CI 0.81 to 1.02).
- Total dairy food intake, of which milk contributed about half, was associated with a significant 6% lower risk of hip fracture per daily serving in men and women (RR = 0.94, CI 0.90 to 0.98).
- **Calcium, vitamin D, and protein from non-dairy sources did not modify the association between milk and hip fracture, nor was it explained by contributions of these nutrients from milk**