UNIVERSITY OF COPENHAGEN

Dairy and CVD risk reduction

New insights based on the food matrix concept

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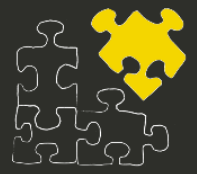
DIETARY GUIDELINES 2015-2020

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

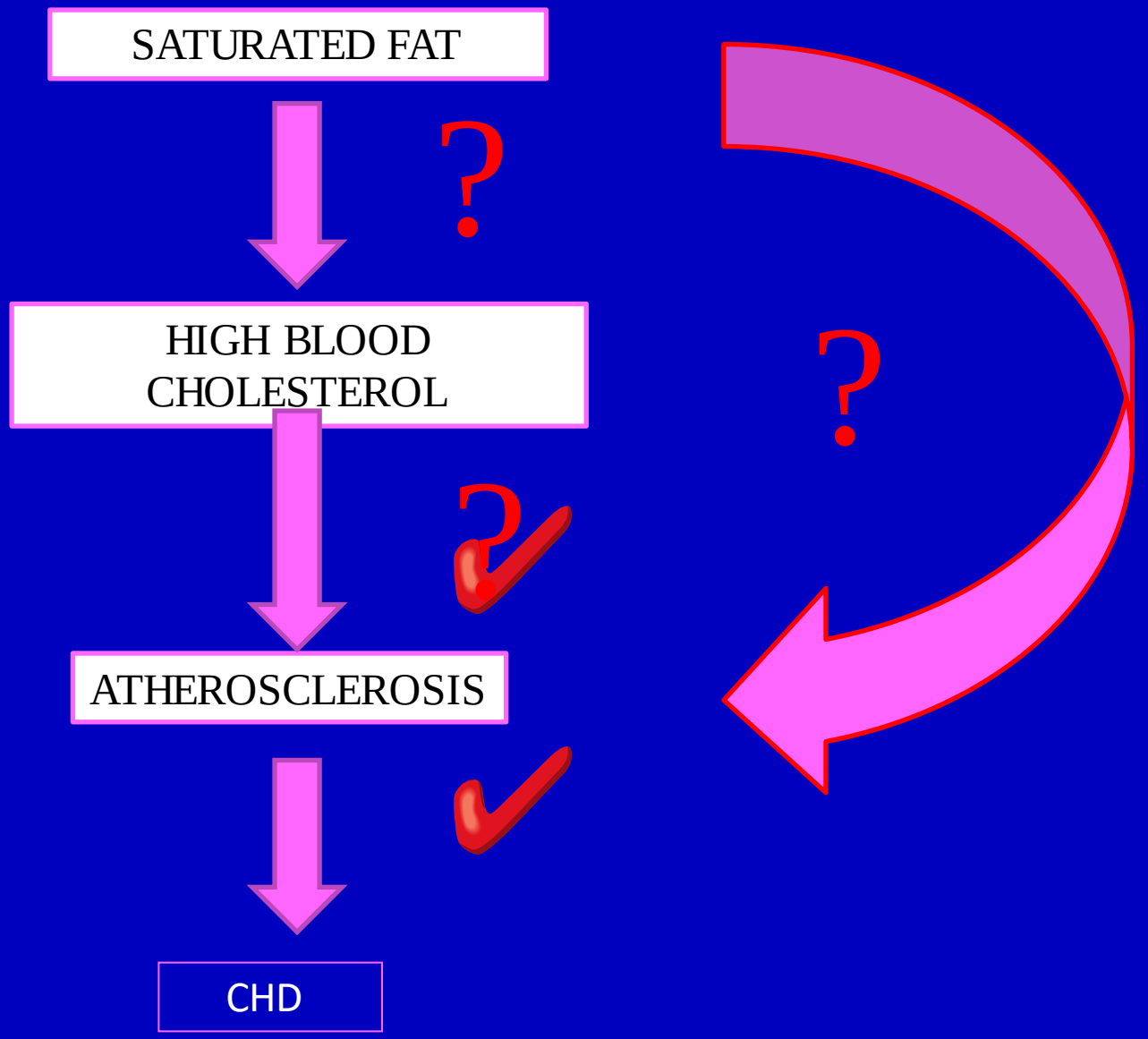
Key Recommendations that are quantitative are provided for several components of the diet that should be limited. These components are of particular public health concern in the United States, and the specified limits can help individuals achieve healthy eating patterns within calorie limits:

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

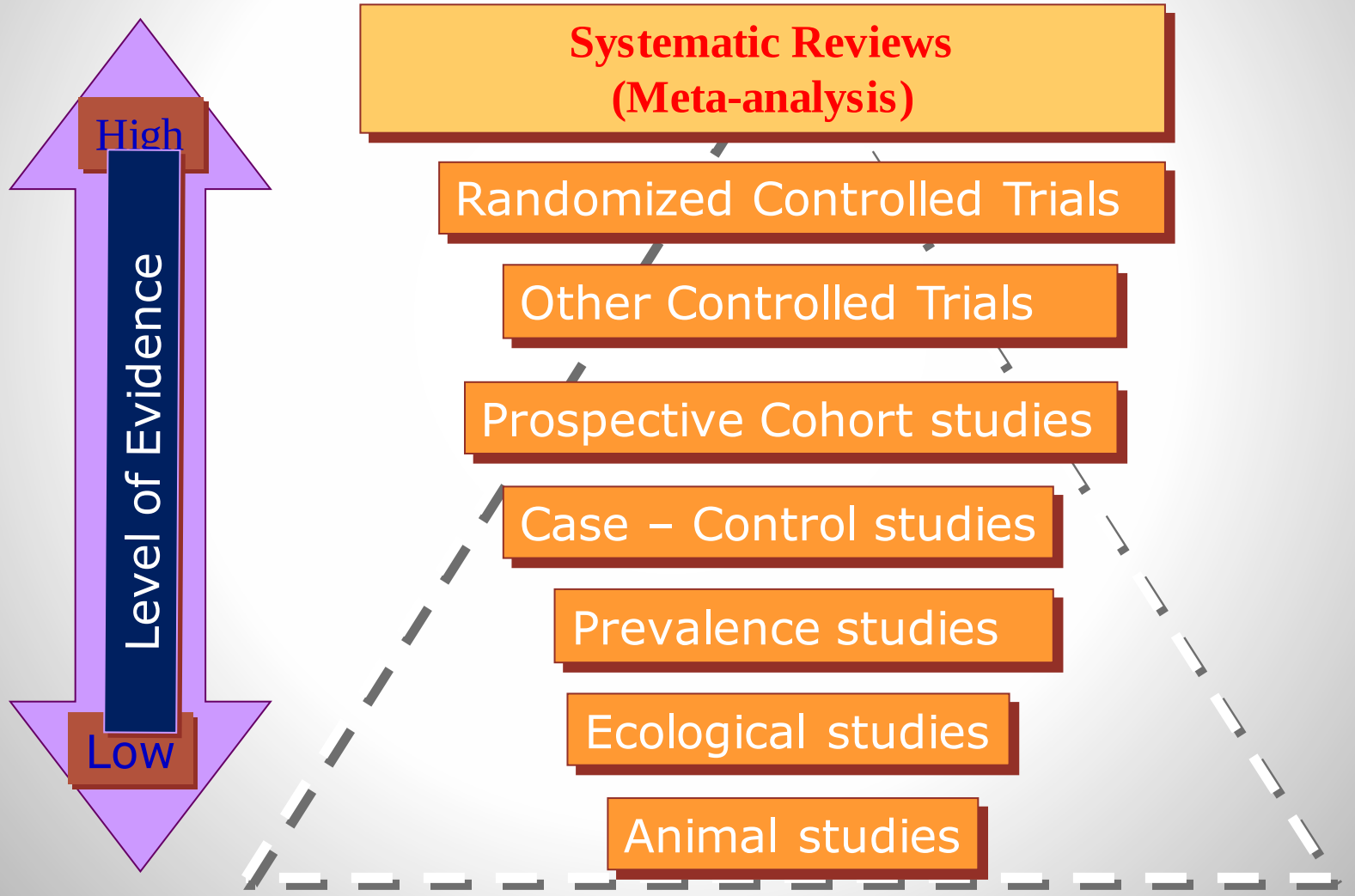
EFSA: As low as possible

- 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]

The lipid hypothesis and CHD

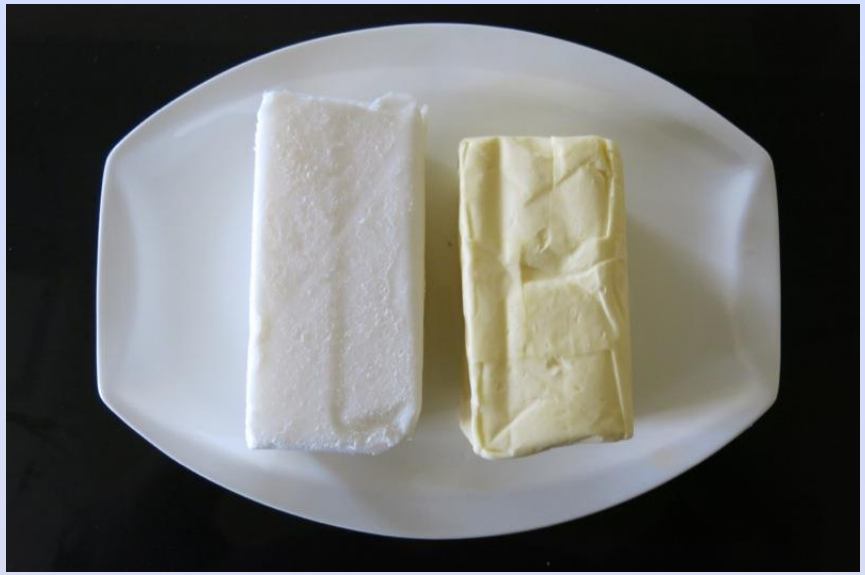


Hierarchy in Scientific Evidence



Saturated fat intake and CVD risk

-the most recent evidence



The WHO evidence: Cochrane analysis by Hooper et al 2020 reviewed RCTs with a minimum of 24 months duration. The review included 15 studies involving approximately 59,000 people and was focused on the impact of saturated fat reduction dying, heart disease and stroke.

There were eight main end-points. Seven of these were non-significant i.e. they found nothing. Again, this is never press-released; it should be the headline.

1) There was no significant effect from reducing saturated fat on total mortality.
2) There was no significant effect from reducing saturated fat on CVD mortality.
3) There was no significant effect from reducing saturated fat on CHD mortality.
4) There was no significant effect from reducing saturated fat on fatal heart attacks.
5) There was no significant effect from reducing saturated fat on non-fatal heart attacks.
6) There was no significant effect from reducing saturated fat on CHD events.
7) There was no significant effect from reducing saturated fat on strokes.

The one significant finding was for CVD events: the risk ratio (RR) for CVD events from meta-analysis was 0.79 (95% CI 0.66 to 0.93). A sensitivity analysis for RCTs that did actually reduce saturated fat – excluding studies that aimed to reduce saturated fat but didn't – showed that the effect on CVD events was no longer significant.

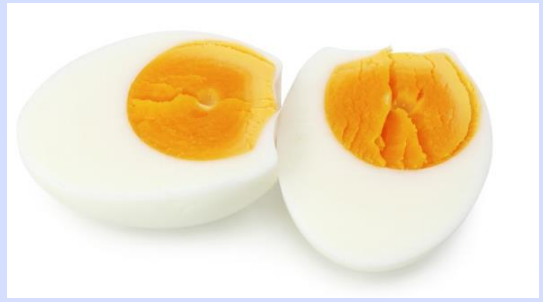
BMJ 2019;366:l4137 doi: 10.1136/bmj.l4137 (Published 3 July 2019)

Questions ?

- Justification to treat Saturated fat as one group ?

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)

thebmj

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

ANALYSIS

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]

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THE PRESENT AND FUTURE

JACC STATE-OF-THE-ART REVIEW

Saturated Fats and Health: A Reassessment and Proposal for Food-Based Recommendations

JACC State-of-the-Art Review

Arne Astrup, MD, DMSc,[a] Faidon Magkos, PhD,[a] Dennis M. Bier, MD,[b] J. Thomas Brenna, PhD,[c,d,e] Marcia C. de Oliveira Otto, PhD,[f] James O. Hill, PhD,[g] Janet C. King, PhD,[h] Andrew Mente, PhD,[i] Jose M. Ordovas, PhD,[j] Jeff S. Volek, PhD, RD,[k] Salim Yusuf, DPhil,[i] Ronald M. Krauss, MD[l,m]

ABSTRACT

The recommendation to limit dietary saturated fatty acid (SFA) intake has persisted despite mounting evidence to the

Previous advice: restrict SFA intake to reduce risk of CVD

Current evidence base: health effects of SFAs depend on the interacting effects from naturally occurring food components and from unhealthy compounds introduced by processing

Whole-fat dairy

Unprocessed red meat

Dark chocolate

=

Complex food matrix with high SFA content but also other nutrients and non-nutritive components (e.g. proteins, micronutrients, phospholipids, probiotics)

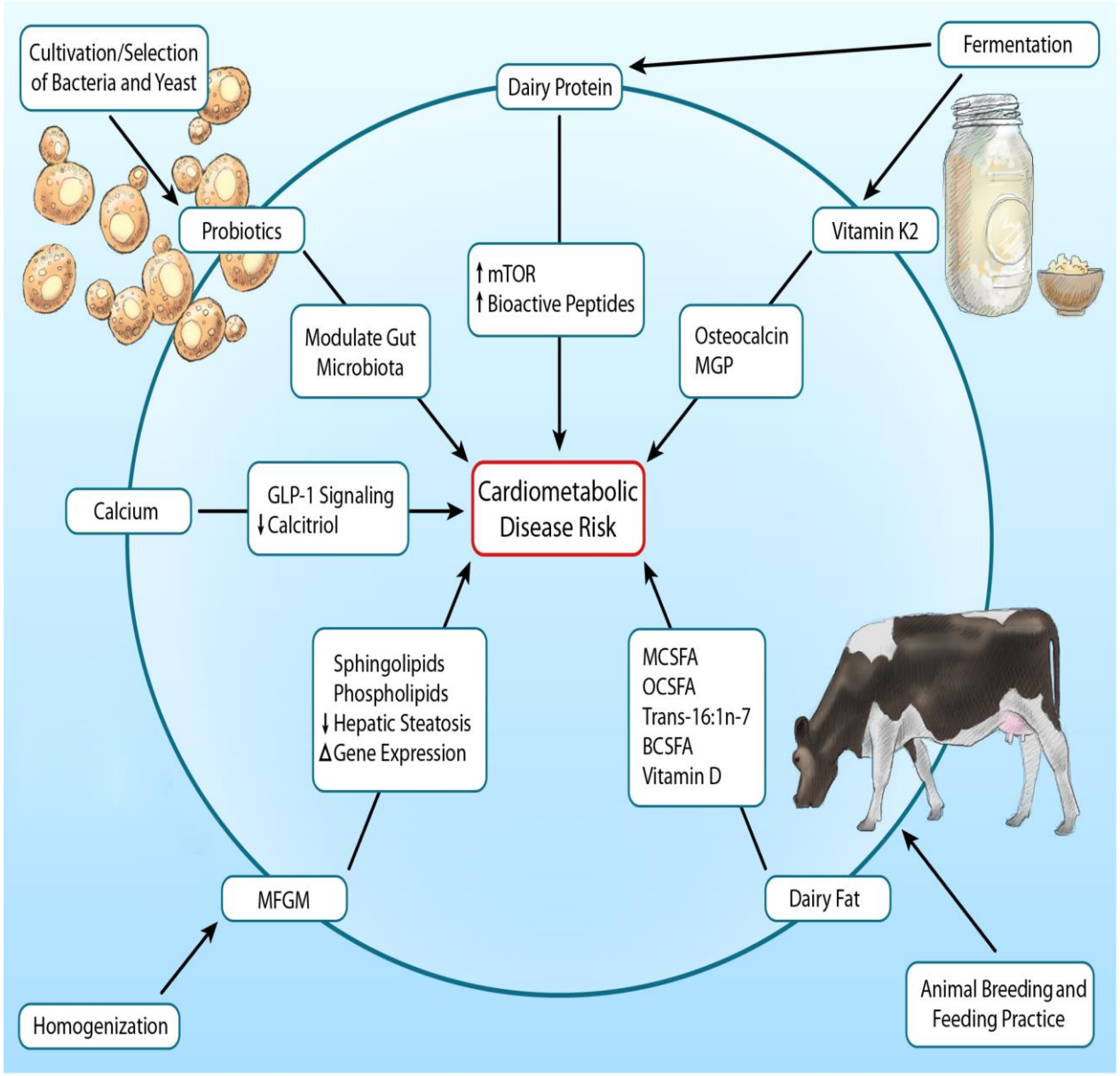
=

No increased CVD or diabetes risk

New recommendations should emphasize food-based strategies that translate for the public into understandable, consistent, and robust recommendations for healthy dietary patterns

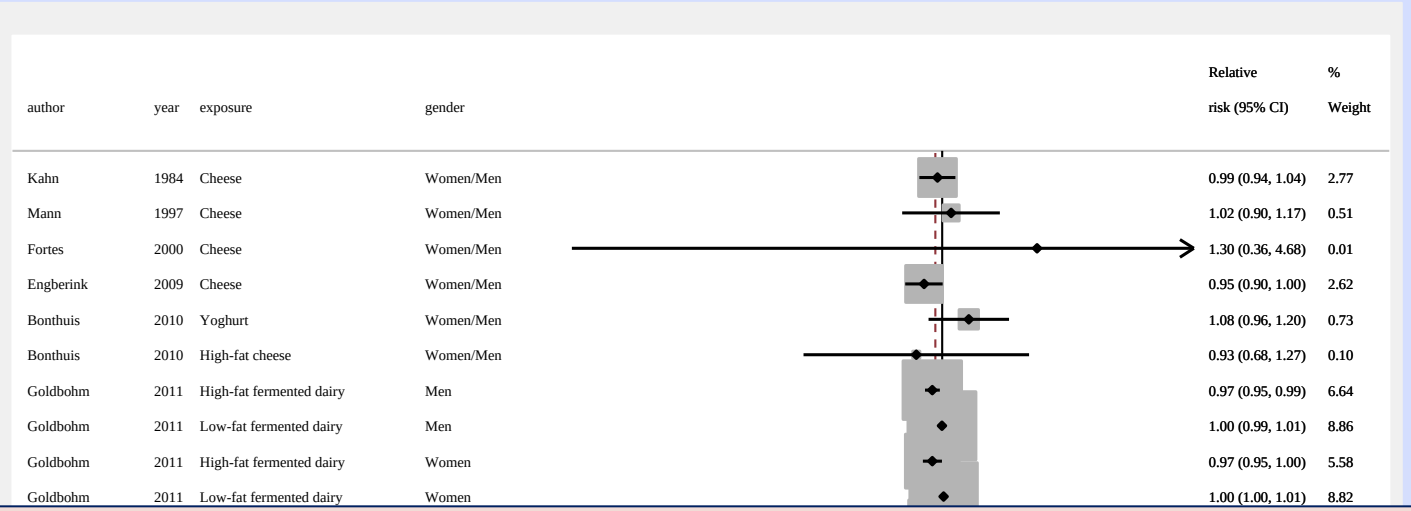
From single nutrients to whole foods: the importance of the food matrix

Dairy & Cardiometabolic Health: Potential Mechanisms



Mozaffarian & Wu, Circulation Res 2018

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 contributes to prevent obesity: Childhood and adult

Meta-analyses of observational studies and RCT's find that dairy in children reduce risk of obesity with beneficial effect on body composition

The NEW ENGLAND JOURNAL of MEDICINE

Milk and Health

June 4, 2020
N Engl J Med 2020; 382:e86
DOI: 10.1056/NEJMc2005220
Metrics

International Journal of Obesity (2012) 1 - 9

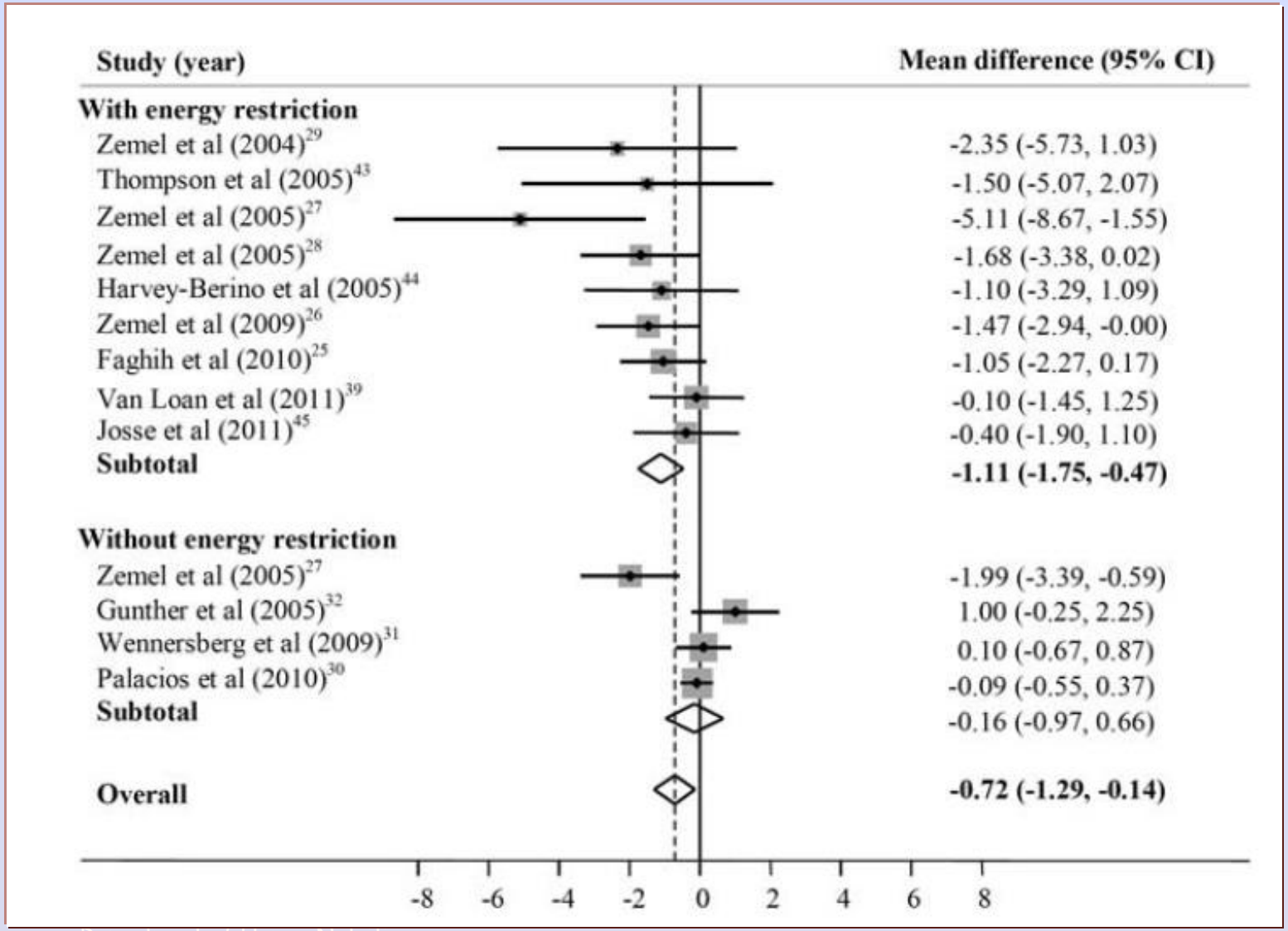
www.nature.com/ijo

ORIGINAL ARTICLE

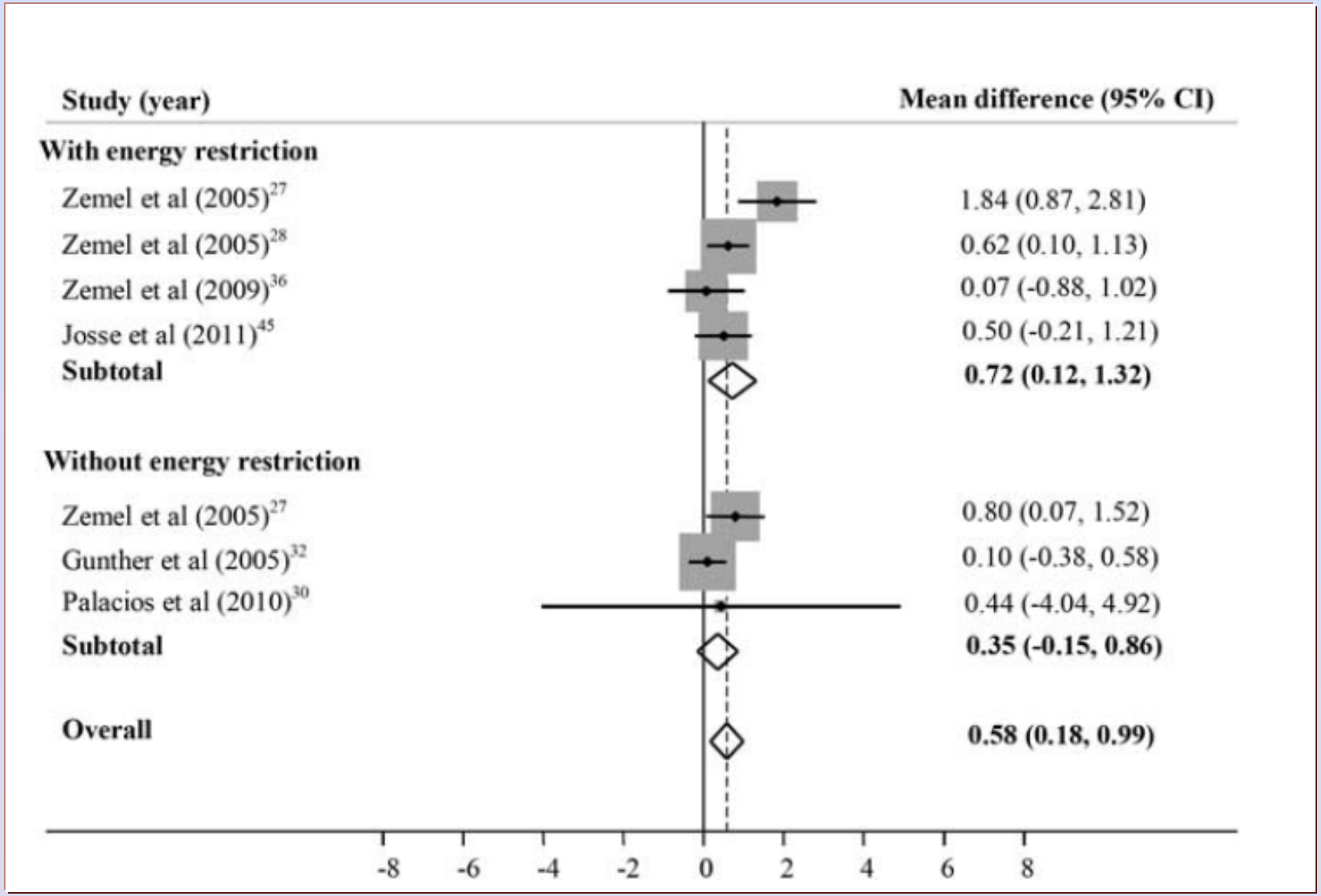
Effect of dairy consumption on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials

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

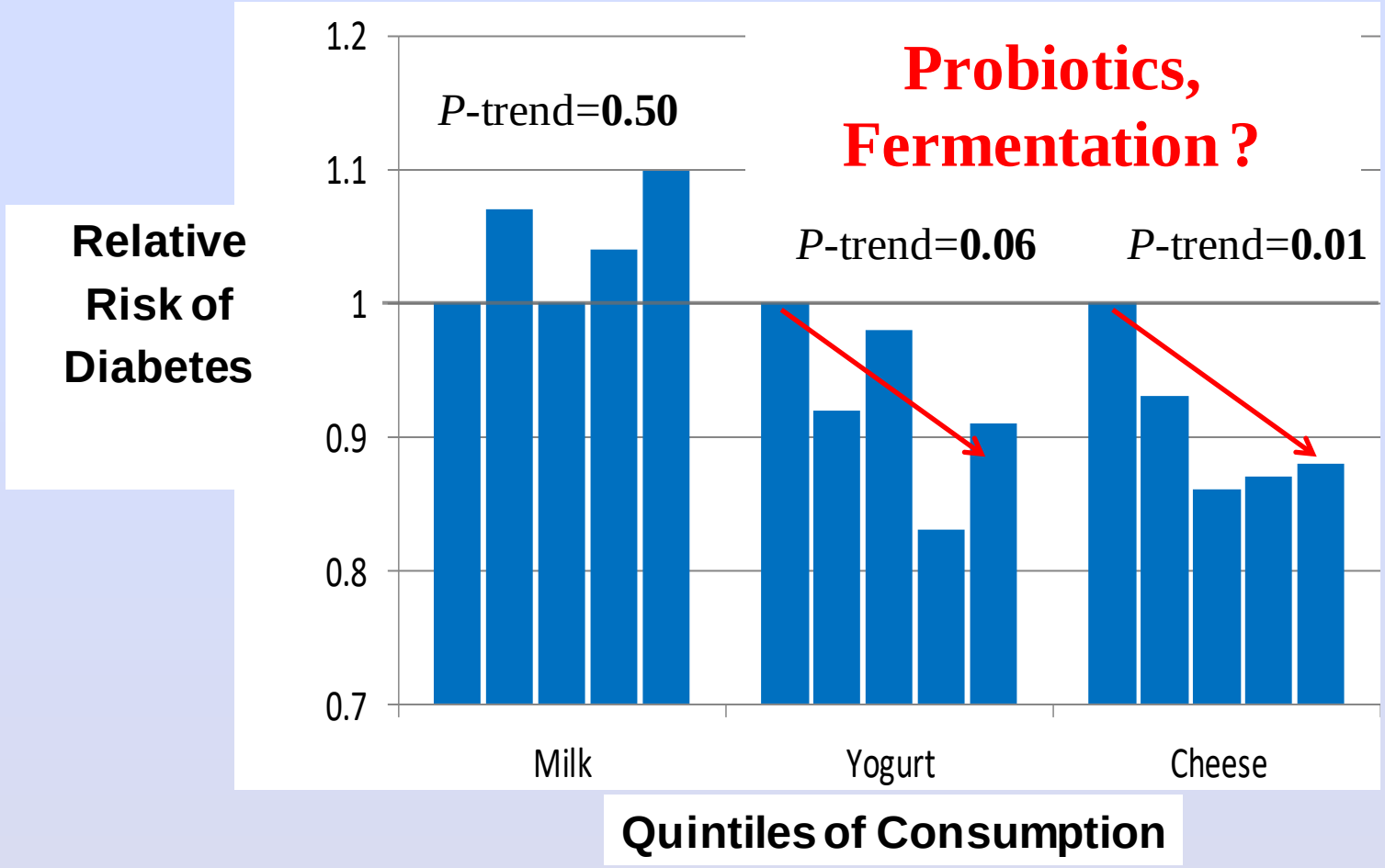


Effect of high vs low dairy on fat free mass



Dairy Foods and Risk of Diabetes

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



Sluijis et al., AJCN 2012

SUPPLEMENT

Effects of Milk and Dairy Product Consumption on Type 2 Diabetes: Overview of Systematic Reviews and Meta-Analyses

Celia Alvarez-Bueno,[1] Ivan Cavero-Redondo,[1] Vicente Martinez-Vizcaino,[1,2] Mercedes Sotos-Prieto,[3,4,5] Jonatan R Ruiz,[6] and Angel Gil[7,8,9,10]

[1]Health and Social Research Center, Universidad de Castilla-La Mancha, Cuenca, Spain; [2]Facultad de Ciencias de la Salud, Universidad Autónoma de Chile, Talca, Chile; [3]Department of Environmental Health, Harvard TH Chan School of Public Health, Boston, MA; [4]Department of Food Sciences and Nutrition, School of Applied Health Sciences and Wellness, [5]Diabetes Institute, Ohio University, Athens, OH; [6]PROFITH (PROmoting FITness and Health through Physical Activity) Research Group, Department of Physical Education and Sport, Faculty of Sport Sciences, [7]Department of Biochemistry and Molecular Biology II, School of Pharmacy, [8]Institute of Nutrition and Food Technology "José Mataix," Biomedical Research Center, University of Granada, Granada, Spain; [9]Instituto de Investigación Biosanitaria ibs GRANADA, Complejo Hospitalario Universitario de Granada, Granada, Spain; and [10]CIBEROBN (CIBER Physiopathology of Obesity and Nutrition CB12/03/30028), Instituto de Salud Carlos III, Madrid, Spain

The participants' ages ranged from 20 to 88 y, and participants were followed up for from 4 to 30 y. Studies included 64,227–566,875 participants and reported 4810–44,474 cases of T2D. Most studies reported an inverse association between T2D incidence and dairy product consumption, especially for *1*) total dairy products (range: 0.86–0.91), *2*) low-fat dairy products (range: 0.81–0.83), *3*) low-fat milk (RR: 0.82), and *4*) yogurt (range: 0.74–0.86). Dose–response analyses showed a decreased T2D risk for *1*) 200–400 g/d of total dairy products (range: 0.93–0.97) and *2*) 200 g/d of low-fat dairy products (range: 0.88–0.91). Total dairy product consumption is associated with a lower risk of T2D, especially for yogurt and low-fat dairy consumption. The association with cheese is moderate. Moreover, dose–response analyses showed that the risk of T2D decreased by each unit increase in consumption of total dairy products and low-fat dairy products. *Adv Nutr* 2019;10:S154–S163.

PLOS | MEDICINE

RESEARCH ARTICLE

Fatty acid biomarkers of dairy fat consumption and incidence of type 2 diabetes: A pooled analysis of prospective cohort studies

Fumiaki Imamura[1]*, Amanda Fretts[2], Matti Marklund[3], Andres V. Ardisson Korat[4], Wei-Sin Yang[5], Maria Lankinen[6], Waqas Qureshi[7], Catherine Helmer[8], Tzu-An Chen[9], Kerry Wong[10], Julie K. Bassett[10], Rachel Murphy[11], Nathan Tintle[12], Chaoyu Ian Yu[13], Ingeborg A. Brouwer[14], Kuo-Liong Chien[5], Alexis C. Frazier-Wood[9], Liana C. del Gobbo[15], Luc Djoussé[16], Johanna M. Geleijnse[17], Graham G. Giles[10,18], Janette de Goede[17], Vilmundur Gudnason[19], William S. Harris[20,21], Allison Hodge[10,18], Frank Hu[4], InterAct Consortium[¶], Albert Koulman[1,22,23,24,25], Markku Laakso[26], Lars Lind[27], Hung-Ju Lin[28], Barbara McKnight[13], Kalina Rajaobelina[8], Ulf Risérus[3], Jennifer G. Robinson[29], Cécilia Samieri[8], David S. Siscovick[30], Sabita S. Soedamah-Muthu[17,31], Nona Sotoodehnia[2], Qi Sun[4], Michael Y. Tsai[32], Matti Uusitupa[6], Lynne E. Wagenknecht[33], Nick J. Wareham[1], Jason HY Wu[34], Renata Micha[35], Nita G. Forouhi[1], Rozenn N. Lemaitre[2], Dariush Mozaffarian[35], Fatty Acids and Outcomes Research Consortium (FORCE)[¶]

PLOS Medicine | https://doi.org/10.1371/journal.pmed.1002670 October 10, 2018

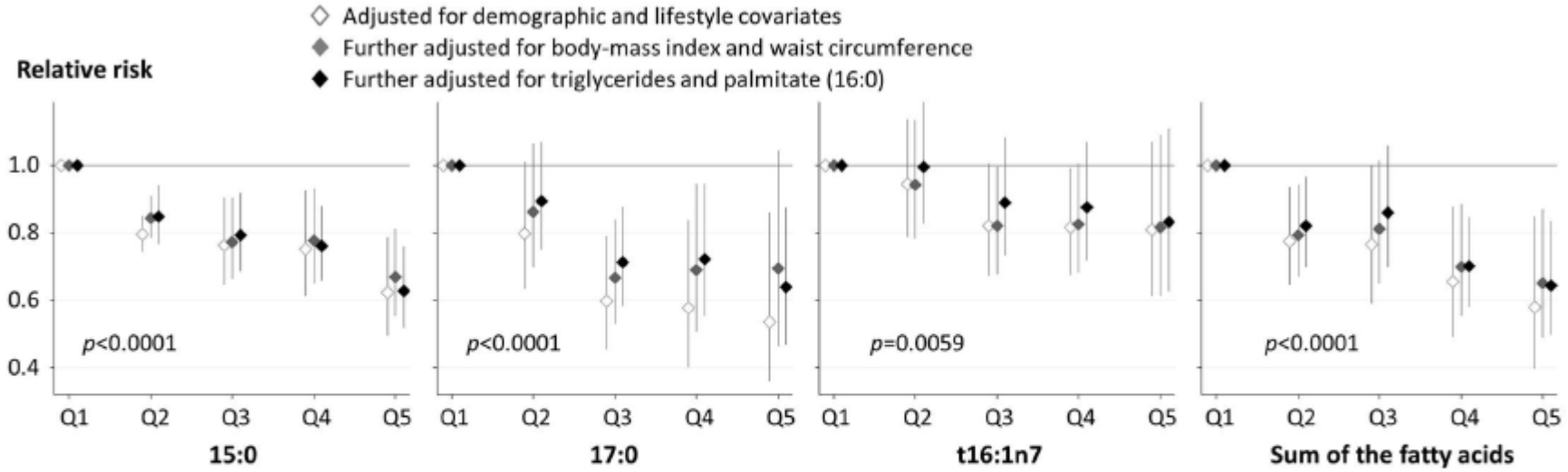


Fig 3. Prospective associations of quintile categories of fatty acid biomarkers for dairy fat consumption with the risk of developing T2D. Cohort-specific associations by quintiles were assessed in multivariable models in each cohort and pooled with inverse-variance–weighted meta-analysis. Cohort-specific multivariable adjustment was made. In the first model (open diamond), estimates were adjusted for sex, age, smoking status, alcohol consumption, socioeconomic status, physical activity, dyslipidaemia, hypertension, and menopausal status (only for women). Then, the estimates were further adjusted for BMI (grey diamond) and further adjusted for triglycerides and palmitic acid (16:0) as markers of de novo lipogenesis (black diamond). To compute *p*-values for a trend across quintiles, each fatty acid was evaluated as an ordinal variable in the most adjusted model. T2D, type 2 diabetes mellitus.

Questions ?

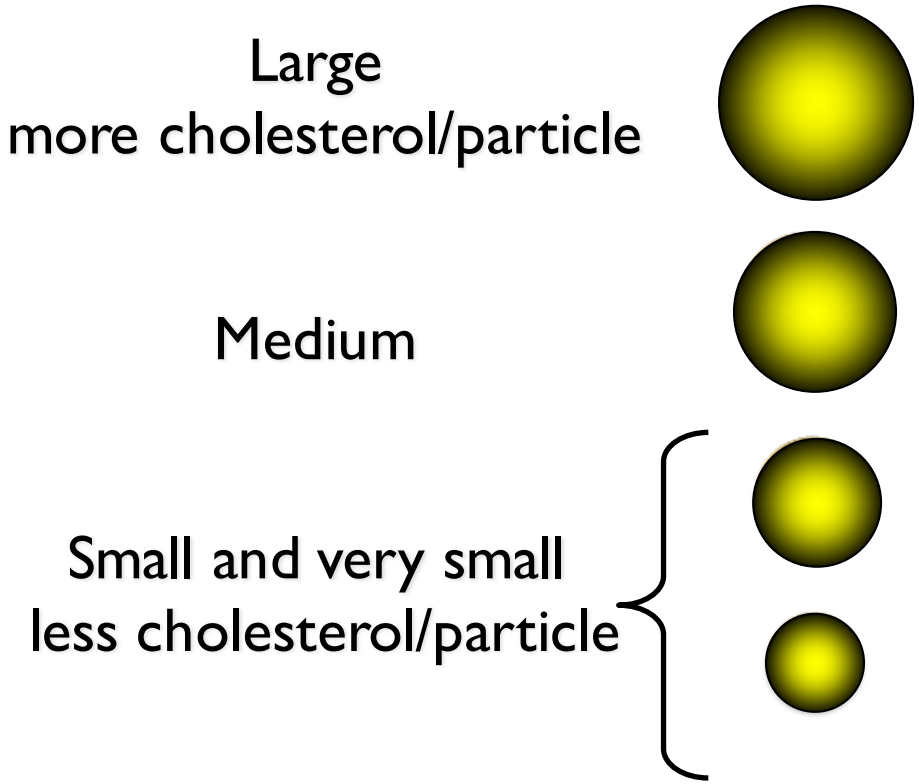
- Justification to treat SFA as one group ?
  - No, the different SFA have very different biological effects on cardio-metabolic health
  - SFA are rarely consumed in a pure form, and the food matrix completely alters the health effects (dark chocolate, cheese, yoghurt)
  - There is good evidence to show that a number of foods with high content of SFA reduces risk of obesity, type 2 diabetes, and CVD.

Pure fats for cooking ?

Questions ?

- Justification to treat Saturated fat as one group ?
- Does Saturated fat increase CVD ?
- Does Saturated fat increase LDL-cholesterol ?

LDL is comprised of subclasses of particles with differing cholesterol content and atherogenic properties

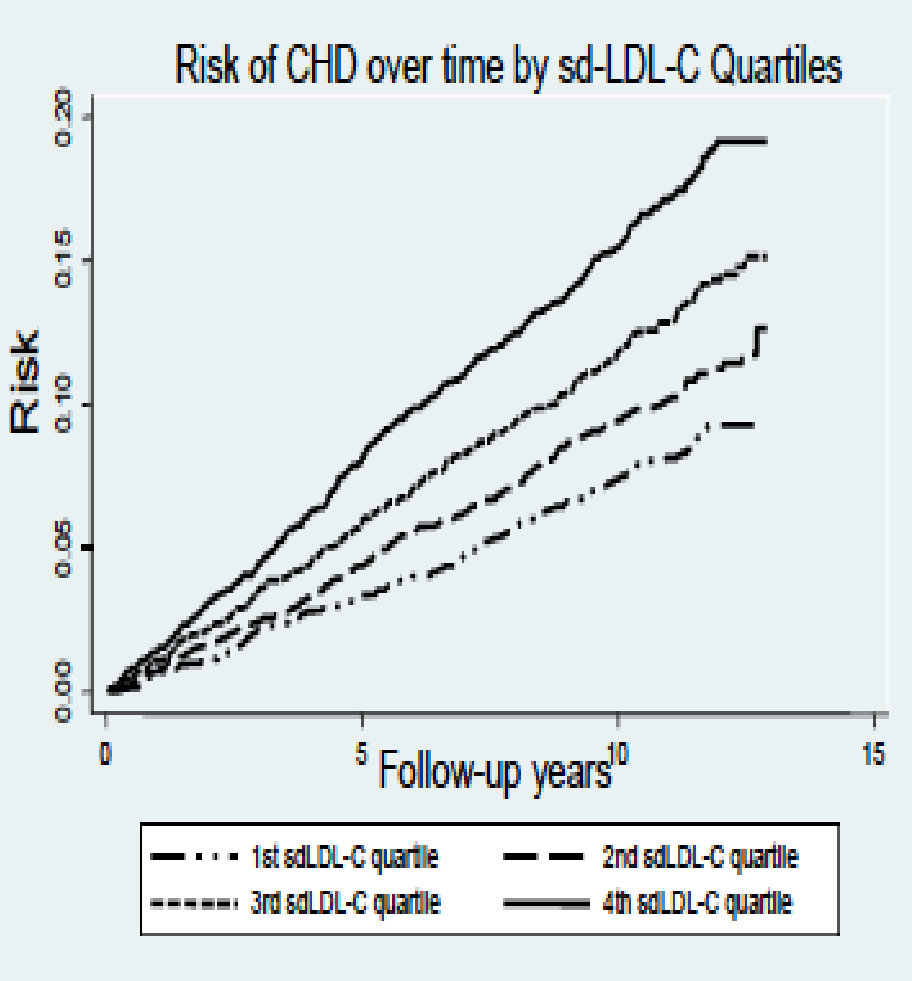


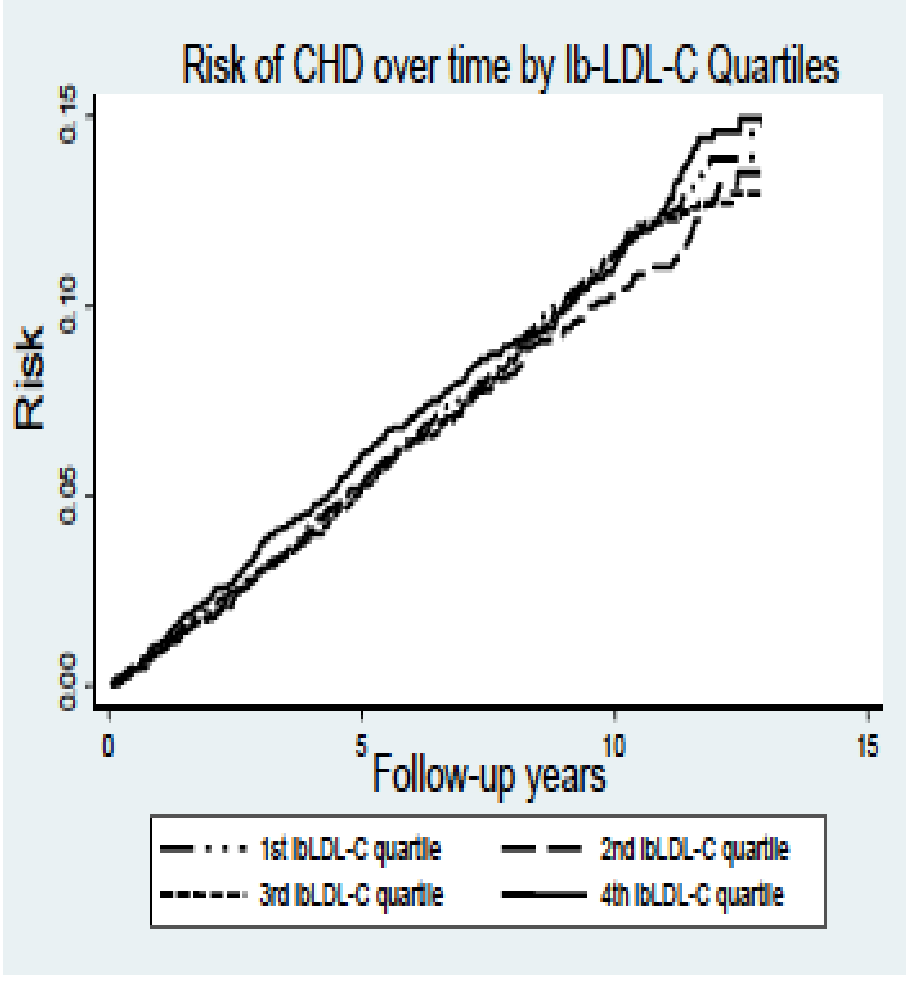
Reduced plasma clearance
Greater entry into artery
Greater retention
Faster oxidation

Distribution of subclasses varies widely among individuals and is independent of total LDL cholesterol

Berneis and Krauss, JLR 43:1155, 2002

Small, dense (sd)-LDL but not large, buoyant (lb)-LDL predicts CHD in ARIC (n=11,419; ~11 yr f/u))

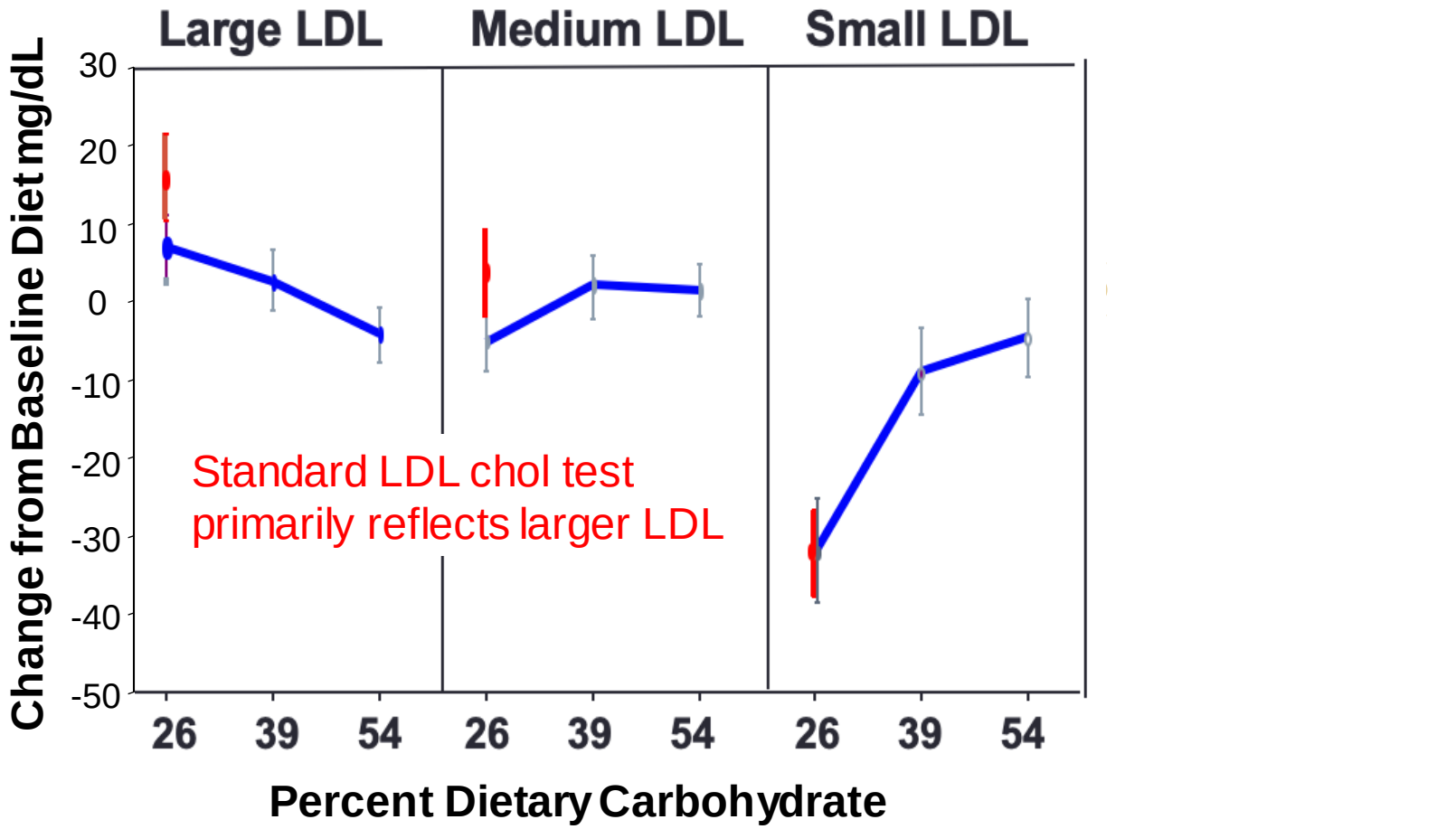




Effects independent of total LDL-C

Hoogeveen et al., ATVB 34:1069, 2014

Divergent effects of dietary carbohydrates and saturated fat on LDL subclasses: higher carbohydrate (blue) raises only small LDL; higher saturated fat (red) raises larger LDL



Krauss et al. AJCN 83:1025, 2006

Questions ?

- Does Saturated fat increase CVD ?
  - No
- Does Saturated fat increase LDL-cholesterol ?
  - SFA changes LDL-cholesterol particles to a less atherogenic distribution

Questions ?

- Justification to treat SFA as one group ?
  - No, the different SFA have very different biological effects on cardio-metabolic health
  - SFA are rarely consumed in a pure form, and the food matrix completely alters the health effects (dark chocolate, cheese, yoghurt)
  - There is good evidence to show that a number of foods with high content of SFA reduces risk of obesity, type 2 diabetes, and CVD.
- Does Saturated fat increase CVD ?
  - No

- Does Saturated fat increase LDL-cholesterol ?
  - SFA changes LDL-cholesterol particles to a less atherogenic distribution
  - Other mechanisms than LDL-cholesterol may also be involved in the dietary effects on CVD risk.

Conclusions

- The totality of evidence i.e. meta-analyses of both observational studies and RCT's cannot find any harmful effects of saturated fat 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.
- The totality of evidence show that "cut down on saturated fat" should be avoided, and recommendations should be food based.

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

Friedrich Nietzsche

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)