Mjölk och hälsa – hur hänger det ihop?

Karl Michaëlsson

Institutionen för kirurgiska vetenskaper

Uppsala universitet

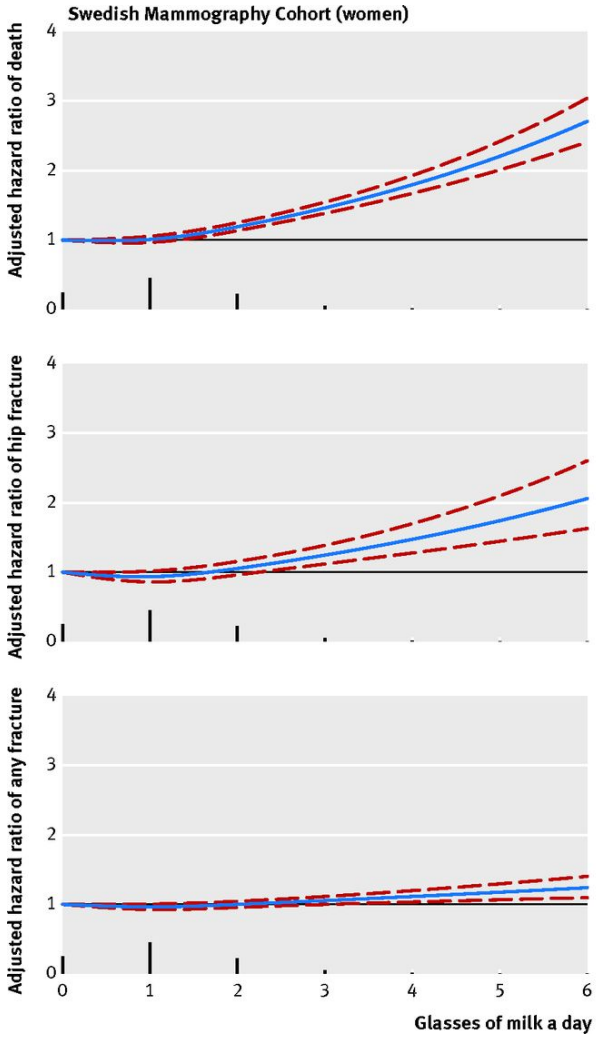
BMJ 2014;349:g6015 doi: 10.1136/bmj.g6015 (Published 27 October 2014)

RESEARCH

Milk intake and risk of mortality and fractures in women and men: cohort studies

Karl Michaëlsson *professor*[1], Alicja Wolk *professor*[2], Sophie Langenskiöld *senior lecturer*[3], Samar Basu *professor*[3], Eva Warensjö Lemming *researcher*[1 4], Håkan Melhus *professor*[5], Liisa Byberg *associate professor*[1]

Sex specific multivariable adjusted spline curves of relation between milk intake with time to death from all causes, hip fracture, and any type of fracture.



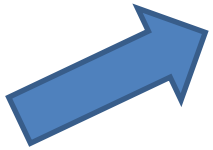
Michaëlsson K et al. BMJ 2014;349:bmj.g6015

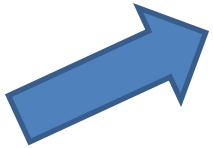
Association with oxidative stress and inflammation markers

SMC-Clinical Women

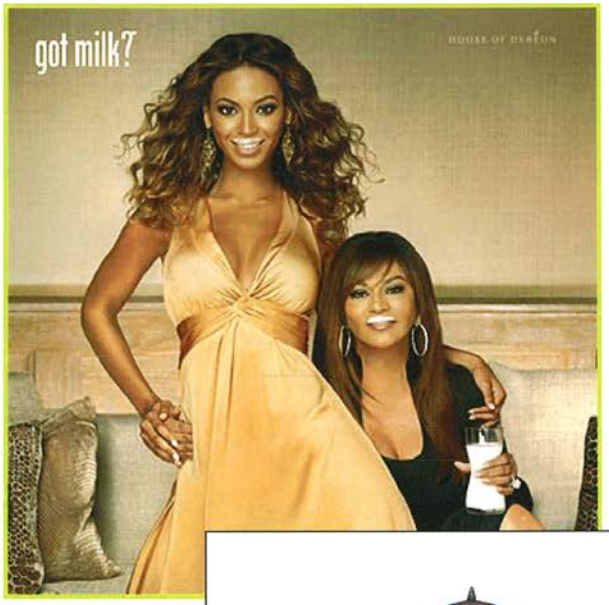
ULSAM – Uppsala Longitudinal Study of Adult Men

Milk

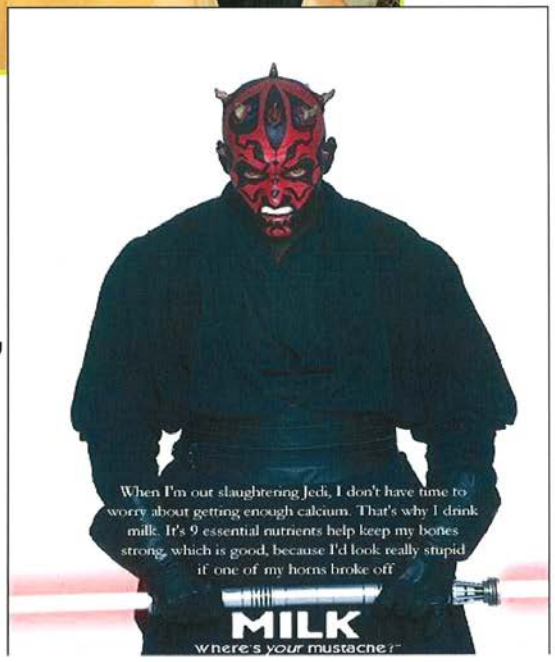
Urin 8-iso-$PGF_{2\alpha}$ 

Serum IL-6 

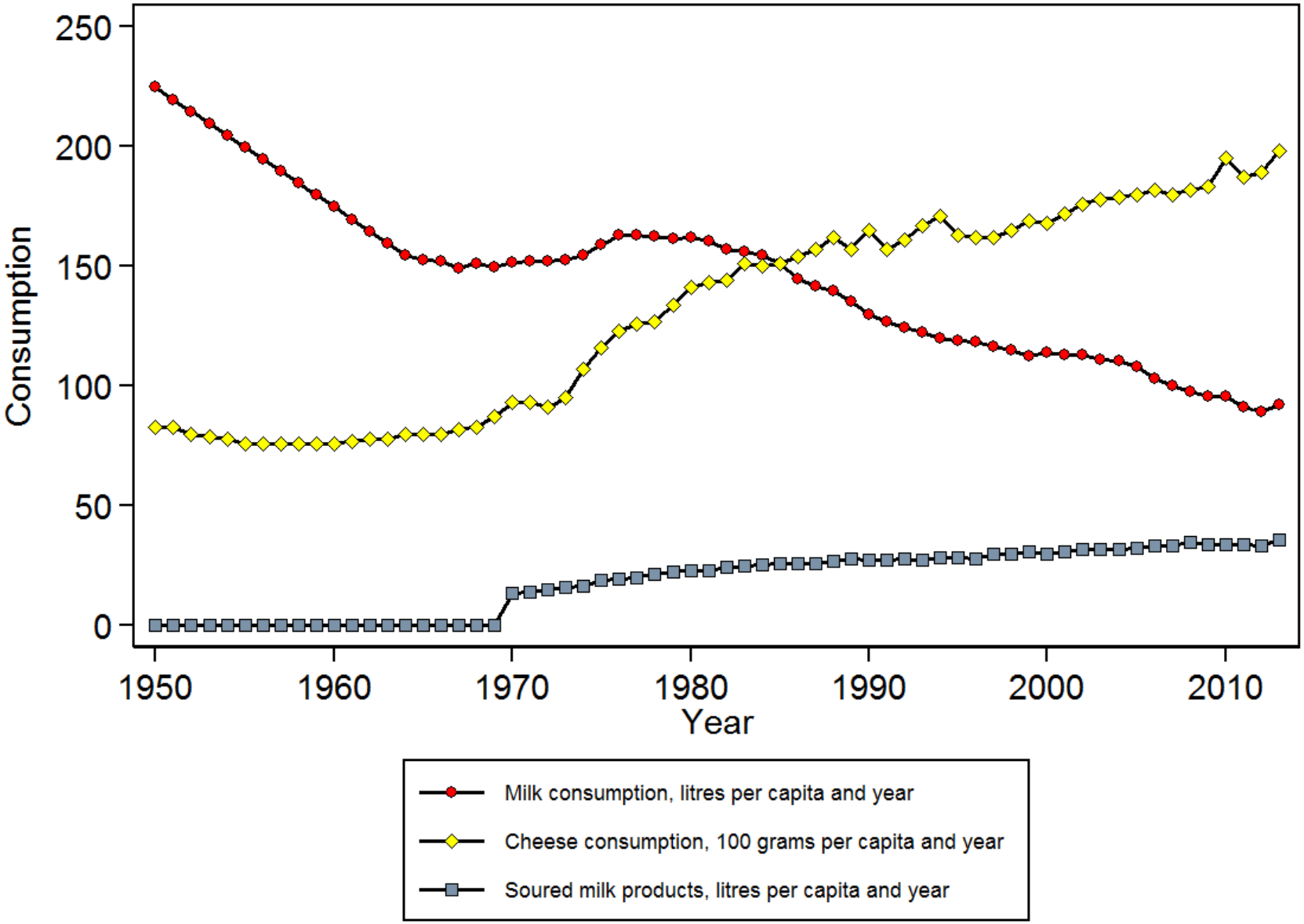

MJÖLK
är hälsa
MJÖLK-BAR
Drick
mjölk!
Ostkaka
35 öre
Ostkaka
35 öre
MJÖLK
Livskraft



”..keep my bones strong”



Dairy consumption in Sweden 1950-2013



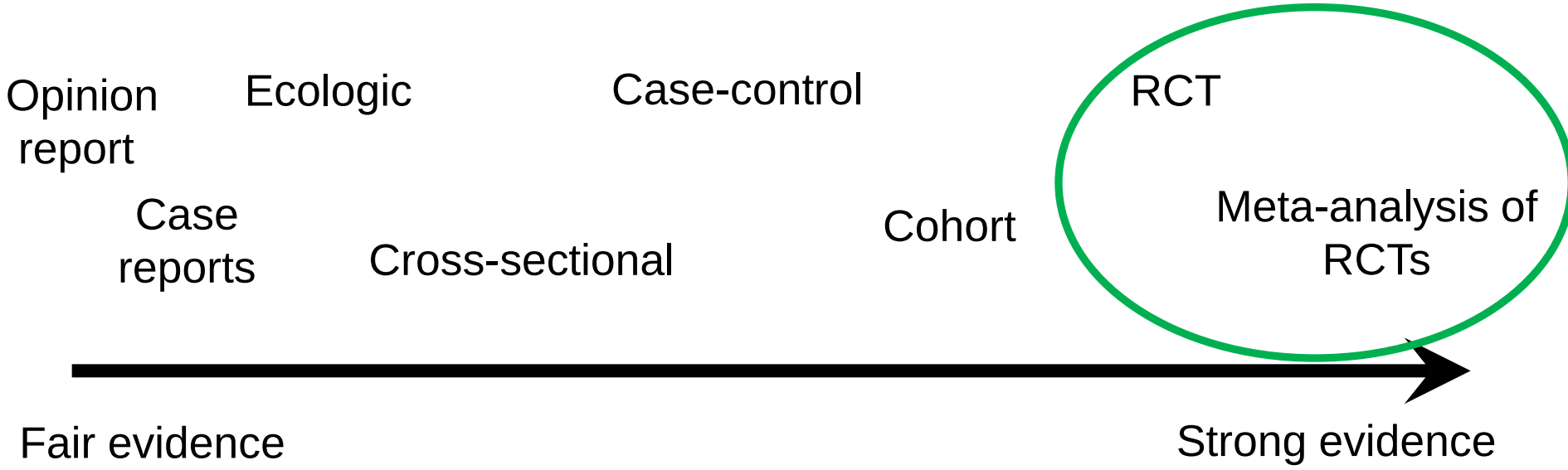
Mjölk och eventuell ohälsa?

Hur studera detta på bästa sätt?

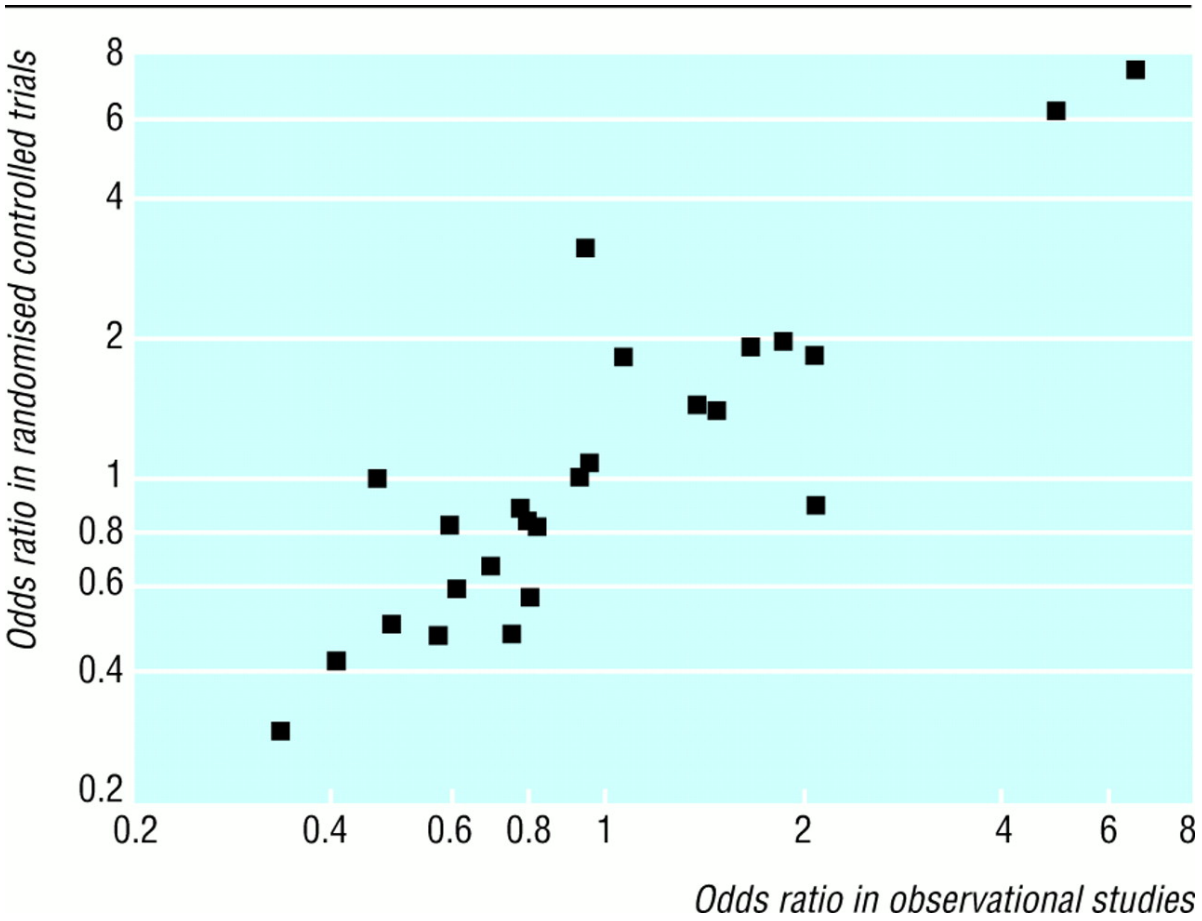
Evidence-based medicine

Community interventions

Cohort studies with instrumental exposure variables such as MR studies



Överensstämmelse mellan RCTs och kohortstudier?



thebmj

John P A Ioannidis et al. BMJ 2001;322:879-880

Färskare analys

Uppföljning t o m 2014

Inom kvinnliga kohorten SMC
22400 dödsfall

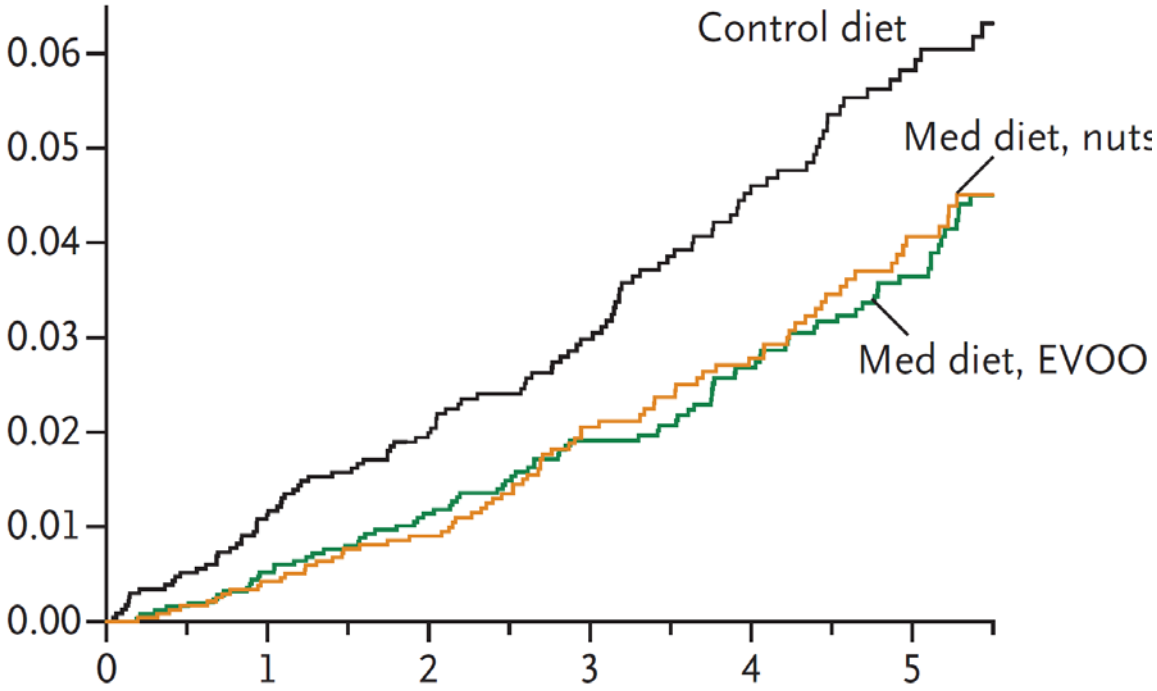
Inom manliga kohorten COSM
15500 dödsfall

Men först en avstickare….

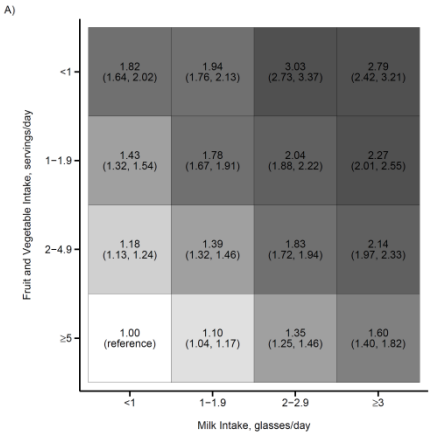
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 4, 2013 VOL. 368 NO. 14

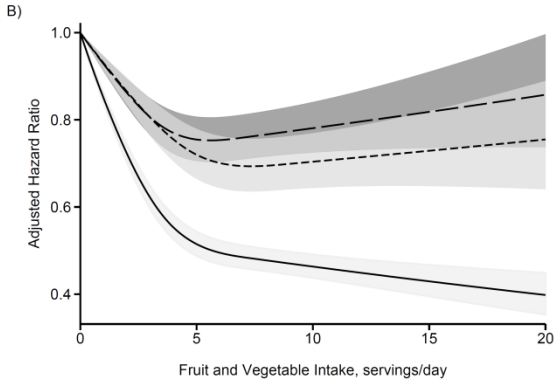
Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

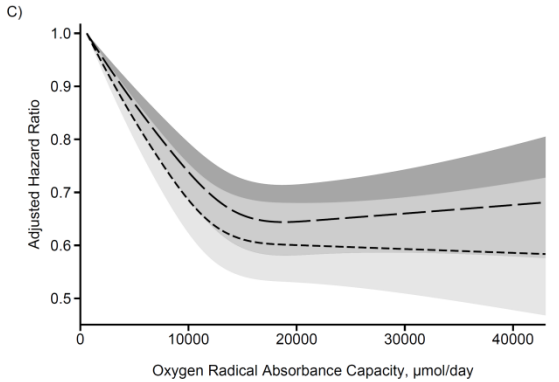


All-cause mortality



Time-updated women





Am J Epidemiol (2017) 185: 345-361

Analys med 6000 höftfrakturer i kvinnokohorten SMC

Mediterranean **Diet** and Hip **Fracture** in Swedish Men and Women.
Byberg L, Bellavia A, Larsson SC, Orsini N, Wolk A, Michaëlsson K.
J **Bone** Miner Res. 2016

Prospective study of dietary Non Enzymatic Antioxidant Capacity on the risk of hip **fracture** in the elderly.
Hantikainen E, Grotta A, Ye W, Adami HO, Surkan PJ, Serafini M, Michaëlsson K, Bellocco R, Trolle Lagerros Y.
Bone. 2016 Sep;90:31-6.

Fruit and Vegetable Intake and Hip **Fracture** Incidence in Older Men and Women: The CHANCES Project.
Benetou V, Orfanos P, Feskanich D, Michaëlsson K, Pettersson-Kymmer U, Eriksson S, Grodstein F, Wolk A, Bellavia A, Ahmed LA, Boffeta P, Trichopoulou A.
J **Bone** Miner Res. 2016 Sep;31(9):1743-52

Fruit and vegetable intake and risk of hip **fracture**: a cohort study of Swedish men and women.
Byberg L, Bellavia A, Orsini N, Wolk A, Michaëlsson K.
J **Bone** Miner Res. 2015 Jun;30(6):976-84.

Nutrients **2015**, *7*, 7749-7763; doi:10.3390/nu7095363

OPEN ACCESS

nutrients

ISSN 2072-6643

www.mdpi.com/journal/nutrients

Article

Milk Consumption and Mortality from All Causes, Cardiovascular Disease, and Cancer: A Systematic Review and Meta-Analysis

Susanna C. Larsson [1,*], Alessio Crippa [1,2], Nicola Orsini [1,2], Alicja Wolk [1] and Karl Michaëlsson [3]

"There was substantial heterogeneity among studies of non-fermented milk consumption in relation to mortality from all causes (12 studies; I^2 = 94%), cardiovascular disease (five studies; I^2 = 93%), and cancer (four studies; I^2 = 75%) as well as among studies of fermented milk consumption and all-cause mortality (seven studies; I^2 = 88%). Thus, estimating pooled hazard ratios was not appropriate."

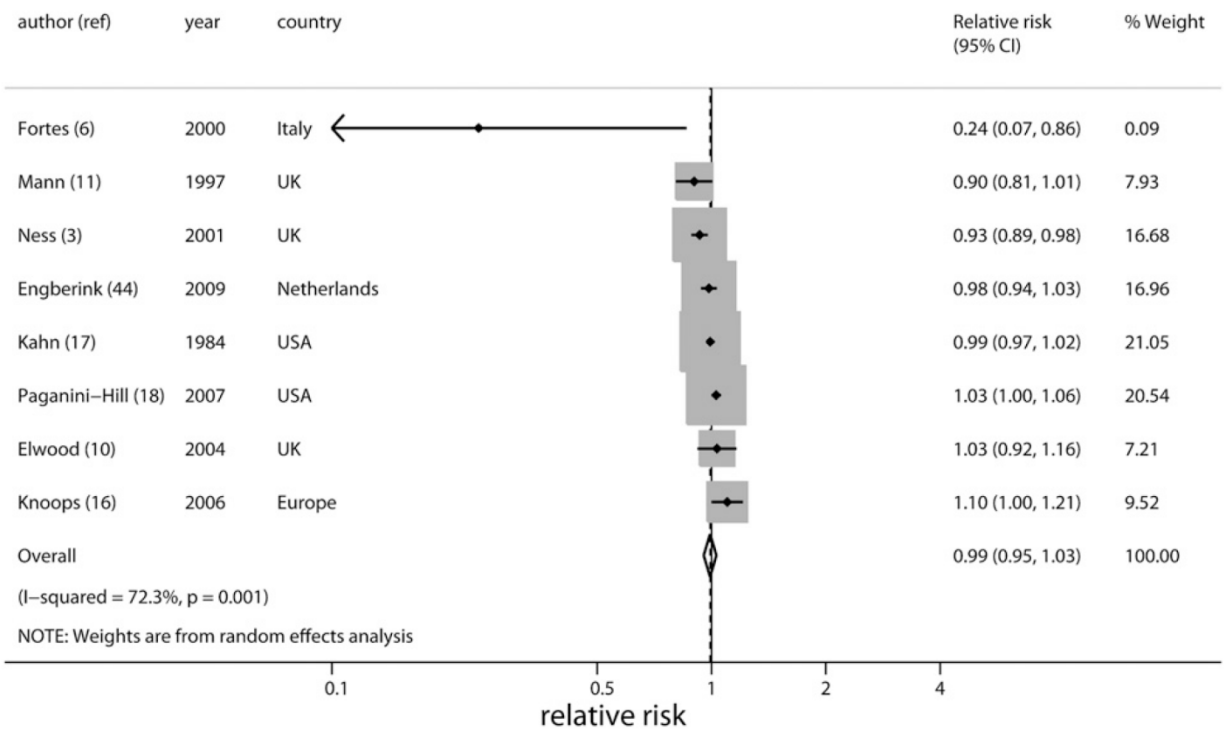
Previous studies?

Am J Clin Nutr 2011

Milk and dairy consumption and incidence of cardiovascular diseases and all-cause mortality: dose-response meta-analysis of prospective cohort studies[1–3]

Sabita S Soedamah-Muthu, Eric L Ding, Wael K Al-Delaimy, Frank B Hu, Marielle F Engberink, Walter C Willett, and Johanna M Geleijnse

Per 200 mL/day



Spurious precision? Meta-analysis of observational studies

BMJ 1998

Matthias Egger, Martin Schneider, George Davey Smith,

-”There is a danger that meta-analyses of observational data produce very precise but equally spurious results”

-”More is gained by carefully examining possible sources of heterogeneity between the results from observational studies”

J Epidemiol 2015;25(1):66-73
doi:10.2188/jea.JE20140081

Original Article

Milk Drinking and Mortality: Findings From the Japan Collaborative Cohort Study

Chaochen Wang[1], Hiroshi Yatsuya[1,2], Koji Tamakoshi[3], Hiroyasu Iso[4], and Akiko Tamakoshi[5]

N=94980
21775 deaths

Aged 40-79 years

40-item FFQ

19 years of follow-up

"An inverse association was also found between drinking milk and mortality from both cardiovascular diseases and cancer."

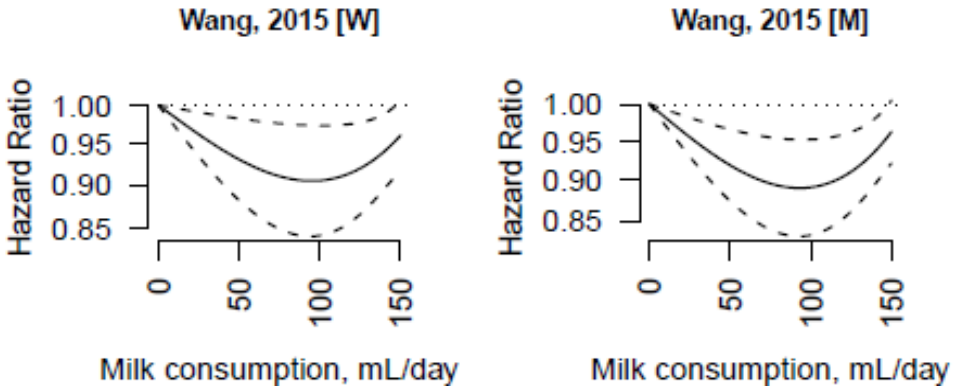
APPENDIX 1.
For each food listed, circle the number in the box indicating how often, you have used.

	Food	Average use: Almost never	1-2 per month	1-2 per week	3-4 per week	Almost every day
1	Beef	1	2	3	4	5
2	Pork (excluding ham or sausage)	1	2	3	4	5
3	Ham or sausage	1	2	3	4	5
4	Chicken	1	2	3	4	5
5	Liver	1	2	3	4	5
6	Eggs	1	2	3	4	5
7	Milk	1	2	3	4	5
8	Yogurt	1	2	3	4	5
9	Cheese	1	2	3	4	5
10	Butter	1	2	3	4	5
11	Margarine	1	2	3	4	5

Hazard ratios (95% CI) for all-cause mortality by daily milk intake

	0 dl/day	5 ml /day	20 ml/day	50 ml/day	100 ml/day	
	Never	1-2 times/month	1-2 times/week	3-4 times/week	Almost every day	Trend P-value
Men	1.0 (Ref)	0.92 (0.86-0.99)	0.91 (0.85-0.96)	0.89 (0.84-0.96)	0.93 (0.89-0.98)	0.09
Women	1.0 (Ref)	1.00 (0.91-1.05)	0.98 (0.91-1.05)	0.91 (0.85-0.98)	0.96 (0.91-1.01)	0.15

No adjustment for energy intake
No adjustment for coffee intake



International Journal of Epidemiology, 2015, 587–603
doi: 10.1093/ije/dyv109
Original article

Mendelian Randomization Causal Analysis

Milk intake is not associated with ischaemic heart disease in observational or Mendelian randomization analyses in 98 529 Danish adults

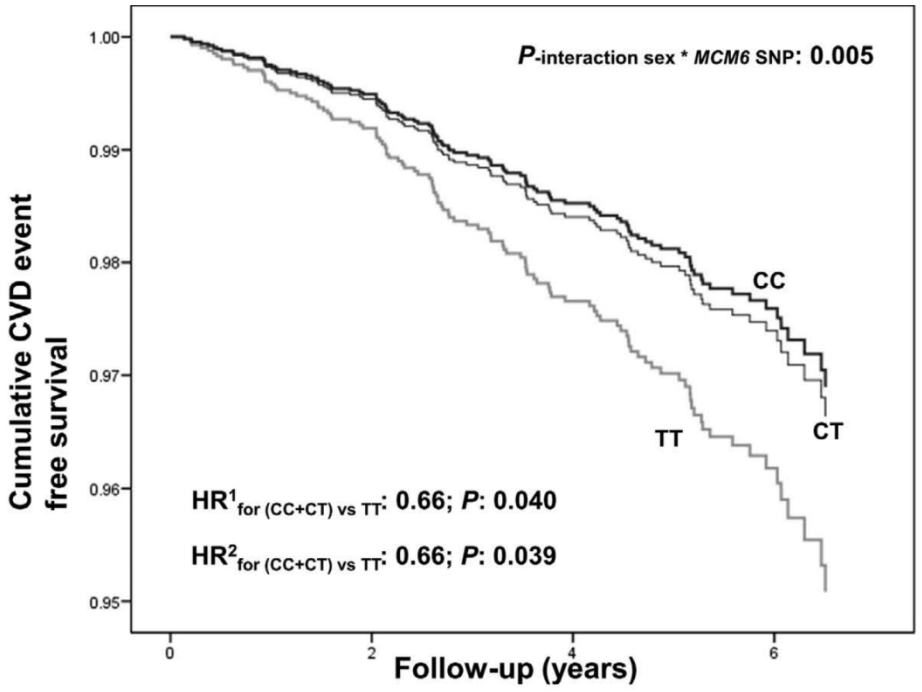
Helle K M Bergholdt,[1,2] Børge G Nordestgaard,[2,3,4] Anette Varbo[2,3] and Christina Ellervik[2,5,6]*

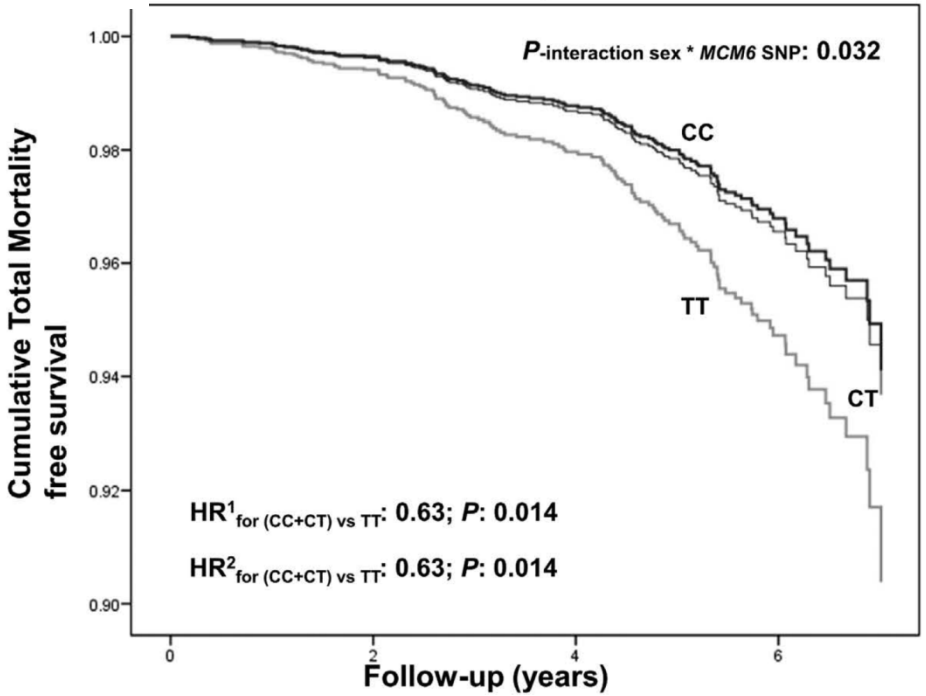
Associations of the MCM6-rs3754686 proxy for milk intake in Mediterranean and American populations with cardiovascular biomarkers, disease and mortality: Mendelian randomization

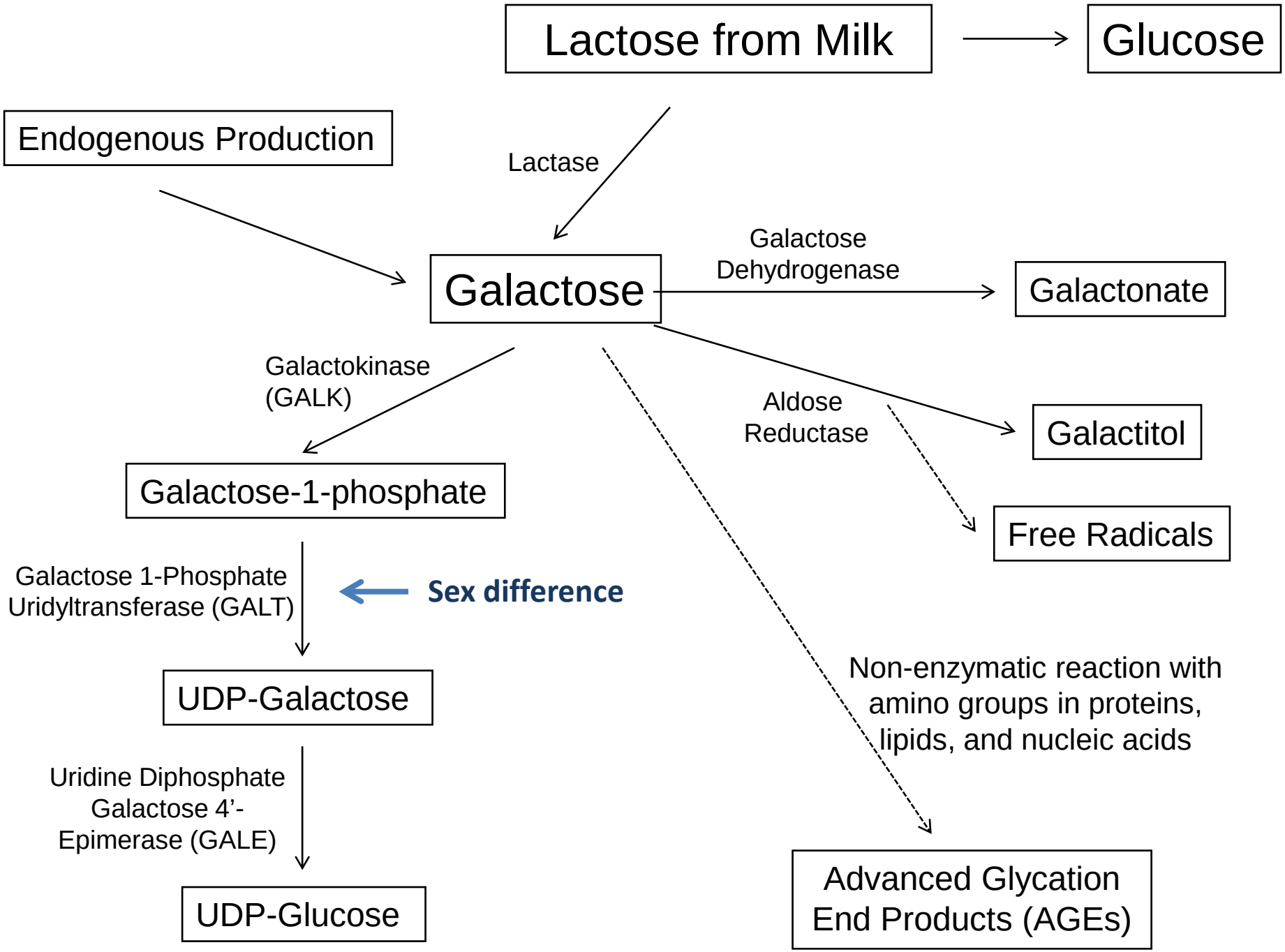
www.nature.com/scientificreports

SCIENTIFIC REPORTS

Caren E. Smith[1], Oscar Coltell[2,3], Jose V. Sorlí[3,4], Ramón Estruch[3,5], Miguel Ángel Martínez-González[3,6], Jordi Salas-Salvadó[3,7], Montserrat Fitó[3,8], Fernando Arós[3,9], Hassan S. Dashti[1], Chao Q. Lai[1], Leticia Miró[3,10], Lluís Serra-Majem[3,11], Enrique Gómez-Gracia[12], Miquel Fiol[3,13], Emilio Ros[3,14], Stella Aslibekyan[15], Bertha Hidalgo[15], Marian L. Neuhouser[16], Chongzhi Di[16], Katherine L. Tucker[17], Donna K. Arnett[15], José M. Ordovás[1,18,19,*] & Dolores Corella[3,4,*]






Lactose from Milk
Glucose
Endogenous Production
Lactase
Galactose
Galactose Dehydrogenase
Galactonate
Galactokinase (GALK)
Aldose Reductase
Galactitol
Galactose-1-phosphate
Free Radicals
Galactose 1-Phosphate Uridyltransferase (GALT)
Sex difference
UDP-Galactose
Non-enzymatic reaction with amino groups in proteins, lipids, and nucleic acids
Uridine Diphosphate Galactose 4'-Epimerase (GALE)
UDP-Glucose
Advanced Glycation End Products (AGEs)

Hur reagerade omvärlden på våra fynd?

Vår artikel i BMJ från 28 oktober 2014

	Abstract	Full	PDF
April 2017	29	8594	576
March 2017	40	14208	566
February 2017	64	16358	551
January 2017	34	12610	567
December 2016	21	11474	1148
November 2016	8	8697	449
October 2016	9	11007	467
September 2016	22	8129	478
August 2016	94	9544	436
July 2016	18	8323	290
June 2016	15	12200	526
May 2016	16	17445	1655
April 2016	14	17216	550
March 2016	23	10551	462
February 2016	22	16416	424
January 2016	27	12910	489
December 2015	10	7220	262
November 2015	13	10238	581
October 2015	11	8441	540
September 2015	23	7224	687
August 2015	12	8363	609
July 2015	12	8083	881
June 2015	10	7592	768
May 2015	32	13116	945
April 2015	57	11010	2158
March 2015	50	20131	2864
February 2015	52	16921	2233
January 2015	52	16558	2562
December 2014	82	24217	3507
November 2014	83	46638	7515
October 2014	32	20025	3700

This research output has an **Altmetric Attention Score** of **2356**. This is our high-level measure of the quality and quantity of online attention that it has received. This Attention Score, as well as the ranking and number of research outputs shown below, was calculated when the research output was last mentioned on **3 May 2017**

All research outputs
#159
of 7,641,242 outputs

Outputs of similar age
#7
of 200,043 outputs

Experts of the National Dairy Council

Confusing message about dairy from Sweden

"The observational study by the Swedish surgeon Karl Michaëlsson and co-workers published in British Medical Journal concluded that high milk intake was associated with increased risk of bone fractures and mortality (Michaëlsson 2014). The message gave rise to global media attention, not least due to the fact that the results of the study seem to go against previous systematic reviews, meta-analyses and recommendations from most authorities in the world. But are the new findings valid and do they change our view on dairy in any way? Or is the study flawed, or are there reasons simply to look at the result as just an outlier that needs to be viewed in the context of the totality of evidence?"

Our response: "Mysteries are in the (milky) eye of the beholder"

Nutritionsfakta.se "**Mjölk och hälsa – färdigmjölkat i kohortstallet?"**
av Åke Nilsson, professor emeritus, Lunds universitet

Vetenskapsrådet

Beredningsgruppens yttrande

Peer review

"The mistake, of course, is to have thought that peer review was any more than a crude means of discovering the acceptability — not the validity — of a new finding. Editors and scientists alike insist on the pivotal importance of peer review. We portray peer review to the public as a quasi-sacred process that helps to make science our most objective truth teller. But we know that the system of peer review is biased, unjust, unaccountable, incomplete, easily fixed, often insulting, usually ignorant, occasionally foolish, and frequently wrong."

Richard Horton, editor-in-chief, Lancet

Konklusion

En enstaka studie är otillräcklig för rekommendationer

Nog viktigt att analysera olika typer av mjölkprodukter separat

Fler studier behövs

Meta-analyser bör göras med omsorg

Var noggrann när du utvärderar olika studiers resultat