Dairy Products and Human Health: The Facts

Professor Ian Givens, *University of Reading*
Professor Peter Elwood, *Cardiff University*
with Janet Pickering and Dr John Gallacher

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The world we live in……

Two major trends……

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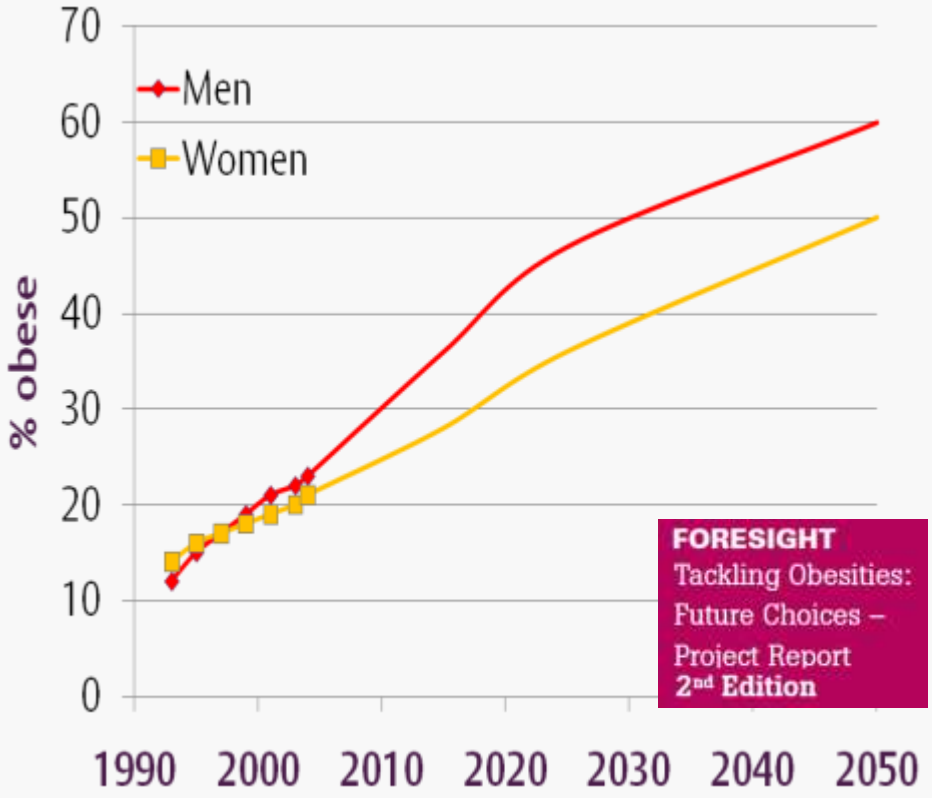
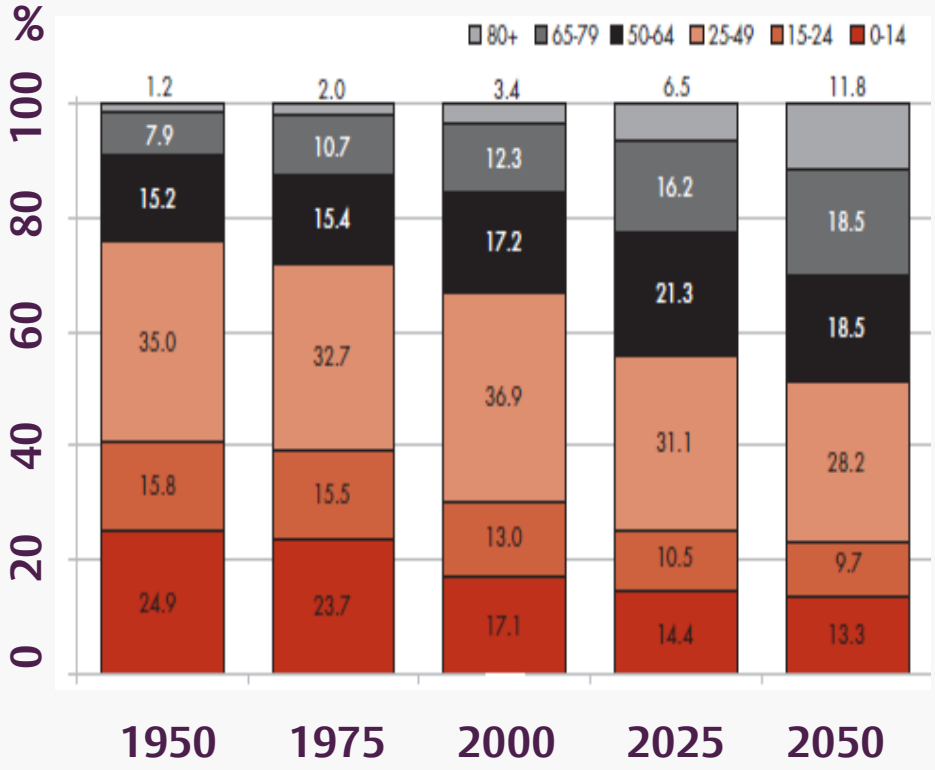
Trend in UK obesity



Trend in EU 25 age structure



Both trends increase chronic disease risk

Overview

- Do milk/dairy foods increase or reduce chronic disease risk?
- What type of evidence should we believe?
- Risk is a balance between good and evil!
- Effects of age; low fat products
- Conclusions

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From The Times

January 20, 2007

It's udder confusion

Is the white stuff good for us or should it carry a health warning? Our correspondent blows away some of the froth

Vivienne Parry

To write about milk is to take your life in your hands. There is probably no food that inspires more vehement accusations and counter-accusations than the white stuff. Some are bound to be aired again in the coming days during Food Allergy and Intolerance Week, as stories of bad reactions to milk are used to promote the oat, soya and rice alternatives available.

In the blue corner we have cow's milk as a cause of hosts of allergies, heart disease and breast cancer, not to mention excess phlegm. In the red corner we have milk as intrinsic to bone health, and protective against cancer, diabetes and heart disease. Meanwhile, on the sidelines, there are those advocating organic milk as nutritionally superior.

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From The Times

May 01, 2006

The demon drink?

Fewer people are drinking milk, but is it f

Peta Bee

Dieters tend to shun milk because they th
as many as 45 per cent of the UK popu
intolerant" and therefore unable to dri

While recently there's been a sl
attributed to the rise in the po
it's clear that milk is hardly th

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Ban butter to save thousands of lives, says heart surgeon

By SEAN POULTER
Last updated at 8:19 AM on 19th January 2010

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Butter should be banned to protect the nation's health, according to a leading heart surgeon.

Shyam Kolvekar says only radical action can save growing numbers of young adults from heart attacks and clogged arteries.

Warning of the dangers of other foods high in saturated fat, he advises people to eat less red meat, take low-fat milk and switch to olive and sunflower oil.

Saturated fat is blamed for a third of the 200,000 premature deaths from heart disease a year.

Adults are eating an average of 800 grams of it a month - 20 per cent more than the recommended limit. Hitting the recommended level could save 3,500 lives a year.

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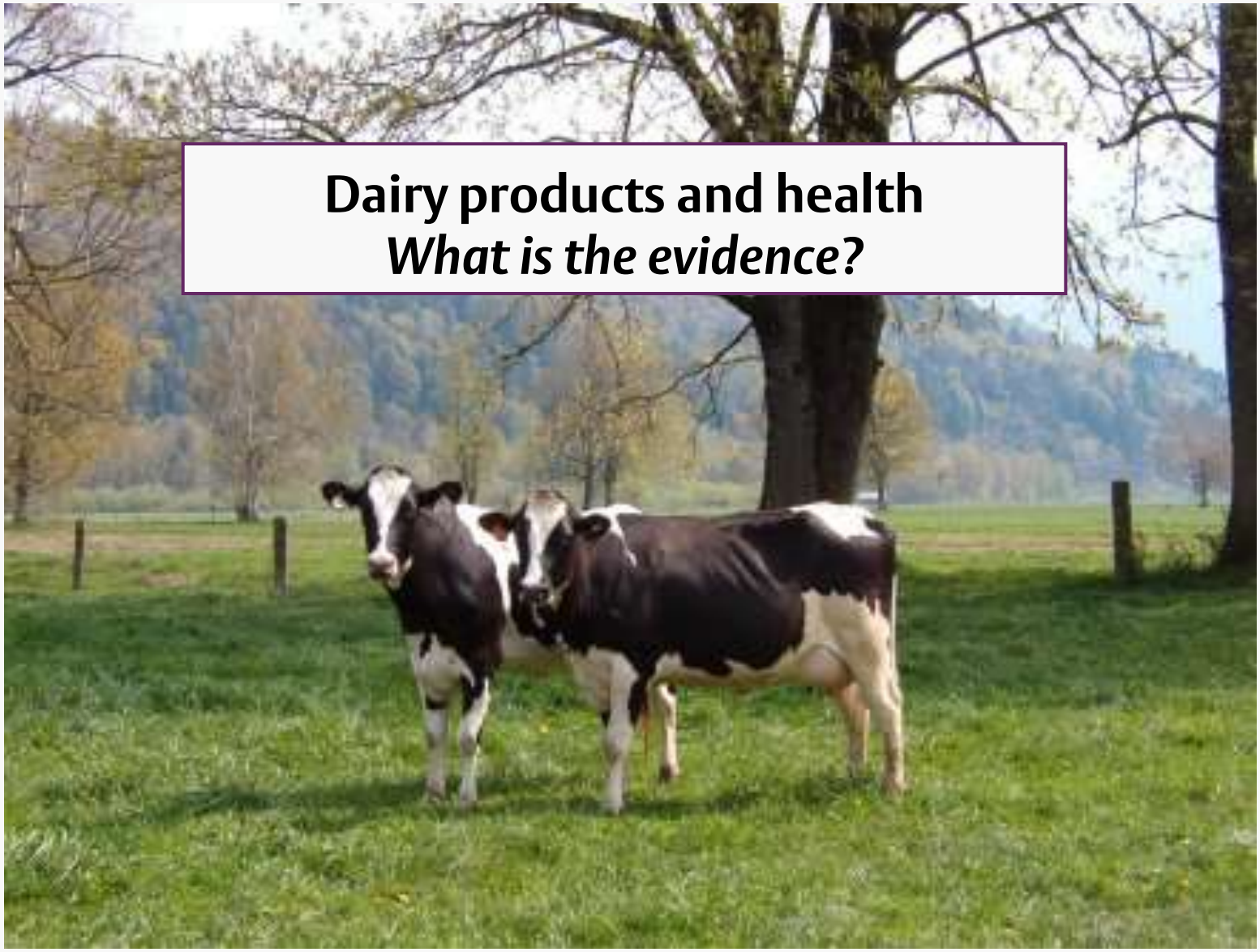

Dairy products and health
What is the evidence?

What are we trying to do?

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Archie Cochrane, inspiration of the Cochrane Collaboration and Evidence Based Medicine, urged that all conclusions within clinical practice be based on ***all the evidence from bias-free studies*****.....**

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On the other hand, Alvarez-Leon has commented:

'Public health nutrition should not be u… for evidence-based conclusions…'

… the benefits and ri… ption cannot be judged fro… bio-pathological variat…

(… Brit J Nutr. 96:594-599)

So, upon what evidence should public health policy on milk and dairy foods be based?

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Sources of evidence

I. Associations with risk-factors for disease

II. Retrospective case-control studies based on patients

III. Prospective cohort studies with disease incidence as outcomes

IV. Randomised controlled trials

and, for each source,
a meta-analysis of all the available studies

BASED ON: the US agency for Health Care Policy and Research (AHCPR 1992)
and the Centre for Health Economics, University of York UK

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I. Associations with risk-factors for disease

Effects of milk on biological mechanisms:

1. ***it raises cholesterol*** *(1,249 papers!)*
2. *heated milk proteins are antigenic (Davies 1969)*
3. *it raises homocysteine (Grant 1998)*
4. *it contains xanthine oxidase (Ho et al 1977)*
5. *it can carry bacteria and fungi (Rank 1986)*
6. *lactose tolerance increases vascular risk (Segal 1980)*
7. *casein A1 enhances atherogenesis (Venn et al 2006)*
8. *the calcium increases arterial calcification (Seely 2000)*
9. *it is low in copper (Strain 1988)*
10. *it contains phytoestrogens (Seely 1982)*
11. *for some people milk is taken as a substitute for alcohol!! (Popham et al 1983)*

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I. Associations with risk-factors for disease

Effects of milk on biological mechanisms:

Cholesterol level in lowest and highest milk drinkers:

A few sample papers:

Abbott et al. (1996)	5.60	5.70 mmol/L	***+ 8% of SD***
Ness et al. (2001)	5.87	5.90	***+10% of SD***
Nagaya et al. (1996)	5.20	5.28	***+ 6% of SD***
Caerphilly	6.05	6.14	***+ 7% of SD***

....but milk is a complex food with many nutrients and bioactive compounds.....

…but which cholesterol?

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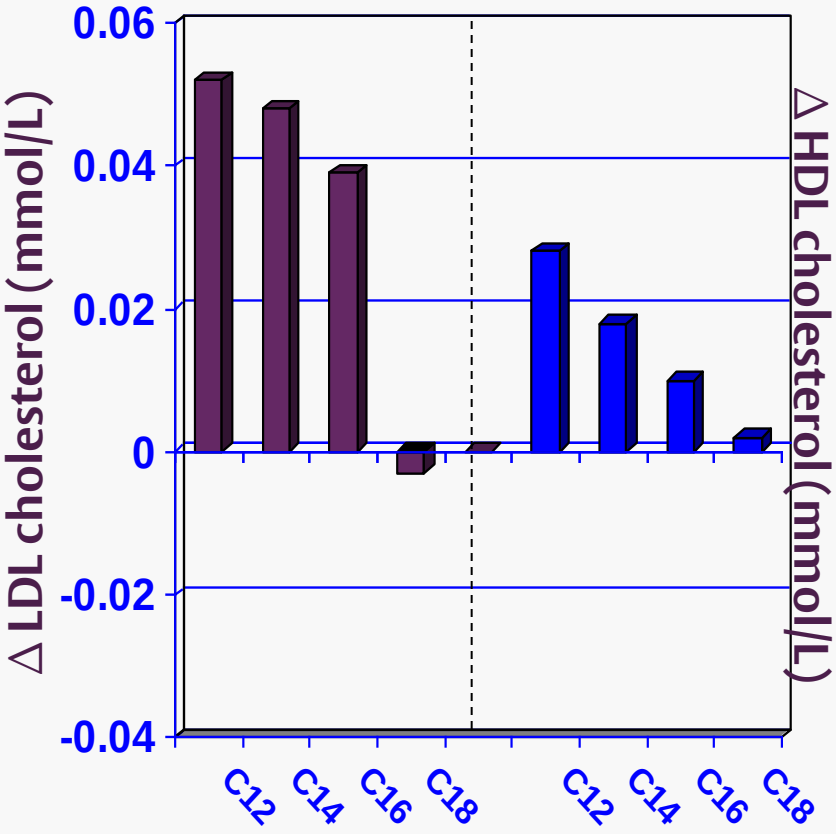
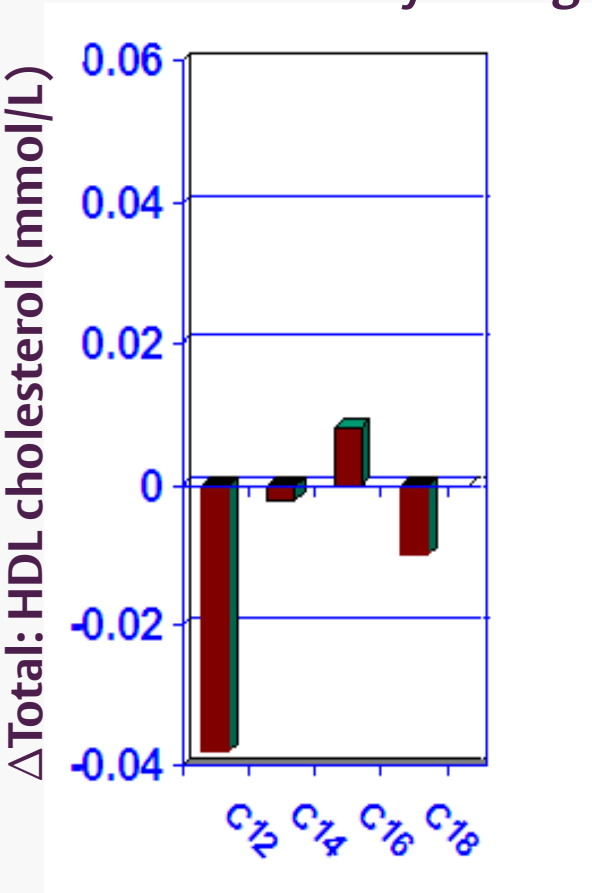


Mensink et al. (2003)

So does SFA profile represent as great a risk as traditionally thought?



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I. Associations with risk-factors for disease

Milk and blood pressure

Again, a few sample papers:

Study	Population	BP in subjects with highest milk intakes
Ackley et al 1983	5,050	- ***6.3% of SD***
Jorde & Bonas 2000	7,735	- ***5.5% of SD***
Shaper et al 1991	1,340	- ***8.3% of SD***
Vivjer et al 1992	1,265	-***10.0% of SD***
Ness et al 2001	5,765	- ***5.5% of SD***
Abbott et al 1996	3,150	- ***6.3% of SD***
Iso et al 1999	34,486	- ***7.5% of SD***
Elwood et al 2004	2,512	- ***10.0% of SD***
Djousse 2006	4,797	- ***6.4% of SD***
PREDIMED study 2009	2,290	- ***10.5% of SD***

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I. Associations with risk-factors for disease

DETERMINANTS

Milk drinki

...and what about other mechanisms?

RISK FACTORS

olesterol *(raised)*

Blood pressure *(lowered)*

? ?

DISEASE

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A heirarchy of evidence

BASED ON: the US agency for Health Care Policy and Research (AHCPR 1992) and the Centre for Health Economics, University of York UK

I. Associations with risk-factors for disease

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and, for each source,
a meta-analysis of all the available studies

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II. Retrospective case-control studies based on patients

Milk consumption in patients prior to a heart attack:

STRATEGY

Patients with a myocardial infarct, and 'control' patients with no evidence of vascular disease, are questioned about their earlier milk consumption etc.

'Overview'

The literature is searched for all relevant case-control studies, the results of these are examined for evidence of heterogeneity, and then all are combined in a meta-analysis to give an overall estimate of risk.

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II. Retrospective case-control studies based on patients

Milk consumption in patients prior to

Study	Nu	
Gramenzi et al. (1990)		
T		
		0.99)
	(107 controls)	

Limitations:

- milk drinking may be associated (positively or negatively) with other health related behaviours
- differences in recall by patients and controls may introduce bias

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A heirarchy of evidence

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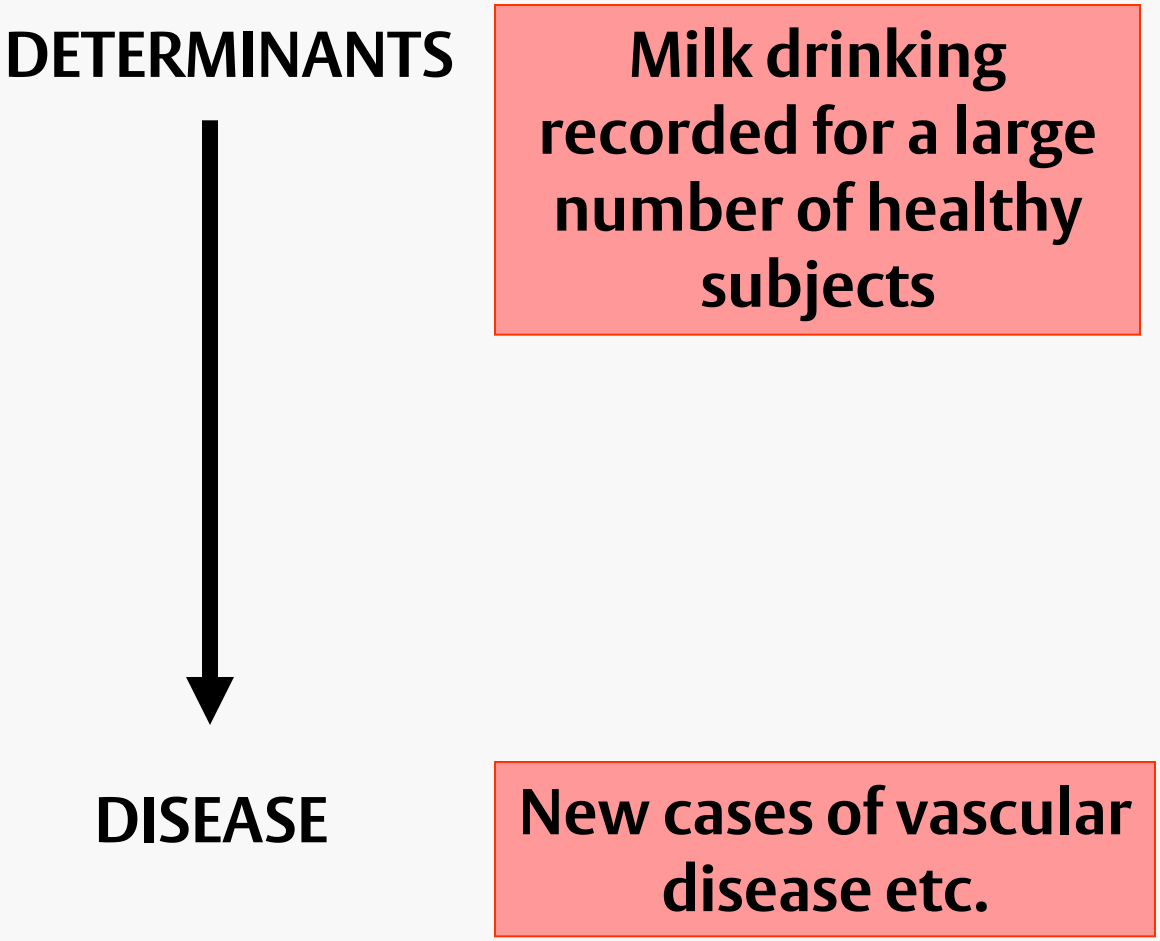
Dairy products and health



III. Prospective cohort studies with disease incidence as outcomes

STRATEGY

Healthy subjects questioned and dietary details etc. recorded. The subjects are then followed and new, incident disease events are related to the earlier diet.

'Overview'

The literature is searched for all relevant cohort studies, the results of these are examined for evidence of heterogeneity, and then all are combined in a meta-analysis to give an overall estimate of risk.

III. Prospective cohort studies with disease incidence as outcomes

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Dairy foods and all-cause mortality

Study	No. of deaths	Adjusted RR
Kahn et al (1984)	6,075	0.98 (n.s.)
Van der Pols (2009)	1,468	0.77 (0.61, 0.98) 0.77 (0.61, 0.97)

Relative risk (95% CI) of death in the highest dairy intake subjects

(***the risk in the 20% of subjects with the highest dairy consumption compared with the risk in the 20% of subjects with the lowest intake***)

0.87 *(0.77, 0.98)*

Three studies with insufficient data for inclusion in a meta-analysis had to be omitted.

LIPIDS DOI 10.1007/s11745-010-3412-5

III. Prospective cohort studies with disease incidence as outcomes

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Dairy foods and ischaemic heart disease events

Study	No. of events	Adjusted RR
Shaper et al (1991)	608	0.88
Mann et al (1997)	63	1.50
Bostic et al (1999)	387	0.94
Lamarche (2004)	217	0.73
Trichopoulou et al (2006)	46	0.95
Umesawa et al (2006)	135	0.80
Umesawa et al (2008)	322	1.09
Van der Pols et al (2009)	378	0.74

RR (95% CI) in subjects with the highest dairy intake
0.92 *(0.80, 0.99)*

Four studies with insufficient data for inclusion in meta-analysis had to be omitted.

J LIPIDS DOI: 10.1007/s11745-010-3412-5

III. Prospective cohort studies with disease incidence as outcomes

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Dairy foods and ischaemic heart disease events

Study	No. of events	Adjusted RR
Shaper et al (1991)	608	0.88
Mann et al (1997)	63	1.50
Bostic et al (1999)	387	0.94
Hu et al (1999)	939	Whole milk 1.67 Skimmed 0.78
Umesawa et al (2008)	322	1.09
Van der Pols et al (2009)	378	0.74

The RR for low-fat milk (0.78) is consistent with all the other RRs, while that for whole milk (1.67) differs significantly, and its inclusion in the meta-analysis introduces marked heterogeneity.

If it is assumed that 20% of women in that cohort had been drinking whole milk and 80% skimmed milk, an overall estimate of RR in Hu et al (20) is **0.96** *(0.74, 1.15) and* putting this estimate into the meta-analysis:

overall estimate for milk and heart disease of 0.91 *(0.77 to 1.07)*

The best estimate of the overall association between milk/dairy and ischaemic heart disease is probably obtained by including Hu et al's estimated for low-fat milk:

0.92 *(0.80, 0.99)*

III. Prospective cohort studies with disease incidence as outcomes

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Dairy foods and new stroke events

Study	*Events*	*Adjusted RR*
Iso et al (1999)	347	0.70 (0.61, 0.97)
Kinjo et al (1999)	3,084	0.85 (0.77, 0.92)
Abbott et al (1996)	229	0.67 (0.45, 1.10)
Larsson et al (2009)	2,702	1.03 (0.96, 1.10)
Umesawa et al (2006)	284	0.53 (0.34, 0.81)
Umesawa et al (2008)	664	0.70 (0.52, 0.94
Van der Pols et al (2009)	121	0.61 (0.27, 1.38)

RR (95% CI) in subjects with the highest dairy intake
0.79 *(0.68, 0.91)*

LIPIDS DOI 10.1007/s11745-010-3412-5

III. Prospective cohort studies with disease incidence as outcomes

Dairy foods and new haemorrhagic strokes

Study	Events	Adjusted RR
Kinjo et al (1999)	4,773	0.74 (0.68, 0.80)
Larsson (2009)	383	1.01 (0.82, 1.20)

RR (95% CI) in subjects with the highest dairy intake
0.75 *(0.60, 0.94)*

LIPIDS DOI 10.1007/s11745-010-3412-5

III. Prospective cohort studies with disease incidence as outcomes

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Dairy foods and new diabetes

Study	Events	Adjusted RR
Choi et al (2005)	1,243	0,91 (0,85, 0.97)
Liu e		67, 0.94)
van D		75, 1.15)
Elwo		20, 1.63)
Villegras et al (2009)	2,270	0.60 (0.41, 0.88)

RR (95% CI) for highest intake groups
0.85 *(0.75, 0.96)*

LIPIDS DOI 10.1007/s11745-010-3412-5

III. Prospective cohort studies with disease incidence as outcomes

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Summary of cohort studies

Outcome	Heterogeneity	Relative Risk
Death	Not significant	0.87 *(0.77, 0.98)*
IHD	Not significant	0.92 *(0.80, 0.99)*
Stroke all Haemorrhagic stroke	Significant Significant	0.79 *(0.68, 0.91)* 0.75 *(0.60, 0.94)*
Diabetes	Not significant.	0.85 *(0.75, 0.96)*

III. Prospective cohort studies with disease incidence as outcomes

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Other reviews of cohort studies

Gibson et al. (2009) identified 12 cohort studies:

> ***'no consistent findings to support the concept that dairy food consumption is associated with a higher risk of coronary heart disease'***

Mente et al. (2009) from 5 cohort studies:

> ***milk has 'no significant association with coronary heart disease' RR = 0.91*** *(0.73, 1.00)*

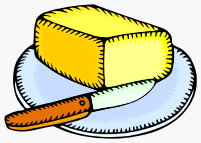
Bonthuis et al. (2010) 16 year Australian cohort:

> ***'a possible beneficial association between intake of full-fat dairy and CV mortality needs further assessment…' HR=0.31*** *(0.12-0.79)*

III. Prospective cohort studies with disease incidence as outcomes

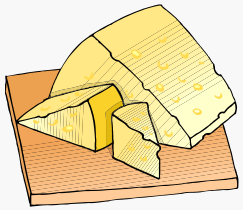
Individual dairy items

BUTTER – **Three cohort studies**: Heterogeneity 0.33; **RR 0.93** *(0.84, 1.02) for VD events*
Two cohorts could not be included: ***RR 1.03*** *and 'increase in CHD'* ***P = 0.026***



Three **case-control studies:**
106 patients, 105 controls: adjusted **OR 2.80** *(1.14, 6.85)*
287 MI women, 649 control women; **OR** adjusted for age alone: **2.3**
144 diabetics with PVD, 288 control patients: **OR 2.06** *(1.15. 3.68)*

CHEESE – **Cohorts**: Two studies (with fixed effects) **RR 0.90** *(0.79, 1.03) for VD events*
Four cohorts not included: ***RRs 0.96; 0.95; 0.97; 0.88***



Three **case-control studies:**
106 patients, 105 control: adjusted **OR 0.42** *(0.18, 1.03)*
111 MI patients, 107 controls: **OR 0.34** *(0.13, 0.91)*
144 diabetic patients with PVD, 288 controls **0.61** *(0.26, 1.45).*
Other case-control studies: **0.77** *(0.54, 1.11)*, and **1.0** *(no CIs stated)*

III. Prospective cohort studies with disease incidence as outcomes

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Summary of cohort studies

Systematic Reviews…….

- Summarise the best available evidence on an issue

- Indicate those issues on which more evidence is required

Butter	Not significant	0.93 (0.84, 1.02)
Cheese	Significant	0.90 (0.79, 1.03)

III. Prospective cohort studies with disease incidence as outcomes

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Dairy foods and cancer

- The literature on this is extensive, though most of the reports are based on retrospective case-control studies

- The World Cancer Research Fund and the American Institute for Cancer Research issued a major report in 2007 on foods and cancer.

III. Prospective cohort studies with disease incidence as outcomes

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Dairy foods and cancer

World Cancer Res. Group American Institute for Cancer Research	No. of studies (heterogeneity)	RR attributable to milk and dairy foods
Colon cancer	4 cohorts (?) 10 cohorts (?)	0.94 (0.85, 1.03) 0.78 (0.69, 0.88)
Bladder cancer	5 case-control (high) 4 cohorts (moderate)	1.00 (0.87, 1.14) 0.82 (0.67, 0.99)
Prostate cancer	5 case-control (low) 8 cohorts (moderate)	1.03 (0.99, 1.07) 1.06 (1.01, 1.11)

No other cancer found to be associated with milk and dairy consumption.

III. Prospective cohort studies with disease incidence as outcomes

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Dairy foods and cancer

Conclusions from the World Cancer Research Fund and the American Institute for Cancer Research report:

"Milk probably protects against colon cancer"

"There is limited evidence suggesting cheese [in contrast to milk] is a cause of colorectal cancer."

"There is limited evidence that milk protects against bladder cancer"

"Diets high in calcium are a probable cause of prostate cancer"

"The probable effect of milk in reducing cancer risk is likely to be mediated at least in part by calcium.... Milk also contains many bioactive constituents however, which may also play a role."

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Sources of evidence

BASED ON: the US agency for Health Care Policy and Research (AHCPR 1992) and the Centre for Health Economics, University of York UK

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and, for each source,
a meta-analysis of all the available studies

IV. Randomised controlled trials

There has been no randomised trial!

That is, no randomised controlled trial with death or survi
outcomes has been reported

A trial with adequate power wo *(?10,000 subjects).*

Half the subjects, sele *ve to agree to drink milk, half would have to agree t* *ntaining milk.*

The t *least 5 years.*

C *ave to be high throughout.*

Probably unacceptable (and un-fundable!)

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Sources of evidence

I. Associations with risk-factors for disease

Invalid, unless all relevant mechanisms are known and can be considered together

II. Retrospective case-control studies based on patients

Limited, but suggestive of benefit

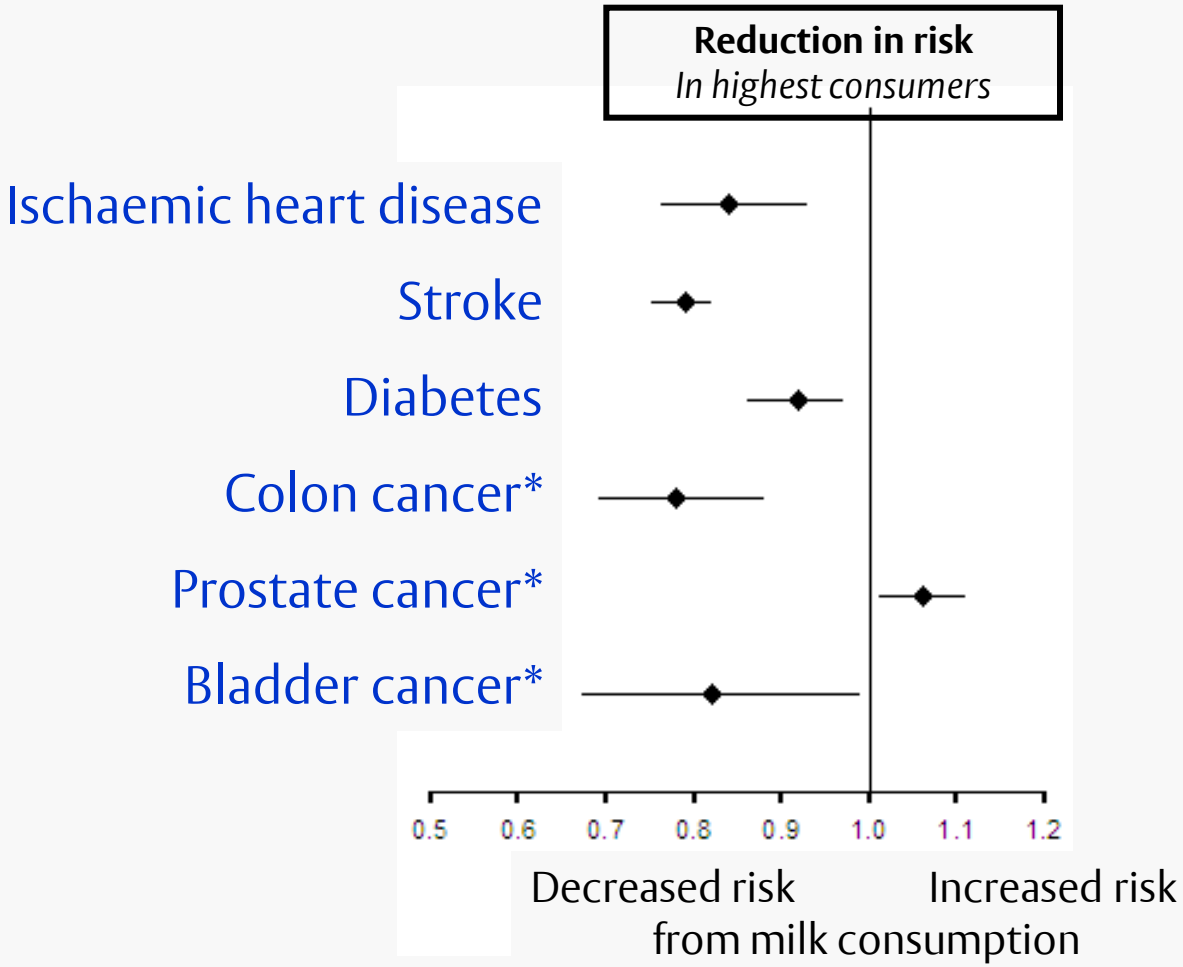
III. Prospective cohort studies with disease incidence as outcomes

Highly suggestive of benefit, though there could be confounding by other health related behaviours

IV. Randomised controlled trials

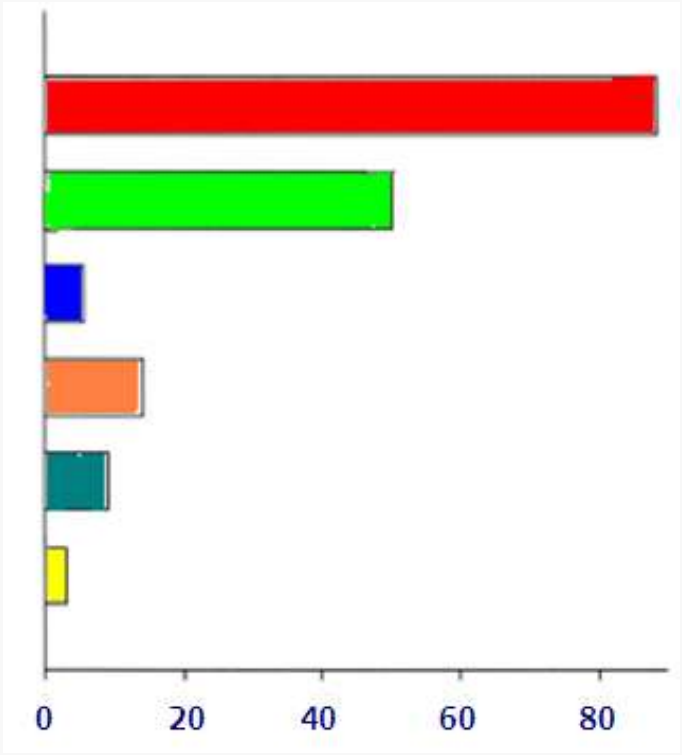
None conducted and none is likely

Summary of evidence from prospective, cohort studies



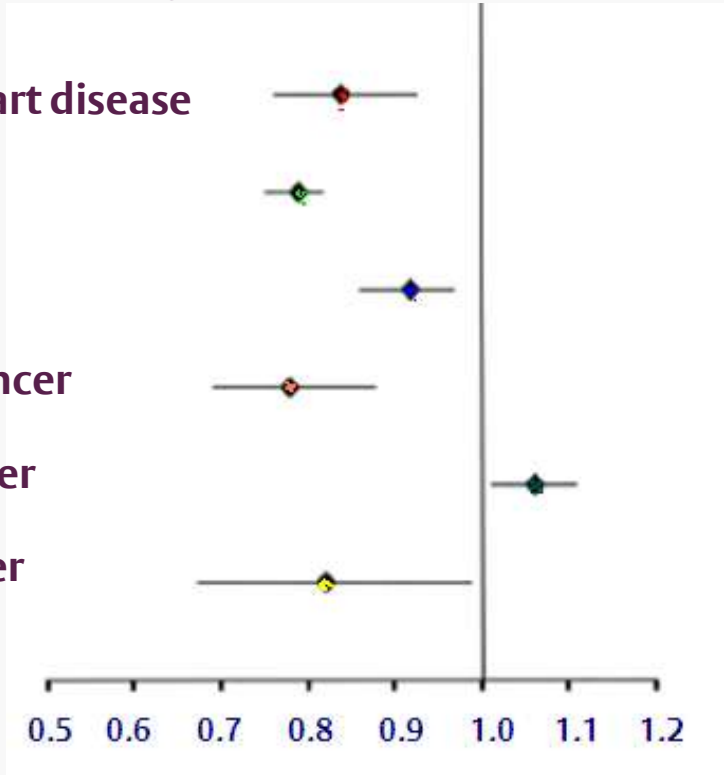
* From the World Cancer Research Fund/American Institute for Cancer Research report

Survival advantage of milk consumption?



Deaths England & Wales 2005 (x1000)

Reduction in risk
In highest consumers



Relative risk (95% CI)

J. Amer Coll Nutr. 2008;27:723S-734S

Hazard ratios according to dairy and calcium intake during childhood in 4374 participants of the Boyd Orr cohort followed up1948–2005 (Van der Pols et al., 2009)

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Outcome	Detail	Hazard ratio
Stroke	Highest *vs.* lowest Ca	0.41
All cause mortality	Highest *vs.* lowest Dairy, Milk or Ca	0.77

The issue of fat-reduced milk and dairy foods

FINALLY: What about low-fat milks etc.....

The appropriate question to ask is:

Do fat-reduced milks and dairy foods provide any additional advantage..... or does the reduction in fat reduce the benefits of whole milk?

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The issue of fat-reduced milk and dairy foods

Study	Subjects	Strategy	RR whole milk		RR fat-reduced
Hu et al.	80,082Females	Prospective	1.67 1.08		0.78 0.82
Lockheart et al	211 subjects	Case-control	0.48		0.96
Kampman et al	16,945 sibjects	Case-control	1.1 0.9		0.8 0.7
Tseng et al	3512 males	Prospective	0.8		1.5
Gallus et al	3247 subjects	Case-control	0.99 1.22 1.06		0.84 0.76 1.11

Although a number of studies report disease rates in su… …ose … … health-related behaviours by subjects on low-fat milk.

Therefore, a statement by German and Dillard is appropriate:

"Such hypotheses [about fat-reduced milks] ***are the basis of sound scientific debate; however they are not the basis of sound public health policy."***

Saturated fats: what dietary intake? Am J Clin Nutr 80:550-9, 2004.

Hazard ratios (and 95% CIs) for 2-y incidence of hypertension by quartile dairy product intake in 2245 Dutch adults aged >=55 y (Engberink et al., 2009)

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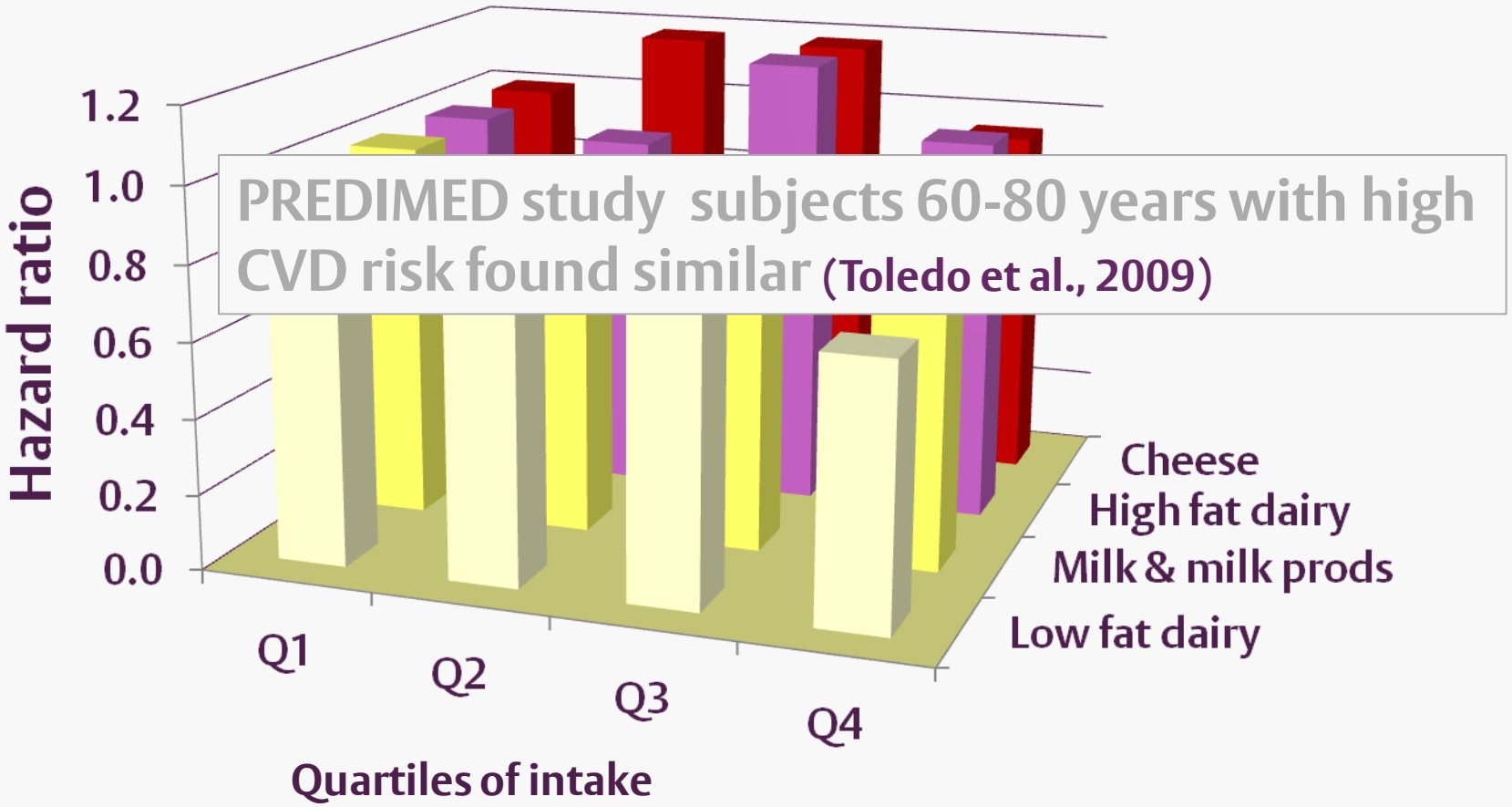
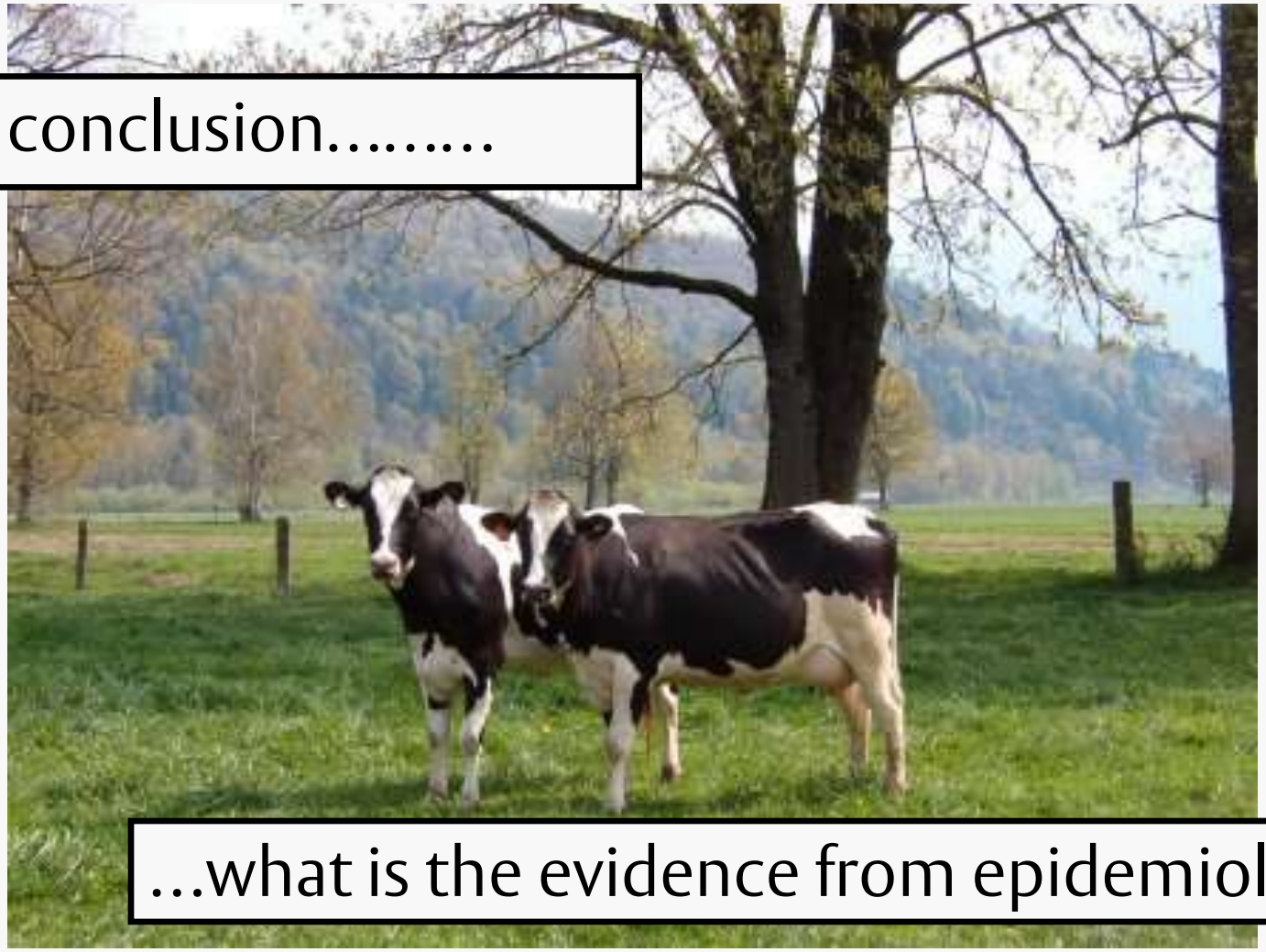


PREDIMED study subjects 60-80 years with high CVD risk found similar (Toledo et al., 2009)

Dairy products and health

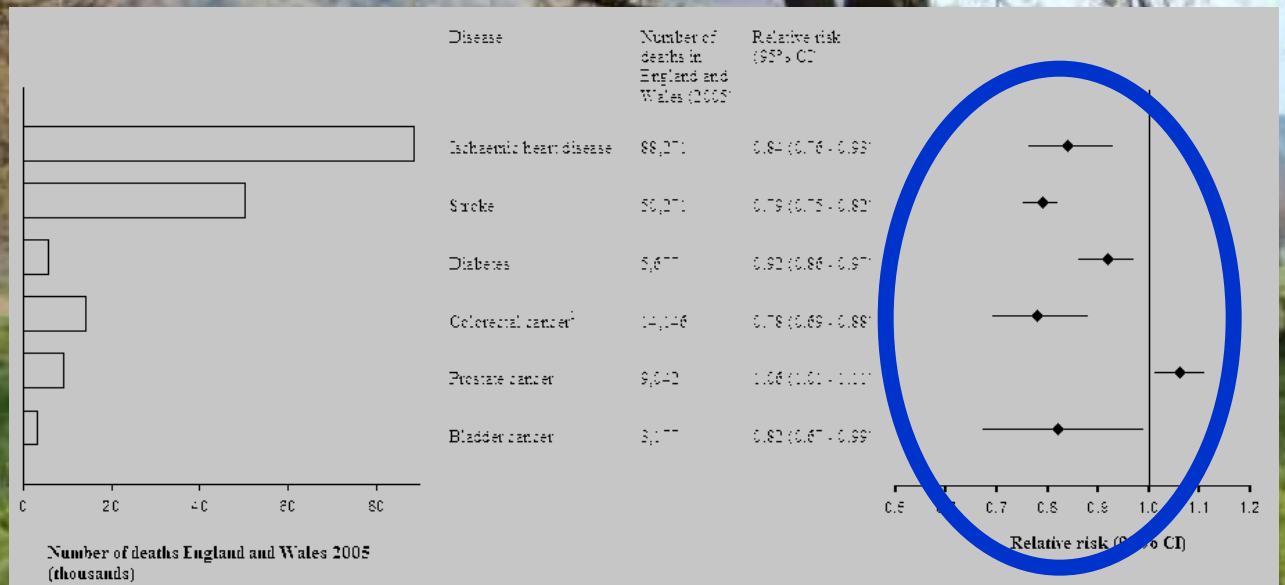
In conclusion……



…what is the evidence from epidemiology?

Dairy products and health

The evidence from epidemiology



Conclusions

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- Milk appears to offer some vascular protection and overall provides a survival advantage
- Vascular benefits may be due to effects on BP and BMI control
- May not apply to cheese and butter and what about fat reduced milk?
- Epidemiology does not assess cause/mechanisms and there is always a risk of confounding factors but…
- ..it should direct and focus research effort
- All of this should remind us that we consume foods not molecules…
- …and milk is perhaps the most misunderstood food..

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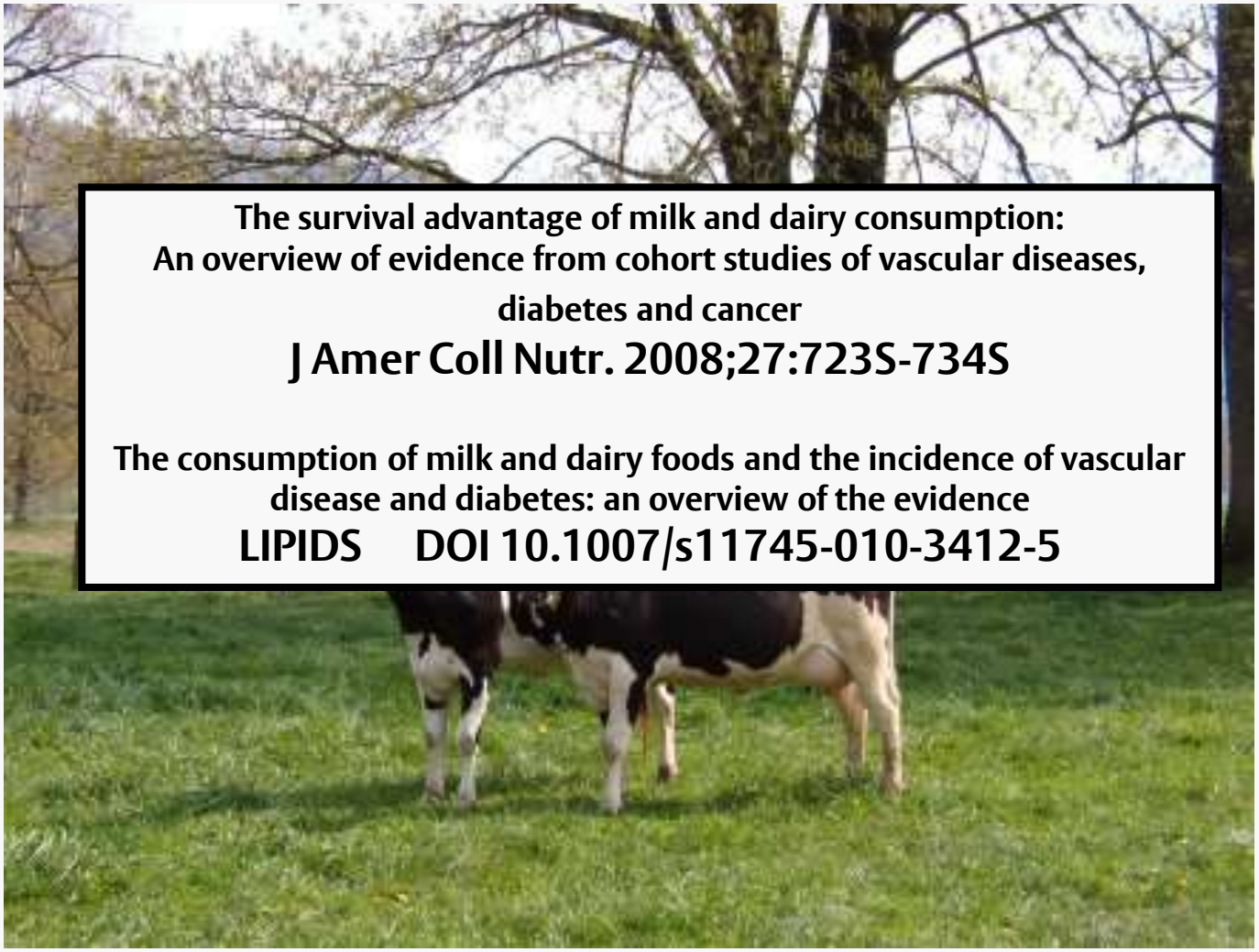
Dairy products and health



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Thank you

Professor Ian Givens, *University of Reading*
Professor Peter Elwood, *Cardiff University*
with Janet Pickering and Dr John Gallacher

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Following slides for possible use in discussion

And really finally, the saturated fat issue

The appropriate question to ask is:

Do milks and dairy foods with reduced saturated fatty acids provide any additional advantage……..

Sources of saturated fats

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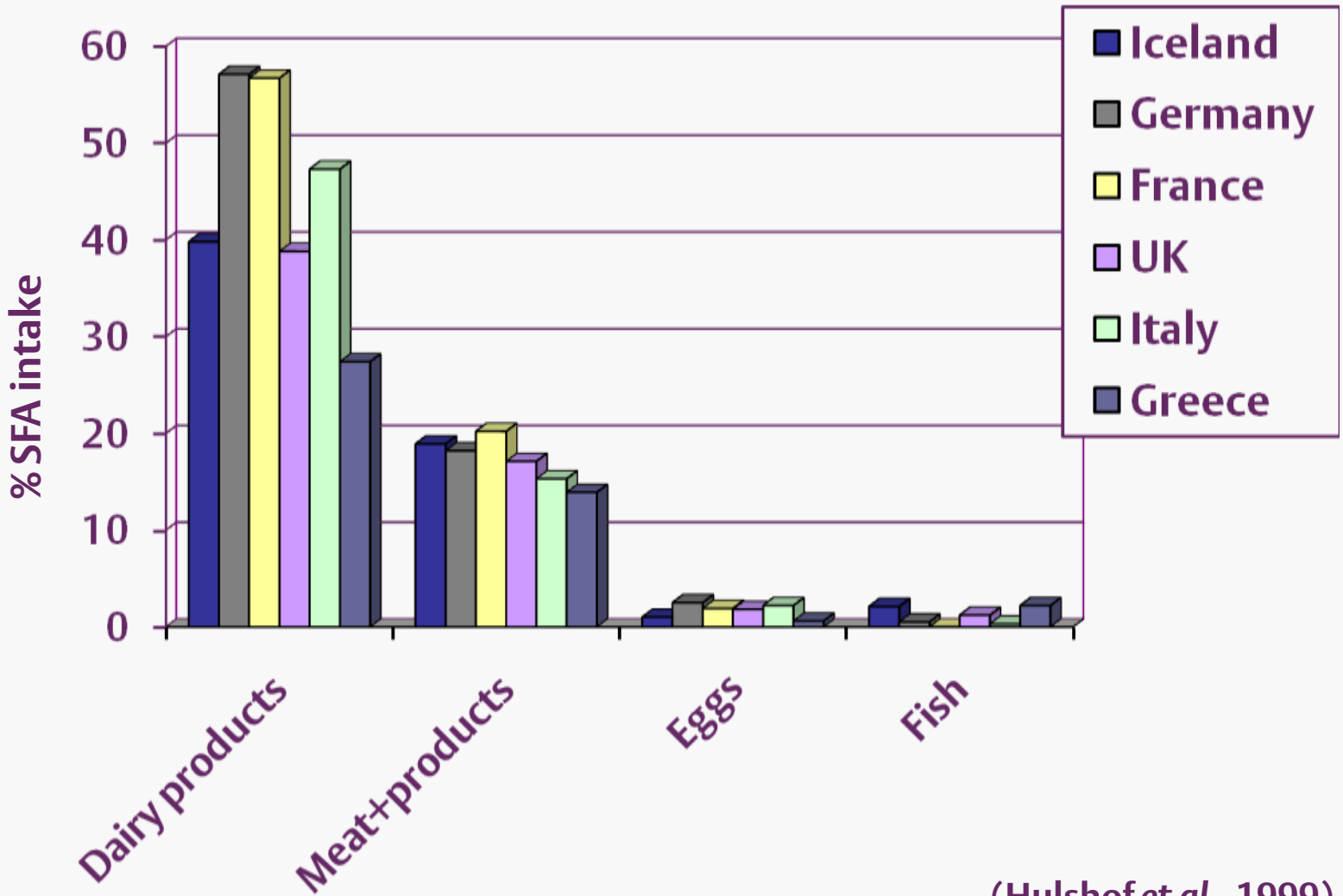

(Hulshof *et al.*, 1999)

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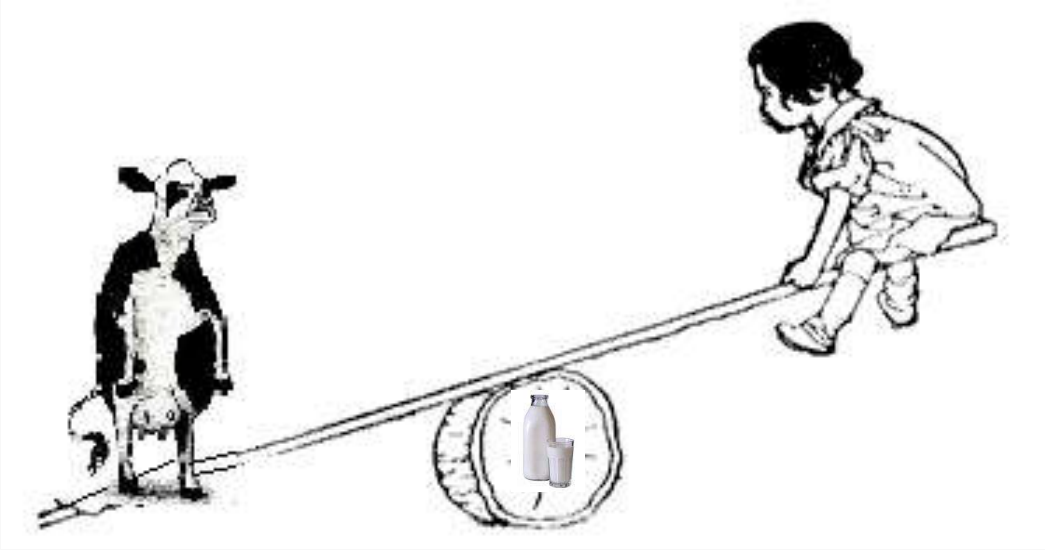
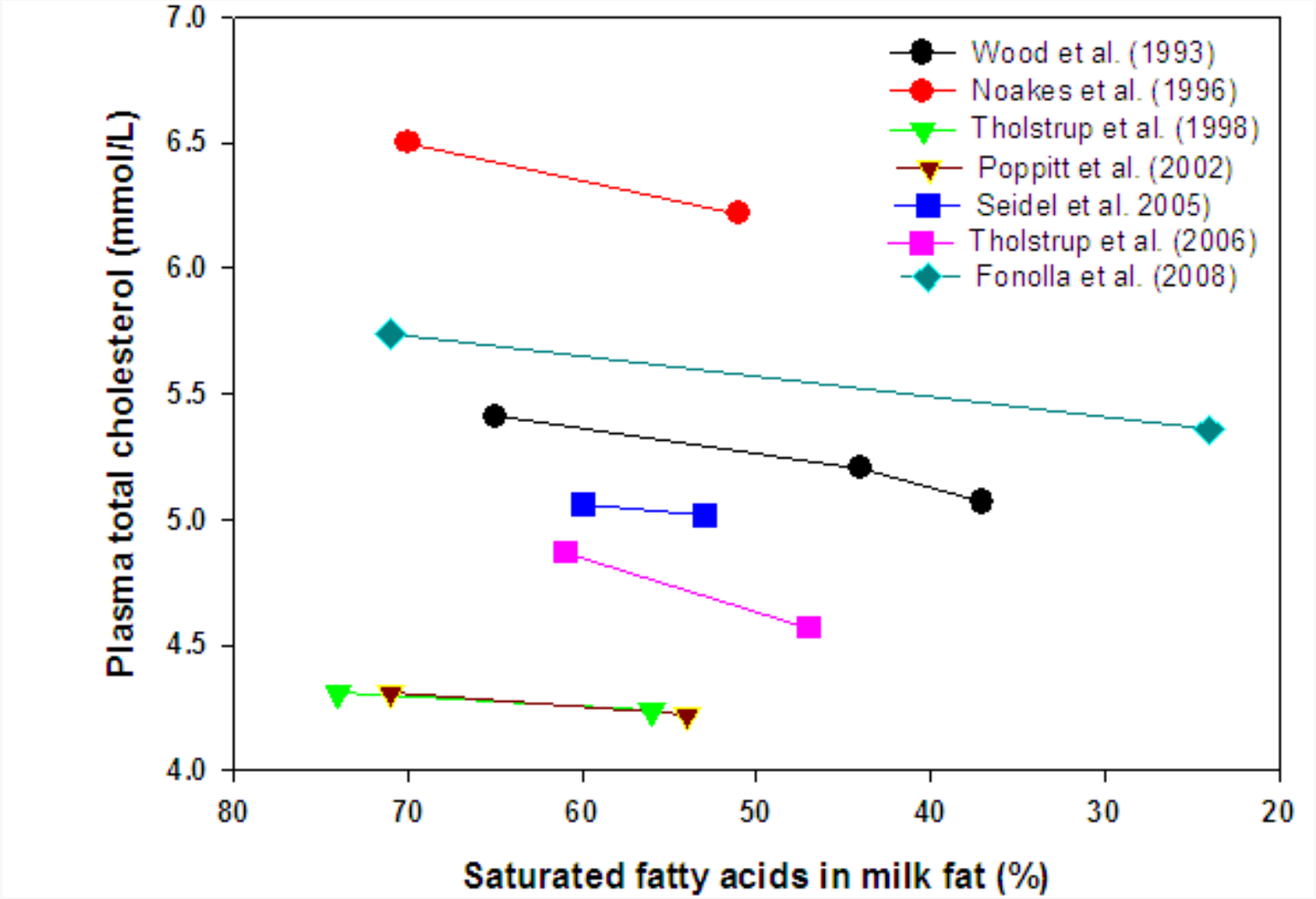
So can we improve the health value of milk?



Effect of reducing SFA in milk fat on total cholesterol



Effect of reducing SFA in milk fat on total:HDL- cholesterol