

Dairy products and vascular disease prevention -evidence from prospective studies



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with Janet Pickering and John Gallacher

Dairy products and vascular disease prevention

The authors have no connection of any kind with the dairy industry or any related industry, nor did they receive any grant for the work to be described.

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The three sources of evidence in medicine:

- **clinical evidence** – *to do with the diagnosis and treatment of disease*
- **laboratory evidence** – *to do with mechanisms in disease*
- **epidemiology** - **the truth!**

Evidence based medicine

"...conclusions within clinical practice be based
on all the evidence from bias-free
and never on a selection of
because they confirm

**So, upon what evidence should public health
nutrition policy be based?**

'Public health nutrition policy should not be unaware of
evidence-based conclusions...'
benefits and risks of dairy product
cannot be judged from 'effects upon
selected physio-pathological variates'. Alvarez-Leon

There are three sources of evidence in medicine:

- **CLINICAL EVIDENCE** – *based on patients;*
focused on the diagnosis and treatment of disease
- laboratory evidence – *to do with mechanisms in disease*
- epidemiology

Evidence from clinical studies based on patients

Milk consumption in patients prior to a heart attack:

STRATEGY

Patients with a myocardial infarct (cases), and 'subjects with no vascular disease (controls) are questioned about their earlier milk consumption

Evidence from clinical studies based on patients

Milk consumption in patients prior to a heart attack:

<i>Study</i>	<i>Numbers</i>	<i>Previous milk consumption by the 'cases'</i>
Gramenzi et al (1990)	287 cases 649 controls	10% lower than in controls
Tavani et al (2002)	507 cases 478 controls	22% lower than in controls
Lockheart et al (2006)	106 cases 105 controls	18% lower than in the controls
Biong et al (2008)	111 patients 107 controls	13% lower dairy fat than controls

Evidence from clinical studies based on patients

Milk consumption in patients prior to a heart attack:

<i>Study</i>	<i>Numbers</i>	<i>Previous milk consumption by the 'cases'</i>
Gramenzi et al	287 cases	10% lower than
(2008)	107 controls	than controls

Probability of a high milk consumption in the cases before the heart attack, relative to the probability in the controls:

0.83 (0.16, 0.99)

Evidence from clinical studies based on patients

Milk consumption in patients prior to a heart attack:

<i>Study</i>	<i>Numbers</i>	<i>Previous milk consumption by the 'cases'</i>
Gramenzi et al	287 cases	10% lower than
<u>Limitations:</u> <ul style="list-style-type: none">- depends on memory of past milk consumption- only patients who have survived a heart attack questioned		
Biong et al (2008)	111 patients 107 controls	15% lower daily fat than controls

There are three sources of evidence in medicine:

- Clinical evidence – *based on patients;*
focused on the diagnosis and treatment of disease
- **LABORATORY EVIDENCE** – *mechanisms in disease*
- Epidemiology

Evidence from laboratory studies

Effects of milk on biological mechanisms:

1. *it raises cholesterol 1,249 papers!*
2. *it lowers blood pressure*
3. *it raises homocysteine*
4. *it contains xanthine oxidase*
5. *it can carry bacteria and fungi*
6. *lactose tolerance increases vascular risk*
7. *casein A2 enhances atherogenesis*
8. *the calcium increases arterial calcification*
9. *it is low in copper*
10. *it contains phytoestrogens*
11. *for some people milk is taken as a substitute for alcohol!!*

Evidence from laboratory studies

Effects of milk on biological mechanisms:

Cholesterol level in lowest and highest milk drinkers :

Study			Chol. In subjects with highest milk intakes
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.....

Evidence from laboratory studies

Effects of milk on biological mechanisms:

Blood pressure in lowest and highest milk drinkers :

STUDY	Population	BP in subjects with highest milk intakes
Ackley et al 1983	5,050	2.5 mmHg Lower
Jorde& Bonas 2000	7,735	2.2 mmHg lower
Shaper et al 1991	1,340	3.3 mmHg lower
Vivjer et al 1992	1,265	4.0 mmHg lower
Ness et al 2001	5,765	2.2 mmHg lower

Evidence from laboratory studies

DETERMINANTS



Mechanisms

Risk factors



DISEASE

Evidence from laboratory studies

DETERMINANTS

Milk drinking



Mechanisms

Risk factors

Cholesterol (raised)

Blood pressure (lowered)



DISEASE

...and what about other mechanisms?

There are three sources of evidence in medicine:

- Clinical evidence – *based on patients;*
focused on the diagnosis and treatment of disease
- Laboratory evidence – *to do with mechanisms in disease*
- **EPIDEMIOLOGY**

Evidence from prospective epidemiological studies

DETERMINANTS

**Milk drinking recorded
for a large number of
healthy subjects**

DISEASE

**New cases of
vascular disease etc.**

Evidence from prospective epidemiological studies

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.*

Limitations:

Milk consumption may be associated with other health related behaviours ('confounding' factors)

'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.

Ischaemic heart disease

Study	Number of subjects (length of follow-up)	Number of heart disease events	Relationship adjusted for...	Adjusted estimate of risk (95% CI)	Predictive factor
Elwood et al (2004) Caerphilly Cohort	2,512 men (Followed for 20 years)	493 Total IHD events	Age, smoking, social class, IHD, BMI, energy, alcohol, fasting cholesterol HDL cholesterol and triglycerides	0.71 (0.40 - 1.26)	One or more pint/day vs little or no milk/day

Ischaemic heart disease

Study	Number of subjects (length of follow-up)	Number of heart disease events	Relationship adjusted for...	Adjusted estimate of risk (95% CI)	Predictive factor
21 cohorts studies	4.5M person years	21,571 IHD events	<i>various</i>		Milk or dairy intake: <i>measured variously</i>

Relative risk in highest milk subjects

RR 0.95 *(0.92 to 0.99)*

Heterogeneity $p=0.747$

Ischaemic stroke

Study	Number of subjects (length of follow-up)	Number of stroke events	Relationship adjusted for...	Adjusted estimate of risk (95% CI)	Predictive factor
Ness et al (2001) Cohort of Scottish men	5,765 men (Followed for 25 years)	196 Stroke deaths	Age, social class, health behaviour	0.84 (0.40 - 1.26)	More than one pint/day vs less than 1/3 per day

Ischaemic stroke

Study	Number of subjects (length of follow-up)	Number of stroke events	Relationship adjusted for...	Adjusted estimate of risk (95% CI)	Predictive factor
11 cohorts studies	8.4M person years	9,725 Stroke events	<i>various</i>		Milk or dairy intake: <i>measured variously</i>

RR 0.79 *(0.68 to 0.91)*

Heterogeneity $p < 0.001$

Haemorrhagic stroke

Study	Number of subjects (length of follow-up)	Number of stroke events	Relationship adjusted for...	Adjusted estimate of risk (95% CI)	Predictive factor
5 cohorts studies	360K person years	5,946 Stroke event	<i>various</i>		Milk or dairy intake: <i>measured variously</i>
<p>RR 0.75 (<i>0.60 to 0.94</i>)</p> <p>Heterogeneity $p < 0.014$</p>					

Subarachnoid bleed

Study	Number of subjects (length of follow-up)	Number of sub-arach. bleeds	Relationship adjusted for...	Adjusted estimate of risk (95% CI)	Predictive factor
3 cohorts studies	960K person years	484 Subarach events	<i>various</i>		Milk or dairy intake: <i>measured variously</i>

RR 0.65 *(0.32 to 1.31)*
Heterogeneity $p < 0.014$

DIABETES

Diabetes

Study	Number of subjects (length of follow-up)	Number of new diabetes	Relationship adjusted for...	Adjusted estimate of risk (95% CI)	Predictive factor
5 cohorts studies	1.7M person years	7,121 New diabetes	<i>various</i>		Milk or dairy intake: <i>measured variously</i>

RR 0.85 (*0.75 to 0.96*)
Heterogeneity $p < 0.122$

Other overviews of milk/dairy foods

Soedamah-Muthu et al. Am J Clin Nutr. 2011;93:158-71

14 prospective studies: CVD **RR 0.94** (0.89,0.99)
6 studies **stroke** **RR 0.87** (0.72,1.05)

Gibson et al. Brit J Nutr 2009;102:1267-75.

12 cohort studies : “...no consistent evidence that dairy food consumption is associated with a higher risk of CHD”

Pitas et al. 2007

4 prospective studies: diabetes **RR 0.86** (0.79, 0.93)

Xing Tong et al: Unpublished

7 prospective studies: diabetes **RR 0.86** (0.79, 0.92)

USE OF BUTTER and CHEESE

Use of butter

Study	Number of subjects (length of follow-up)	Number of vascular events	Relationship adjusted for...	Adjusted estimate of risk (95% CI)	Predictive factor
5 cohorts studies	360K person years	3,310 vascular events	<i>various</i>		Butter use: <i>measured variously</i>

RR 0.93 *(0.84 to 1.02)*

Heterogeneity $p < 0.333$

Use of cheese

Study	Number of subjects (length of follow-up)	Number of vascular events	Relationship adjusted for...	Adjusted estimate of risk (95% CI)	Predictive factor
6 cohorts studies	400K person years	2,766 vascular events	<i>various</i>		Cheese use: <i>measured variously</i>

RR 0.90 (*0.79 to 1.03*)
Heterogeneity $p < 0.032$

SUMMARY

Ischaemic heart disease:

Published estimate

0.92 (0.80-0.99)

Ischaemic stroke:

Published estimate:

0.79 (0.68, 0.91)

Diabetes

Published estimate

0.85 (0.75, 0.96)

BUTTER:

Published estimate

0.93 (0.84, 1.02)

CHEESE:

Published estimate

0.90 (0.79, 1.03)

SUMMARY

Ischaemic heart disease:

Published estimate **0.92** (0.80-0.99)
With 2 more recent studies **0.95** (0.92, 0.99)

Ischaemic stroke:

Published estimate: **0.79** (0.68, 0.91)
With 1 more recent studies **0.81** (0.71,0.92)

Diabetes

Published estimate **0.85** (0.75, 0.96)
With 2 more recent studies **0.91** (0.80, 1.03)

BUTTER:

Published estimate **0.93** (0.84, 1.02)
With 2 more recent studies **0.95** (0.87, 1.03)

CHEESE:

Published estimate **0.90** (0.79, 1.03)
With 4 more recent studies **0.89** (0.81, 0.97)

Dairy foods and cancer

Dairy foods and cancer

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

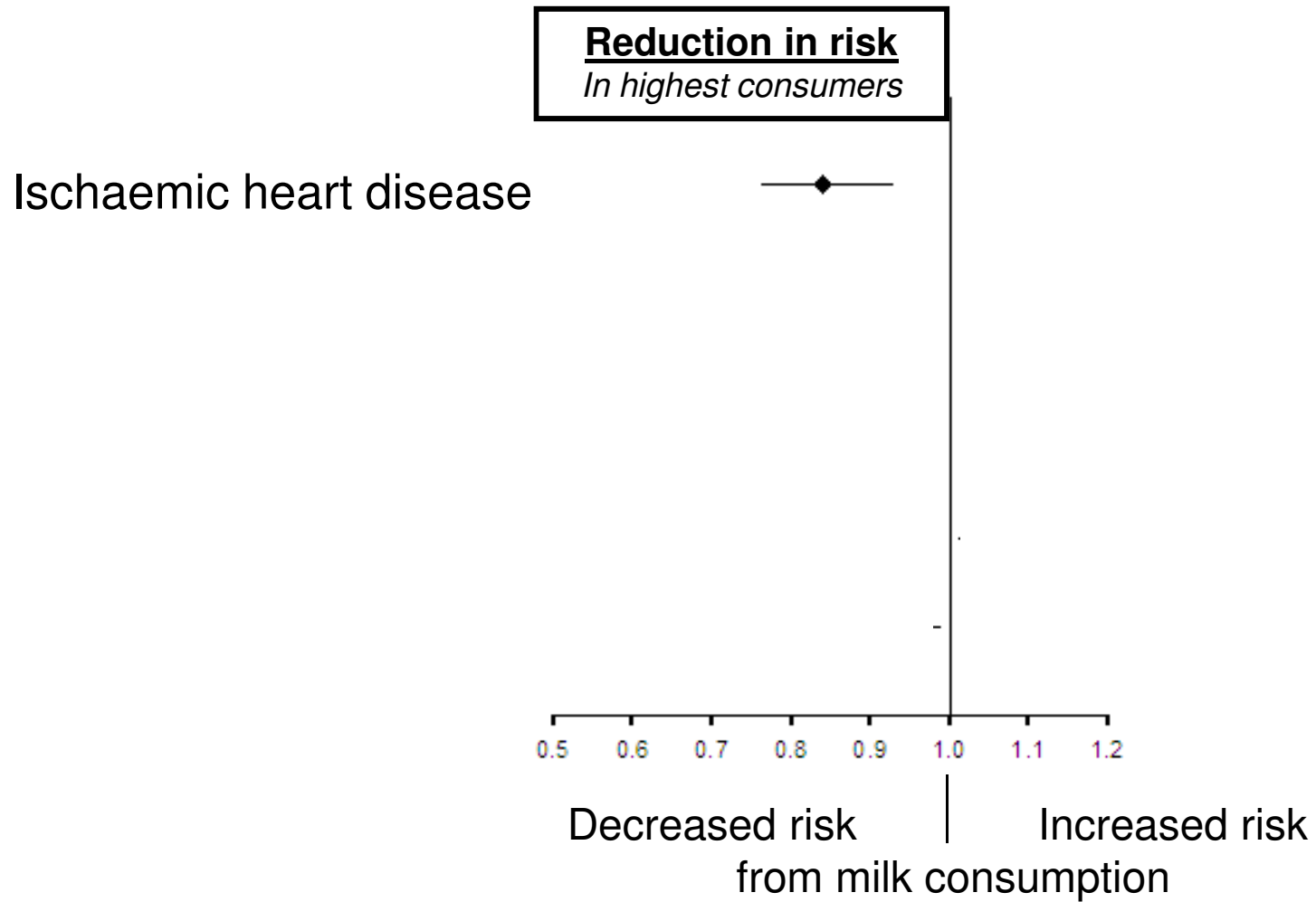
The World Cancer Research Fund and the American Institute for Cancer Research issued a major report in 2007 on foods and cancer.

Dairy foods and cancer

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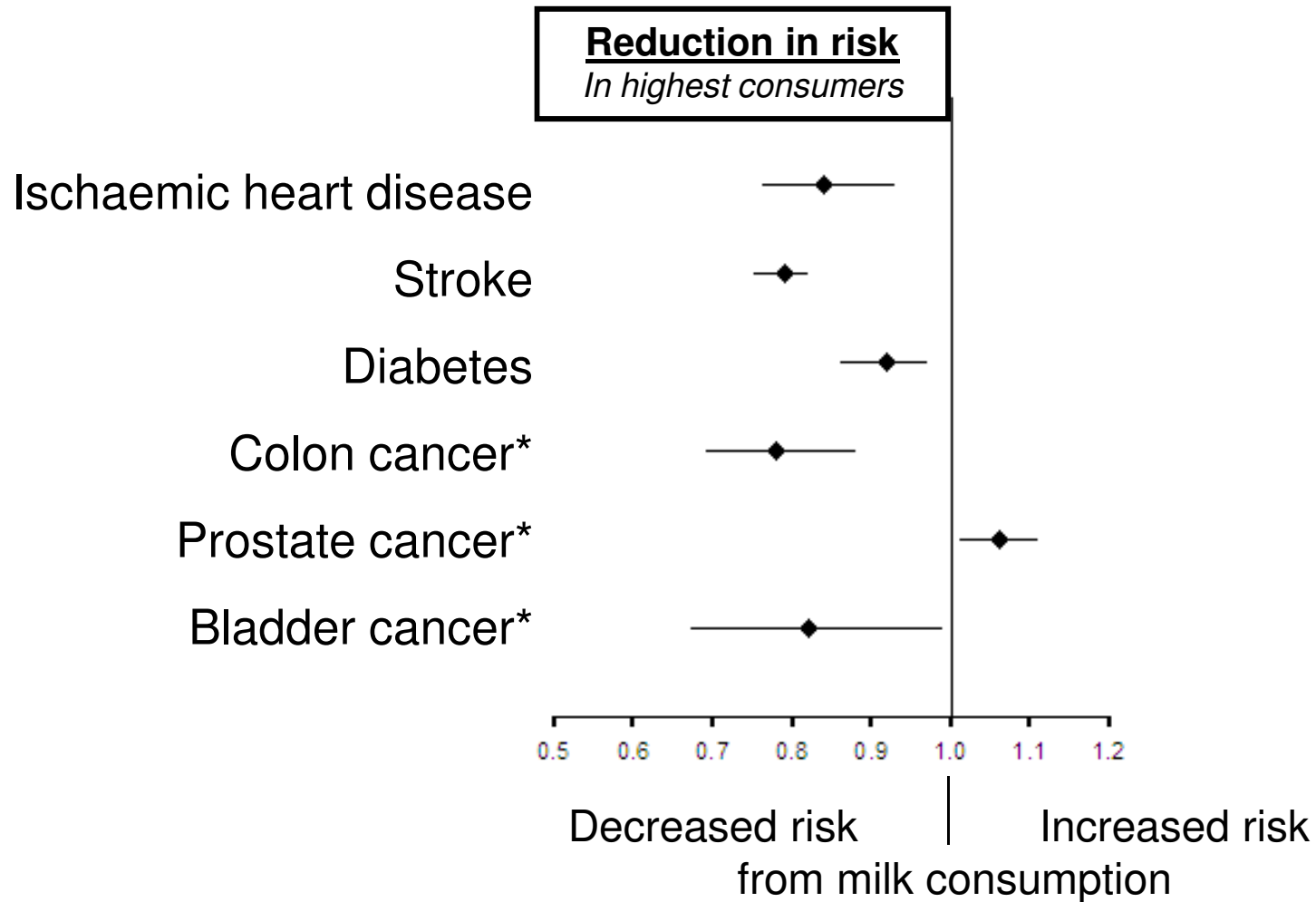
World Cancer Res. Group American Institute for Cancer Research	No. of studies (<i>heterogeneity</i>)	RR attributable to milk and dairy foods
<u>Colon cancer</u>	4 cohorts (<i>not stated</i>)	0.94 (0.85, 1.03)
	10 cohorts (<i>not stated</i>)	0.78 (0.69, 0.88)
<u>Bladder cancer</u>	4 cohorts (<i>moderate</i>)	0.82 (0.67, 0.99)
<u>Prostate cancer</u>	8 cohorts (<i>moderate</i>)	1.06 (1.01, 1.11)

SUMMARY



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

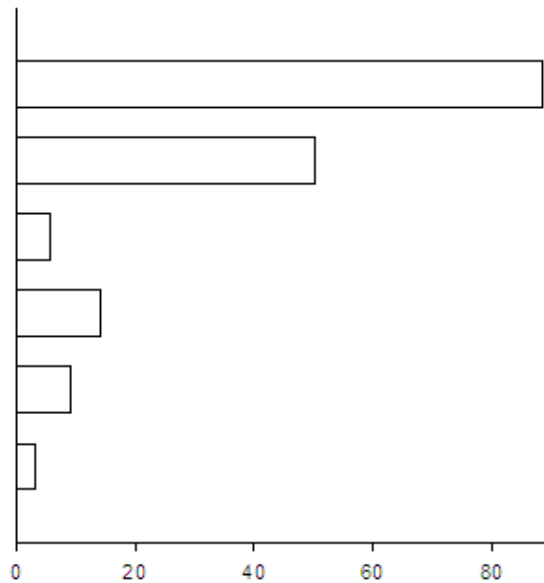
SUMMARY



FROM: J Amer Coll Nutr. 2008;27:723S-734S and *The World Cancer Report

SUMMARY

Number of deaths in UK

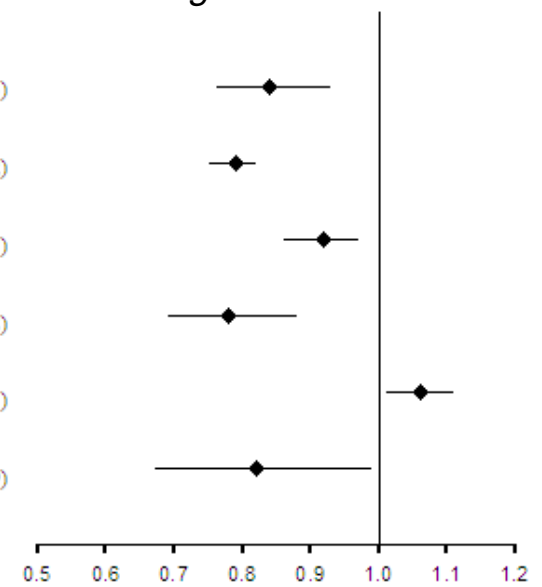


Number of deaths England and Wales 2005 (thousands)

Disease	Number of deaths in England and Wales (2005)	Relative risk (95% CI)
Ischaemic heart disease	88,271	0.84 (0.76 - 0.93)
Stroke	50,271	0.79 (0.75 - 0.82)
Diabetes	5,677	0.92 (0.86 - 0.97)
Colorectal cancer ¹	14,146	0.78 (0.69 - 0.88)
Prostate cancer	9,042	1.06 (1.01 - 1.11)
Bladder cancer	3,177	0.82 (0.67 - 0.99)

Reduction in risk

In highest consumers



Relative risk (95% CI)

FROM: J Amer Coll Nutr. 2008;27:723S-734S and The World Cancer Report

FINALLY: What about low-fat dairy produce.....

Low fat dairy products

First, note that cohort studies are long-term, and most of the evidence already presented comes from cohorts of subjects who were drinking whole milk.

Low fat dairy products

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?***

A recent study in the USA reported an association between a unique fatty acid in whole milk (*trans*-palmitoleic acid) and a 'substantial' reduction in diabetes.

Mosafarian et al 2010

Low fat dairy products

Study	Subjects	Strategy	RR whole milk	RR fat-reduced
Hu et al.	80,082 Females	Prospective	1.67	0.78
			1.08	0.82
Lockheart et al.	211 subjects	Case-control	0.48	0.96

Although a number of studies report disease rates in subjects who consume natural dairy foods, and in those who consume reduced fat dairy foods, the data are hopelessly confounded due to the adoption of other health-related behaviours by subjects on low-fat milk.

Kampman et al.	16,945 subjects	Case-control	1.1	0.8
			0.9	0.7
Tseng et al.	3512 males	Prospective	0.8	1.5
Gallus et al.	3247 subjects	Case-control	0.99	0.84
			1.22	0.76

SUMMARY

Study	Subjects	Strategy	RR whole milk	RR fat-reduced
Hu et al.	80,082 Females	Prospective	1.67	0.78
			1.08	0.82
Lockheart et al	211 subjects	Case-control	0.48	0.96
Lui et al.	10,066 females	Case-control	0.71	0.78

Although a number of studies report disease rates in subjects who consume natural dairy foods and

in data of the relation

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.

LOW-fat MILK.

Tseng et al	3512 males	Prospective	0.8	1.5
Gallus et al	3247 subjects	Case-control	0.99	0.84
			1.22	0.76
			1.06	1.11

Dairy products and vascular disease prevention

The bottom line: Survival.....



All-cause deaths

All-cause deaths

Study	Number of subjects (length of follow-up)	Number of deaths	Relationship adjusted for...	Adjusted estimate of risk (95% CI)	Predictive factor
10 cohorts studies	0.76M person years	21,402 deaths	<i>various</i>		Milk or dairy intake: <i>measured variously</i>
<p>RR 0.96 (<i>0.88 to 1.06</i>)</p> <p>Heterogeneity $p < 0.07$</p>					

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**The survival advantage of milk and dairy consumption:
An overview of evidence from cohort studies of vascular diseases,
diabetes and cancer**

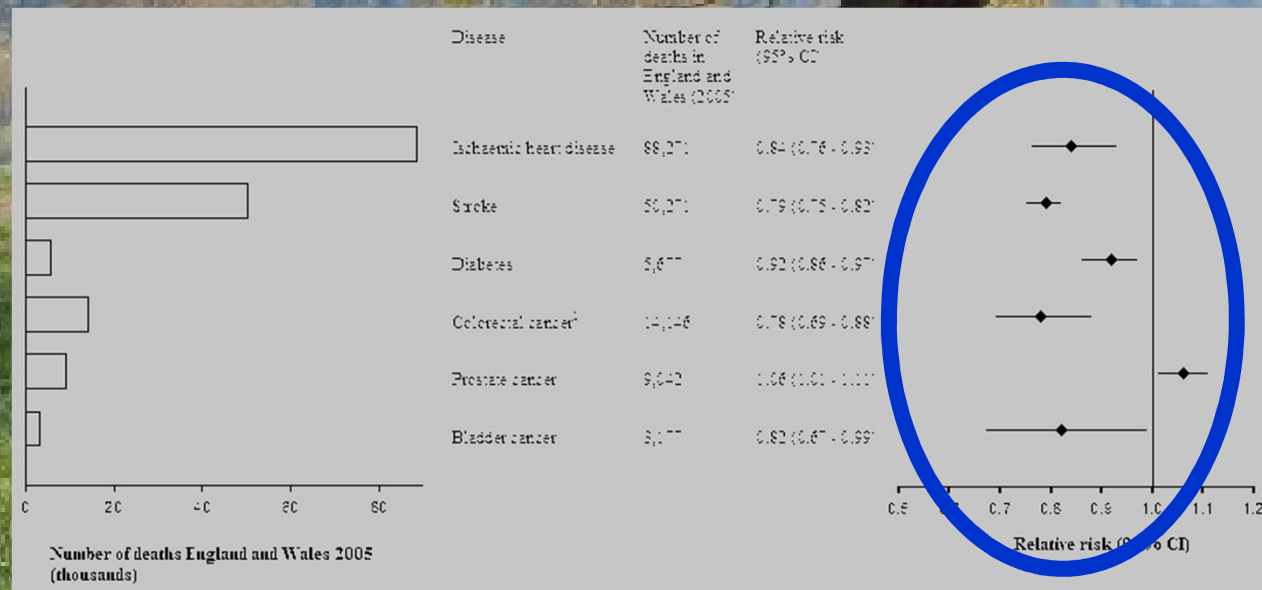
J Amer Coll Nutr. 2008;27:723S-34S

**The consumption of milk and dairy foods and the incidence of
vascular disease and diabetes: an overview of the evidence**

Lipids: 2010;45:925-

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Dairy products and (vascular) disease prevention



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with Janet Pickering and John Gallacher