Forebyggelse af metabolisk syndrom vha. mejeriprodukter

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Mejeriforskningens Dag 2. marts 2017, Hotel Legoland

Metabolic Syndrome (MeS) (IDF-definition)

20 – 25 % of adults in Western countries have MeS

- Apple form (central obesity)
- + (two of the following 4 factors):
- Increased fasting Triglyceride
- Reduced HDL Cholesterol
- Increased blood pressure
- Increased fasting glucose





Agenda: Can we combat features of the metabolic syndrome?

- Dairy products and weight
- Dairy products and triglycerides
- Dairy products and blood pressure
- Dairy products, blood glucose and risk of type 2 diabetes

Agenda

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Weight change between dairy and control groups

		No effect
	Study (year)	Mean difference (95% CI)
With energy restriction	With energy restriction Zemel et al $(2004)^{29}$ Thompson et al $(2005)^{43}$ Zemel et al $(2005)^{27}$ Zemel et al $(2005)^{28}$ Harvey-Berino et al $(2005)^{44}$ Zemel et al $(2009)^{26}$ Faghih et al $(2010)^{25}$ Van Loan et al. 2011 $(2011)^{39}$ Smilowitz et al $(2011)^{40}$ Josse et al $(2011)^{45}$ Subtotal	-4.47 (-10.45, 1.51) -1.80 (-5.45, 1.85) -5.07 (-8.61, -1.54) -1.64 (-3.17, -0.11) -1.20 (-4.88, 2.48) -1.46 (-3.19, 0.27) -1.56 (-2.61, -0.51) -0.30 (-1.70, 1.10) -1.70 (-8.01, 4.61) 0.20 (-1.73, 2.13) -1.29 (-1.98, -0.60)
Without energy restriction	Without energy restriction Barr et al, Females $(2000)^{34}$ Barr et al, Males $(2000)^{34}$ Zemel et al(maintenance) $(2005)^{27}$ Gunther et al $(2005)^{32}$ Wennersberg et al $(2009)^{31}$ Palacios et al $(2010)^{30}$ Subtotal Overall	1.40 (-2.31, 5.11) 4.00 (-0.99, 8.99) 0.20 (-1.33, 1.73) 0.70 (-0.74, 2.14) 0.00 (-0.94, 0.94) 0.90 (-5.02, 6.82) 0.33 (-0.35, 1.00) -0.61 (-1.29, 0.07)

Abargouei et al Int J Obes 2012, 36:1484-1493

Conclusion

Increased dairy consumption without energy restriction may not lead to a change in weight or body composition.

Inclusion of dairy products in energy-restricted weight loss diets affects body weight, body fat mass, lean body mass and waist circumference compared with that in usual weight loss diets.

Weight loss in short-term (< 1 year) and long-term studies

Short-term < 1 y

Long-term > 1 y

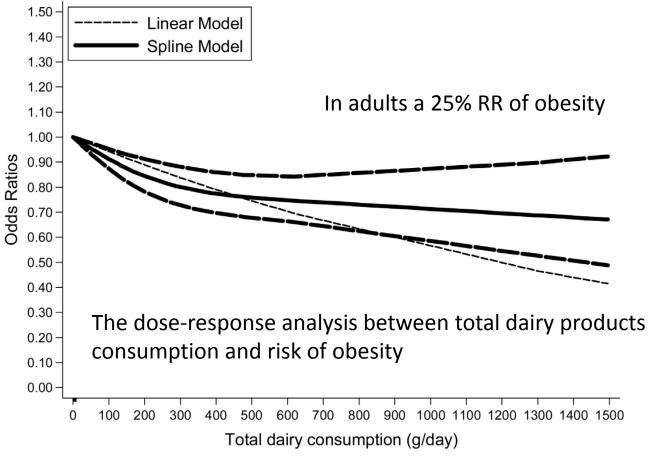
Chen et al Am J Clin Nutr 2012,96:735-747

Study A body weight ID WMD 95% CI(kg) Weight(%) Short-term (<1y) Barr, 2000 (3) 0.54 (-0.30, 1.38) 4.61 Bowen et al, 2005 (14) 0.08 (-2.10, 2.26) 2.74 Buchowski et al, 2010 (15) -1.30 (-3.15, 0.55) 3.16 Faghih et al, 2011 (25) -1.56 (-2.61, -0.51) 4.31 Ghadirian et al. 1995 (16) 0.50 (-0.69, 1.69) 4.12 Gilbert et al, 2011 (26) -2.15 (-4.61, 0.31) 2.43 0.20 (-2.00, 2.40) Josse et al, 2011 (20) 2.72 1.00 (-1.95, 3.95) 1.96 Palacios et al, 2011 (6) Rosado et al, 2011 (29) -0.40 (-0.63, -0.17) 5.18 -1.50 (-2.05, -0.95) 4.94 Stancliffe et al, 2011 (36) 1.60 (-1.03, 4.23) Thomas et al, 2010 (40) 2.26 Thomas et al. 2011 (32) -1.40 (-4.03, 1.23) 2.26 Van Loan et al. 2011 (37) -0.30 (-1.70, 1.10) 3.81 van Meijl et al, 2010 (39) 0.30 (-0.69, 1.29) 4.40 Wagner et al, 2007 (28) 1.60 (-0.62, 3.82) 2.70 Wennersberg et al, 2009 (38) 0.00 (-0.94, 0.94) 4.47 -4.47 (-10.45, 1.51) 0.67 Zemel et al, 2004 (9) Zemel et al. 2005a (35) -5.07 (-9.46, -0.68) 1.12 -0.20 (-1.73, 1.33) Zemel et al. 2005a(maintenance) (35) 3.62 Zemel et al, 2005b (7) -1.64 (-3.17, -0.11) 3.61 Zemel et al, 2009 (8) -1.46 (-3.19, 0.27) 3.33 Subtotal (I-squared = 59.2%, p < 0.001) -0.47 (-0.90, -0.03) 68.39 Long-term (≥1y) 0.80 (-1.54, 3.14) Baran et al, 1990 (13) 2.56 Chee et al. 2003 (30) -0.12 (-0.90, 0.66) 4.69 Gunther et al. 2005a (17) 0.31 (-0.80, 1.42) 4.23 Gunther et al, 2005b (18) 0.10 (-2.15, 2.35) 2.66 Harvey-Berino et al, 2005 (33) -2.30 (-6.00, 1.40) 1.45 1.00 (0.30, 1.70) 4.78 Kukuljan et al, 2009 (27) Lau et al, 2001 (31) 0.78 (0.02, 1.54) 4.71 Manios et al. 2009 (5) 2.10 (1.73, 2.47) 5.10 Thompson et al, 2005 (34) 0.30 (-3.40, 4.00) 1.45 0 Subtotal (I-squared = 80.7%, p < 0.001) 0.66 (-0.14, 1.46) 31.61 Overall (I-squared = 86.3%, p < 0.001) 100.00 -0.14 (-0.66, 0.38) NOTE: Weights are from random effects analysis -10 -5 10 Ω Favors dairy Kg Favors control

Conclusion

Dairy products may have modest benefits in facilitating weight loss in short-term or energy-restricted RCTs.

In 2016 this meta-analysis showed a positive effect of total dairy intake on obesity



Wang et al Annals of Epidemiology 26 (2016) 870e882

Explanations for the weight reducing effect

- Increased calcium intake (reduced lipogenesis; reduced fat absorption)
- Whey protein (beneficial effects on muscle sparing and lipid metabolism)
- Conjugated linolenic acid (regulate adipogenesis)
- Other milk fats?

Long-term study

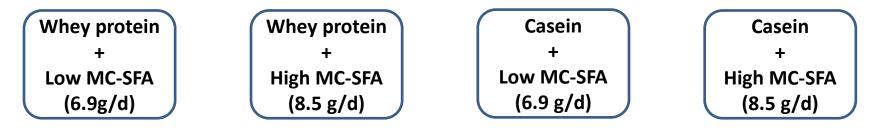
ORIGINAL ARTICLE The effects of proteins and medium-chain fatty acids from milk on body composition, insulin sensitivity and blood pressure in abdominally obese adults

M Bohl¹, A Bjørnshave^{1,2}, MK Larsen³, S Gregersen¹ and K Hermansen¹

Bohl M et al Eur J Clin Nutr. 2017 Jan;71(1):76-82

Design of DairyHealth

- 12-week, randomized, double-blinded, diet intervention study.
- Inclusion: abdominal obese participants, weight stable > 3 month, min. 18 years old.
 - 63 subjects randomized into four diets.
 - 60 g protein supplement
 - 63 g milk fat supplement

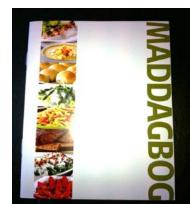


Dietary supplementation (12-week intervention)

- 60 g protein (powder + shaker)
- 63 g milk fat/day (2 rolls, 1 cake, 25 g butter)
 - 6.9 g/day of MCFA in low-MCFA butter
 - 8.5 g/day of MCFA in high-MCFA butter
 - A relative increase of 24% in high- compared with low-MCFA
- Daily energy intake from test products: 6,200 kJ (baseline mean daily energy intake ~ 8.200 kJ)







Body composition

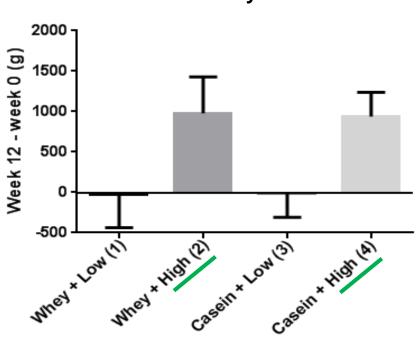
• Evaluated by Dual-Energy X-ray Absorptiometry (DEXA) scans





Bohl M et al Eur J Clin Nutr. 2017 Jan;71(1):76-82

Results

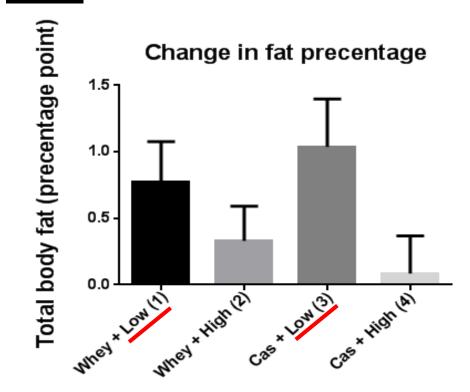


Lean body mass

Lean body mass increased with **981 g** (P = 0.010) **after high**compared with low-MCFA

Bohl M et al Eur J Clin Nutr. 2017 Jan;71(1):76-82

Results



Body fat percentage increased by

0.70 percentage points (P = 0.024) after <u>low</u>- compared with high-MCFA.

	Whey + low	Whey + high MC-SFA (n = 13)		Casein +	Two-factor ANOVA, P value			
Characteristic	-			high MC-SFA (n = 13)	Protein	Fatty acid composition	Interaction	
Total body mass (g), change	1030 (128, 1932)	1846 (469 <i>,</i> 3222)	1295 (400, 2190)	1500 (603 <i>,</i> 2397)	0.923	0.295	0.527	
Lean body mass (g), change	-26 (-930 <i>,</i> 879)	981 (4, 1 958)	-18 (-653, 617)	938 (28, 1 593)	0.961	0.010	0.946	
Lean body percentage (% of total body mass), change	-0.7 (-1.4, - 0.1)	-0.2 (-0.8, 0.3)	-1.0 (-1.8, - 0.2)	0.1 (-0.6 <i>,</i> 0.8)	0.919	0.015	0.367	
Body fat mass (g), change	1060 (523, 1596)	885 (184 <i>,</i> 1586)	1318 (444, 2192)	635 (-163, 1433)	0.997	0.208	0.460	
Body fat percentage (percentage points), change	0.8 (0.1, 1.4)	0.3 (-0.2, 0.9)	1.0 (0.3, 1.8)	0.1 (-0.5, 0.7)	0.991	0.024	0.406	

Changes after the 12-week dietary intervention of body composition¹

Conclusion

- Enhanced intake of MC-SFA increased the lean body mass and caused a significantly lower total body-fat percentage compared with lower intake of MC-SFA.
- Consequently, the composition of dairy fat should also be considered when evaluating the impact of dairy products on body composition.

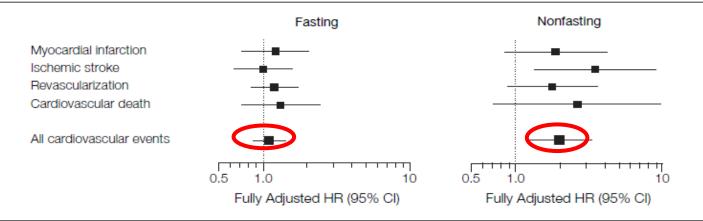
Agenda

- Dairy products and weight
- Dairy products and triglycerides
- Dairy products and blood pressure
- Dairy products, blood glucose and risk of type 2 diabetes

Association of TG with CVD

N = 27,000 womens health study; follow up 11.4 years

Figure 2. Association of Triglyceride Levels With Individual Cardiovascular End Points, According to Fasting Status

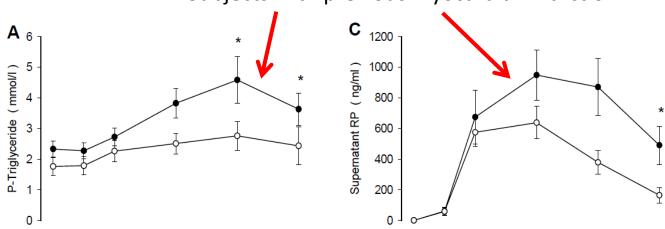


Hazard ratio (HR) and 95% confidence interval (CI) for highest vs lowest tertiles of triglyceride level (see Table 3 for values), adjusted for age, blood pressure, smoking, hormone use, levels of total and high-density lipoprotein cholesterol, diabetes mellitus, body mass index, and high-sensitivity C-reactive protein level.

Differential Postprandial Lipoprotein Responses in Type 2 Diabetic Men with and without Clinical Evidence of a Former Myocardial Infarction

Marius Carstensen¹, Claus Thomsen¹, Ole Gotzsche², Jens Juul Holst³, Jürgen Schrezenmeir⁴, and Kield Hermansen¹

Rev Diabetic Stud (2004) 1:175-184



Subjects with previous myocardial infarction

Black circles = Myocardial infarction (MI) (n=17)
Open circles = Matched control subjects without prior MI (n=15)

Test meal: 1027 kcal (86 g fat, 51 g CHO, 8 g protein and vitamin A)

Conclusion

Type 2 diabetic males with prior MI had higher postprandial triglyceride-rich lipoprotein responses than those without MI, indicating that high responses may be a marker for a high-risk population.



Acute differential effects of dietary protein quality on postprandial lipemia in obese non-diabetic subjects

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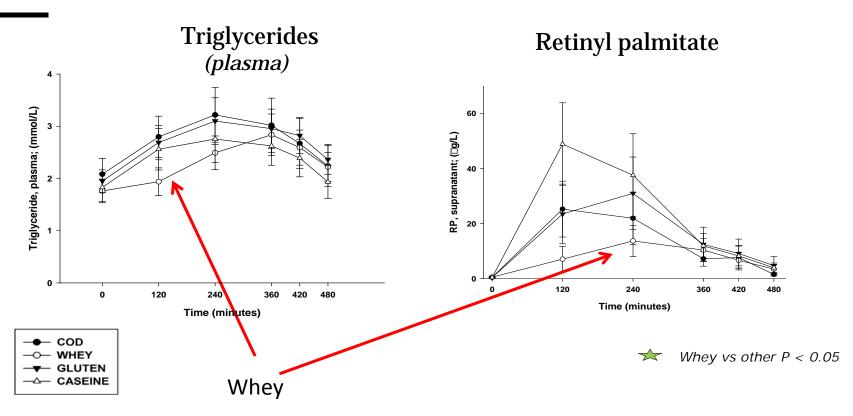
Keywords: Obesity Postprandial lipemia Triglyceride Atherosclerosis Dietary protein Cross-over

ABSTRACT

Non-fasting triglyceridemia is much closer associated to cardiovascular risk compared to fasting triglyceridemia. We hypothesized that there would be acute differential effects of four common dietary proteins (cod protein, whey isolate, gluten, and casein) on postprandial lipemia in obese non-diabetic subjects. To test the hypothesis we conducted a randomized, acute clinical intervention study with crossover design. We supplemented a fat rich mixed meal with one of four dietary proteins i.e. cod protein, whey protein, gluten or casein. Eleven obese non-diabetic subjects (age: 40-68, body mass index: 30.3-42.0 kg/m²) participated and blood samples were drawn in the 8-h postprandial period. Supplementation of a fat rich mixed meal with whey protein caused lower postprandial lipemia (P = .048) compared to supplementation with cod protein and gluten. This was primarily due to lower triglyceride concentration in the chylomicron rich fraction (P = .0293). Thus, we have demonstrated acute differential effects on postprandial metabolism of four dietary proteins supplemented to a fat rich mixed meal in obese non-diabetic subjects. Supplementation with whey protein caused lower postprandial lipemia compared to supplementation with cod and gluten. As postprandial lipemia is closely correlated to cardiovascular disease, long-term dietary supplementation with whey protein may prove beneficial in preventing cardiovascular disease in obese non-diabetic subjects.

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Results



N = 11; obese non-diabetic subjects

Holmer-Jensen J et al Nutr Res 2013;33:34-40

Conclusion

In conclusion, we accept the hypothesis of acute differential effects of dietary proteins on postprandial lipemia in obese non-diabetic subjects. A fat rich meal supplemented with whey protein caused lower postprandial lipemia compared to cod and gluten due to lower triglyceride concentrations in the chylomicron rich supernatant.

Lifestyle intervention

• Dairy proteins as dietary intervention on lipid metabolism:

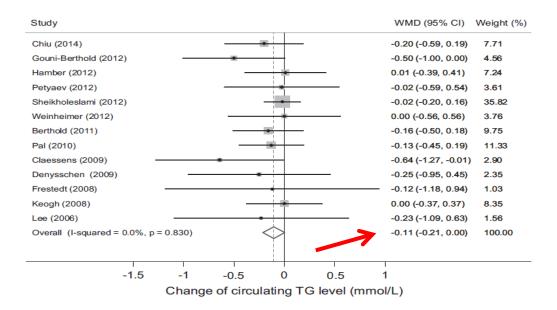
Milk protein (g)	Study design (duration)	Effect	Comparison group	Subjects (n)	Reference
WPI or casein + fat-rich meal (45 g)	Acute	↓ TG response	Cod- and gluten protein	Obese non-diabetic (11)	[39]
WPI + fat-rich meal (45 g	Acute	↓ TG response	Casein, cod- and gluten protein	T2D (12)	[40]
WPI (45 g)	Acute	↓ TG response	Casein, glucose	Postmenopausal women (20)	[53]
WPI or casein + fat-rich meal (45 g)	Acute	↓ TG concentration in chy lomicron-rich fraction	Cod- and gluten protein	Obese non-diabetic (11)	[39]
Casein combined with carbohydrates and a fat- rich meal (45 g)	Acute	↓ TG concentration in chy lomicron-rich fraction	Control meal, control meal + carbohydrates, control meal + casein	T2D (11)	[64]
WPI + fat-rich meal (45 g	Acute	→ TG response	WP specific fractions	Obese non-diabetic (11)	[47]
WPI + fat-rich meal (45 g	Acute	→ TG response	WP specific fractions	T2D (12)	[46]
WPI or casein + fat-rich meal (45 g)	Acute	↓ FFA	Cod- and gluten protein	Obese non-diabetic (11)	[39]
WPI + fat-rich meal (45 g	Acute	↓ FFA	Casein, cod- and gluten protein	T2D (12)	[40]
WPI (2x27 g/d)	Chronic (12 weeks)	↓ Fasting TG, ↓ total cho- lesterol, ↓ LDL cholestero	Glucose	Overweight and obese (70)	[31]
Casein (35 g/d)	Chronic (6 weeks)	↓ Total cholesterol	Baseline	Hypercholesterolemic (43)	[65]
WP (2x25 g/d)	Chronic (12 weeks)	\rightarrow Fasting lipids	Casein	Moderate obese (48)	[48]

Table 2. Effects of milk proteins on lipid metabolism in human subjects

Bjørnshave A, Hermansen K Rev Diabet Stud. 2014 Summer;11(2):153-66

Whey protein and TG – a meta-analysis

Whey protein and blood lipid profiles J-W Zhang *et al*



a. RCT of whey protein or derivates; b. Treatment > 4 weeks; c. A control or a comparison group

Zhang JW et al Eur J Clin Nutr 2016;70:879-885

Whey protein and TG – a meta-analysis

REVIEW

Effect of whey protein on blood lipid profiles: a meta-analysis of randomized controlled trials

J-W Zhang^{1,4}, X Tong^{1,4}, Z Wan¹, Y Wang², L-Q Qin^{1,3} and IMY Szeto²

CONCLUSION

Our findings demonstrated the modestly favorable effects of whey protein supplementation on circulating TG levels. No effects of whey protein on TC, LDL-C and HDL-C levels were found. Considering the limited studies and possible heterogeneity of trials, additional well-designed RCTs are needed to further clarify the effect of supplemental whey protein on TC and lipoprotein cholesterol.

Agenda

- Dairy products and weight
- Dairy products and triglycerides
- Dairy products and blood pressure
- Dairy products, blood glucose and risk of type 2 diabetes

Dose-response relationship (pr increment of 200g/d) between total dairy intake and hypertension (meta-analysis)

Α

Author	Year	Country	Study Population			_	Relative Risk (95% Cl)	% Weight
Alonso	2005	ES	SUN cohort		_	-	0.91 (0.80–1.03	3) 2.83
Steffen	2005	USA	CARDIA Study			÷	0.93 (0.88–0.99	9.80
Engberink	2009	NL	Rotterdam Study			+	0.94 (0.89–0.99) 12.65
Wang	2008	USA	Women's Health Study			•	0.96 (0.94–0.98	30.81
Alonso	2009	USA	ARIC Study				0.97 (0.93–1.01) 18.06
Heraclides	2012	UK	1946 National Birth Cohort			÷	1.01 (0.92–1.12	?) 4.25
Engberink	2009	NL	MORGEN Study			1	1.01 (0.96–1.07) 12.18
Dauchet	2007	FR	SU.VI.MAX cohort			÷	1.02 (0.93–1.12	2) 4.88
Snijder	2008	NL	Hoorn Study			-	1.04 (0.95–1.14) 4.54
Overall					\longrightarrow	d	0.97 (0.95–0.99) 100.00
(<i>l</i> ²=28.3%,	P=0.19	93)			•			
NOTE: We	ights a	re from ran	dom-effects analysis					
			0.1		0.5	1.0	2.0	
			F	Relative Risk				

Soedamah-Muthu SS et al Hypertension. 2012 Nov;60(5):1131-7

Conclusion

• Total dairy, low-fat dairy and milk may contribute to the prevention of hypertension.

• Intervention studies are needed to confirm this!

Whey protein, blood pressure and endothelial function

Whey protein lowers blood pressure and improves endothelial function and lipid biomarkers in adults with prehypertension and mild hypertension: results from the chronic Whey2Go randomized controlled trial^{1,2}

Ágnes A Fekete,^{3,4} Carlotta Giromini,⁵ Yianna Chatzidiakou,³ D Ian Givens,⁴ and Julie A Lovegrove³*

Design: The trial was a double-blinded, randomized, 3-way–crossover, controlled intervention study. Forty-two participants were randomly assigned to consume 2×28 g whey protein/d, 2×28 g Ca caseinate/d, or 2×27 g maltodextrin (control)/d for 8 wk separated by a 4-wk washout. The effects of these interventions were examined with the use of a linear mixed-model ANOVA.

Whey protein, blood pressure and endothelial function

This novel study revealed that the consumption of whey protein (56 g/d) for 8 wk resulted in clinically relevant reductions in 24-h SBP ($-2.9 \pm 1.1 \text{ mm Hg}$) and DBP ($-2.0 \pm 0.7 \text{ mm Hg}$) compared with the effect of the control in adults with prehypertension and mild hypertension

In conclusion, this novel RCT has several important observations. Compared with the control, whey protein significantly lowered 24-h SBP and DBP, central and peripheral SBP, and mean arterial pressure. Furthermore, compared with the control, both whey protein and calcium caseinate improved endothelial function, reduce adhesion molecules and vascular biomarkers of risk, and improved blood lipids. The magnitude of changes in the CVD risk markers observed is modest but may have important implications for public health.

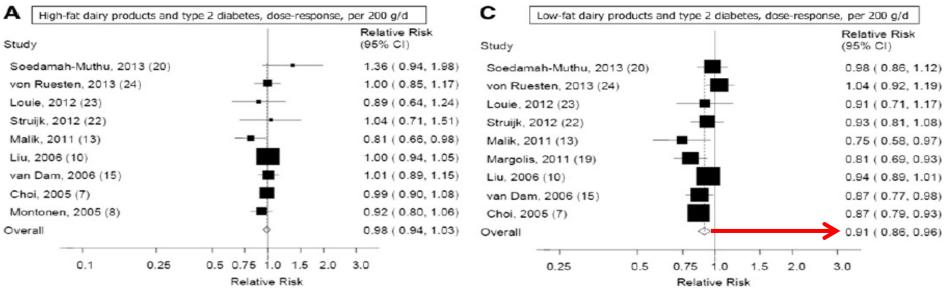
FMP: Flow Mediated Dilation (Gold standard for endothelial dysfunction)

Agenda

- Dairy products and weight
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Dairy products and risk of type 2 diabetes

High fat dairy products



Low fat dairy products

Youghurt intake and diabetes risk

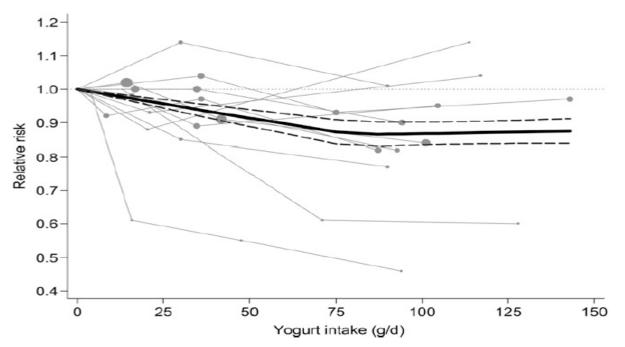


FIGURE 4 Spaghetti plot for the nonlinear association (*P*-nonlinearity: <0.001) between yogurt intake and diabetes risk (RR: 0.86 at 80 g/d compared with 0 g/d; 95% CI: 0.83, 0.90; P < 0.001), including 11 studies (12 study populations; n = 438,140 individuals).

Summary: can we combat features of the metabolic syndrome?

- Dairy products and weight
 - at least in energy restricted or short term trials
- Dairy products and triglycerides
 - in paticular with whey protein
- Dairy products and blood pressure
 - at least low fat dairy, milk and possibly whey protein
- Dairy products, blood glucose and risk of type 2 diabetes
 - in fat reduced dairy products and youghurt





Conclusion

To know better how to combat metabolic syndrome we need more intervention studies e.g. on the impact of:

- Specific dairy products as such and as part of a Healthy diet both with and without energy restriction (diurnal blood pressure, insulin sensitivity, low grade inflammation).
- Different dairy fat types (e.g. medium chain saturated fatty acids) on the body composition (lean body mass, fat mass) measured with different methods (DEXA scan, MR scan).

