VUmc (

Dairy foods and diabetes – a protective role?

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Content

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- Dairy consumption
- Dairy consumption and diabetes risk
- Cardiometabolic effects of dairy
- Compounds: vitamin K, probiotics



Introduction

- Dairy is widely consumed source of vitamins, minerals, but also saturated fat and sodium
- Studies suggest health benefits for dairy consumption on type 2 diabetes





Dairy consumption in Europe





Dietary recommendations

 Have some dairy or dairy alternatives (such as soya drinks); choosing lower fat and lower sugar options

Handhaving van de consumptie aanbevolen:



390 g/day for men, 325 g/day for women

InterAct – EPIC substudy on Type 2 Diabetes (



Discover how genetic and lifestyle behavioural factors, particularly diet and physical activity, interact in their influence on the risk of developing type 2 diabetes

- 8 European countries, 26 centres
- Mean follow-up 12 years
- Case-cohort design



Dairy consumption and type 2 diabetes- EPIC-InterAct



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Meta-analysis dairy consumption vumc (Meta-analysis dairy consumption

22 prospective cohort studies

- 579.832 individuals and 43.118 diabetes cases
- Total dairy consumption 111 400 g/day
- N=16 on total, low-fat and high-fat dairy
- N=11 on milk intake
- N=5 on fermented dairy



Total dairy consumption and diabetes risk

		-		Relative	76
Author	Year	Country	Gender	nsk (95% CI)	weight
Zong	2014	China	Men/Women	• 0.65 (0.53, 0.80)	1.50
Elwood	2007	UK	Men	.78 (0.47, 1.32)	0.28
Kiri	2009	Japan	Women	0.85 (0.73, 1.00)	2.49
Diaz-López	2015	Spain	Men/Women	0.85 (0.75, 0.97)	3.31
Llu	2006	USA	Women	0.88 (0.82, 0.96)	6.28
Grantham	2013	Australia	Men/Women	• · · · · · · · · · · · · · · · · 0.89 (0.77, 1.04)	2.67
van Dam	2006	USA	Women		6.76
Margolis	2011	USA	Women	0.97 (0.93, 1.00)	10.77
Ericson	2015	Sweden	Men/Women	0.98 (0.95, 1.01)	11.54
Chen - HPFS	2014	USA	Men	0.99 (0.95, 1.02)	10.90
Sluijs	2012	Europe	Men/Women	0.99 (0.94, 1.04)	9.22
Chen - NHS II	2014	USA	Women		11.34
Chen - NHS	2014	USA	Women		11.83
Struijk	2013	Denmark	Men/Women	1.07 (0.93, 1.23)	2.94
Kirli	2009	Japan	Men	• 1.08 (0.95, 1.23)	3.30
Soedamah-Muthu	2013	UK	Men/Women	1.10 (0.99, 1.22)	4.39
Louie	2013	Australia	Men/Women	1.12 (0.76, 1.64)	0.49
Overall (I-squared	- 66.49	%, p = 0.000))	0.97 (0.95, 1.00)	100.00
NOTE: Weights an	e from r	andom effec	cis analysis		
			.4	.6 .8 1 1.2 1.4 <u>16 18</u>	
				Relative risk	5-1
			040	5.57, 5.5	



Low-fat dairy consumption and diabetes risk

							Relative	%
Author	Year	Country	Gender				risk (95% CI)	Weight
					_			
Margolis	2011	USA	women	-			0.81 (0.70, 0.93)	5.85
Díaz-López	2015	Spain	Men/Women			-	0.84 (0.71, 0.98)	5.37
Llu	2006	USA	Women				0.84 (0.75, 0.95)	7.75
van Dam	2006	USA	Women			-	0.89 (0.78, 1.00)	7.17
Nettleton	2008	USA	Men/Women			+	0.91 (0.71, 1.15)	2.91
Louie	2013	Australla	Men/Women	-	•		0.93 (0.69, 1.26)	2.02
O'Connor	2014	UK	Men/Women				0.95 (0.82, 1.09)	6.10
Chen - NHS II	2014	USA	Women			-	0.97 (0.93, 1.01)	13.30
Soedamah-Muthu	2013	UK	Men/Women			•	0.98 (0.86, 1.11)	6.99
Chen - HPFS	2014	USA	Men		-	•	0.98 (0.94, 1.03)	12.93
Chen - NHS	2014	USA	Women			•	1.02 (0.99, 1.06)	13.76
Struijk	2013	Denmark	Men/Women			•	1.04 (0.90, 1.21)	5.64
Ericson	2015	Sweden	Men/Women				1.12 (1.03, 1.22)	10.22
Overall (I-squared	- 68.09	%, p = 0.000	0		(<	7)	0.96 (0.92, 1.00)	100.00
NOTE: Weights are	e from r	andom effe	cts analysis					
				6	.8	1 1.2	1.4	
					Relative risk		0.96; 0.92-	1.00



High-fat dairy consumption and diabetes risk

			Relative %	5
Author	Year Countr	Gender	risk (95% CI) W	Veight
Díaz-López	2015 Spain	Men/Women 🔹	0.51 (0.26, 0.99) 0.0	.61
Struijk	2013 Denma	rk Men/Women	0.75 (0.26, 2.15) 0.2	.25
Ericson	2015 Swede	Men/Women -	0.87 (0.81, 0.93) 15	5.29
Montonen	2005 Finland	Men/Women -	0.92 (0.80, 1.05) 8.9	.99
Louie	2013 Austral	a Men/Women •	0.92 (0.66, 1.28) 2.3	.31
Nettleton	2008 USA	Men/Women	0.97 (0.62, 1.50) 1.3	.35
Chen - HPFS	2014 USA	Men	0.99 (0.93, 1.07) 15	5.15
Chen - NHS	2014 USA	Women	1.01 (0.95, 1.07) 16	6.81
Liu	2006 USA	Women	1.01 (0.89, 1.14) 9.3	.76
van Dam	2006 USA	Women	1.01 (0.90, 1.14) 9.4	.89
Chen - NHS II	2014 USA	Women	1.04 (0.97, 1.11) 15	5.23
O'Connor	2014 UK	Men/Women	1.28 (0.90, 1.83) 2.0	.04
Soedamah-Muthu	2013 UK	Men/Women	- 1.29 (0.93, 1.79) 2.3	.32
Overall (I-squared	d = 51.6%, p = (.016)	0.98 (0.93, 1.04) 10	00.00
NOTE: Weighter	- from modern			
NOTE: weights an	re from random	errects analysis		
		.2 .5 1 1.5 Deletive riek	2 2.5	

Total milk consumption and diabetes risk

Author	Year	Country	Gender	Relative risk (95% CI)	% Weight
Zong	2014	China	Men/Women -	 0.71 (0.58, 0.88) 	3.65
Elwood	2007	UK	Men	• 0.88 (0.66, 1.18)	2.05
Díaz-López	2015	Spain	Men/Women		4.66
Kirli	2009	Japan	Women	0.90 (0.75, 1.07)	4.74
Fuhrman	2009	Puerto Rico	Men	0.94 (0.90, 0.99)	15.84
Grantham	2013	Australia	Men/Women		3.87
Soedamah-Muthu	2013	UK	Men/Women	0.99 (0.87, 1.14)	6.75
Vang	2008	USA	Men/Women	1.00 (0.94, 1.05)	15.24
Kiri	2009	Japan	Men	1.00 (0.86, 1.16)	6.02
Siuljs	2012	Europe	Men/Women	1.01 (0.94, 1.08)	13.23
Ericson	2015	Sweden	Men/Women	• 1.04 (1.00, 1.08)	17.83
Struljk	2013	Denmark	Men/Women	1.07 (0.93, 1.24)	6.11
Overall (I-squared	- 57.4	%, p = 0.007)		0.97 (0.93, 1.02)	100.00
NOTE: Weights an	e from r	andom effects	analysis		
			.5	.75 1 1.25 1.5 Relative risk	

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VUmc (1)

Low-fat milk consumption and diabetes risk

							Polativo	9/
								<i>/</i> •
Author	Year	Country	Gender				nsk (95% CI)	Weight
Grantham	2013	Australia	Men/Women		•		0.80 (0.66, 0.98)	3.31
Liu	2006	USA	Women -				0.81 (0.59, 1.12)	1.31
Díaz-López	2015	Spain	Men/Women		•		0.82 (0.68, 1.00)	3.33
Chen - NHS II	2014	USA	Women		÷	•	1.00 (0.97, 1.03)	22.65
Chen - HPFS	2014	USA	Men		-		1.02 (0.98, 1.05)	22.50
Chen - NHS	2014	USA	Women			-	1.05 (1.02, 1.07)	24.61
Ericson	2015	Sweden	Men/Women				1.06 (1.02, 1.10)	22.29
Overall (I-squ	ared =	71.6%, p =	0.002)		<	\Diamond	1.01 (0.97, 1.05)	100.00
NOTE NUMBER								
NOTE: Weight	is are fr	rom randoi	n emects analysis					
			.5	.7	5 viels	1 1.3	25	
				Relative	ISK			

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VUmc (1)

High-fat milk consumption and vumc (ME diabetes risk

						Relative	*
Author	Year	Country	Gender			risk (95% CI)	Weight
		country	Consci			104 (30 % 01)	
Villegas	2009	China	Women			0.62 (0.54, 0.72)	13.05
Ericson	2015	Sweden	Men/Women		-	0.94 (0.88, 1.00)	15.89
Montonen	2005	Finland	Men/Women		-	1.00 (0.94, 1.06)	15.91
Chen - NHS II	2014	USA	Women			1.04 (0.86, 1.27)	11.20
Chen - HPFS	2014	USA	Men		· · ·	1.11 (0.97, 1.27)	13.66
Chen - NHS	2014	USA	Women		•	1.12 (1.00, 1.26)	14.39
Grantham	2013	Australia	Men/Women		· · ·	1.15 (0.93, 1.41)	10.77
Llu	2005	USA	Women	-	•	1.20 (0.76, 1.90)	4.58
Diaz-López	2015	Spain	Men/Women		· ·	1.34 (0.29, 6.09)	0.55
Overali (I-squa	red = 84	.1%, p = 0.0	00)		\diamond	0.99 (0.88, 1.11)	100.00
NOTE: Weights	are fron	n random ef	fects analysis				
			.25	.5 .75	1 1.25 1.5	2	
				Relative risk			

Fermented dairy consumption and diabetes risk



Cheese consumption and diabetesvume (ME risk

Author	Year	Country	Gender								Relative risk (95% CI)	% Weight
Vang	2008	USA	Men/Women				-				0.89 (0.69, 1.15)	0.53
Grantham	2013	Australia	Men/Women		•	+					0.91 (0.80, 1.03)	1.94
Kirli	2009	Japan	Men								0.93 (0.63, 1.39)	0.22
Struijk	2013	Denmark	Men/Women			÷-					0.96 (0.88, 1.05)	3.80
Llu	2006	USA	Women								0.97 (0.88, 1.06)	3.53
Sluijs	2012	Europe	Men/Women		-	+					0.98 (0.95, 1.00)	17.00
Ericson	2015	Sweden	Men/Women		- 1	+					0.99 (0.98, 1.00)	19.50
Chen - NHS II	2014	USA	Women		- 1	-					1.00 (0.97, 1.04)	12.88
Chen - NHS	2014	USA	Women			+					1.01 (1.00, 1.03)	20.55
Chen - HPFS	2014	USA	Men								1.06 (1.02, 1.09)	13.05
Soedamah-Muthu	2013	UK	Men/Women		-	•	_				1.06 (0.96, 1.17)	3.04
Diaz-López	2015	Spain	Men/Women				_				1.08 (0.99, 1.19)	3.76
Kirli	2009	Japan	Women	-			•				1.19 (0.77, 1.84)	0.19
Overall (I-squared	- 61.7%	6, p = 0.002))			\$					1.00 (0.99, 1.02)	100.00
NOTE: Weights are	e from ra	andom effec	ts analysis									
			.6		Relative	1 e risk	1.2	1.4	1.6	1.8 2	2	



Sources of heterogeneity

Milk intake

- Asian versus European populations
- Adjustment for major confounding factors

Fermented dairy

Stronger association among women



Underlying mechanism: cardiometabolic outcomes

Figure2: Effects of whole & low fat dairy food on weight*

	Increa	sed dairy		USU	al diet			Mean Difference	Mean Difference	
Study or Subgroup	Mean [kg]	SD [kg]	Total	Mean [kg]	SD [kg]	Total	Weight	IV, Random, 95% CI [kg]	IV, Random, 95% CI [kg]	
Low fat										
Sunther 2005	1.5	4.1	48	0.8	2.8	42	7.8%	0.70 [-0.74, 2.14]		
Vanios 2009	1.4	3	26	-0.7	2	36	8.7%	2.10 [0.77, 3.43]		
Chrichton 2012	1.8	2.4	36	0.2	3	36	9,4%	1.60 (0.35, 2.85)		
an Mellj 2011	1	2.6	35	0.7	2.6	35	9.8%	0.30 [-0.92, 1.52]		
kulijan 2009	1.3	2.2	45	0	2	44	14.4%	1.30 (0.43, 2.17)		
Chee 2003	0.04	2.6	91	0.16	2.6	82	16.1%	-0.12[-0.90, 0.66]		
.au 2001	0.52	2.6	95	-0.26	2.7	90	18.3%	0.78 (0.02, 1.54)		
Barr 2000	1.2	2.5	98	0.6	2.5	102	17.7%	0.60 [-0.09, 1.29]		
lotal (95% CI)			474			467	100.0%	0.82 [0.35, 1.28]	+	
Whole fat						_	-			
Stancliffe 2011	-0.4	2	20	1.1	4.8	20	2.6%	-1.501-3.78.0.781		
Palacios 2009	0.3	2.6	8	-0.6	2	B	2.6%	0.90 [-1.37, 3.17]		
Baran 1990	1.4	3	20	0.2	3.1	17	3.5%	1.20[-0.77, 3.17]	3	
3hadirian 1995	0.1	5.9	81	-0.4	5.9	77	4.0%	0.50 [-1.34, 2.34]	***	
Zemmel 2005	0.4	2.6	17	0.2	2	16	5.3%	0.20 [-1.38, 1.78]		
Eagon 2006	0.3	3	19	0.4	1.7	18	5.4%	-0.10 [-1.65, 1.46]		
Vennesberg 2009	-0.1	2.5	56	-0.1	2.6	57	12.9%	0.00 [-0.94, 0.94]		
Fardy 2009	0.4	2	20	0.5	0.2	19	14.4%	-0.20 [-1.08, 0.68]		
Vonso 2009	1	2	45	-0.2	2.2	55	15.9%	1.20 (0.38, 2.02)		
Benatar 2013	0.4	1.3	56	-0.2	1.2	59	33.5%	0.60 [0.14, 1.06]		
fotal (95% CI)			342			346	100.0%	0.41 [0.04, 0.79]	*	
Catal JOEN CD			816			813	100.0%	100 0 02 01 03 0	•	

* Total number =1629, 82% female, mean baseline weight 77.7 (SD 16.2) kg, median study duration 26 (IQR10-39)weeks

No effect on glycaemic parameters, blood lipids or blood pressure Benatar et al. Plos one 2013 18



Mendelian randomization

Mendelian Randomization Study

Randomized Controlled Trial



Milk intake and type 2 diabetes- vumc (ME Mendelian Randomization



Bergholdt et al. AJCN 2015 ²⁰



Milk intake and type 2 diabetes-Mendelian Randomization



Genetic risk of type 2 diabetes per1 glass/wk of milk intake:
0.99 (0.93-1.06)

Intake of vitamin K2 and diabetes^{vumc (ME}risk

Table 2—Energy-adjusted p	hylloquinon	e and menaquinone	type 2 diabetes an	iong 38.094	Dutch men and women	
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P _{trend} value	Per 50 µg
Phylloquinone						
Intake (µg/day)	100.1	155.7	211.4	308.1		
Age-, sex-, waist-adjusted	1.0	0.89 (0.73-1.08)	0.95 (0.79–1.14)	0.89 (0.74–1.07)	0.35	1.00 (0.97 - 1.03) P = 0.92
Multivariate adjusted*	1.0	0.89 (0.74–1.09)	0.94 (0.78–1.14)	0.88 (0.73–1.06)	0.26	0.99 (0.96 - 1.02) P = 0.65
Multivariate adjusted†	1.0	0.87 (0.71–1.06)	0.90 (0.74–1.09)	0.81 (0.66–0.99)	0.08	0.98 (0.95 - 1.02) P = 0.31
Menaquinones						
Intake (µg/day)	16.0	24.5	32.9	46.1		Per 10 µg
Age-, sex-, waist-adjusted	1.0	1.03 (0.85–1.25)	0.95 (0.78–1.15)	0.86 (0.71–1.05)	0.07	$0.95 (0.91 - 1.01) \tilde{P} = 0.060$
Multivariate adjusted*	1.0	1.04 (0.86–1.26)	0.97 (0.80–1.17)	0.88 (0.73–1.08)	0.13	0.96 (0.91 - 1.02) P = 0.12
Multivariate adjusted†	1.0	0.99 (0.82–1.21)	0.89 (0.72–1.10)	0.80 (0.62–1.02)	0.04	0.93 (0.87 - 1.00) P = 0.038



Probiotics and insulin sensitivity





Take home message

Dairy consumption is suggested to be associated with a reduced risk of type 2 diabetes, in particular low-fat dairy and fermented dairy.

Substantial heterogeneity is present between different studies and should be accounted for in recommendations on dairy intake.

Recent Dutch recommendations on maintaining an intake of 2-3 consumptions per day also apply to risk of type 2 diabetes.



THANK YOU!