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Effects of Dairy Matrix on Musculoskeletal Health

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Disclosure

Speaker Bureau or Member of Scientific Advisory Boards for
Abiogen, Danone, Echolight, Effryx, Mylan, Nestlé, ObsEva, Pfizer, Radius Health, Sandoz, TEVA/Theramex

The Bone Bank (BBC,Bone Bank Corp)

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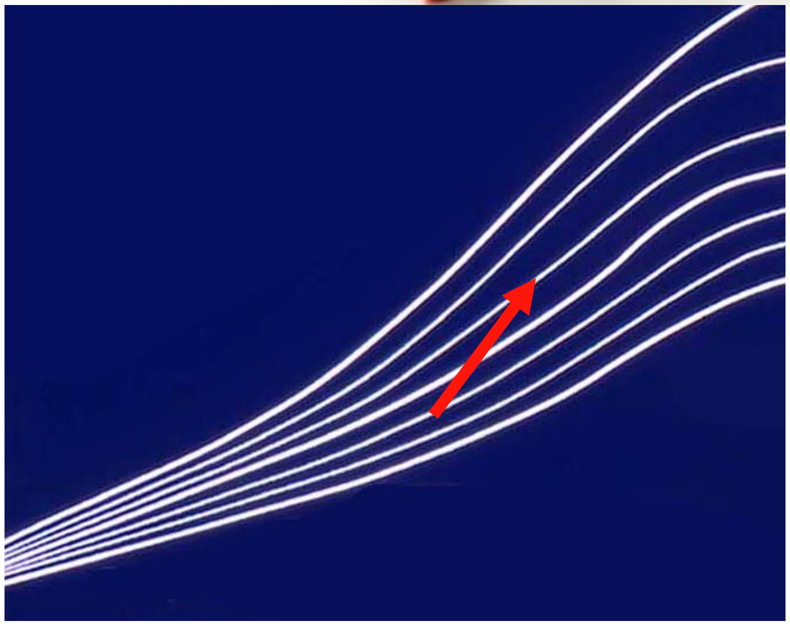
Dairy ?

Income
(Bone Accrual)

Expenses
(Bone Loss)

Capital:		
	Gold	Mass/Density
	Currencies	Geometry
	Equities	Microstructure
	Bonds	Matrix/Mineral

Can Bone Mineral Mass Trajectory be Changed ?
Nutritional Factors: Calcium, Protein (Dairy)



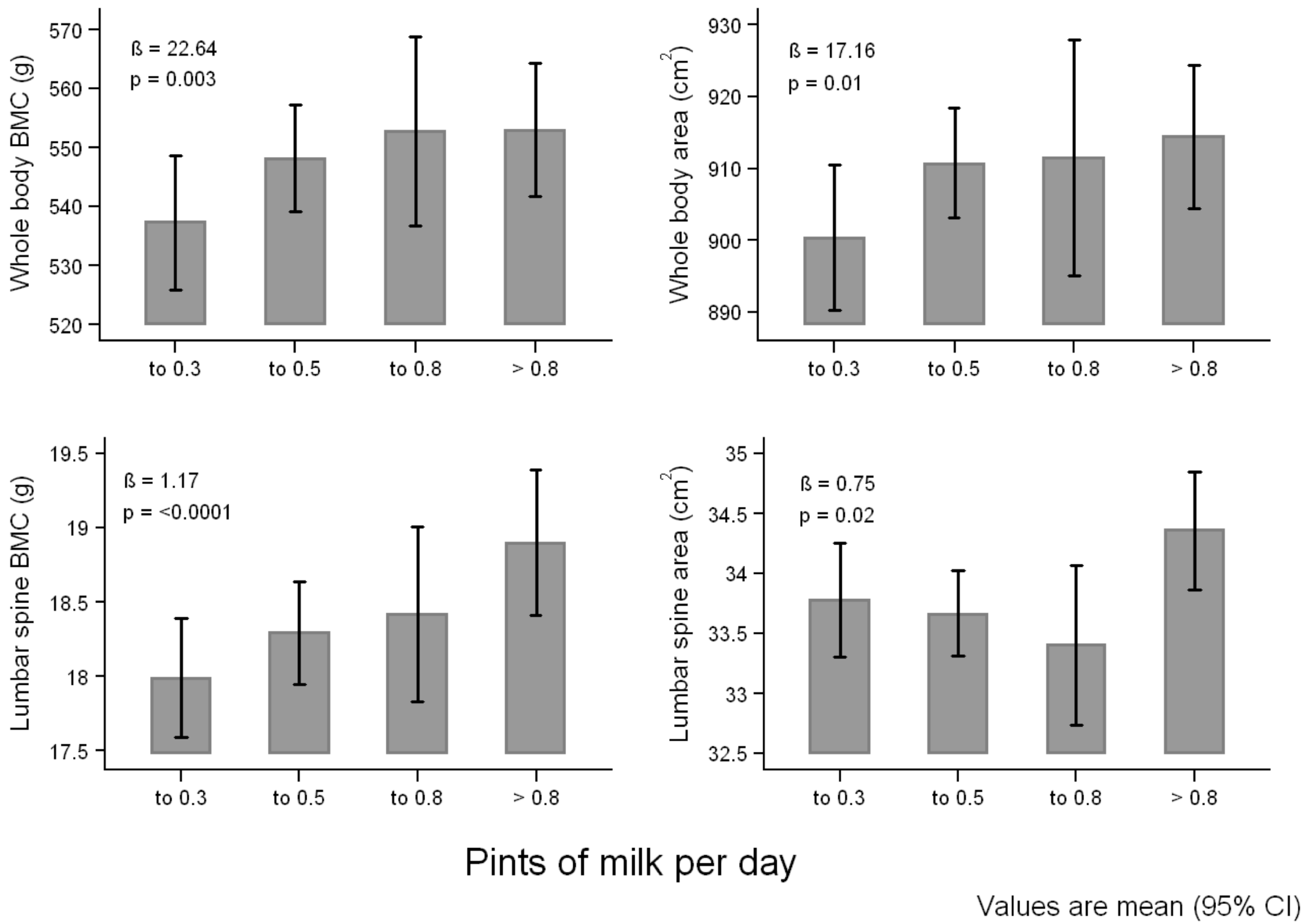
Children Bone Mass in Relation to Mother Nutritional Status during Pregnancy

- WB BMD at Age of 6 Yrs was Positively Correlated to Milk Products and Calcium-rich Foods Consumption During Pregnancy *(Ganpule et al 2006)*

- At the Age of 8-9 Years, aBMD (WB-BMC) was Higher if Born from a Mother with a Prudent Diet (Fruits, Vegetables, Pasta, yoghourt, Cheese) (Cole et al 2009)

> Cross-sectional Case Control Studies

6 year milk intake and offspring (at 6 years) associated bone mass



Kindly provided by Cole et al 2013

Randomized Controlled Trials

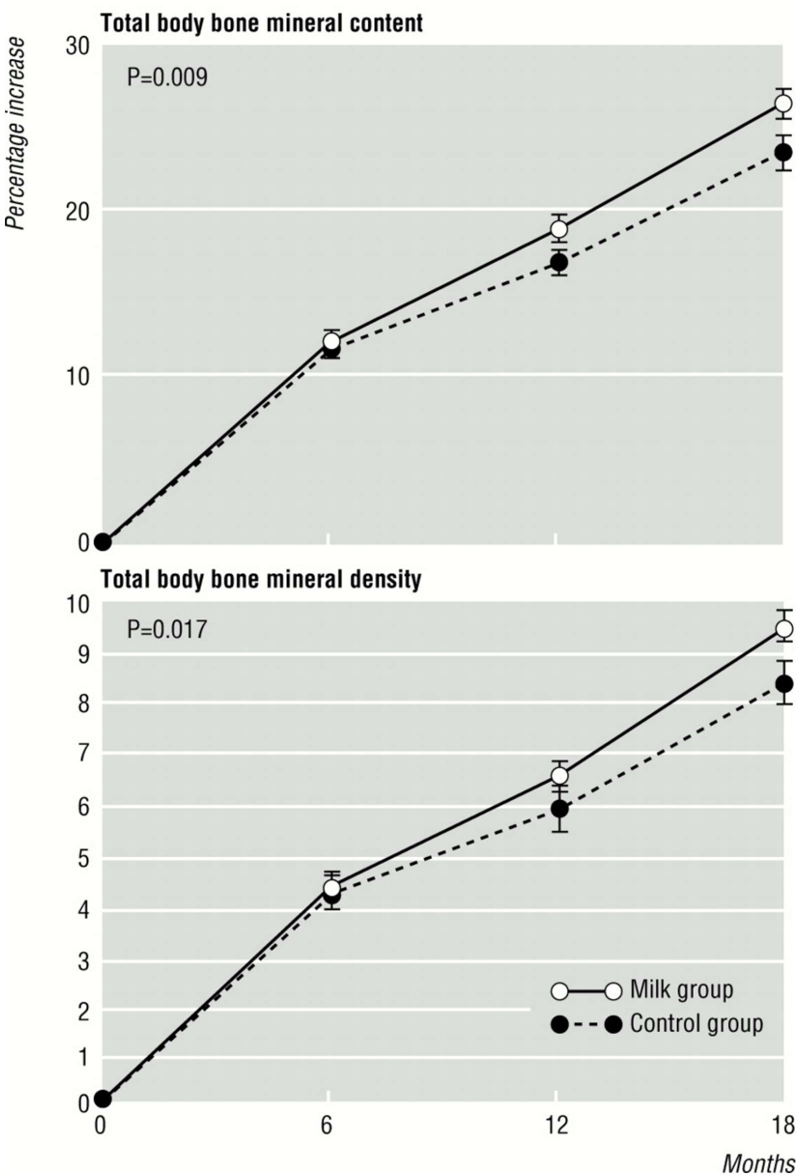
Milk consumption and the growth of school children

Orr	BMJ 1928
Leighton & Clark	BMJ 1929

400-600 ml Milk -> Greater Height Gain

Milk Intake and BMC Acquisition in Adolescent Girls

Cadogan et al, BMJ 1997



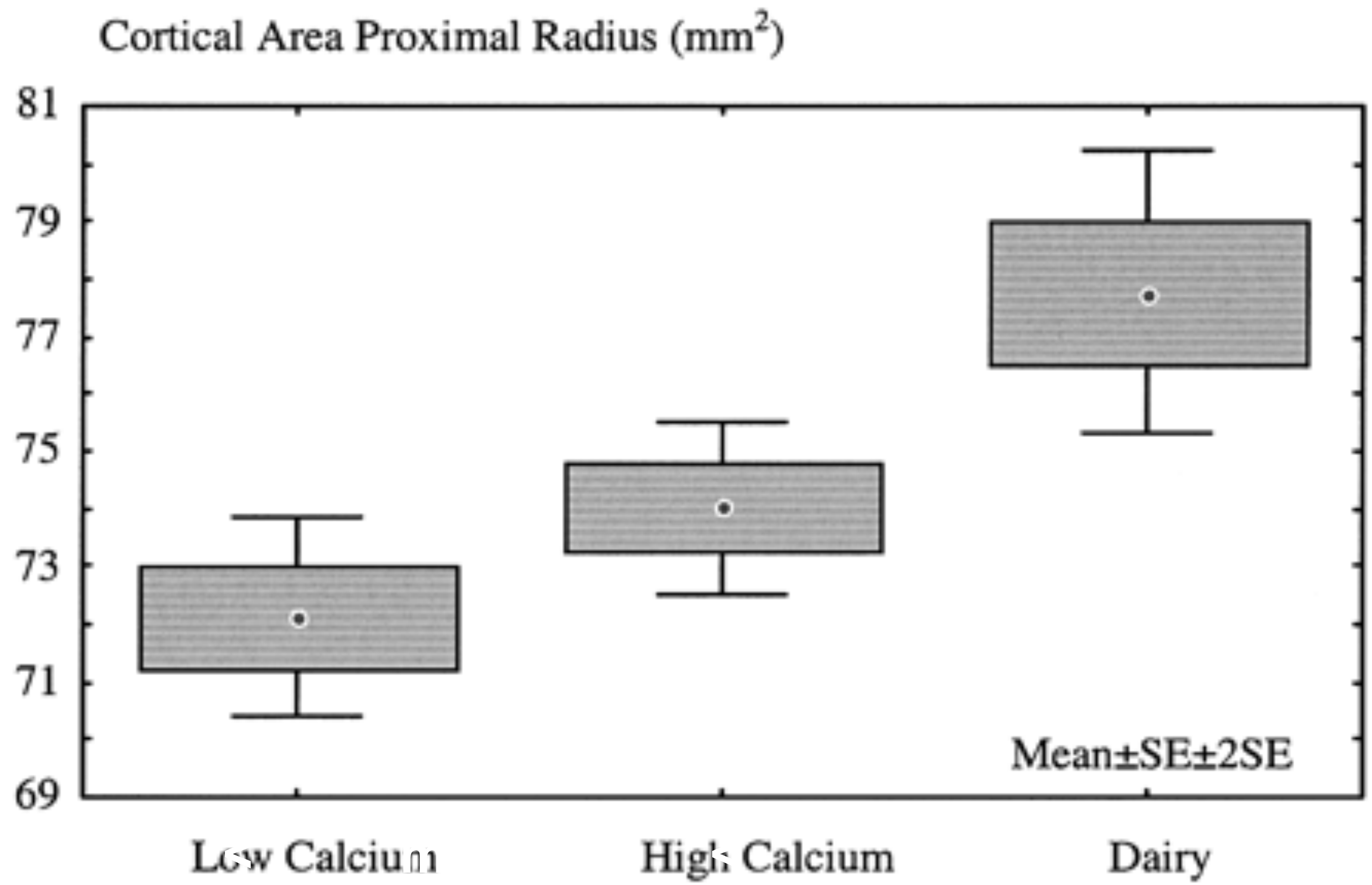
82 Girls, 12.2 Yrs, RCT ± 1 Pint Milk (568 ml)

		Baseline	18 Mo
Calcium	(supp)	739	1025 *
	(cont.)	753	703
Protein	(supp)	59	71 *
	(cont.)	56	56
IGF-I	(supp)	390	522 *
	(cont.)	385	448

Effect of Dairy on Bone Mass Accrual in Children and Adolescents (RCT)

Study	n	Age(yr)	Duration	Intervention	Main Results
Matkovic 1990	28	14	2 yr	Milk 900 ml	NS
Chan 1995	46	11	1 yr	Dairy (1437 mg/d calcium	Increased LS BMD & WB BMC
Cadogan 1997	80	12.2	18 mo	Milk (486 ml/d)	Increased WB BMC & BMD
Renner 1998	129	15.5	1 yr	Dairy (1150 mg/d calcium)	Increased Forearm BMD
Merrilees 2000	73	15.5	1 yr	Dairy (1160 mg/d calcium)	Increased LS, FN & Troch BMD
Volek 2003	28	14.3	12 wks	Dairy (3 servings)	Increased WB BMD
Gibbons 2004	123	9.4	18 mo	Dairy	NS (LS, Hip & WB BMD)
Lau 2004	324	10	18 mo	Dairy (fortified milk)	Increased LS & Hip BMD
Du 2004	698	10	2 yr	Dairy	Increased WB BMC & BMD
Cheng 2005	173	11	2 yr	Dairy (Cheese)	Increased WB BMD & Tibia Cortical Thickness
Albala 2008	93	9 yr	16 wks	Dairy (3 Servings)	NS (WB BMC)

Nutritional Influences on Bone Growth in Children

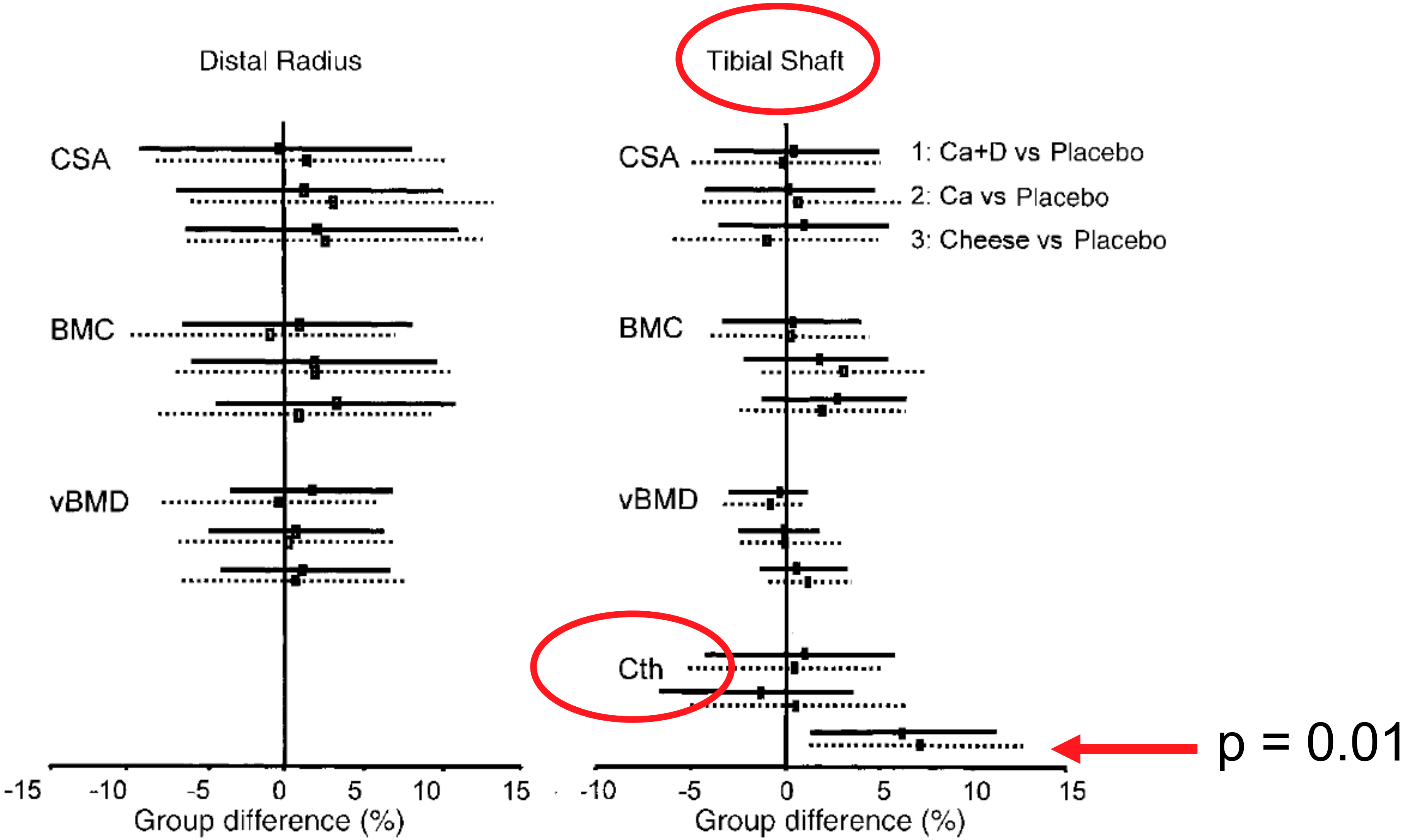


Dairy versus high or low calcium, P=0.0003 by ANOVA

Matkovic et al J Nutr 2004

Effects of Calcium, Dairy Products or Vitamin D on Bone Mass Accrual in 10-12 Years Old Girls: a 2-Year RCT

Cheng et al, AJCN 2005



ITT and Per Protocol

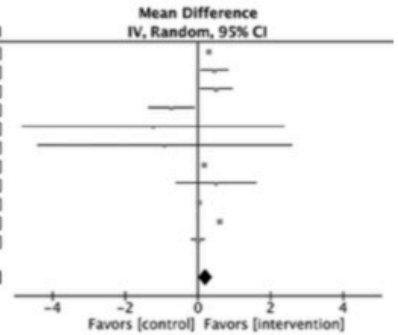
Effects of Milk and Milk-Product Consumption on Growth among Children and Adolescents Aged 6–18 Years: A Meta-Analysis of Randomized Controlled Trials

Lean Mass

A

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Albala et al. (22)	0.92	0.1	47	0.62	0.11	46	15.0%	0.30 [0.26, 0.34]
Cadogan et al. (25)	5.5	0.99	44	5.05	0.81	38	9.5%	0.45 [0.06, 0.84]
Chan et al. (26)	4.3	0.6	22	3.8	1	26	8.3%	0.50 [0.04, 0.96]
Cheng et al. (27)	7.64	1.41	39	8.37	1.46	38	5.8%	-0.73 [-1.37, -0.09]
Cohen et al. 1 (28)	0.1	6.69	24	1.33	6.32	26	0.3%	-1.23 [-4.84, 2.38]
Cohen et al. 2 (28)	0.41	6.19	23	1.33	6.32	26	0.3%	-0.92 [-4.43, 2.59]
Gibbons et al. (30)	3.98	0.19	74	3.81	0.18	80	14.9%	0.17 [0.11, 0.23]
Lambourne et al. (31)	2.2	1.9	36	1.7	2.9	38	2.6%	0.50 [-0.61, 1.61]
Lappe et al. (32)	0.05	0.35	136	0.03	0.26	138	14.8%	0.02 [-0.05, 0.09]
Merrilees et al. (33)	0.72	0.09	45	0.12	0.06	46	15.0%	0.60 [0.57, 0.63]
Volek et al. (38)	2.4	0.3	14	2.4	0.2	14	13.3%	0.00 [-0.19, 0.19]
Total (95% CI)			504			516	100.0%	0.21 [0.01, 0.41]

Heterogeneity: Tau² = 0.07; Chi² = 369.71, df = 10 (P < 0.00001); I² = 97%
Test for overall effect: Z = 2.10 (P = 0.04)



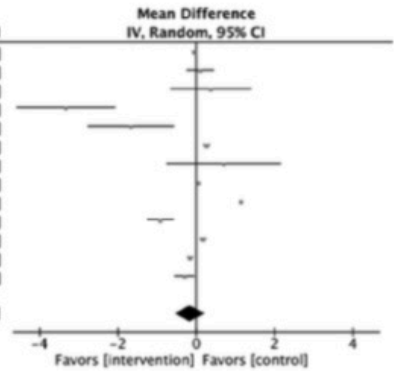
+ 21%

Fat Mass

B

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Albala et al. (22)	0.84	0.15	47	0.89	0.15	46	9.3%	-0.05 [-0.11, 0.01]
Cadogan et al. (25)	1.84	0.75	44	1.74	0.86	38	8.6%	0.10 [-0.25, 0.45]
Cheng et al. (27)	3.42	2.31	39	3.05	2.33	38	5.3%	0.37 [-0.67, 1.41]
Cohen et al. 1 (28)	-0.06	2.55	24	3.27	1.96	26	4.4%	-3.33 [-4.60, -2.06]
Cohen et al. 2 (28)	1.6	1.98	23	3.27	1.96	26	5.0%	-1.67 [-2.78, -0.56]
Gibbons et al. (30)	2.59	0.25	74	2.33	0.29	80	9.2%	0.26 [0.17, 0.35]
Lambourne et al. (31)	1.1	2.8	36	0.4	3.6	38	3.7%	0.70 [-0.77, 2.17]
Merrilees et al. (33)	2.62	0.05	45	2.56	0.09	46	9.3%	0.06 [0.03, 0.09]
Mobarhan et al. 1 (34)	-2.26	0.1	33	-3.4	0.02	35	9.3%	1.14 [1.11, 1.17]
Mobarhan et al. 2 (34)	-4.32	0.94	28	-3.4	0.02	35	8.6%	-0.92 [-1.27, -0.57]
Vogel et al. 2 (37)	1.68	0.2	47	1.51	0.17	32	9.2%	0.17 [0.09, 0.25]
Vogel et al. 3 (37)	1.35	0.15	55	1.51	0.21	47	9.3%	-0.16 [-0.23, -0.09]
Volek et al. (38)	-1.1	0.4	14	-0.8	0.3	14	8.9%	-0.30 [-0.56, -0.04]
Total (95% CI)			509			501	100.0%	-0.15 [-0.52, 0.22]

Heterogeneity: Tau² = 0.38; Chi² = 2846.32, df = 12 (P < 0.00001); I² = 100%
Test for overall effect: Z = 0.80 (P = 0.42)

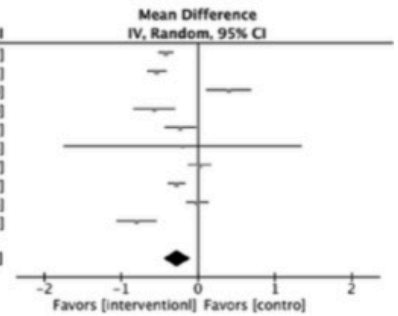


% Fat

C

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Albala et al. (22)	0.36	0.24	47	0.78	0.25	46	12.1%	-0.42 [-0.52, -0.32]
Cadogan et al. (25)	-0.42	0.29	44	0.12	0.31	38	11.8%	-0.54 [-0.67, -0.41]
Chan et al. (26)	1.6	0.6	22	1.2	0.4	26	9.4%	0.40 [0.11, 0.69]
Cohen et al. 1 (28)	-0.67	0.59	24	-0.1	0.35	26	9.7%	-0.57 [-0.84, -0.30]
Cohen et al. 2 (28)	-0.33	0.39	23	-0.1	0.35	26	10.7%	-0.23 [-0.44, -0.02]
Lambourne et al. (31)	-0.2	3.3	36	0	3.5	38	1.2%	-0.20 [-1.75, 1.35]
Lappe et al. (32)	0.27	0.6	136	0.25	0.7	138	11.5%	0.02 [-0.13, 0.17]
Mobarhan et al. 1 (34)	-1.78	0.18	33	-1.5	0.29	35	12.0%	-0.28 [-0.39, -0.17]
Mobarhan et al. 2 (34)	-1.51	0.3	28	-1.5	0.29	35	11.6%	-0.01 [-0.16, 0.14]
Volek et al. (38)	-2.2	0.3	14	-1.4	0.4	14	9.9%	-0.80 [-1.06, -0.54]
Total (95% CI)			407			422	100.0%	-0.27 [-0.45, -0.09]

Heterogeneity: Tau² = 0.07; Chi² = 90.15, df = 9 (P < 0.00001); I² = 90%
Test for overall effect: Z = 3.00 (P = 0.003)



- 27%

Kang et al Nutr Rev 2019

Dairy Products and Fracture Risk In Childhood and Adolescence

1.Children who avoid drinking cow's milk are at increased risk for prepubertal bone fractures
Goulding et al, JADA 2004

-> 0 - 13 yrs: 22 observed fractures vs 8.4 expected

2. Fractures during growth: potential role of a milk-free diet
Konstantynowicz et al, Osteoporos Int 2007

-> 2 - 20 yrs: OR 4.6 in girls and 1.3 (NS) in boys

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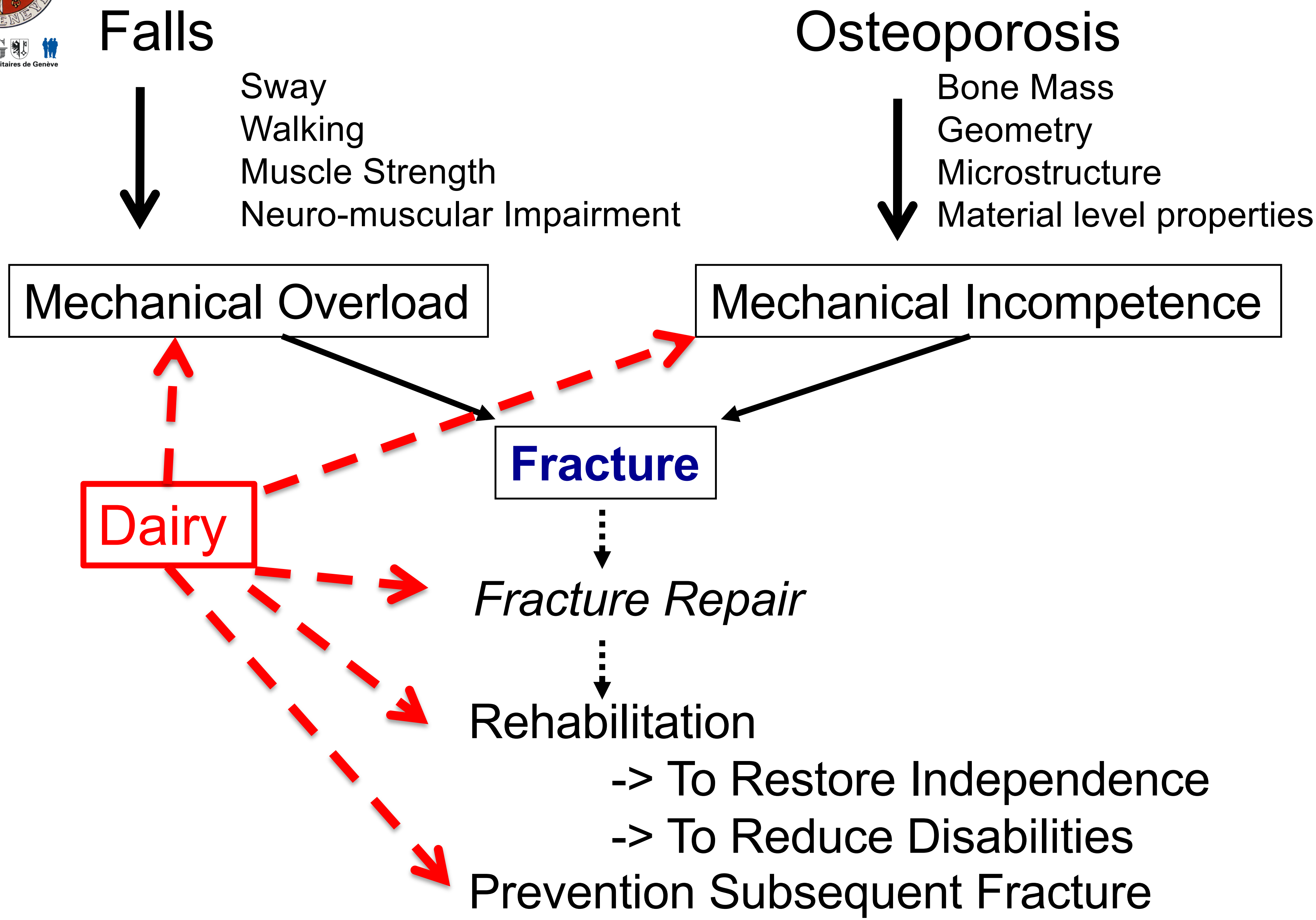
Recommended Milk Intakes

US Department of Agriculture Food Pyramid
US Department of Health & Human Services Dietary Guidelines for American

Children	2 - 8 Yrs	480 ml or Equivalent
	> 9 Yrs	730 ml or Equivalent

3 Equivalents / day

Osteoporotic Fracture



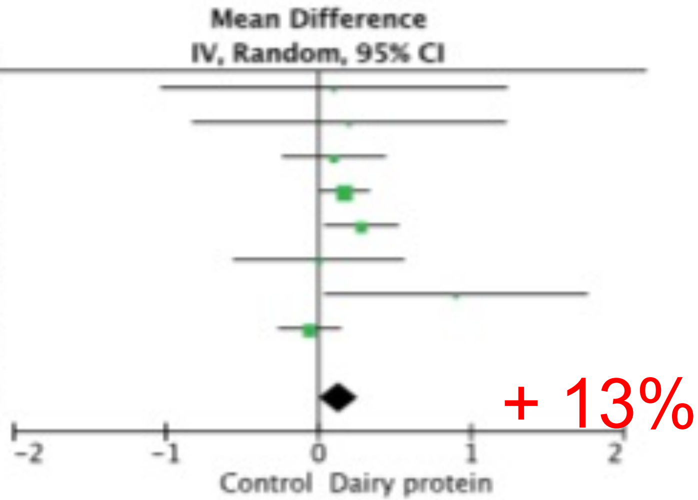
Adapted from Rizzoli, Best Pract Res Clin Endocrinol Metab 2014

The Impact of Dairy Protein Intake on Muscle Mass, Muscle Strength, and Physical Performance in Middle-Aged to Older Adults with or without Existing Sarcopenia: A Systematic Review and Meta-Analysis

Study or Subgroup	Dairy protein Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Alemán-Mateo et al. (20)	0.3	1.9	20	0.2	1.77	20	1.2%	0.10 [−1.04, 1.24]
Alemán-Mateo et al. (26)	0	2.62	49	−0.2	2.59	49	1.4%	0.20 [−0.83, 1.23]
Arnarson et al. (27)	0.6	1.2	66	0.5	0.8	75	11.5%	0.10 [−0.24, 0.44]
Bauer et al. (21)	0.25	0.68	124	0.08	0.68	135	34.2%	0.17 [0.00, 0.34]
Norton et al. (33)	0.27	0.59	31	−0.01	0.36	29	19.8%	0.28 [0.03, 0.53]
Tieland et al. (24)	0.1	1.13	31	0.1	1.13	31	4.6%	0.00 [−0.56, 0.56]
Verreijen et al. (28)	0.4	1.2	30	−0.5	2.1	30	2.0%	0.90 [0.03, 1.77]
Zhu et al. (30)	−0.03	0.67	93	0.03	0.75	88	25.4%	−0.06 [−0.27, 0.15]
Total (95% CI)			**444**			**457**	**100.0%**	**0.13 [0.01, 0.26]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 8.17$, df = 7 (P = 0.32); $I^2 = 14\%$

Test for overall effect: Z = 2.08 (P = 0.04)



Hanach et al Adv Nutr 2019

A DAIRY-BASED PROTEIN, CALCIUM AND VITAMIN D SUPPLEMENT REDUCES FALLS AND FEMORAL NECK BONE LOSS IN AGED CARE RESIDENTS: A CLUSTER RANDOMISED TRIAL

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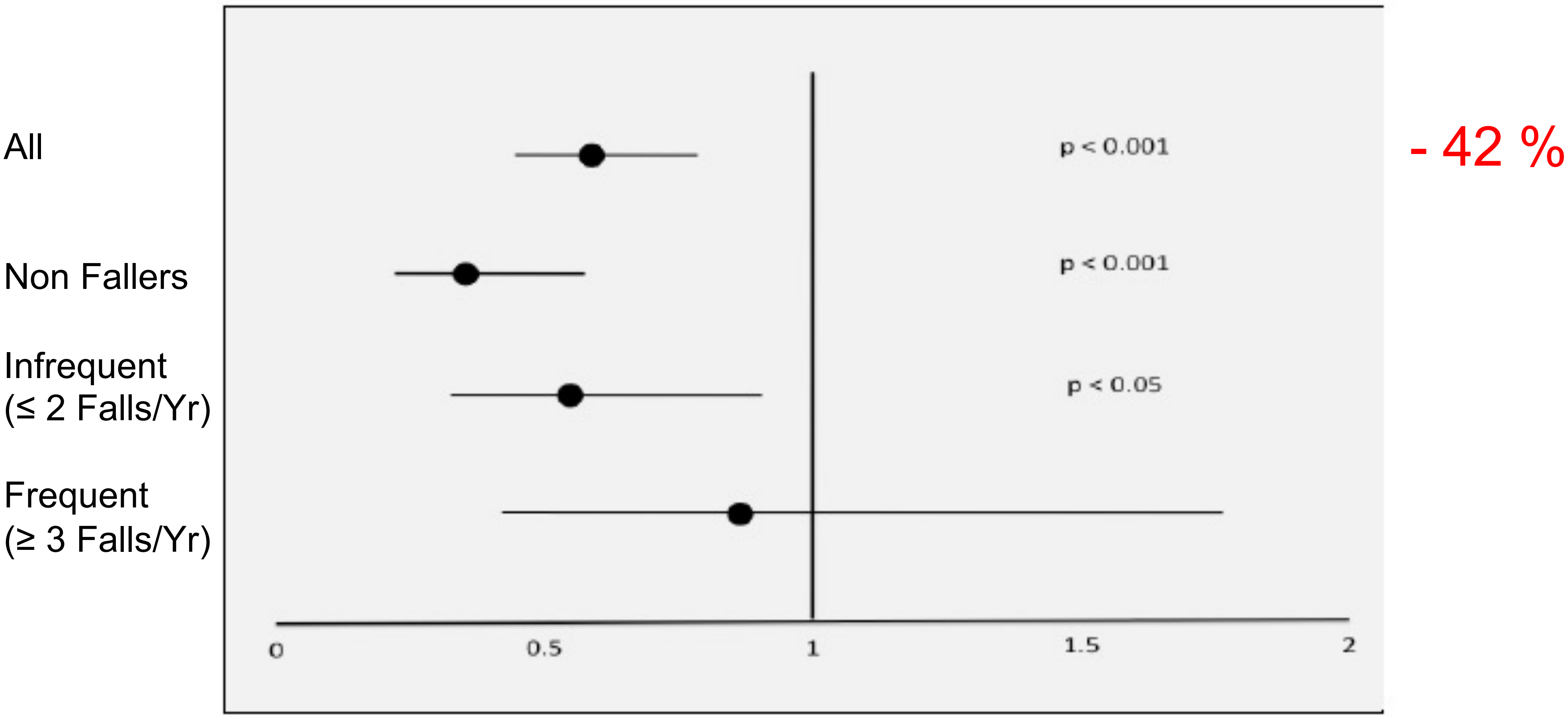
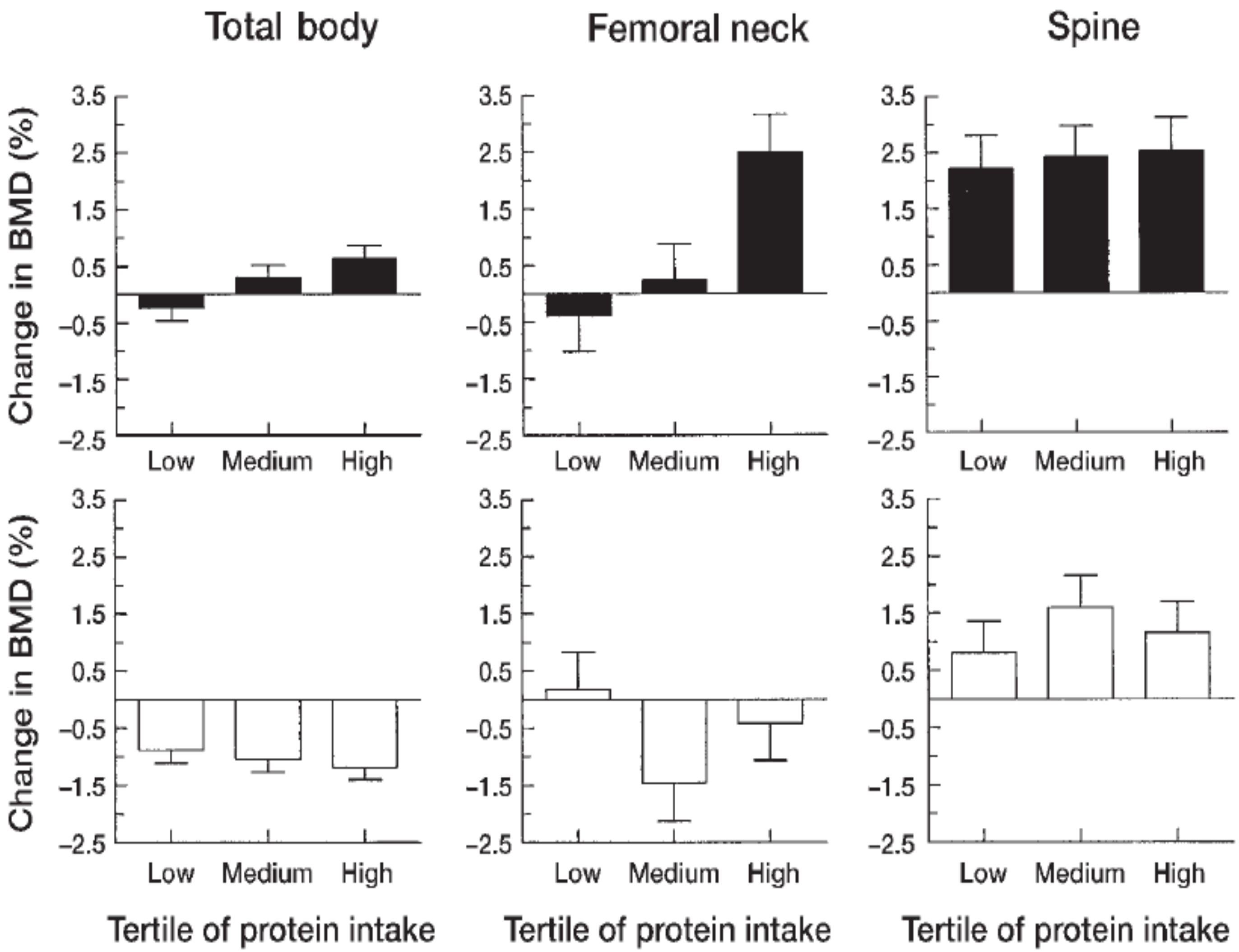
813 Age Care Residents, 86.1±5.9 Yrs, 76% Women, ± Dairy-based protein (9 g/d), calcium (600 mg/d) and vitamin D (960 IU/d), for 8 Months after a 12-Month observation Period

OR for Risk of Falls



Iuliano-Burns et al J Aging Res Clin Pract 2012

Change in BMD by tertile of protein intake (% energy) in 342 men and women (aged ≥ 65 yr) treated with calcium (500 mg/d) and vitamin D (700 IU/d) (■) or placebo (□) for 3 years



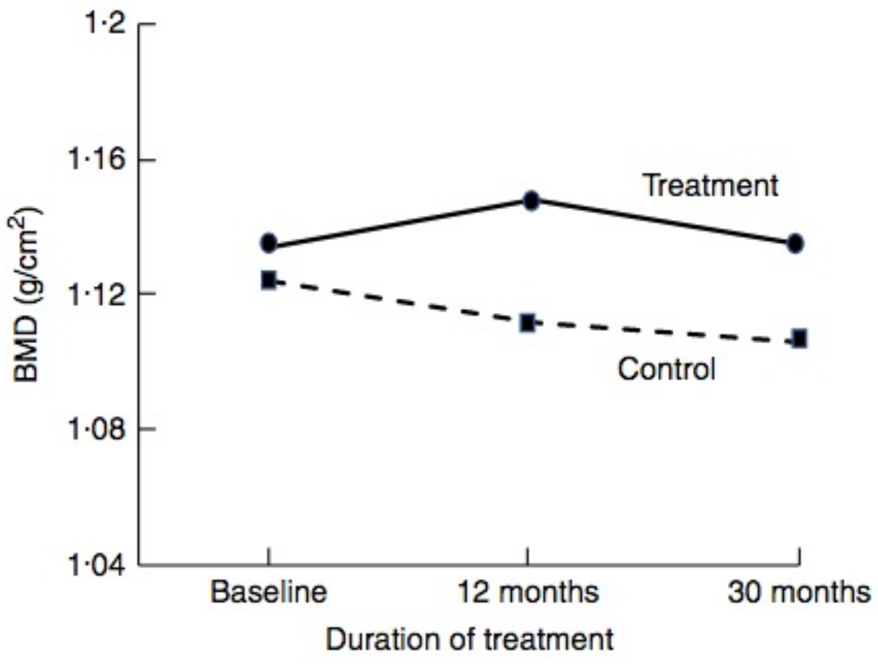
Ca x Protein
P=0.044

High vs low
P=0.011 and
middle P=0.042

Dawson-Hughes et al AJCN 2002

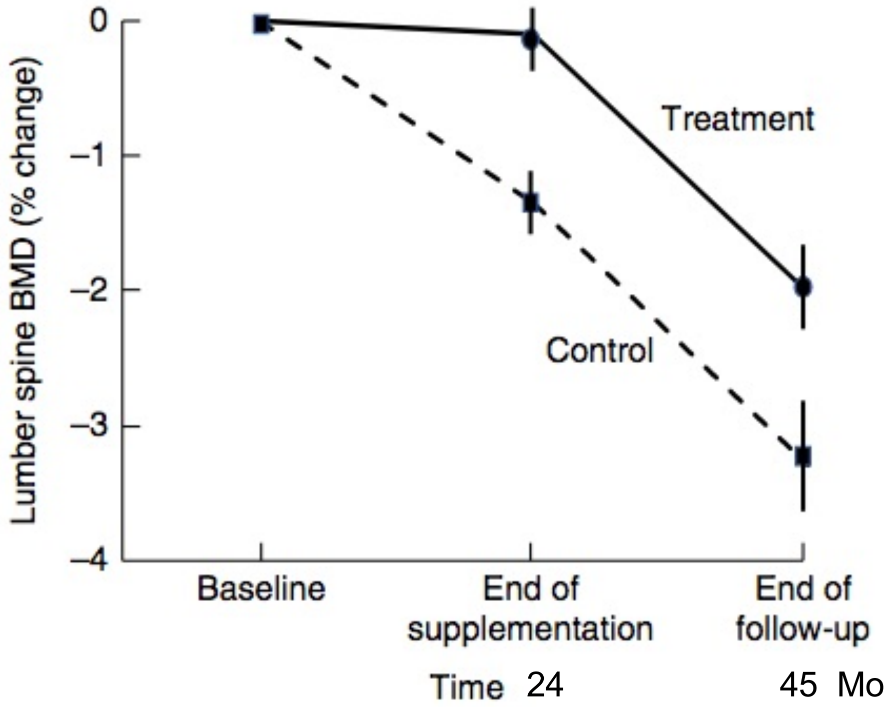
Effects of Fortified Dairy Products

Whole Body BMD



Moschonis et al Br J Nutr 2010

Lumbar Spine BMD



Ting et al JNHA 2007

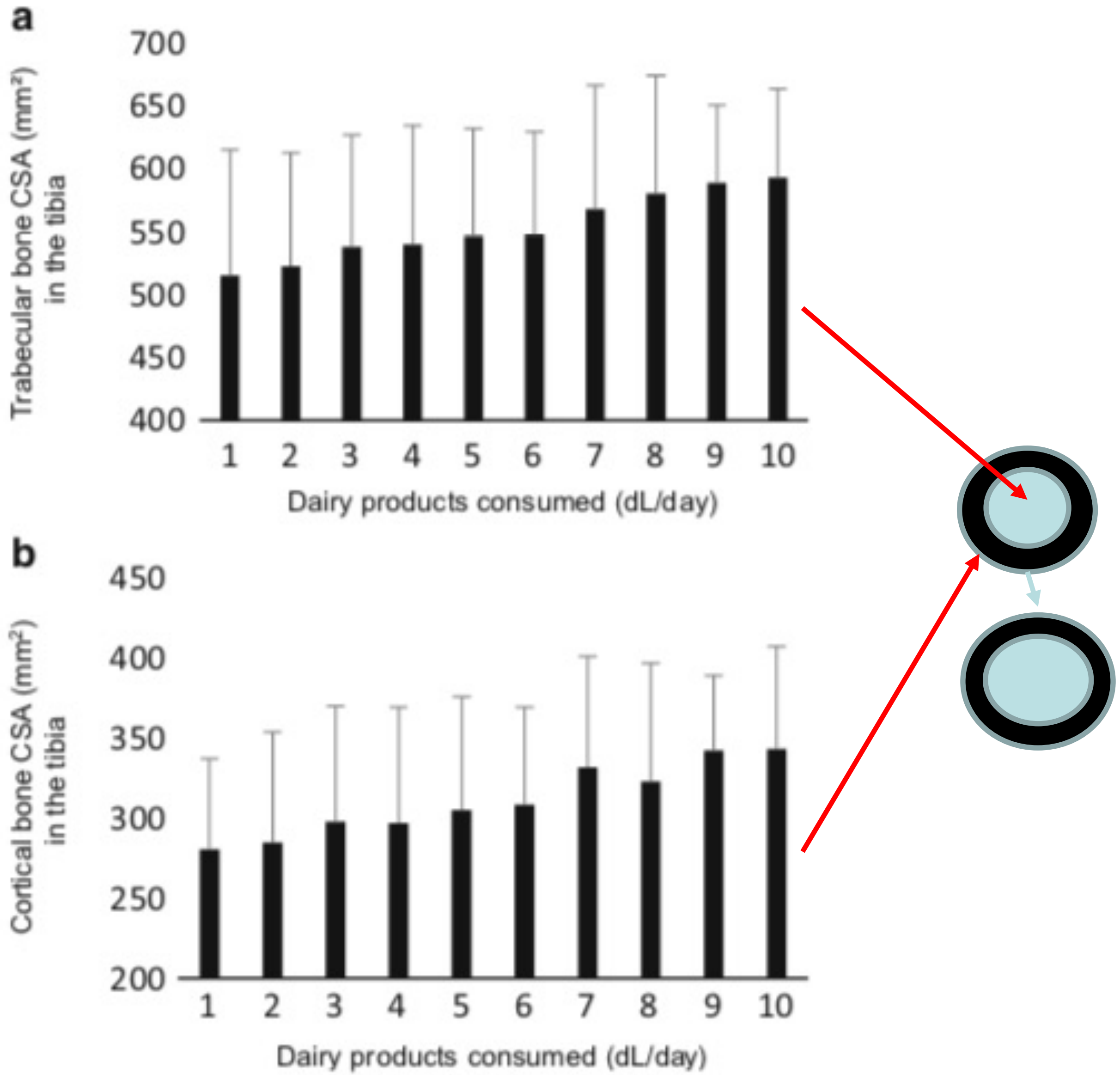
Effect of Dairy on Bone Mineral Density in Adults (RCT)

Study	n	Age(yr)	Duration	Intervention	Main Results
Lau 2001	185	PM Women	2 yr	Milk Powder	Lower BMD Decrease
Chee 2003	173	55-65	2 yr	Milk Powder	Lower BMD Decrease
Manios 2007	101	PM Women	5 mo	Milk & Yogurt	Higher LS and WB BMD
Daly 2006	111	50-87	2 yr	Fortified Milk	Lower Hip & Radius BMD Decrease
Thorpe 2008	130	30-65	1 yr	Dairy	Lower BMD Decrease
Moschonis 2010	66	55-65	30 mo	Fortified Milk & Yogurt	Increased WB BMD
Moschonis 2011	115	PM Women	12 mo	Fortified Milk & Yogurt	Increased WB BMD
Gui 2012	141	45-65	18 mo	Milk	Lower Hip BMD Decrease

Adapted from Rizzoli et al Osteoporos Int 2018

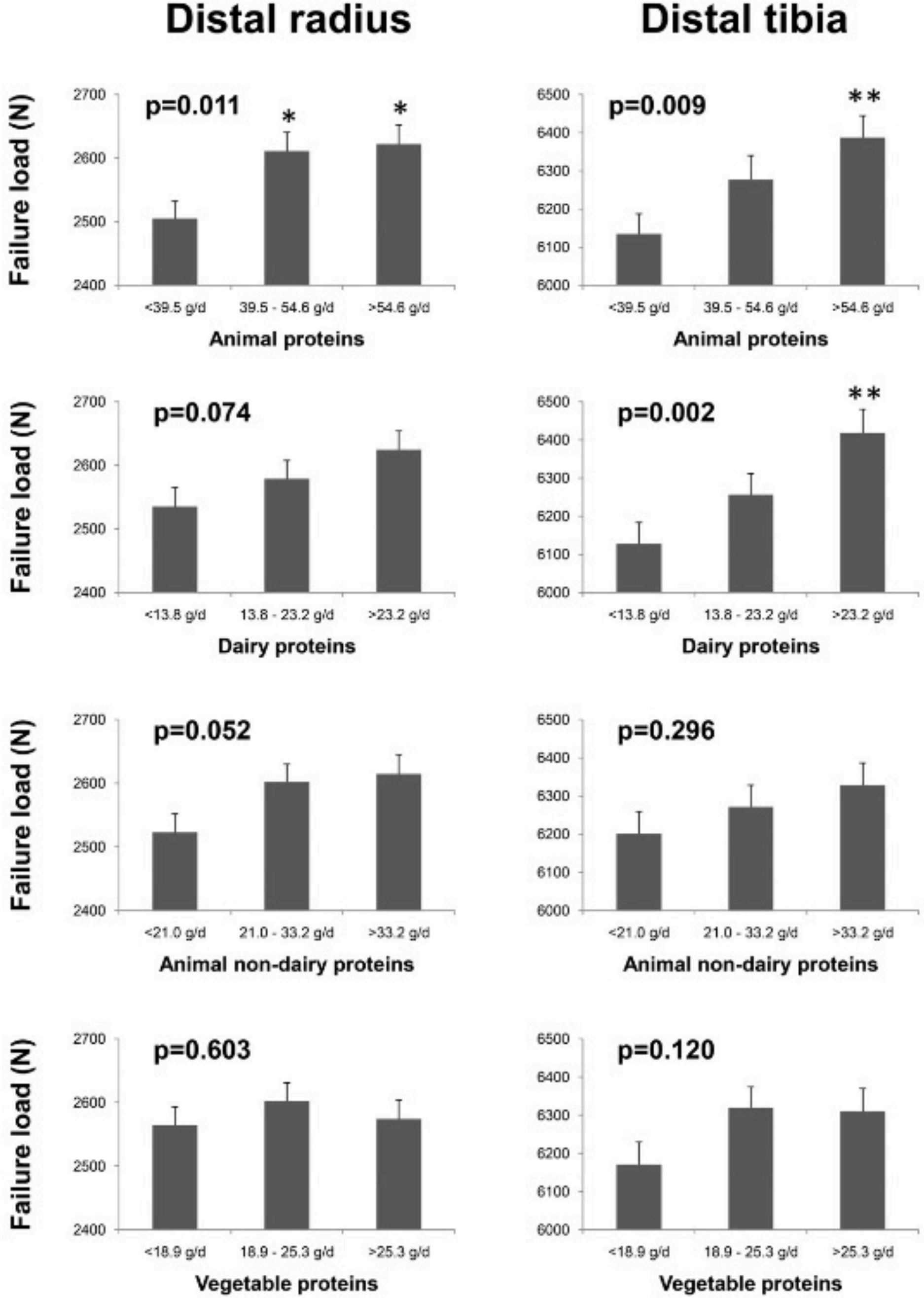
Dairy product intake and bone properties in 70-year-old men and women

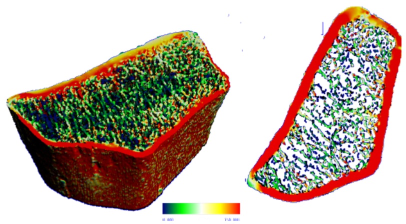
n=2040
(1000 W &
1040 M)



Hallkvist et al Arch Osteoporos 2018

Peripheral skeleton bone strength is positively correlated with total and dairy protein intakes in healthy postmenopausal women[1,2]





Durosier-Izart et al
AJCN 2017

High dairy protein intake is associated with greater bone strength parameters at the distal radius and tibia in older men: a cross-sectional study

L. Langsetmo[1] · J. M. Shikany[2] · A. J. Burghardt[3] · P. M. Cawthon[4,5] · E. S. Orwoll[6] · J. A. Cauley[7] · B. C. Taylor[1,8,9] · J. T. Schousboe[10,11] · D. C. Bauer[12] · T. N. Vo[1] · K. E. Ensrud[1,8,9] · for the Osteoporotic Fractures in Men (MrOS) Study Research Group

Osteoporosis International 29:69-77,2018

1016 Men, Mean Age 84.3 Yrs (MrOs),
FFQ, Protein Intakes in Percent of Energy Intakes
HR-pQCT

- Dairy Protein
  -> Higher Calculated Bone Strength
  (Effect Size: 0.17 at radius et 0.13 at tibia)
- Non Dairy Animal Protein
  -> Higher Calculated Bone Strength (radius)
- Vegetable Protein: No Effect

Milk and other dairy foods and risk of hip fracture in men and women

D. Feskanich[1] · H. E. Meyer[2,3] · T. T. Fung[4] · H. A. Bischoff-Ferrari[5] · W. C. Willett[1,6]

Osteoporosis International 29:385-396, 2018

Nurses' Health Study & Health Professionals Follow-up Study:

80'600 Postmenopausal Women
43'306 Men -> 32 Yrs Follow-Up
(Survey every 4 Yrs)
2138 & 694 Hip Fractures

Hip Fracture Risk :

- - 8 % per Milk Serving (240 ml)
- - 9 % per Cheese Serving (28 g) (NS)
- - 6 % per Dairy Products Serving

Fermented Dairy Products and Hip Fracture Risk

Swedish Mammographic Cohort
61'433 Women 39-74 ans; Follow-up: 20.1 aYrs
4'259 Hip Fractures

- Yogurt and Fermented Milk

	<1g/d	1-199g/d	200-399g/d	>=400g/d
HR	1	0.73 (0.68-0.79)	0.84 (0.70-0.93)	0.70 (0.57-0.86)

- Cheese

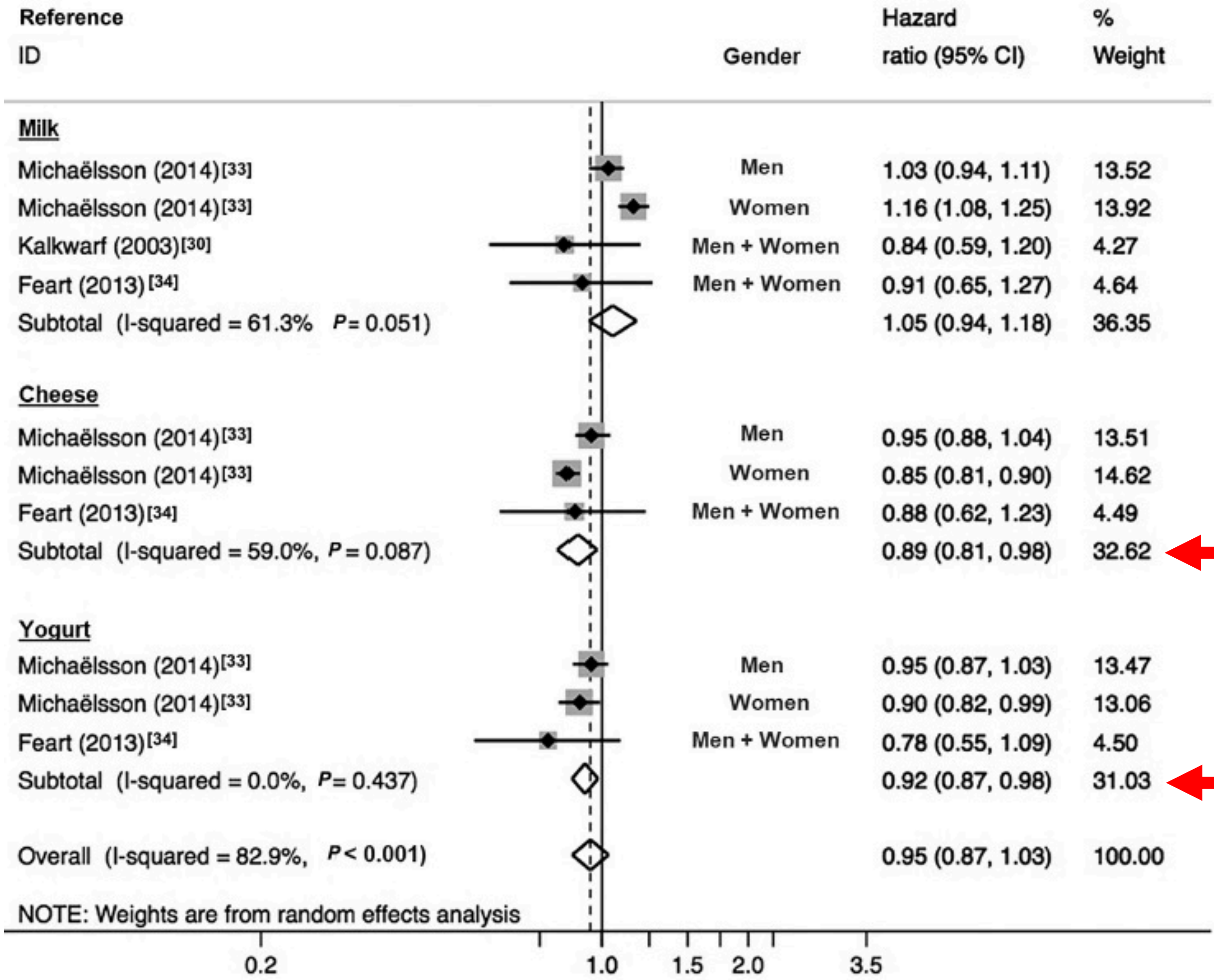
	<20g/d	20-39g/d	40-59g/d	>=60g/d
HR	1	0.72 (0.67-0.78)	0.88 (0.80-0.97)	0.64 (0.55-0.74)

For each Serving
(200 g Yogurt
Or 20g Cheese):
Minus 10 -15% Hip
Fracture Risk

Michaëlsson K et al. BMJ 2014

Effects of Milk and Dairy Products on the Prevention of Osteoporosis and Osteoporotic Fractures in Europeans and Non-Hispanic Whites from North America: A Systematic Review and Updated Meta-Analysis

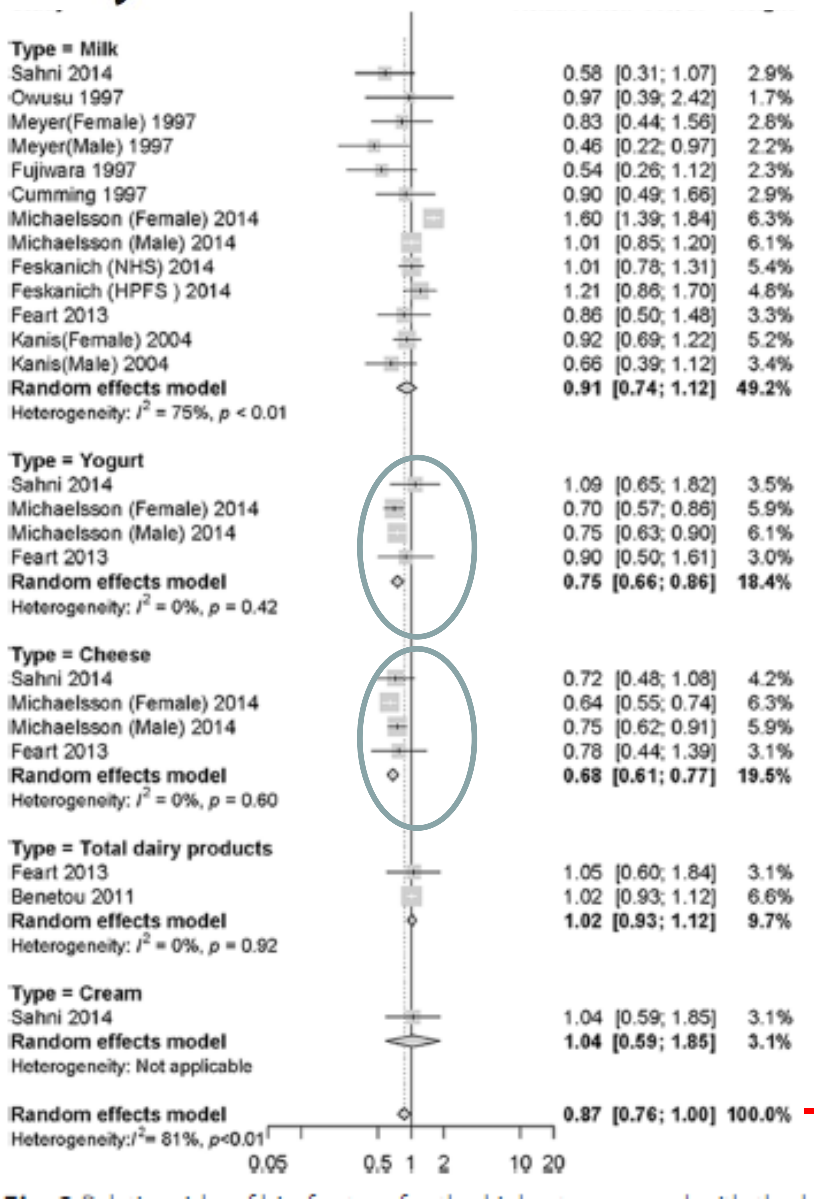
HR for Incident Fracture at any Site (n=109'134)



Matia-Martin et al Adv Nutr 2019

Dairy product consumption and risk of hip fracture: a systematic review and meta-analysis

Cohort



- 25%

- 32%

- 13%

Bian et al BMC Public Health 2018

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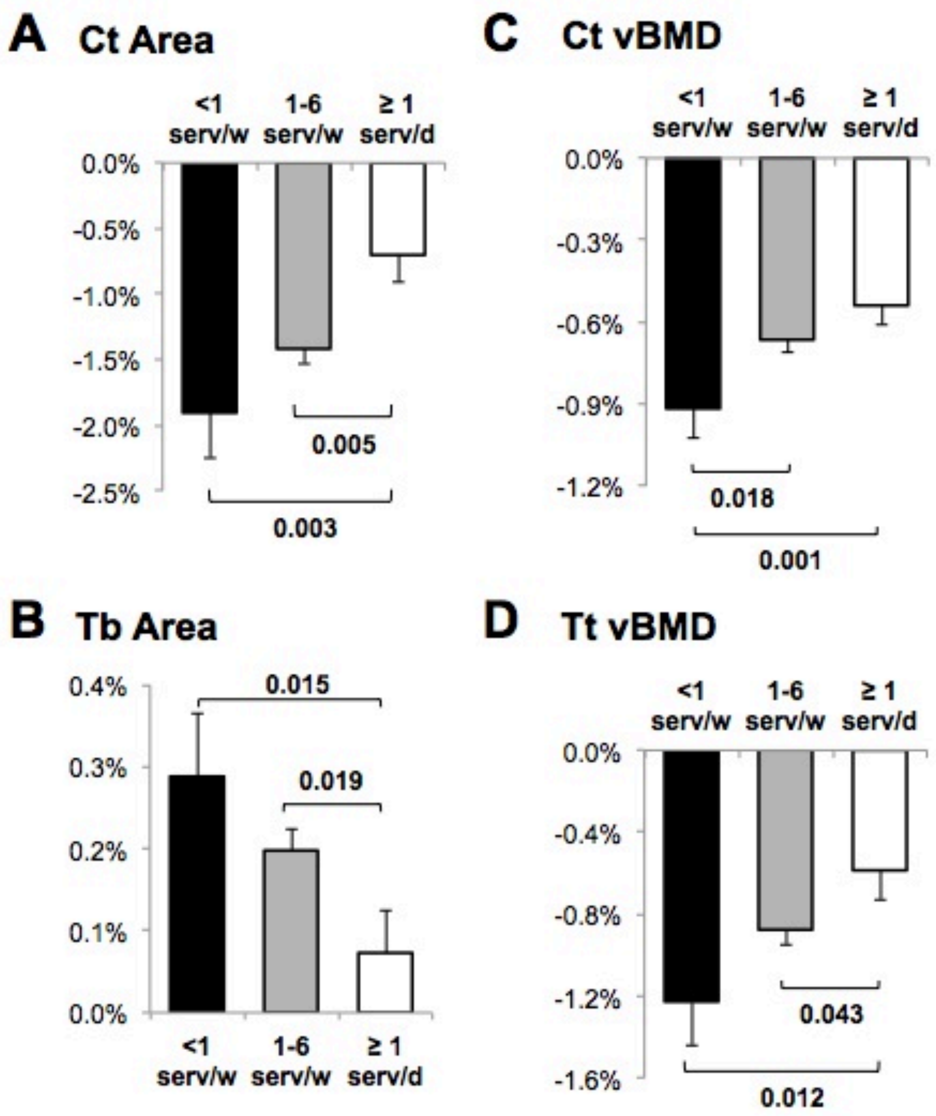
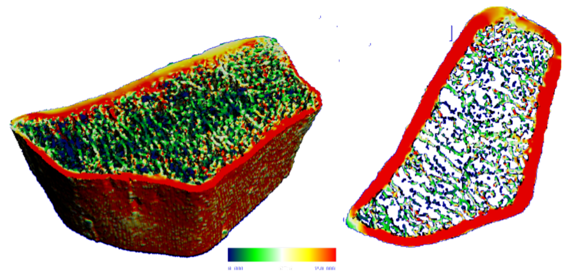
Fermented dairy products consumption is associated with attenuated cortical bone loss independently of total calcium, protein and energy intakes in healthy postmenopausal women





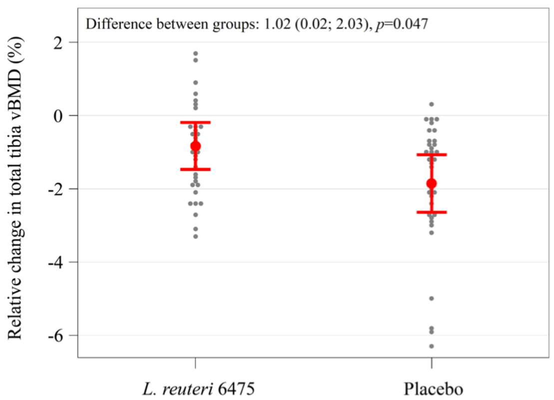
Biver et al Osteoporos Int 2018

Effects of *Lactobacillus reuteri* on Bone in Older Women – The ELBOW Trial

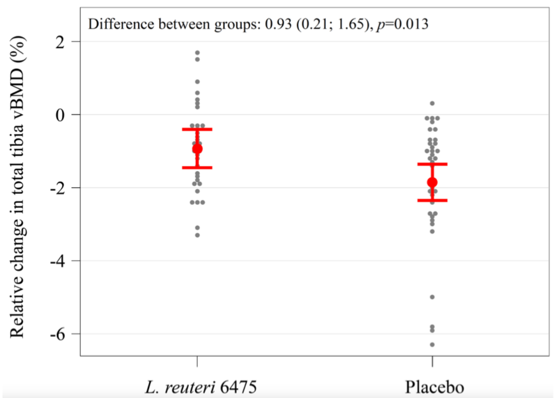
- A randomized, double-blind, placebo-controlled trial, ± daily supplementation with L.reuteri 6475 in older women with low BMD
- 90 women, 76 years old, randomized to placebo or L.reuteri 6475 for 12 months
- The primary and predefined outcome was relative change in volumetric BMD at the ultradistal tibia (measured with HRpQCT).

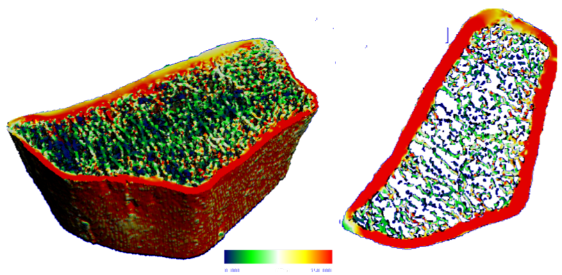
- Results

Intention to treat population, n=90



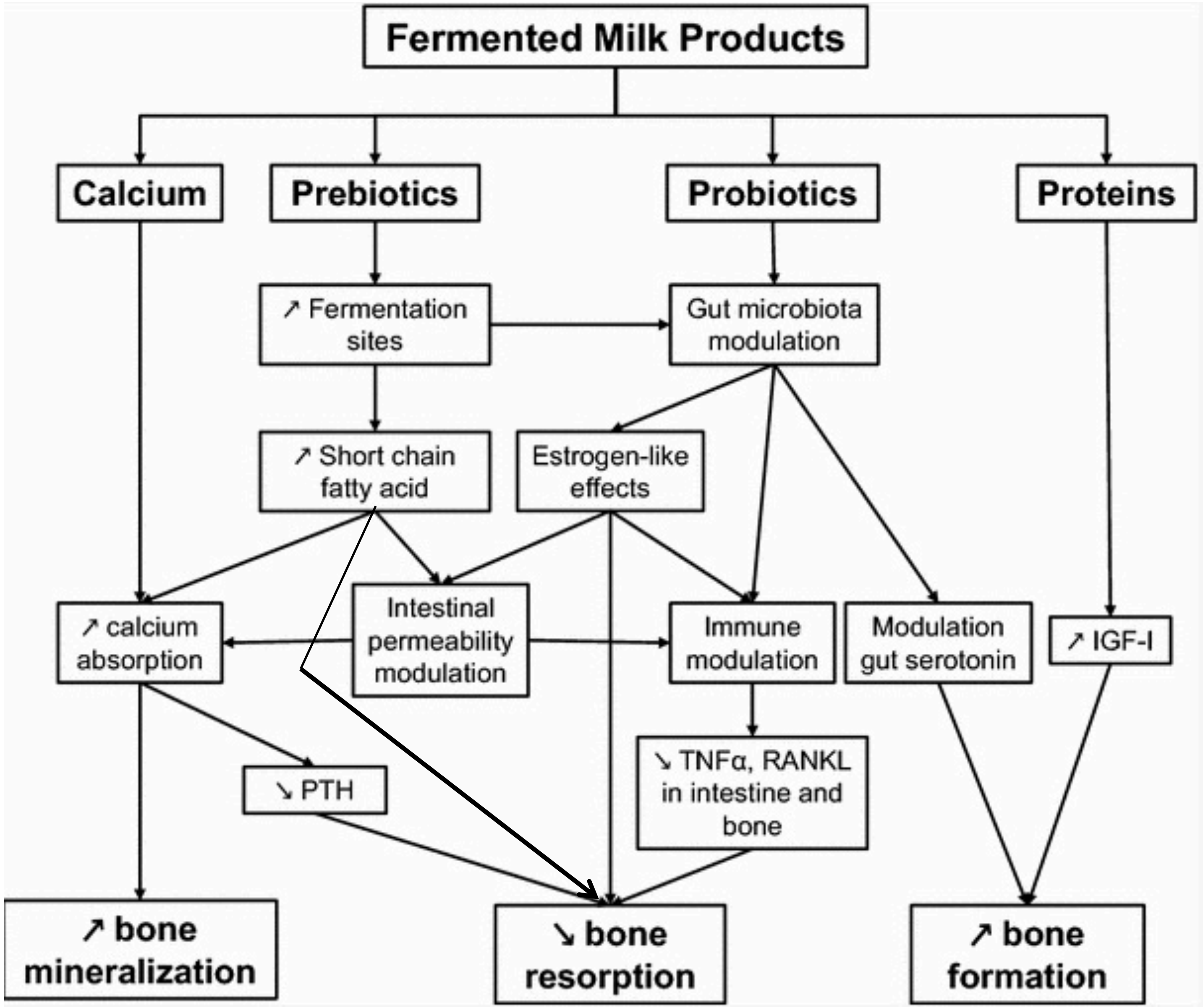
Per protocol population, n=68





Nilsson et al J Int Med 2018

Effects of Fermented Milk Products on Bone



Rizzoli & Biver CTI 2018

Veganism, vegetarianism, bone mineral density, and fracture risk: a systematic review and meta-analysis

HUG Hôpitaux Universitaires de Genève

Fracture

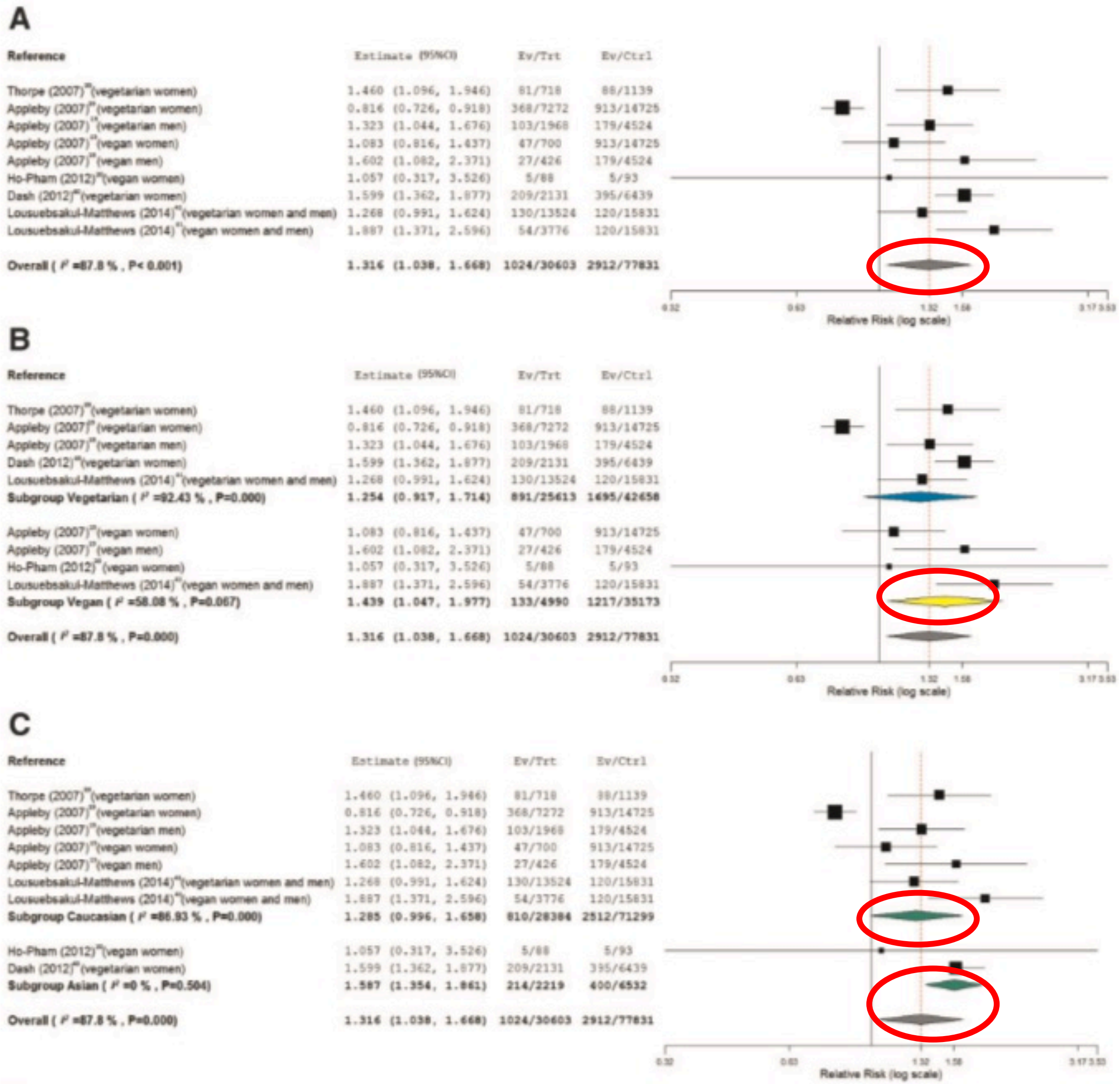
Vegetarians & Vegans
vs Omnivores

Vegetarians
vs Omnivores

Vegans
vs Omnivores

Caucasians

Asians



◆-Vegetarians and vegans, ◆-Only vegetarians, ◆-Only vegans, ◆-Overall results.

Iguacel et al Nutr Rev 2019

The Bone Bank (BBC,Bone Bank Corp)

Dairy ?

Income: Yes
(Bone Accrual)

Expenses: Yes
(Bone Loss)

Capital:	Gold	Mass/Density	-> Bone Strength
	Currencies	Geometry	
	Equities	Microstructure	
	Bonds	Matrix/Mineral	

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