



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)



Capital:

Gold

Currencies

Equities

Bonds

Mass/Density

Geometry

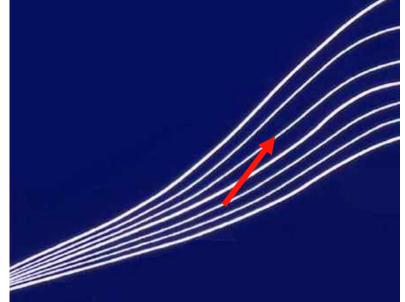
Microstructure

Matrix/Mineral



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











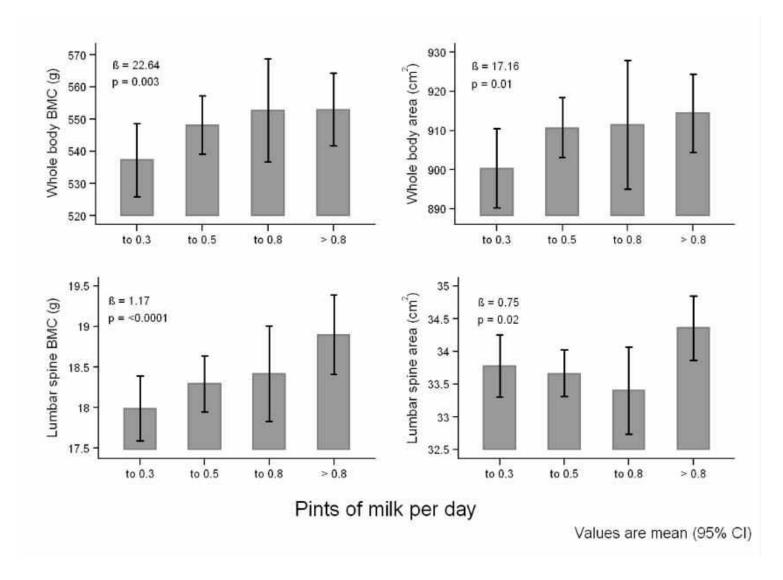
Children Bone Mass in Relation to Mother Nutritional Status during Pregnancy

- 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





Randomized Controlled Trials

Milk consumption and the growth of school children

Orr BMJ 1928

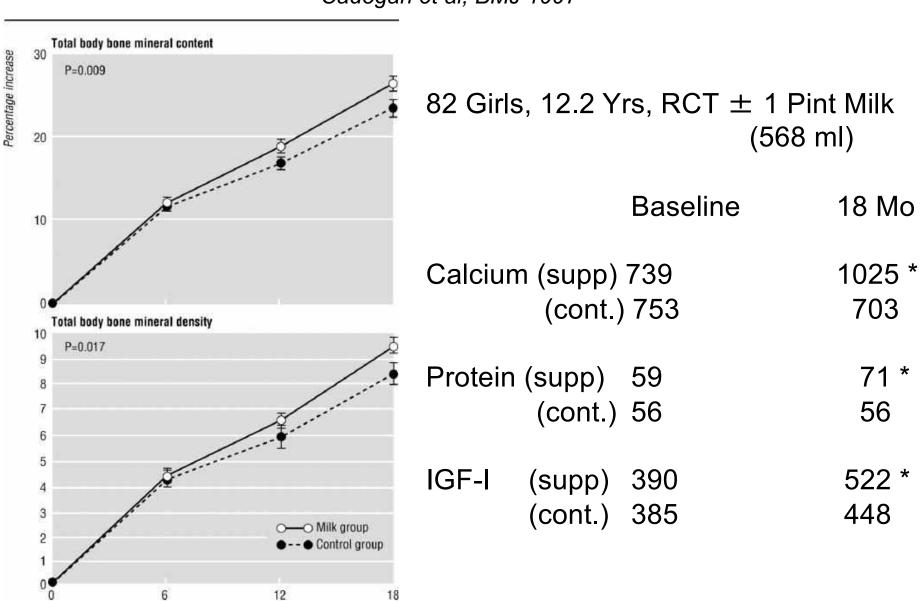
Leighton & Clark BMJ 1929

400-600 ml Milk -> Greater Height Gain



Milk Intake and BMC Acquisition in Adolescent Girls

Cadogan et al, BMJ 1997



Months

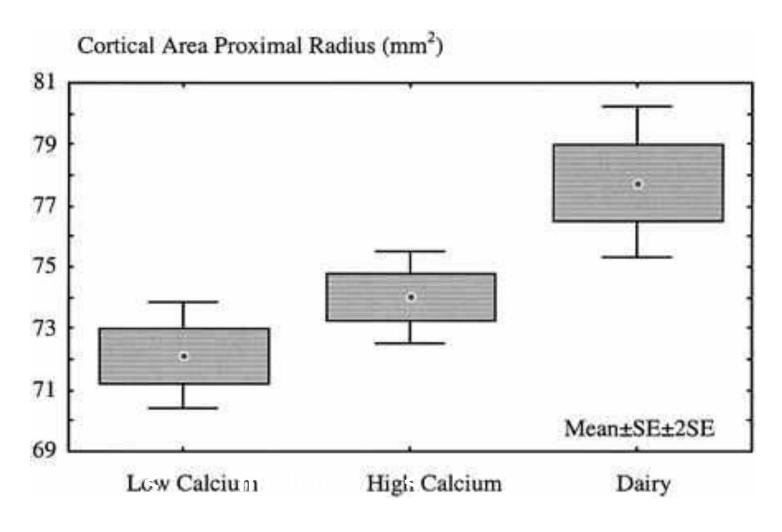


Effect of Dairy on Bone Mass Accrual in Children and Adolescents (RCT)

Study	n	Age(yr)	Duration	Intervention	Main Results
Matkovic 1990	28	14	2 yr	r 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



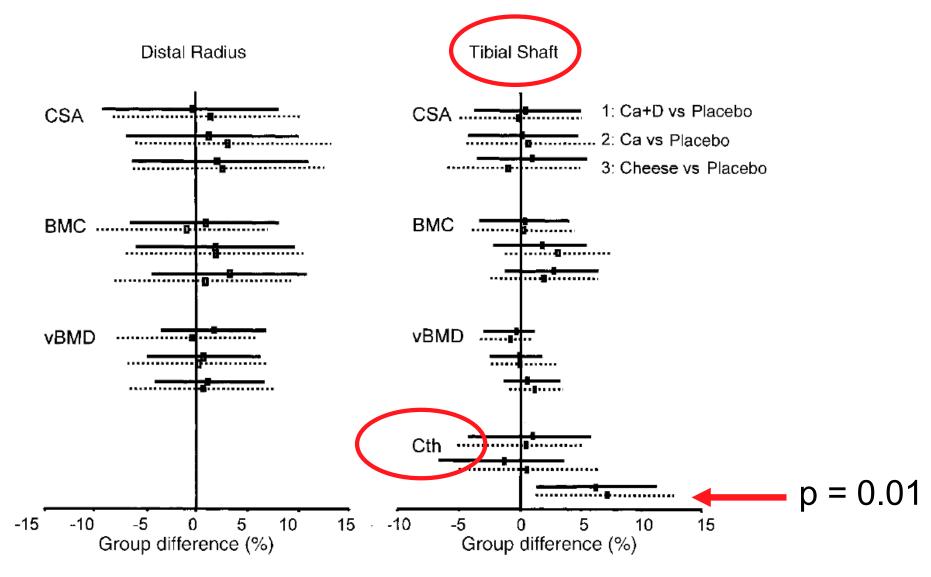
Dairy versus high or low calcium, P=0.0003 by ANOVA

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

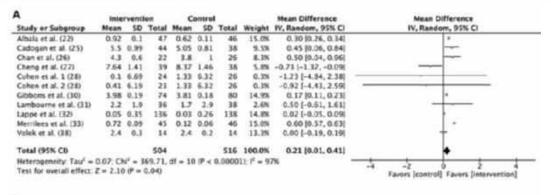


ITT and Per Protocol



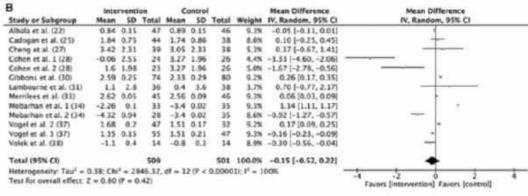
Effects of Milk and Milk-Product Consumption on Growth among Children and Adolescents Aged 6–18 Years: A Meta-Analysis of Randomized Controlled Trials

Lean Mass



+ 21%

Fat Mass



% Fat

0	Inte	rventi	O-M	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	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, -0.10]	
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)	+
Vrdek et al. (34)	-2.2	0.1	1.4	-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: Tau ⁴ = 0	07: CN	- 90	15.4	- 9 P	< 0.00	10011	F = 90%		
Test for overall effect: 2									Favors [intervention]] Favors [control]

- 27%



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



Recommended Milk Intakes

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

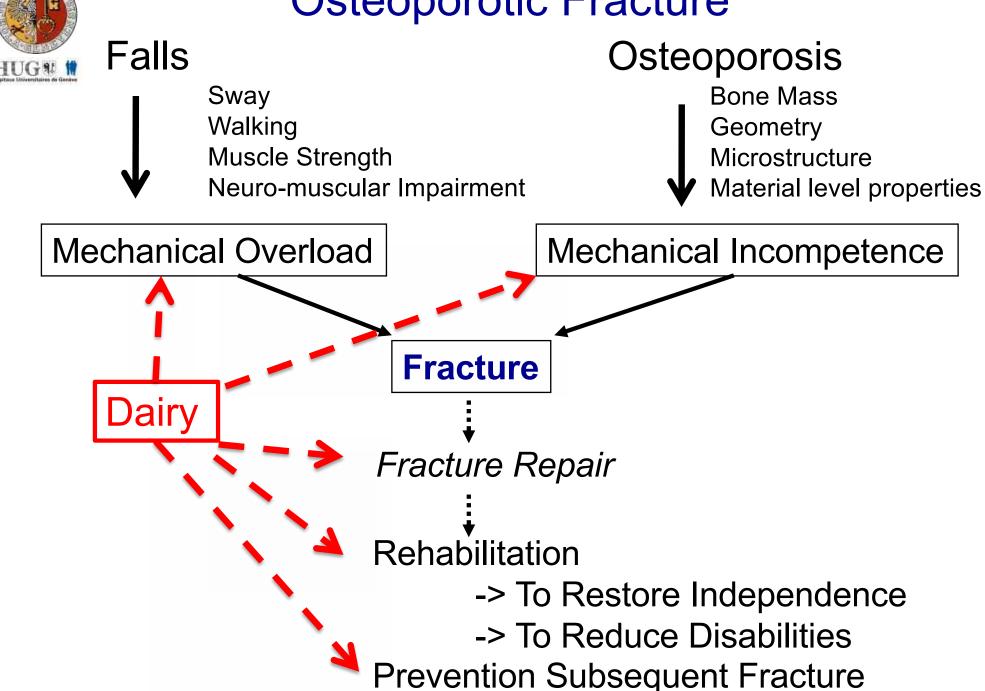
Children 2 - 8 Yrs 480 ml or Equivalent

> 9 Yrs 730 ml or Equivalent

3 Equivalents / day



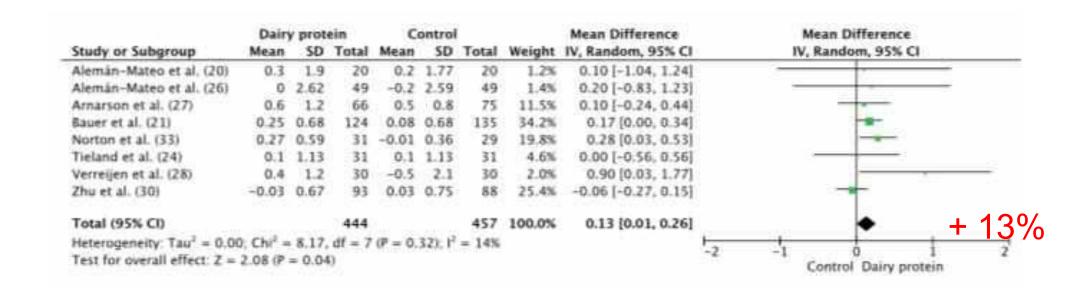
Osteoporotic Fracture



Adapted from Rizzoli, Best Pract Res Clin Endocrinol Metab 2014



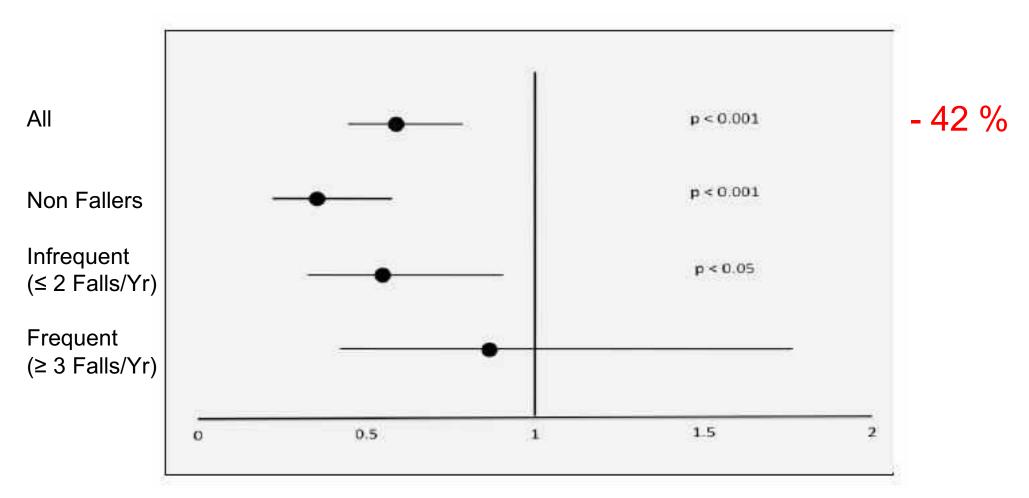
The Impact of Dairy Protein Intake on Muscle Mass, Muscle Strength, and Physical Performance in Middle-Aged to Older Adults with or without Existing Sarcopenia: A Systematic Review and Meta-Analysis





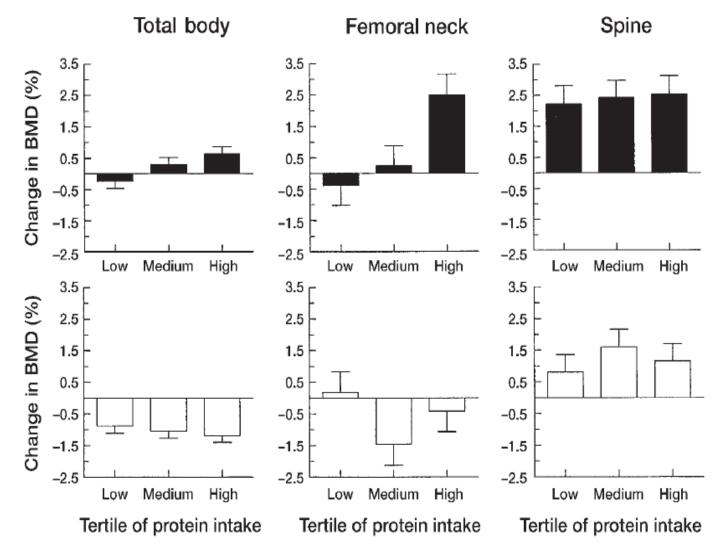
A DAIRY-BASED PROTEIN, CALCIUM AND VITAMIN D SUPPLEMENT REDUCES FALLS AND FEMORAL NECK BONE LOSS IN AGED CARE RESIDENTS: A CLUSTER RANDOMISED TRIAL

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





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



Ca x Protein P=0.044 High vs low P=0.011 and middle P=0.042

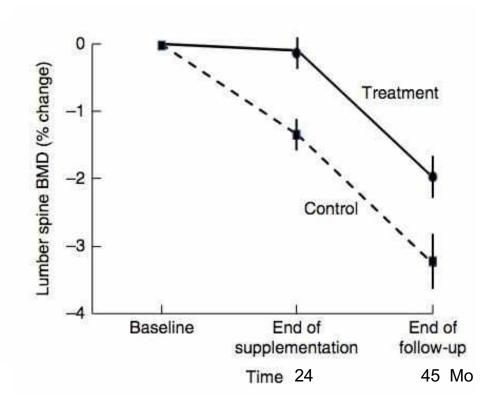


Effects of Fortified Dairy Products

Whole Body BMD

1·16 - Treatment 1·108 - Control 1·08 - Baseline 12 months Duration of treatment

Lumbar Spine BMD





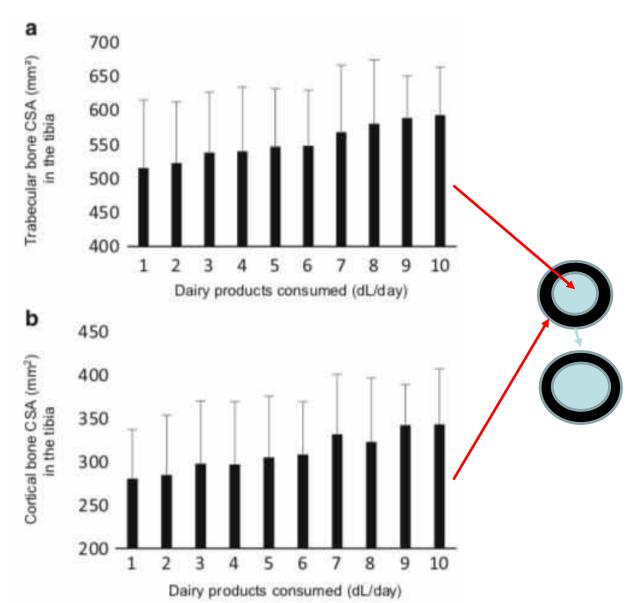
Effect of Dairy on Bone Mineral Density in Adults (RCT)

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



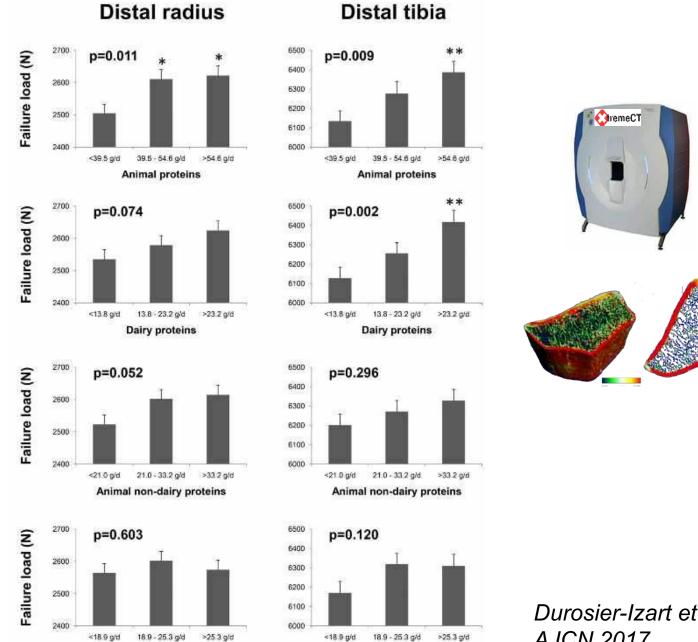
Dairy product intake and bone properties in 70-year-old men and women

n=2040 (1000 W & 1040 M)





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



Vegetable proteins

Vegetable proteins

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

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L. Langsetmo<sup>1</sup> J. M. Shikany<sup>2</sup> · A. J. Burghardt<sup>3</sup> · P. M. Cawthon<sup>4,5</sup> · E. S. Orwoll<sup>6</sup> · J. A. Cauley<sup>7</sup> · B. C. Taylor<sup>1,8,9</sup> · J. T. Schousboe<sup>10,11</sup> · D. C. Bauer<sup>12</sup> · T. N. Vo<sup>1</sup> · K. E. Ensrud<sup>1,8,9</sup> · 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 0 · 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

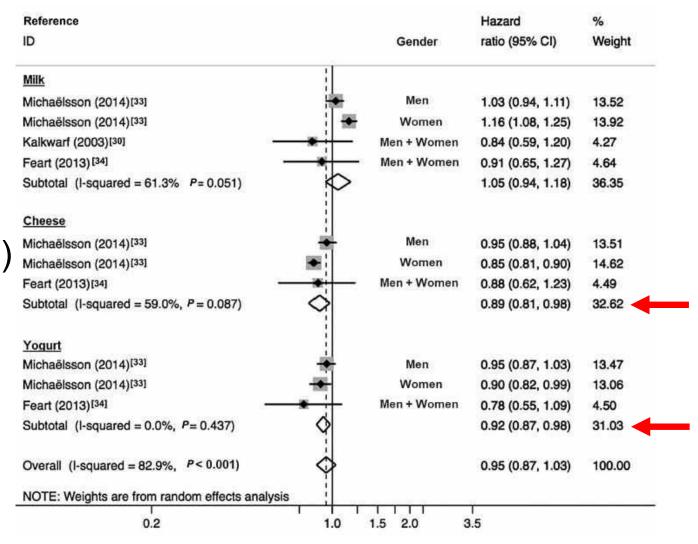
	<20g/d	20-39g/d	40-59g/d	>=60g/d
HR	1	0.72 (0.67-0.78)	0.88 (0.80-0.97)	0.64 (0.55-0.74)

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



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

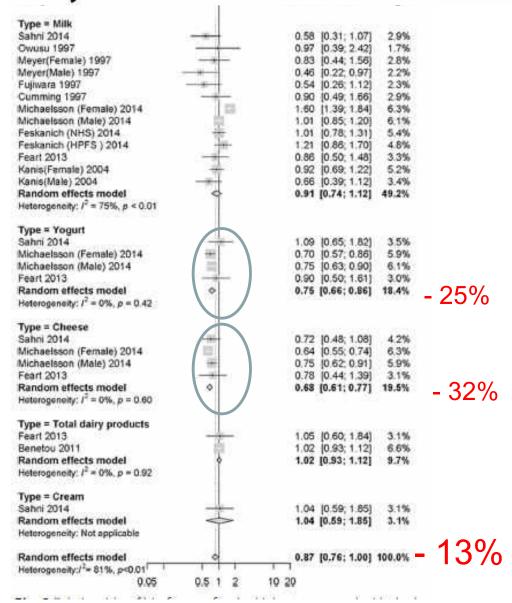
HR for Incident Fracture at any Site (n=109'134)





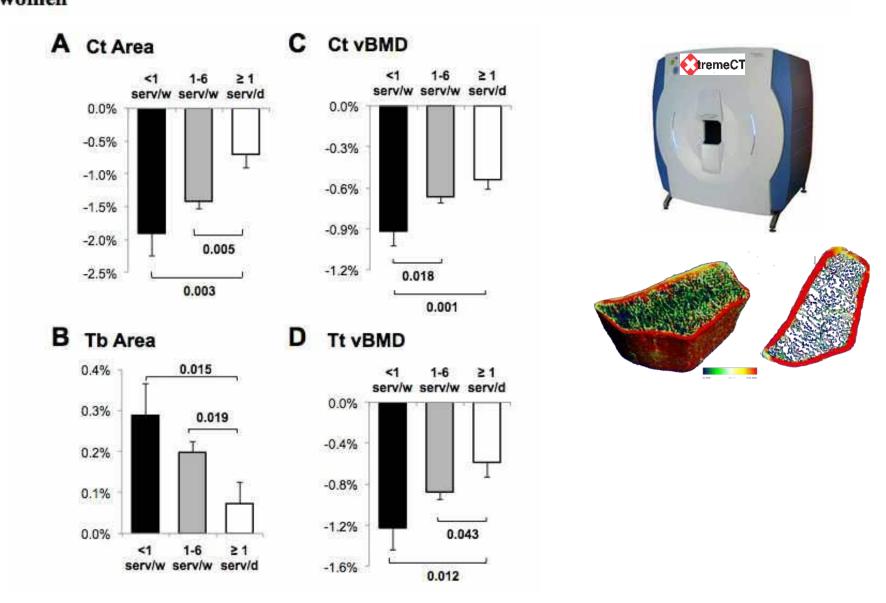
Cohort

Dairy product consumption and risk of hip fracture: a systematic review and metaanalysis





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



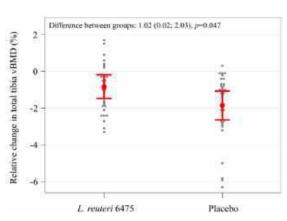


Effects of Lactobacillus reuteri on Bone in Older Women – The ELBOW Trial

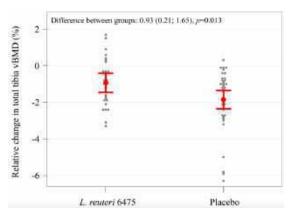
- A randomized, double-blind, placebo-controlled trial, ± daily supplementation with L.reuteri 6475 in older women with low BMD
- 90 women, 76 years old, randomized to placebo or L.reuteri 6475 for 12 months
- The primary and predefined outcome was relative change in volumetric BMD at the ultradistal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

Results

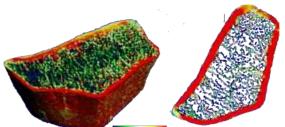
Intention to treat population, n=90



Per protocol population, n=68

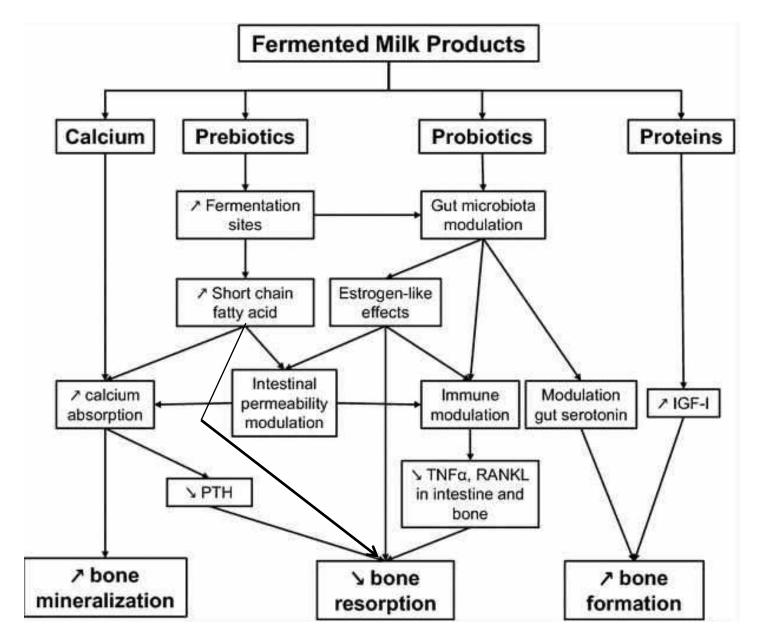








Effects of Fermented Milk Products on Bone





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

Fracture

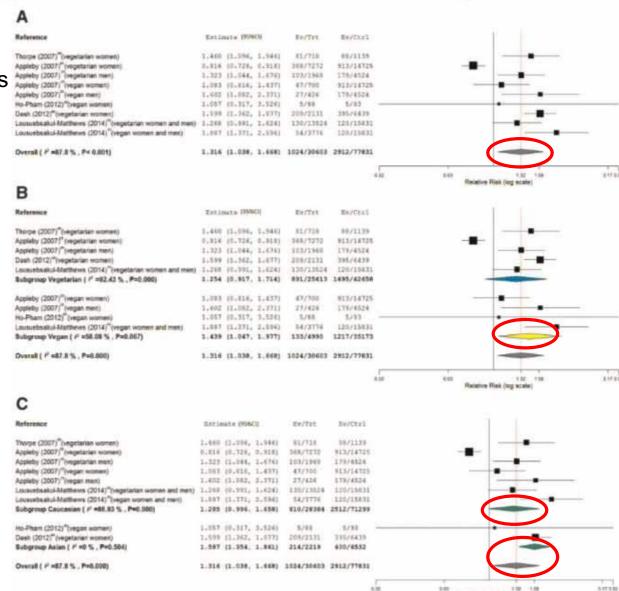
Vegetarians & Vegans vs Omnivores

Vegetarians vs Omnivores

Vegans vs Omnivores

Caucasians

Asians





Relative Risk (top scale)



The Bone Bank (BBC,Bone Bank Corp)



Capital:

Gold

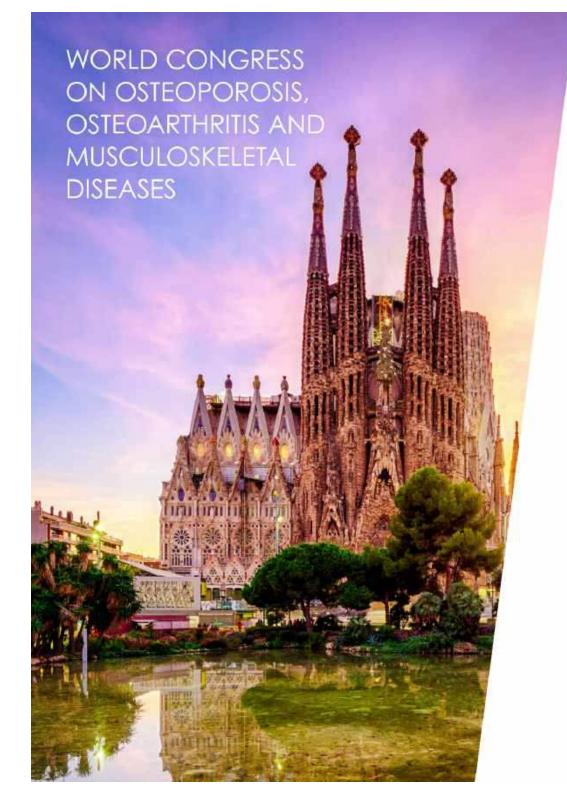
Currencies

Equities

Bonds

Mass/Density
Geometry
Microstructure
Matrix/Mineral

-> Bone Strength





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