Mælkematricen og knogler

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Interessekonfligter

Board membership: Amgen, Eli Lilly, MSD, Novartis, Nycomed, Gilead.

Payment for lectures: Amgen, Eli Lilly, MSD, Gilead.

Research grants: Eli Lilly, Amgen

Disposition

Nøgletal for osteoporose
Symptomer og diagnostik af osteoporose
Effekter af mælkeindtag på knoglemassen
Effekter af mælkeindtag på risiko for knoglebrud
Effekter af mælkeprotein på knoglemasse og brud
Spørgsmål

Nøgletal for osteoporose

550.000 har osteoporose, og omkring 130.000 er i behandling

Af personer ældre end 50 år har :

41% af alle kvinder sv. til 4 ud af 10 kvinder har osteoporose

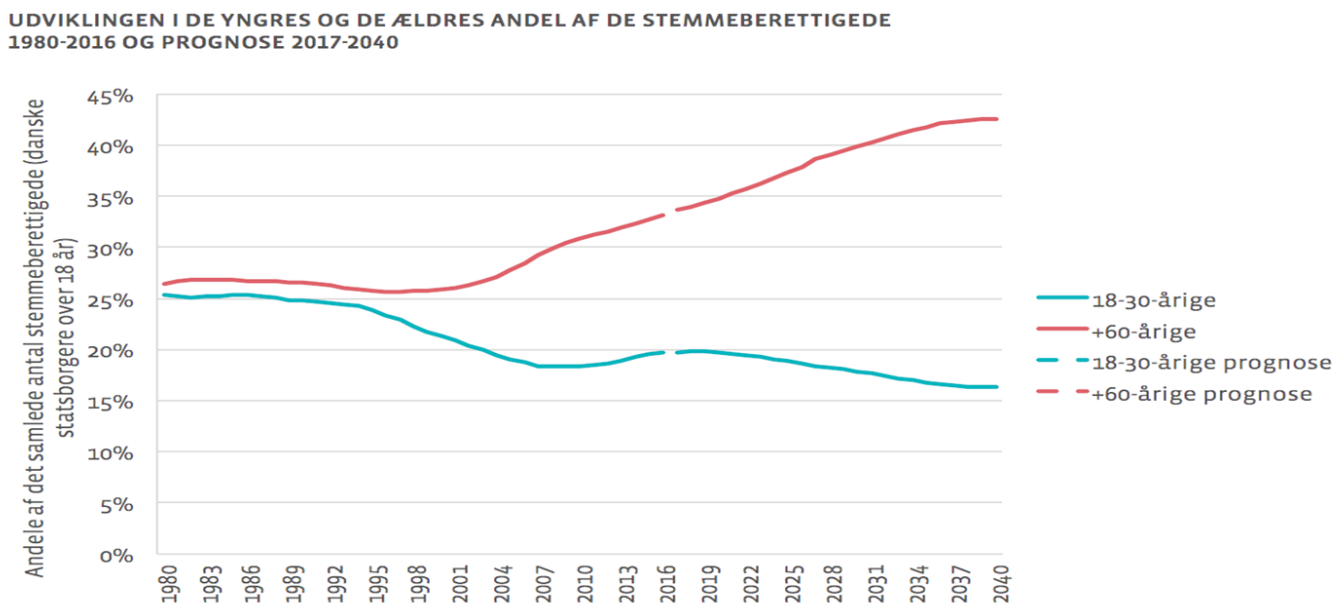
18% af alle mænd sv. til 2 ud af 10 mænd har osteoporose

9.000 hoftebrud (3.000 er mænd) om året koster
4,6 milliarder kroner

Udgiften til kommunerne udgør 75% af de samlede udgifter

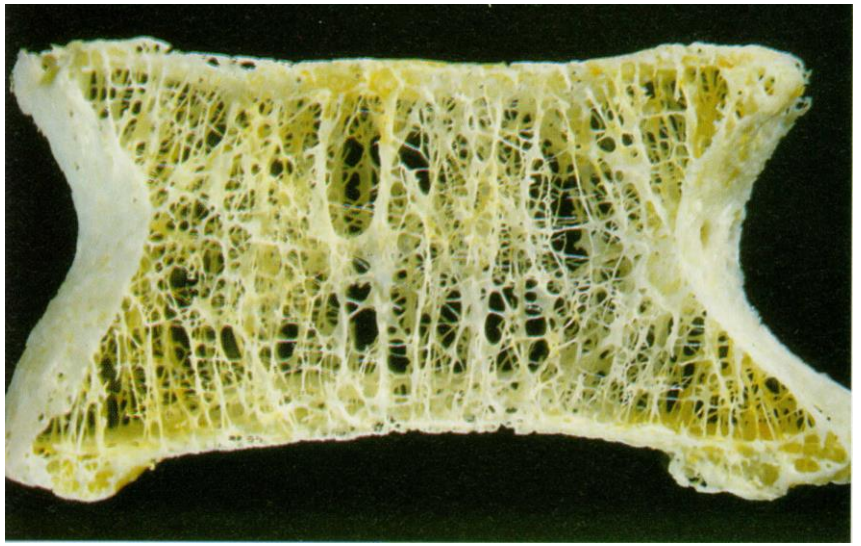
Baggrund

Befolkningssammensætningen ændres



Knoglestrukturen

Rask yngre person



Person med osteoporose

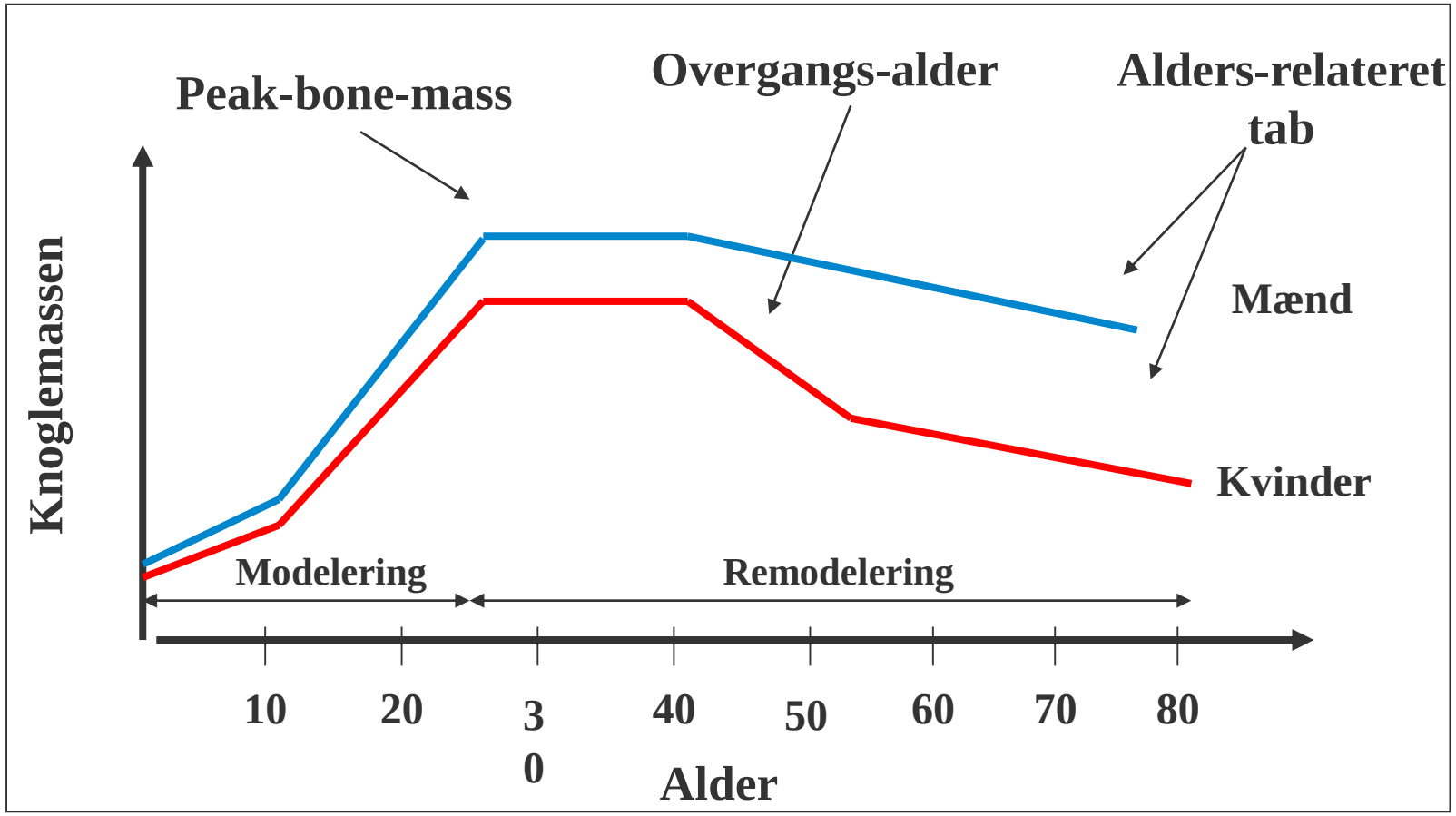
Knoglemassen gennem livet

Ved fødsel ca. 25 g Calcium

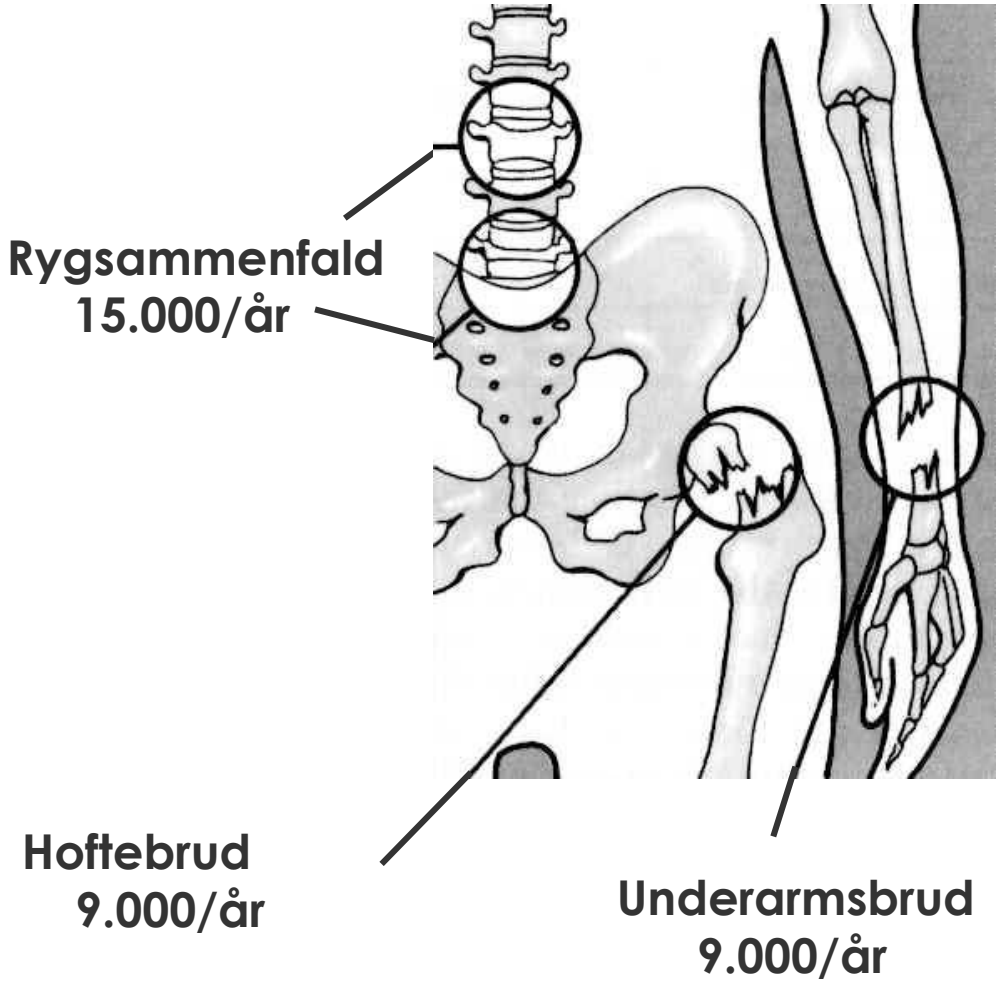
Voksne kvinder ca. 1000 g calcium

Voksne mænd ca. 1200 g calcium

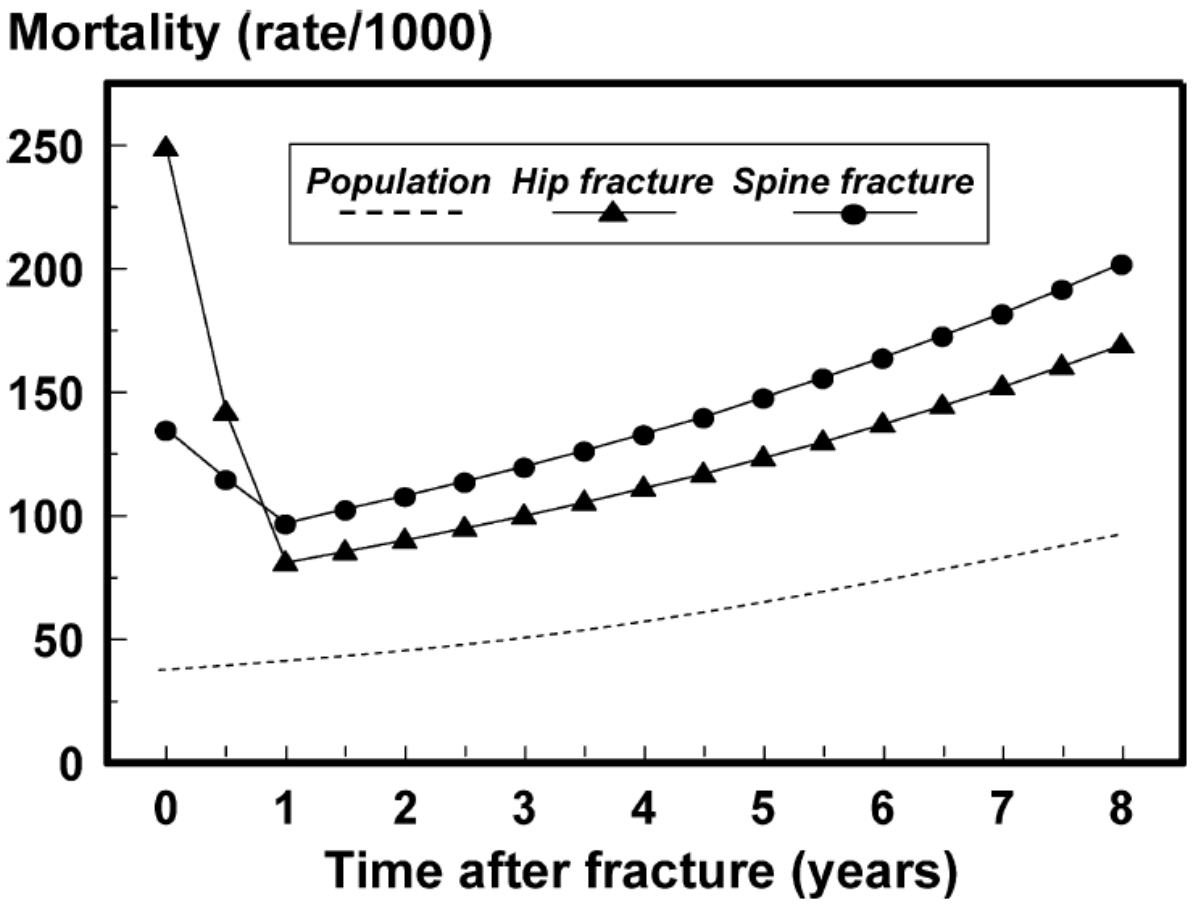
Svarer til vækst på 135 mg/dag



Klassiske osteoporotiske brud

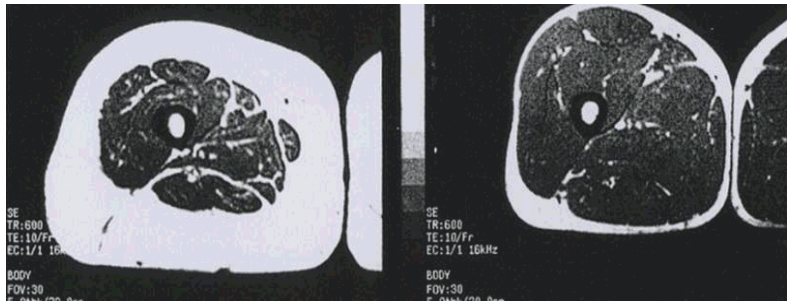


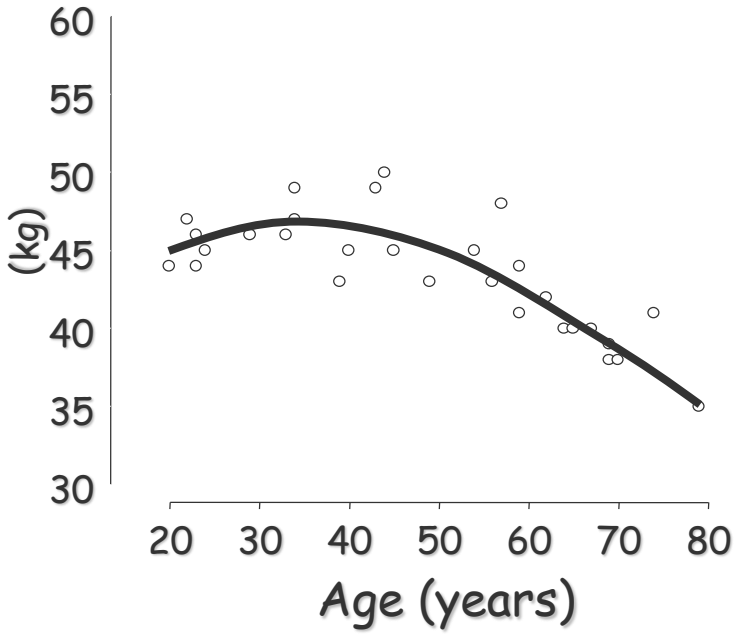
Osteoporose og mortalitet



Kanis et al. Osteoporosis Int 2004;15:108-12

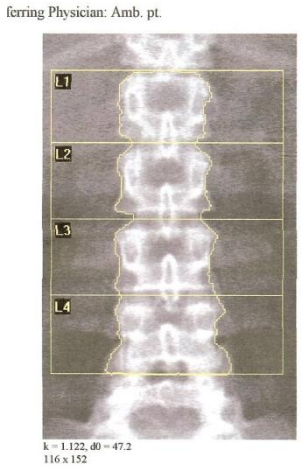
Osteoporose og livskvalitet

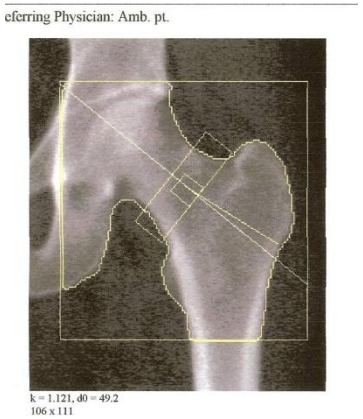


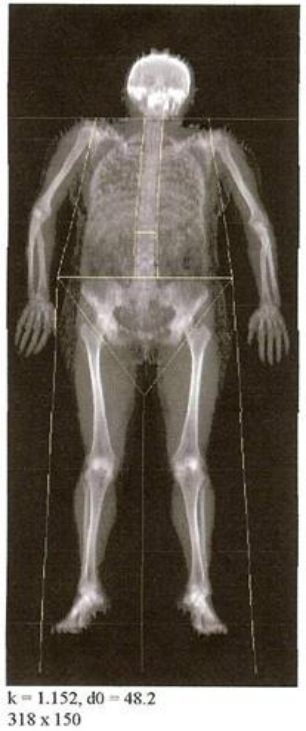


Holloszy. Mayo Clinic Proceedings, 2000

DXA-scanning







Mælkeprodukter hos børn og yngre voksne
Effekt på knoglerne

TABLE 2
Beneficial effects of dairy products on bone growth in children and adolescents: data from observational studies[1]

First author, year (reference)	Subjects	Age	Sex	Duration	Type of dairy	Outcome
	n	*y*		*mo*		
Alexy, 2005 (28)	229	6–18	F/M	48	Protein	Positive association between protein intake and diaphyseal bone stability and strength; increased BMC
Black, 2002 (33)	50	3–10	F/M	12	Milk (vs milk avoiders for 4.5 ± 2.5 y)	Milk avoiders had significantly shorter height and lower femoral neck, hip, spine, and radius BMC/BMD
Budek, 2007 (34)	109	17	F/M	Cross-sectional study	Milk	Dietary milk protein (but not dietary meat protein) significantly associated with BMC
Esterle, 2009 (35)	192	12–22	F	Cross-sectional study	Milk	Milk consumption (but not other calcium sources) associated with higher lumbar BMC/BMD
Matković, 1979 (36)	72	30–40	F/M	Cross-sectional study	All dairy	Dairy intake associated with bone mass in young adults
Matković, 2004 (37)	264	15	F	≥36	Milk	Dairy consumption associated with higher trochanter BMD and proximal radius cortical area
Teegarden, 1999 (38)	224	1–19	F	Cross-sectional study	Milk	Milk intake in adolescence correlates with total-body, radius, and spine BMC/BMD

[1] BMC, bone mineral content; BMD, bone mineral density.

Rizzoli An J Clin Nutri 2014

Mælkeprodukter i puberteten
Effekt på knoglerne

TABLE 3
Effect of dairy products on bone mineral mass accrual: results from randomized clinical trials in adolescents[1]

First author, year (reference)	Subjects	Age	Sex	Duration	Type of dairy	Skeletal site[2]	Difference between intervention and control groups
	n	*y*		*mo*			%
Cadogan, 1997 (39)	82	12	F	18	Milk (568 mL)	Whole-body	2.9
Chan, 1995 (40)	48	11	F	12	Dairy	Spine/whole-body	9.9/6.6
Cheng, 2005 (41)	195	11	F	24	Cheese (= 1000 mg Ca)	Tibia shaft	4.4
Du, 2004 (42)	757	10	F	24	Milk (330 mL)	Whole-body	4.2
Gibbons, 2004 (43)	154	8–10	F/M	18	Fortified dairy drink	Whole-body/hip/spine	NSD
Ho, 2005 (44)	199	14–16	F	12	Fortified soy drink (375 mL)	Spine/hip	NSD
Lau, 2004 (45)	344	10	F/M	18	Milk powder (= 650 mg Ca)	Spine/hip	1.4/1.1
Merrilees, 2000 (46)	91	16	F	24	Milk (= 1160 mg Ca)	Spine/femoral neck/trochanter	1.5/4.8/4.8
Zhu, 2005 (47)	606	10	F	24	Milk (330 mL)	Metacarpal cortical thickness, periosteal diameter	5.7/1.2

Rizzoli An J Clin Nutri 2014

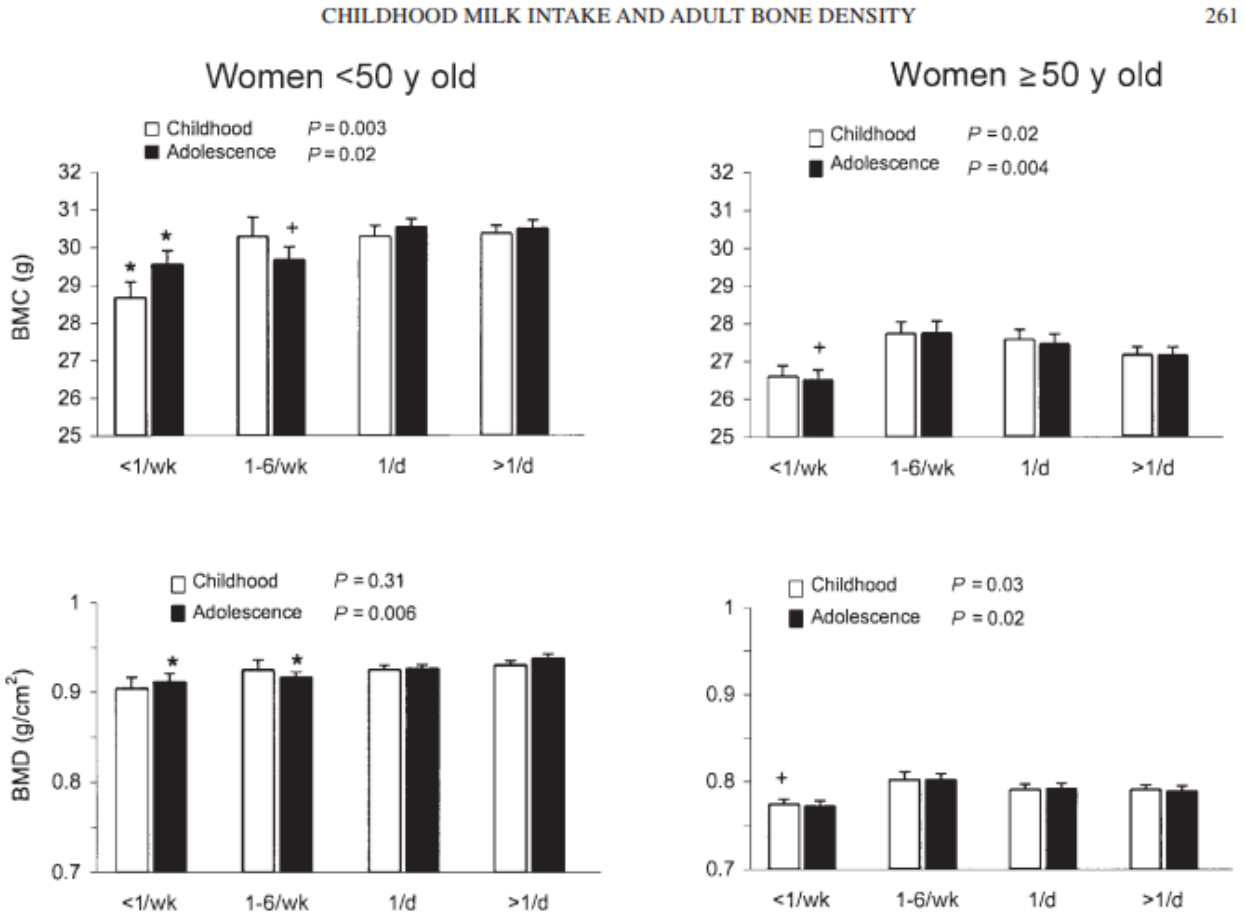
Mælkeprodukter hos voksne
Effekt på knogleomsætningen

First author, year (reference)	Subjects	Age	Sex	Duration	Type of dairy	Outcome
	n	*y*		*mo*		
Adolphi, 2009 (56)	85	58.7 ± 0.3[2]	F	0.5	Fortified fermented milk (175 mL)	Reduction in nocturnal deoxypyridinoline excretion
Bonjour, 2008 (57)	30	59.3 ± 0.3	F	1.5	Milk	Reduction in PTH, CTX, PINP, osteocalcin
Bonjour, 2009 (58)	37	84.8 ± 8.1	F	1	Skimmed soft cheese, 2 servings/d	Reduction in PTH, CTX, TRAP 5b; increase in IGF-I, 25(OH)D
Bonjour, 2012 (59)	71	56.6 ± 3.0	F	1.5	Skimmed soft cheese, 2 servings (100 g)/d	Reduction in PTH, CTX, TRAP 5b; increase in IGF-I
Bonjour, 2013 (60)	89	85.5	F	2	Either vitamin D– and calcium-fortified yogurt (2 × 125 g/d) (vitamin D 10 μg/d and calcium 800 mg/d) or nonfortified control yogurt providing calcium of 280 mg/d	Reduction in PTH, CTX, TRAP 5b
Josse, 2010 (51)	20	22.4 ± 2.4	F	3	Milk (2 × 500 mL/d)	Reduction in PTH, CTX
Kruger, 2006 (61)	82	20–35	F	4	Fortified milk	Reduction in CTX
Kruger, 2010 (62)	1898	>55	F	4	Fortified milk	Reduction in PTH, CTX, PINP, osteocalcin
Kruger, 2012 (63)	63	>55	F	3	Fortified milk	Reduction in CTX
Manios, 2007 (64)	101	60.5 ± 0.7	F	12	Fortified milk and yogurt, 3 servings/d	Reduction in PTH, CTX; increase in BMD
Thorpe, 2008 (65)	130	45.6 ± 8.9	F/M	12	High-protein dairy	Attenuated bone loss

[1] BMD, bone mineral density; CTX, cross-linked teleopeptide of type 1 collagen; IGF-I, insulin-like growth factor I; PINP, procollagen type I N-propeptide; PTH, parathyroid hormone; TRAP 5b, tartrate-resistant acid phosphatase isoform 5b; 25(OH)D, 25-hydroxyvitamin D.
[2] Mean ± SD (all such values).

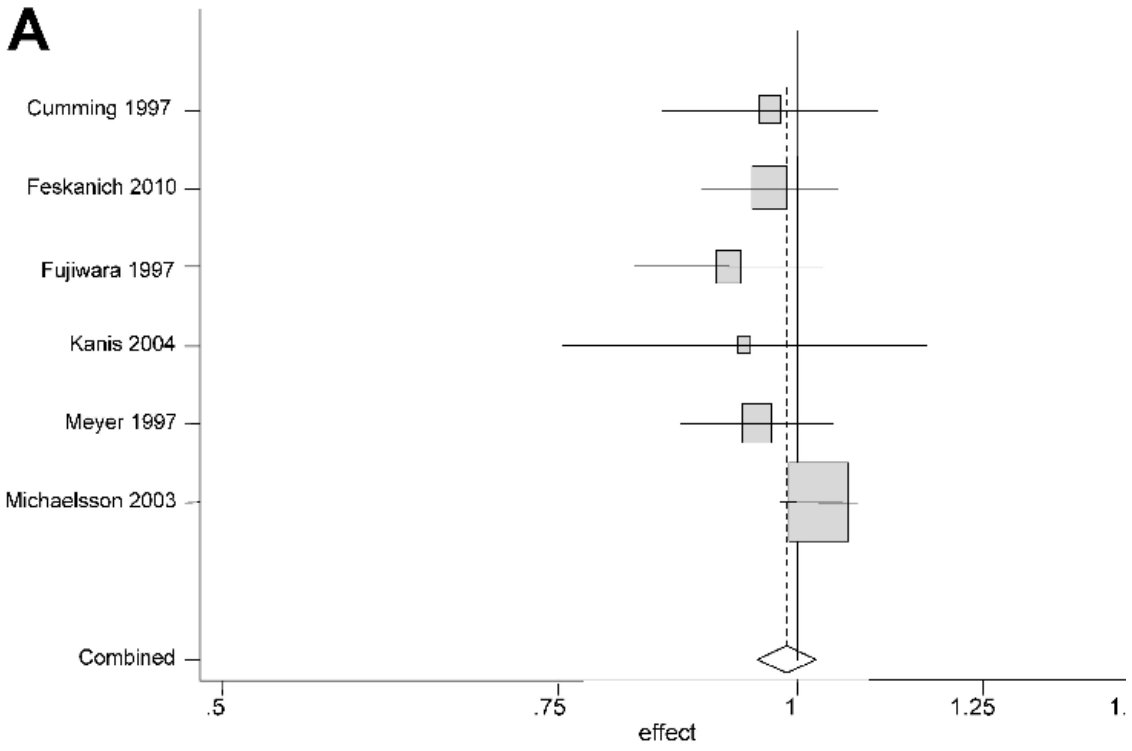
Rizzoli An J Clin Nutri 2014

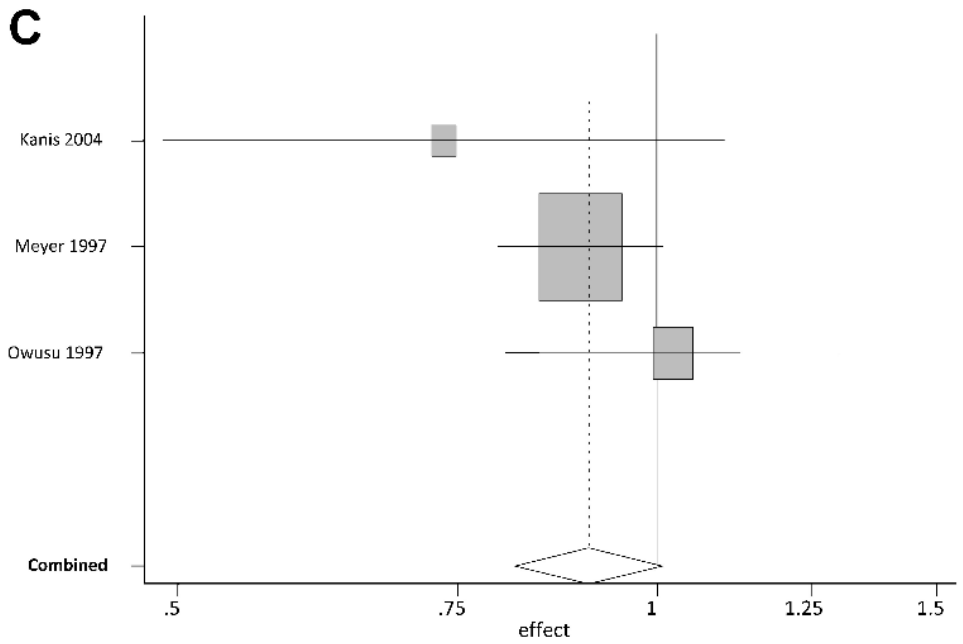
Antal glas mælk i barndommen relateret til knoglemassen som voksen



KalkWarf Am J Clin Nutr 2003

Meta analyse af prospektive kohorte studier med mælkeindtag 1 glas/d og Hoftebrud udfra spørgeskemaer





Bischoff-Ferrari JBMR 2011

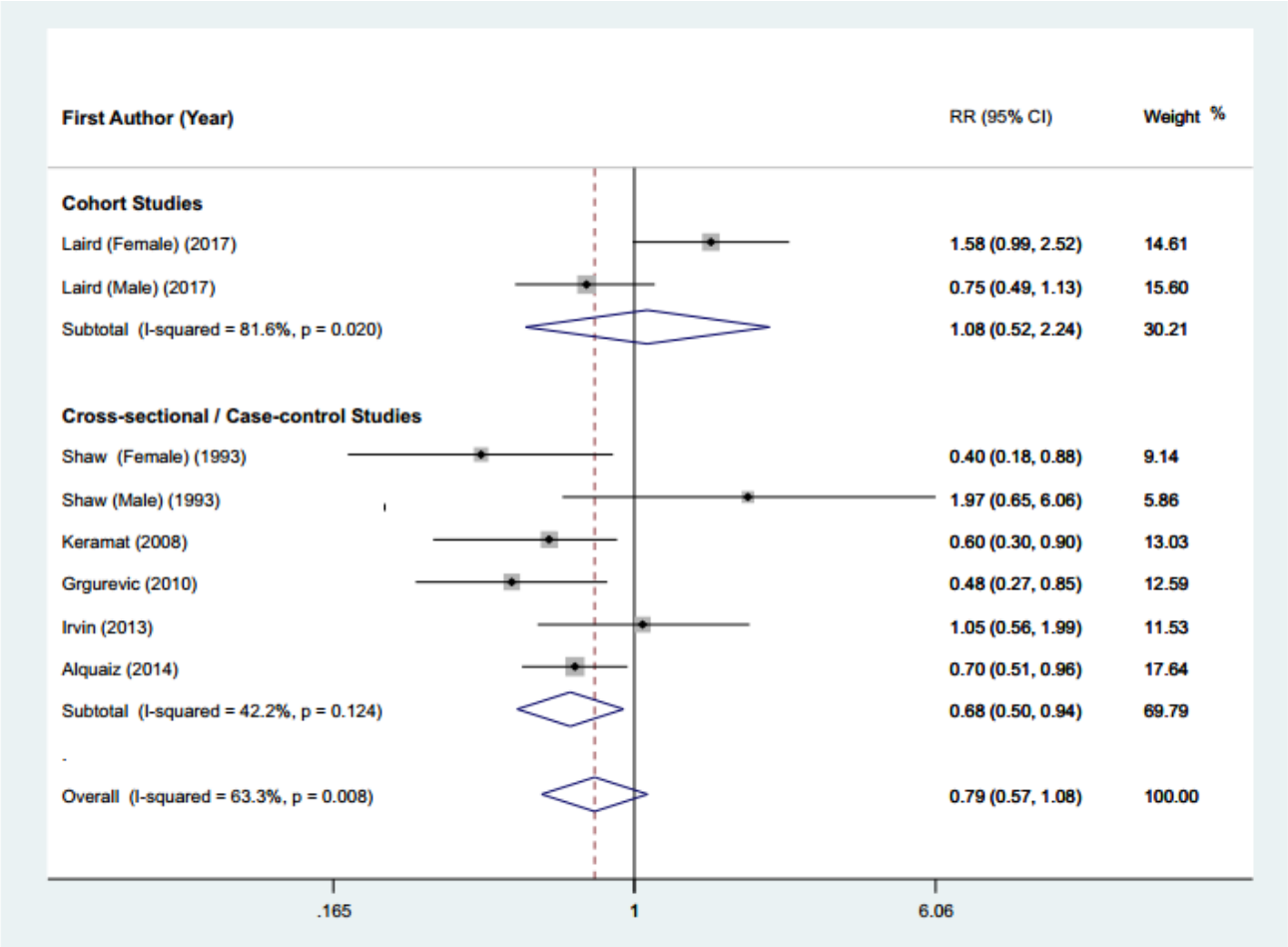
Hofterbrudsrisiko for

80,600 postmenopausal women and 43,306 men over 50 years of age were followed for up to 32 years
Mean Age Women 74 years
Mean Age Men 78 Years
Undersøgt hvert 4 år

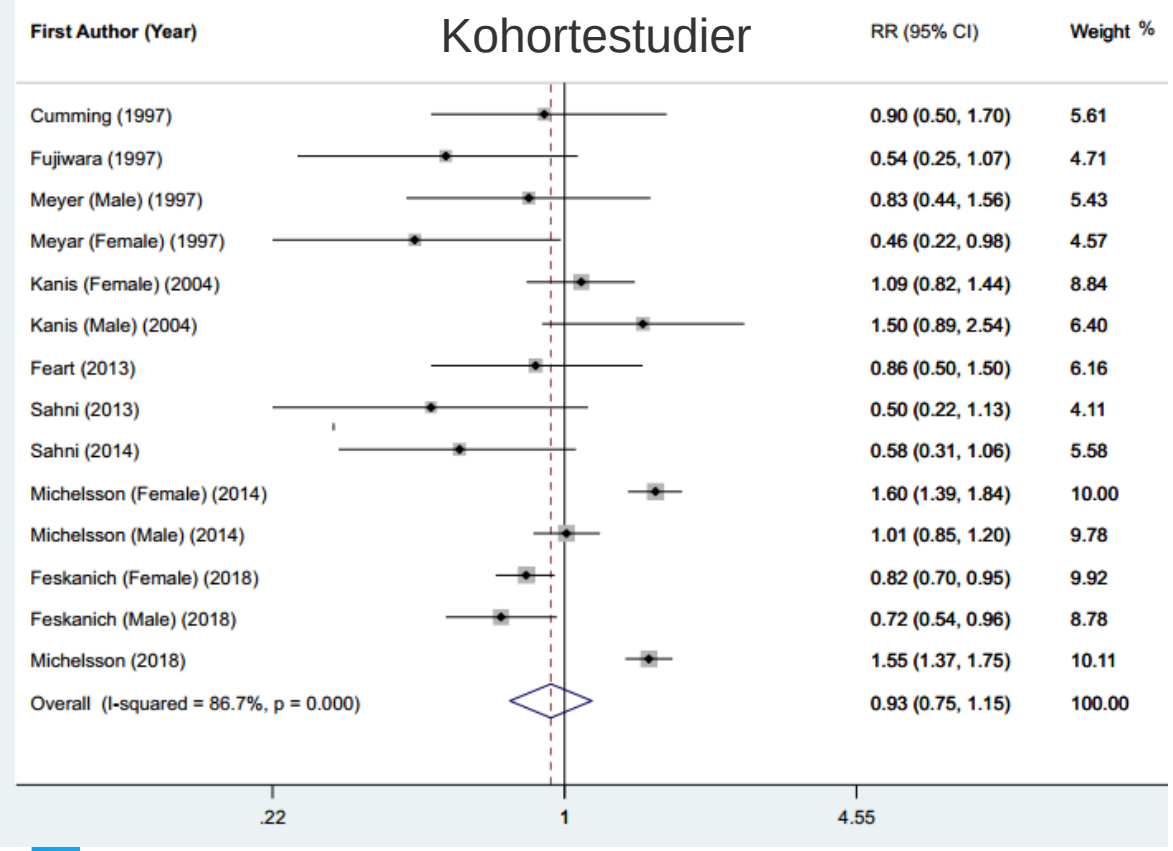
	Cumulative average consumption[a]				Current consumption[a]			Baseline consumption[a]		
	Cases	p-y	Basic model[b]	Multivariable[c]	Cases	p-y	Multivariable[c]	Cases	p-y	Multivariable[c]
Milk[d]										
Women										
< 1/week	285	249	1.00	1.00	492	350	1.00	413	274	1.00
1/week	173	140	0.86 (0.71–1.04)	0.89 (0.73–1.08)	184	146	0.89 (0.75–1.05)	348	286	0.95 (0.82–1.09)
2–4/week	578	422	0.88 (0.76–1.02)	0.94 (0.81–1.09)	591	419	0.96 (0.85–1.08)	382	311	0.92 (0.80–1.07)
5–6/week	331	240	0.83 (0.71–0.98)	0.90 (0.76–1.07)	352	259	0.91 (0.79–1.05)	176	139	0.97 (0.81–1.16)
1/day	550	420	0.81 (0.70–0.94)	0.88 (0.75–1.03)	602	491	0.83 (0.73–0.94)	591	453	0.93 (0.81–1.06)
≥ 2/day	221	207	0.75 (0.62–0.90)	0.77 (0.64–0.94)	334	264	0.82 (0.70–0.95)	361	290	0.87 (0.75–1.02)
Per 1 a day	2138	1678	0.91 (0.86–0.97)	0.92 (0.86–0.98)	2555	1929	0.93 (0.88–0.98)	2271	1753	0.96 (0.92–1.01)
Men										
< 1/week	109	134	1.00	1.00	163	168	1.00	122	119	1.00
1/week	66	64	0.99 (0.72–1.36)	1.00 (0.72–1.37)	48	61	0.78 (0.56–1.09)	99	123	0.85 (0.64–1.12)
2–4/week	179	198	0.84 (0.65–1.07)	0.81 (0.63–1.04)	149	182	0.78 (0.62–0.99)	175	164	1.04 (0.81–1.32)
5–6/week	107	109	0.84 (0.64–1.11)	0.79 (0.59–1.05)	117	111	0.88 (0.68–1.13)	88	90	0.88 (0.66–1.17)
1/day	142	155	0.80 (0.61–1.04)	0.73 (0.58–0.96)	154	172	0.72 (0.57–0.91)	129	168	0.67 (0.52–0.87)
≥ 2/day	91	99	0.92 (0.68–1.23)	0.77 (0.58–1.05)	93	105	0.72 (0.54–0.96)	140	134	0.83 (0.63–1.10)
Per 1 a day	694	759	0.98 (0.88–1.08)	0.91 (0.82–1.02)	724	799	0.91 (0.82–1.00)	753	798	0.94 (0.86–1.03)
Pooled[e]										
Per 1 a day	2832	2437	0.93 (0.88–0.98)	0.92 (0.87–0.97)	3279	2728	0.92 (0.88–0.97)	3024	2551	0.96 (0.92–1.00)
Cheese[d]										
Women										
< 1/week	126	112	1.00	1.00	391	220	1.00	178	152	1.00
1/week	323	251	1.02 (0.83–1.26)	1.09 (0.88–1.35)	430	338	0.94 (0.82–1.08)	402	328	1.10 (0.92–1.32)
2–4/week	1017	740	0.93 (0.77–1.12)	1.03 (0.85–1.24)	1079	825	0.95 (0.84–1.07)	830	639	1.14 (0.97–1.35)
5–6/week	393	314	0.90 (0.74–1.11)	1.00 (0.81–1.24)	355	292	0.91 (0.78–1.06)	375	279	1.07 (0.89–1.29)
≥ 1/day	279	261	0.85 (0.68–1.06)	0.94 (0.75–1.17)	300	254	0.94 (0.80–1.11)	486	355	1.06 (0.89–1.27)
Per 1 a day	2138	1678	0.88 (0.79–0.99)	0.91 (0.81–1.02)	2555	1929	0.92 (0.86–1.04)	2271	1753	0.97 (0.90–1.04)
Men										
<1 /week	90	93	1.00	1.00	125	116	1.00	114	108	1.00
1/week	123	144	0.85 (0.64–1.18)	0.89 (0.67–1.19)	129	146	0.90 (0.69–1.17)	157	170	0.97 (0.75–1.25)
2–4/week	333	343	0.90 (0.71–1.16)	0.96 (0.75–1.24)	285	334	0.88 (0.70–1.11)	273	308	0.89 (0.70–1.13)
5–6/week	70	101	0.66 (0.48–0.92)	0.72 (0.51–1.01)	92	109	0.80 (0.60–1.07)	99	105	0.85 (0.63–1.13)
≥ 1/day	78	78	1.01 (0.73–1.40)	1.08 (0.77–1.51)	93	94	0.96 (0.71–1.29)	110	107	0.96 (0.72–1.28)
Per 1 a day	694	759	1.03 (0.84–1.26)	1.04 (0.85–1.28)	724	799	1.01 (0.85–1.20)	753	798	1.01 (0.87–1.17)[g]
Pooled[e]										
Per 1 a day	2832	2437	0.93 (0.81–1.07)	0.94 (0.85–1.03)	3279	2728	0.96 (0.88–1.04)	3024	2551	0.98 (0.91–1.04)

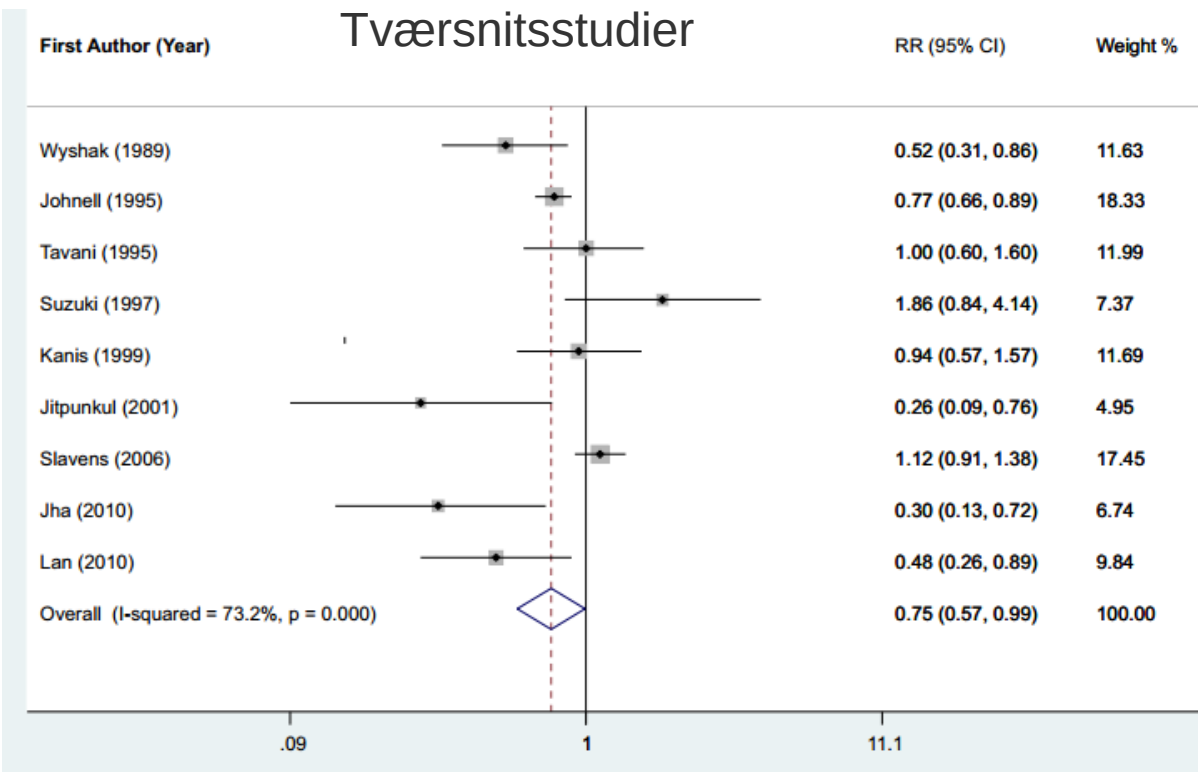
Multivariable models are adjusted for age, follow-up cycle, total energy intake, calcium and vitamin D from non-dairy foods plus supplements, protein from non-dairy foods, retinol from supplements, vitamin K, caffeine, alcohol, milk during teenage years, body mass index, height, physical activity, smoking, use of postmenopausal hormones (women), use of thiazide diuretics, furosemide-type diuretics and oral steroids, and diagnoses of cancer, diabetes and cardiovascular disease. In addition, milk, cheese and yogurt are adjusted for one another

Mælkeindtag på 200 g/d og risiko for osteoporose

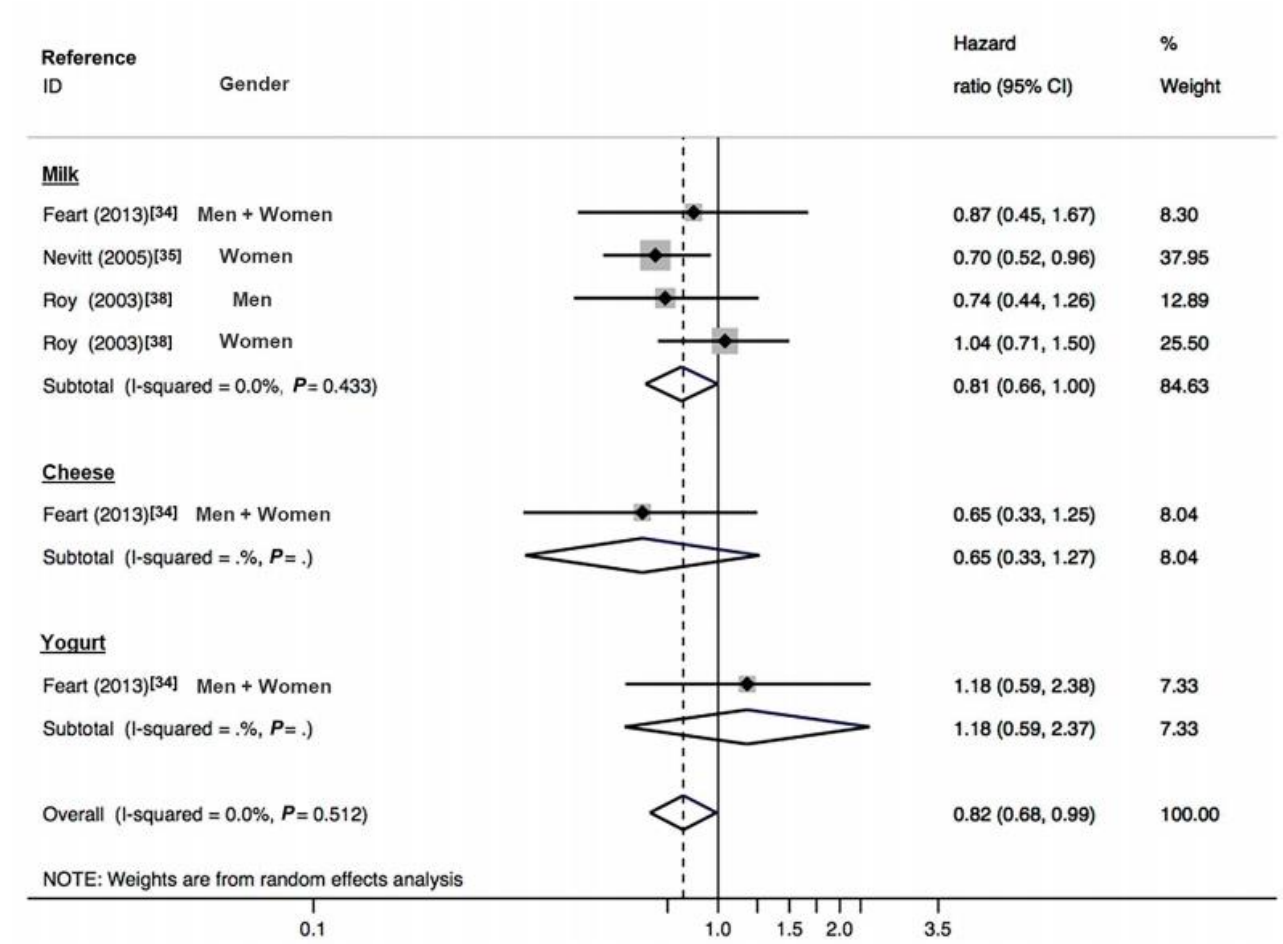


Mælkeindtag (200g/d) og risiko for hoftebrud



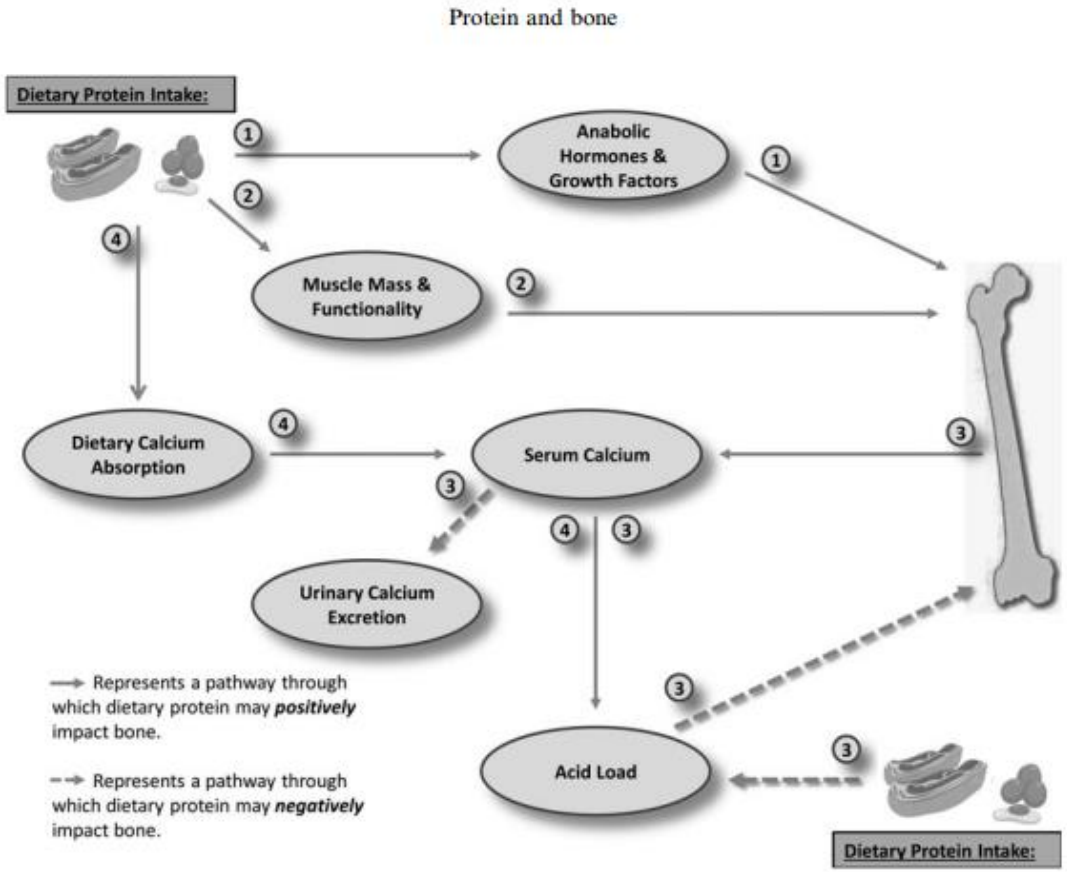


Metanalyse af kohortestudier med nye vertebrale frakturer (rygsammenfald) n = 11,893; 3 cohort studies



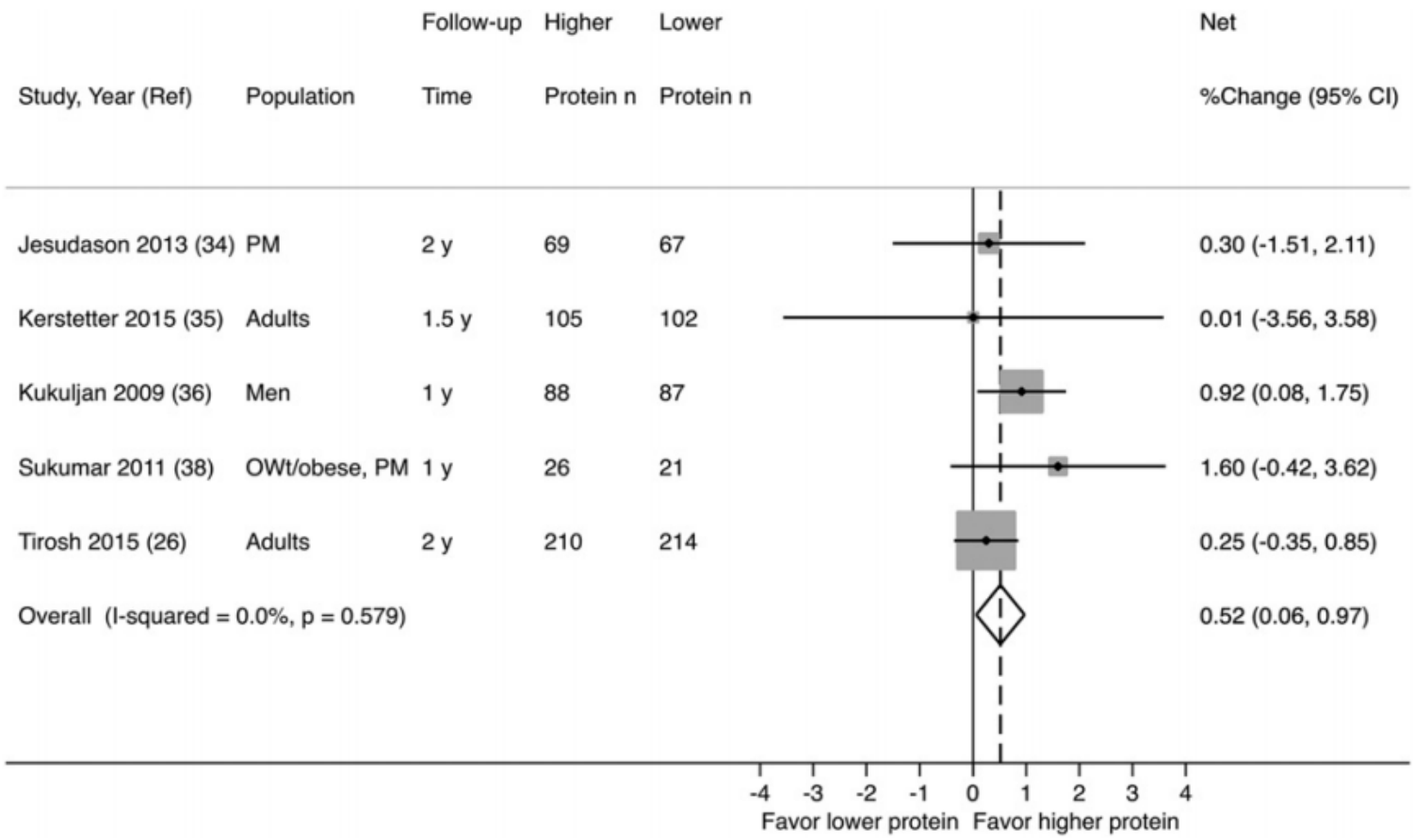
Matia-Martin Adv Nutr 2019

Proteins påvirkning af calcium, knogler og muskler



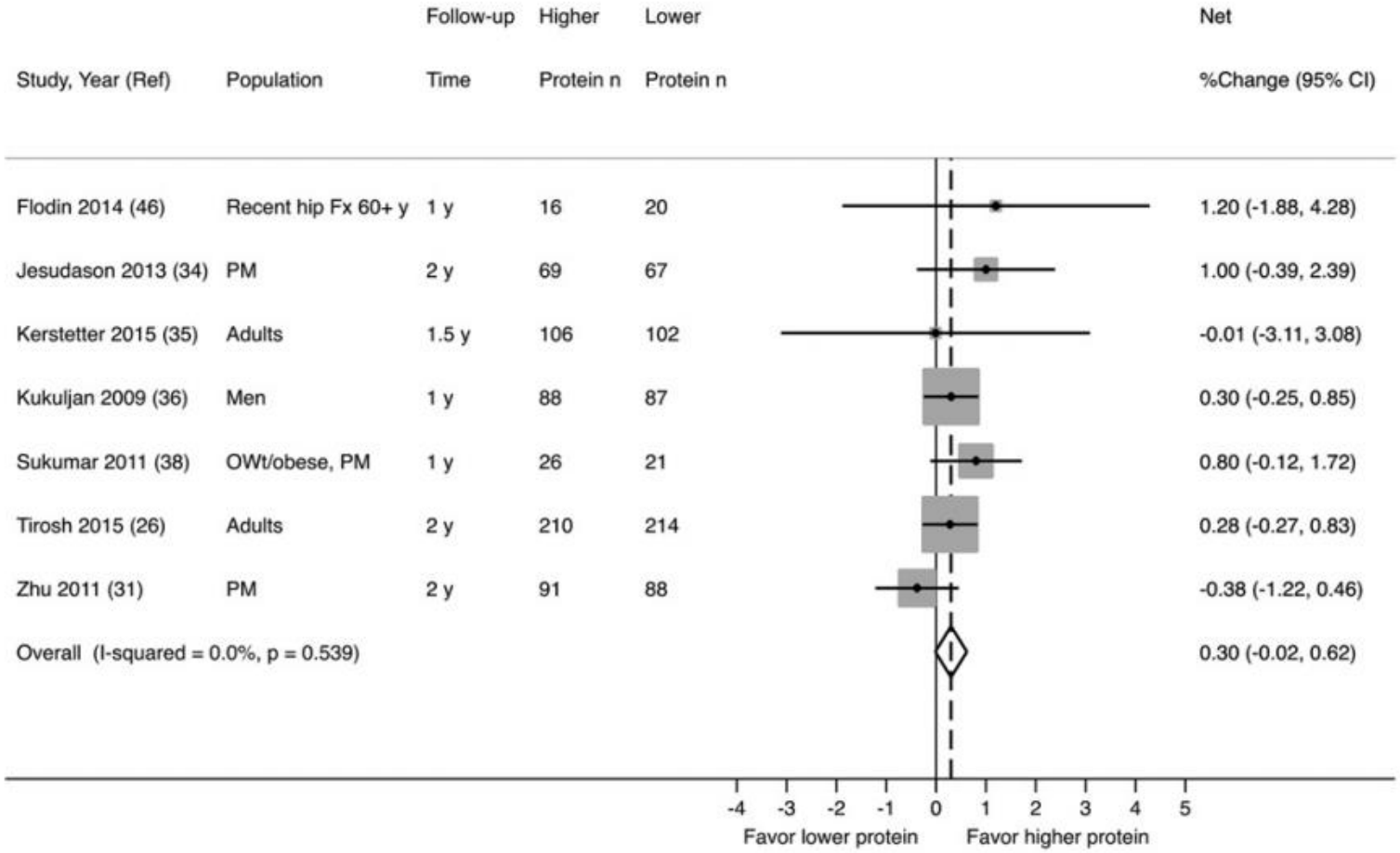
Dolan. Proceedings of the Nutrition Society (2019)

BMD i columna ved højt proteinindtag >90 g/d mod lavt < 80 g/d ved enten tilskud af mælkeprotein eller kostomlægning



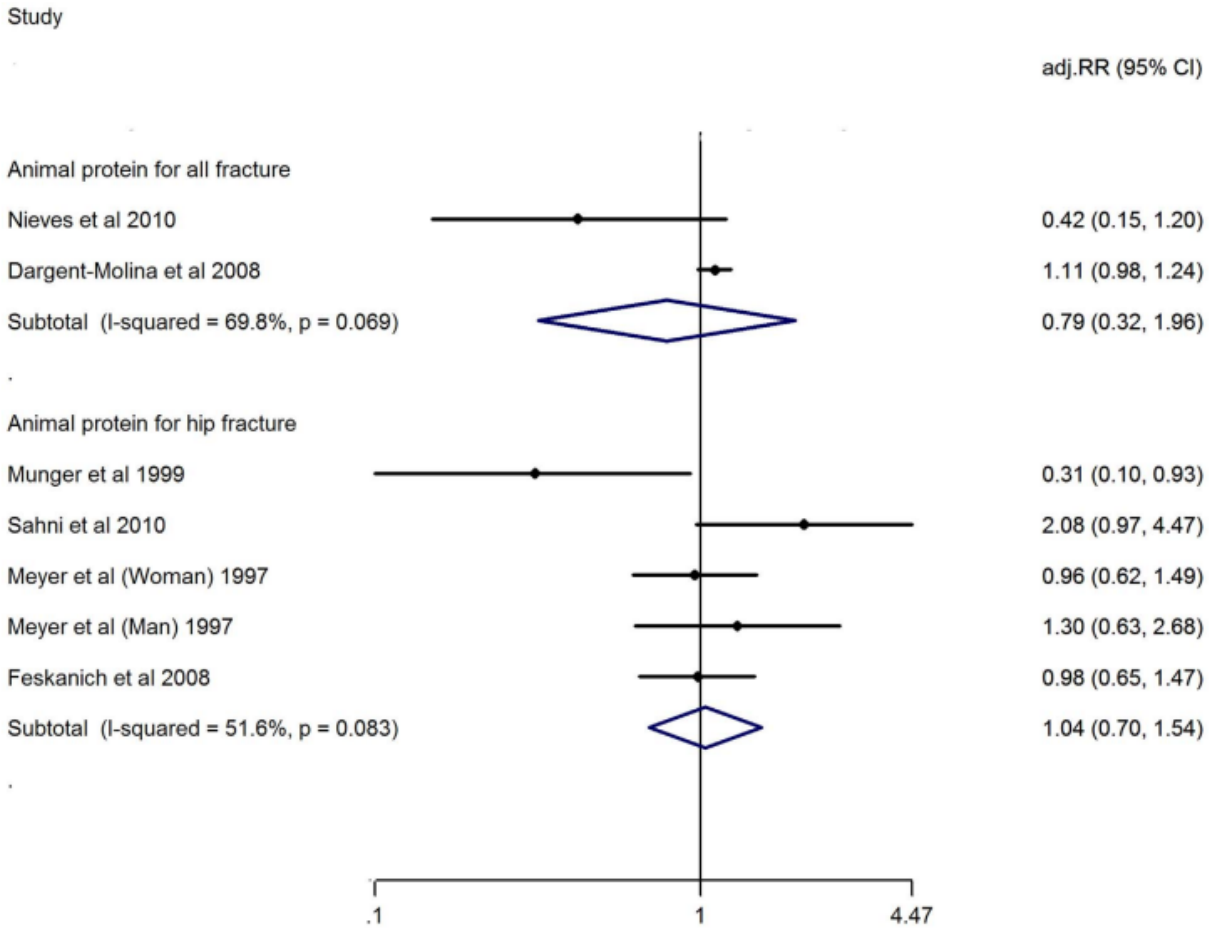
Shams-White. Am J Clin Nutr 2017

BMD i total hip ved højt proteinindtag >90 g/d mod lavt < 80 g/d ved enten tilskud af mælkeprotein eller kostomlægning



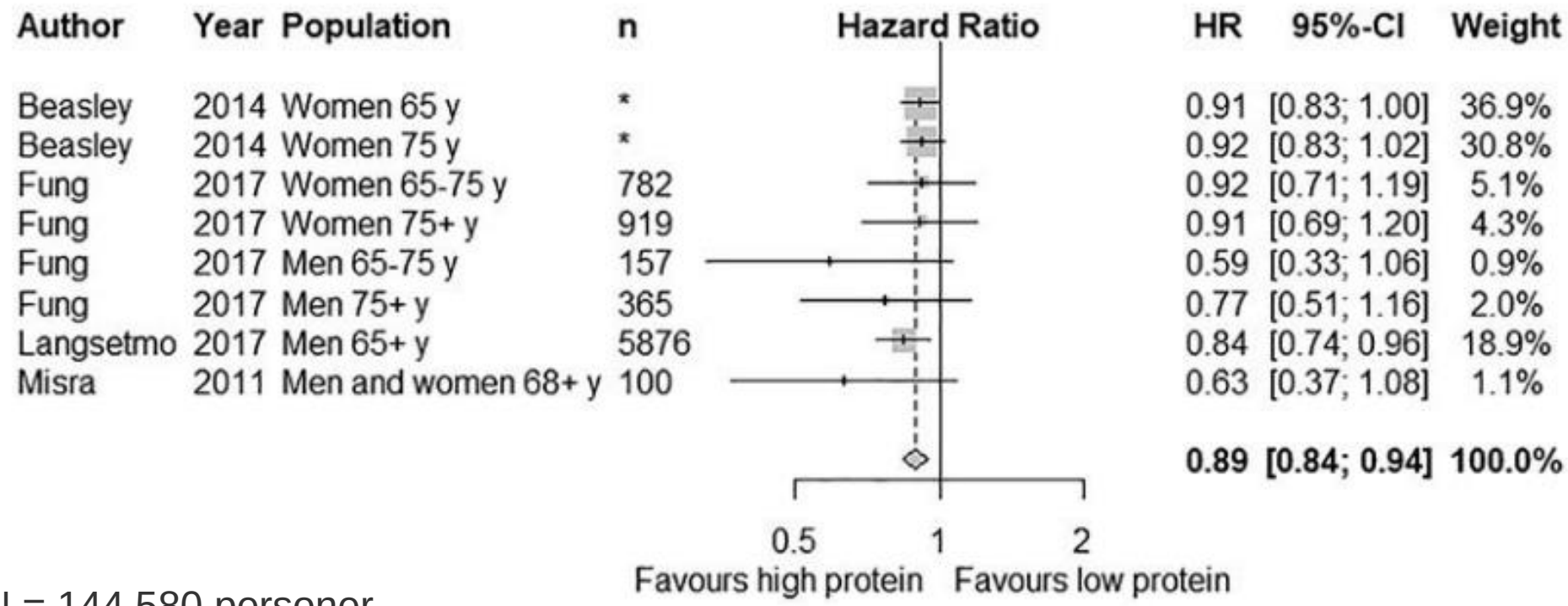
Shams-White. Am J Clin Nutr 2017

Risiko for alle frakturer og hoftefraktur ved højt (51-98 g/d)versus lavt (41-68g/d) animalsk protein indtag.



WU. SCI report 2015

Kohortestudier af hoftefrakturer i relation til høj versus lavt proteindtag (range 0,52 – 1,41 g/bw/d).



N = 144,580 personer

Valle proteintilskud til hoftefraktur patienter i 2 uger efter operation

Table 1
Ingredients of whey protein.

Nutritional ingredients	42 g (162 kcal)
Protein	32.2 g
Lipid	2.0 g
Carbohydrate	3.8 g
Sodium	32–180 mg
Niacin	13.6 mg
Folic acid	84 μg
Pantothenic acid	1.52 mg
Vitamin B_1	4.0 mg
Vitamin B_2	2.4 mg
Vitamin B_6	0.98 mg
Vitamin B_{12}	2.8 μg
Vitamin C	148 mg

Protein (% of energy): 76.6%, Lipid (% of energy): 0.04%, Carbohydrate (% of energy): 0.09%.

ADL (Barthel index).

Item	Per-protocol analysis			
	Whey protein (n = 15)		Control (n = 17)	
	Baseline	Post	Baseline	Post
Toilet use	5(5–7.5)	10(10–10)[a]	5(0–5)	5(0–5)
Transfer	10(10–10)	15(10–15)[a]	10(10–10)	10(10–10)
Walking	10(0–10)	15(15–15)[a]	10(0–10)	10(10–15)
Stair	5(0–5)	5(5–5)	0(0–5)	5(5–5)

Median (interquartile range).
[a] Statistically significant ($P < 0.05$).

Niitsu et al. Clinical Nutrition 2016

Konklusion

Indtag af mælk ser ud til at øge knoglemassen hos børn og unge. Specialt hvis indtaget i forvejen er lavt.
Mælk har en mindre men signifikant effekt på knoglemassen hos voksne.
Mælk kan hos ældre muligvis reducere forekomsten af hoftebrud og rygsammenfald
Mælkeprotein ser ud til at øge knoglemassen en smule og reducere antal hoftebrud hos ældre
Der er ikke fundet negative effekter af mælk på knogler
Der mangler veldesignede randomiserede kontrollerede studier.

Supplerende slides

CALCIUM REKOMMANDATIONER

Nordiske rekommandationer	
alder / køn	mg / dag
Børn	
0-6 mdr	360
6-12 mdr	540
1-6 år	600
7-10 år	700
Voksne mænd	
11-20 år	900
20-75 år	800
> 75 år	800
Voksne kvinder	
11-20 år	900
20-75 år	800
> 75 år	800
gravide	900
ammende	1200

Amerikanske rekommandationer	
alder / køn	mg / dag
Børn	
0-6 mdr	**400**
6-12 mdr	**800**
1-5 år	**800**
6-10 år	**800-1200**
Voksne mænd	
11-24 år	**1200-1500**
25-55 år	**1000**
> 55 år	**1500**
Voksne kvinder	
11-24 år	**1200-1500**
24-55 år	**1000**
> 50 postmenop.+ HRT	**1000**
> 50 postmenop.- HRT	**1500**
> 65 år	**1500**
gravide og ammende	**1200-1500**

ET EKSEMPEL

Mælk og mælkeprodukter i alt		
Antal deciliter x 110 mg	(½ l mælk) =	550 mg
Ost og osteprodukter		
Antal gram x 6 mg	(2 skiver a´20 g) =	240 mg
Basisindtag	=	300 mg
I alt		1090 mg

CALCIUMABSORPTION

TABLE 4 Content and Absorbability of Calcium from Different Sources[a]

Supplement	Calcium content of supplement (mg/g)	Fractional absorption (%)
Carbonate	400	27
Tricalcium phosphate	390	25
Citrate malate	210	35
Milk[b]	—	29

[a] Absorption from a meal containing 250 mg of calcium was determined by a double isotope method [45–48].
[b] Contains 1200 mg calcium per quart.

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