Associazione Medici Endocrinologi

Primo Congresso Interregionale AME Sud - Italia

Primo Congresso Interregionale ANIED Sud - Italia

Matera, 9-10 Maggio 2014 - HILTON GARDEN INN

LE DIETE IPERPROTEICHE: TRA RISULTATO CLINICO E POSSIBILI RISCHI

Ambulatorio di Nutrizione Clinica

U.O.C. Oncologia Medica

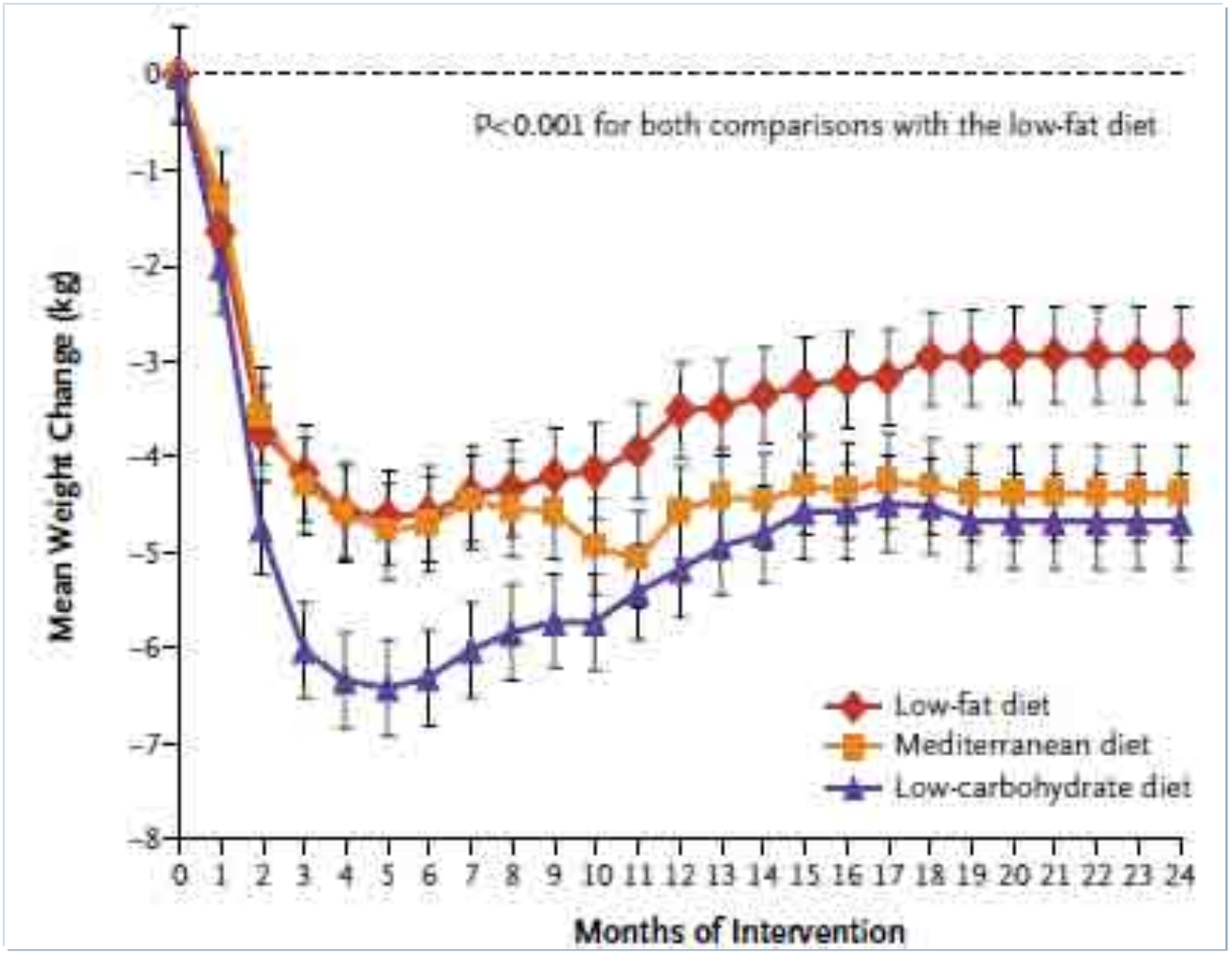
Dipartimento Scienze Biomediche e Oncologia Umana

Dr. Alessandro Nitti

dietista

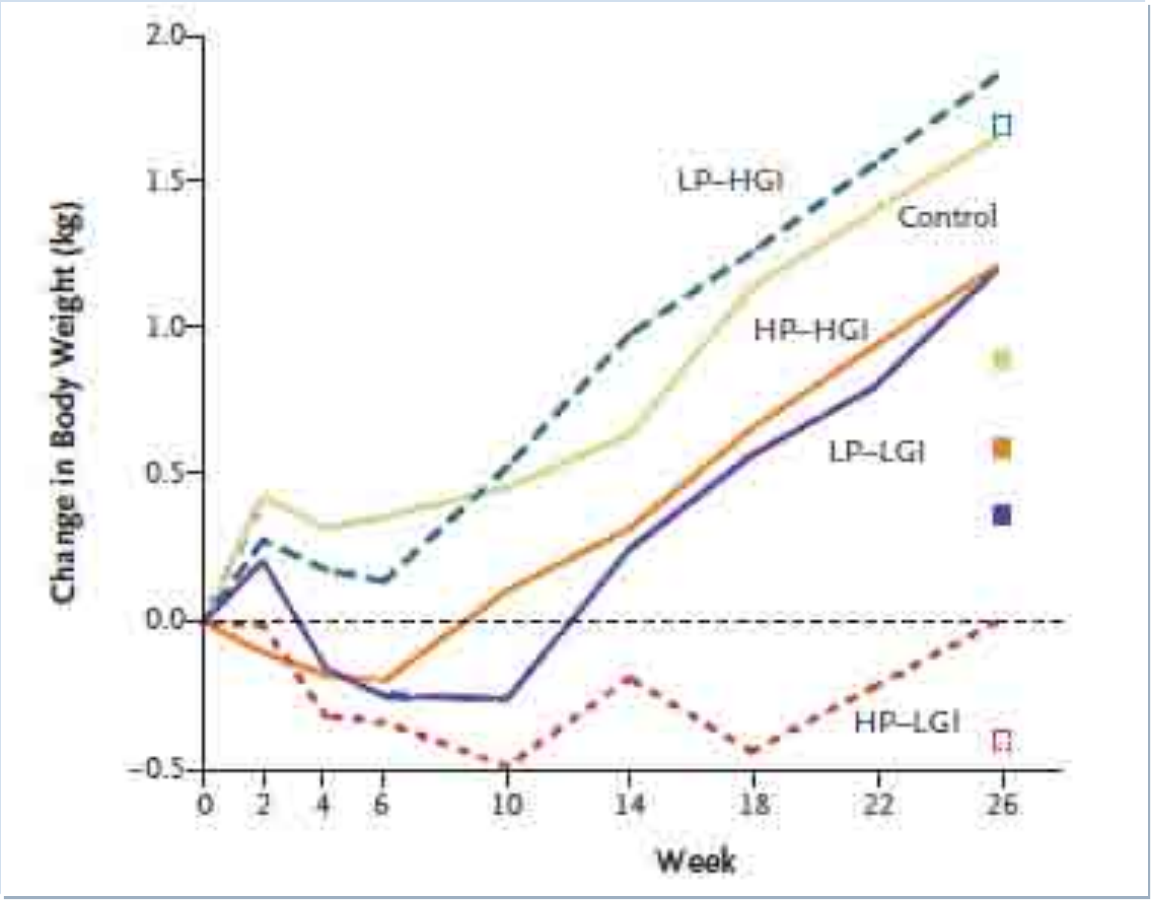
Weight Loss with a Low-Carbohydrate, Mediterranean, or Low-Fat Diet

Esaminati **322 soggetti** in moderato eccesso ponderale



Shai I et al, *NEJM*, 359: 229-241, 2008

Diets with High or Low Protein Content and Glycemic Index for Weight-Loss Maintenance



Larsen TM et al, NEJM, 363: 2102-2113, 2010

DIETE IPERPROTEICHE E MODULAZIONE DELLA COMPOSIZIONE CORPOREA

- I **trials a breve termine** dimostrano che, rispetto ad una dieta ipocalorica con normale percentuale di proteine (10-15% delle calorie totali), un'alimentazione ipocalorica caratterizzatata da **aumento delle proteine** e **riduzione dei carboidrati** induce **incremento della perdita di massa grassa** e limita la **perdita di massa magra**

Clifton PM et al, NMCD, 24: 224-235, 2014

SYSTEMATIC REVIEW AND META-ANALYSIS

Long term weight maintenance after advice to consume low carbohydrate, higher protein diets – A systematic review and meta analysis

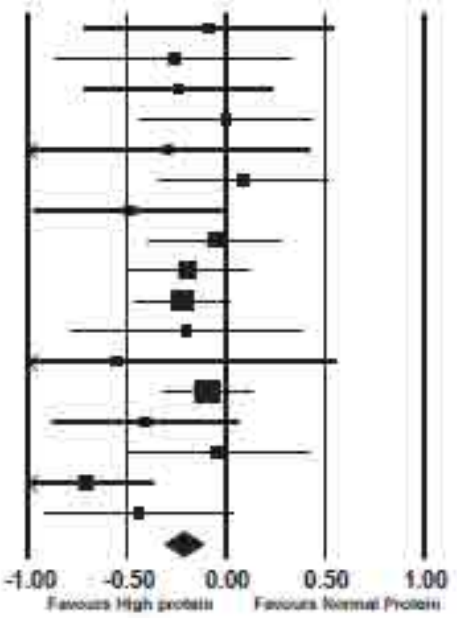
Almeno 12 mesi di follow up

La metanalisi ha preso in esame 32 studi condotti negli adulti (N=3492), in cui il rapporto tra % delle proteine e % dei carboidrati era elevato

Un aumento ≥ 5% della % di proteine risultava associato ad un aumento di 3 volte dell'effetto di riduzione della massa grassa ($p < 0.038$)

Fat Mass

Study name	Std diff in means	Standard error	p-Value	High Protein	Control
Brinkworth 2004a	-0.086	0.325	0.791	19	19
Brinkworth 2004b	-0.263	0.306	0.390	21	22
Brinkworth 2009	-0.241	0.242	0.320	33	36
Clifton 2008	0.000	0.225	1.000	41	38
Das 2007	-0.295	0.367	0.422	15	15
Delbridge 2009	0.085	0.221	0.702	42	40
Due 2004	-0.489	0.249	0.049	36	31
Foster 2010	-0.058	0.174	0.740	66	66
Frisch 2010	-0.193	0.157	0.219	86	78
Gardner 2007	-0.222	0.127	0.080	129	120
Jesudason 2013	-0.202	0.300	0.500	21	24
Keogh 2007b	-0.553	0.567	0.330	7	6
Krebs 2012	-0.093	0.117	0.425	144	150
Layman 2009	-0.408	0.243	0.093	41	30
Mcauley 2006	-0.045	0.238	0.849	28	48
Soenen 2012	-0.713	0.180	0.000	66	66
Wycherley 2012	-0.441	0.246	0.073	33	35
	-0.215	0.050	0.000	828	824

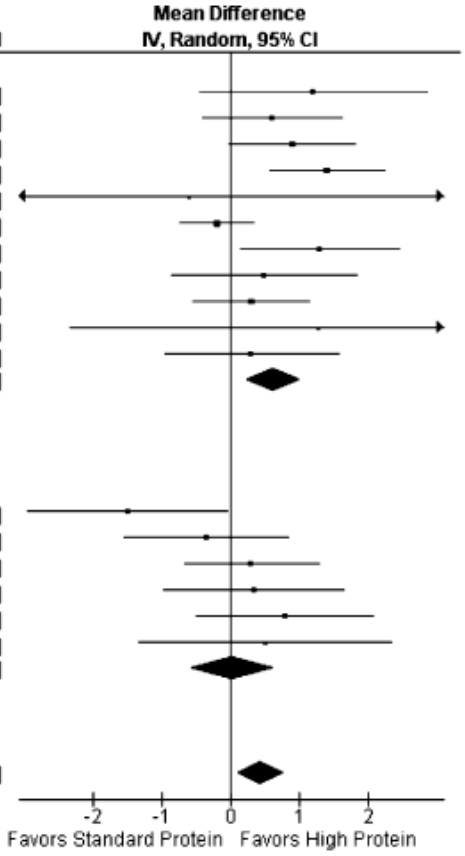


Clifton PM et al, NMCD, 24: 224-235, 2014

Effects of energy-restricted high-protein, low-fat compared with standard-protein, low-fat diets: a meta-analysis of randomized controlled trials[1–3]

Meta-analysis for changes in fat-free mass (kg) in randomized controlled trials that compared high-protein, low-fat diets with isocalorically prescribed standard-protein, low-fat, energy-restricted diets

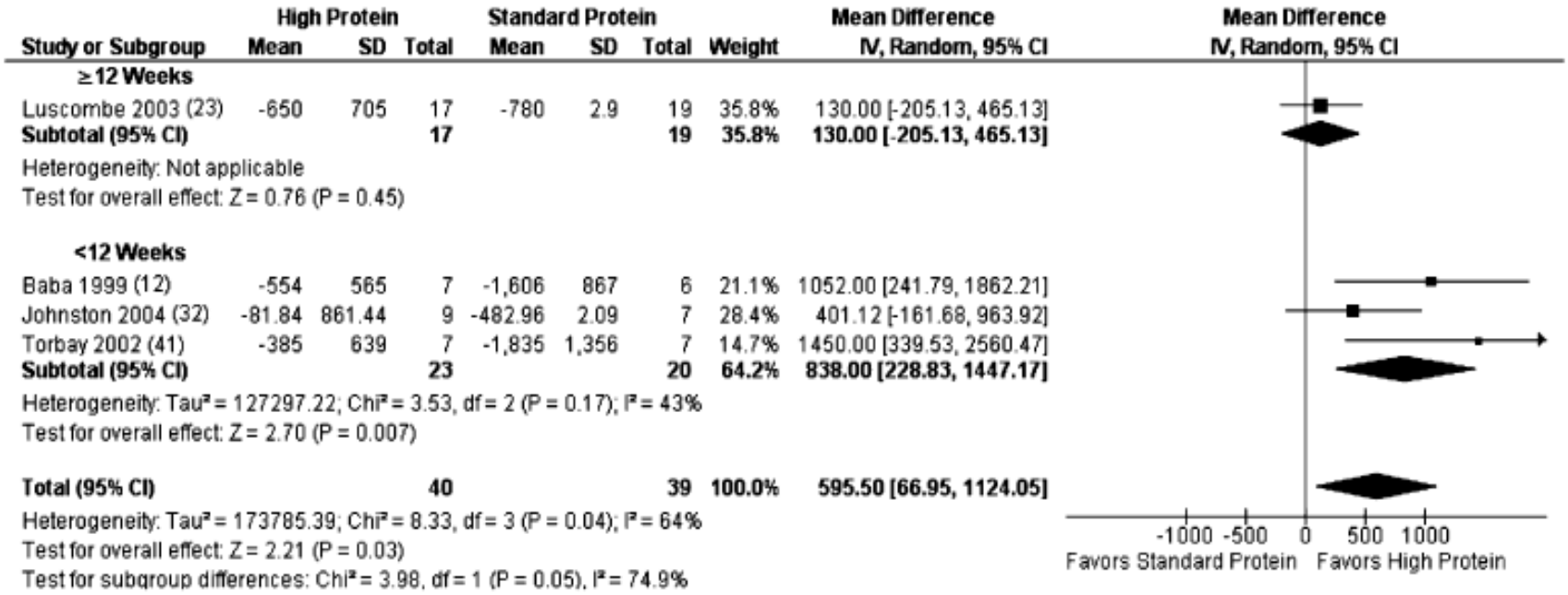
Study or Subgroup	High Protein Mean	SD	Total	Standard Protein Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
≥12 Weeks								
Belobrajdic 2010 (27)	-1.9	3	34	-3.1	4.3	42	3.6%	1.20 [-0.45, 2.85]
Campbell 2010 (28)	-1.6	1.1	13	-2.2	1.6	15	7.4%	0.60 [-0.41, 1.61]
Evangelista 2009 (30)	0.6	1	5	-0.3	0.3	5	8.3%	0.90 [-0.02, 1.82]
Farnsworth 2003 - F (11)	-0.1	1.4	21	-1.5	1.4	22	9.2%	1.40 [0.56, 2.24]
Farnsworth 2003 - M (11)	-2.5	7.4	7	-1.9	5.6	7	0.2%	-0.60 [-7.47, 6.27]
Layman 2009 (39)	-2.6	1.4	52	-2.4	1.4	51	13.4%	-0.20 [-0.74, 0.34]
Leidy 2007 (10)	-1.5	1.4	21	-2.8	2.5	25	6.2%	1.30 [0.15, 2.45]
Luscombe 2003 (23)	-1.2	2.45	17	-1.69	1.49	19	4.9%	0.49 [-0.85, 1.83]
Noakes 2005 (8)	-1.5	2.2	52	-1.8	2.1	48	9.1%	0.30 [-0.54, 1.14]
Treyzon 2008 (42)	-2.78	4.11	44	-4.06	11.14	41	0.9%	1.28 [-2.34, 4.90]
Wycherley 2010 (43)	-1.9	1.5	12	-2.2	1.9	16	5.4%	0.30 [-0.96, 1.56]
Subtotal (95% CI)			**278**			**291**	**68.6%**	**0.61 [0.20, 1.02]**
Heterogeneity: Tau² = 0.14; Chi² = 14.80, df = 10 (P = 0.14); I² = 32%								
Test for overall effect: Z = 2.94 (P = 0.003)								
< 12 Weeks								
Baba 1999 (12)	-1.2	1.1	7	0.3	1.5	6	4.4%	-1.50 [-2.95, -0.05]
Johnston 2004 (32)	-2.1	1.3	9	-1.74	1.12	7	5.9%	-0.36 [-1.55, 0.83]
Kasim-Karakas 2009 (33)	-0.3	1.3	11	-0.6	1.1	13	7.7%	0.30 [-0.67, 1.27]
Layman 2003 (9)	-0.88	1.14	12	-1.21	2.01	12	5.1%	0.33 [-0.98, 1.64]
Parker 2002 (24)	-0.61	1.87	26	-1.4	2.88	28	5.3%	0.79 [-0.50, 2.08]
Torbay 2002 (41)	-0.2	2.1	7	-0.7	1.3	7	3.0%	0.50 [-1.33, 2.33]
Subtotal (95% CI)			**72**			**73**	**31.4%**	**0.03 [-0.58, 0.64]**
Heterogeneity: Tau² = 0.15; Chi² = 6.78, df = 5 (P = 0.24); I² = 26%								
Test for overall effect: Z = 0.10 (P = 0.92)								
Total (95% CI)			**350**			**364**	**100.0%**	**0.43 [0.09, 0.78]**
Heterogeneity: Tau² = 0.15; Chi² = 23.74, df = 16 (P = 0.10); I² = 33%								
Test for overall effect: Z = 2.45 (P = 0.01)								
Test for subgroup differences: Chi² = 2.38, df = 1 (P = 0.12), I² = 57.9%								



Wycherley TP et al, Am J Clin Nutr, 96: 1281-98, 2012

Effects of energy-restricted high-protein, low-fat compared with standard-protein, low-fat diets: a meta-analysis of randomized controlled trials[1–3]

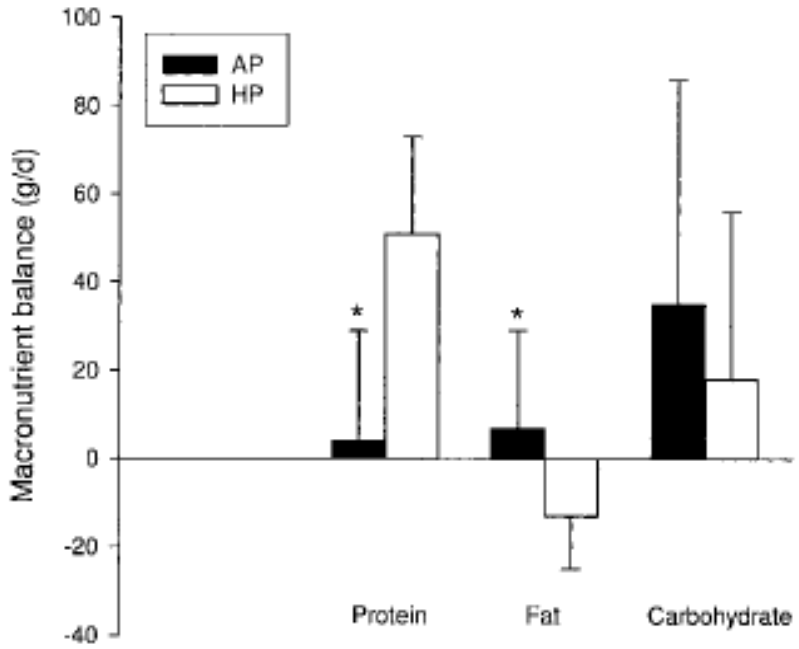
Meta-analysis for changes in resting energy expenditure (kJ/d) in randomized controlled trials that compared high-protein, low-fat diets with isocalorically prescribed standard-protein, low-fat, energy-restricted diets.



Wycherley TP et al, Am J Clin Nutr, 96: 1281-98, 2012

EFFETTO DELLE PROTEINE SUL BILANCIO ENERGETICO

BILANCIO DEI MACRONUTRIENTI
DOPO 4 GIORNI DI DIETA HP O AP

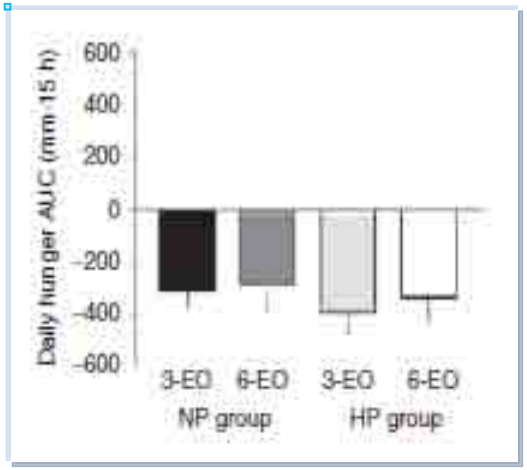


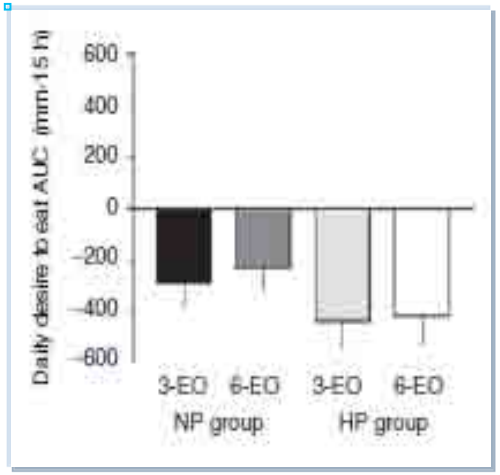
Le diete ad elevato contenuto proteico inducono

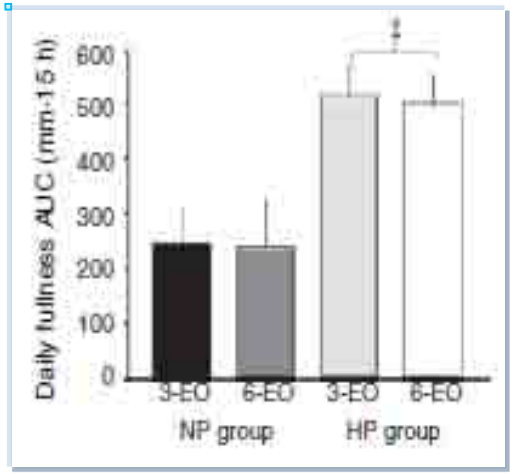
1) un maggiore incremento della **DIT** (*diet-induced thermogenesis*)
2) una riduzione del quoziente respiratorio (rapporto ossidazione dei carboidrati / ossidazione del lipidi)
3) un aumento del metabolismo durante il sonno

Lejeune et al, Am J Clin Nutr, 83: 89-94, 2006

SAZIETÀ

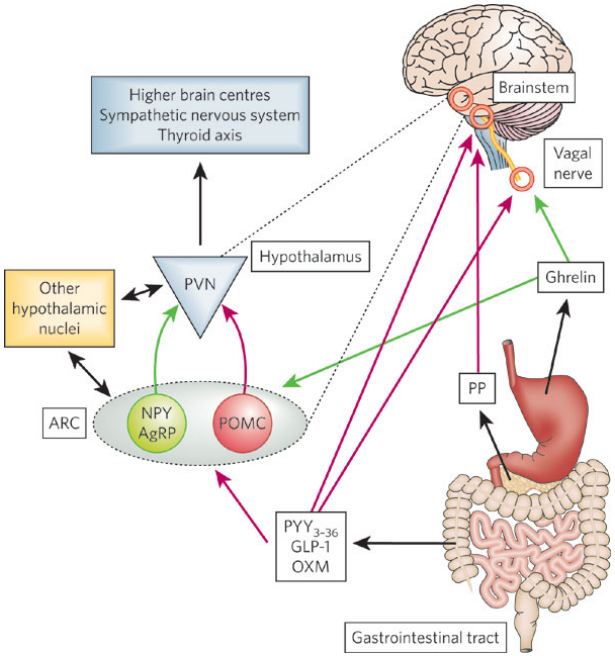






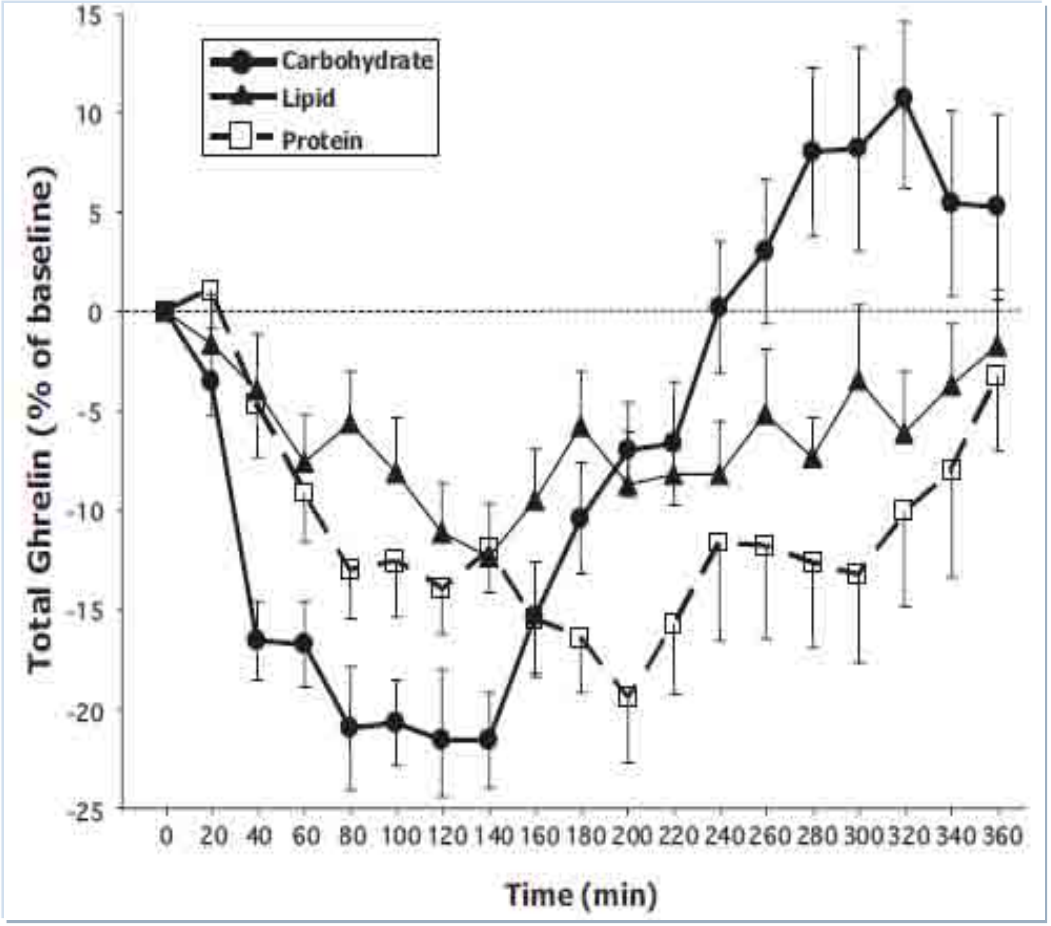
Leidy HJ et al, Obesity, 19: 818-824, 2010

L'effetto saziante maggiore delle proteine rispetto a quella degli altri macronutrienti, può essere in parte attribuito al rilascio di come il **GLP-1** e il **PYY.**
Inoltre il pasto iperproteico rallenta lo svuotamento gastrico, prolungando i tempi di digestione e il senso di sazietà.



Acyl and Total Ghrelin Are Suppressed Strongly by Ingested Proteins, Weakly by Lipids, and Biphasically by Carbohydrates

Ghrelin is an orexigenic hormone that can increase body weight. Its circulating levels increase before meals and are suppressed after food ingestion.



Foster-Schubert KE et al, JCEM, 93: 1971-1979, 2008

INSULINEMIA

28 STUDI

SYSTEMATIC REVIEW AND META-ANALYSIS

Long term weight maintenance after advice to consume low carbohydrate, higher protein diets – A systematic review and meta analysis

Clifton PM et al, NMCD, 24: 224-235, 2014

Fasting insulin was also lower with high protein diets with effect sizes of 0.22 ($p < 0.042$)

Long-term effects of low-fat diets either low or high in protein on cardiovascular and metabolic risk factors: a systematic review and meta-analysis

Schwingshackl et al, Nutrition Journal 2013, 12:48

15 studi
Non Diabetici, RCT a lungo termine (almeno 12 mesi)
HP: >25% delle calorie
LP: <20% delle calorie

Study or Subgroup	HP Mean	HP SD	HP Total	LP Mean	LP SD	LP Total	Weight	Mean Difference IV, Random, 95% CI
Brinkworth et al. 2004	13	9.16	21	11.8	5.15	22	2.1%	1.20 [-3.27, 5.67]
Brinkworth et al. 2004 II	17	12.64	19	17.6	13.51	19	0.6%	-0.60 [-8.92, 7.72]
Clifton et al. 2007	-2.92	3.5	40	-1.23	6.88	38	7.1%	-1.69 [-4.13, 0.75]
Dansinger et al. 2005	-5.4	14	40	-3	6.3	40	1.9%	-2.40 [-7.16, 2.36]
Das et al. 2007	-2.56	2.02	14	-1.89	1.58	15	24.1%	-0.67 [-2.00, 0.66]
Due et al. 2004	6.5	10.43	18	8.45	5.88	23	1.5%	-1.95 [-7.33, 3.43]
Gardner et al. 2007	-1.5	4.9	79	-1	4.45	155	25.5%	-0.50 [-1.79, 0.79]
Keogh et al. 2007	7.28	4.97	11	5.11	1.69	12	4.4%	2.17 [-0.92, 5.26]
McAuley et al. 2006	6.77	2.95	28	7.77	2.8	24	17.3%	-1.00 [-2.56, 0.56]
Sacks et al. 2009	11	8	201	12	10	201	13.5%	-1.00 [-2.77, 0.77]
Wycherley et al. 2012	5.41	2.53	32	7.03	13.29	34	2.0%	-1.62 [-6.17, 2.93]
Total (95% CI)			503			583	100.0%	-0.71 [-1.36, -0.05]

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.84$, df = 10 (P = 0.83); $I^2 = 0\%$
Test for overall effect: Z = 2.12 (P = 0.03)

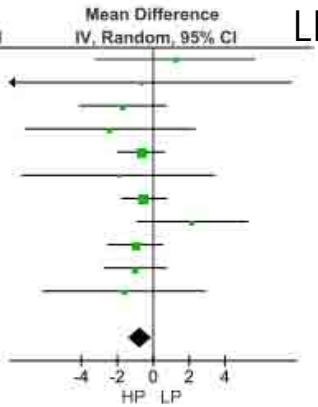


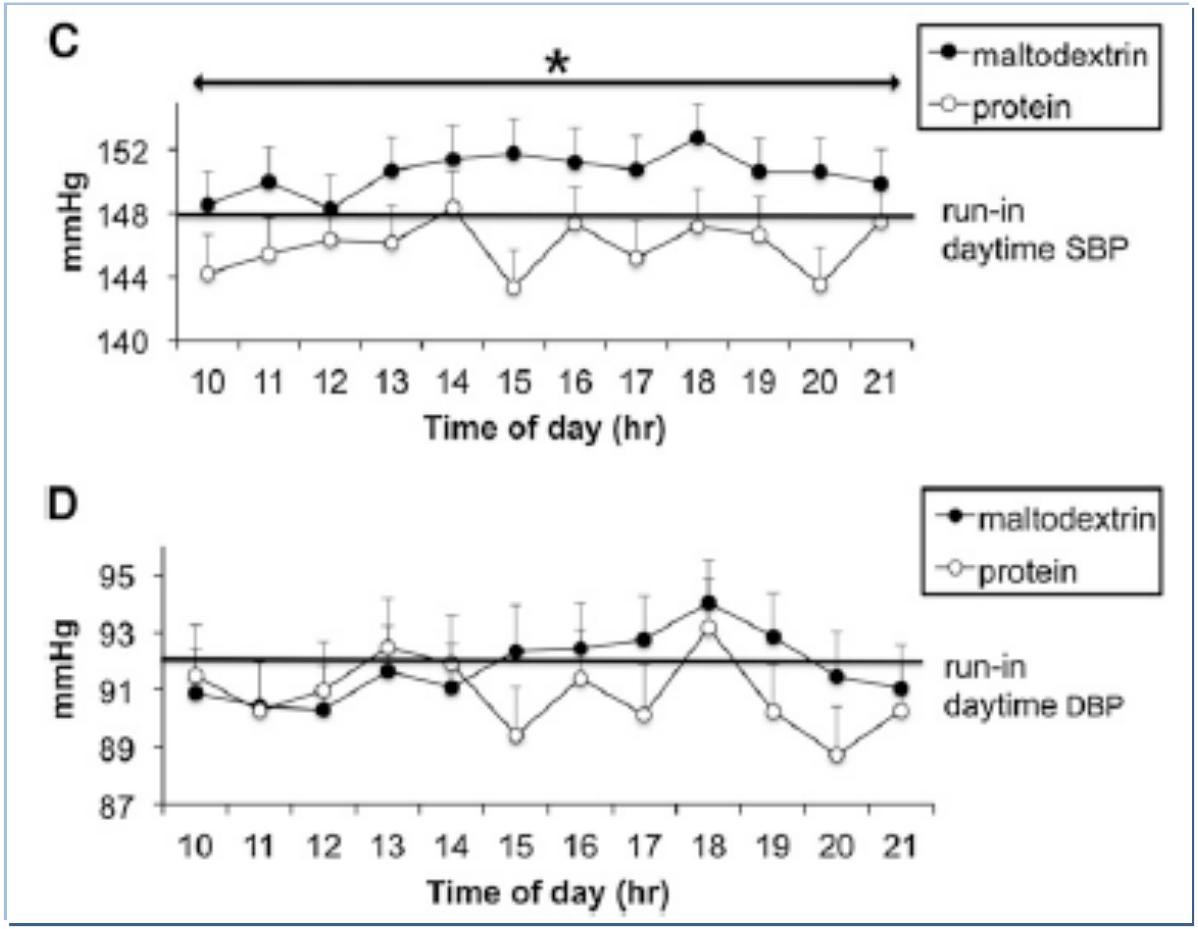
Figure 3 Forest plot showing pooled WMD with 95% CI for fasting insulin (μIU/ml) for 10 randomized controlled high-protein diet studies. For each high-protein study, the shaded square represents the point estimate of the intervention effect. The horizontal line joins the lower and upper limits of the 95% CI of these effects. The area of the shaded square reflects the relative weight of the study in the respective meta-analysis. The diamond at the bottom of the graph represents the pooled WMD with the 95% CI for the 10 study groups. Abbreviations: HP = high-protein; LP = low-protein; I^2 = Inconsistency.

IPERTENSIONE

Protein supplementation lowers blood pressure in overweight adults: effect of dietary proteins on blood pressure (PROPRES), a randomized trial[1–3]

Pazienti affetti da Pre-ipertensione o Ipertensione grado 1

L'aumento percentuale di proteine (25% invece del 15% delle calorie giornaliere) , con riduzione isoenergetica dei carboidrati (maltodestrine), riduce la pressione arteriosa delle 24 ore dopo 4 settimane di trattamento



Teunissen-Beekman et al, AJCN, 2012

INCIDENZA MORTALITÀ

Low Protein Intake Is Associated with a Major Reduction in IGF-1, Cancer, and Overall Mortality in the 65 and Younger but Not Older Population

Ha esaminato 6,381 adulti di età > 50 anni (età media di 65 anni).

Cross-sectional study dove i soggetti dello studio sono stati categorizzati in base all'assunzione proteica:

1) ***high protein group*** (20% o più delle calorie da proteine),
2) ***moderate protein group*** (10%– 19% delle calorie da proteine),
3) ***low protein group*** (< 10% delle calorie da proteine)

RISULTATI:

- **Riduzione del 28%** della mortalità per tutte le cause (HR: 0.72)
- **Riduzione del 60%** della mortalità per cancro (HR: 0.40) rispetto ai soggetti con basso contenuto di proteine

SOLAMENTE NEI SOGGETTI CON ETÀ SUPERIORE AI 65 ANNI

Levin ME et al, Cell Metab, 19: 407-417, 2014

INCIDENZA MORTALITÀ

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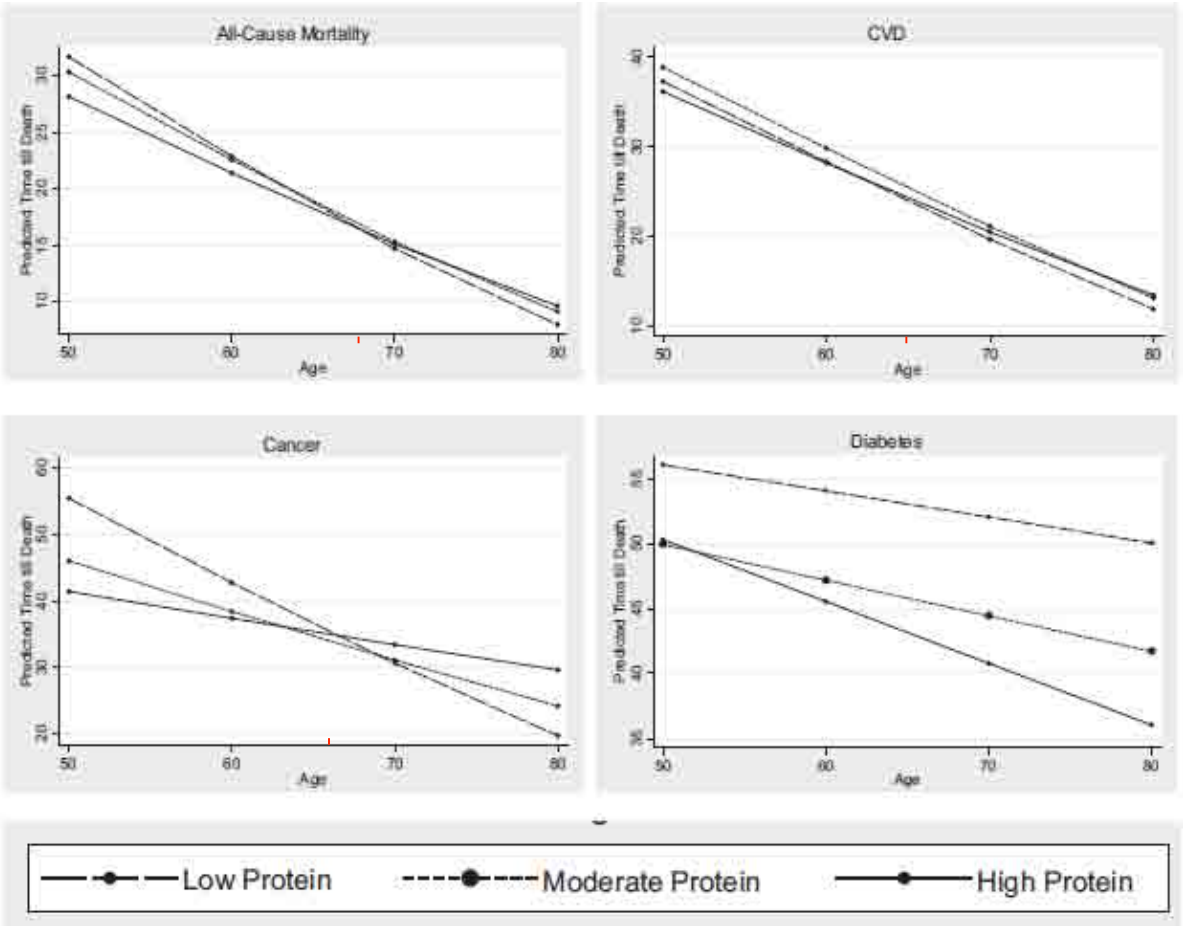
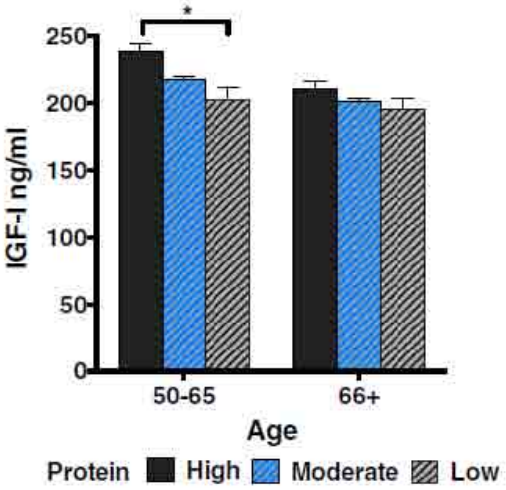


Tra i 50-65 anni i gruppi di popolazione con un consumo di proteine elevato ha mostrato **un incremento del 74%** di rischio di morte ed un **rischio 4 volte** maggiore di incidenza di **cancro**, rispetto ai soggetti con consumo proteico basso



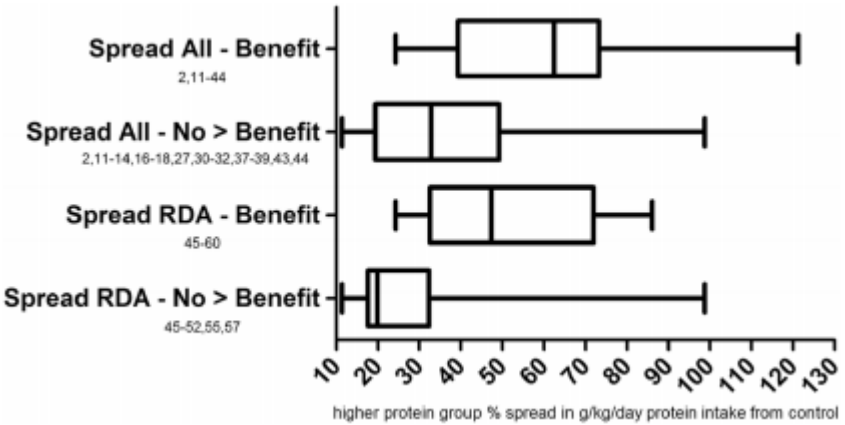
SPREAD vs CHANGE THEORY

Dietary protein in weight management: a review proposing protein spread and change theories

Review di 51 studi sulla quantità di proteine efficace per il mantenimento del peso

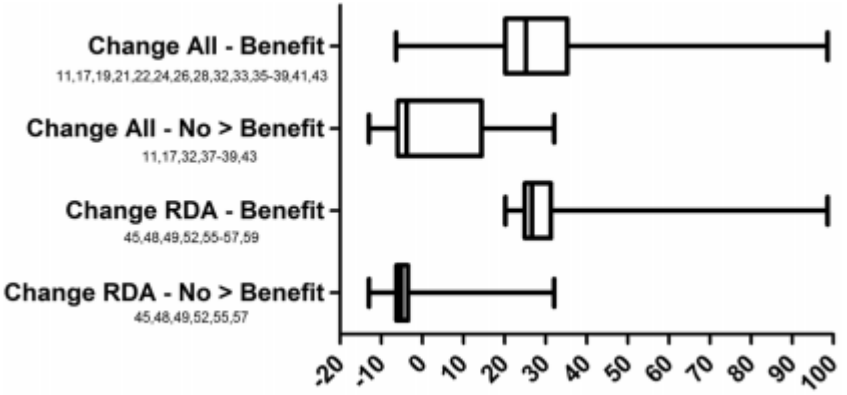
PROTEIN SPREAD THEORY (differenza proteica certa tra gruppo di controllo e gruppo di intervento)

- Se la differenza proteica tra i 2 gruppi è in media il **58,4%**, la dieta iperproteica è efficace
- Se la differenza è al di sotto del **38,8%**, non si ottengono grandi risultati



PROTEIN CHANGE THEORY (si considera solamente l'aumento proteico rispetto alla normale alimentazione dei 2 gruppi:

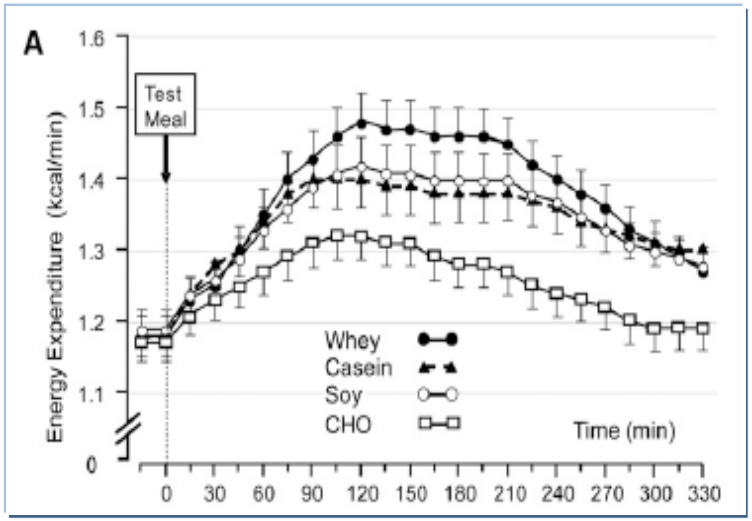
- Se la differenza proteica è del **28,6%**, si ha un risultato significativamente efficace
- Gli stessi risultati non sono ottenuti se la differenza proteica è in media del **4,9%**

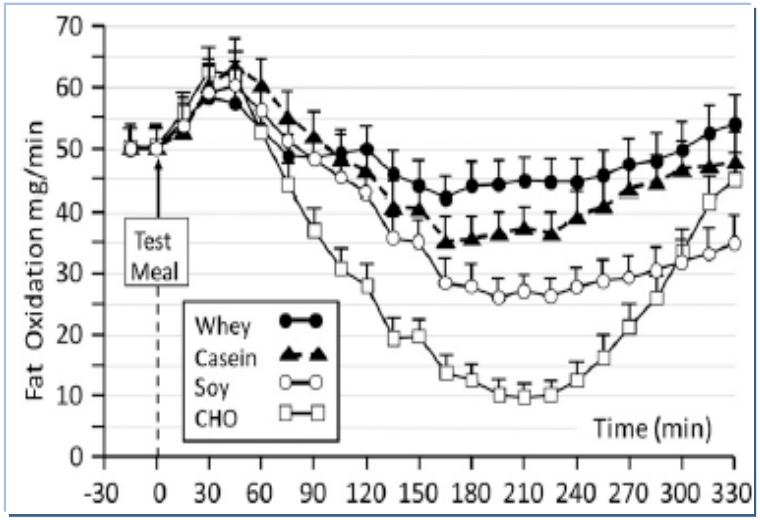


J Bosse et al, Nutrition & Metabolism 2012, 9:81

SCELTA DELLE FONTI PROTEICHE

Protein choices targeting thermogenesis and metabolism[1–3]



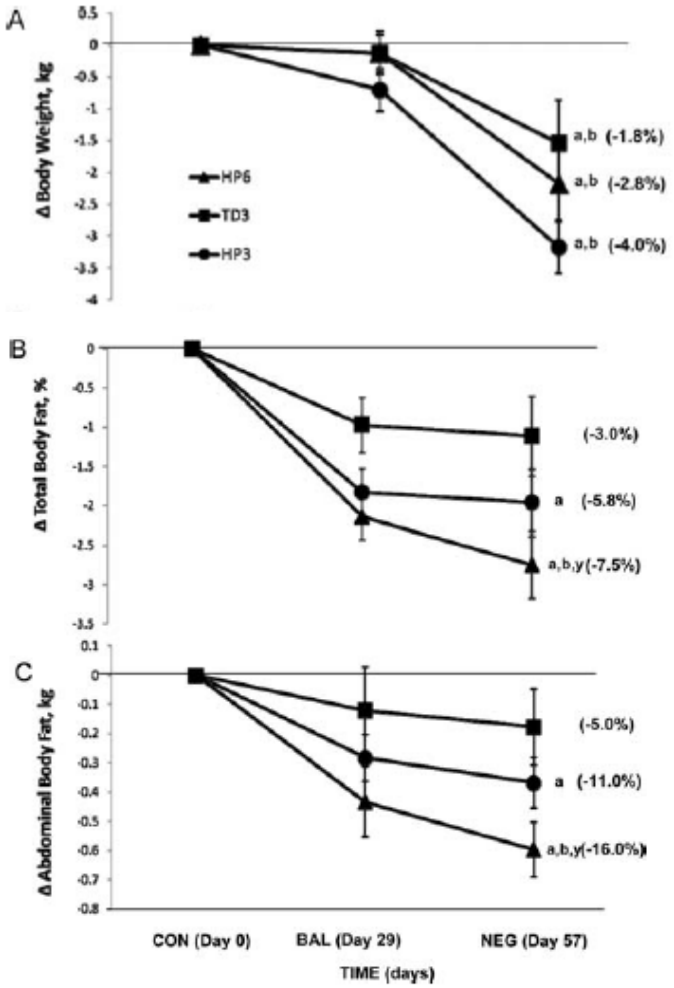


Le proteine del siero del latte **(whey protein)** sono risultate più efficaci sull'aumento del dispendio energetico e sull'ossidazione dei grassi

Acheson KJ et al, Am J Clin Nutr, 93: 525-534, 2011

Increased Protein Intake and Meal Frequency Reduces Abdominal Fat During Energy Balance and Energy Deficit

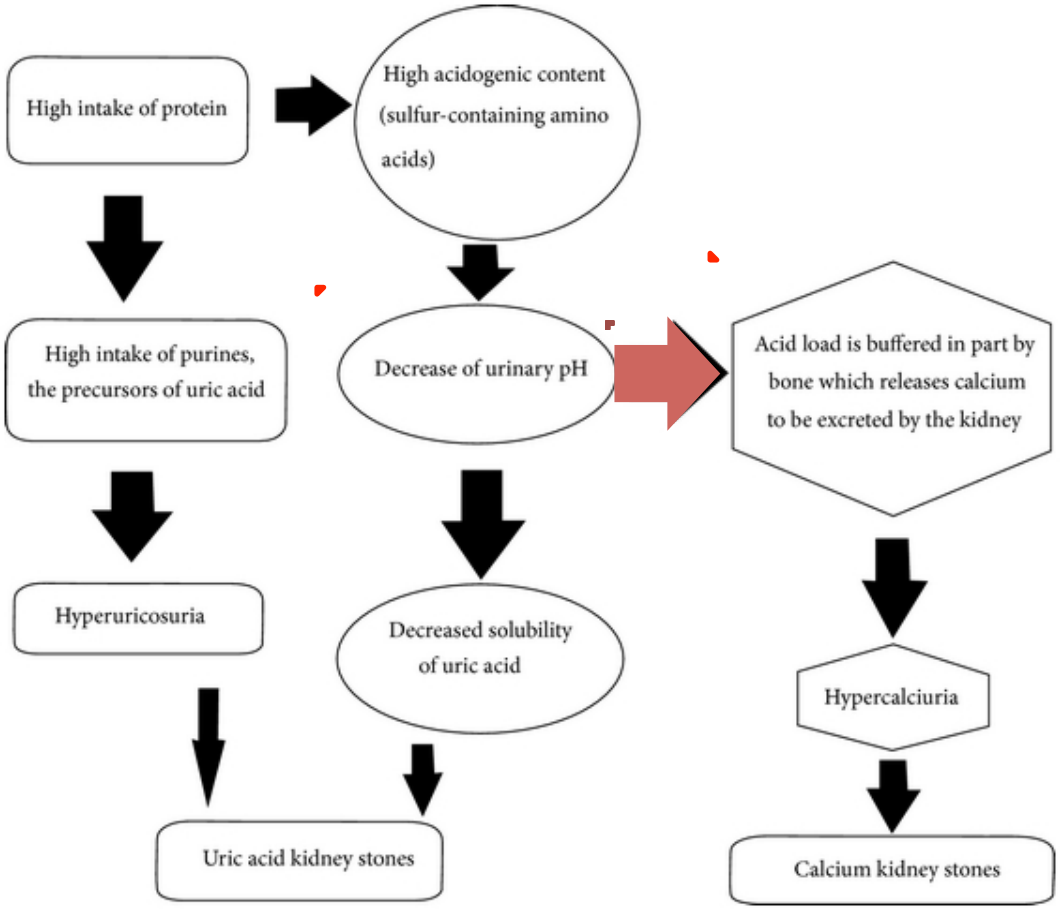
15% (TD) vs 35% proteine (HP3 e HP6)



A parità di quantità di proteine, la somministrazione in 6 pasti induce un aumento della LBM e della spesa energetica post-prandiale

Arciero PJ et al, Obesity, 2013

Metabolismo osseo



Le proteine della dieta rappresentano un fattore determinante della escrezione urinaria di calcio.
In media, per ogni g di proteine introdotte con la dieta la calciuria delle 24 ore aumenta di 1 mg

Metabolismo osseo

- Dietary protein and bone health: a systematic review and meta-analysis[1–3]

Andrea L Darling, D Joe Millward, David J Torgerson, Catherine E Hewitt, and Susan A Lanham-New
Am J Clin Nutr 2009;90:1674–92. Printed in USA.

The effect of dietary protein on the skeleton appears to be **favorable** to a small extent or, at least, is **not detrimental**. However, the long-term clinical importance of the effect is unclear.

Curr Opin Clin Nutr Metab Care. 2010 Nov;13(6):698-702. doi: 10.1097/MCO.0b013e32833df691.

Acid diet (high-meat protein) effects on calcium metabolism and bone health.

Cao JJ[1], Nielsen FH.

On the basis of recent findings, consuming protein (including that from meat) higher than current Recommended Dietary Allowance for protein is **beneficial** to calcium utilization and bone health, especially in the elderly. A high-protein diet with adequate calcium and fruits and vegetables is important for bone health and osteoporosis prevention.

Curr Opin Clin Nutr Metab Care. 2014 Jan;17(1):69-74. doi: 10.1097/MCO.0000000000000013.

Dietary protein is beneficial to bone health under conditions of adequate calcium intake: an update on clinical research.

Mangano KM[1], Sahni S, Kerstetter JE.

Dietary protein may positively impact bone health by increasing muscle mass, increasing calcium absorption, suppressing parathyroid hormone, and augmenting insulin-like growth factor 1 production

The positive effects of protein intake on bone health may only be beneficial under conditions of adequate calcium intake.

FUNZIONALITÀ RENALE

Effect of short-term high-protein compared with normal-protein diets on renal hemodynamics and associated variables in healthy young men[1–3]

HP diet (2.4 g/kg/peso ideale) vs NP diet (1.2 g/kg/peso ideale)

TABLE 3
Urinary chemical variables in healthy men who consumed a normal-protein (NP) or a high-protein (HP) diet[1]

	NP diet	HP diet	*P* value[2]
Urinary albumin (mg/24 h)	8.7 ± 7	18.3 ± 7	<0.05
Urine pH	6.45 ± 0.39	5.79 ± 0.47	<0.05
Specific gravity	1020 ± 10	1020 ± 5	NS
Sodium excretion (mmol/d)	173.4 ± 64	215.6 ± 53	<0.05
Urea nitrogen excretion (mg/d)	9094 ± 1599	13915 ± 2275	<0.01
Creatinine excretion (mg/d)	1796 ± 292	1989 ± 381	0.12

[1] All values are means ± SDs. Excretion of albumin, sodium, urea nitrogen, and creatinine was measured in 22 participants who completed 24-h urine collections. Urinary pH and specific weight were measured by using a spot urine probe in 24 participants.

Frank H et al, Am J Clin Nutr, 90: 1509-1516, 2009

Review Article

Health effects of protein intake in healthy adults: a systematic literature review

Agnes N. Pedersen[1]*, Jens Kondrup[2] and Elisabet Børsheim[3]

[1]DTU Food, National Food Institute, Lyngby, Denmark; [2]Clinical Nutrition Unit, Rigshospitalet University Hospital, Copenhagen, Denmark; [3]Department of Surgery, The University of Texas Medical Branch, Galveston, TX, USA

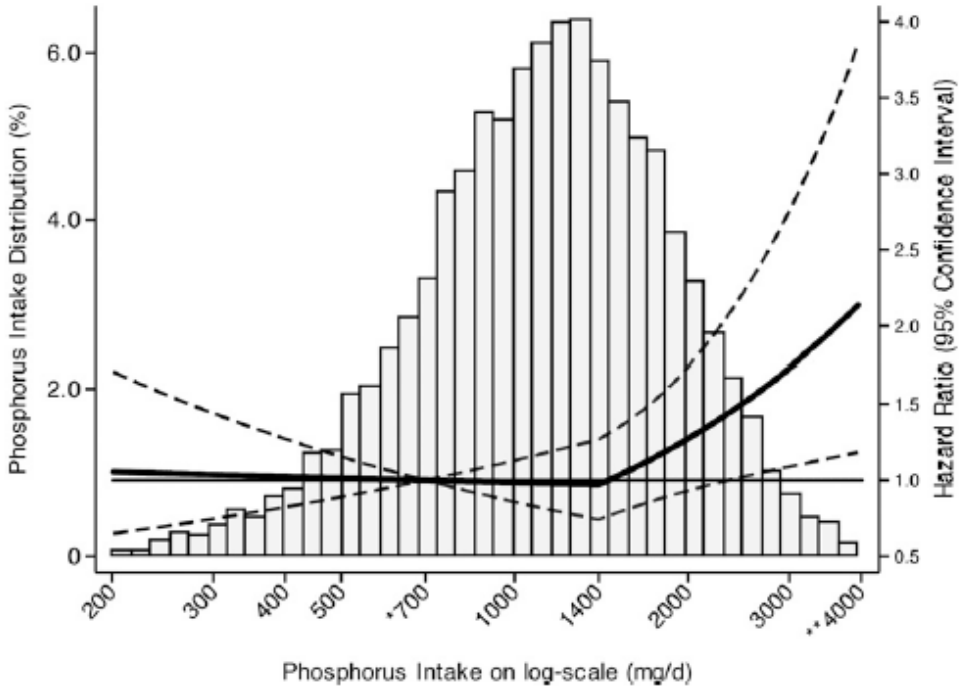
Exposure/Intervention	Outcome variable	Study	Number of participants (age) Men (M), Women (W)	Association of protein/effect (in RCT) Total	Animal	Vegetable	Rating A B C	Strength of evidence: Convincing, probable, Suggestive, no conclusion
Experimental normal (1.2 g/kg per day) or high protein intake (2.4 g/kg per day)	GFR	RC cross-over intervention study (61)	24 men, average age 24 years	POS	POS	NA	B	No conclusion
Experimental normal (1 ≈ g/kg per day) or high protein intake (≈ 2 g/kg per day) in young and elderly.	GFR	Balance study (9)	10 young (24 years), 10 elderly (70 years), 5 women in each group	POS (young) NS (elderly)	NA	NA	B	
Quintiles of estimated protein intake (24-h N)	eGFR	Cohort(11)	6,000 with 24 h urinary albumin ≥10 mg/L. 2,592 with 24 h urinary albumin <10 mg/L Average age: 50.	NS	NA	NA	C	
Protein intake (FFQ) in gram per day and in quintiles	eGFR	Cohort (60)	1,624 W	NS INVERSE in women with mild kidney insufficiency at baseline	NA	NA	C	
Experimental normal (1.2 g/kg per day) or high protein intake (2.4 g/kg per day)	Microalbuminuria	Experimental study (61)	24 men, average age: 24 years	POS	POS	NA	B	No conclusion
Experimental normal (1.5 g/kg per day) or high protein intake (3.0 g/kg per day)	Microalbuminuria	Experimental study (63)	24 men, average age: 24 years	NS	NA	NA	A	
Quintiles of estimated protein intake (24 h N)	Microalbuminuria	Cohort (11)	6,000 with 24 h urinary albumin ≥10 mg/L. 2,592 with 24 h urinary albumin <10 mg/L Average age: 50	NS	NA	NA	C	
Protein intake (FFQ) in gram per day and in quintiles)	Microalbuminuria	Cohort (60)	1,624 W	NS	NA	NA	C	
Spontaneous intake (FFQ) energy-adjusted gram per day and quintiles	Kidney stone	Cohort (64)	96,245 W (27-44 years (average: 36 years)	NA	NS	NA	C	No conclusion
Spontaneous intake (FFQ) energy-adjusted in quintiles	Kidney stone	Cohort (65)	45,619 M. Average age not given, range of age groups: 40- ≥70 years	NA	POS (Increase in group BMI <25, not overall)	NA	C	

Regarding the associations between protein kidney function and kidney stones, the evidence is regarded **as inconclusive** (GFR, Microalbuminuria, Calcolosi)

INTAKE FOSFORO

High dietary phosphorus intake is associated with all-cause mortality: results from NHANES III[1–3]

Median phosphorus intake was 1166 mg/d



Healthy population free of diabetes, cardiovascular disease, and chronic kidney disease.

In analyses adjusted for demographics, cardiovascular risk factors, kidney function, and energy intake, higher phosphorus intake was associated with **higher all-cause mortality** in individuals who consumed **> 1400 mg/d** (P = 0.03).

Chang AR et al, Am J Clin Nutr, 2014

TAKE HOME MESSAGE

- Le diete iperproteiche si sono dimostrate nei trial a breve termine più efficaci nella **riduzione** del peso corporeo e sul **mantenimento** del peso raggiunto.

- Considerando il solo intervento nutrizionale, le diete iperproteiche hanno dimostrato una riduzione maggiore della massa grassa, una riduzione più contenuta della perdita di massa priva di grasso e un incremento del dispendio energetico rispetto alle altre diete

- Una riduzione significativa della **mortalità** per tutte le cause, e una riduzione dell'incidenza di tumori in una popolazione di over 65

- Un miglioramento della densità ossea, purché si assumano adeguate porzioni di vegetali e di calcio

Grazie per l'attenzione