



Associazione
Medici
Endocrinologi



ITALIAN CHAPTER

16 Congresso Nazionale Ame

Joint Meeting with AACE Italian Chapter

Update in Endocrinologia Clinica

9-12 novembre 2017

Roma

**Ormoni sessuali,
metabolismo osseo e longevità**

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Servizio Ambulatoriale di Endocrinologia

P.O. San Massimo Penne AUSL Pescara

Aspetti neuroendocrini dell'invecchiamento

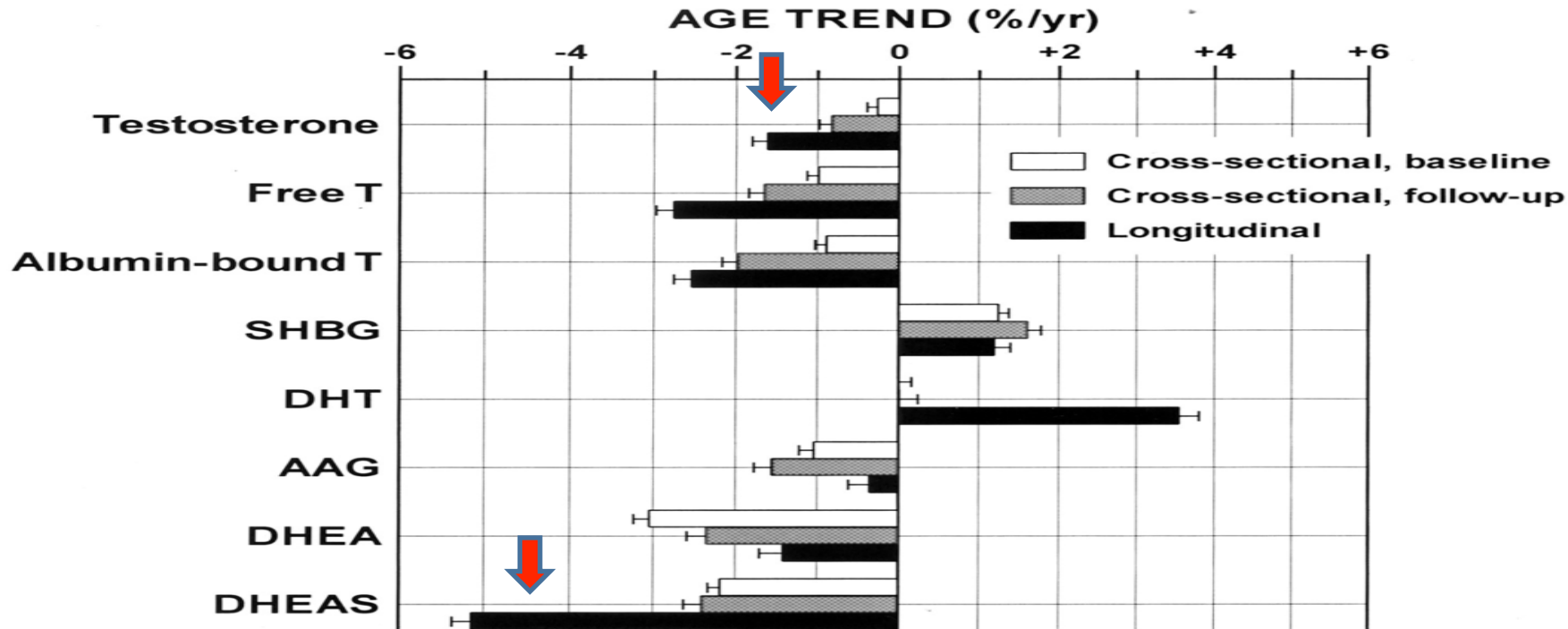
L'invecchiamento è un processo multifattoriale molto complesso

Invecchiamento come espressione di un progressivo squilibrio funzionale neuroendocrino: alterazione della secrezione ormonale e del rapporto inibitorio fra vari assi endocrini

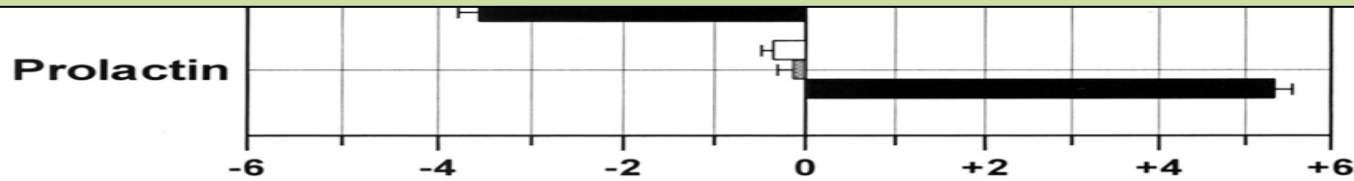
Teoria neuroendocrina.

Age Trends in the Level of Serum Testosterone and Other Hormones in Middle-Aged Men: Longitudinal Results from the Massachusetts Male Aging Study

Henry A. et al. *The Journal of Clinical Endocrinology & Metabolism*, 87, 2, 1 February 2002,



*Prevalenza di valori patologici di testosterone totale:
-nel 20% negli uomini di 60 anni
-> 35% negli uomini di 80 anni e più.*



Comorbidità nell'anziano e deficit di testosterone

Malattie acute	Qualsiasi malattia acuta
Malattie croniche	Obesità (insulino-resistenza) DM in scompenso metabolico BPCO OSAS Scompenso cardiaco Insufficienza respiratoria cronica Emocromatosi Insufficienza renale cronica Epatopatia cronica Malattie endocrine (Cushing , prolattinomi, altre patologia tumorali ipofisarie) Malattie neoplastiche Artropatie Fragilità
Stile di vita e trattamenti farmacologici	Alcolismo Sedentarietà Malnutrizione Glucocorticoidi Farmaci neurolettici Ketochenazolo Spironolattone Agenti chemioterapici alchilanti Oppiacei Cannabinoidi

Multiple Hormonal Deficiencies in Anabolic Hormones Are Found in Frail Older Women: The Women's Health and Aging Studies

Anne R. Cappola et al. Journal of Gerontology: MEDICAL SCIENCES 2009. Vol. 64A, No. 2, 243–248

Methods. The relationships of serum levels of total IGF-1, DHEAS, and free testosterone (T) with frailty status (nonfrail, prefrail, or frail) were analyzed in 494 women aged 70 – 79 years enrolled in the Women's Health and Aging Studies. Using multivariate polytomous regression,.

Conclusioni: Questi risultati suggeriscono una disfunzione endocrina generalizzata nella sindrome da fragilità.

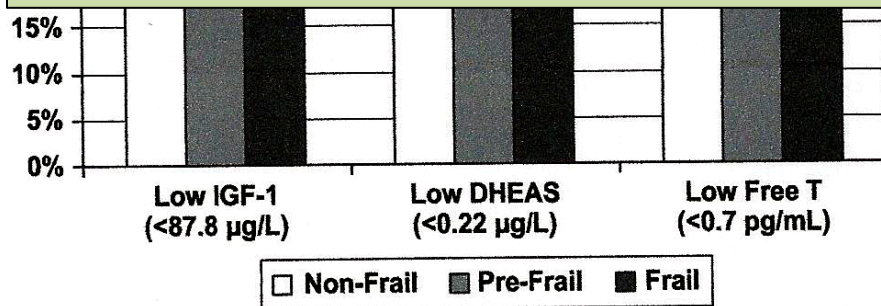


Figure 1. Prevalence of hormone deficiency by frailty status.

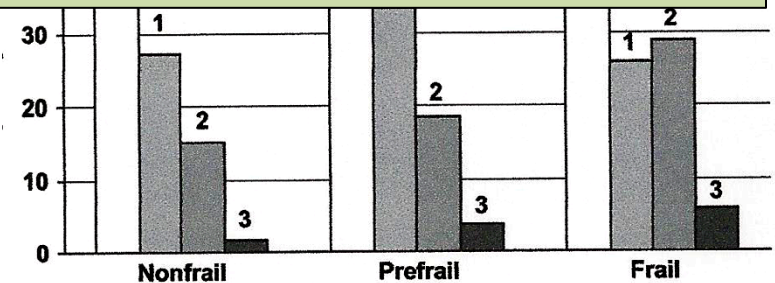
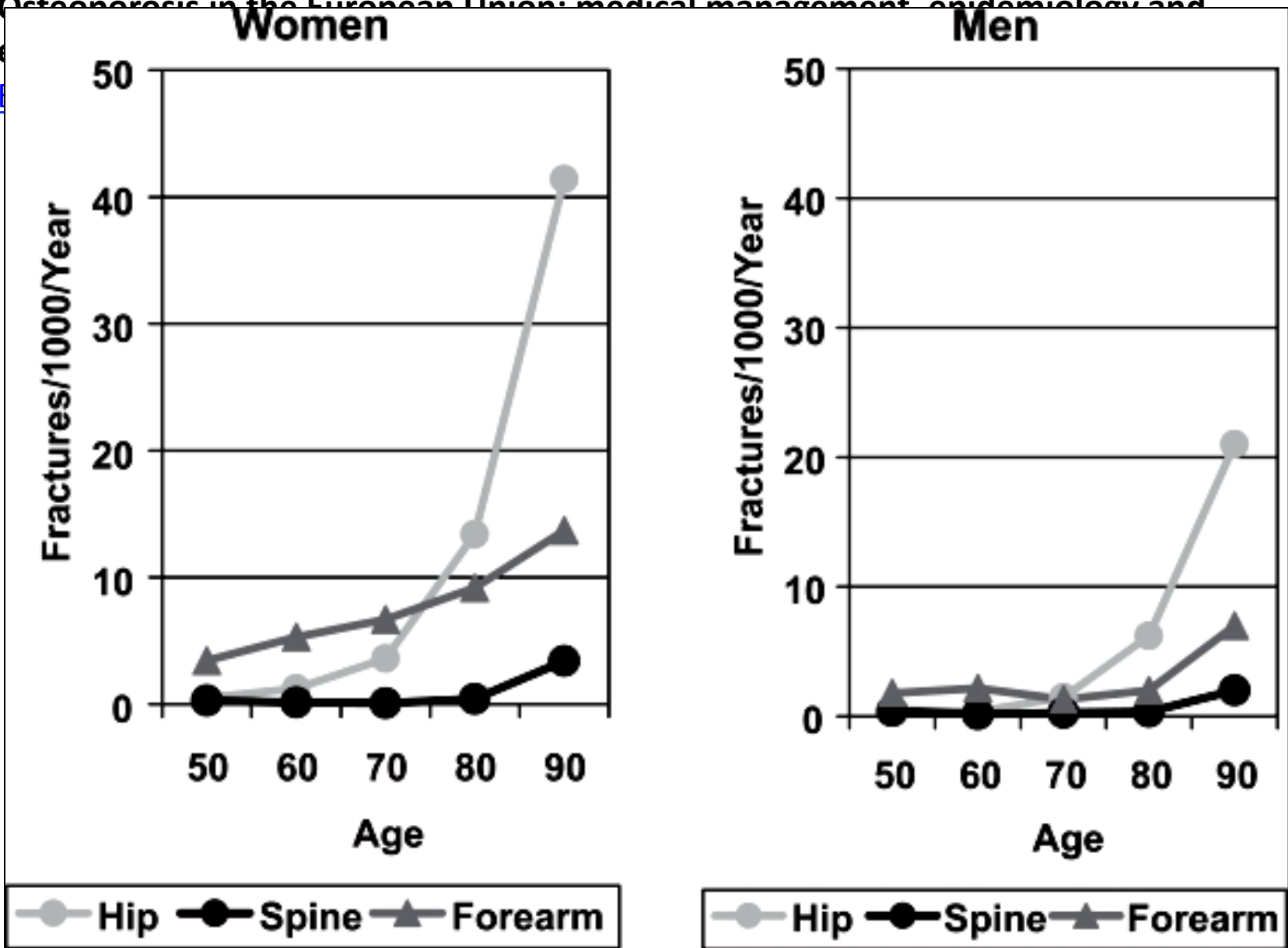


Figure 2. Number of abnormal hormones by frailty status.



The site specific pattern of osteoporotic fractures between the ages of 50-54 and 85-89 years in women from Sweden

DHEA Replacement for Postmenopausal Women

Susan R., et al., Volume 96, Issue 6, 1 June 2011, Pages 1642–1653,

First author, year (Ref.)	Study design	Duration (wk)	Dose (mg/d)	Total no.	Age of postmenopausal	Significant effects on BMD measured by dual photon x-ray absorptiometry
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Considerati complessivamente , i risultati di questa revisione della letteratura non supportano l'uso di DHEA.

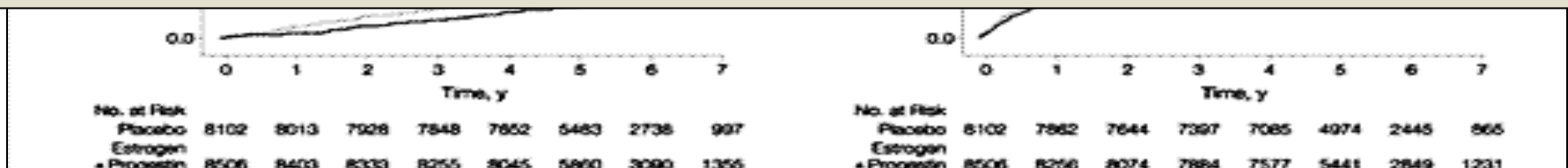
*Non si rilevano inoltre benefici sugli altri endpoint: **funzione sessuale, sensazione di benessere, parametri metabolici e cognitivi.***

2006 (97)	controlled double blind	26	50	(70 men)	60-80	both women and men
Villareal, 2000 (98)	Randomized placebo-controlled double blind	26	50	20 Women (16 men)	64-82	Significant increases in total body and lumbar spine BMD in women and men
Morales, 1998 (88)	Randomized placebo-controlled double blind, crossover	26	100	10 Women (9 men)	50-65	No significant effects on BMD
Baulieu, 2000 (71)	Randomized placebo-controlled double blind	52	50	140 Women (140 men)	60-79	Increased BMD in women femoral neck and Ward's triangle in 60-69 yr group, upper and total radius in 70-79 yr group, no effect in men
Casson, 1998 (87)	Randomized placebo-controlled double blind	26	25	13 Women		No significant effects on BMD

Long-term hormone therapy for perimenopausal and postmenopausal woman. J.Marjoiribanks et al. 17 January 2017

We included **22 double-blinded randomised controlled trials (RCTs) (43,637 women)** of HT **versus placebo** taken for at least 1 year by perimenopausal or postmenopausal women. HT included oestrogens, with or without progestogens, via the oral, transdermal, subcutaneous or intranasal route.

Anche se HT è considerata efficace per la prevenzione dell'osteoporosi in post-menopausa, è generalmente raccomandata come opzione solo per donne a rischio fratturativo significativo per le quali le terapie classiche risultassero inadeguate.



Testosterone Use in Men and Its Effects on Bone Health. A Systematic Review and Meta-Analysis of Randomized Placebo-Controlled Trials

Michal J. Tracz et al. Volume 91, Issue 6, 1 June 2006 central.



Date source Medline Embase Cochrane

Study	SMD 95% CI	SMD 95% CI
Intramuscular group		

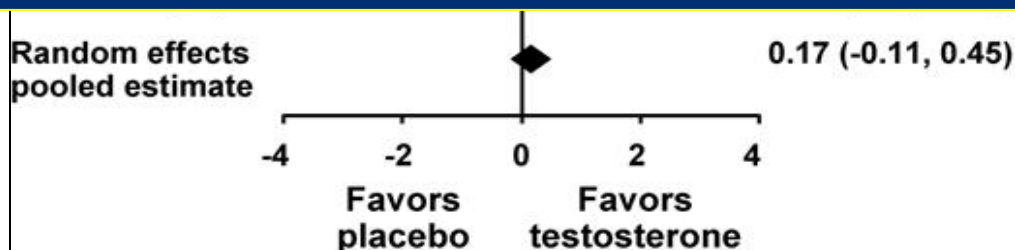
erone no greater than

Il testosterone presenta un evidente effetto sul metabolismo osseo:

a) di tipo diretto sul recettore androgenico

- stimolazione dell'attività osteoblastica nella formazione di osso trabecolare
- attivazione degli osteociti nel prevenire la perdita ossea trabecolare correlata all'invecchiamento
- non chiaro il ruolo del recettore androgenico nell'attività osteoclastica

b) di tipo indiretto tramite – aromatizzazione in estrogeni a livello osteoblastico



Random-effects meta-analysis of testosterone on ***femoral neck bone mineral density***.

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Table 4. Adverse Events during the First Year (Treatment Period) of the Testosterone Trials.*

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Event	Placebo (N = 394) <i>no. of participants</i>	Testosterone (N = 394)
Prostate-related event		
Increase in PSA level by ≥ 1.0 ng/ml	8	23
Prostate cancer	0	1
IPSS > 19 †	26	27
Hemoglobin ≥ 17.5 g/dl	0	7
Cardiovascular event‡		
Myocardial infarction (definite or probable)	1	2
Stroke (definite or probable)	5	5
Death from cardiovascular causes	1	0
Myocardial infarction, stroke, or death from cardiovascular causes	7	7
Serious adverse events		
Death	7	3
Hospitalization	78	68
Other§	6	7

		Fracture risk									BMD								
		Testosterone			Estrogen			SHBG			Testosterone			Estrogen			SHBG		
Study	Characteristics	H	V	O	H	V	O	H	V		O	H	V	O	H	V	O	H	V
CHAMP	Observational study 958 Australian men over 70	N	-	N	N	-	N	Y	-	Y	Y	-	-	Y	-	-	Y	-	-

- L'analisi multivariata ha evidenziato come solo l'estrogene bio-

Al momento pertanto il trattamento sostitutivo con testosterone va proposto al soggetto anziano

- **con bassi livelli di testosterone verificati in differenti valutazioni**
- **con sintomi clinici significativi di carenza androgenica**
- **dopo esplicita discussione riguardante l'incertezza sui rischi e benefici del trattamento**

mROS US	1234 men over 65 Average follow-up of 4.6 years	-	-	-	-	-	-	-	-	-	N	-	-	Y	-	-	Y	-	-
mROS US	Observational study 1436 American men over 65 Average follow-up of 4.7 years	N	-	N	N	-	Y	Y	-	Y	-	-	-	-	-	-	-	-	-
mROS Hong Kong	Observational study 1498 men over 65 from Hong Kong Average follow-up of 4 years	N	-	N	N	-	Y	N	-	N	N	-	N	Y	-	Y	N	-	N
Rotterdam	Prospective case-control study 179 men over 55 from Rotterdam Average follow-up of 6.5 years	-	-	-	-	N	-	-	N	-	-	-	-	-	Y*	-	-	N*	-



Grazie