12° Congresso Nazionale AME
Associazione Medici Endocrinologi
6th Joint Meeting with AACE
American Association of Clinical Endocrinologists

Bari,
7-10 novembre 2013

Ipogonadismo maschile : La terapia tra tabù e libero mercato

Dott. Mauro Schiesaro UOC Medicina Interna, AULSS 22 Bussolengo (VR)

LOH (Late onset Hypogonadism) o TDS

Bari,
7-10 novembre 2013

- TDS è una sindrome *clinica E biochimica*
- È caratterizzata da ipotestosteronemia e sintomi specifici
- Associata con il processo di invecchiamento
- Interessa molteplici organi ed apparati e determina alterazioni della QOL
- E' responsabile di disturbi sessuali

Epidemiologia

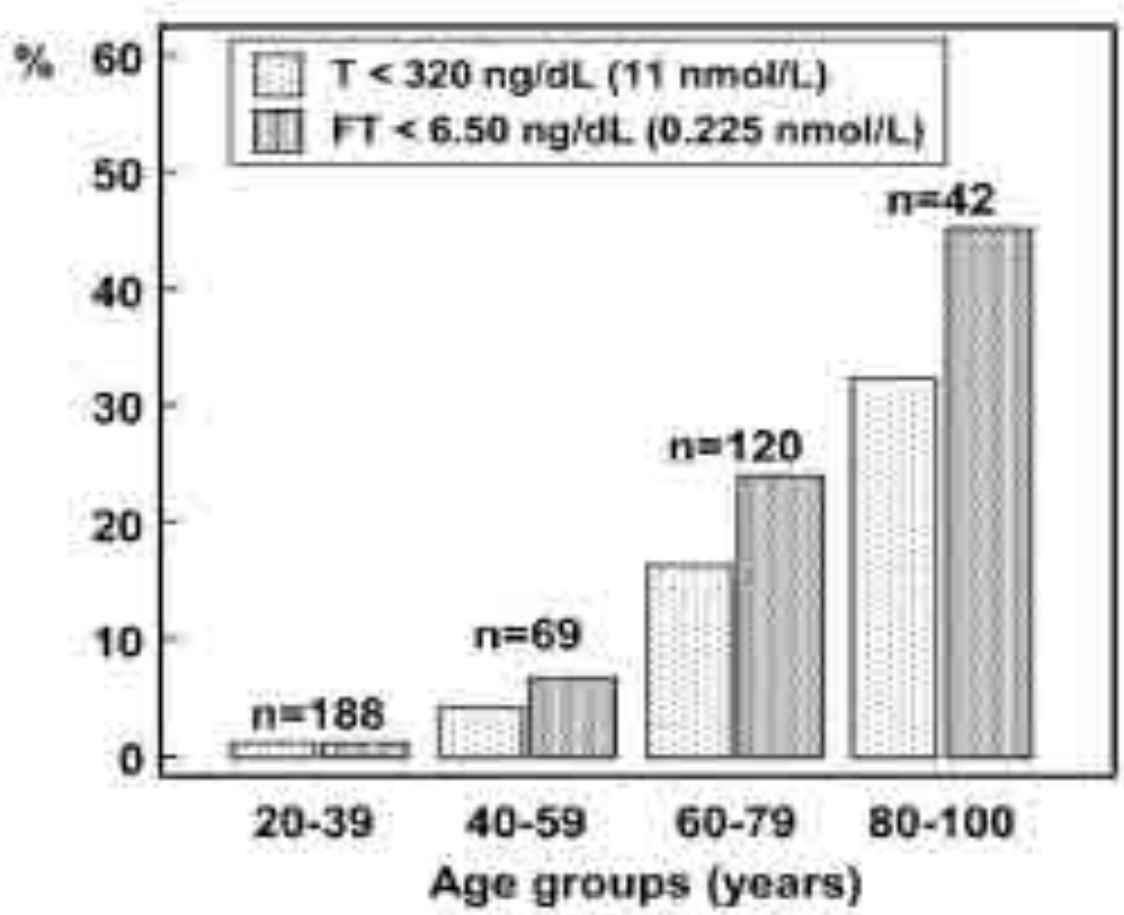

FIG. 5. Proportion of healthy men with serum testosterone (T) and FT below the laboratory reference range for young men, according to data in Refs. 20 and 35. [Adapted from Ref. 41 with permission from Elsevier.]

Clinical Endocrinology (2008) 69, 515–525

REVIEW ARTICLE

Measurement of testosterone in the diagnosis of hypogonadism in the ageing male

M. J. Wheeler and S. C. Barnes

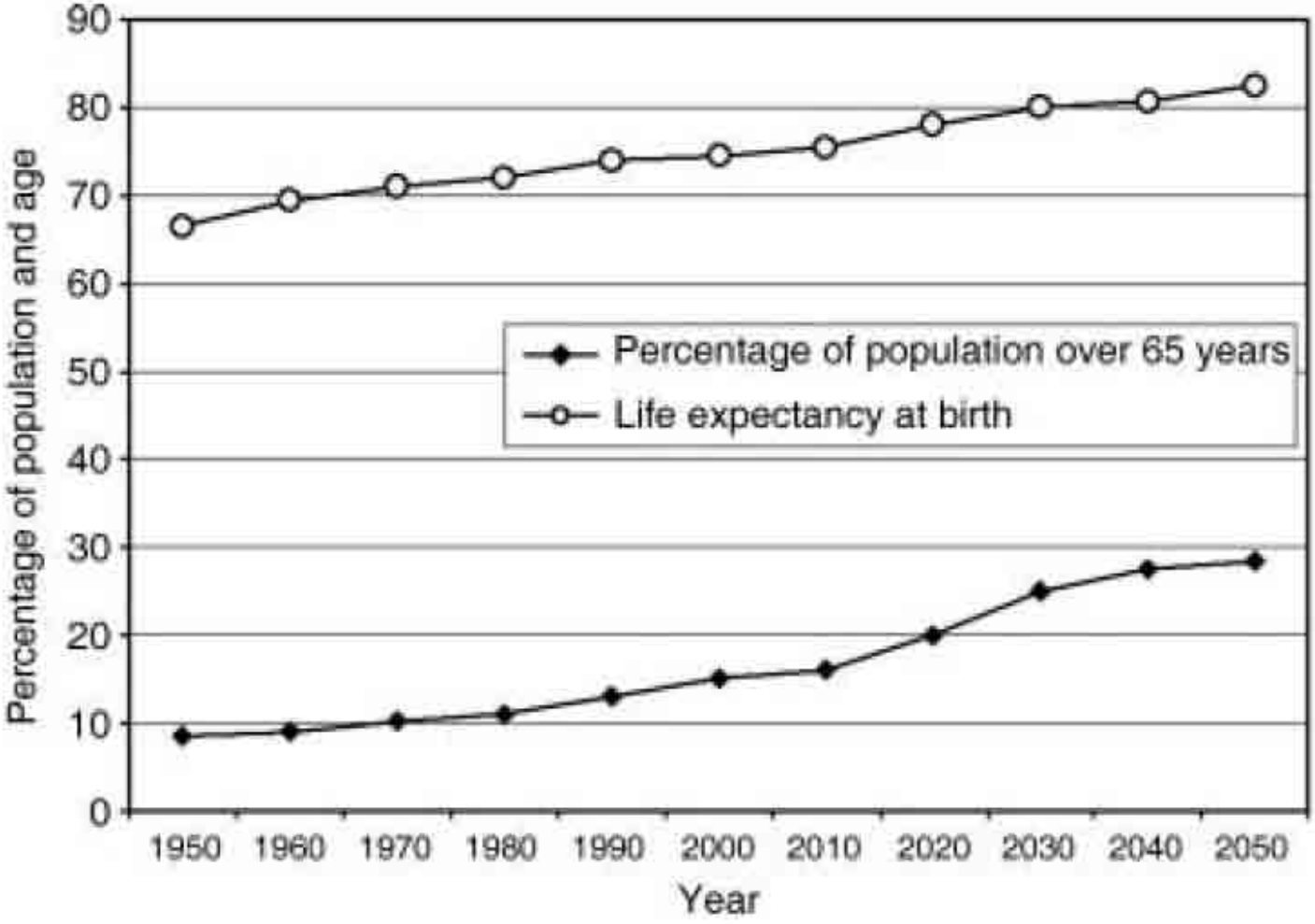

Fig. 1 Trends in life expectancy and percentage of population over 65 years.

Symptoms in Hypoandrogenism

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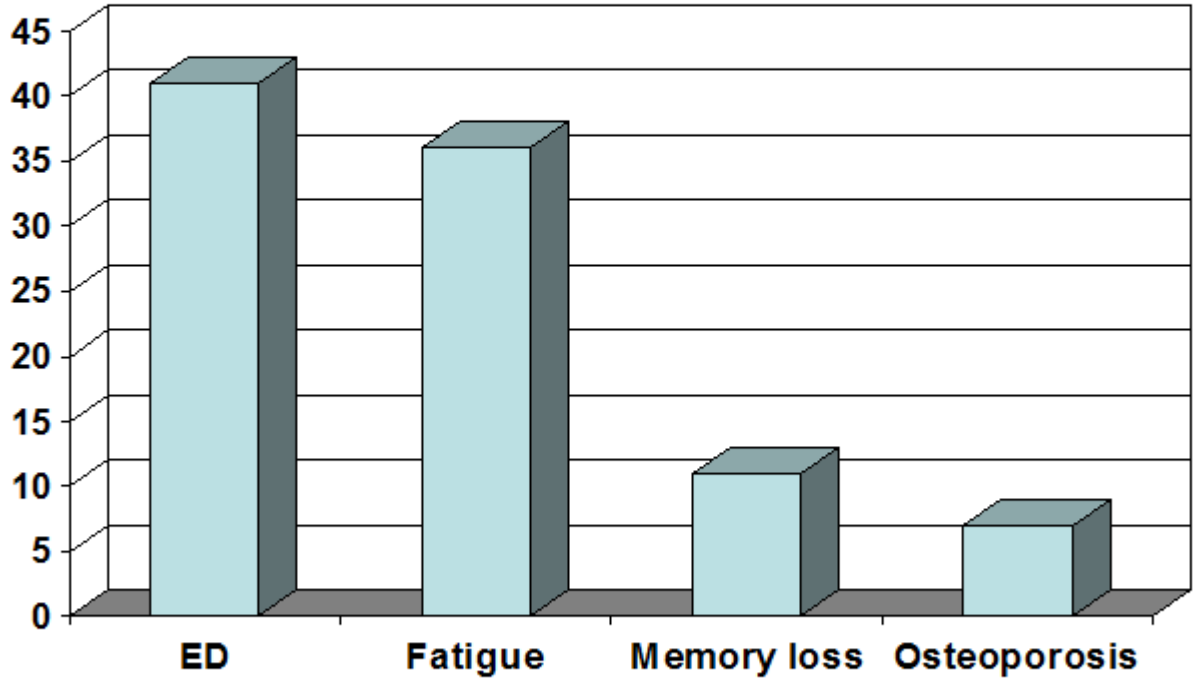
7-10 novembre 2013



Tan, 1999

Diagnosi

Bari,
7-10 novembre 2013

Journal of Andrology, Vol. 30, No. 1, January/February 2009

Investigation, Treatment, and Monitoring of Late-Onset Hypogonadism in Males: ISA, ISSAM, EAU, EAA, and ASA Recommendations

C. WANG*, E. NIESCHLAG,† R. SWERDLOFF*,

Recommendation 7: Biochemical diagnosis. Grade C

- Serum sample for total testosterone (TT) determination.

Diagnosi

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7-10 novembre 2013

Ad oggi non vi è concordanza su quale sia il livello di testosterone che definisca il deficit androgenico nell'anziano.

E' accettato comunque un valore 2 SD al di sotto dei valori del giovane.

Testosterone : < 8 nmol/l (231 ng/dl)

Free testosterone < 174 pmol/l (50 ng/l)
Testosterone biodisponibile : < 3.8 nmol/l


T (ng/ml)
T (nM)
No terapia con testosterone
5,0
17
3,5
12
3,0
10,4
2,31
8
Terapia con testosterone
0,5
2

Chi studiare?

Bari,
7-10 novembre 2013

Fattori di rischio per TDS

Bari,
7-10 novembre 2013

- ✓ Obesità
- ✓ Sindrome metabolica
- ✓ DM 2
- ✓ Iperprolattinemia
- ✓ Farmaci
- ✓ BPCO

T e Obesità

Bari,
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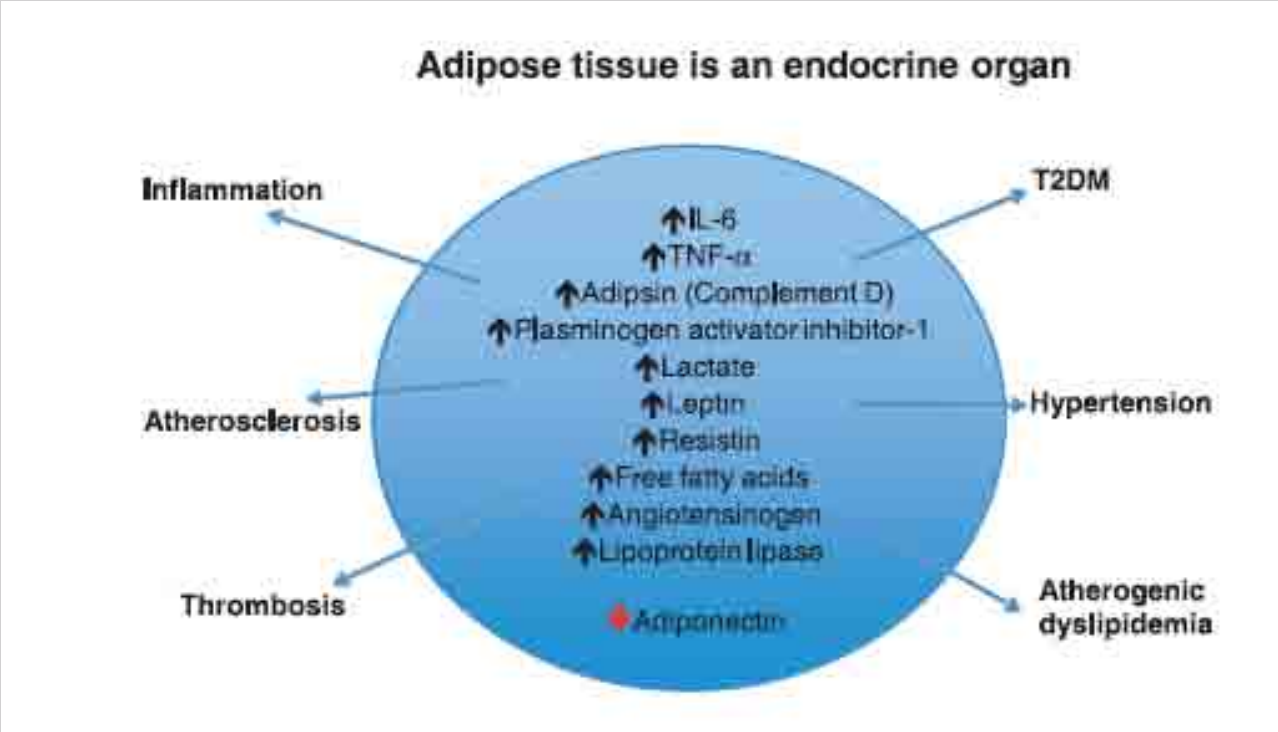
Tessuto adiposo



Obesity is often associated with reduced Testosterone
(Pasquali et al Metabolism 1991)

Central obesity predicts T reduction better than BMI
(Svartberg et al Eur J Epidemiol 2004)

Table 1. Definition of the metabolic syndrome

	WHO	IDF	NCEP III
Essential feature	diabetes, impaired glucose tolerance or insulin resistance[a]	central obesity (men >94 cm waist, women >80 cm waist)	no essential feature
Diagnosis requires	essential feature plus 2 from: hypertension (>140/90) hypertriglyceridaemia (>1.7 mmol/l) low HDL cholesterol[b] central obesity[c] microalbuminuria[d]	essential feature plus 2 from; hypertension (>130/85) hypertriglyceridaemia (>1.7 mmol/l) low HDL cholesterol (<1.03 mmol/l) raised fasting glucose (>5.6 mmol/l)	diagnosis requires three factors from; hypertension (>130/85) hypertriglyceridaemia (>1.7 mmol/l) low HDL cholesterol (<1.03 mmol/l) raised fasting glucose (>5.6 mmol/l) central obesity[e]

WHO = World Health Organisation definition of the metabolic syndrome; IDF = International Diabetes Federation definition of the metabolic syndrome; NCEP = National Cholesterol Education Program Expert Panel III definition of the metabolic syndrome.

[a]Impaired glucose tolerance = glucose >7.8 mmol on 2-hour glucose tolerance test. Insulin resistance = in highest quartile of relevant population.

[b]HDL cholesterol <0.9 mmol/l in men, <1.0 mmol/l in women.

[c]Waist-to-hip ratio >0.9 in men, >0.85 in women or BMI greater than 30.

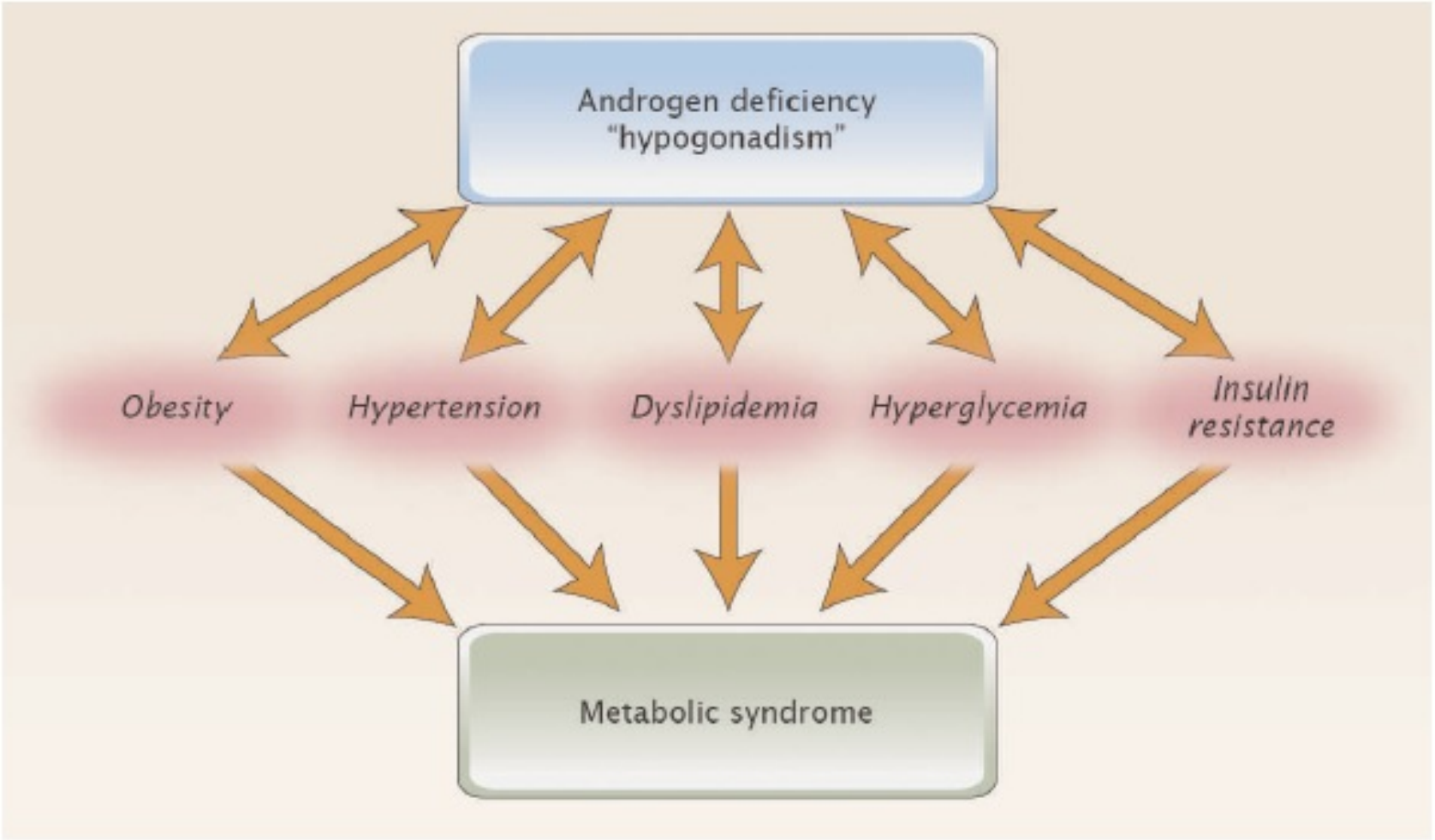
[d]Albumin-creatinine ratio >30.

[e]Waist circumference >102 cm in men, >88 cm in women.

The Emerging Link Between Hypogonadism and Metabolic Syndrome

ANDRÉ T. GUAY

Bari,
7-10 novembre 2013



Journal of Andrology, Vol. 30, No. 4, July/August 2009

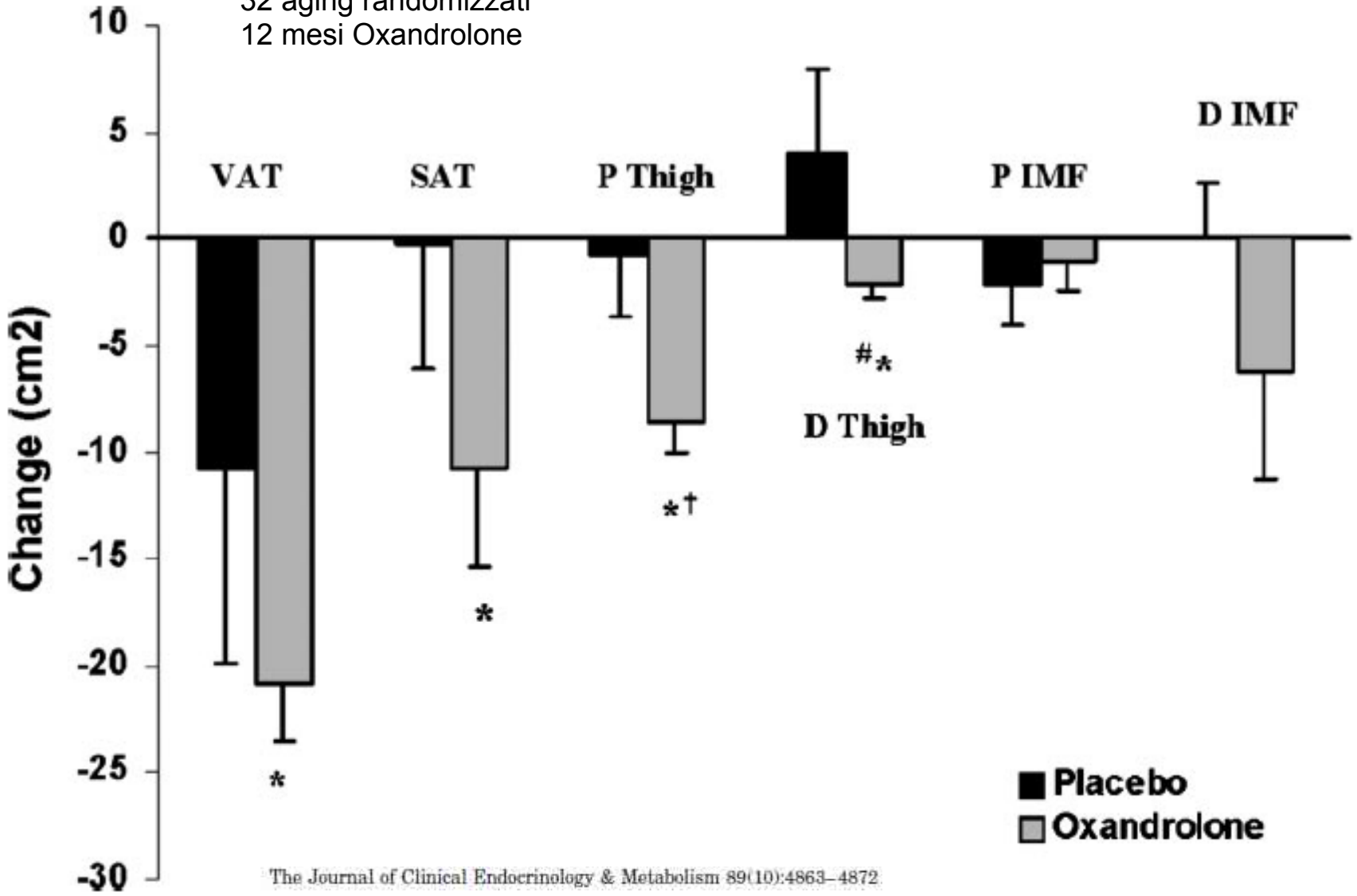
Obesity, MeTS and Hypogonadism

Bari,
7-10 novembre 2013

Effects of Androgen Therapy on Adipose Tissue and Metabolism in Older Men

E. TODD SCHROEDER, LING ZHENG, MICHELLE D. ONG, CARMEN MARTINEZ, CARLA FLORES, YOLANDA STEWART, COLLEEN AZEN, AND FRED R. SATTLER

32 aging randomizzati
12 mesi Oxandrolone

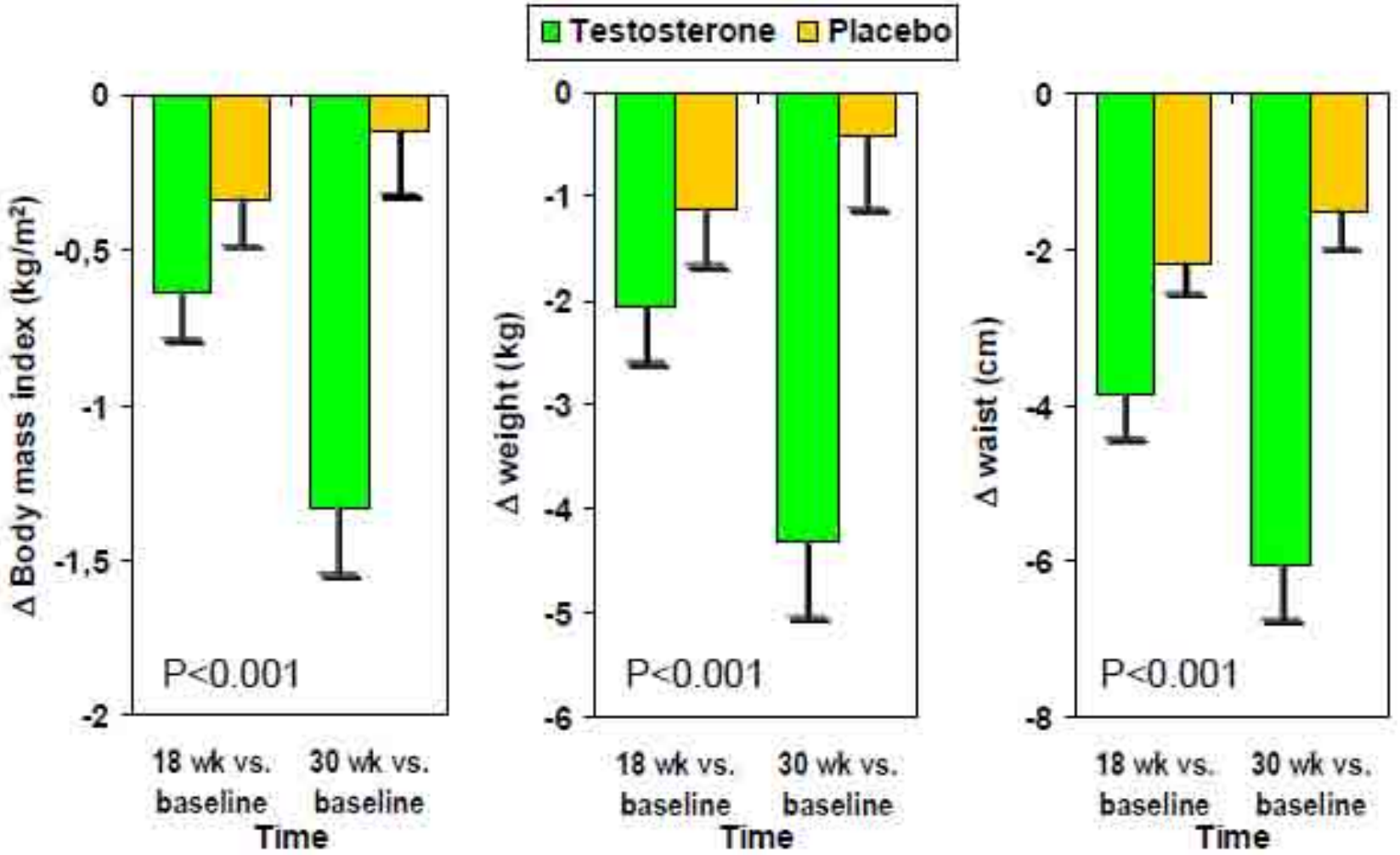


The Journal of Clinical Endocrinology & Metabolism 89(10):4863–4872

Testosterone as Potential Effective Therapy in Treatment of Obesity in Men with Testosterone Deficiency: A Review

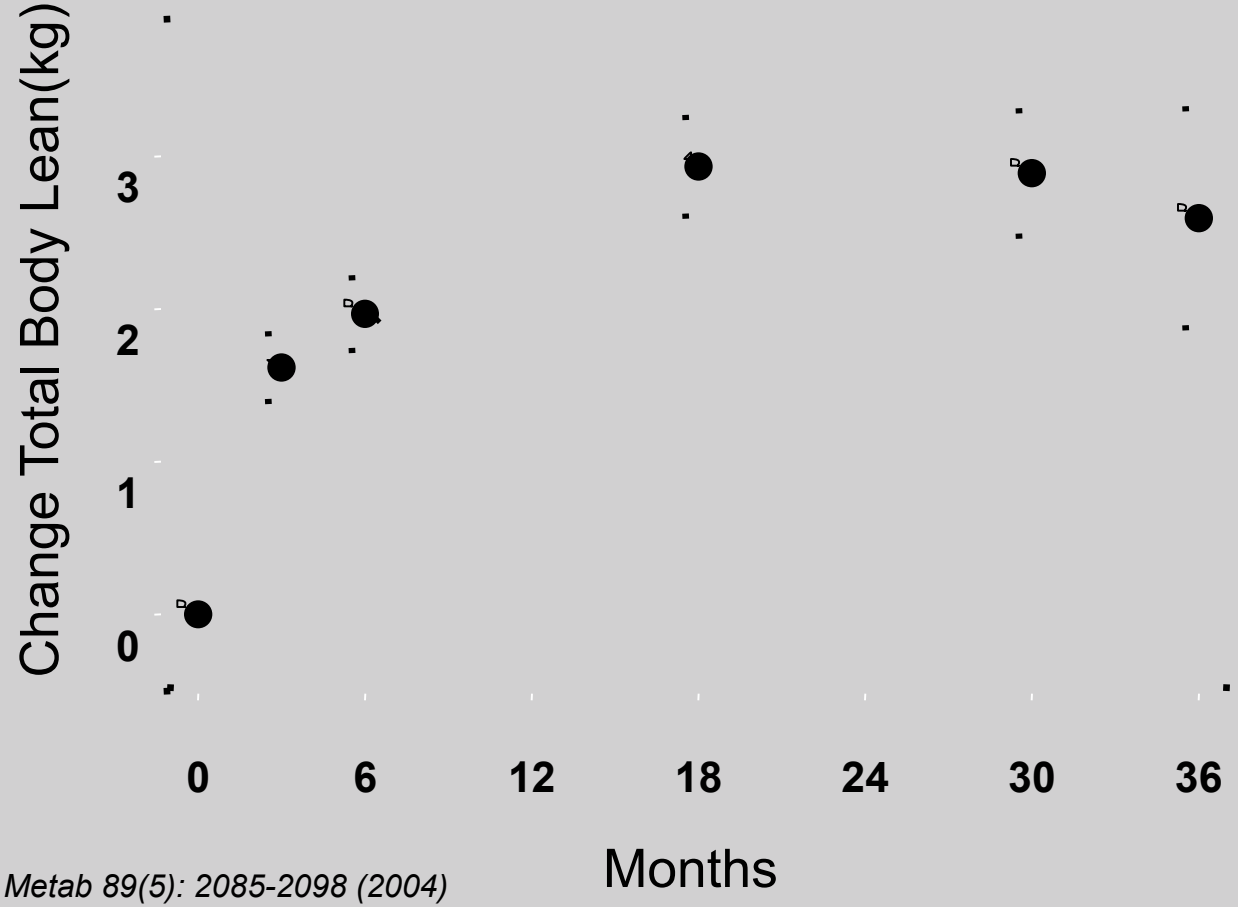
Farid Saad[1,*], Antonio Aversa[2], Andrea M. Isidori [2] and Louis J. Gooren[3]

184 MS



Total Body Lean Mass after T-gel

Bari,
7-10 novembre 2013

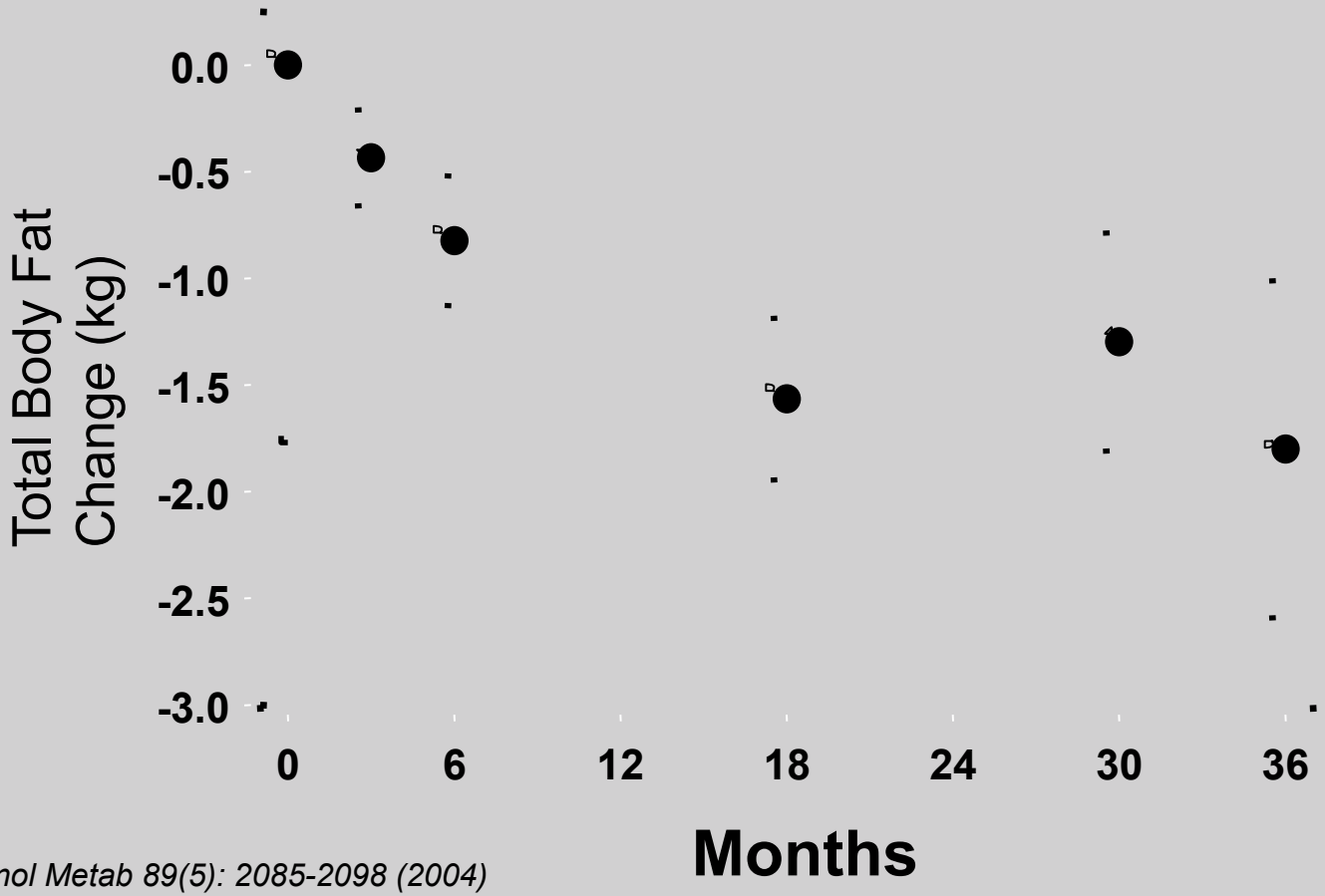


Mean values of all dose groups

Wang C et al. J Clin Endocrinol Metab 89(5): 2085-2098 (2004)

Body Fat Mass after T-gel

Bari,
7-10 novembre 2013



Mean values of all dose groups

Wang C et al. J Clin Endocrinol Metab 89(5): 2085-2098 (2004)

T e diabete

Bari,
7-10 novembre 2013

Hypogonadism and diabetes

M Betancourt-Albrecht[1] and GR Cunningham[1]*

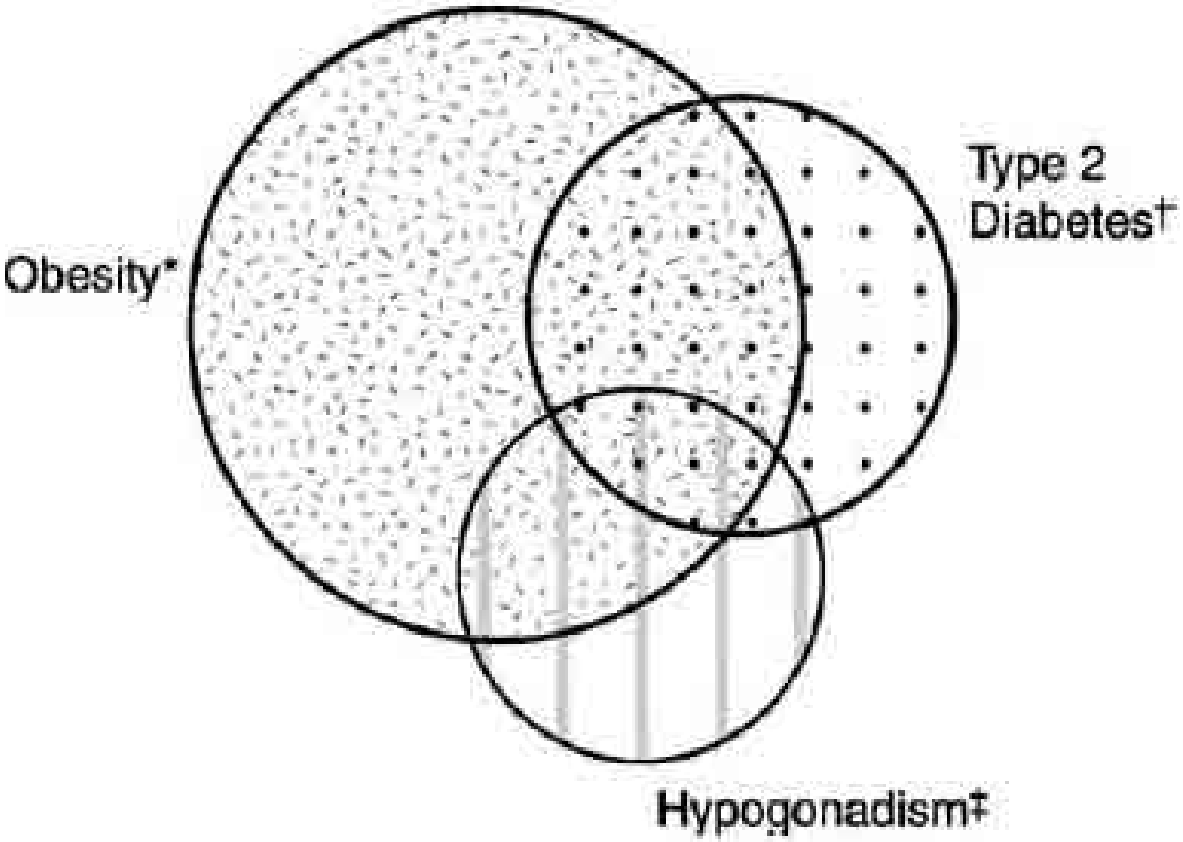


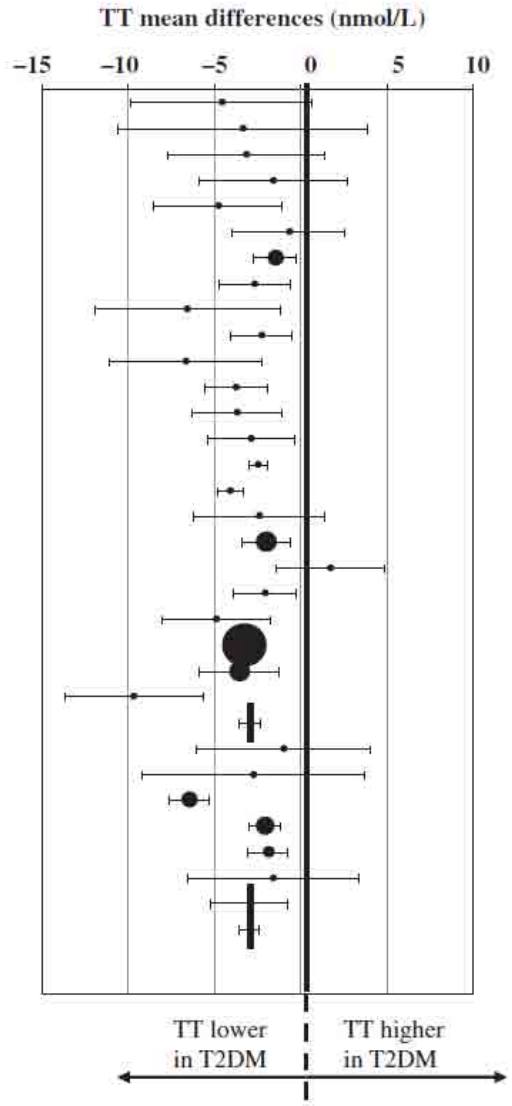
Figure 1 Populations of American men with obesity, type II diabetes, and hypogonadism display a high degree of overlap. *21.4 million men were considered obese in 2001.[45] †6.9 million men had type II diabetes in 2001.[45] ‡5 million men are thought to be hypogonadal.[46]

International Journal of Impotence Research (2003) 15, Suppl 4, S14–S20
 0955-9930/03 $25.00

Type 2 diabetes mellitus and testosterone: a meta-analysis study

G. Corona,*§[1] M. Monami,†[1] G. Rastrelli,* A. Aversa,‡ A. Sforza,§ A. Lenzi,‡ G. Forti,* E. Mannucci† and M. Maggi*

Bari,
7-10 novembre 2013



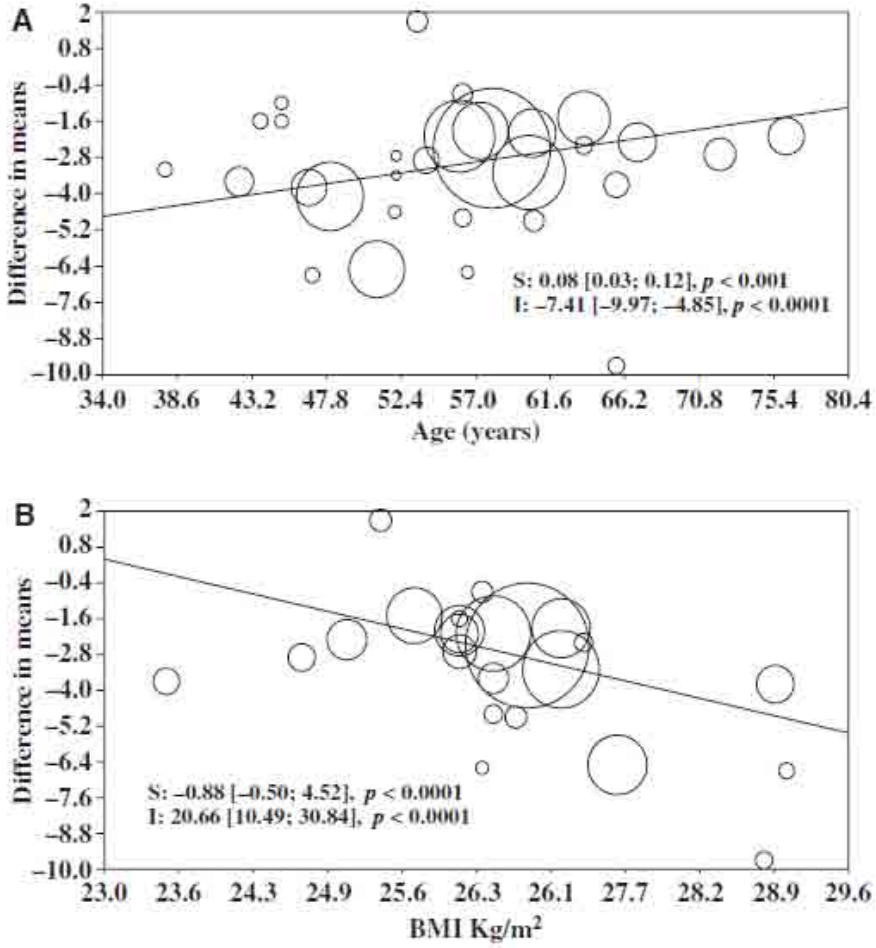
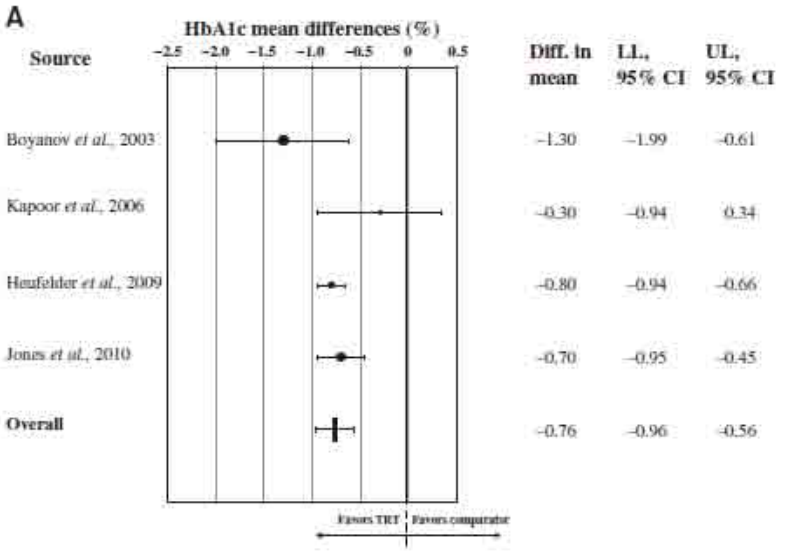


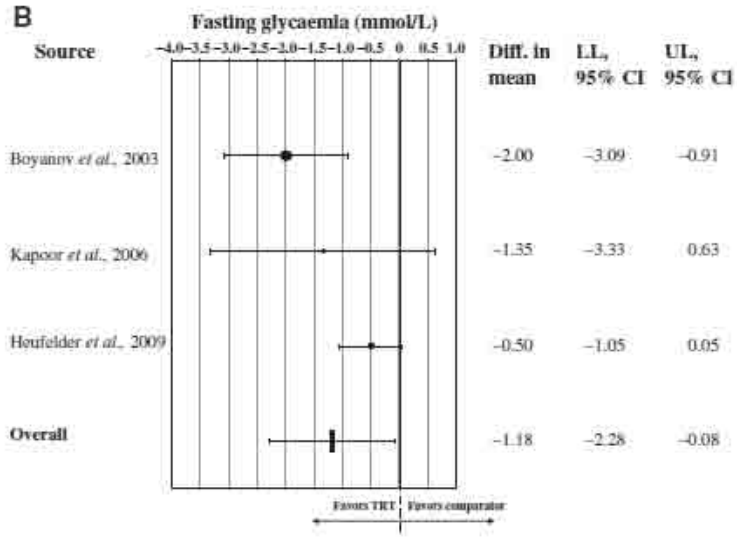
Figure 4 Influence of age (A) and body mass index (B) on total testosterone weighted mean differences between type 2 diabetes mellitus and controls.

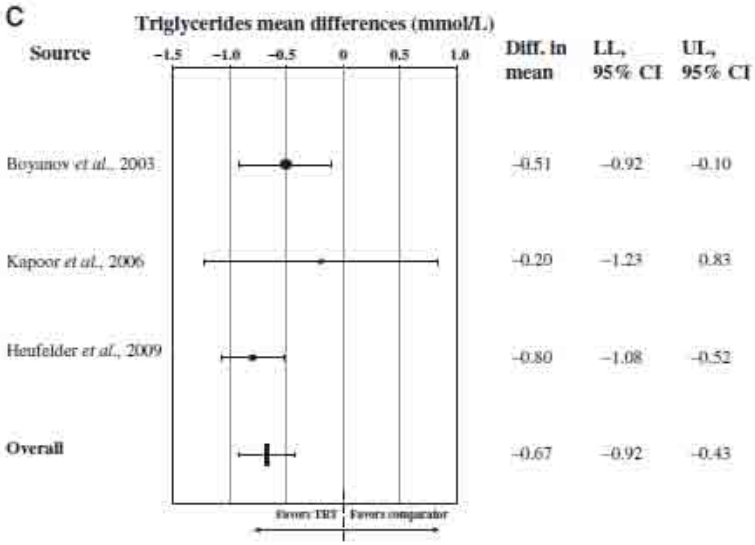
Type 2 diabetes mellitus and testosterone: a meta-analysis study

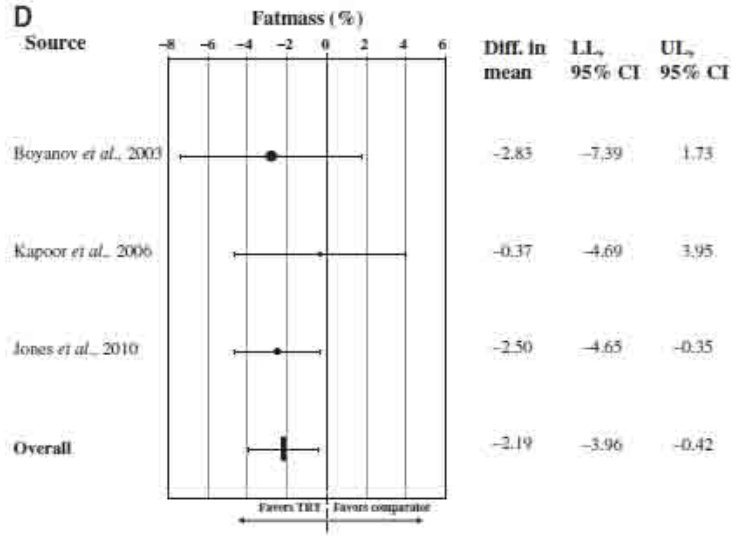
G. Corona,*§[1] M. Monami,†[1] G. Rastrelli,* A. Aversa,‡ A. Sforza,§ A. Lenzi,‡ G. Forti,* E. Mannucci† and M. Maggi*

Bari,
7-10 novembre 2013







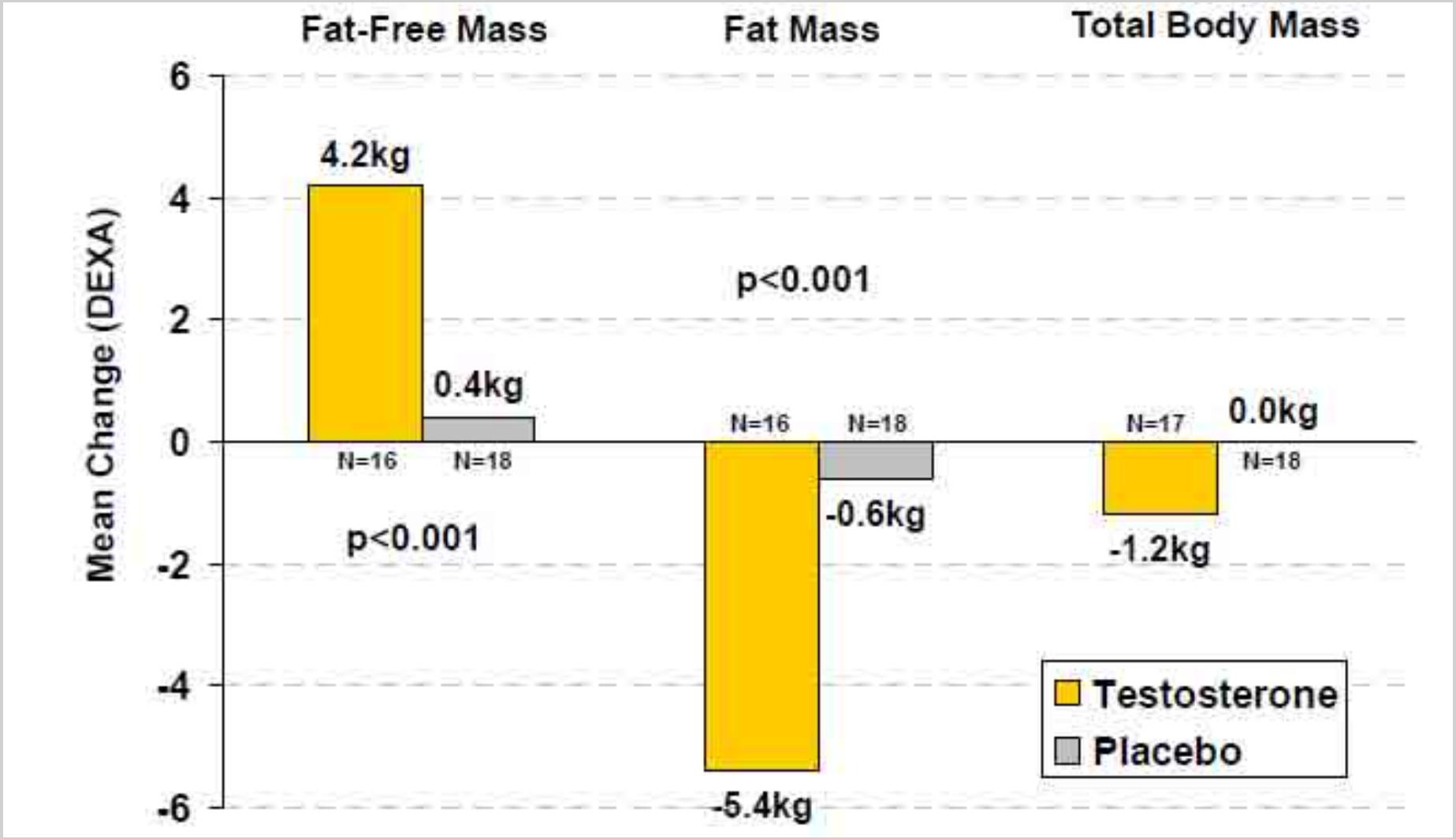


Testosterone as Potential Effective Therapy in Treatment of Obesity in Men with Testosterone Deficiency: A Review

Farid Saad[1,*], Antonio Aversa[2], Andrea M. Isidori [2] and Louis J. Gooren[3]

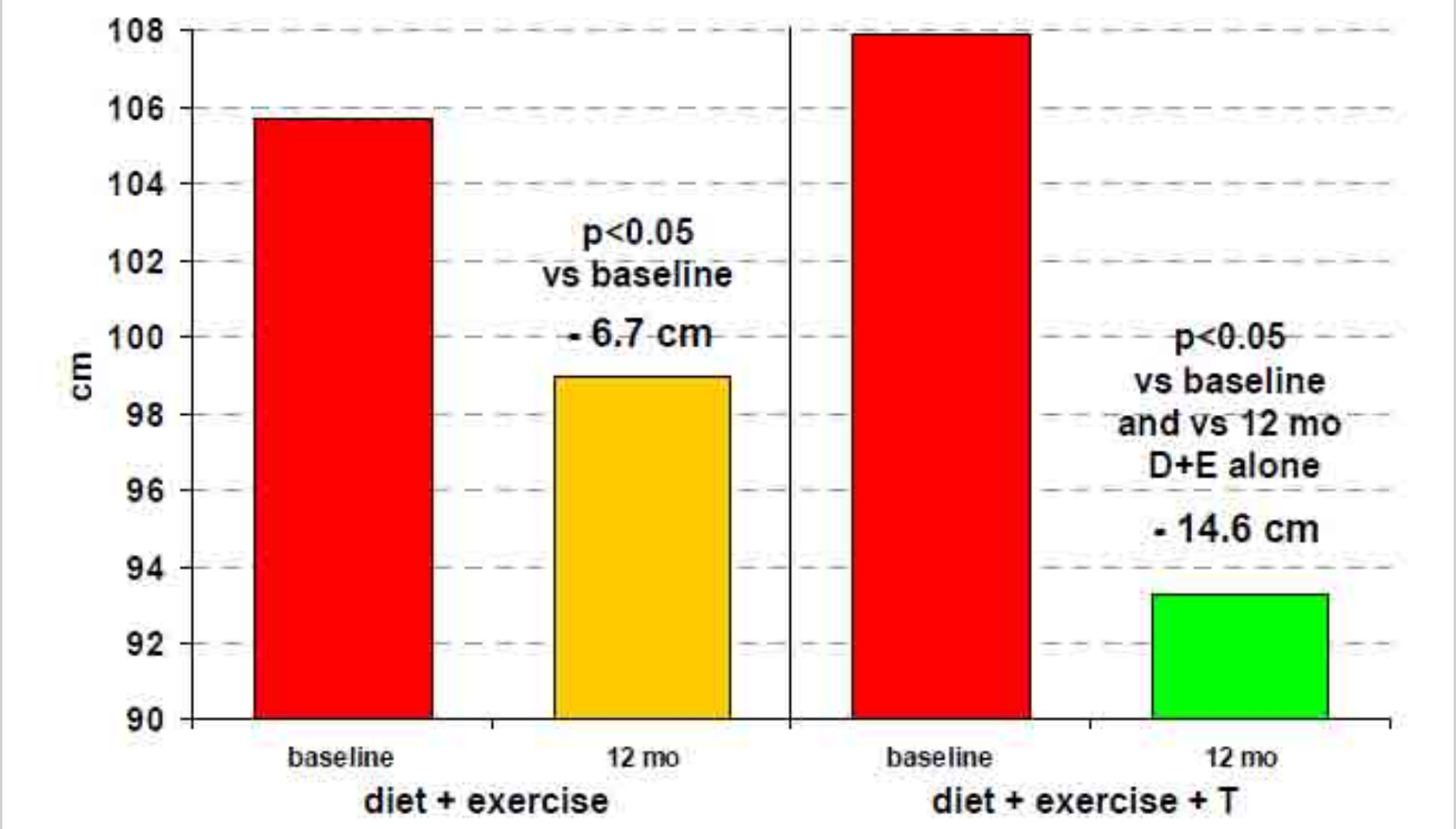
Bari,
7-10 novembre 2013

32 DM trattati con uT i.m.



Current Diabetes Reviews, 2012, *8*, 131-143

32 DM


108
106
104
102
100
98
96
94
92
90
cm
p<0.05
vs baseline
- 6.7 cm
p<0.05
vs baseline
and vs 12 mo
D+E alone
- 14.6 cm
baseline
12 mo
baseline
12 mo
diet + exercise
diet + exercise + T

Low Testosterone in Men with Type 2 Diabetes: Significance and Treatment

Mathis Grossmann

Bari,
7-10 novembre 2013

TABLE 2. RCT assessing the effect of testosterone therapy on glucose metabolism in men with type 2 diabetes or the MetS

First author (Ref.)	n	Diagnosis	Age (yr)	BMI (kg/m^2)	T-Rx type	T-Rx duration (wk)	Dropout %	Total T baseline (nmol/liter)	Total T achieved (nmol/liter)	HbA1c baseline (%)	Effect on WC (cm)	Effect on HOMA-IR	Effect on HbA1c (%)	Other reported effects
Kapoor (92)	24	T2D	64	33	TE 200 mg im 2- weekly	12	0	8.6	12.8	7.3	−1.6[a]	−1.7[a] (−39%)	−0.37%[a]	Decrease in total cholesterol (−0.4 mmol/liter[a]). No effect on LDL, HDL, Tg or blood pressure.
Gopal (93)	22	T2D	44	24	TE 200 mg im 2- weekly	12	0	10.1	N.R.	7.0	N.S.	N.S.	N.S.	No effects on lipids, blood pressure.
Heufelder (94)	32	MetS and newly diagnosed T2D	57	31	Transdermal T 50 mg/d with DE compared to DE alone	52	0	10.5	15.4[b] (11.2[a] DE)	7.5	−6.0	−0.9[b] (−59%)	−0.8%[a]	Decrease in CRP[b], increase in adiponectin[a]
Kalinchenko (95)	184	MetS and T2D (28%)	52	35	TU 1000 mg im 12-weekly	30	7	6.7	13.1	N.R.	−4.6[b]	−1.7[a] (−31%)	N.R.	Decrease in body weight (−3.9 kg[b]). Decrease in IL-1β[a], TNF-α[a], CRP[b], but not in IL-6, IL-10. No effect on fasting glucose, lipids. Increase in HCT (+2.0%[b]). No change in IPSS, PSA.
Aversa (96)	50	MetS and T2D (30%)	58	30	TU 1000 mg im 12-weekly	52	8	8.3	14.2[b]	5.7	−8.0[b]	−2.6[b] (60%)	−1.1%[a]	Decrease in CRP[b]. No change in PSA, prostate volume. Increase in HCT (+3.8%)[a]. No change in lipids, blood pressure.
Jones (97)[c]	220	T2D (62%) and/or MetS (80%)	60	32.0	Transdermal T 60 mg/d	26	29	9.4	>17[b]	6.7	N.S.	−0.8[a] (15%)	N.S.	Decrease in lipoprotein a[a] and in HDL[a]. No change in % body fat.
Solvay RCT[d]	180	T2D	N.R.	N.R.	Transdermal T 1%	26	11	<13.9	N.R.	7.0–9.5	N.R.	N.S.	N.S.	2.0 kg increase in lean body mass[b]

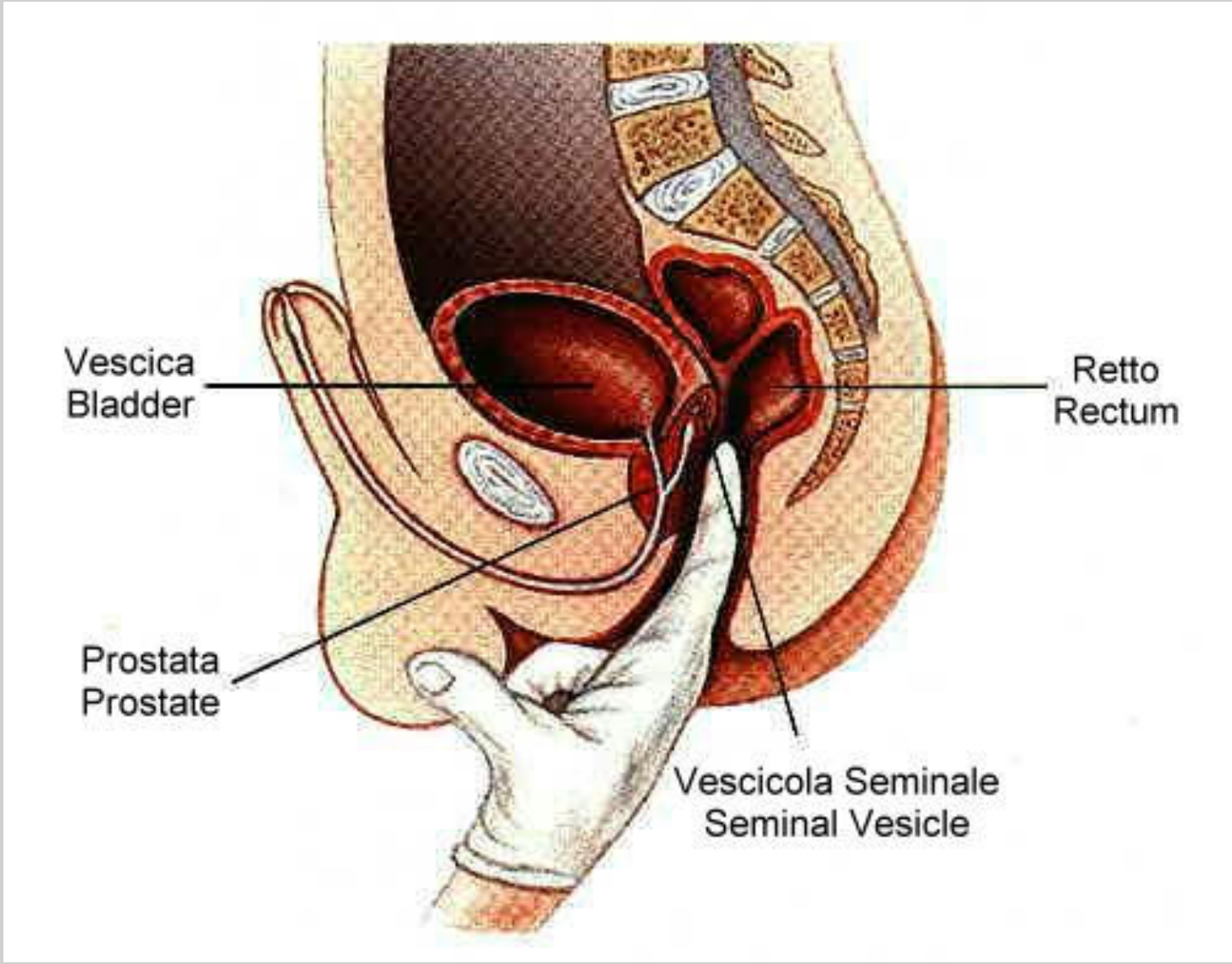
Effect is relative to control. Patients were included on the basis of subnormal testosterone levels and symptoms compatible with androgen deficiency. n, Number of patients; Rx, therapy; WC, waist circumference; T, testosterone; TE, T esters; DE, diet and exercise; TU, T undecanoate; N.R., not reported; N.S., not significant; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HCT, hematocrit; PSA, prostate-specific antigen; CRP, C-reactive protein; Tg, triglyceride; T2D, type 2 diabetes; IPSS, International Prostate Symptom Score.

Nonostante potenziali benefici, scarsità di evidenze
La decisione di trattare deve essere guidata dalla presenza di altri disturbi (Osso, massa grassa, disturbi sessuali ecc.)

J Clin Endocrinol Metab, August 2011, 96(8):2341–2353

T e Prostata

Bari,
7-10 novembre 2013



Prostate cancer and age

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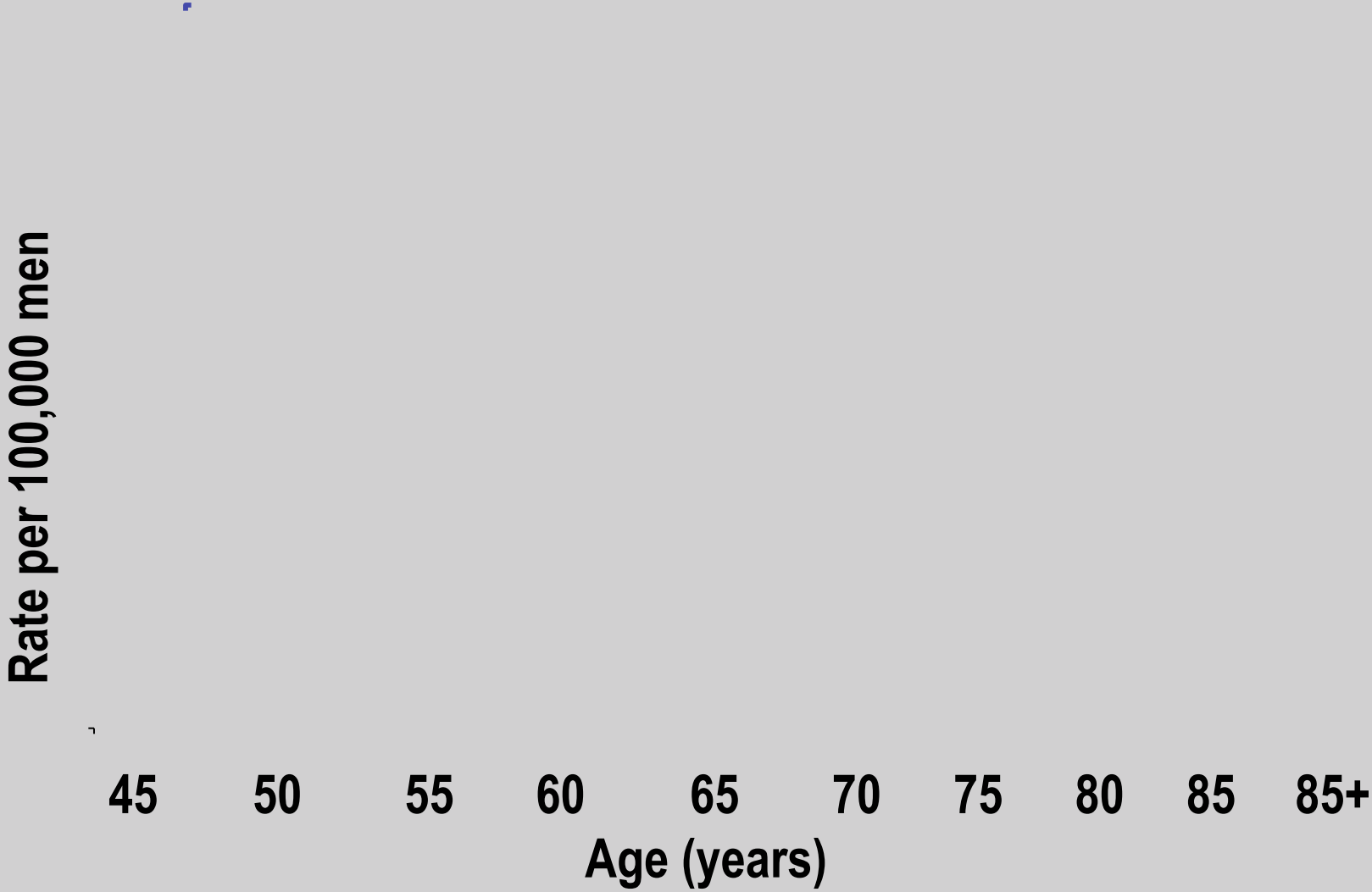

Relative importance in analysis of prostate cancer in MMAS

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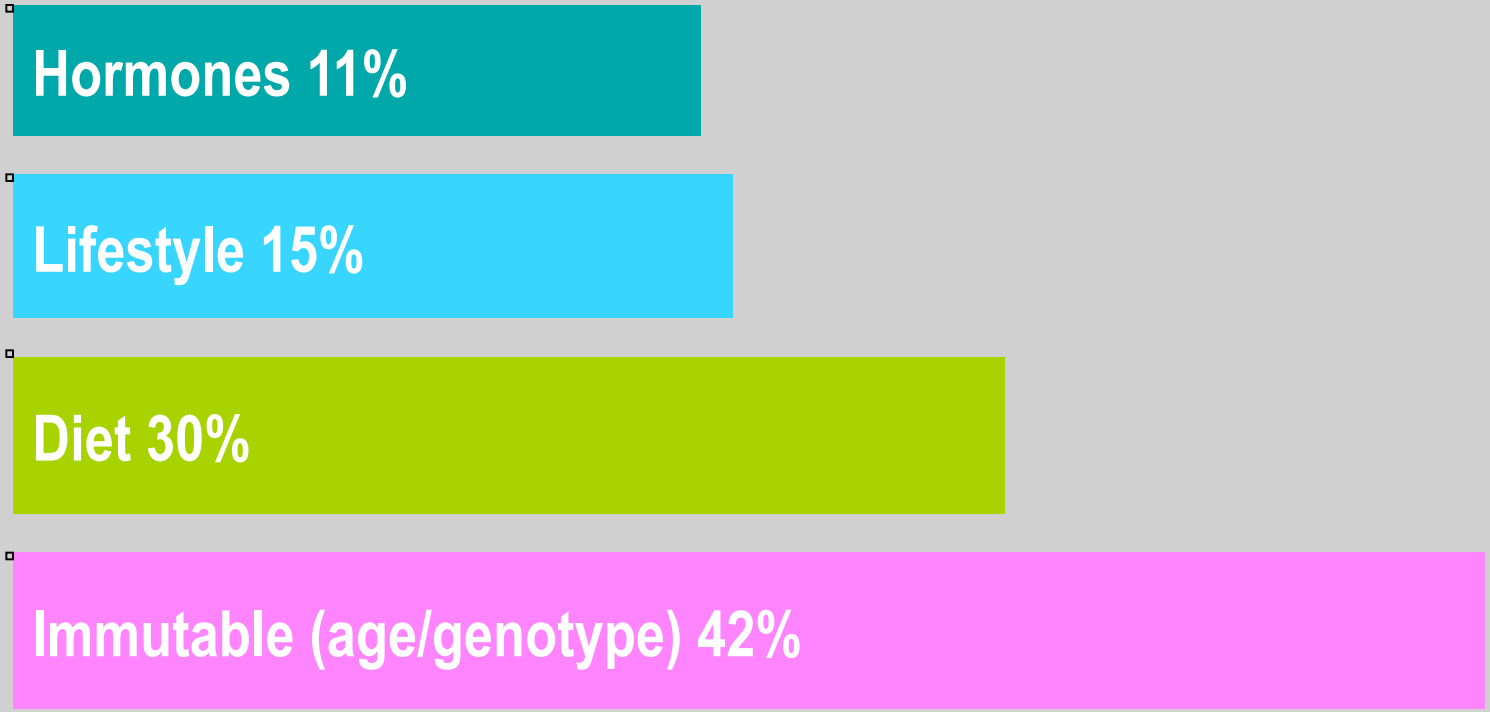
7-10 novembre 2013



Percentage of total known risk factors

Kleinman & McKinlay, 2000

Testosterone Therapy in Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline

Bari,
7-10 novembre 2013

We recommend that clinicians assess prostate cancer risk in men being considered for testosterone therapy. We recommend against testosterone therapy without further urological evaluation in patients with palpable prostate nodule or induration or PSA greater than 4 ng/ml or PSA greater than 3 ng/ml in men at high risk of prostate cancer, such as African-Americans or men with first-degree relatives with prostate cancer. (1|⊕◯◯◯)

We recommend against testosterone therapy in patients with breast (1|⊕◯◯◯) or prostate cancer. (1|⊕⊕◯◯)

Hormonal Predictor of Prostate Cancer: Meta-Analysis

Bari,
7-10 novembre 2013

- Only prospective cohort and case control studies
- 3/31 included
- Men whose total T in highest quartile are 2.34 times more likely to develop prostate cancer

Shaneyfelt et al. 2000, J. Clinical Oncology 18(4):847-853.

25 Studies:
T Levels and Prostate Cancer

Bari,
7-10 novembre 2013

1993 overview of unselected studies comparing testosterone levels in controls and patients with prostate cancer at time of diagnosis

Outcome of study	No. of studies	No. of participants in the studies	
		patients	controls
Total	25	1481	2767
Mean testosterone level higher than in controls	4	343	503
Mean testosterone level same in patients vs controls	15	758	2004
Mean testosterone level lower in patients than control	6	380	260

Slater and Oliver 2000, Drugs & Aging 17(6): 431-439.

Hormones and prostate cancer: a prospective study

Bari,
7-10 novembre 2013

- Massachusetts Male Aging Study

- 1576 men
- Follow-up: 1987–1997
- 70 men diagnosed with prostate cancer
- No association with any hormonal parameter (testosterone, DHT, estradiol)

Testosterone deficiency syndrome: Treatment and cancer risk☆

Jean-Pierre Raynaud

Université Pierre & Marie Curie, 4 Place Jussieu, Paris, France

Journal of Steroid Biochemistry & Molecular Biology 114 (2009) 96–105

Bari,
7-10 novembre 2013

- TDS insorge in età in cui emergono patologie prostatiche benigne e maligne
- Epitelio androgeno dipendente (anche early stage)
- Ruolo del recettore androgenico e di DHT
- Polimorfismo di CAG

- *Thompson , NEJM 349(2003)* : Finasteride riduce del 25% rischio K prostata per riduzione DHT, ma aumenta rischio di K ad alto grado
- *Nishiyama, J Urol 176(2006)* : 47 soggetti, Basso DHT in Prostata aumenta Gleason score
- *Mearini, Urol Int 80 (2008)* : 63 IPB e 65 K prostata; T più alto in IPB; 37% dei K erano TDS
- *McLaren, Br J Urol 102(2008) :* 85 pz; no sintomi durante TRT; 8 mappe e 3 K
- *Gerstenbluth , J Androl 23(6) 2002* : 54 TDS trattati con eT i.m. : aumento n.s. PSA (da 1.8 a 2.8), 1 K
- *Morgentaler, Clin N Am 34(2007)* : Mai dimostrato che TRT comporti progressione di K prostata
- *Rhoden, J Urol 170(2003)* : TRT in PIN non comporta differenze in PSA e rischio K rispetto ai nPIN

Effect of Testosterone Replacement Therapy on Prostate Tissue in Men With Late-Onset Hypogonadism

A Randomized Controlled Trial

Bari,
7-10 novembre 2013

Table 2. Clinical, Hormonal, and Histological Results for Baseline vs 6 Months*

	Testosterone Replacement Therapy (n = 21)			Placebo (n = 19)		
	Baseline	6 mo	*P* Value†	Baseline	6 mo	*P* Value†
Clinical						
International Prostate Symptom Score (voiding symptoms)	13.0 (0-26.0)	12.5 (0-30.0)	.43	11.0 (0-27.0)	9.5 (2.0-28.0)	.50
Uroflowmetry rate, mL/s	14.0 (4.0-31.0)	10.6 (4.8-18.9)	.09	10.6 (7.3-22.7)	8.5 (3.0-20.1)	.13
Prostate volume, mL						
Whole	43.8 (15.5-112.0)	42.0 (19.8-117.9)	.16	36.8 (17.2-105.0)	29.4 (17.8-93.0)	.20
Transition zone	21.8 (4.8-76.5)	15.4 (4.1-74.8)	.58	18.4 (6.44-54.0)	16.0 (6.9-55.2)	.47
Prostate-specific antigen, ng/mL						
Total	1.55 (0.30-5.80)	2.29 (0.40-7.10)	<.001	0.97 (0.10-2.50)	1.10 (0.02-6.90)	.006
Free	0.49 (0.20-1.60)	0.68 (0.20-2.13)	<.001	0.21 (0.04-0.66)	0.30 (0.01-5.47)	.13
Hemoglobin, g/dL	14.5 (11.0-18.0)	15.9 (12.1-20.4)	<.001	14.9 (12.6-16.1)	14.8 (12.8-16.0)	.30
Hematocrit, %	43.2 (35.2-50.5)	47.6 (38.8-57.4)	<.001	43.6 (37.4-48.2)	43.4 (37.8-47.6)	.20
Hormonal						
Testosterone						
Total, ng/dL	282 (182-444)	640 (272-1190)	<.001	282 (135-391)	273 (89-715)	.11
Free, pg/mL‡	48 (17-102)	162 (35-309)	<.001	51 (16-66)	42 (8-114)	.16
Dihydrotestosterone, ng/dL	28 (18-56)	47 (20-121)	.002	28 (11-52)	26 (7-40)	.20
Estradiol, pg/mL	22 (6-41)	37 (18-95)	.006	15 (12-36)	17 (10-19)	.67
Luteinizing hormone, IU/L	4.50 (1.10-16.00)	0.10 (0.03-13.00)	<.001	4.80 (1.80-32.00)	4.10 (1.20-40.00)	.79
Sex hormone-binding globulin, µg/dL	0.6 (0.2-2.0)	0.6 (0.1-1.2)	.005	0.7 (0.1-1.3)	0.8 (0.2-1.7)	.82
Testosterone tissue, ng/g	0.91 (0.15-16.46)	1.55 (0.10-23.11)	.29	2.00 (0.11-6.92)	0.88 (0.02-20.12)	.05
Dihydrotestosterone tissue, ng/g	6.79 (3.26-19.59)	6.82 (1.57-39.82)	.51	8.15 (1.21-18.70)	5.10 (0.70-22.37)	.01
Histological						
Carcinoma, No.	0	2		0	4	
High-grade intraepithelial neoplasia, No.	5	2		3	3	
Atrophy score, % of glands	8 (1-50)	1 (1-25)	.01	8 (1-75)	6 (1-75)	.23
Stroma-epithelial ratio	2.06 (0.86-3.80)	2.47 (0.54-5.54)	.69	2.18 (0.50-4.98)	2.65 (0.11-7.95)	.21
Biomarkers						
MIB1 (Ki-67), % of positive cells	0.53 (0.27-1.34)	0.63 (0.33-1.38)	.09	0.45 (0.23-0.86)	0.49 (0.29-1.52)	.70
Androgen receptor, % of positive cells						
Epithelium	80 (50-90)	80 (55-90)	.75	80 (60-90)	85 (65-90)	.18
Stroma	16 (5-60)	33 (8-75)	.02	24 (8-70)	48 (13-60)	.09
CD34, microvessel/200 × field	63.0 (25.0-97.5)	66.0 (48.5-89.0)	.37	65.5 (42.0-90.0)	71.5 (36.0-90.5)	.89

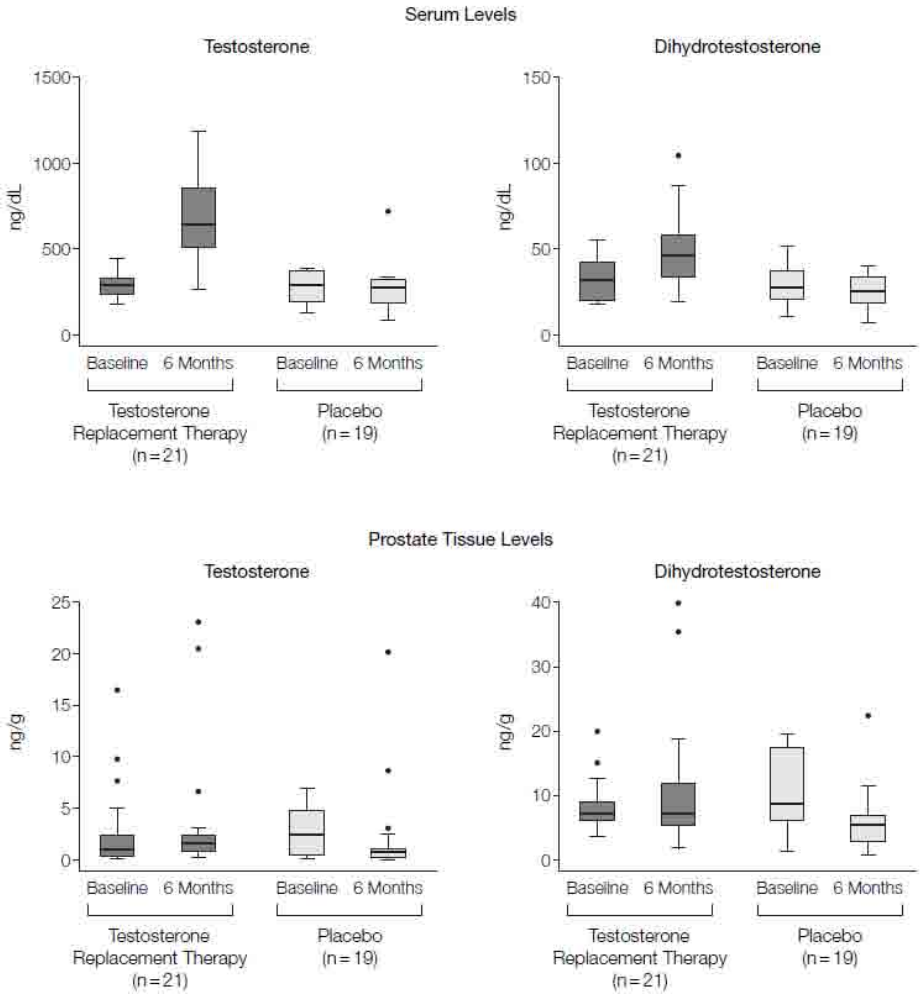
SI conversion factors: To convert estradiol to pmol/L, multiply by 3.671; total testosterone to nmol, multiply by 0.0347.
*Values are expressed as median (range) unless otherwise indicated. Of the 44 men randomized, 3 did not complete the trial and a fourth was excluded because baseline serum testosterone was higher than 700 ng/dL, indicating an error in screening.
†Calculated using the signed rank test.
‡Normal value for adult males is 52 to 280 pg/mL. Free testosterone at baseline was less than 70 pg/mL in 90% of participants.

Effect of Testosterone Replacement Therapy on Prostate Tissue in Men With Late-Onset Hypogonadism

A Randomized Controlled Trial

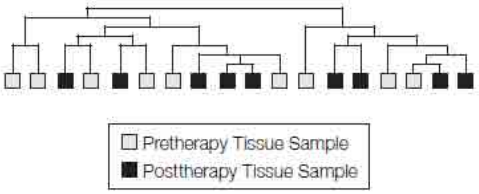
Bari,
7-10 novembre 2013

Figure 2. Effects of Treatment on Serum and Prostatic Androgen Levels



Both testosterone and dihydrotestosterone levels increased in serum after 6 months of treatment with testosterone replacement therapy ($P<.001$ by signed rank test). However, despite an increase in serum levels for testosterone to the mid-normal range, prostate tissue levels of the androgens did not change significantly. Boxes contain 50% of data with the inside horizontal line representing the median value; whiskers contain 100% of data, except for statistical outliers shown as individual data points.

Figure 4. Gene Expression Cluster Analysis of Prostate Tissue Before and After Testosterone Replacement



The relationships of prostate tissue samples obtained at baseline and 6 months from men undergoing active treatment are grouped based on unsupervised hierarchical clustering of the 500 most-variably expressed genes (see "Methods" section for explanation of horizontal and vertical distances). Individuals included were those who at 6 months exhibited the greatest increase in tissue androgens. Testosterone replacement therapy did not cause sufficient alterations in gene expression to cluster samples based on pretreatment vs posttreatment.

TRT per 6 mesi :
- non si accumula a livello prostatico,
- non produce incremento significativo di DHT
- Non causa mutazioni biologiche ghiandolari

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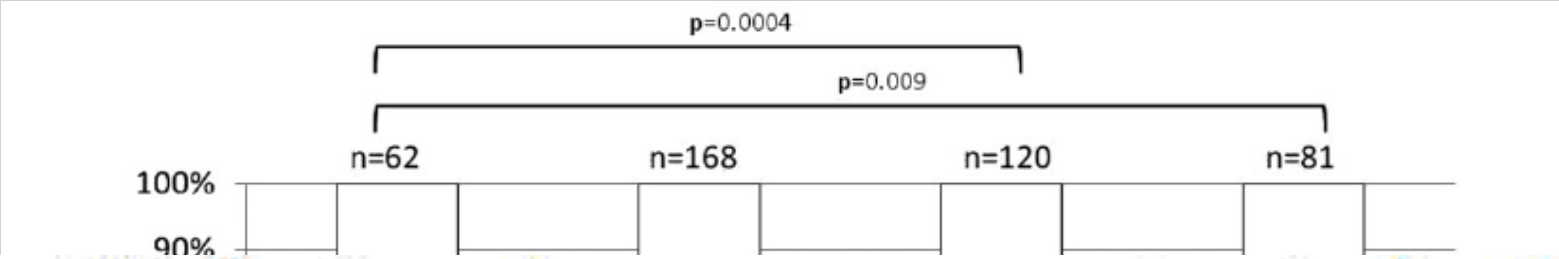
High Incidence of Predominant Gleason Pattern 4 Localized Prostate Cancer is Associated With Low Serum Testosterone

Henry Botto,* Yann Neuzillet, Thierry Lebret, Philippe Camparo, Vincent Molinie and Jean-Pierre Raynaud



While these data are provocative, it should still be emphasized that the standard of care for prostate cancer screening should be followed in age-appropriate men with ADAM. In addition, hypogonadal men with prostate cancer should only be treated with testosterone in conjunction with careful counseling and ongoing monitoring.

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Androgen Administration to Hypogonadal Men with PIN

Bari,
7-10 novembre 2013

- 75 men, 59.6 years, all biopsied before Rx
  - 55 PIN negative, 20 PIN positive
  - No difference in PSA changes after 1 year
  - Repeat Bx if DRE abnl or PSA up 1 ng/mL
  - Cancer in 1/2 PIN pos, 0/4 PIN neg
  - T therapy safe even in high risk group

Morgentaler et al. 2003, J. Urol. 170(6):2348-51.

Prostate safety of ageing men receiving testosterone

Bari,
7-10 novembre 2013

- Factors determining transition of carcinoma *in situ* to clinical carcinoma not known
- A priori likelihood that androgens are one of the factors is not large but cannot be excluded either
- A clinical intervention trial with administration of T to ageing men would require inclusion of more than 6000 men

- **Impossible !!**

Could Testosterone Have a Therapeutic Role in Prostate Cancer?

- Fosfatidilinositolo 3 Kinasi (PI-3) controlla sopravvivenza cellulare, trasformazione maligna ed invasività
- Regolata da FAK (Focal adhesion kinase) e da Cdc42/Rac1
- FAK elevato in malattia metastatica
- Cdc42/Rac1 aumentato da complesso T/Alb.
- Cdc42/Rac1 inibisce migrazione cellulare ed invasività

TRT : benefici e rischi

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- Benefici:
  - Osteoporosi
  - Massa muscolare
  - Massa grassa
  - Sessualità
  - Cognitività
  - Depressione
  - Anemia

- Rischi:
  - Profilo lipidico
  - Alterazioni cardiovascolari
  - Alterazioni ematologiche
  - Tossicità epatica
  - Disturbi del sonno (Sleep apnea)
  - Cambiamenti del comportamento
  - Sicurezza prostatica

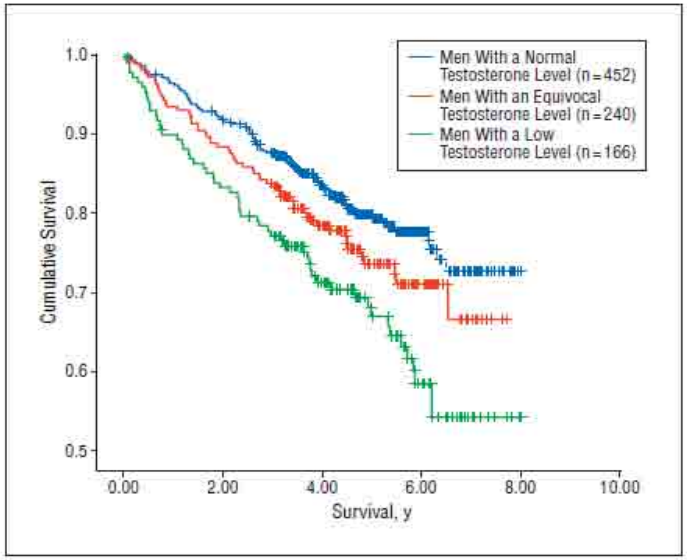
Low Serum Testosterone and Mortality in Male Veterans

Molly M. Shores, MD; Alvin M. Matsumoto, MD; Kevin L. Sloan, MD; Daniel R. Kivlahan, PhD

Bari,
7-10 novembre 2013

Table 1. Baseline Characteristics of Men With Low, Equivocal, and Normal Testosterone Levels*

Characteristic	Men With a Normal Testosterone Level (n = 452)	Men With an Equivocal Testosterone Level (n = 240)	Men With a Low Testosterone Level (n = 166)	*P* Value†
Age, y‡	60.5 (10.9)	61.4 (10.9)	63.6 (11.3)	.007§
Body mass index‡‖	28.4 (5.1)	29.9 (6.3)	30.0 (6.9)	<.001§¶
Medical morbidity‡#	4.7 (2.9)	4.9 (3.2)	5.1 (3.0)	.28
No. of testosterone measurements‡	2.05 (0.22)	2.00 (0.06)	2.07 (0.26)	.001¶**
Testosterone level, ng/dL‡				
Total	520 (270)	400 (440)	190 (150)	<.001§¶**
Free	1.33 (0.55)	0.92 (0.54)	0.46 (0.20)	<.001§¶**
White race	328 (72.6)	198 (82.5)	128 (77.1)	.01
Married	250 (55.3)	138 (57.5)	90 (54.2)	.78
Diabetes mellitus	94 (20.8)	57 (23.8)	52 (31.3)	.01
COPD	100 (22.1)	61 (25.4)	47 (28.3)	.25
HIV	5 (1.1)	2 (0.8)	1 (0.6)	.83
Hyperlipidemia	93 (20.6)	43 (17.9)	33 (19.9)	.70
CAD	92 (20.4)	50 (20.8)	36 (21.7)	.94
Prescription				
Narcotic	168 (37.2)	96 (40.0)	70 (42.2)	.49
Glucocorticoid	70 (15.5)	38 (15.8)	31 (18.7)	.62



Accesso alle cure

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T Propionato i.m.
T Enantato i.m.
T Undecanoato os

T Gel
T Patch
T Gengivale
T Undecanoato i.m.

Nota 36

testosterone	*La prescrizione a carico del SSN, su diagnosi e piano terapeutico di strutture specialistiche, secondo modalità adottate dalle Regioni e dalle Province autonome di Trento e Bolzano, è limitata alle seguenti condizioni:* -ipogonadismi maschili primitivi e secondari caratterizzati da ridotte concentrazioni di testosterone totale (< 12 nmoli/L o 350 ng/dL) in presenza di sintomi tipici (riduzione del desiderio e potenza sessuale, osteoporosi, riduzione forza muscolare, obesità viscerale, alterazioni del tono dell'umore)

Conclusioni

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- Usare solo dosaggio di TT
- No screening di massa
- TRT sicuramente utile nel modificare rapporto massa magra/massa grassa
- Non evidenze per il trattamento di DM2, ma considerare altri sintomi specifici
- Pur se sembra «safe», TRT controindicato se PSA elevato o K prostata manifesto
- Comunque attenzione e stretto monitoraggio clinico e bioumorale
- No evidenza TRT utile in Parkinson
- Terapia comunque da individualizzare e discutere con pz.

Quasi…. Finito!!!

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