

Male hypogonadism therapy: when gonadotropins and when testosterone

VA GIAGULLI MD,PhD

*Outpatient Clinic for Endocrinology and Metabolic
Diseases*

Conversano Hospital ASL BA

LEAD-IN

- **How could one define male hypogonadism ?**
- **How, when and why one should treat with Testosterone**
- **How, when and why one should treat with Gonadotropin**
- **Does the therapeutic appropriateness match the reimbursement for T and Gn in our health system?**

How one can define male hypogonadism

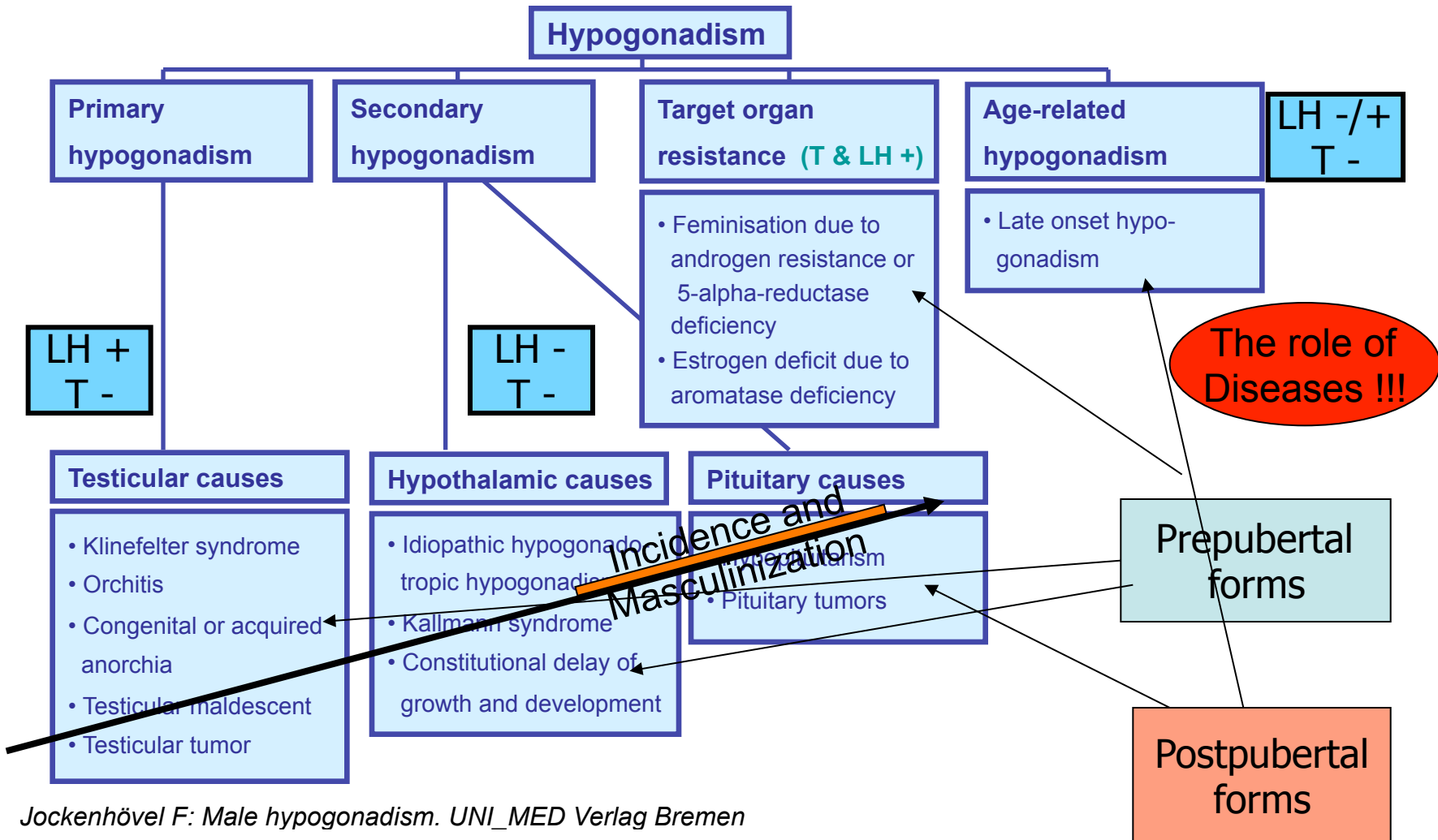
Definizione di ipogonadismo

- *L'ipogonadismo maschile è una **sindrome clinica** provocata dall'**incapacità dei testicoli di produrre una quantità fisiologica di testosterone** (deficit di ormone androgeno) e un numero normale di spermatozoi dovuta all'interruzione in uno o più livelli del funzionamento dell'asse ipotalamo-ipofisi-gonadi*
- **Linee guida per la pratica clinica della Endocrine Society (2010)**

• *L'ipogonadismo nel maschio adulto (LOH, Late Onset Hypogonadism anche noto come TDS, **sindrome da deficit di testosterone**) è una **sindrome clinica e biochimica**, caratterizzata quindi da **sintomi e ridotti livelli sierici di testosterone** (al di sotto del range riferimento nei maschi giovani sani)*

Raccomandazioni da: ISA, ISSAM, EAU, EAA, e ASA (2009)

Male hypogonadism - classification



Co-morbidity prevalence with low serum T levels in adult end elderly men

(Mulligan T et al, Int J Clin Prac, 2006)

	AACE, 2002 TT<7 nmol/L	ISA, ISSAM, EAU, EAA and ASA TT<8 nmol/L and FT<225 pmol/L		EMAS TT<11nmol/L and FT<220 pmol/L	
	<ul style="list-style-type: none"> • Low libido • Erectile dysfunction 	<ul style="list-style-type: none"> • Low libido • Erectile dysfunction 		<ul style="list-style-type: none"> • Low libido • Erectile dysfunction 	
	<ul style="list-style-type: none"> • Decreased muscle mass • Menopausal-type hot flushes (with acute onset of hypogonadism) • Slow growth of body hair • Poor ability to concentrate • Oligospermia and azoospermia 	<ul style="list-style-type: none"> • Decreased muscle mass and strength • Increased body fat • Decreased body mineral density and osteoporosis • Decreased vitality • Depressed mood 		<ul style="list-style-type: none"> • Decreased frequency of morning erection 	
<i>Condition</i>					<i>% CI</i>
Hypertension			0.342	43.5 (36.8–50.3)	1.40 (1.04–1.86)
Hyperlipidemia			0.013	41.3 (36.4–46.2)	1.29 (1.03–1.62)
Diabetes			0.405	38.8 (33.7–44.0)	1.13 (0.89–1.44)
Obesity			0.101	32.1 (25.3–38.8)	0.81 (0.58–1.11)
Prostatic disease/disorder			0.195		
Chronic pain			nr		
Insomnia/sleep disturbance	129 (15.4)	185 (14.0)	0.342	43.5 (36.8–50.3)	1.40 (1.04–1.86)
Asthma/COPD	102 (12.2)	118 (8.9)	0.013	41.3 (36.4–46.2)	1.29 (1.03–1.62)
Headaches (within the last 2 weeks)	70 (8.4)	125 (9.4)	0.405	38.8 (33.7–44.0)	1.13 (0.89–1.44)
Rheumatoid arthritis	28 (3.3)	29 (2.2)	0.101	32.1 (25.3–38.8)	0.81 (0.58–1.11)
Osteoporosis	15 (1.8)	15 (1.1)	0.195		
Not reported	0 (0.0)	4 (0.3)	nr		

CI, confidence interval; COPD, chronic obstructive pulmonary disease.

Clinical features

**How, when and why one should
treat with Testosterone and/or
Gonadotrophins or others drugs**

**Straight frontal
hairline**

**Hypotrophic
musculatuera**

**Reduction of pubic and
Body hair**

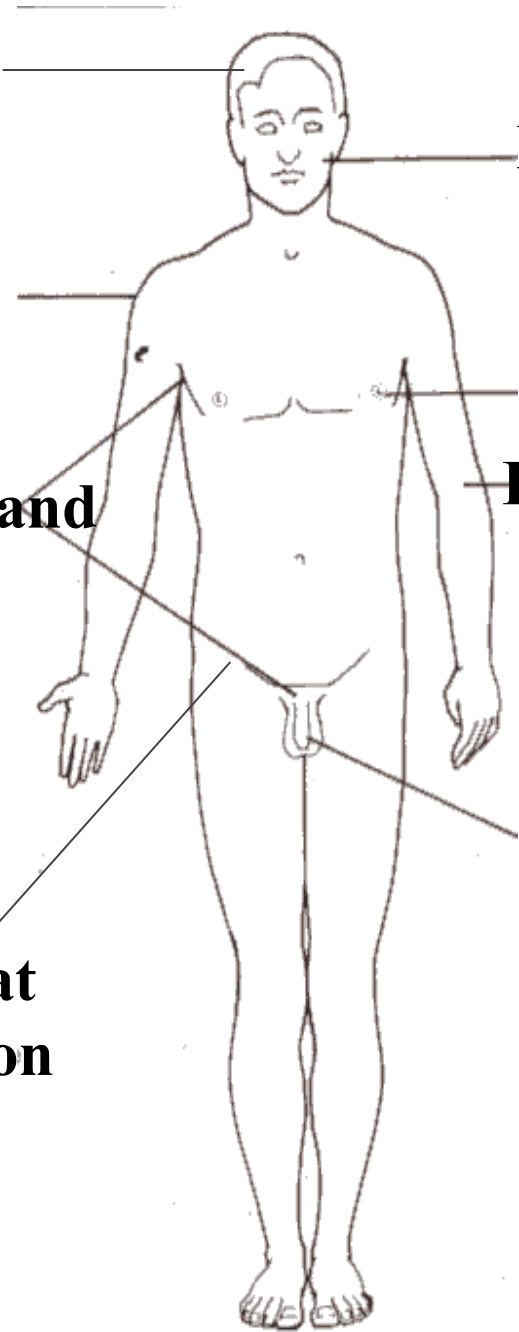
**Female fat
distribution**

**Diminution of
Beard growth**

Gynecomastia

**Eunucoid tall
stature**

**Reduction of
Testicular size**



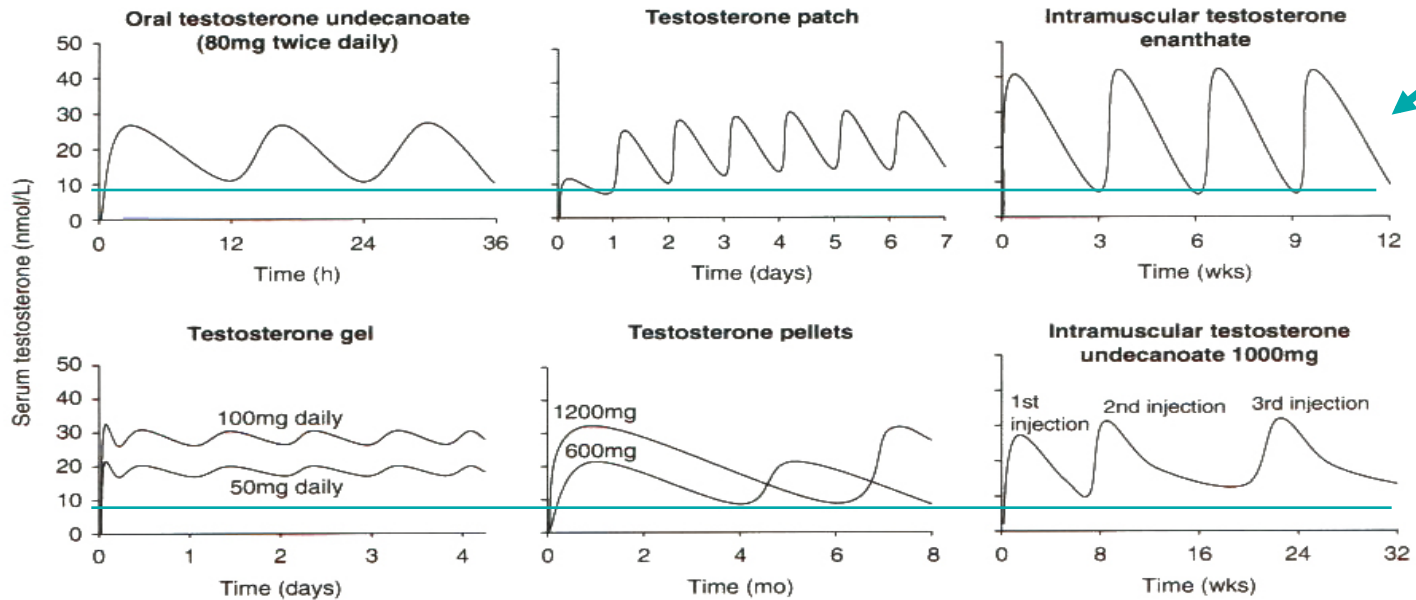
REPLACEMENT TESTOSTERONE THERAPY (TRT):GENERAL CONSIDERATIONS

Current Testosterone Formulations on Market

	Generic name	Commercial name	Doses
INJECTABLE	<i>Testosterone propionate</i>	Testovis®	100 mg every 2-4 weeks
	<i>Testosterone enantate</i>	Testoviron® Dep.	200-400 mg every 2-4 weeks
	<i>Testosterone undecanoate</i>	Nebid®	1000 mg every 10-14 weeks
ORAL	<i>Testosterone undecanoate</i>	Andriol® (N 36)	120-240 mg /day
TRANS-DERMAL	<i>Testosterone patch</i>	Androderm®	2.5-5 mg/day
		Testopatch®	1.8-2.4 mg/day
	<i>Testosterone gel</i>	Testogel® Androgel® Testim®	50-100 mg/day
		Tostrex®	60-80 mg/day
BUCCAL	<i>Buccal Testosterone</i>	Striant®	30 mg 2 times a day

Testosterone Pellets ???

Serum T in different forms of T application



Properties of Different T preparations

	T over 24h	Dose Flexibility
Injectable T esters	-	-
Oral TU	±	+
Scrotal T patch	+	-
Nonscrotal T patch	+	-
T gel	+	+
T implants	+	±
Injectable TU	+	-

DHT = 5 α -dehydrotestosterone; E₂ = 17 β -estradiol; TU = testosterone undecanoate; + indicates favourable; ± indicates reasonable; - indicates faulty.

To date, there has been a few evidence about Patients Satisfaction with TRT in Literature, however.

TRT outcomes

TRT Main outcomes in hypogonadism male

(Bhasin S et al JCEM, 2010; Buvat J et al J Sex Med, 2012)



- 1) Pubertal development and sex characteristics induction
- 2) Maintain normal androgenization and sexual activity
- 3) Prevent co-morbidities (obesity, diabetes mellitus, osteoporosis, etc)
- 4) The target T levels should be around 4 to 7 ng/ml as in most adult men (40-50 yrs), while in older ones, T levels above the mid-range (> 4 ng/ml) of young adult men should be avoided.

Puberty induction

Schema terapeutico con T per l' induzione della pubertà

Induction of puberty in boys using testosterone esters
Increasing dose schedule every 6 months:
25 mg/m² per 2 weeks i.m.

However, there have been no guidelines in
Literature until now !

**Main warning: growth velocity, while testis
size remains stable.**

Delmarre et al, 2008

The Role of Long-Acting Parenteral Testosterone Undecanoate Compound in the Induction of Secondary Sexual Characteristics in Males with Hypogonadotropic Hypogonadism

Vito A. Giagulli, MD, PhD,^{*†} Vincenzo Triggiani, MD,^{*} Maria D. Carbone, MD,^{††} Giovanni Corona, MD, PhD,[§] Emilio Tafaro, MD,^{*} Brunella Licchelli, MD,^{*} and Edoardo Guastamacchia, MD^{*}

^{*}Endocrinology and Metabolic Diseases, University of Bari "Aldo Moro," Bari, Italy; [†]Biomedical Research Association "Guglielmo Telesforo," Foggia, Italy; ^{††}Institute of Clinical and Hormonal Research, Foggia, Italy; [§]Sexual Medicine and Andrology Unit, Department of Clinical Physiopathology, University of Florence and Endocrinology Unit, Medical Department, Azienda Usl, Maggiore-Bellaria Hospital, Bologna, Italy

Table 1 Clinical characteristics, hormonal levels, and number of CAG repeats of patients and controls

Groups	Diagnosis	Case no.	Age (years)	BMI (kg/m ²)	Testis (volume)	Penis length (cm)	CAG no.	FSH (IU/L)	LH (IU/L)	T (ng/dL)	SHBG (nm/L)	FT (ng/dL)	BioT (ng/dL)
CG	Normospermic men	15	19.5 ± 1.0	23.9 ± 1.1	22.3 ± 1.5	12.7 ± 2.0	19.8 ± 1.0	6.6 ± 2.5	7.5 ± 2.5	645.5 ± 79.5	41.8 ± 3.8	12.5 ± 1.9	275 ± 61
HHG	Idiopathic	1	18	23	4	4.5	19	1.5	1.0	120	60	1.49	35.1
	Idiopathic	2	17	24	4	4.5	25	1.8	1.2	100	59	1.25	29.3
	Idiopathic	3	17	26	6	5.5	21	0.9	1.7	130	56	1.71	40.2
	Idiopathic	4	17	23	6	4.8	20	1.6	1.1	89	53	1.21	28.4
	Idiopathic	5	19	24	4	3.8	27	2.1	0.9	92	49	1.31	31.1
	Idiopathic	6	17	25	4	4.8	22	1.8	0.9	132	50	1.88	44.1
	Intermediate BT	7	20	24	8	3.5	25	2.2	1.5	141	54	1.91	44.9
	Major BT	8	21	25	6	4.5	20	2.4	1.1	180	59	2.31	54.1
	Major BT	9	20	24	10	5.8	18	1.50	1.2	160	52	2.23	53.4
			18.50 ± 1.50	24.22 ± 1.31	5.78 ± 2.71**	4.7 ± 0.7**	21.89 ± 2.92	1.78 ± 0.43**	1.19 ± 0.27**	127.2 ± 29.2**	53.7 ± 3.8**	1.7 ± 0.39**	40.01 ± 9.27**

P* < 0.01; *P* < 0.001 (Mann-Whitney *U*-test).

BT - β-thalassemia; BioT - biologically active testosterone; BMI - body mass index; CAG - cytosine-adenine-guanine; CG - control group; FSH - follicle-stimulating hormone; FT - testosterone-free fraction; HHG - hypogonadotropic hypogonadic group; LH - luteinizing hormone; SHBG - sex hormone binding globulin; T - total testosterone.

Table 2 Height, centile, and midparent target height in hypogonadal subjects in basal condition and after 1 and 2 years of parenteral testosterone undecanoate therapy

Diagnosis	Case no. (age [years])	Basal height (cm)	Centile	Height (cm) at 1 year	Centile	Height (cm) at 2 years	Centile	MPTH (cm)
Idiopathic	1 (18)	168.5	20	172	35	174	50	170
Idiopathic	2 (17)	170	25	174	50	176.5	60	172
Idiopathic	3 (17)	173	50	177	75	180	80	182
Idiopathic	4 (17)	170.5	25	174	50	177	60	169
Idiopathic	5 (19)	174	50	178.5	75	182	80	183
Idiopathic	6 (17)	177	70	181.5	80	183	85	185
Intermediate β -thalassemia	7 (20)	168	20	169.5	<50	171	<50	174
Major β -thalassemia	8 (21)	166	10	168	<50	169.5	<50	172
Major β -thalassemia	9 (20)	166.5	10	168	<50	169	<50	174

Calculated centile according to Italian cross-sectional growth charts.

MPTH = Midparental target height.

Body composition, metabolic and cardiovascular diseases

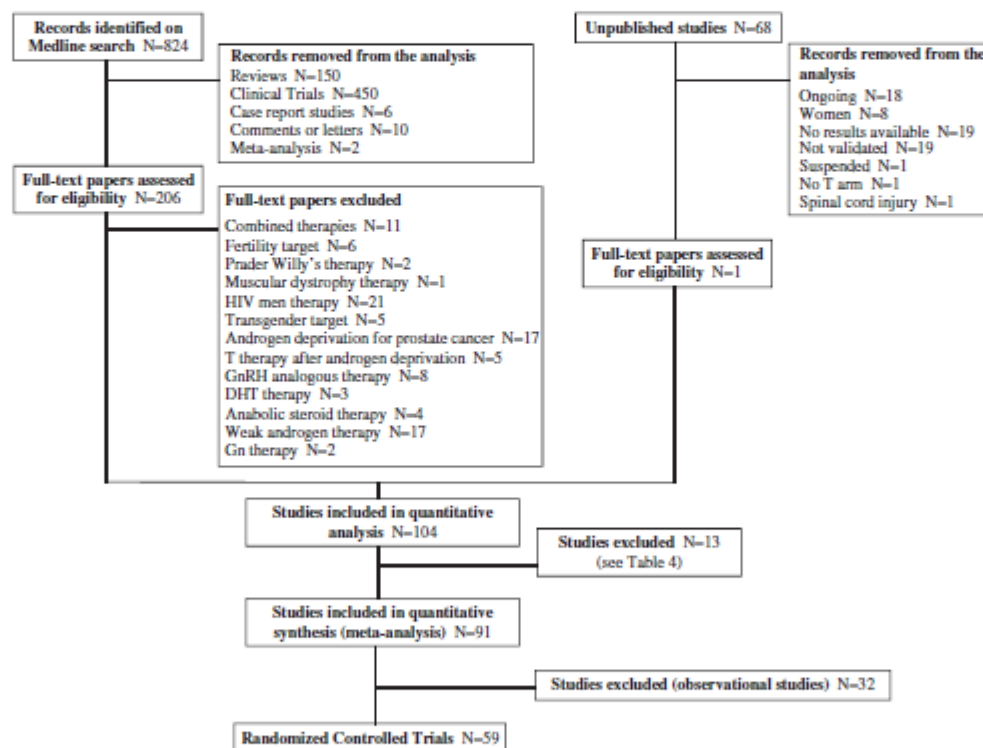
THERAPY OF ENDOCRINE DISEASE

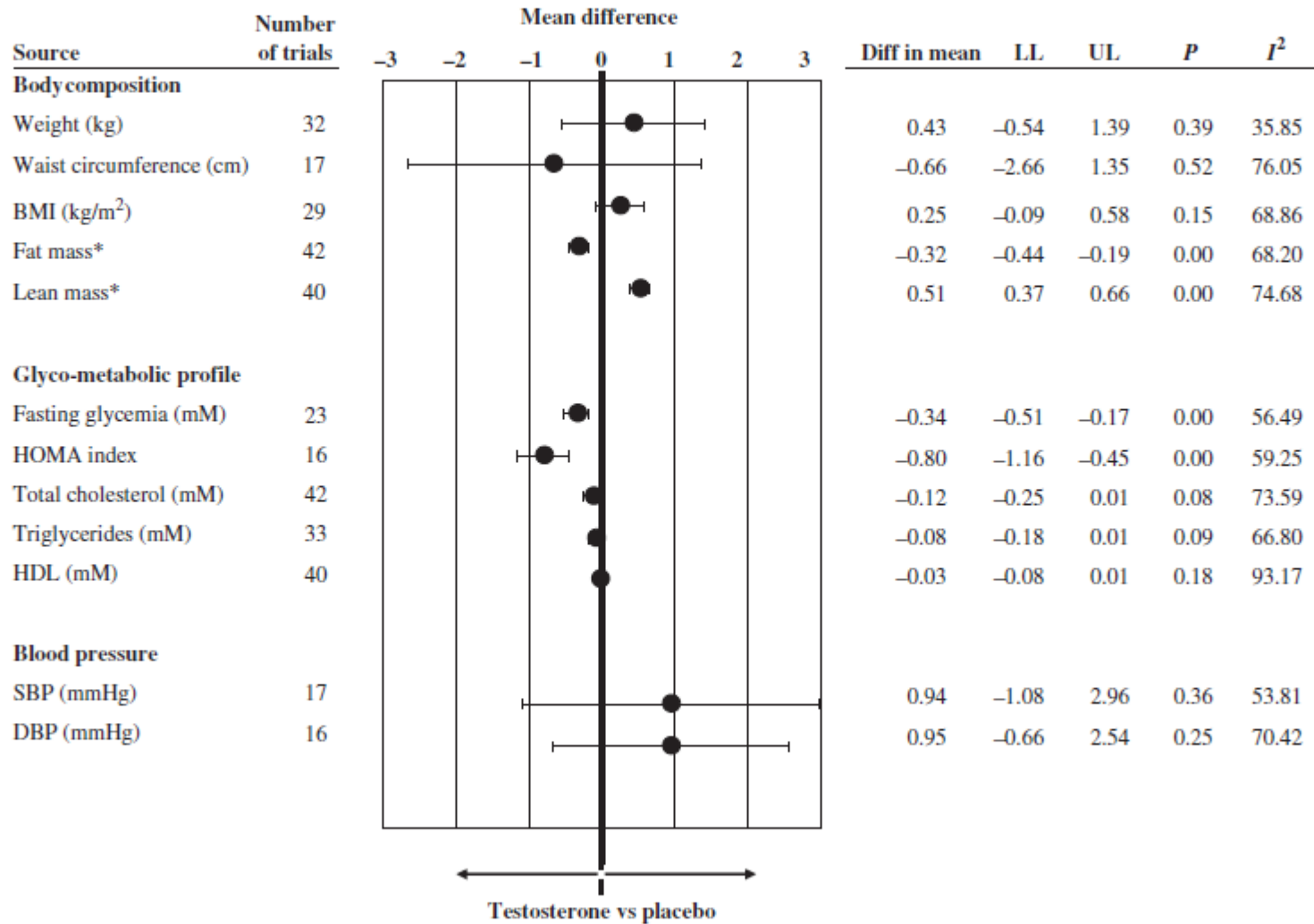
Testosterone supplementation and body composition: results from a meta-analysis study

Giovanni Corona, Vito A Giagulli¹, Elisa Maseroli², Linda Vignozzi², Antonio Aversa³, Michael Zitzmann⁴, Farid Saad^{5,6}, Edoardo Mannucci⁷ and Mario Maggi²

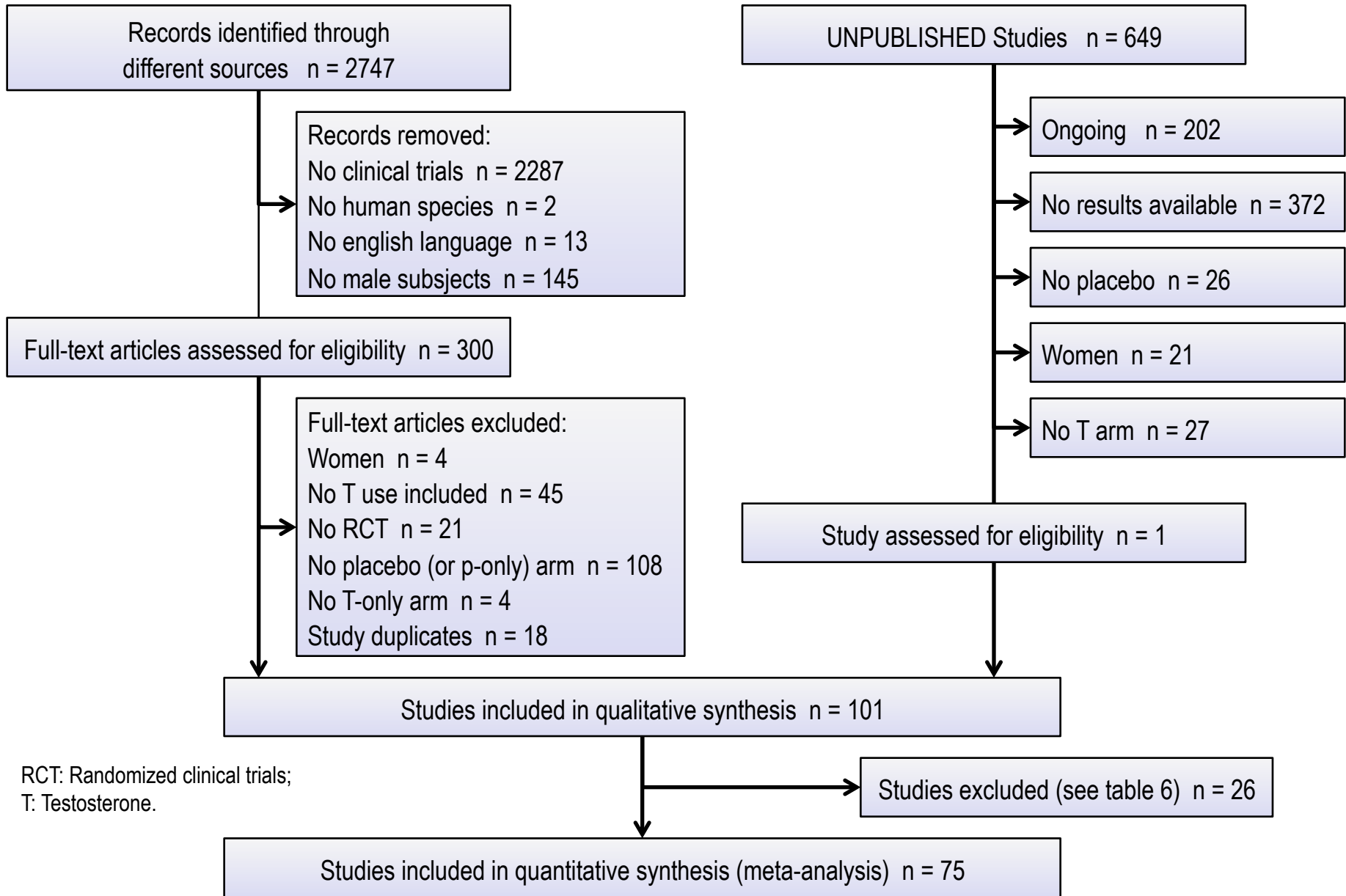
Endocrinology Unit, Medical Department, Azienda Usl Bologna Maggiore-Bellaria Hospital, Bologna, Italy, ¹Unit of Metabolic Diseases and Endocrinology, Conversano, Italy, ²Andrology and Sexual Medicine Unit, Department of Experimental and Clinical Biomedical Sciences, University of Florence, Viale Pieraccini 6, 50139 Florence, Italy, ³Department of Experimental Medicine, Sapienza University of Rome, Rome, Italy, ⁴Centre for Reproductive Medicine and Andrology, Muenster, Germany, ⁵Bayer Pharma, Global Medical Affairs Andrology, Berlin, Germany, ⁶School of Medicine, Gulf Medical University, Ajman, United Arab Emirates and ⁷Diabetes Agency, Careggi Hospital, Florence, Italy

Correspondence should be addressed to M Maggi
Email
m.maggi@dfc.unifi.it



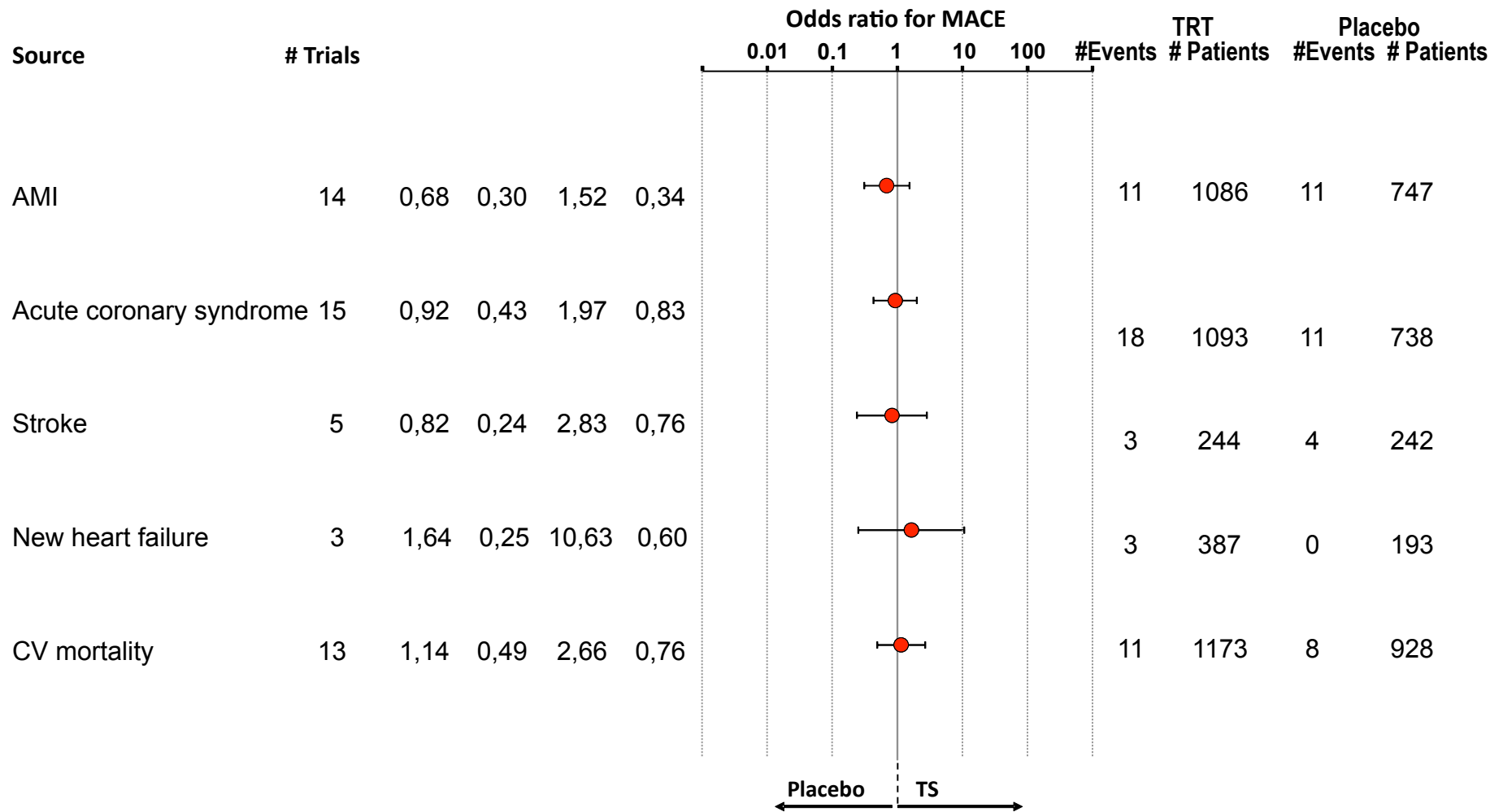


Trial Flow Diagram



RCT: Randomized clinical trials;
T: Testosterone.

Odds Ratio for Acute Myocardial Infarction (AMI), Acute Coronary Syndrome, Stroke, Heart Failure, and Cardiovascular (CV) Mortality in Subjects Treated with Testosterone or Placebo



LL: Lower limit; MACE: Major adverse cardiovascular events; MH-OR: Mantel-Haenszel odds ratio; UL: Upper limit

Sexual Dysfunction and TRT in Hypogonadal men

Testosterone Supplementation and Sexual Function: A Meta-Analysis Study

Giovanni Corona, MD,* Andrea M. Isidori, MD,[†] Jaques Buvat, MD,[‡] Antonio Aversa, MD,[†] Giulia Rastrelli, MD,[§] Geoff Hackett, MD,[¶] Vincenzo Rochira, MD,^{**} Alessandra Sforza, MD,* Andrea Lenzi, MD,[†] Edoardo Mannucci, MD,^{††} and Mario Maggi, MD[§]

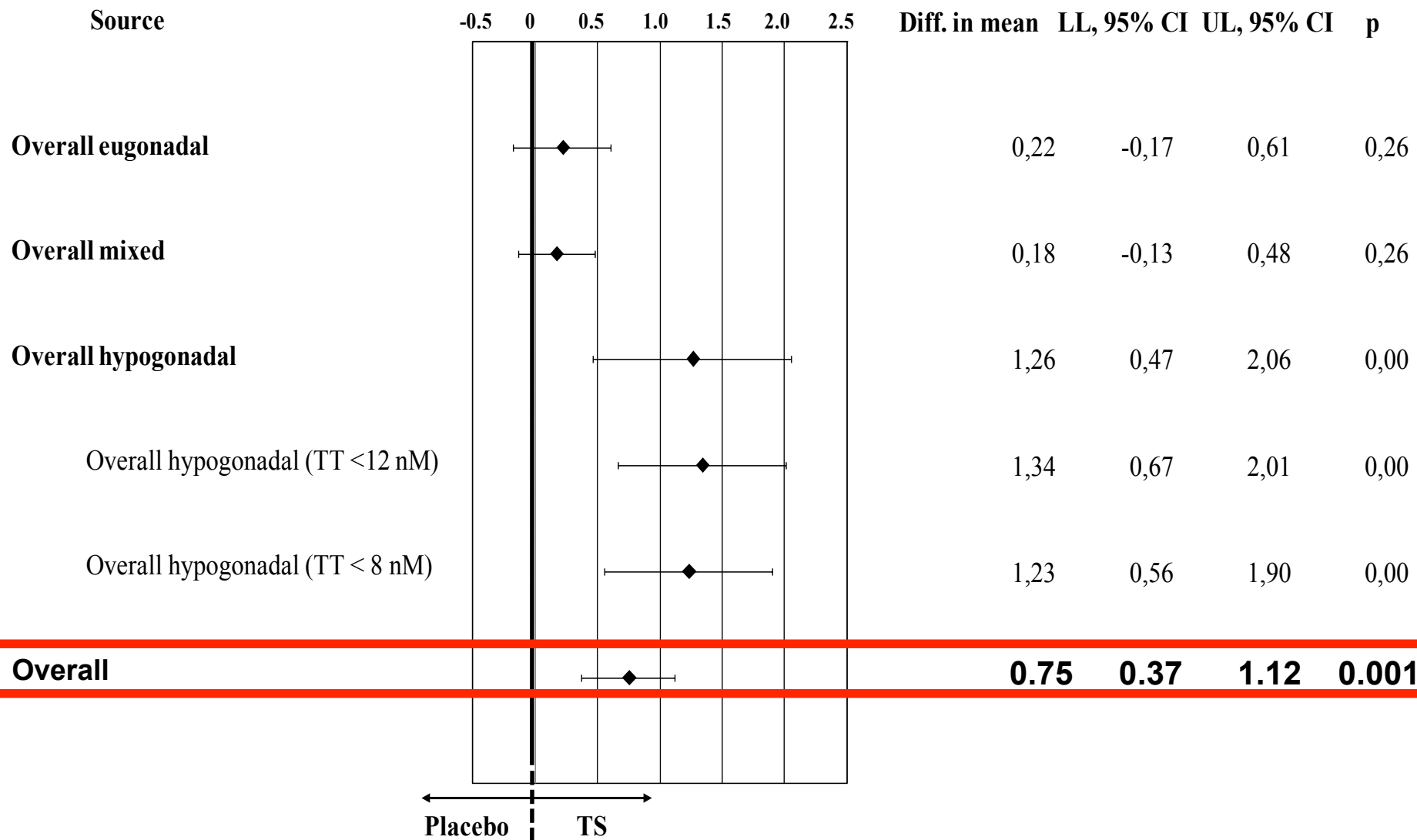
*Endocrinology Unit, Medical Department, Azienda USL Bologna, Maggiore-Bellaria Hospital, Bologna, Italy; [†]Department of Experimental Medicine, Sapienza University of Rome, Rome, Italy; [‡]Centre ETPARP, Lille, France; [§]Sexual Medicine and Andrology Unit, Department of Biomedical, Clinical and Experimental Sciences, University of Florence, Florence, Italy; [¶]Good Hope Hospital, Sutton Coldfield, UK; ^{**}Chair of Endocrinology, Department of Biochemical, Metabolic and Neural Sciences, University of Modena & Reggio Emilia & Azienda USL of Modena, Italy; ^{††}Diabetes Agency, Careggi Hospital, Florence, Italy

f



Effect size (with 95%CI) of testosterone supplementation (TS) vs placebo on erectile function component (including only sexual-related erections)

Sexual-related erectile function component standardized mean differences



**TRT in hypogonadal diabetic
male**

ORIGINAL ARTICLE

Correspondence:

Vito A. Giagulli, Outpatient Clinic for Endocrinology and Metabolic Diseases, Conversano Hospital, ASL Bari, Via De Amicis, 70014 Conversano, Italy.
E-mail vitogiagulli@alice.it

Keywords:

erectile dysfunction, glucagon-like peptide-1 agonist, hypogonadism, obesity, testosterone replacement therapy, type 2 diabetes mellitus

Received: 24-Jan-2015

Revised: 18-Jul-2015

Adding liraglutide to lifestyle changes, metformin and testosterone therapy boosts erectile function in diabetic obese men with overt hypogonadism

^{1,2}V. A. Giagulli, ³M. D. Carbone, ¹M. I. Ramunni, ²B. Licchelli, ⁴G. De Pergola, ⁵C. Sabbà, ²E. Guastamacchia and ²V. Triggiani

Prepubertal onset hypogonadism men with obesity and T2DM

G2 N (n = 10)	T1	T2	p1 (p)	T3	p2 (p)
Age (years)	50.0 ± 4.7	–	–	–	–
Duration of diabetes (years)	3.2 ± 0.8	–	–	–	–
Height (cm)	172.9 ± 2.5	–	–	–	–
Weight (kg)	105.3 ± 9.8	102.5 ± 7.1	<0.05	98.0 ± 8.3	<0.01
BMI (kg/m ²)	34.8 ± 2.6	33.5 ± 2.0	<0.05	32.5 ± 2.3	<0.05
WC (cm)	106.8 ± 11.0	104.5 ± 9.9	<0.05	99.2 ± 9.8	<0.001
SBP (mmHg)	151.5 ± 8.8	147.5 ± 8.3	<0.05	142.0 ± 8.6	<0.01
DBP (mmHg)	89.5 ± 4.4	87.7 ± 2.6	<0.06	85.9 ± 4.1	<0.05
Gly (mg/dL)	211.4 ± 25.7	169.9 ± 15.3	<0.01	133.9 ± 12.8	<0.01
HbA1c (%)	8.8 ± 0.8	8.2 ± 0.3	<0.04	7.4 ± 0.6	<0.01
TC (mg/dL)	189.9 ± 12.4	176.5 ± 25.7	<0.01	175.8 ± 19.0	<0.15
TG (mg/dL)	319.1 ± 152.7	270.3 ± 104.9	<0.01	226.0 ± 48.7	<0.001
HDL (mg/dL)	35.7 ± 3.7	37.1 ± 3.0	<0.34	37.9 ± 3.5	<0.12
LDL (mg/dL)	105.6 ± 12.4	94.3 ± 19.5	<0.05	92.4 ± 18.9	<0.05
T (ng/dL)	304.8 ± 30.4	395.5 ± 40.0	<0.01	420.0 ± 27.5	<0.01
SHBG (nmol/L)	37.1 ± 2.6	38.4 ± 2.0	<0.02	40.8 ± 1.5	<0.02
FT (ng/dL)	5.6 ± 0.7	7.2 ± 0.8	<0.01	7.6 ± 0.6	<0.16
BioT (ng/dL)	132.8 ± 16.2	170.7 ± 18.0	<0.01	178.4 ± 13.6	<0.18
IIEF (score)	14.2 ± 1.8	16.5 ± 1.6	<0.01	19.9 ± 1.1	<0.001

Statistically significant *p* values are in bold. p1, significance T2 vs. T1; p2, significance T3 vs. T2; Met, metformin; TU, testosterone undecanoate; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; Gly, glycaemia; HbA1c, glycosylated haemoglobin; TC, total cholesterol; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; T, testosterone; SHBG, sex hormone binding globulin; FT, free T; BioT, bioavailable T; IIEF, International Index of Erectile Function.

Postpubertal onset Hypogonadal men with obesity and T2DM

G1N (n = 16)	T1	T2	p1 (p)	T3	p2 (p)
Age (years)	52.7 ± 4.5	–	–	–	–
Duration of diabetes (years)	3.8 ± 0.8	–	–	–	–
Height (cm)	171.2 ± 5.7	–	–	–	–
Weight (kg)	102.7 ± 9.1	99.0 ± 7.6	<0.01	93.7 ± 6.3	<0.01
BMI (kg/m ²)	35.2 ± 2.3	34.0 ± 3.1	<0.01	32.6 ± 2.0	<0.01
WC (cm)	103.7 ± 7.0	99.1 ± 6.2	<0.01	92.5 ± 5.3	<0.001
SBP (mmHg)	155.8 ± 13.7	150.1 ± 12.0	<0.01	145.7 ± 9.6	<0.001
DBP (mmHg)	86.4 ± 4.5	85.5 ± 4.2	<0.07	82.5 ± 2.6	<0.01
Gly (mg/dL)	180.4 ± 24.8	155.5 ± 19.7	<0.001	130.3 ± 15.6	<0.001
HbA1c (%)	9.1 ± 0.4	8.3 ± 0.3	<0.001	7.3 ± 0.3	<0.001
TC (mg/dL)	226.6 ± 20.8	216.8 ± 16.8	<0.01	206.9 ± 10.8	<0.01
TG (mg/dL)	202.8 ± 28.6	190.1 ± 27.3	<0.001	175.4 ± 19.4	<0.001
HDL (mg/dL)	38.6 ± 2.8	39.0 ± 2.6	<0.61	39.6 ± 3.0	<0.07
LDL (mg/dL)	147.3 ± 21.3	133.6 ± 15.4	<0.001	125.5 ± 10.7	<0.001
T (ng/dL)	285.8 ± 25.0	466.1 ± 63.6	<0.001	481.7 ± 57.3	<0.001
SHBG (nmol/L)	36.0 ± 3.2	37.1 ± 2.8	<0.05	39.1 ± 2.2	<0.01
FT (ng/dL)	5.4 ± 0.6	8.7 ± 1.6	<0.001	9.0 ± 1.3	<0.13
BioT (ng/dL)	124.6 ± 13.4	204.0 ± 37.1	<0.001	211.1 ± 30.0	<0.14
IIEF (score)	12.2 ± 2.2	14.6 ± 1.7	<0.05	19.9 ± 2.0	<0.001

Statistically significant *p* values are reported in bold. p1, significance T2 vs. T1; p2, significance T3 vs. T2; Met, metformin; TU, testosterone undecanoate; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; Gly, glycaemia; HbA1c, glycosylated haemoglobin; TC, total cholesterol; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; T, testosterone; SHBG, sex hormone binding globulin; FT, free T; BioT, bioavailable T; IIEF, International Index of Erectile Function.

TRT in ageing male

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

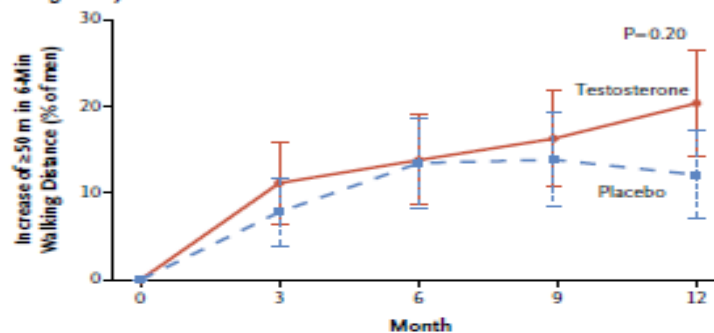
FEBRUARY 18, 2016

VOL. 374 NO. 7

Effects of Testosterone Treatment in Older Men

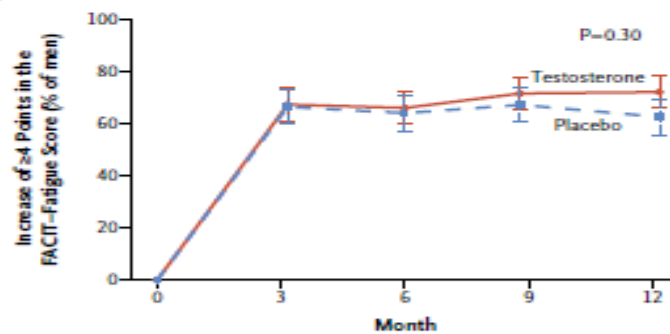
P.J. Snyder, S. Bhasin, G.R. Cunningham, A.M. Matsumoto, A.J. Stephens-Shields, J.A. Cauley, T.M. Gill, E. Barrett-Connor, R.S. Swerdloff, C. Wang, K.E. Ensrud, C.E. Lewis, J.T. Farrar, D. Cella, R.C. Rosen, M. Pahor, J.P. Crandall, M.E. Molitch, D. Cifelli, D. Dougar, L. Fluharty, S.M. Resnick, T.W. Storer, S. Anton, S. Basaria, S.J. Diem, X. Hou, E.R. Mohler III, J.K. Parsons, N.K. Wenger, B. Zeldow, J.R. Landis, and S.S. Ellenberg, for the Testosterone Trials Investigators*

B Walking Ability



No. at Risk	0	3	6	9	12
Testosterone	193	179	174	172	172
Placebo	197	179	171	159	165

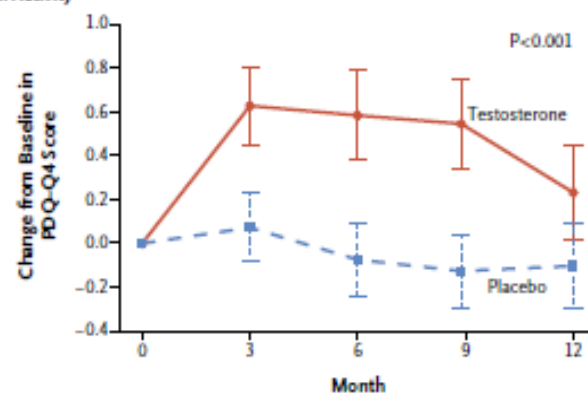
C Vitality



No. at Risk	0	3	6	9	12
Testosterone	236	219	217	206	203
Placebo	238	207	196	188	191

The NEW ENGLAND JO

A Sexual Activity



No. at Risk	0	3	6	9	12
Testosterone	230	205	208	205	193
Placebo	229	198	189	190	193

© 2016 Massachusetts Medical Society

TRT and Prostatic Cancer

- Until now there has been no data showing a direct correlation between TRT and Prostatic Cancer (Morgantale)
 - Some men have a significant difference in prostate cancer risk when treated with TRT vs. not treated (Cunningham GR & Toma SM, JCEM, 2010)
 - Krieg et al 1993
 - Slater et al 2000
 - Heikkila et al 1999
 - Hsing et al 2001
 - Zitzmann et al, 2013
- However, to have a definitive evidence, there would be almost 6000 hypogonadal men who have been treating with T for 5 yrs at least. (Cunningham GR & Toma SM, JCEM, 2010)
- Fernandez results were found by another

Contraindications of testosterone therapy

Absolute contraindications

- Suspected or diagnosed carcinoma of the prostate or breast.
- Significant polycythemia, untreated sleep apnea, severe heart failure, severe symptoms of lower urinary tract obstruction or clinical findings of bladder outflow obstruction due to benign prostate hypertrophy.

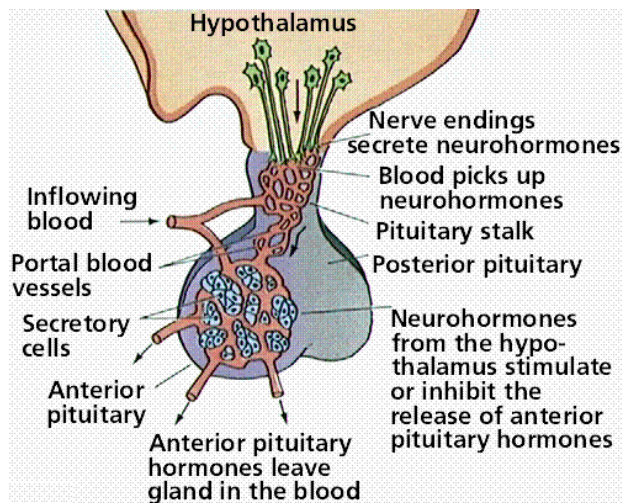
Partial contraindications

- Moderate urinary obstruction (contraindication lifted after successful treatment)
- ▶ In the absence of definite contraindications, **age** as such is not a contraindication to initiate testosterone substitution.

Appropriatezza/prescrivibilità

- **Nota 36 Determinazione 29 luglio 2010 (GU 18 novembre 2010, n. 270): modifica alla nota AIFA 36 di cui alla determinazione del 4 gennaio 2007**
- 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)
- Farmaci : Andriol cp 40 mg e Testo Enant fl 250 mg
- Ricetta non ripetibile prescritta da endocrinologi, urologi, andrologi e ginecologi (determina AIFA n 199 del 05/02/2016).

SPERM INDUCTION THERAPY



Posologia:

1. hCG 1500-2000 U
x2-3/w i.m. o
s.c. per 4-6m
2. aggiungere hMG
i.m. o s.c. o rFSH
(s.c.) (75)-150 U.
x 3/w

hCG

+ FSH

Vantaggi:

1. Facile da usare
2. Utile anche in difetti GnRHr
3. Meno costoso di GnRH

Svantaggi:

1. Ginecomastia (↑ produzione endogena di E2)
2. Non utile nell'ipogonadismo primitivo

Il Mercato

PRODOTTO	AZIENDA	CONTENUTO	MOLECOLA	DATA DI LANCIO	PREZZO €
GONAL F	MERCK SERONO	75 UI rFSH 150,300,450,900,1 050	FOLLITROPINA α DA DNA RICOMBINANTE	Ottobre '95	40,61 .. 564,86
PUREGON	SCHERING PLOUGH ORGANON	50 UI rFSH 100,300,600	FOLLITROPINA β DA DNA RICOMBINANTE	Maggio '96	27,50 ... 489,30
MEROPUR	FERRING	75UI FSH + 75 UI LH 10 FIALE	MENOTROPINA	Aprile 2006	279,71

Fostimon 10 fiale 75 UI FSH: € 145.22

Classe A
Nota 74

Beta HCG in commercio

- **Gonasi** (gonadotropina di sintesi) con fiale da 250, 1000, 2000, 5000 e 10000 UI (**fascia C**; 80 E/mese);
- **Pregnyl** (gonadotropina estrattiva) con fiale di 1500 e 5000 UI (**fascia A**; 57 E/mese) .
- **Ovitrelle** (HCG ricombinante; 250 mcgr/fl) ha un costo più elevato e (come da scheda tecnica) non ha indicazioni nel maschio.

REVIEW ARTICLE

Correspondence:

Mario Maggi, Andrology Unit, Department of Biomedical, Experimental and Clinical Sciences, Viale Piersanti 6, 50139 Florence, Italy.
E-mail: m.maggi@dfc.unifi.it

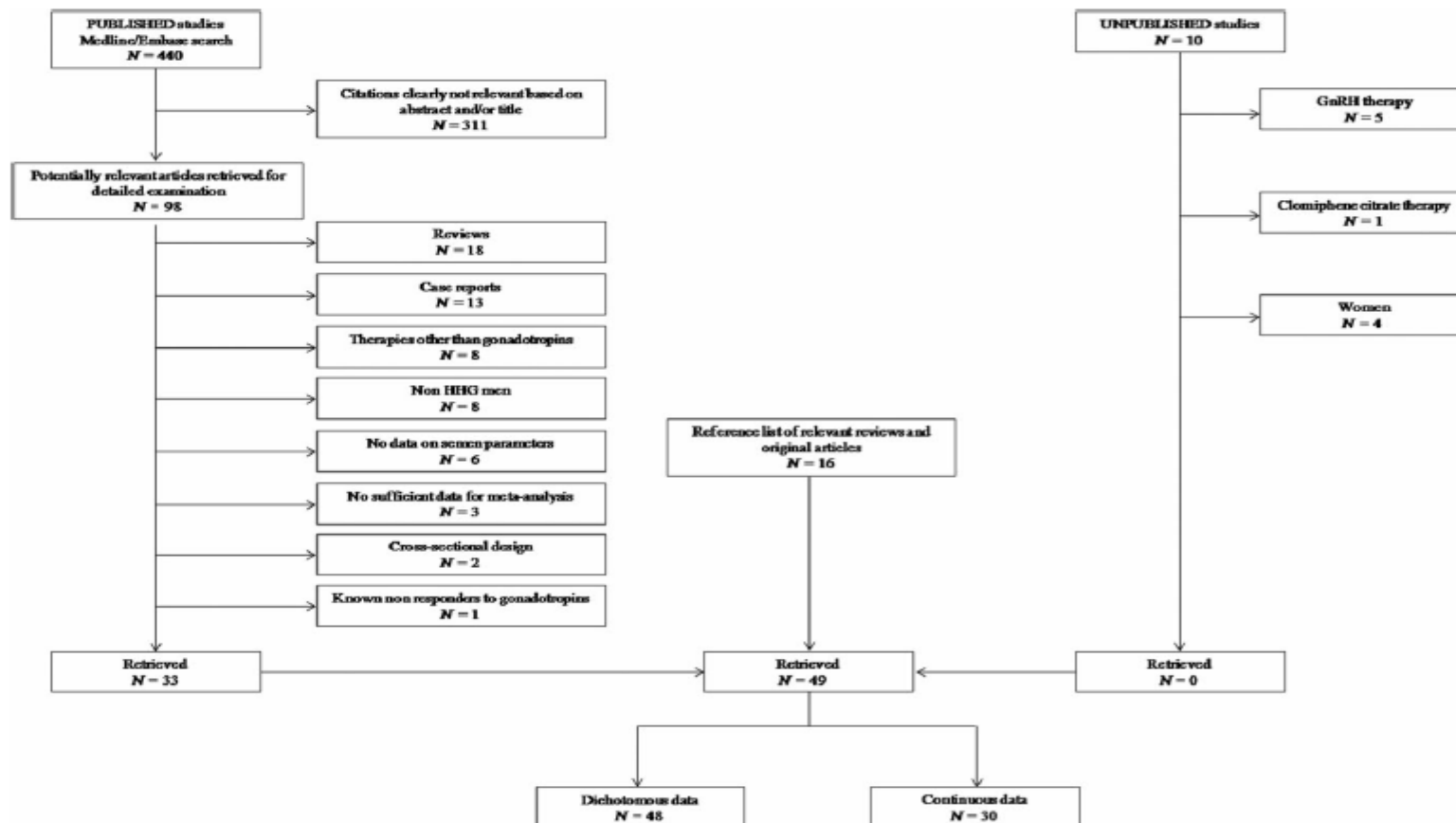
Keywords:

gonadotrophins, hypogonadism, sperm count,

Factors affecting spermatogenesis upon gonadotropin-replacement therapy: a meta-analytic study

¹G. Rastrelli, ^{1,2}G. Corona, ³E. Mannucci and ¹M. Maggi

Figure 1 Study flow diagram on gonadotropin therapy. HHG, Hypogonadotropic hypogonadism; GnRH, gonadotropin releasing hormone



FSH



Pituitary related HHG

Hypothalamic related HHG

Mixed pre- and post-pubertal onset HHG

Only pre-pubertal onset of HHG

Urinary-derived FSH

Purified FSH

Recombinant FSH

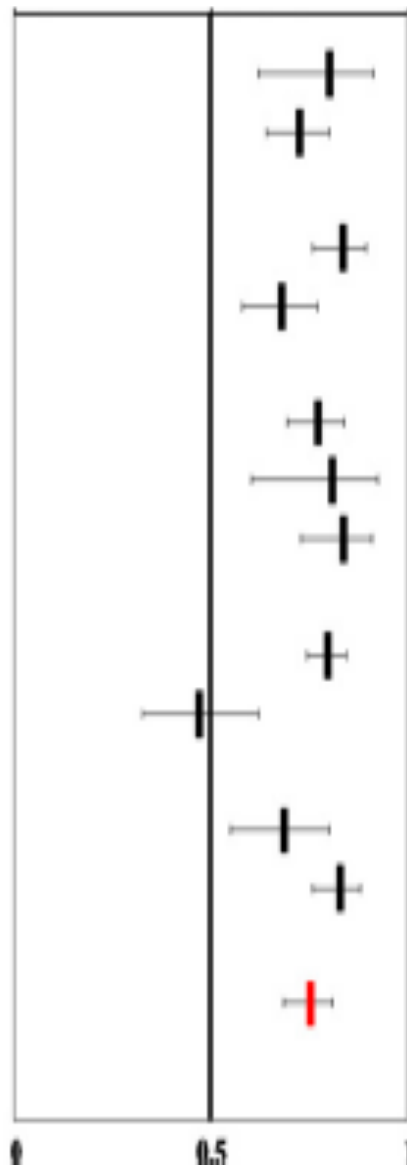
hCG+FSH

Only hCG

No previous THF
(0% of previously treated subjects)

Previous THF
(at least 1 previously treated subject)

OVERALL



# Studies	# Subjects	Event Rate	LL	UL
9	39	0.80	0.62	0.91
29	501	0.73	0.64	0.80
6	126	0.84	0.76	0.89
26	445	0.68	0.58	0.77
20	366	0.77	0.69	0.84
5	100	0.81	0.60	0.92
10	236	0.84	0.73	0.91
36	723	0.80	0.74	0.84
10	151	0.47	0.33	0.62
8	152	0.69	0.55	0.80
25	355	0.83	0.76	0.88
48	897	0.75	0.69	0.81

Q = 0.680
p = 0.410

Q = 6.52
p = 0.011

Q = 1.127
p = 0.569

Q = 18.623
P < 0.0001

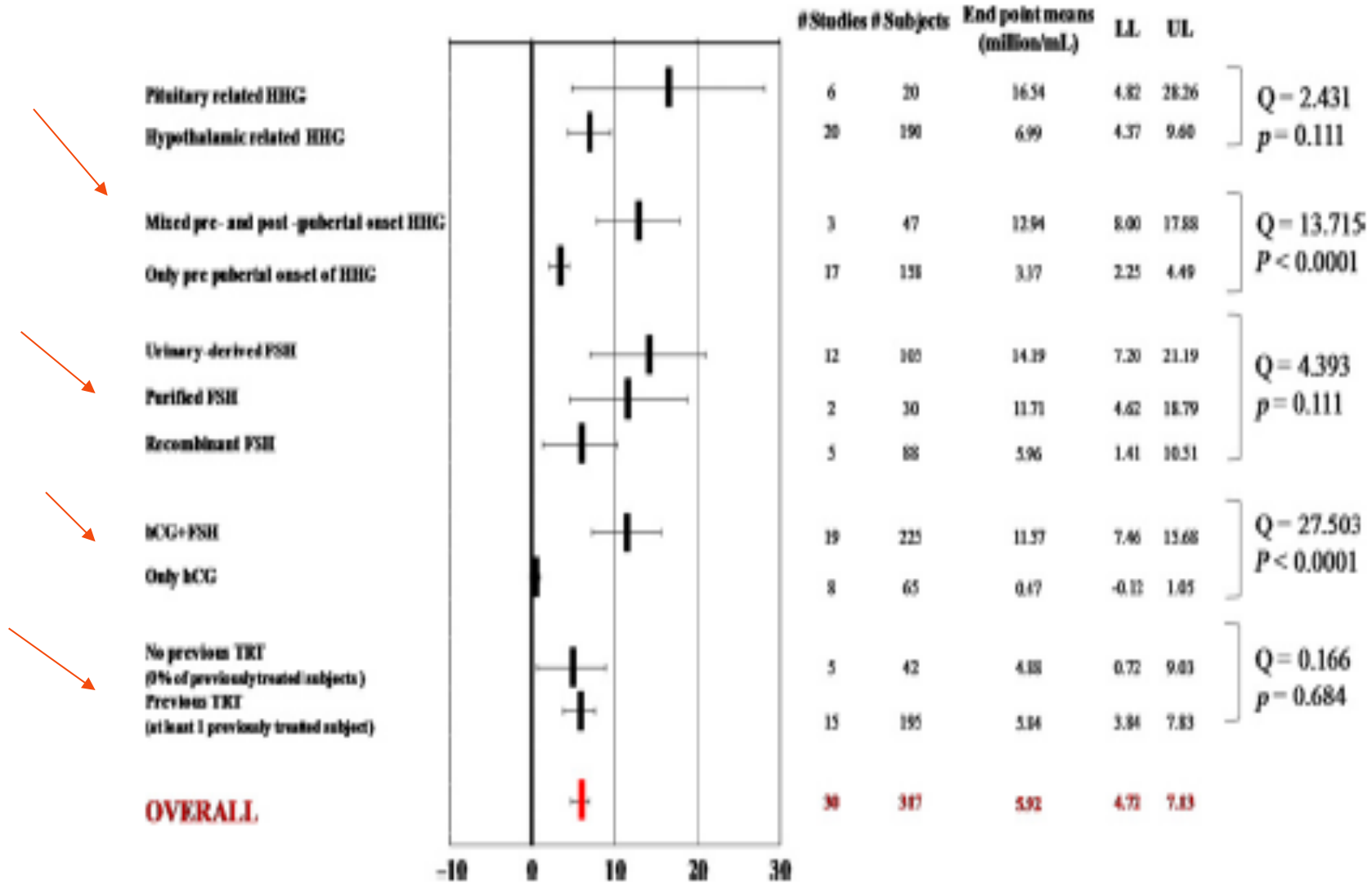
Q = 4.562
p = 0.051

Overall success rate 75%

Mean Sperm Concentration 5,9 mil/ml

Appearance a sperm

FSH



Sperm concentration

Summing up

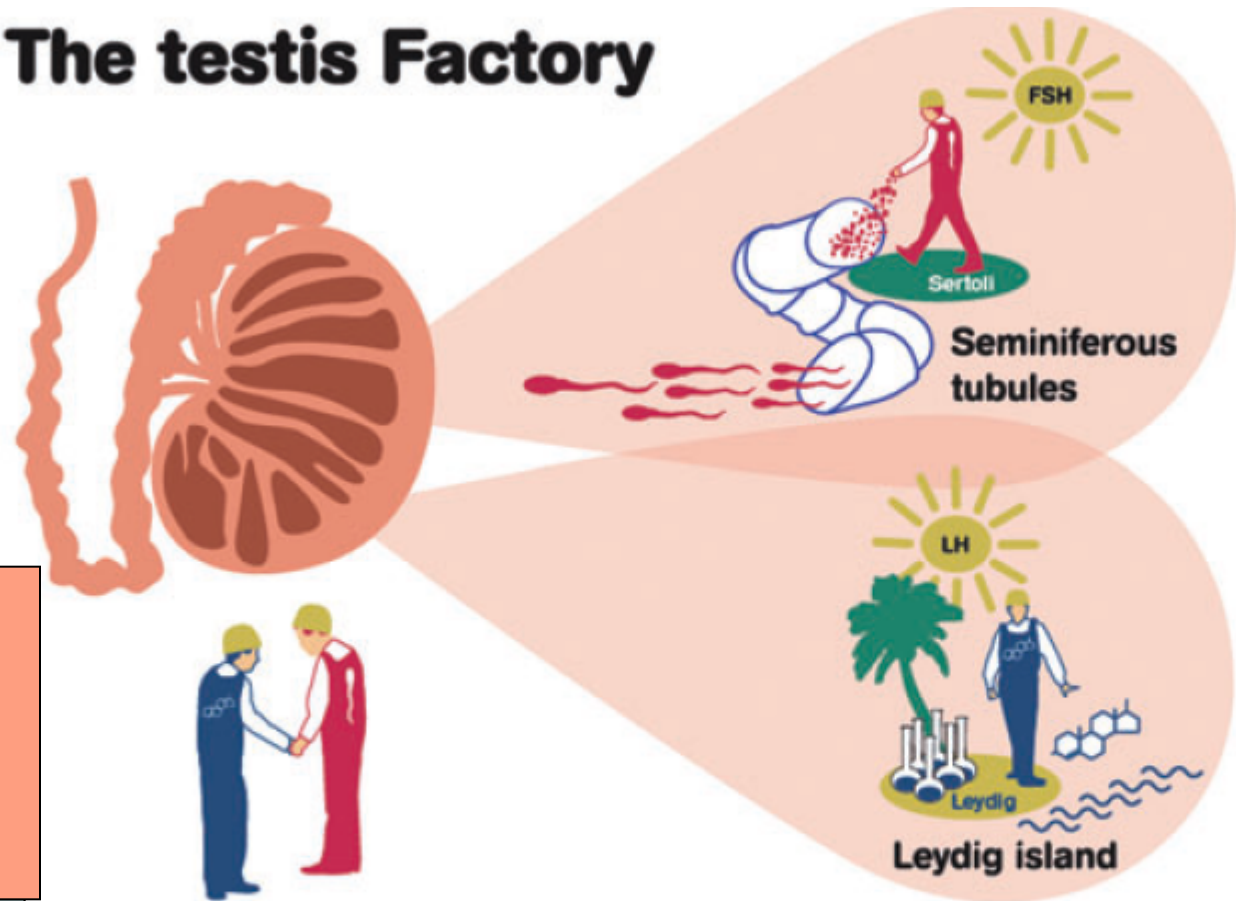
**Chronic Syndrome
showing important
clinical sequences**

It is typified by
the starting age and the
testis functions
mainly compromised

Main clinical problems:
-Sex differentiation
-Sex maturation with
normal androgenization
-Fertility

Sequences:
Low libido and
Erectile Dysfunction
Weakness
Obesity
Diabetes mellitus type 2
Osteoporosis

The testis Factory



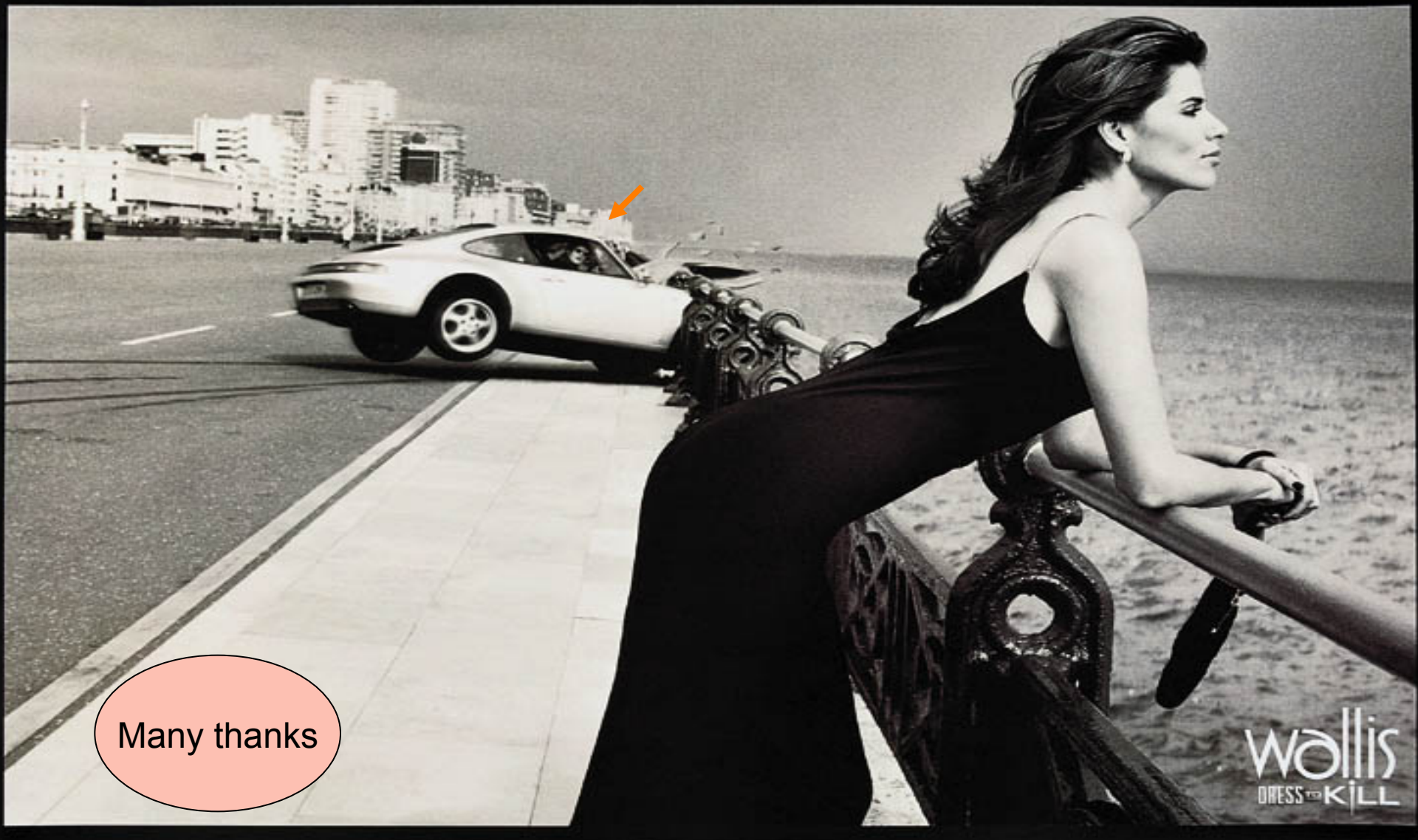
Terapia dell' ipogonadismo

Obiettivi:

- **rimuovere la causa (se possibile)**
- **ripristinare la fertilità e curare i sintomi**
- **non ripristinare la fertilità ma curare i sintomi**

But...one should add some established alternatives for its sequences!

- Glucose metabolism
diet, exercise, metformin,...
- Mobility, muscle strength
exercise, diet,...
- Cardiovascular risk
lifestyle, statins,
- Osteoporosis
bisphosphonates
-



Many thanks

Wallis
DRESS TO KILL