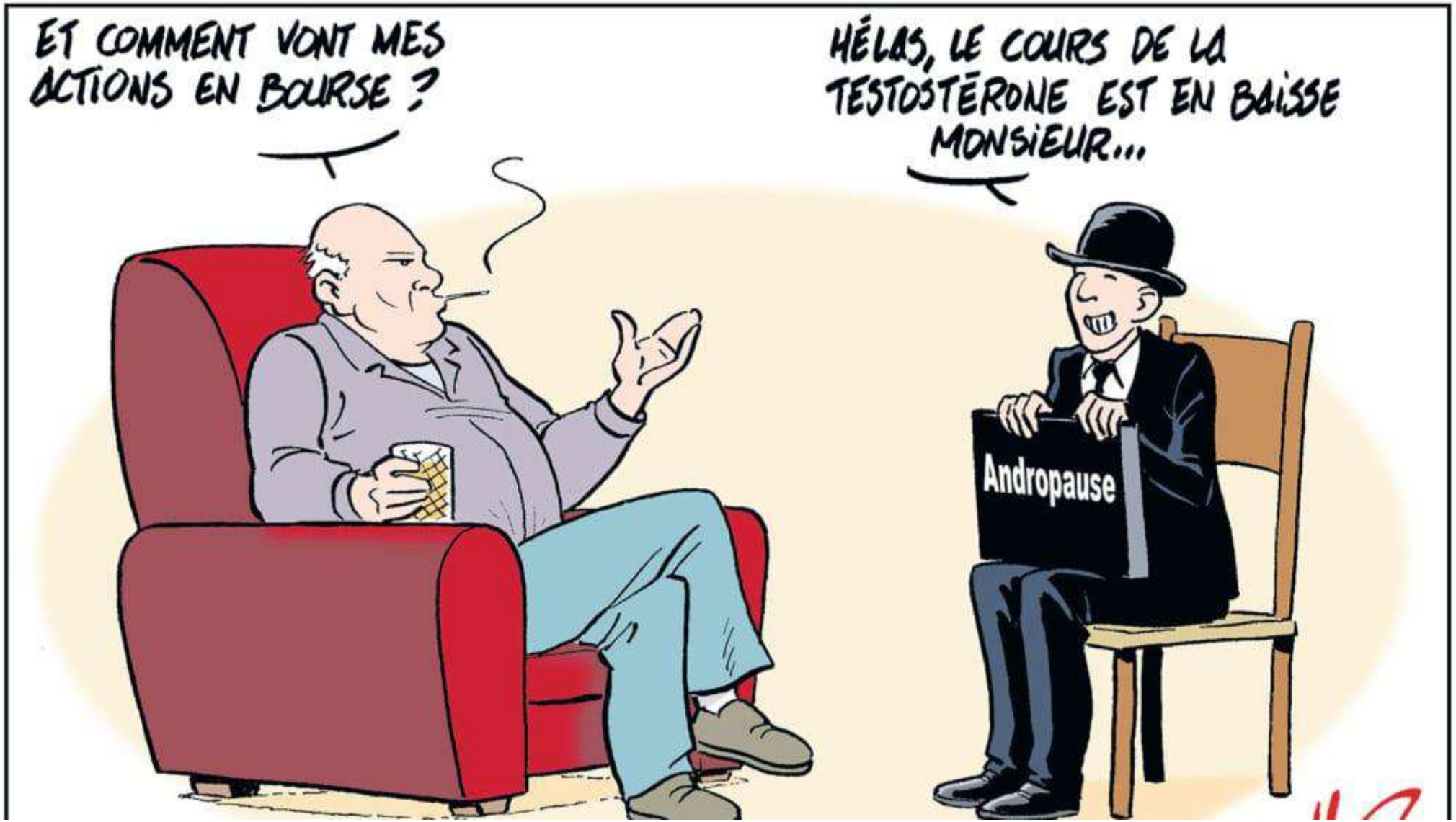
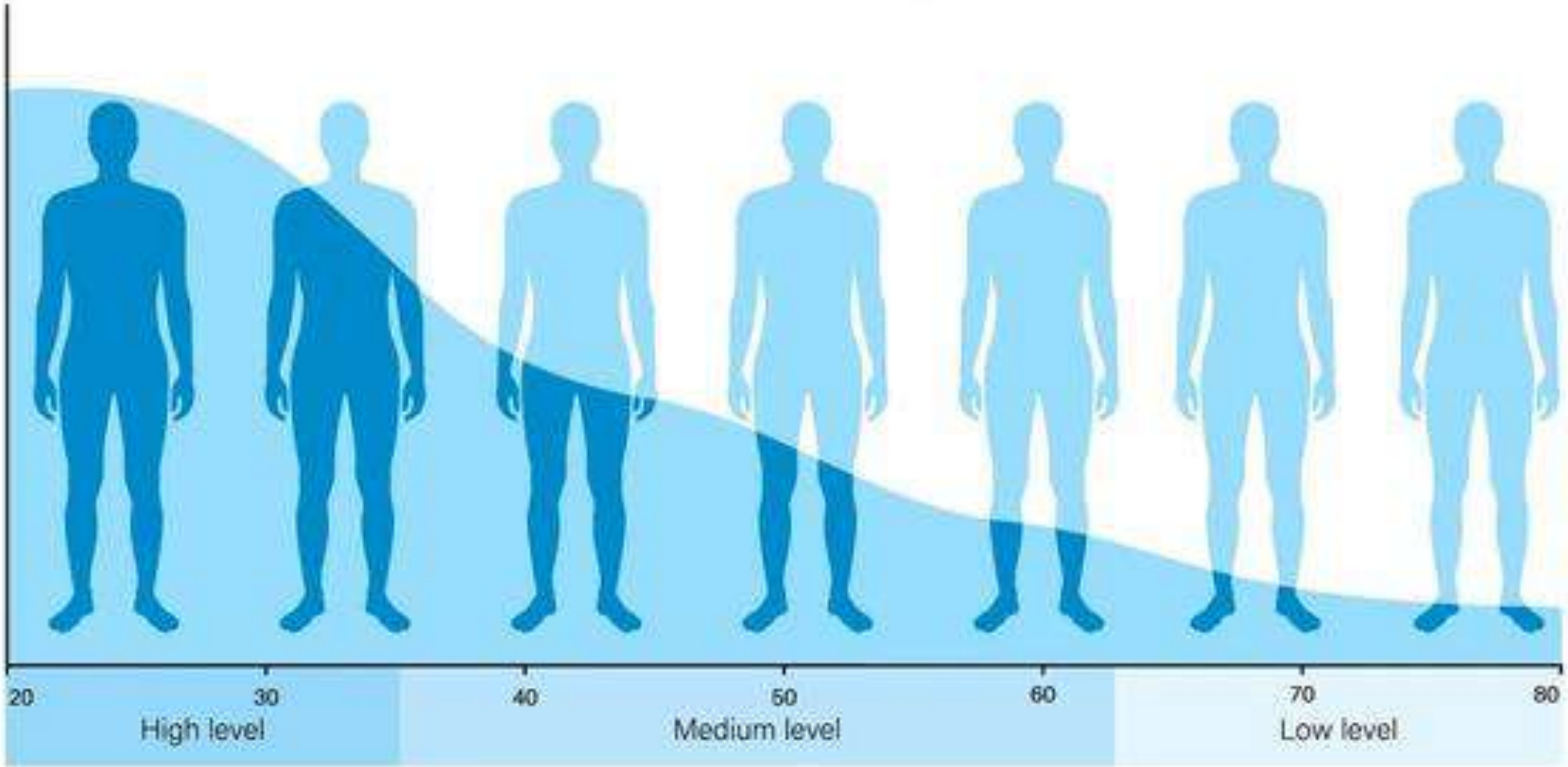
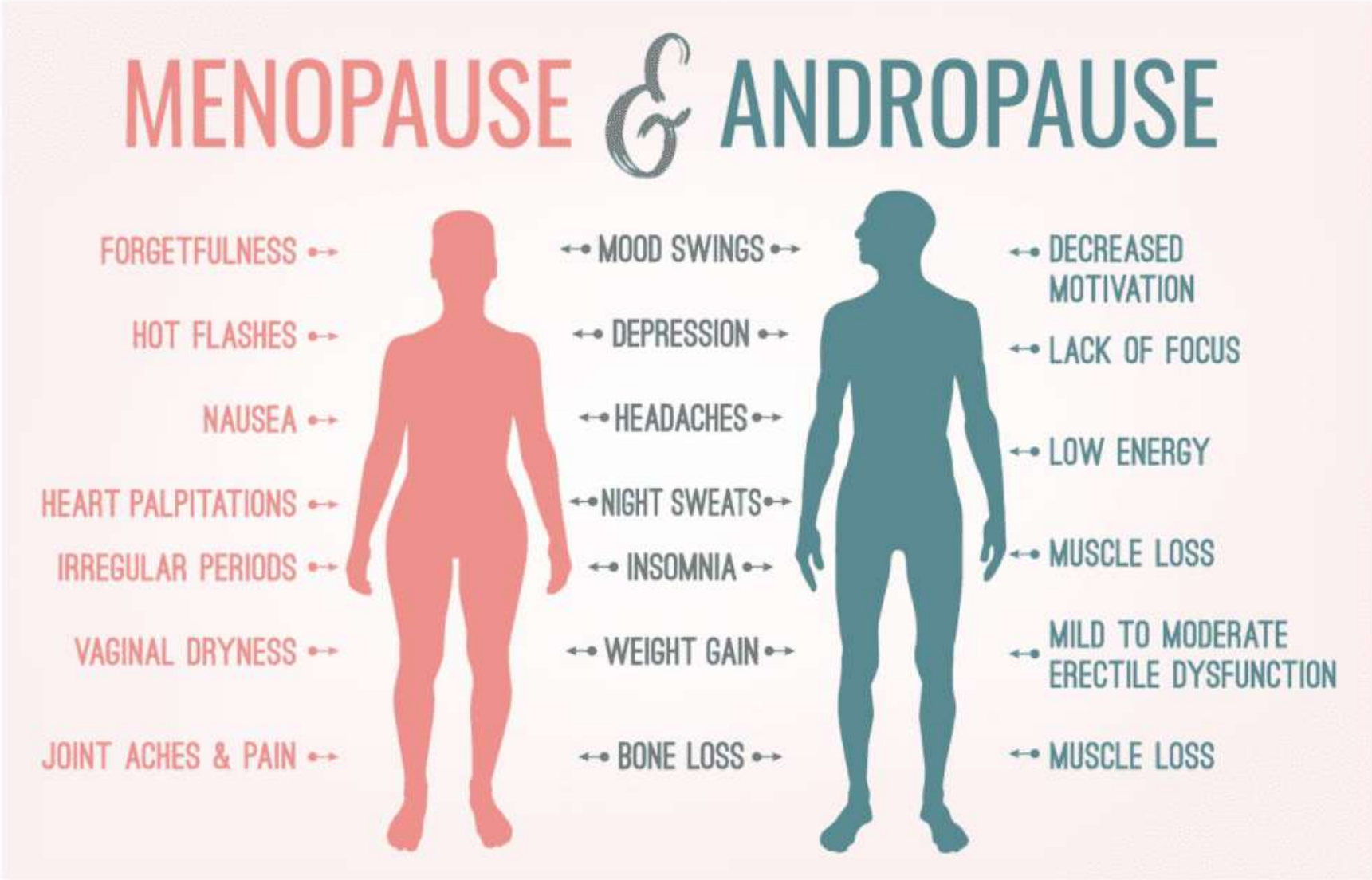
Andropause: mythe or reality



TESTOSTERONE LEVEL BY AGE

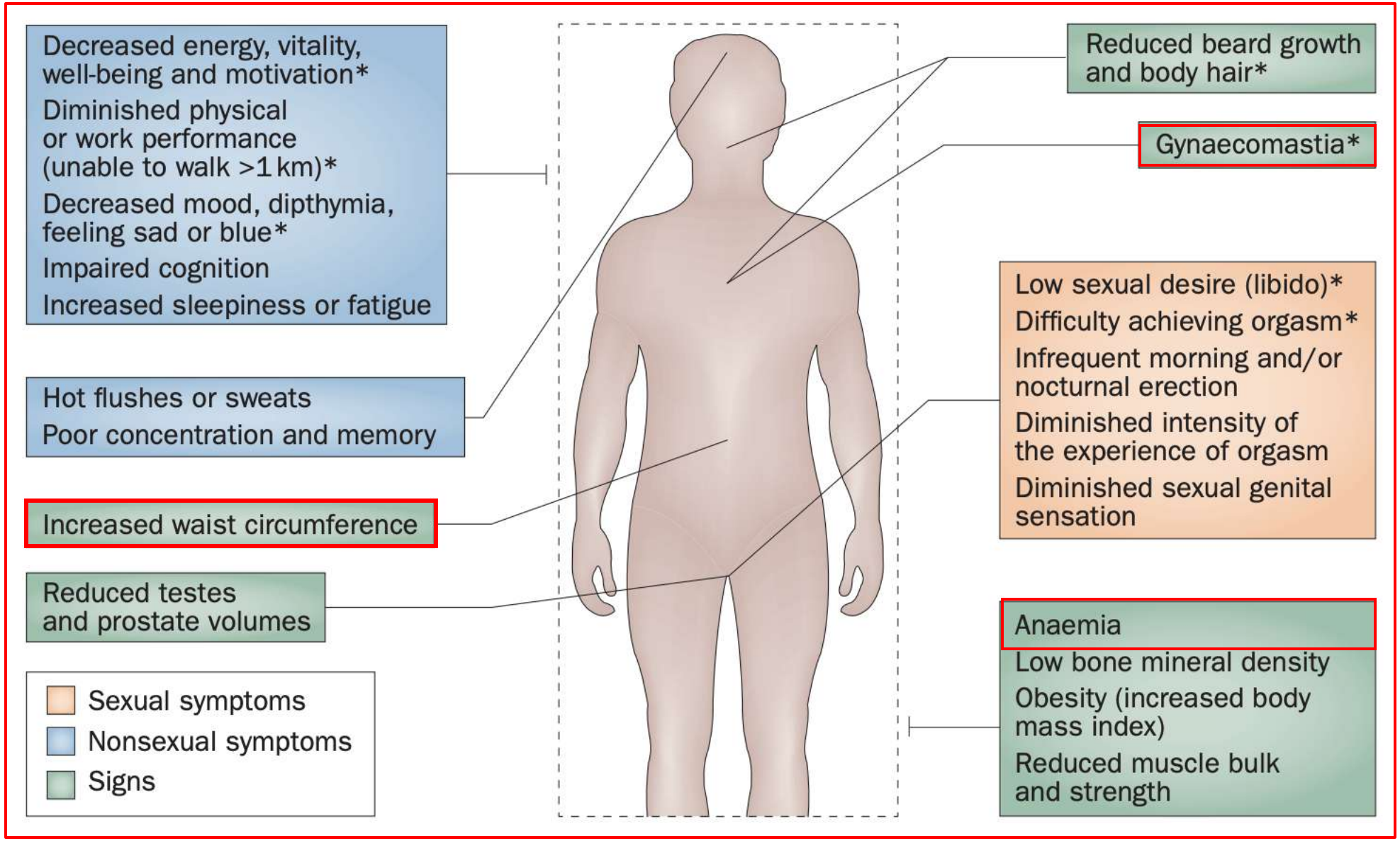


Andropause Or “Male Menopause”

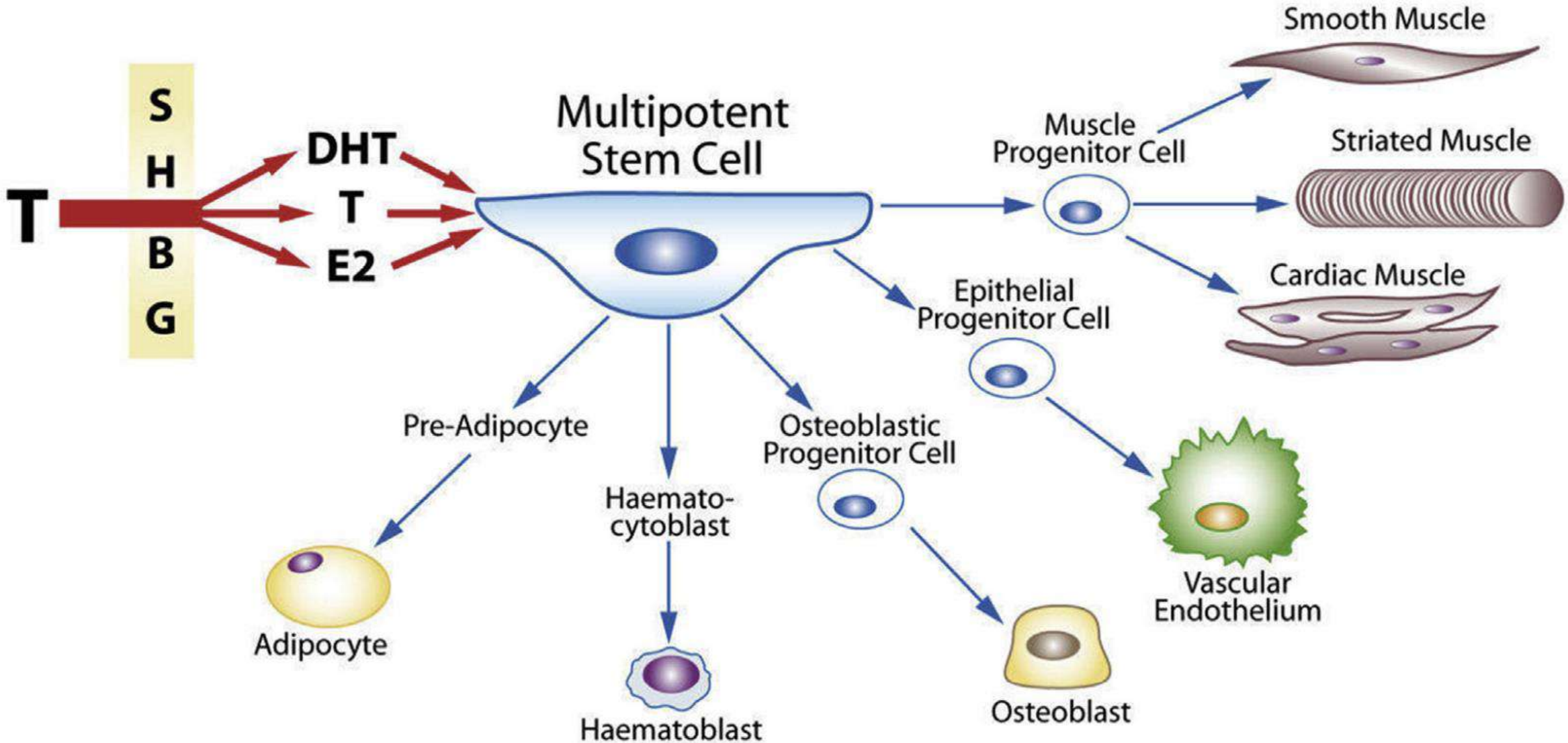


https://balancedmedicalsolutions.com/andropause-or-male-menopause-20-symptoms-that-every-man-should-know/

Symptoms and signs of testosterone deficidency



The practical management of testosterone deficiency in men. Antonio Aversa & Abraham Morgentaler *Nature Reviews Urology* volume 12, pages641–650 (2015)

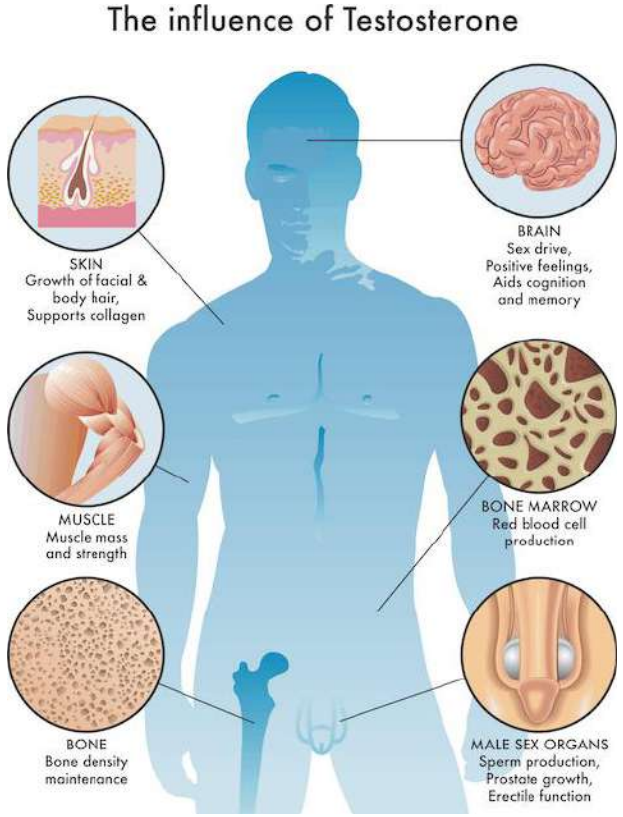


Testosterone, directly or through conversion to 5a-dihydrotestosterone or estradiol, modulates multipotent stem cell metabolism and function to promote differentiation to progenitor cells for muscle, endothelium, bone, and red blood cells. DHT ¼ 5adihydrotestosterone; E2 ¼ estradiol; T ¼ testosterone. From Carruthers M, Trinick TR, Jankowska E, et al.

Benefits and Health Implications of Testosterone Therapy in Men With Testosterone Deficiency. Abdulmaged M. Traish PhD. Sexual Medicine ReviewsVolume 6, Issue 1, January 2018, Pages 86-105

Testosterone Is a Metabolic Hormone and Plays a Vital Role in Human Physiology

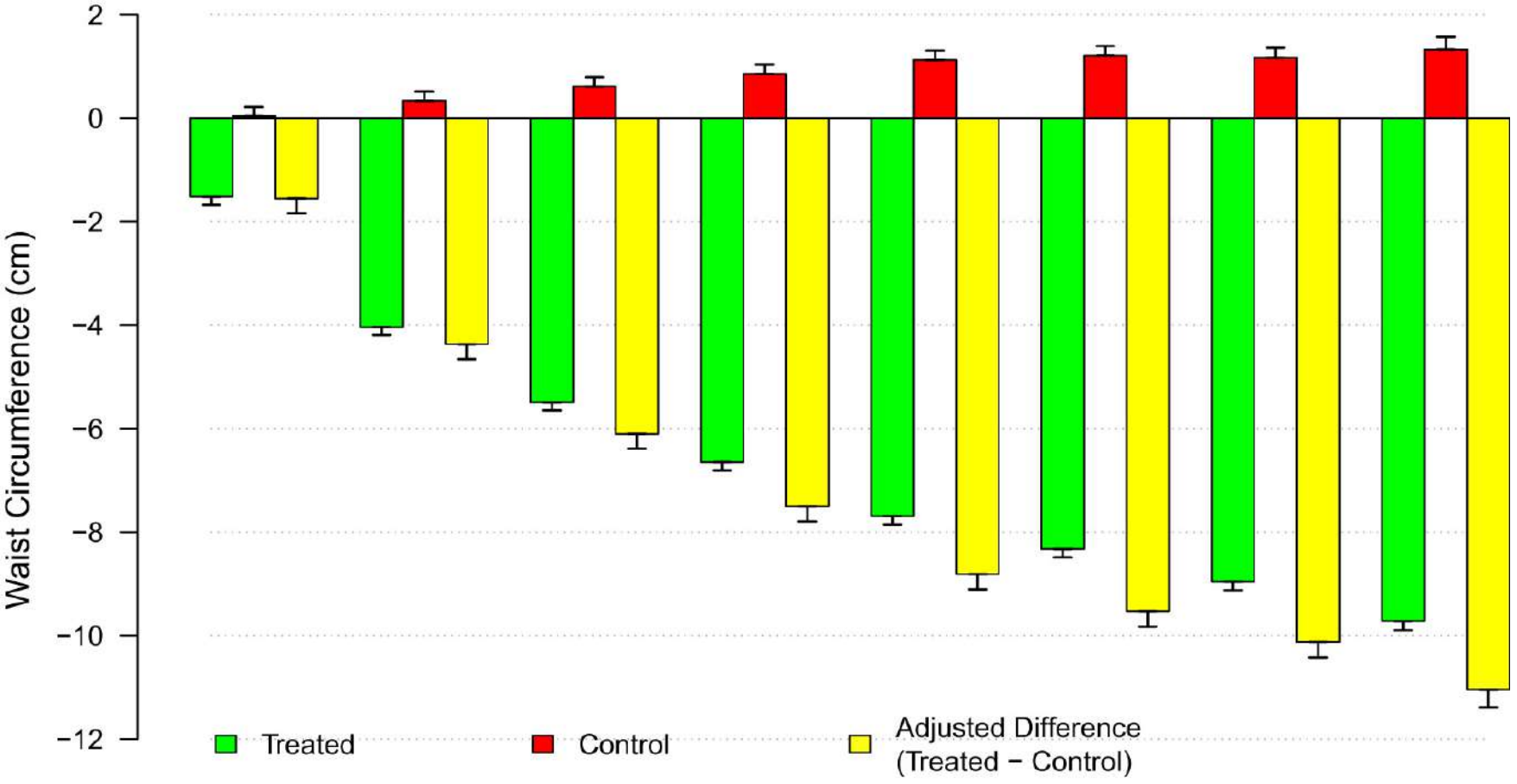
- Regulate energy metabolism
- Nitrogen retention
- Muscle growth and maintenance
- Inhibit adipogenesis
- Modulate male reproductive and sexual function
- Exerts an important metabolic and functional role in many tissues and organs
- Regulation of bone metabolism
- Erythropoiesis
- Endothelial function
- Liver functions,
- Hair growth



The wide distribution of androgen receptors in various tissues, including the central nervous system, strongly supports the premise that T plays a key physiologic role in regulating human physiology and that T is an integral hormone in maintaining human health

Benefits and Health Implications of Testosterone Therapy in Men With Testosterone Deficiency. Abdulmaged M. Traish PhD. Sexual Medicine ReviewsVolume 6, Issue 1, January 2018, Pages 86-105

Changes in waist circumference in testosterone-treated and untreated (control) groups



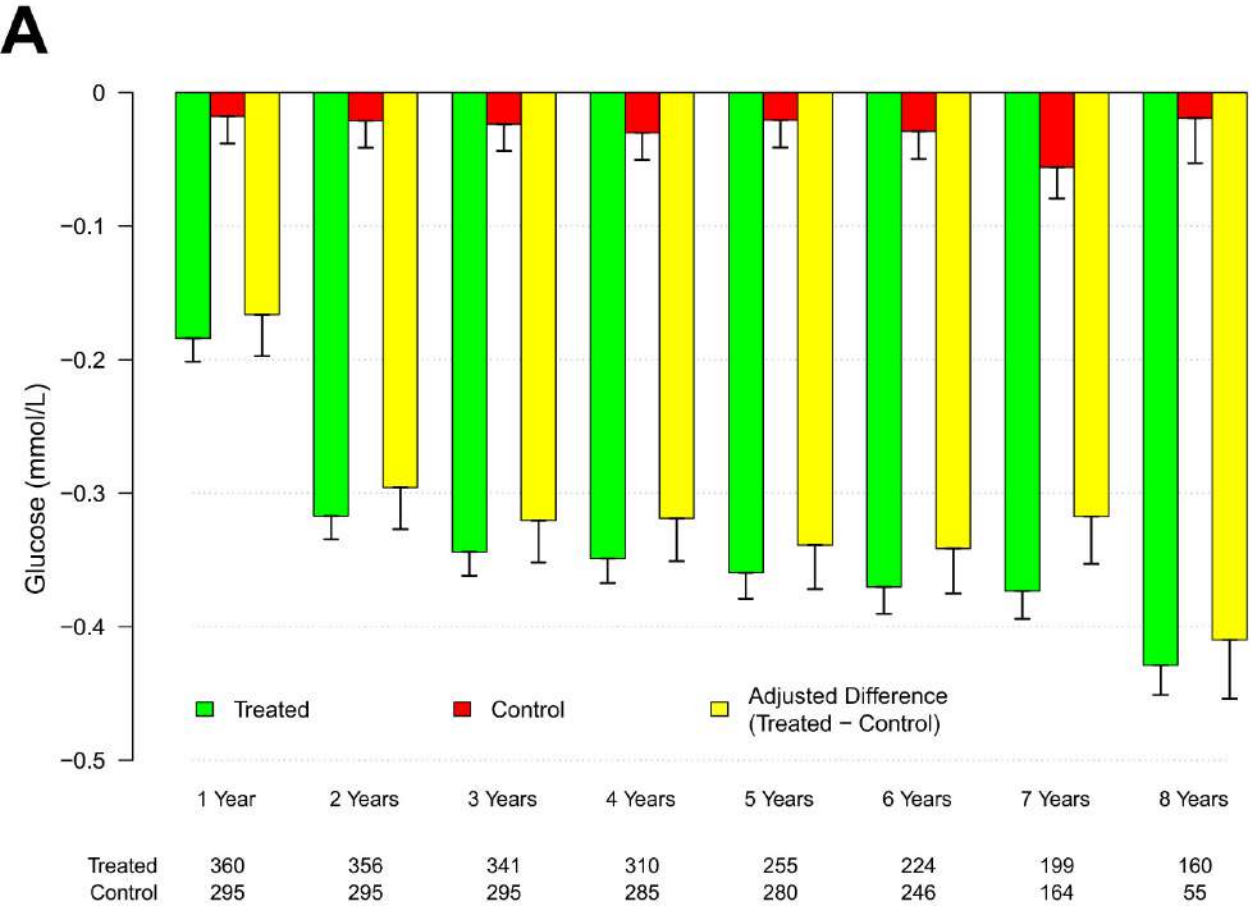
	1 Year	2 Years	3 Years	4 Years	5 Years	6 Years	7 Years	8 Years
Treated	360	356	341	310	255	224	199	160
Control	295	295	295	285	280	246	164	55

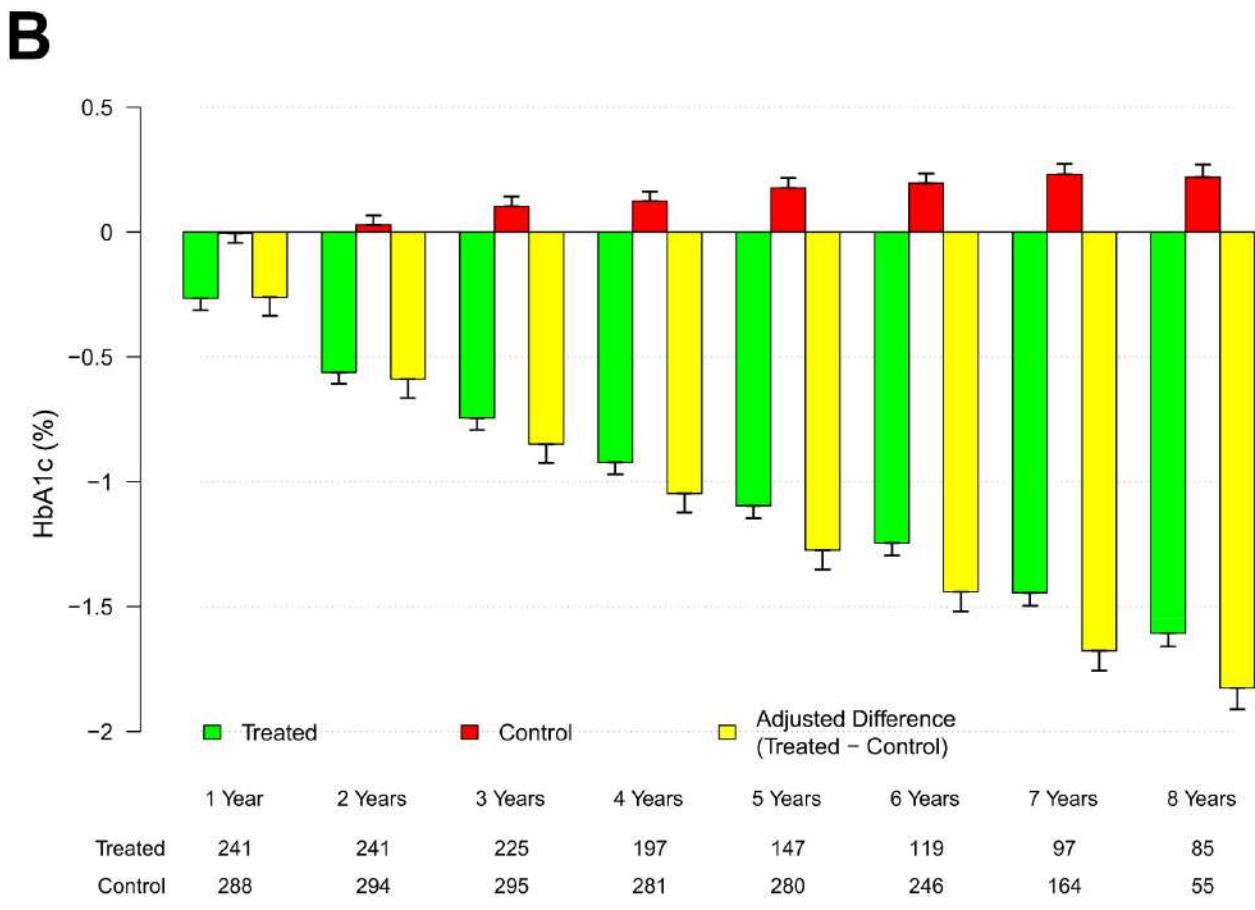
TTh Ameliorates Components of MetS, Increases Insulin Sensitivity, and Lowers Risk of T2DM.

Benefits and Health Implications of Testosterone Therapy in Men With Testosterone Deficiency. Abdulmaged M. Traish PhD. Sexual Medicine ReviewsVolume 6, Issue 1, January 2018, Pages 86-105

Changes in fasting blood glucose and HbA1c in testosterone-treated and untreated (control) groups

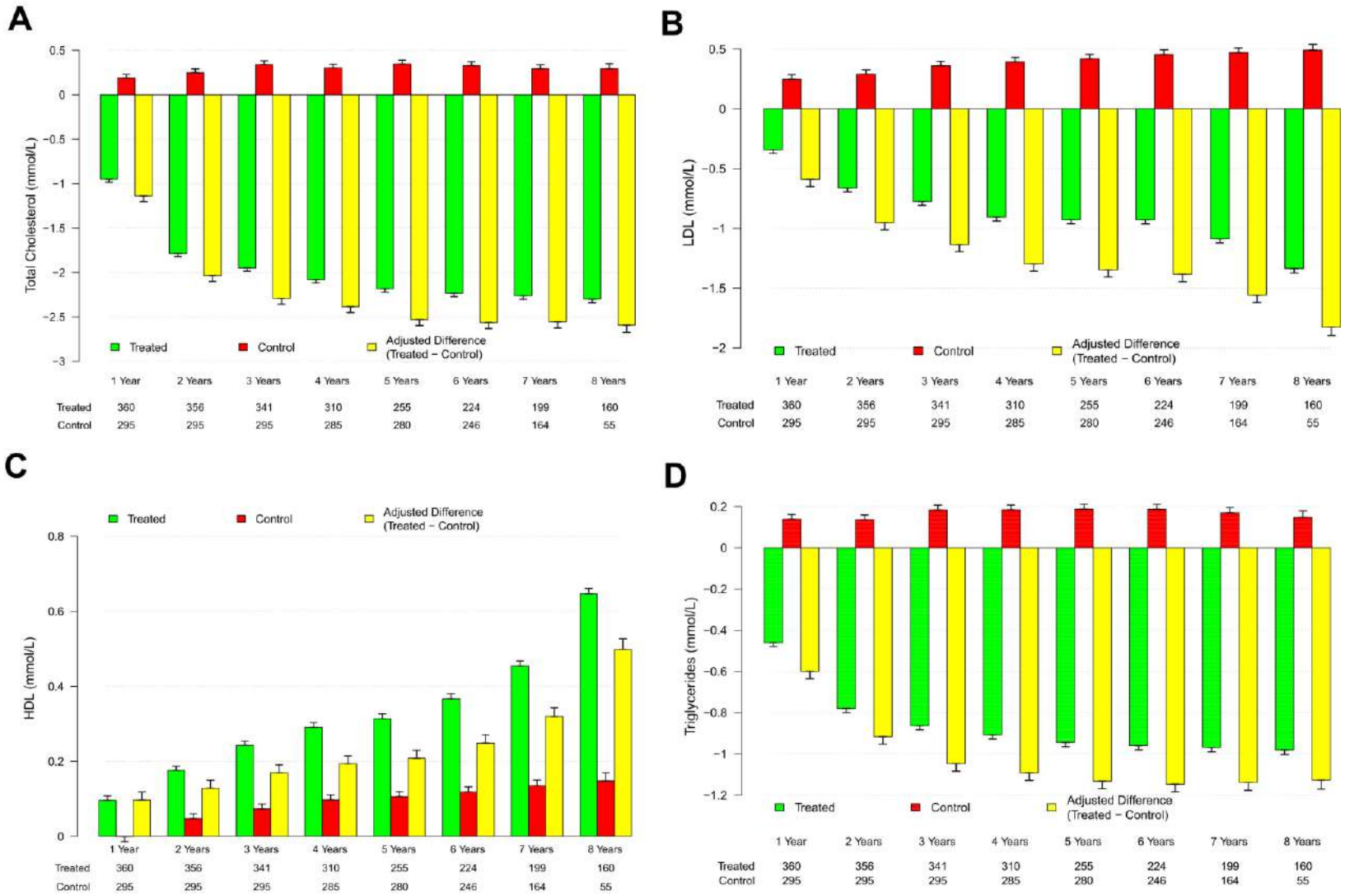
TTh ameliorates components of MetS, improves lipid profiles, lowers blood glucose and HbA_{1c}, improves insulin sensitivity, attentuates inflammation, decreases systolic and diastolic blood pressures, and improves cardiometabolic functions.





Benefits and Health Implications of Testosterone Therapy in Men With Testosterone Deficiency. Abdulmaged M. Traish PhD. Sexual Medicine ReviewsVolume 6, Issue 1, January 2018, Pages 86-105

Changes (yellow bars) in lipid profile in testosterone-treated (green bars) and untreated control (red bars) groups



TTh ameliorates components of MetS, improves lipid profiles, lowers blood glucose and HbA_{1c}, improves insulin sensitivity, attentuates inflammation, decreases systolic and diastolic blood pressures, and improves cardiometabolic functions.

Meta-analyses have shown that TTh decreases total cholesterol, low-density lipoprotein cholesterol, and triglycerides and improves high-density lipoprotein and systolic and diastolic blood pressures.

Higher T levels have been shown to produce a 42% lower risk of T2DM[82] and T2DM has been associated with lower total T levels.

In 2 meta-analyses, Corona et al[184], [185] showed that TTh significantly ameliorates hyperglycemia, HbA_{1c}, and HOMA-IR index.

Benefits and Health Implications of Testosterone Therapy in Men With Testosterone Deficiency. Abdulmaged M. Traish PhD. Sexual Medicine ReviewsVolume 6, Issue 1, January 2018, Pages 86-105

Testosterone deficiency, insulin resistance and the metabolic syndrome

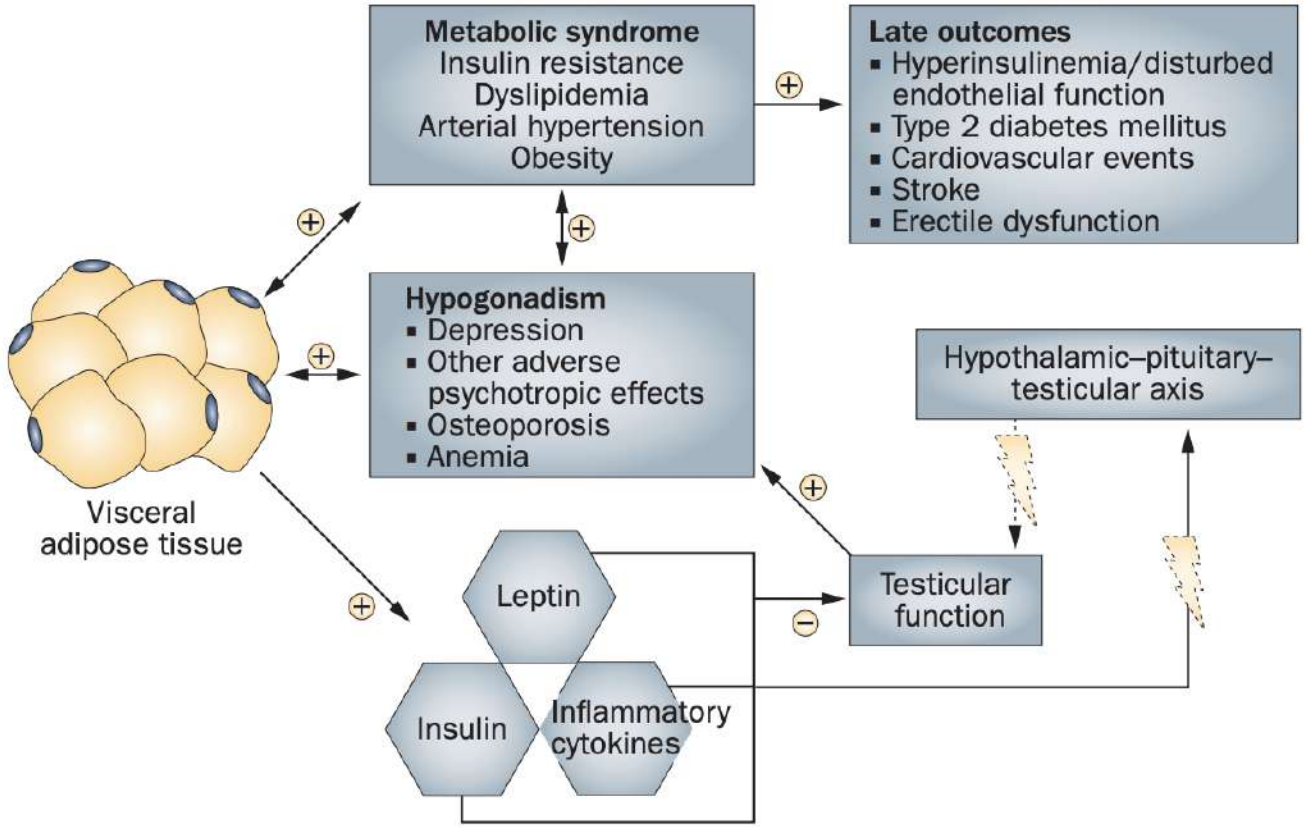
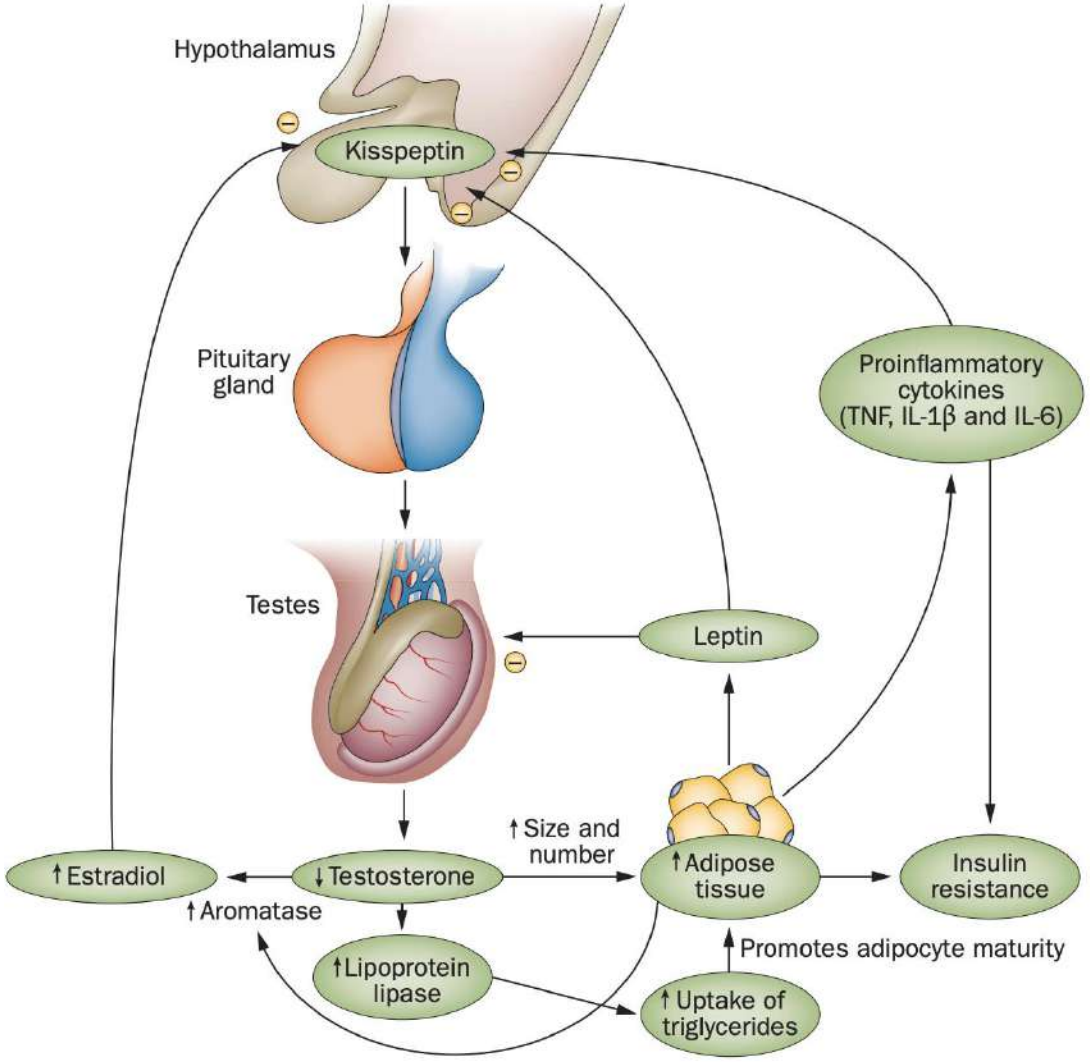


Figure 1 | Self-perpetuating pathogenic circle between adverse metabolic parameters, with visceral adipose tissue as a pivotal component. Inflammatory cytokines are shed by adipocytes and cause dysfunctions of the hypothalamic–pituitary–testicular axis, leading to clinically relevant end points and, potentially, increased mortality. The 'lightning' signs symbolize disturbance of function.

Testosterone deficiency, insulin resistance and the metabolic syndrome. Michael Zitzmann. *Nature Reviews Endocrinology* volume 5, pages673–681. Published: 27 October 2009

The hypogonadal–obesity–adipocytokine hypothesis



Increased amounts of adipose tissue increase the activity of aromatase (which converts testosterone to estradiol) in adipocytes.

Estradiol directly inhibits the hypothalamic–pituitary–testes axis via Kisspeptin, which leads to decreased testosterone production.

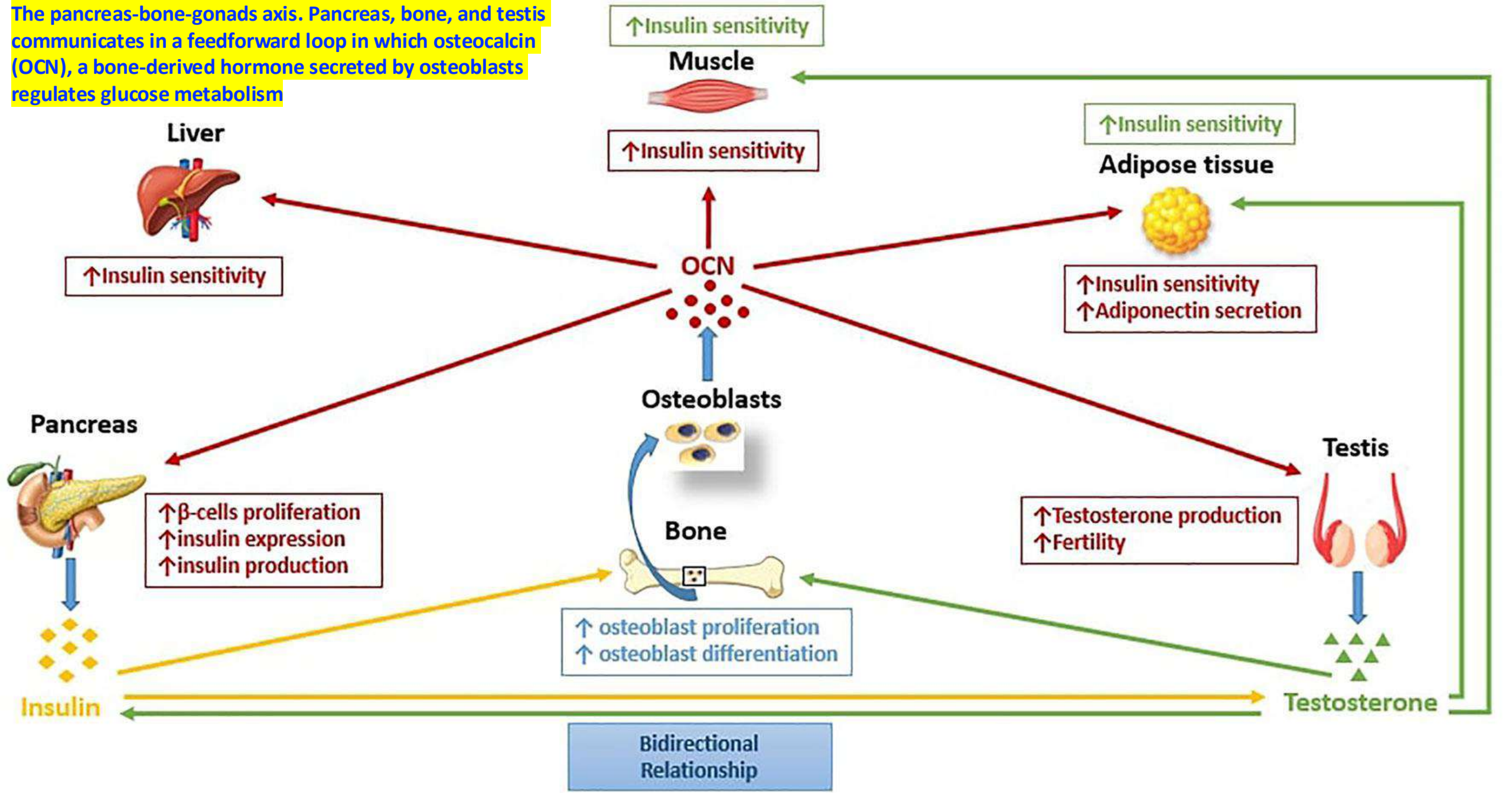
Adipose tissue also produces leptin and proinflammatory cytokines that have a negative feedback effect on the hypothalamic–pituitary–gonadal axis.

Leptin also inhibits the stimulatory action of gonadotropins on the Leydig cells of the testes, which results in decreased androgen production from the testes.

Reduced levels of testosterone in the tissues facilitates triglyceride storage in adipocytes by increasing the activity of lipoprotein lipase.

Testosterone and insulin resistance in the metabolic syndrome and T2DM in men. Preethi M. Rao, Daniel M. Kelly & T. Hugh Jones. *Nature Reviews Endocrinology* volume 9, pages479–493 Published: 25 June 2013

The pancreas-bone-gonads axis. Pancreas, bone, and testis communicates in a feedforward loop in which osteocalcin (OCN), a bone-derived hormone secreted by osteoblasts regulates glucose metabolism



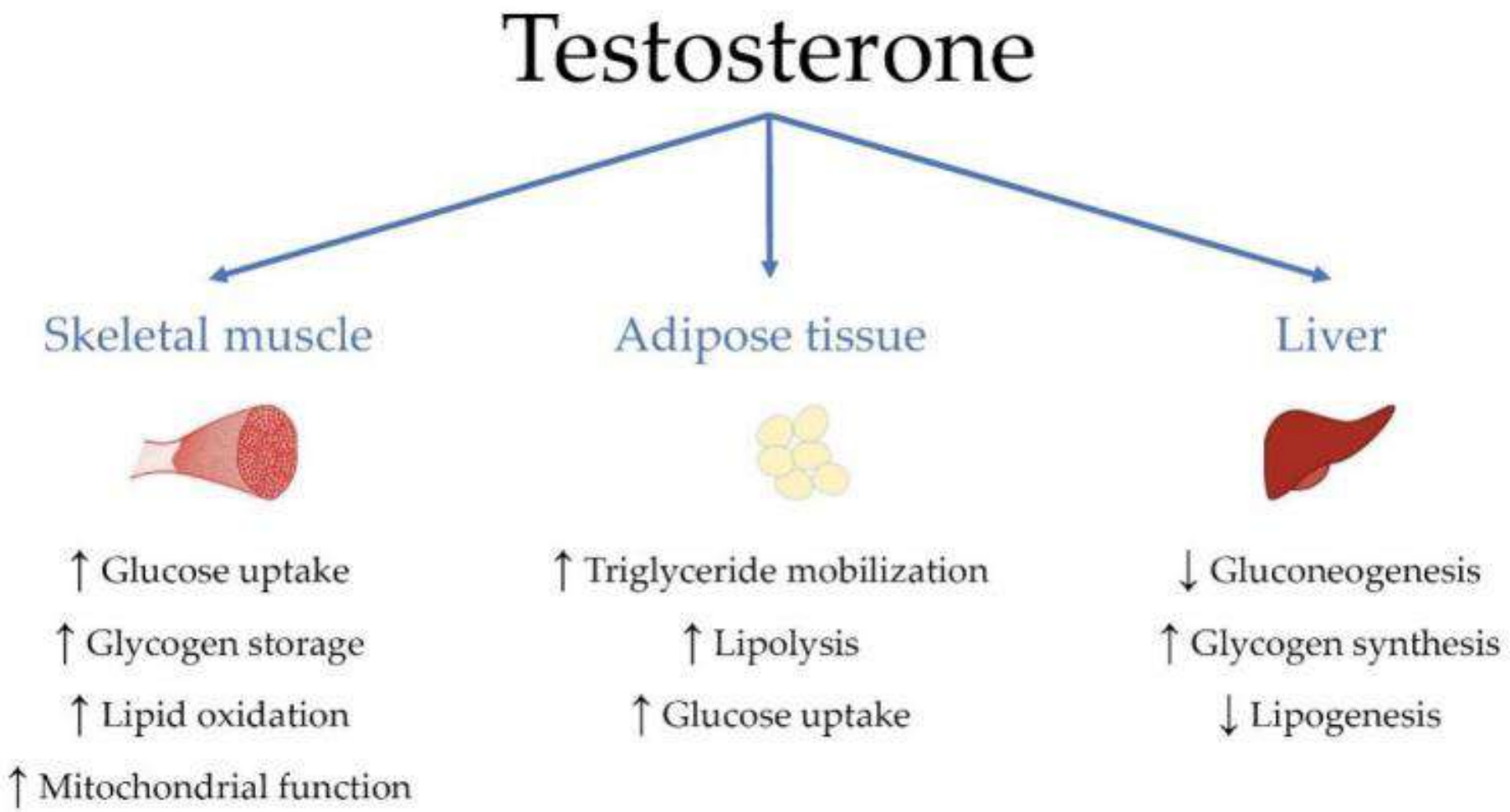
Hypogonadism, Type-2 Diabetes Mellitus, and Bone Health: A Narrative Review. Front. Endocrinol., 18 January 2021. Sec. Endocrinology of Aging Volume 11 - 2020

Testosterone and insulin resistance in the metabolic syndrome and T2DM in men

- Testosterone deficiency is highly prevalent in men with the metabolic syndrome and type 2 diabetes mellitus
- Low levels of testosterone are an independent risk factor that predicts subsequent development of the metabolic syndrome and type 2 diabetes mellitus
- Population studies in community-dwelling men have shown that testosterone deficiency is associated with increased all-cause mortality and cardiovascular mortality
- The hypogonadal–obesity–adipocytokine hypothesis summarises the complex interaction of the above components and their contribution to the vicious cycle of obesity causing hypogonadism and vice versa
- Interventional studies of testosterone replacement therapy have shown improvements in insulin resistance, body composition, glycaemic control, lipid metabolism and other cardiovascular risk factors
- The benefit of testosterone on insulin sensitivity might be attributable to a complex regulatory influence on insulin signalling and glucose homeostasis in the major insulin-responsive target tissues

Testosterone and insulin resistance in the metabolic syndrome and T2DM in men. Preethi M. Rao, Daniel M. Kelly & T. Hugh Jones. *Nature Reviews Endocrinology* volume 9, pages479–493 Published: 25 June 2013

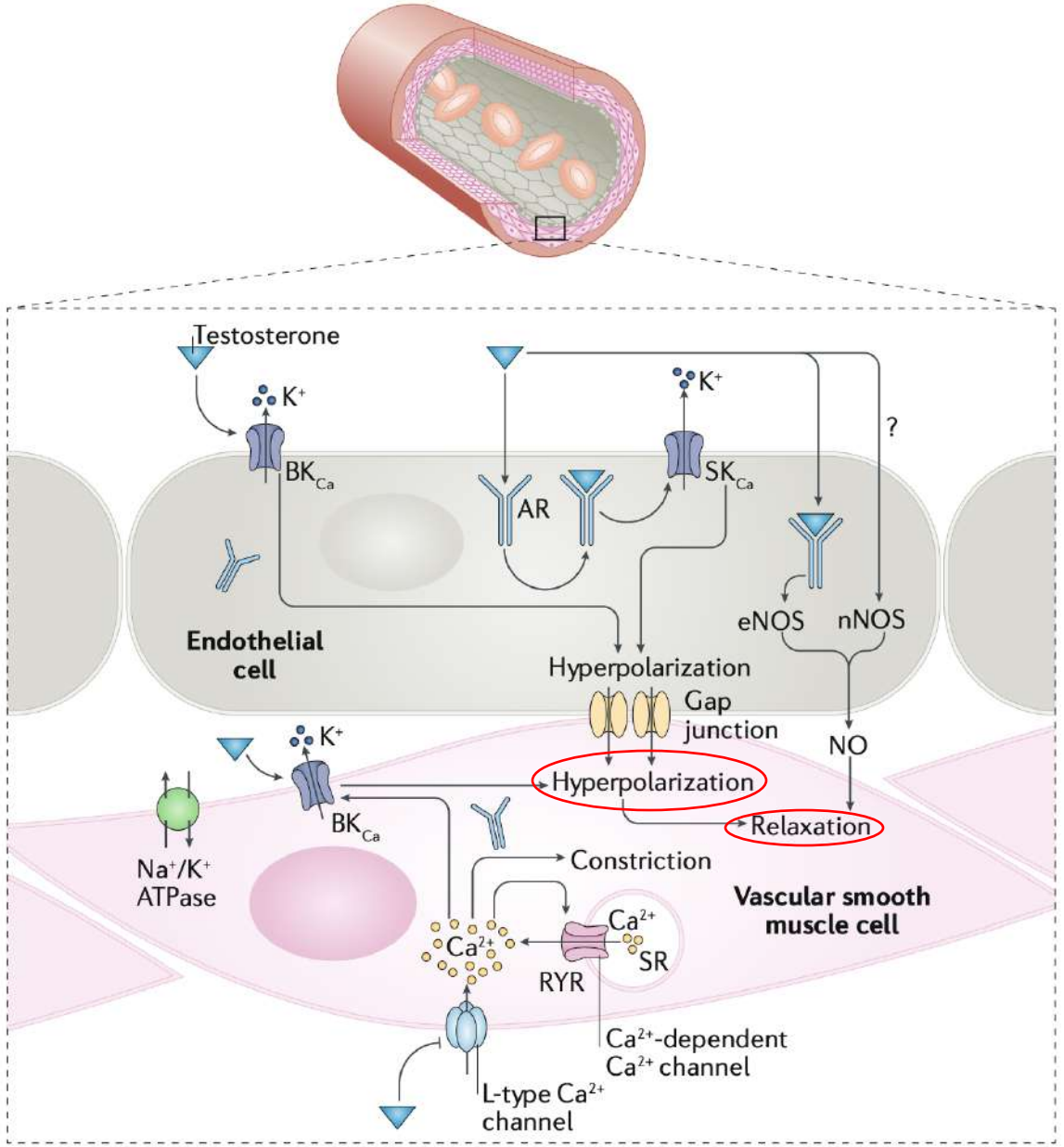
Potential actions of testosterone treatment on insulin-sensitive tissues



Glucose Homeostasis, Diabetes Mellitus, and Gender-Affirming Treatment. Charalampos Milionis, Ioannis Ilias , Evangelia Venaki and Eftychia Koukkou. *Biomedicines* 2023, *11*(3), 670; Published: 22 February 2023

Molecular mechanisms of testosterone modulation of vascular tone

- Testosterone has effects in both vascular endothelial cells and vascular smooth muscle cells, which together produce changes in vascular tone.
- Testosterone relaxes the vascular smooth muscle by inhibiting the L-type calcium current through voltagedependent L-type calcium channel subunit α1C (Cav1.2), independently of the vascular endothelium or the androgen receptor (AR).
- Testosterone also induces vascular smooth muscle relaxation via the opening of big-conductance calcium-activated and voltage-activated potassium channels (BKCa) in vascular smooth muscle cell as well as in endothelial cells.
- In addition, testosterone induces nitric oxide (NO) synthesis in the endothelial cell by endothelial nitric oxide synthase (eNOS) via an AR-dependent, nontranscriptional mechanism; neuronal nitric oxide synthase (nNOS) in the endothelium might also contribute to the testosterone-induced increase in endothelial NO synthesis.
- Involvement of small-conductance calcium-activated potassium channels (SKCa) in addition to BKCa in the endothelium-dependent vasodilatory effects of testosterone has also been suggested. RYR, ryanodine receptor; SR, sarcoplasmic reticulum



Nature Reviews Cardiology volume 16, pages555–574 (2019)

RESEARCH SUMMARY

Cardiovascular Safety of Testosterone-Replacement Therapy

Lincoff AM et al. DOI: 10.1056/NEJMoa2215025

CLINICAL PROBLEM

The cardiovascular effects of testosterone-replacement therapy in middle-aged and older men with hypogonadism have not been determined. Studies have yielded conflicting results or have been of inadequate size or duration.

CLINICAL TRIAL

Design: A phase 4, multicenter, double-blind, randomized, placebo-controlled, noninferiority trial assessed the effects of testosterone-replacement therapy on the incidence of cardiovascular events among men with hypogonadism and established cardiovascular disease or an elevated cardiovascular risk.

Intervention: 5246 men who were 45 to 80 years of age with preexisting cardiovascular disease or an increased cardiovascular risk, at least one symptom of hypogonadism, and two fasting serum testosterone levels <300 ng per deciliter were assigned to receive either daily transdermal 1.62% testosterone gel (dose adjusted to maintain testosterone levels between 350 and 750 ng per deciliter) or placebo gel. The primary cardiovascular safety end point was the first occurrence of any component of a composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke, assessed in a time-to-event analysis.

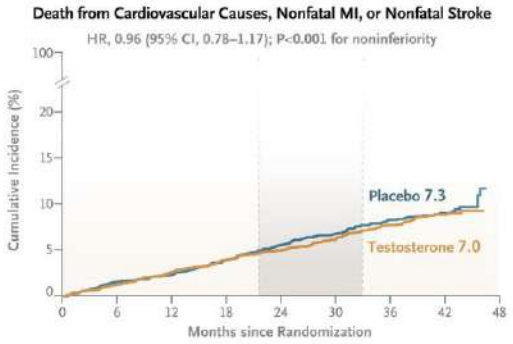
RESULTS

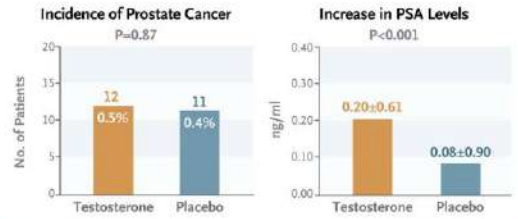
The mean duration of treatment was 22 months; the mean duration of follow-up was 33 months. Testosterone-replacement therapy was noninferior to placebo with respect to the incidence of major adverse cardiac events. The incidence of prostate cancer was similar in the two groups. The increase in prostate-specific antigen levels from baseline was greater in patients in the testosterone group than in those in the placebo group.

LIMITATIONS

- Levels of adherence and retention were lower in this trial than in most cardiovascular outcome studies; the effect of nonretention in particular is difficult to quantify, and bias due to informative censoring is possible.

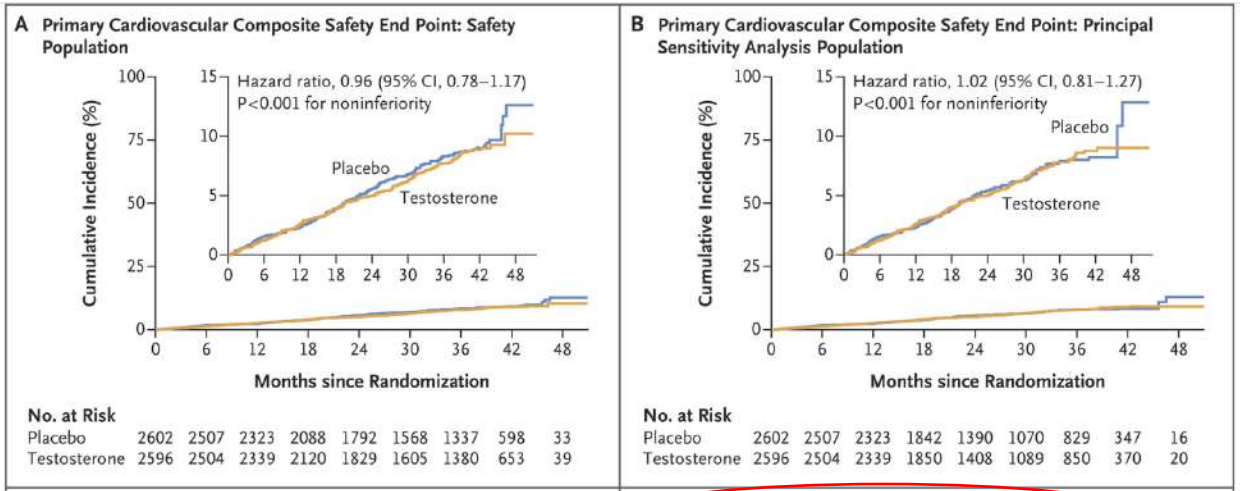
Links: Full Article | NEJM Quick Take | Editorial

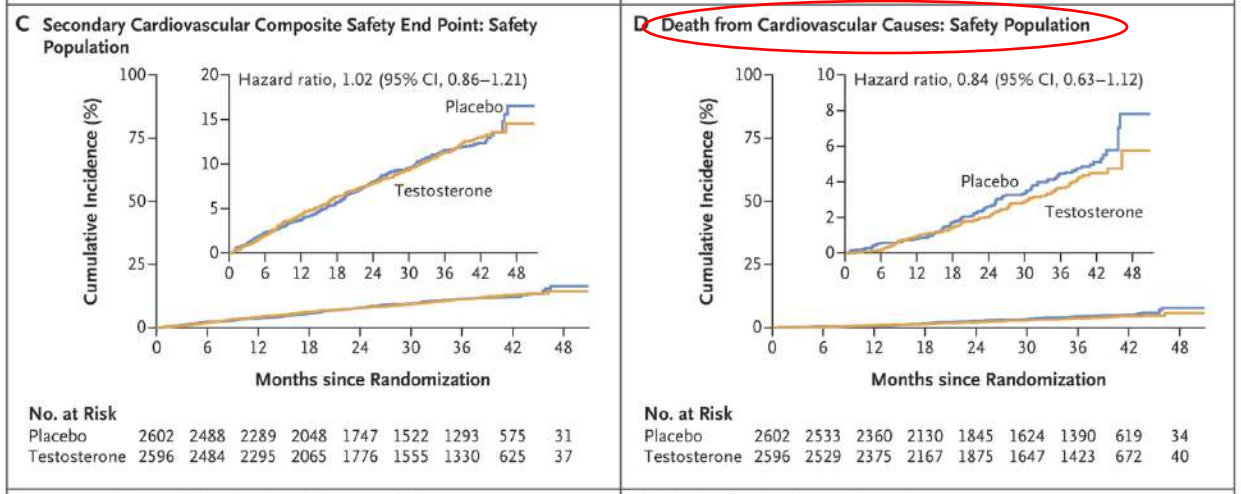


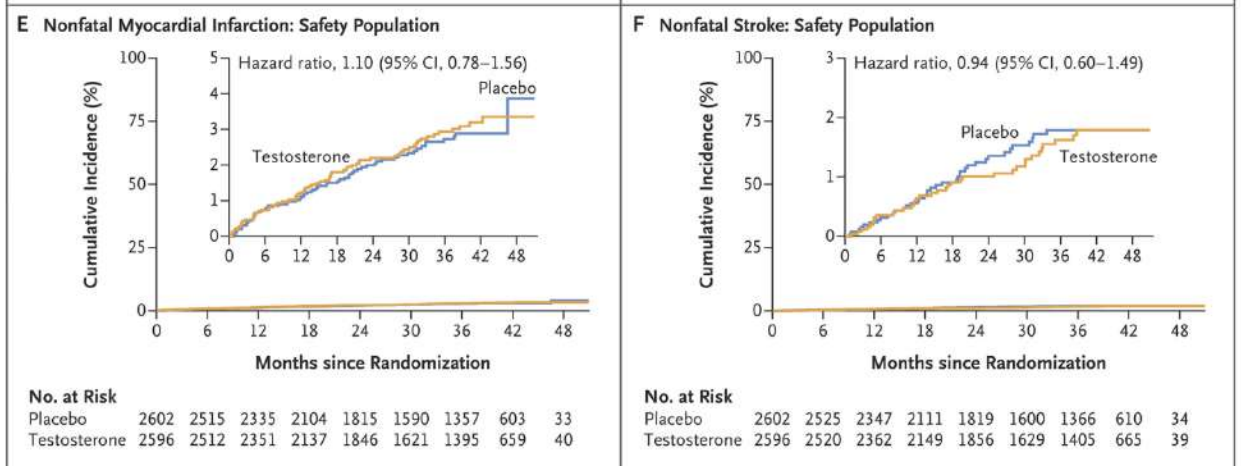


CONCLUSIONS

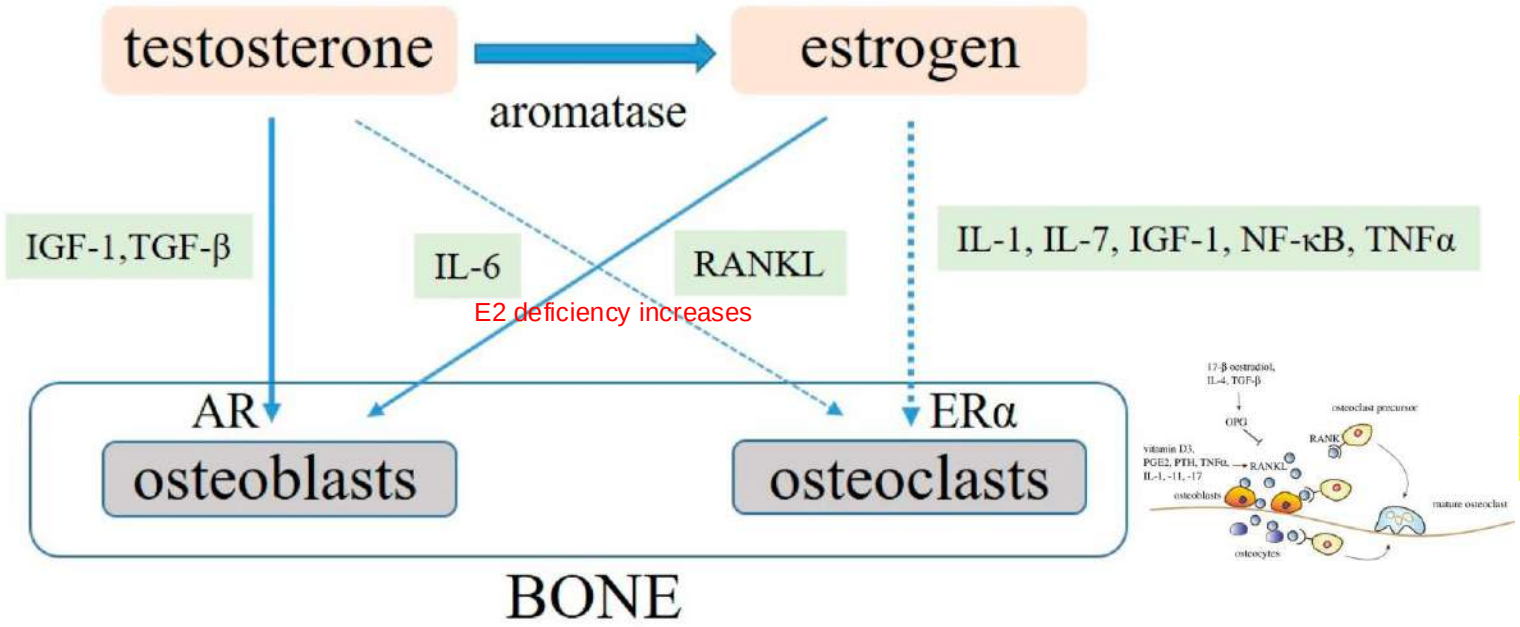
In middle-aged and older men with hypogonadism and preexisting cardiovascular disease or an increased cardiovascular risk, daily treatment with transdermal testosterone for approximately 2 years was noninferior to placebo with respect to the incidence of major adverse cardiac events.







Molecular rules of testosterone and estrogen in bone metabolism



AR is present in chondrocytes and osteoblasts, although its expression level widely varies by age and bone sites.

Testosterone acts directly on osteoblasts by AR and can consequently promote bone formation.

In addition, testosterone has some indirect effects on bone metabolism through various cytokines and growth factors.

Furthermore, testosterone can increase AR expression level in osteoblasts, resulting in differentiation promotion and osteoblast and chondrocyte apoptosis proliferation.

E2 and ERα also play important roles in maintaining BMD in men and women.

Estrogen has a greater effect than androgen in inhibiting bone resorption in men.

Consequently, men with loss of ERα function exhibit extremely low BMD.

Male patients with aromatase deficiency have a marked decrease in BMD in trabecular and cortical bone.

E2 generally regulates apoptosis and function of osteoclast, which contributes to BMD maintenance.

IL-1, IL-6, IL-7, IGF-1, nuclear factor-κB (NF-κB), RANKL, and tumor necrotic factor-α (TNFα) are the E2 target genes.

However, E2 deficiency increases IL-6, which reduces osteoblast proliferation and activity while increasing osteoclastic activity and increasing the expression of RANKL-mediated osteoclastogenesis.

Testosterone and Bone Health in Men: A Narrative Review. Kazuyoshi Shigehara, Kouji Izumi, Yoshifumi Kadono, Atsushi Mizokami. *J. Clin. Med.* 2021, *10*(3), 530; https://doi.org/10.3390/jcm10030530

Low serum testosterone is associated with tumor aggressiveness and poor prognosis in prostate cancer

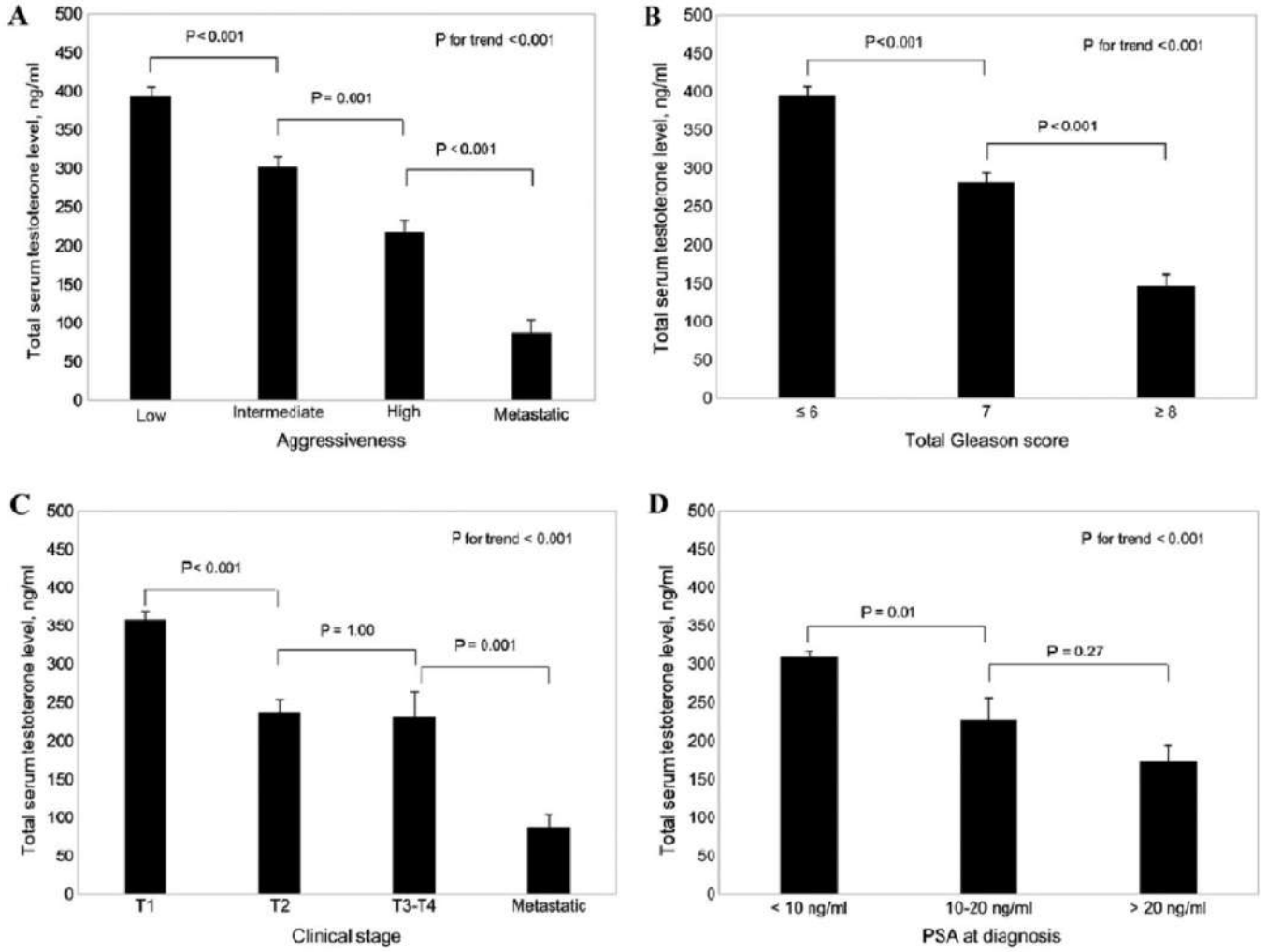


Figure 1. Association bet we en total serum testo sterone levels in patients with prostate cancer and (A) tumor aggressiveness, (B) total Gleason score, (C) clinical stage of tumor and (D) PSA levels at diagnosis. Results are presented as the mean ± standard error. PSA, prostate-specific antigen.

HUAKANG TU, XIFENG WU ans All. **ONCOLOGY LETTERS Received April 14, 2016; Accepted November 1, 2016. DOI: 10.3892/ol.2017.5616**

Low serum testosterone is associated with tumor aggressiveness and poor prognosis in prostate cancer

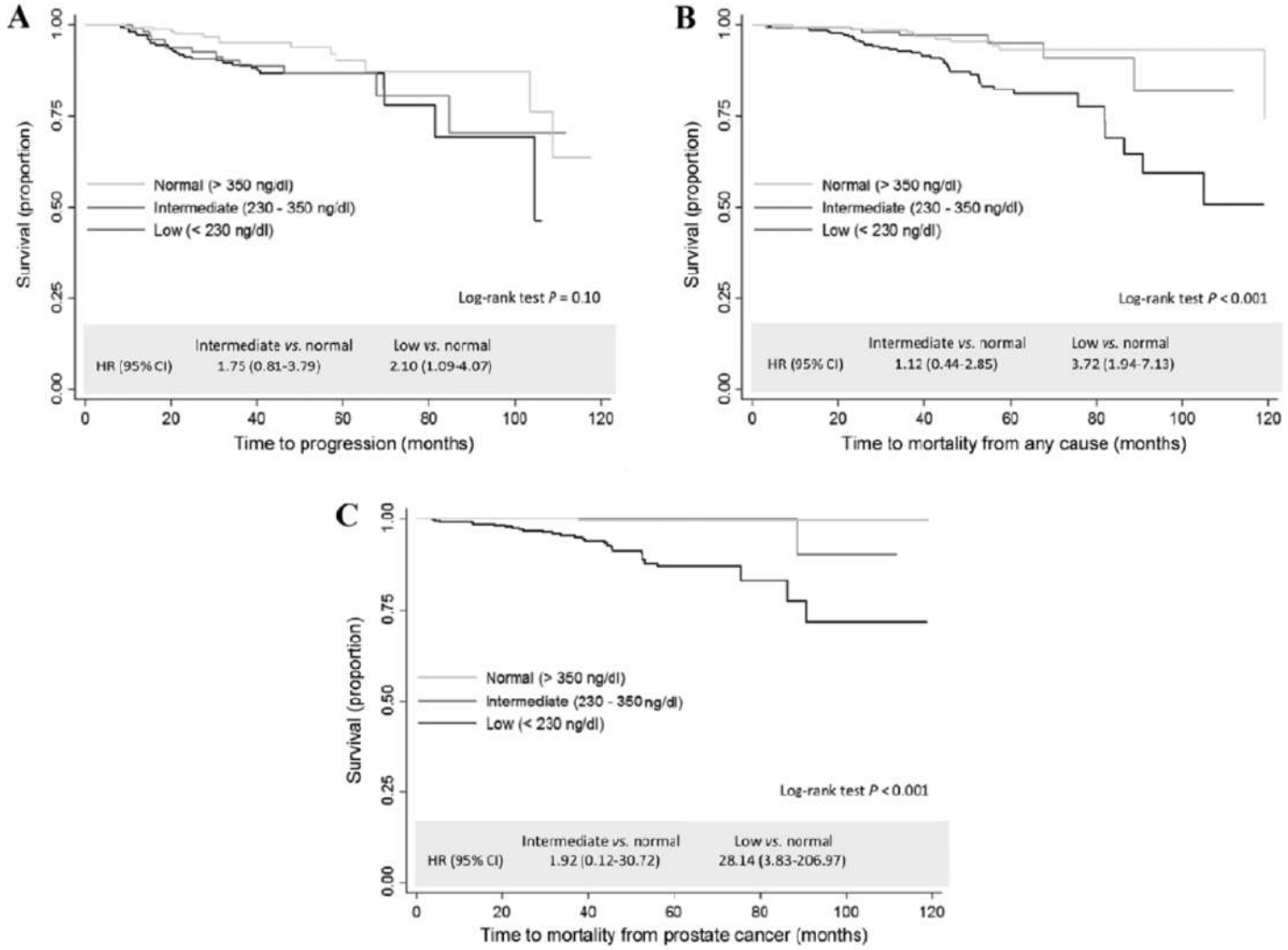


Figure 4. Unadjusted Kaplan-Meier estimator survival curves and HRs for the association between total serum testosterone levels and (A) disease progression, (B) mortality from all causes and (C) mortality due to prostate cancer. HR, hazard ratio; CI, confidence interval.

HUAKANG TU, XIFENG WU ans All. **ONCOLOGY LETTERS Received April 14, 2016; Accepted November 1, 2016. DOI: 10.3892/ol.2017.5616**

Testosterone treatment is not associated with increased risk of prostate cancer or worsening of lower urinary tract symptoms: prostate health outcomes in the Registry of Hypogonadism in Men

Frans M J Debruyne [1], Hermann M Behre [2], Claus G Roehrborn [3], Mario Maggi [4], Frederick C W Wu [5], Fritz H Schröder [6], Thomas Hugh Jones [7], Hartmut Porst [8], Geoffrey Hackett [9], Olivia A Wheaton [10], Antonio Martin-Morales [11], Eric Meuleman [12], Glenn R Cunningham [13], Hozefa A Divan [10], Raymond C Rosen [10]; RHYME Investigators

Collaborators, Affiliations + expand

PMID: 27409523 DOI: 10.1111/bju.13578

Conclusions
In this longitudinal disease registry of 999 hypogonadal men in 6 European countries, no evidence was seen of increased PCa rates or LUTS/BPH progression in men receiving TRT compared to untreated hypogonadal men in our cohort. PCa incidence rates in RHYME were similar to rates reported in large population studies and with findings from other single country or single product registries. PSA was minimally affected and slight improvements in voiding symptoms were observed in our study in men on TRT. These findings warrant confirmation in further long-term, registries or randomized trials.

Abstract

Objectives: To evaluate the effects of testosterone-replacement therapy (TRT) on prostate health indicators in hypogonadal men, including rates of prostate cancer diagnoses, changes in prostate-specific antigen (PSA) levels and lower urinary tract symptoms (LUTS) over time.

Patients and methods: The Registry of Hypogonadism in Men (RHYME) is a multi-national patient registry of treated and untreated, newly-diagnosed hypogonadal men (n = 999). Follow-up assessments were performed at 3-6, 12, 24, and 36 months. Baseline and follow-up data collection included medical history, physical examination, blood sampling, and patient questionnaires. Prostate biopsies underwent blinded independent adjudication for the presence and severity of prostate cancer; PSA and testosterone levels were measured via local and central laboratory assays; and LUTS severity was assessed via the International Prostate Symptom Score (IPSS). Incidence rates per 100 000 person-years were calculated. Longitudinal mixed models were used to assess effects of testosterone on PSA levels and IPSS.

Results: Of the 999 men with clinically diagnosed hypogonadism (HG), 750 (75%) initiated TRT, contributing 23 900 person-months of exposure. The mean testosterone levels increased from 8.3 to 15.4 nmol/L in treated men, compared to only a slight increase from 9.4 to 11.3 nmol/L in untreated men. In all, 55 biopsies were performed for suspected prostate cancer, and 12 non-cancer related biopsies were performed for other reasons. Overall, the proportion of positive biopsies was nearly identical in men on TRT (37.5%) compared to those not on TRT (37.0%) over the course of the study. There were no differences in PSA levels, total IPSS, or the IPSS obstructive sub-scale score by TRT status. Lower IPSS irritative sub-scale scores were reported in treated compared to untreated men.

Conclusions: Results support prostate safety of TRT in newly diagnosed men with HG.

Keywords: #PCSM; #ProstateCancer; benign prostatic hyperplasia; disease registry; hypogonadism; testosterone.

BJU Int. 2017 Feb;119(2):216-224. doi: 10.1111/bju.13578. Epub 2016 Aug 14

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World J Mens Health. 2020 Jan; 38(1): 132–136.
Published online 2019 May 2. doi: 10.5534/wjmh.180130
PMCID: PMC6920078
PMID: 31081296

Testosterone Replacement Therapy for Patients with Hypogonadism after High Dose-Rate Brachytherapy for High-Risk Prostate Cancer: A Report of Six Cases and Literature Review

Suguru Kadomoto, Kazuyoshi Shigehara,✉ Hiroaki Iwamoto, Hiroshi Yaegashi, Kouji Izumi, Yoshifumi Kadono, and Atsushi Mizokami

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Abstract

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We had six cases of patients who were treated with long-term testosterone replacement therapy (TRT) after high dose-rate (HDR) brachytherapy and androgen deprivation therapy for high-risk prostate cancer. All patients were given testosterone enanthate by intramuscular injection every 3 to 4 weeks. Blood biochemistry including prostate specific antigen (PSA) level was evaluated every 3 to 6 months after TRT, and radiological imaging was performed every 12 months. All patients had slight increases in PSA within the normal range and not indicative of biochemical recurrence. A sudden increase in PSA was observed in one patient, but it finally decreased. Aging male symptoms scale and various metabolic factors were improved by TRT in all of cases. Although adverse events included polycythemia in one patient, no patients experienced disease recurrence or progression during TRT. Our results suggest TRT for high risk-patients with HDR brachytherapy for prostate cancer may be beneficial and safe.

Keywords: Hypogonadism, Prostatic neoplasms, Safety, Testosterone

Testosterone Therapy in Men on Active Surveillance

Tristan Chun, Jacob Tannenbaum, Haley Watts, Igor Voznesensky, Wael Almajed, and Wayne J.G. Hellstrom

Published Online: 22 Dec 2022 | https://doi.org/10.1089/andro.2022.0004

Abstract

In recent decades, although prostate cancer (PCa) mortality has dramatically decreased, addressing the quality of life for PCa survivors has become an area of great interest. This is especially important among men who are enrolled in active surveillance (AS) to manage their PCa. Since men with PCa are likely to experience erectile dysfunction, decreased libido, and loss of lean muscle mass secondary to testosterone deficiency (TD) as a consequence of antitumor therapies or advanced age, testosterone therapy (TTh) is typically the indicated treatment to alleviate the symptoms of TD. However, due to the theoretical causal relationship of increased testosterone levels leading to PCa development, the usage of TTh in men who have been diagnosed with PCa has long been the subject of debate. As there is an increased number of men with PCa who are enrolling in AS for the management of PCa, there needs to be an evaluation of the safety and efficacy of TTh in this cohort. Recently, the previous relationship between TTh and PCa has been challenged, and emerging evidence suggests that TTh may not be directly associated with PCa development or progression. Instead, TTh usage may safely improve the quality of life for those men on AS. This review summarizes and analyzes the latest findings on the use of TTh in men on AS for PCa.

Urologic Oncology: Seminars and Original Investigations
Volume 38, Issue 8, August 2020, Pages 661-670

Clinical-Prostate cancer

Testosterone replacement therapy (TRT) and prostate cancer: An updated systematic review with a focus on previous or active localized prostate cancer

Louis Lenfant M.D. [a 1], Priscilla Leon M.D. [b c 1], Géraldine Cancel-Tassin Ph.D. [c d], Marie Audouin M.D. [c], Frédéric Staerman M.D. [e], Morgan Rouprêt M.D., Ph.D. [c d a], Olivier Cussenot M.D., Ph.D. [c d]

Abstract

Often contraindicated because of the theoretical risk of progression based on the dogma of hormone dependent prostate cancer (CaP), testosterone replacement therapy (TRT) is increasingly discussed and proposed for hypogonadal patients with localized CaP. To perform a systematic literature review to determine the relationship between TRT and the risk of CaP with a focus on the impact of TRT in the setting of previous or active localized CaP. As of October 15, 2019, systematic review was performed via Medline Embase and Cochrane databases in accordance with the PRISMA guidelines. All full text articles in English published from January 1994 to February 2018 were included. Articles were considered if they reported about the relationship between total testosterone or bioavailable testosterone and CaP. Emphasis was given to prospective studies, series with observational data and randomized controlled trials. Articles about the safety of the testosterone therapy were categorized by type of CaP management (active surveillance or curative treatment by radical prostatectomy, external radiotherapy or brachytherapy). Until more definitive data becomes available, clinicians wishing to treat their hypogonadal patients with localized CaP with TRT should inform them of the lack of evidence regarding the safety of long-term treatment for the risk of CaP progression. However, in patients without known CaP, the evidence seems sufficient to think that androgen therapy does not increase the risk of subsequent discovery of CaP.

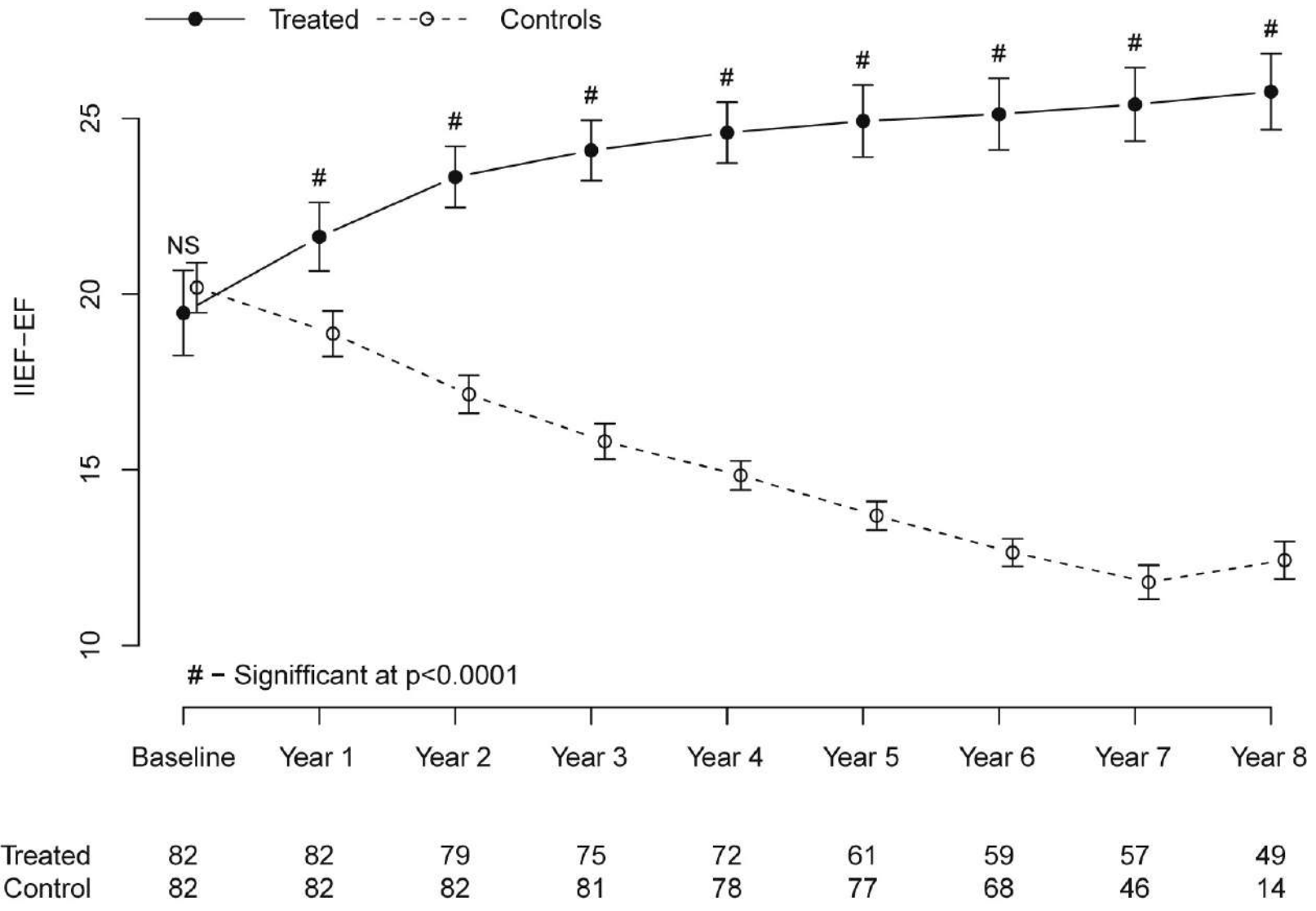
The use of 5 alpha reductase inhibitors reduces the risk of CaP

Five alpha reductase inhibitor (5 ARI), are enzymes that convert testosterone into its active metabolite, dihydrotestosterone (DHT). This treatment provides a selective form of androgen deprivation by severely reducing intracellular concentrations of DHT. Using these 5 ARI for 3 to 12 months would reduce, but to a lesser extent than castration, the prostate-specific antigen (PSA level) (approximately 50%) and prostatic volume (by one-third) [7]. The CaP Prevention Trial showed that compared to…

Conclusion

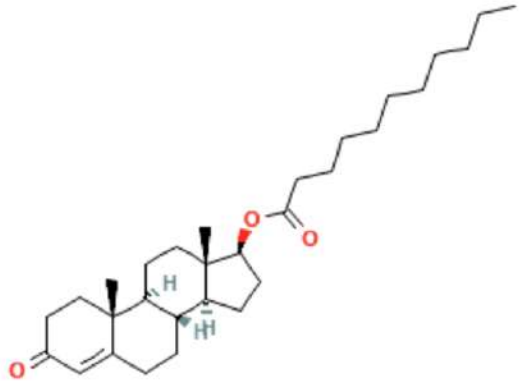
For patients without known CaP, evidence seems sufficient to suggest that androgen therapy does not increase the risk of subsequent CaP discovery. Although no controlled studies to date have been conducted to document the safety of androgen therapy in men with CaP, the available evidence suggests that such treatment does not increase the risk of recurrence or progression of CaP. The risk of CaP recurrence after administration of testosterone is likely to be lower in patients whose initial…

The primary outcome of the Sexual Function



Changes in IIEF-EF score in testeosterone-treated and untreated propensity-matched groups during 8-year follow-up period. IIEF-EF = International Index of Erectile Function erectile function domain. From Haider KS, Haider A, Doros G, et al. Long-term testosterone therapy improves urinary and sexual function and quality of life in men with hypogonadism: results from a propensity-matched subgroup of a controlled registry study. J Urol https://doi.org/10.1016/j.juro 2017.07.039.

Benefits and Health Implications of Testosterone Therapy in Men With Testosterone Deficiency. Abdulmaged M. Traish PhD. Sexual Medicine ReviewsVolume 6, Issue 1, January 2018, Pages 86-105



Natural T is rapidly inactivated by first-pass hepatic metabolism, making oral therapy an ineffective means of delivering unmodified T.

Esterification at carbon 17-beta yields T undecanoate, preferentially absorbed into the lymphatic system when taken orally, and hydrolysed in vivo to yield native T.

The efficacy of oral T undecanoate is limited because of unreliable oral bioavailability, fluctuating serum levels and short half-life, necessitating 3-4 40-mg capsules daily for full TRT taken with meals to improve absorption.

Reported gastrointestinal and liver adverse effect precluded the marketing of oral T undecanoate for TRT in the USA.

Other oral T derivatives include 17-alpha-methyltestosterone and fluoxymesterolone, which are associated with hepatotoxicity and have disappeared from the market in Europe.

The patches are available in 2 or 4 mg/d formulations. The recommended starting dose is one 4 mg/d patch every 24 hours applied nightly to the back, abdomen, upper arms or thighs.37 Sites should be rotated and not re-used for 7 days. Two weeks after initiation of therapy, a serum T level should be measured (early morning after patch application the night before). Levels < 400 ng/dL require a dose escalation to 6 mg/d, while levels > 930 ng/dL should require a dose reduction to 2 mg/d.

A 2% T gel comes in a metered-dose dispenser that includes a hands-free cap applicator for precise dispensing and application. This avoids exposure to the hands, which minimizes the risk of *transfer*
Based on serum T levels, the dose can be increased in 25 mg increments up to 100 mg of T daily. The 1.62% concentration is also available in a metered-dose pump and unit-dose packets in the USA market only. The metered-dose pump provides 20.25 mg of T per actuation, while the unit-dose packets contain either 20.25 mg/1.25 g or 40.5 mg/2.5 g of T. The recommended starting dose of 1.62% gel is 40.5 mg applied topically once daily in the morning. Serum T levels should be measured 14 and 28 days after initiation prior to the morning dose

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Testosterone enanthate

TE is available in 100, 200 mg/mL or 250 mg/mL prepared in sesame oil.

For both groups, levels plateaued below the therapeutic range (300 ng/dL) by week 3 and week 4, respectively.

The authors concluded that the TE doses of 200 mg have to be injected every two weeks or doses of 300 mg every 3 weeks to guarantee effective substitution therapy.

TE-associated adverse events are similar to those of TC. The short-acting IM injections have the highest incidence of erythrocytosis approaching 40% It is suggested that T formulation, dose and pharmacokinetics collectively determine the risk of erythrocytosis by establishing the duration of supraphysiological T levels.

Short-acting IM T formulations (TE) are associated with the most rapid and significant increases in serum T levels, with supraphysiological T levels achieved within days of an injection and a return to baseline by 10-14 days, followed by a decrease to subphysiological levels within 3 weeks if not re-dosed.

Caution should be exercised in prescribing short-acting IM formulations in at-risk populations (T2DM, smokers, obese, thrombophilic conditions)

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- Clinicians must consider the unique characteristics of each patient and make the necessary adjustments in the management of LOH in order to provide the safest and most beneficial results.
- Different formulations of T are available for replacement therapy to relieve symptoms and signs of androgen deficiency in men with LOH.
- T therapy is associated with multiple benefits highly relevant to the patient including amelioration of sexual function, depressive mood, muscle function, anaemia, vertebral and femoral BMD, and body composition.
- The recommendations given in different guidelines on TRT are based on data from a limited number of RCTs, as well as on non-randomized clinical studies and on observational studies. This is the case for the safety of a long-term TRT in LOH. No evidence is provided indeed on the effects of TRT on endpoints such as deterioration of heart failure suggesting a cautious approach to T replacement in older men with a history of heart failure.
- The TRAVERSE trial, the first trial of testosterone therapy that is adequately powered to assess cardiovascular events, began in 2018, and its findings might take a decade to become available.
- Clinicians must consider the unique characteristics of each patient and make the necessary adjustments in the management of LOH in order to provide the safest and most beneficial results

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