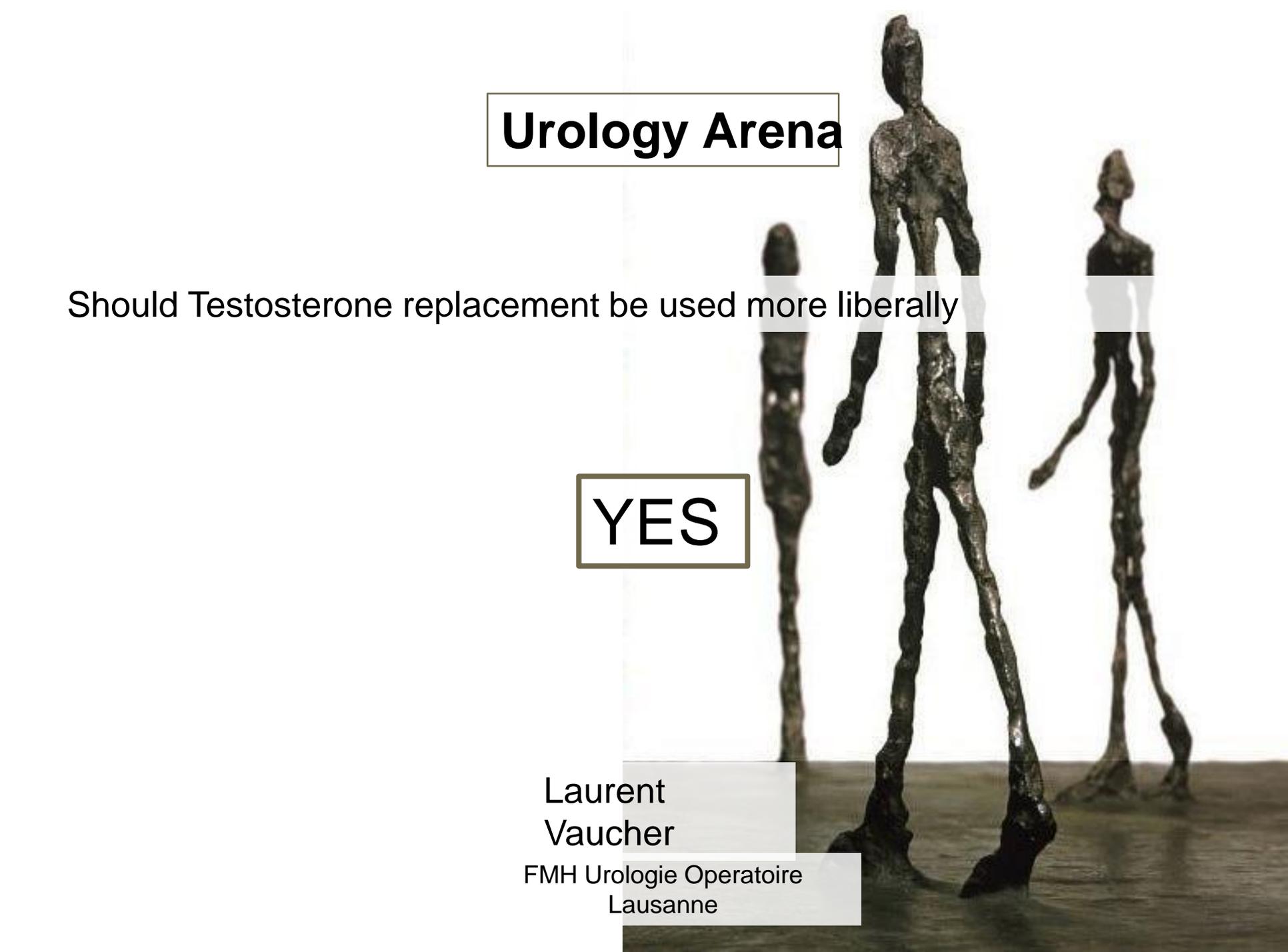


Urology Arena

The background of the slide features three bronze sculptures of human figures. The figures are extremely thin and elongated, with long, spindly legs and thin torsos. They are standing on a dark, reflective surface. The central figure is the tallest and most prominent, flanked by two shorter figures. The overall aesthetic is that of a modern art installation.

Should Testosterone replacement be used more liberally

YES

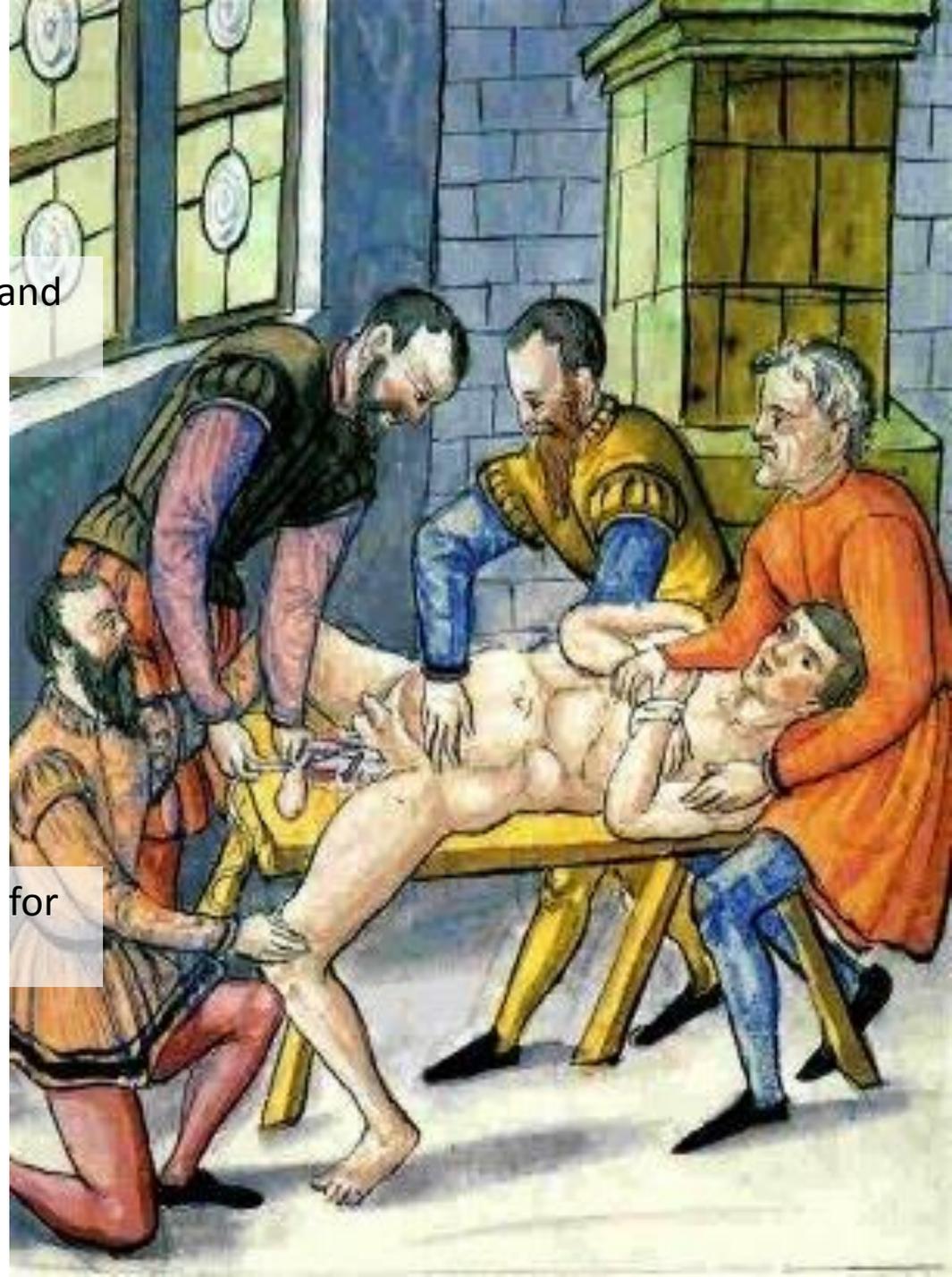
Laurent
Vaucher

FMH Urologie Operatoire
Lausanne

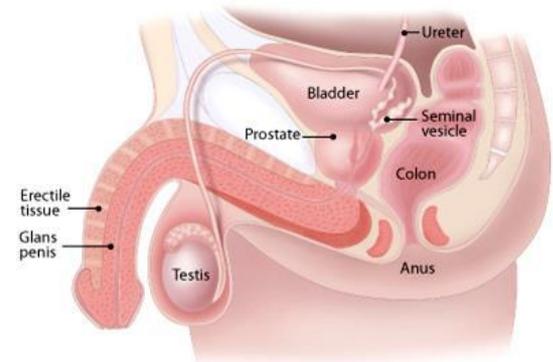
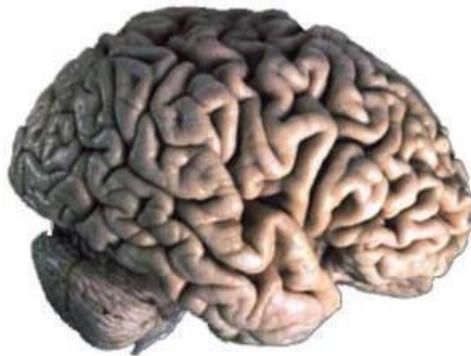
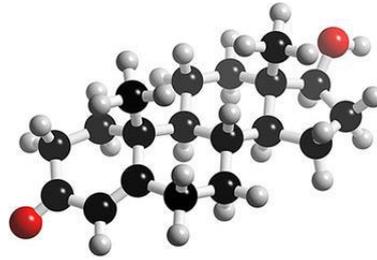
Male Factor, responsible for strength and
« manhood »

200 AC: Castration for sex crimes

8th century: Chinese use testis extract for
treatment of impotence



TESTOSTERONE



- Sex Drive

- Mood disorder

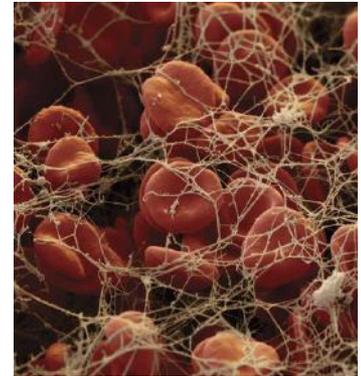
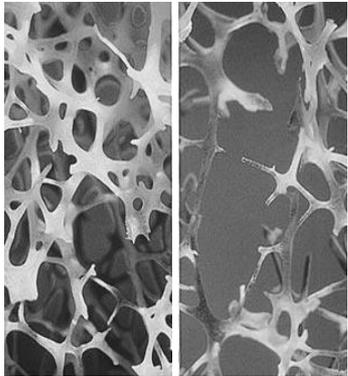
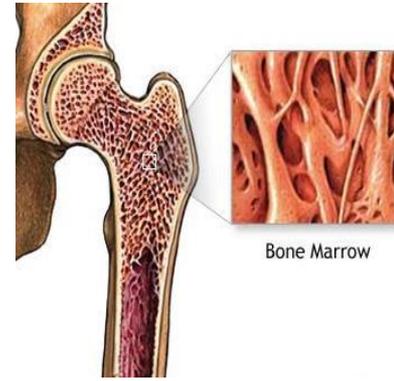
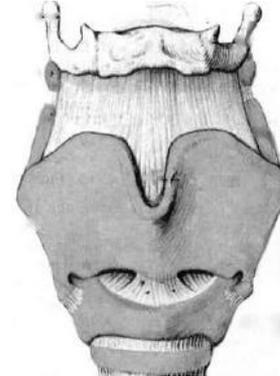
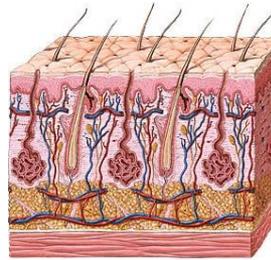
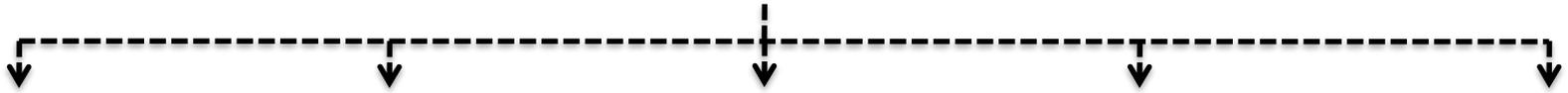
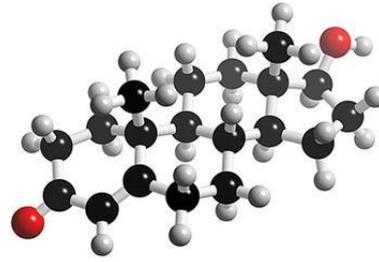
- (Cognitive function)

- Prostate, Seminal vesicles

- Fertility

- Erectile and ejaculatory function

TESTOSTERONE

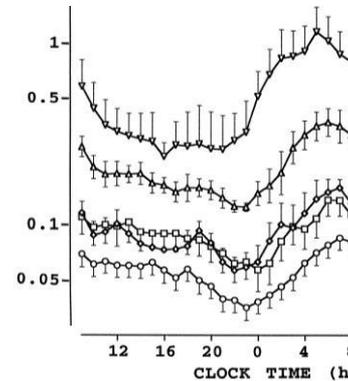


Immunoassay vs Mass spectrometric methods

Daily variation: 35%

Individual variation: 10%

1-6% Variability



Basaria S, Lancet 2014 383; 1250

Morning total serum testosterone value:

- Post castration: < 1 nmol/l
- Physiological: 12-30 nmol/l
- hypogonadic: 1-8 nmol/l
- supra-physiological: >30 nmol/l

No clear cut threshold

TD symptoms and signs become more likely with decreasing T levels.

Consensus



International Society of Andrology
International Society for Study of Aging Male
European Association of Urology
European Association of Andrology
American Society of Andrology

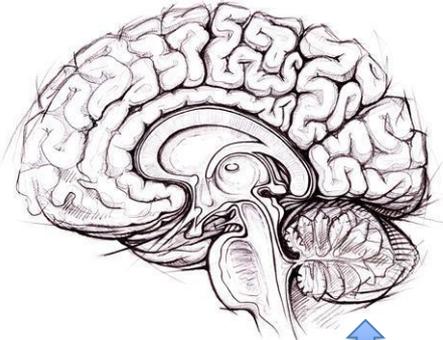
>12 nmol/l
< 8 nmol/l

No Substitution
Substitution

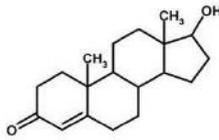
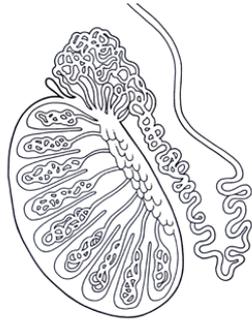
Primary hypogonadism

Classical Hypogonadism

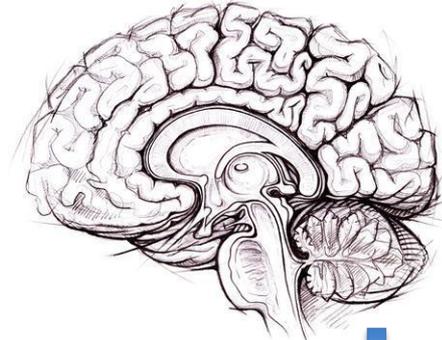
Secondary Hypogonadism



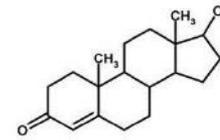
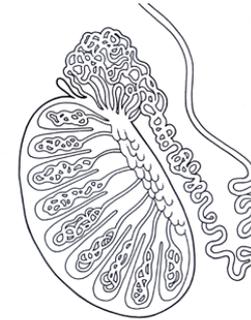
LH, FSH ↑



Toxic
Trauma
Cryptorchidism
Klinefelter...



LH, FSH ↓



Kallmann Syndrom
Hyperprolactinemia
Traitement (steroid, opiate)
Pituitary lesion

Age related
Testosterone
Deficiency Syndrome

Age related Testosterone Deficiency Syndrome

Serum total T decreases after the age of 55 years by 1–2% per year

- Leydig cell decrease
- Arterial Sclerosis and testis volume
- Alteration in neuroendocrine regulation
LH Pulsatility, \downarrow GnRH)
- SHBG \nearrow (1.2% per year)

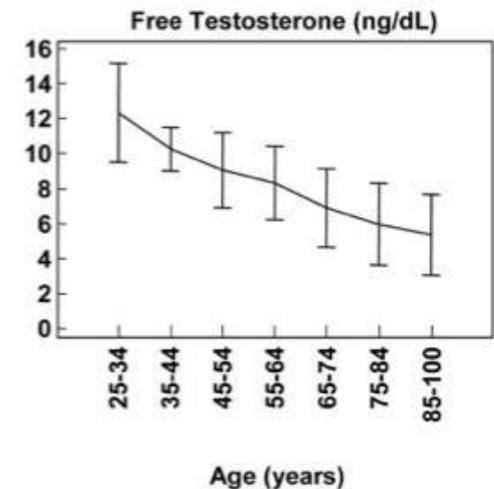
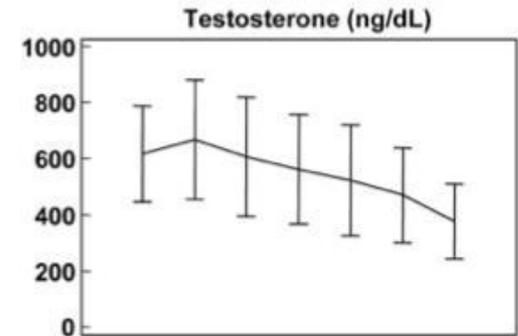
Treatment: Steroids, opiate, neuroleptics

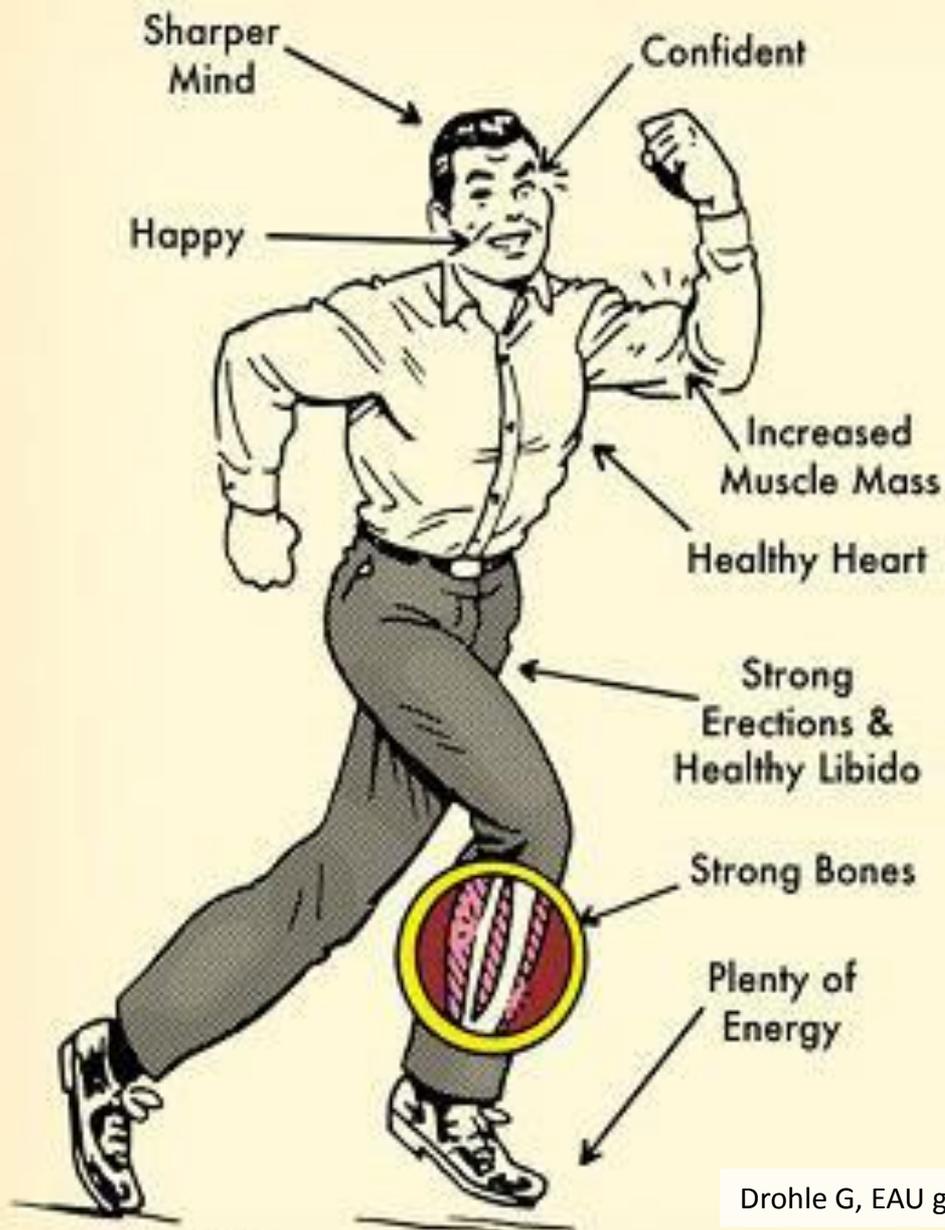
Pathologies: Obesity , Diabetes, \downarrow kidney function ...

Feldman HA, JCI 2002,87;589

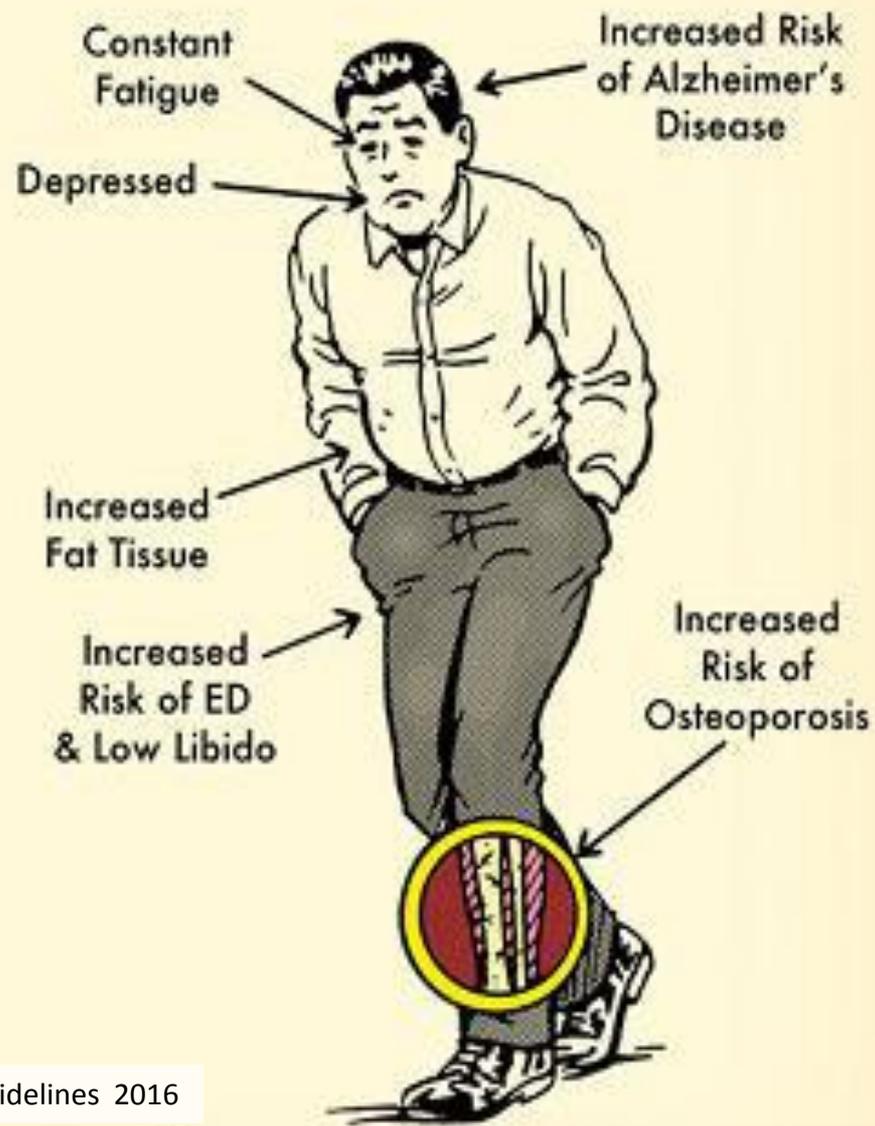
Slow decrease \neq menopause

GH + IGF-1 decrease





Man with Optimal Testosterone



Man with Deficient Testosterone

Drohle G, EAU guidelines 2016

TDS = Testosterone deficiency syndrome

Well established medical condition that negatively impacts male sexuality, general health and quality of life



☞ Combination of

Symptoms

T concentration ≤ 11 nmol/l/L

Rosenthal B. Urology 2006 67: 571

Prevalence of Low serum Testosterone:

Total serum testosterone < 11 nmol/ml **38.7%** male > 45 ans

Mulligan T, Int J Clin Pract 2006 60: 762

Prevalence of testosterone deficiency syndrome

Low serum Testosterone

Libido ↘ +

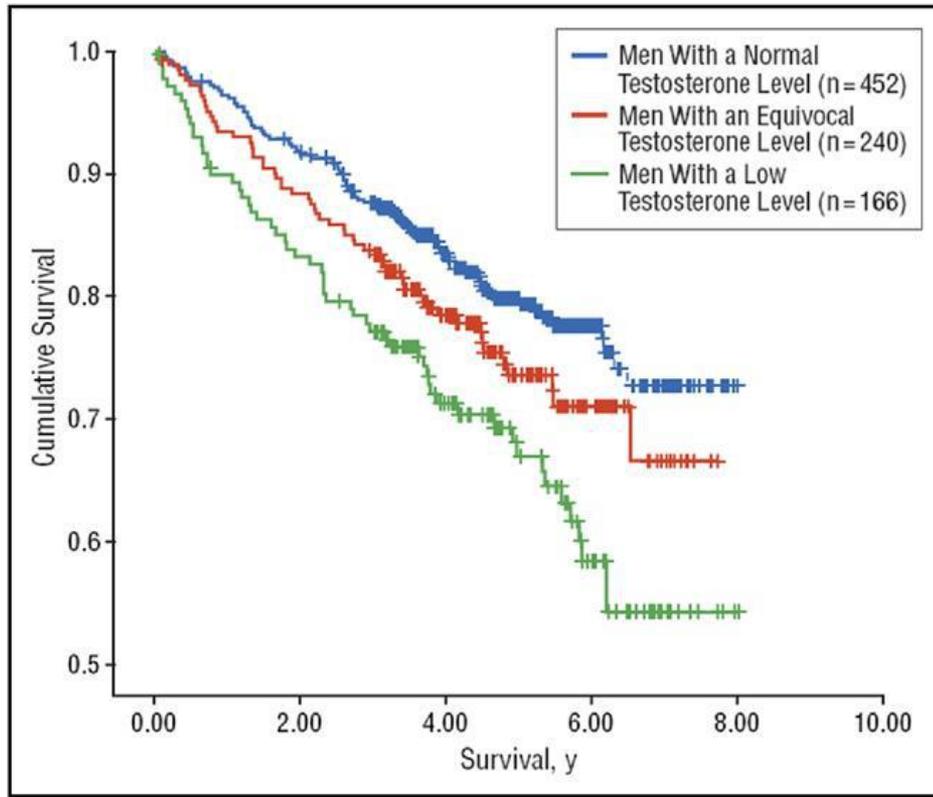
ED

Bone mineral density ↘

2-4 % men 39 – 70 years

18.7% men > 70 years

Araujo AB, JCEM, 2007, 92:4241



The Rancho Bernardo study longitudinal study 794 men, aged 50-91 years, average follow-up 11.8 years, but up to 20 years)

Associations between T levels and all-cause and cardiovascular death in general populations of men aged 40 years old

Laughlin GA, *J Clin Endocrinol Metab.* 2008;93: 68-75.

Only 12% of T-deficient men, defined by the combination of symptoms and T concentrations of less than 11 nmol/L received T therapy despite adequate access to medical care

Hall SA, *Arch Intern Med.* 2008;168(10):1070

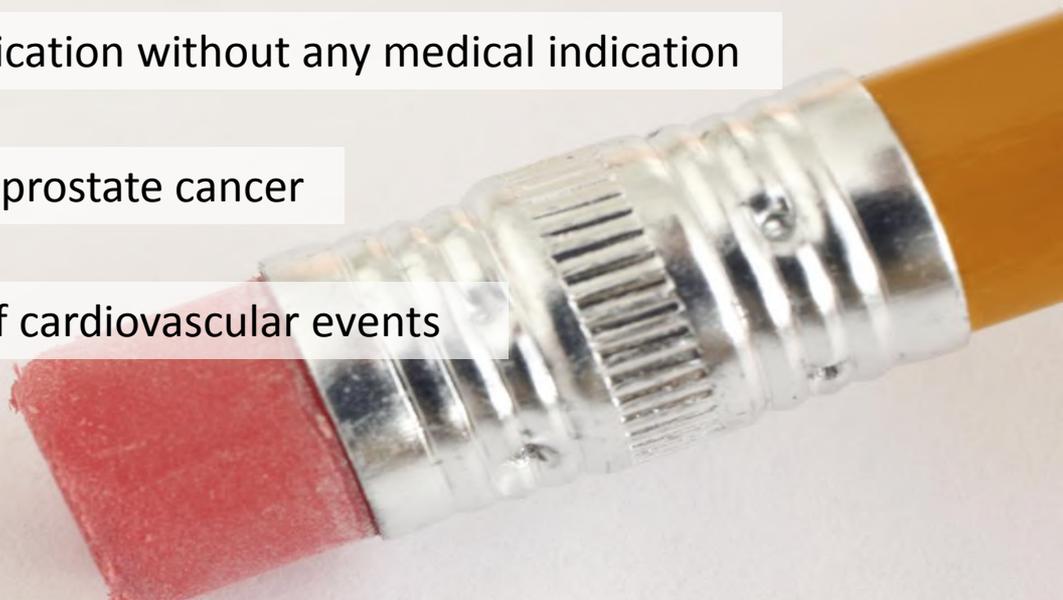
Major factors for not prescribing testosterone treatment

Testosterone is a well being medication without any medical indication

Testosterone increase the risk of prostate cancer

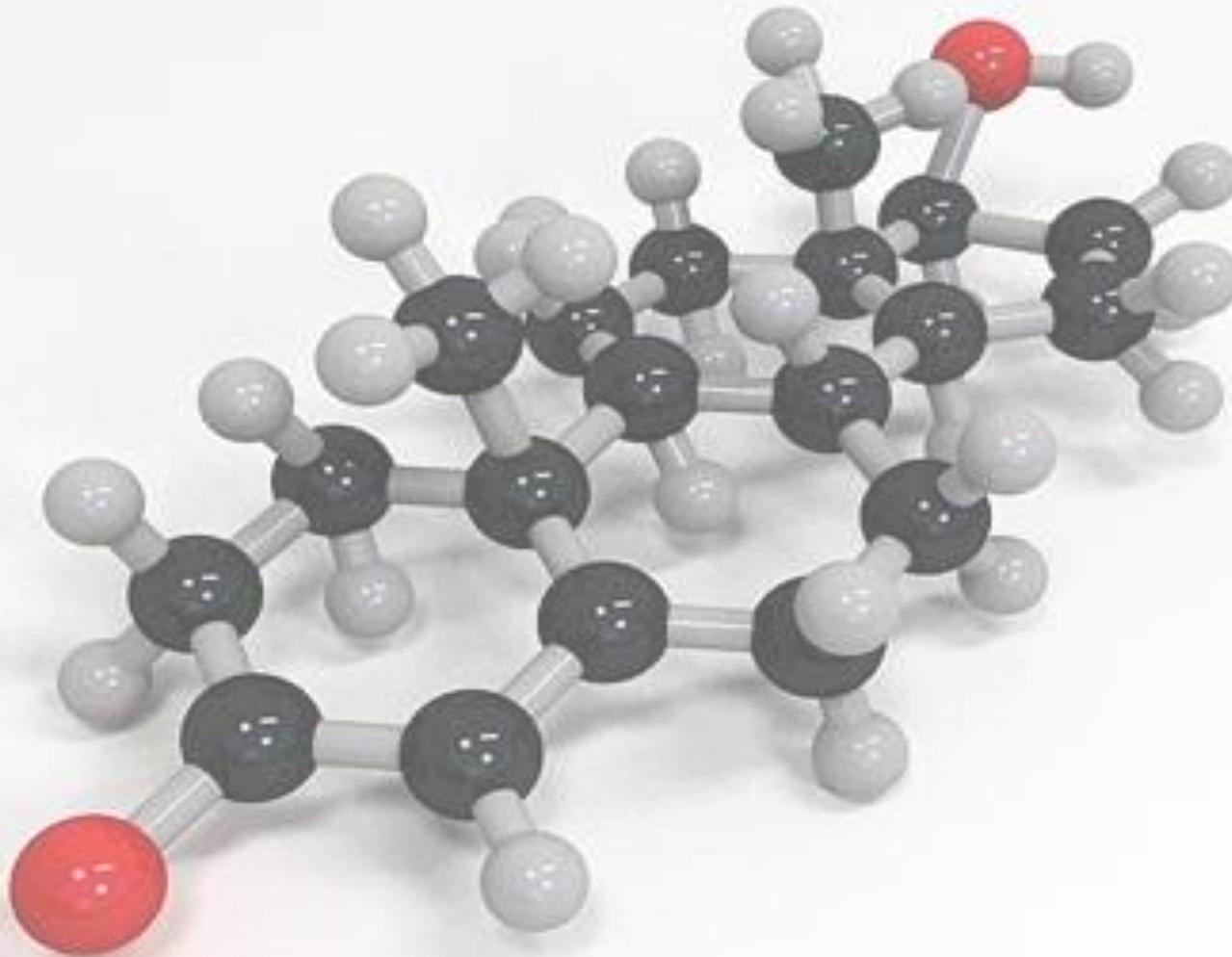
Testosterone increase the risks of cardiovascular events

Giving testosterone is risky



FEAR

T therapy for men with TD is effective, rational, and evidence based



The goal of TT is to restore T levels to normal physiological ranges and to reverse the physiological effects of hypogonadism

High level of evidence shows that Testosterone treatment effectively

Increase sex desire (libido) and erectile function

Metaanalysis 29 RCT, 1930 participants

Corona G, et al. J Sex Med. 2014;11(6):1577

Increase lean body mass

Decrease fat mass

Metaanalysis 59 RT, 5078 participants

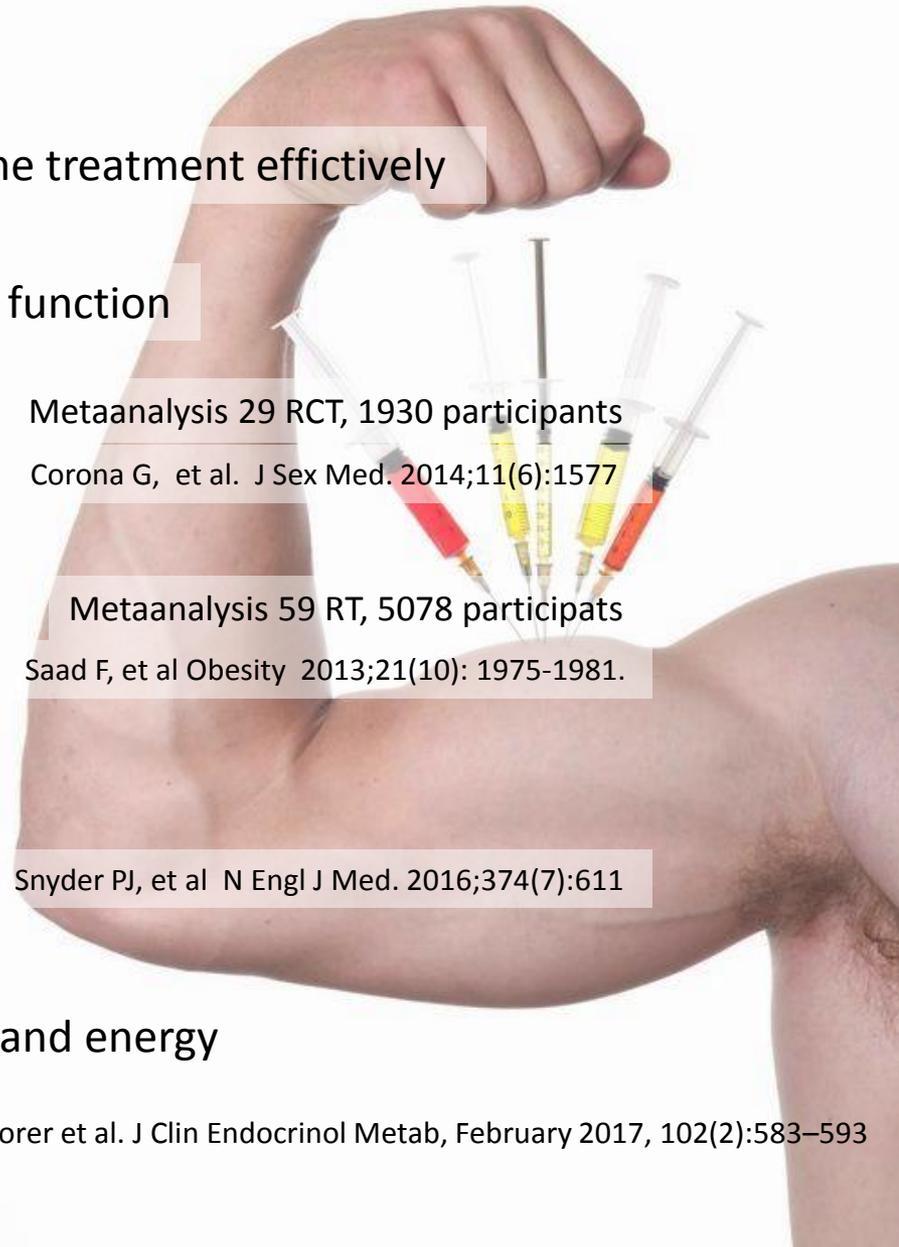
Saad F, et al Obesity 2013;21(10): 1975-1981.

Improve bone mineral density

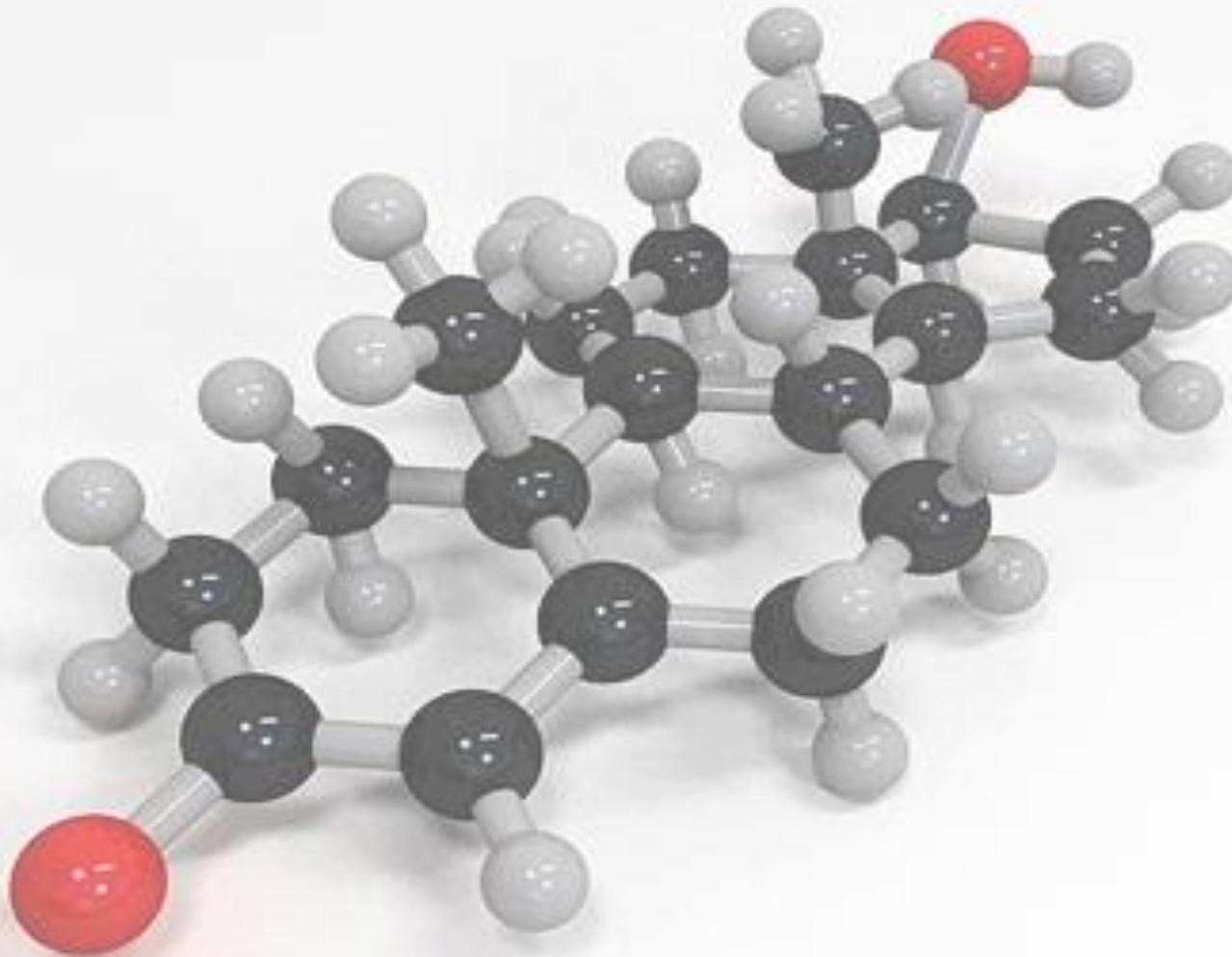
Snyder PJ, et al N Engl J Med. 2016;374(7):611

Strongly suggest improvement in mood and energy

T Storer et al. J Clin Endocrinol Metab, February 2017, 102(2):583–593



The evidence does not support increased risk of PCa with T therapy



Greatest concern of physicians with regard to T therapy as potentially stimulating Pca



1941: Huggins & Hodges

Androgen deprivation



Regression of advanced prostate cancer

Huggins C, Cancer res 1941 1:293

High serum androgen concentrations are not associated with increased risk of PCa or aggressive PCa

3886 men with PCa

6438 age-matched controls



PCa risk

Serum concentrations of T
calculated free T
dihydrotestosterone

T therapy has no greater risk than placebo for development of PCa

Meta-analysis of 19 studies

no greater risk of PCa

men diagnosed with TD who received placebo

men diagnosed with TD who received T therapy

Calof OM, et al.. *J Gerontol A Biol Sci Med Sci.* 2005;60:1451-1457.

VOLUME 35 · NUMBER 13 · MAY 1, 2017

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT



Testosterone Replacement Therapy and Risk of Favorable and Aggressive Prostate Cancer

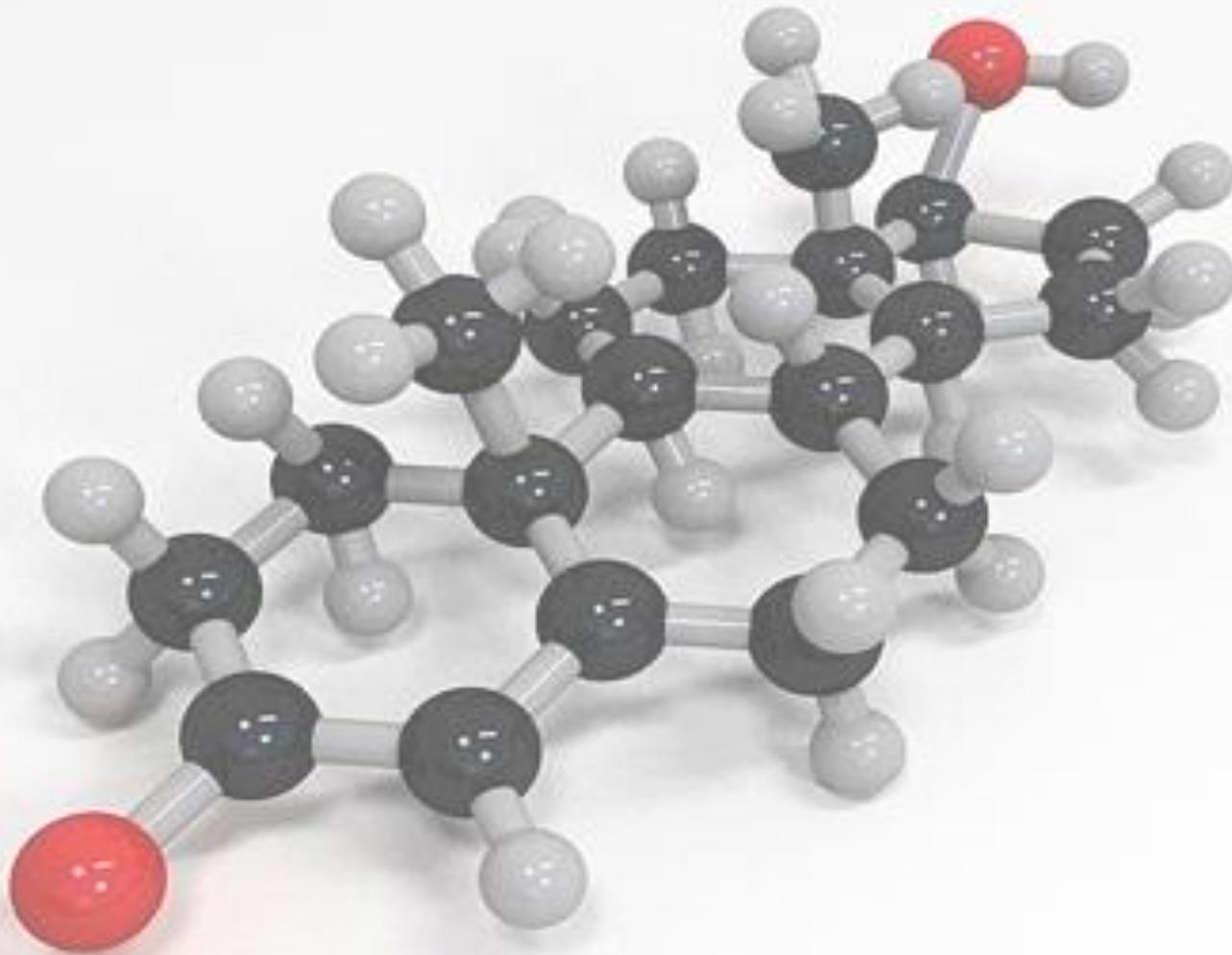
Stacy Loeb, Yasin Folkvaljon, Jan-Erik Damber, Joseph Alukal, Mats Lambe, and Pär Stattin

Loeb S et al, JCO 2017; 35 (13) 1430

Patients with TD who received TRT might a decrease in risk of aggressive prostate cancer

Evidence accumulated over the last 15 years strongly indicates that beyond the near-castrate range, there is no impact of serum T on PCa growth.

The evidence does not support increased risks of CV events with T therapy



Most epidemiological studies have suggested that low T is associated with increased atherosclerosis, coronary artery disease, obesity, diabetes, and mortality

There are controversies about the effects of TRT on CV events and mortality.

TOM Trial

Testosterone in Older Men With Mobility Limitations

RCT on Adverse events associated with testosterone administration

Effects of exogenous T gel or placebo on lower extremity strength in men 65 years and older who had baseline limited mobility and low total serum T levels

CV-related adverse events 23 men in the T group vs 5 in the placebo group

2 MI + Minor event (edema, ectopy on electrocardiogram [ECG], tachycardia with fatigue, carotid bruit, elevated blood

population of older, immobile men with a high prevalence of chronic conditions including pre- existing CV disease

Received very high doses of T



Observational studies reported increased CV risks with T therapy

Vigen R, et al. Association of testosterone therapy with mortality, myocardial infarction, and stroke in men with low testosterone levels [JAMA. 2013;310(17):1829-1836.

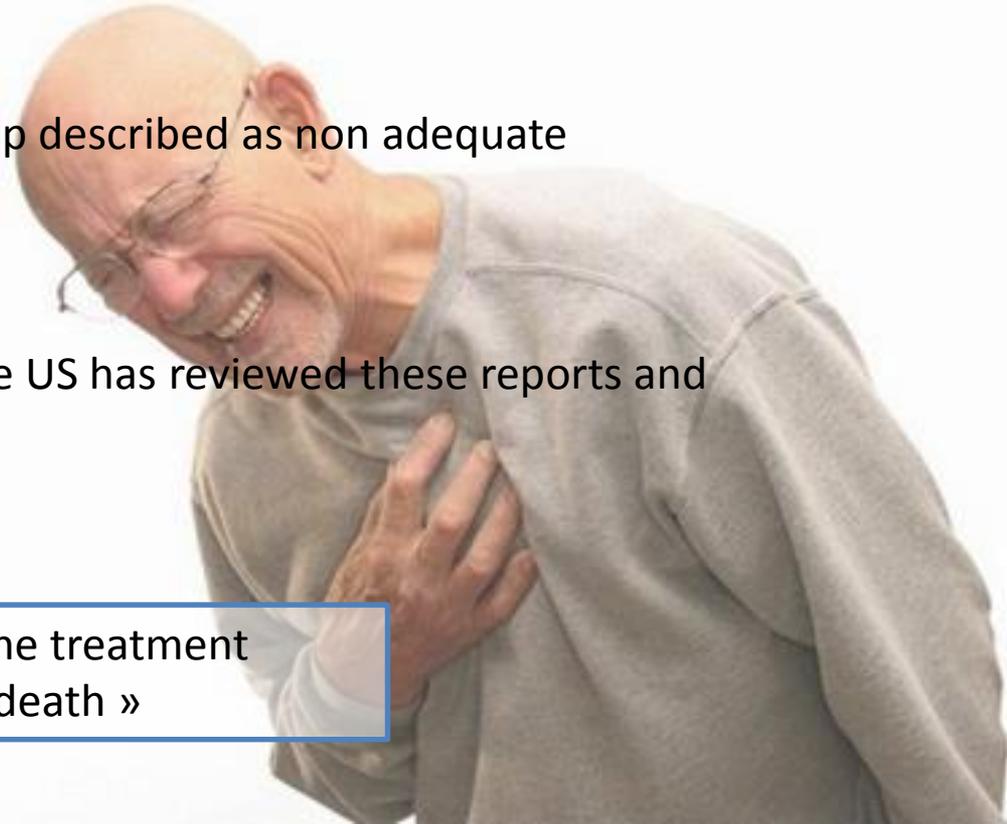
Raw data showed contrary than statistical analysis
investigators have printed some corrections to the study

Finkle WD, Greenland S, Ridgeway GK, et al. Increased risk of non-fatal myocardial infarction following testosterone therapy prescription in men. PLoS One. 2014;9(1):e85805.

3 month treatment, Follow up described as non adequate

the Food and Drug Administration in the US has reviewed these reports and found them to be seriously flawed.

« FDA can not conclude that Testosterone treatment increases risks of stoke, heart attack or death »



More than 100 studies have reported

- Reduced CV risk with physiological endogenous T concentration
- Improvement of known CV risk factors with T therapy
- Reduced mortality in T-deficient men who underwent T therapy compared with untreated men

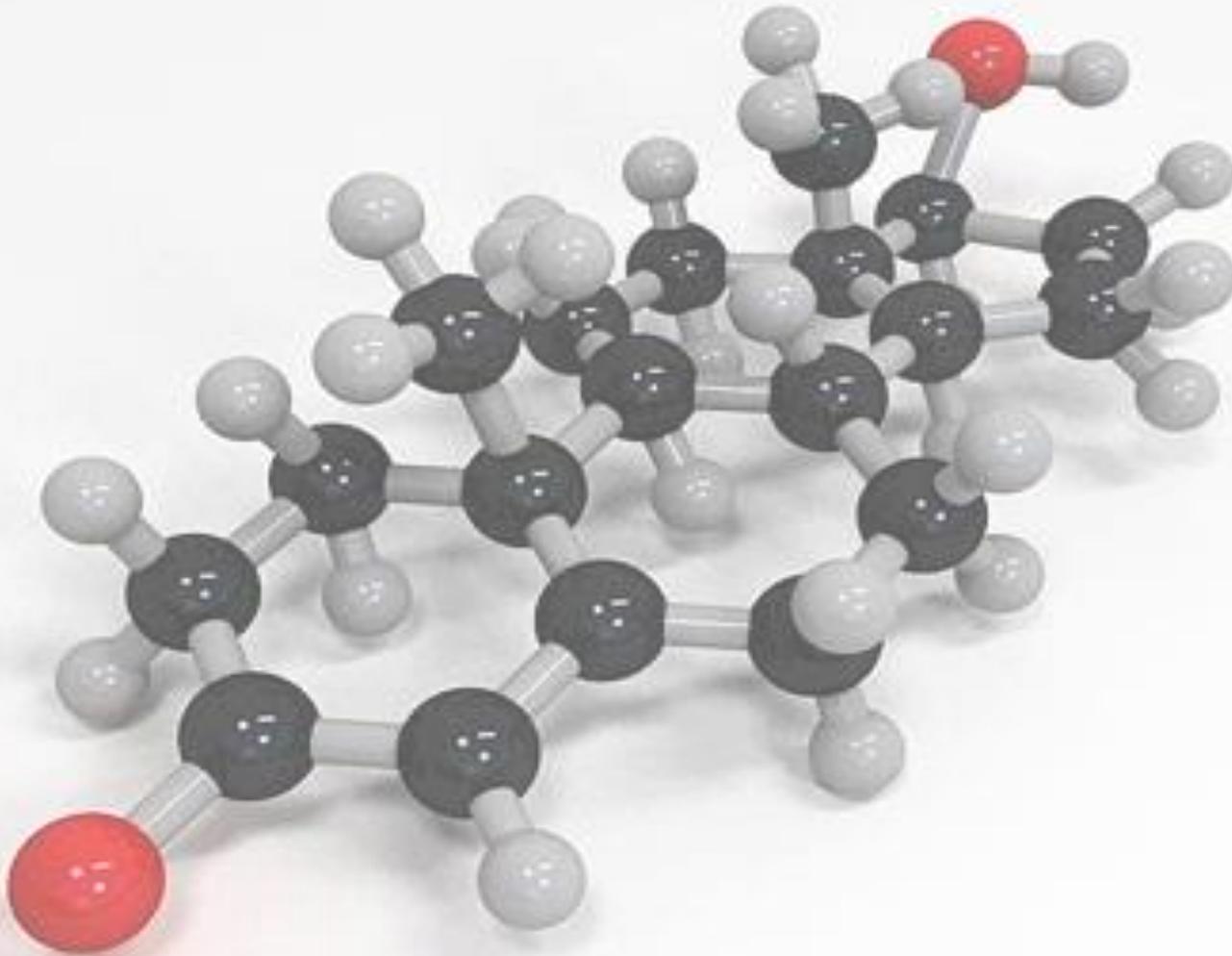
Corona G, et al Expert Opin Drug Saf. 2014; 13(10):1327
Shores MM, et al. J Clin Endocrinol Metab 2012;97:2050.
Layton JB, et al. JAMA Intern Med 2015;175: 1187

At the present time, the issue of the CV safety of T remains controversial

- The use of T in older men and those with known coronary artery disease is controversial
- Asymptomatic, middle-aged and older men without a history of heart disease should be counseled about the uncertain CV risk.

Large prospective, long-term study with a primary endpoint of adverse cardiovascular events is needed

Testosterone therapy does not represent major risk when used wisely



Known risks of Testosterone therapy include

Acne
Gynecomastia
Infertility
Decreased testicular volume
Erythrocytosis

Reversible with discontinuation of treatment



Evidence fails to support
-risks on Prostate Cancer
-increase CV risks in not High CV risk population

Testosterone Deficiency syndrome is a common and well established medical condition

Testosterone may improve significantly quality of life of some of your patients

When prescribed wisely, and with a shared decision, there are no major risks

APRIL 24, 2000 \$3.99 www.time.com AOL Keyword: TIME

COLUMBINE A YEAR LATER:
CAN YOU SPOT A KILLER KID?

STOCKS: IS THIS
DIP DIFFERENT?

TIME

TESTOSTERONE

It restores sex drive.
It boosts muscle mass.
And soon you can get it
as a gel. But it also
can be dangerous.
Is the edge worth it?