

Testosterone Deficiency in Men (Hypogonadism)

Men's Health Forum

November 18th, 2009

Richard Bebb MD ABIM FRCPC



Department of
UROLOGIC SCIENCES
UBC

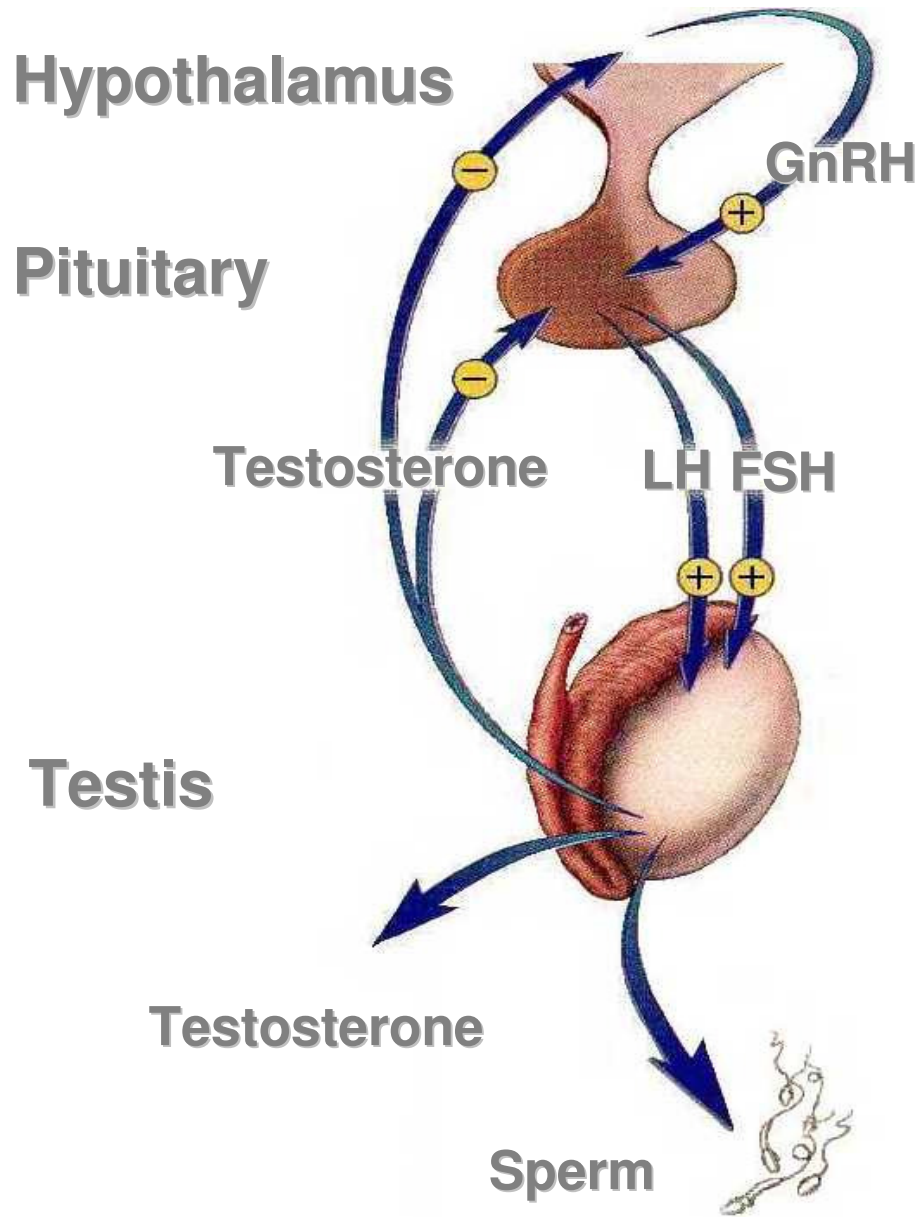


mensHEALTH
INITIATIVE OF BC

Vancouver
CoastalHealth
Promoting wellness. Ensuring care.

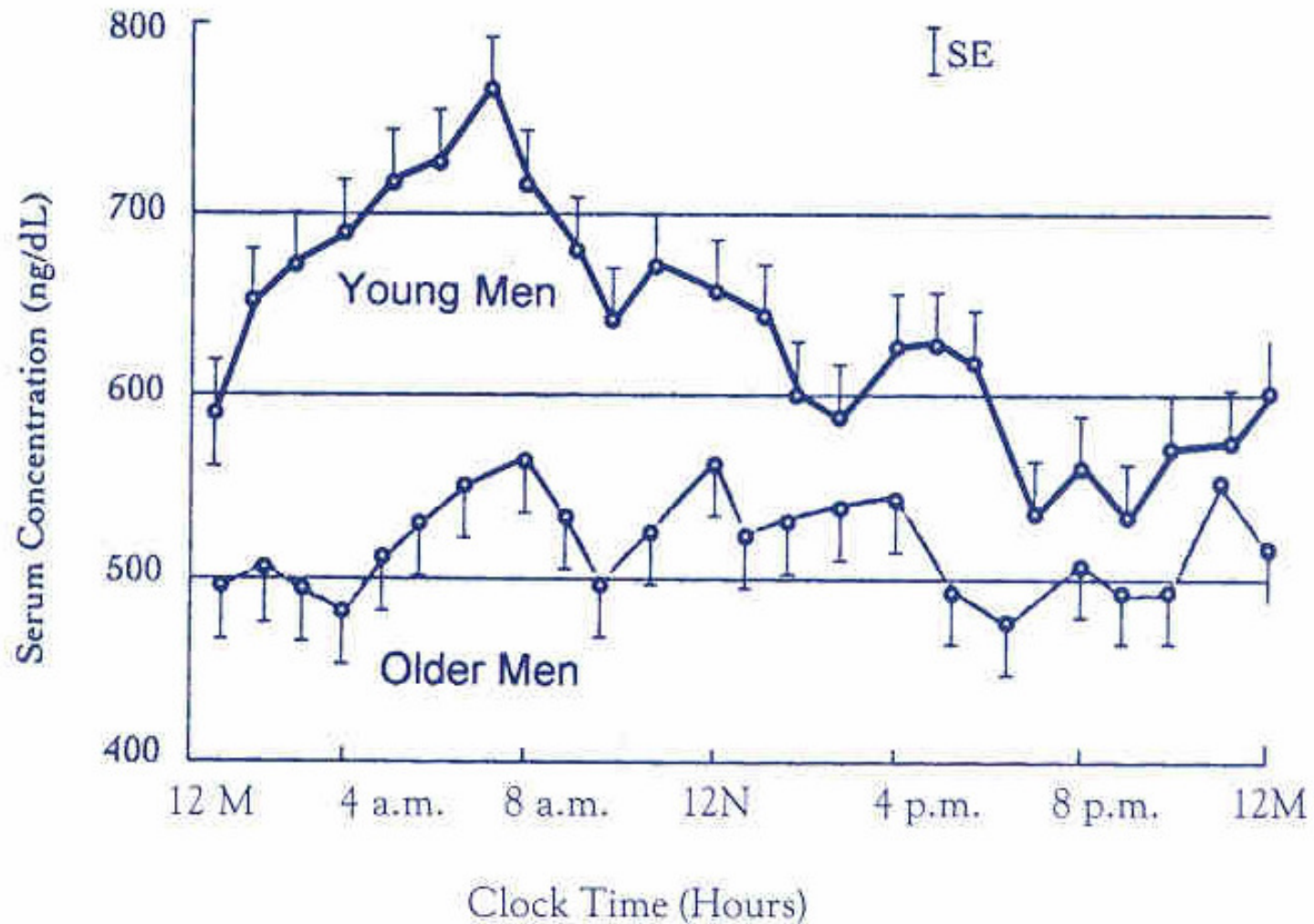


VGH&UBC
HOSPITAL FOUNDATION
*Advancing world-class health care
for people in British Columbia*



Adapted from Bagatell CJ, Bremner WJ. *N Engl J Med.* 1996;334:707-715.

Diurnal Cycle of Testosterone



ACTION SITES OF TESTOSTERONE

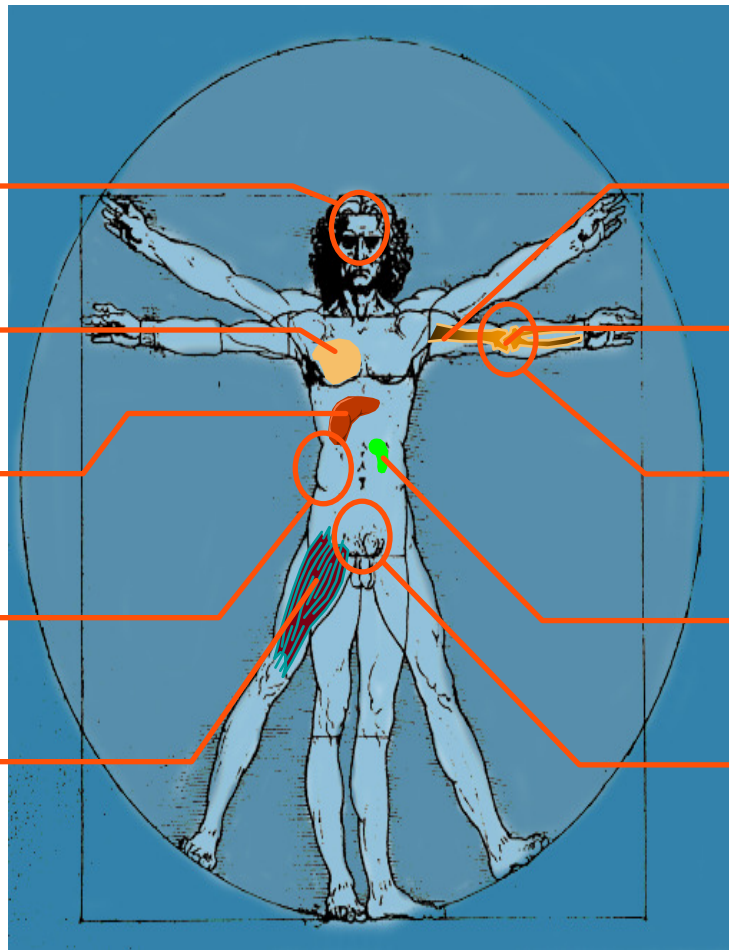
Brain:

Skin:
hair growth,
sebaceous glands

Liver:
protein synthesis

Adipose tissue:
control of leptin

Muscles:
volume & strength



Marrow:
hematopoietic cells

Joints:
synovial sheaths

Bone:
protein matrix

Kidney:
erythropoietin

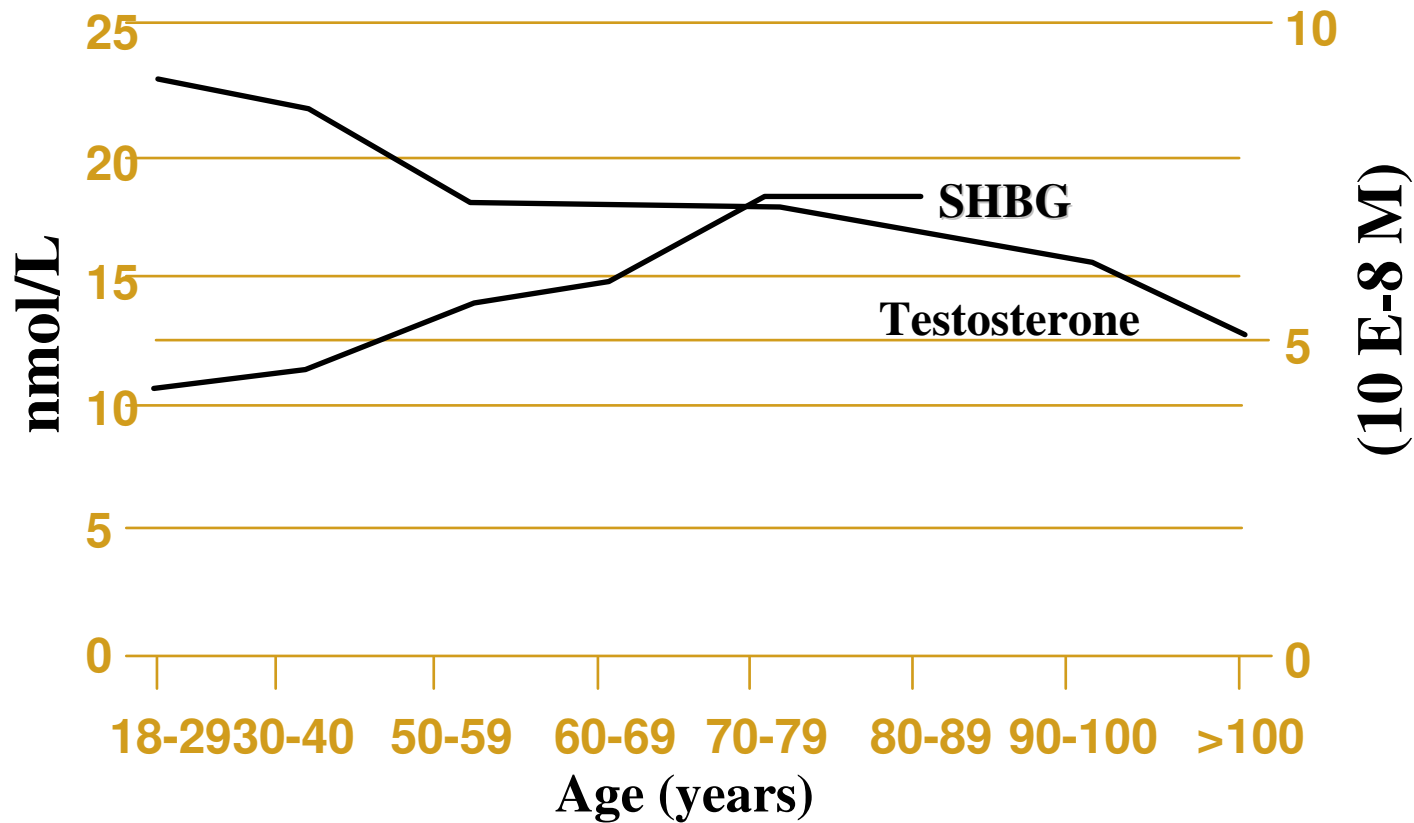
Prostate:
development and function



mensHEALTH
INITIATIVE OF BC



INFLUENCE OF AGE ON TOTAL TESTOSTERONE AND SHBG



Department of
UROLOGIC SCIENCES
UBC

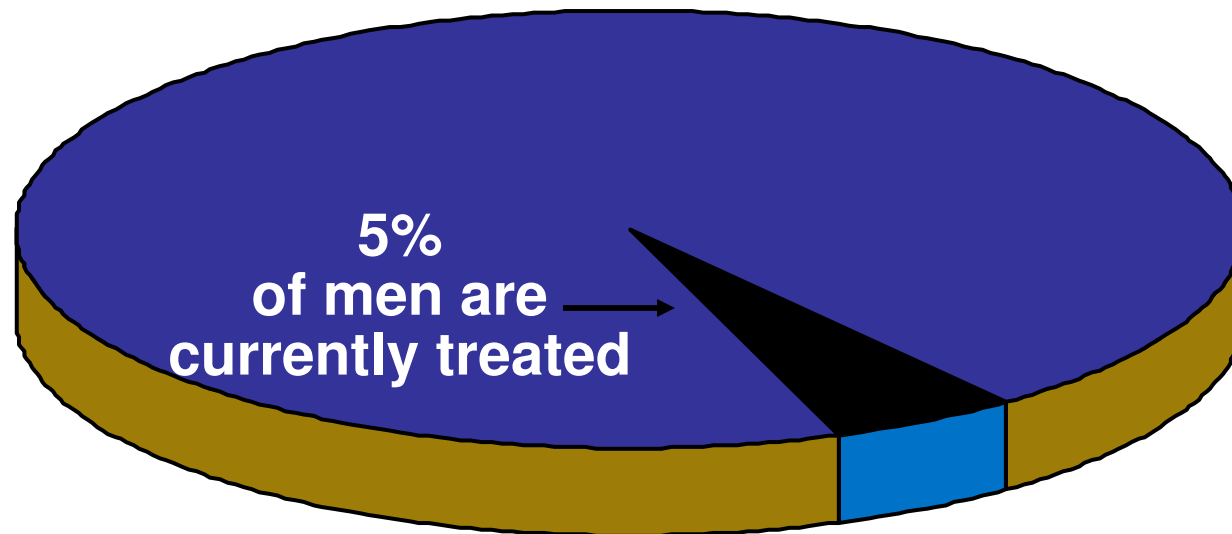


mensHEALTH
INITIATIVE OF BC



Prevalence and Treatment of Hypogonadism

4 to 5 Million Men with Hypogonadism



Adapted from US Food and Drug Administration Updates. May 23, 2003.



mensHEALTH
INITIATIVE OF BC



Hypogonadism: Signs & symptoms

Loss of strength, energy, motivation^{1,2}

Decrease in lean body mass, muscle volume;
increased visceral fat^{1,2}

Fatigue, lethargy, sleep disturbance^{1,2}

Decrease in body hair; skin alterations²

Diminished libido, erectile dysfunction^{1,2}

Mood and cognitive changes^{1,2}

1. Practice Committee (ASRM). *Fertil Steril* 2004;81:1437-1440.
2. Nieschlag E, Swerdloff R, Behre HM et al. *The Aging Male* 2005;8(2):56-8.



Department of
UROLOGIC SCIENCES
UBC

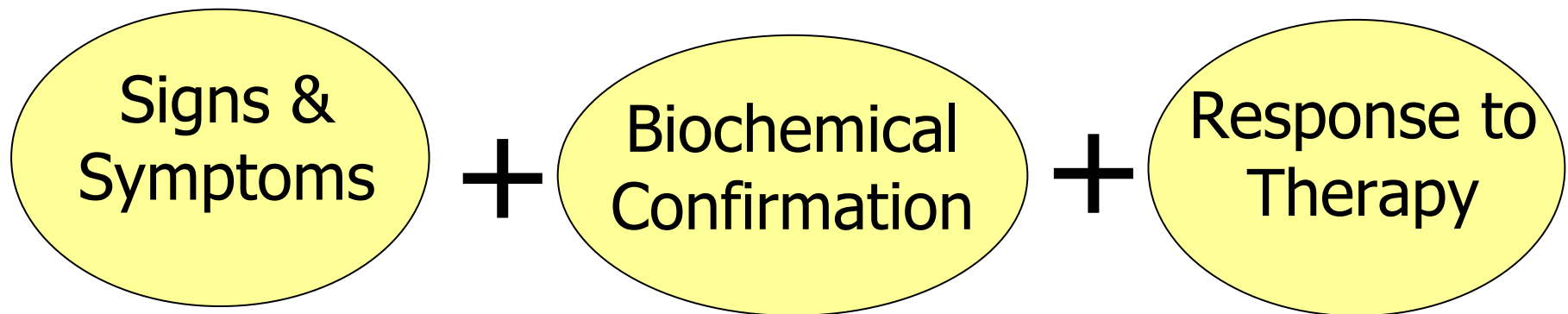


mensHEALTH
INITIATIVE OF BC



VGH&UBC
HOSPITAL FOUNDATION
Advancing world-class health care
for people in British Columbia

Diagnostic Criteria for Hypogonadism (Low testosterone)



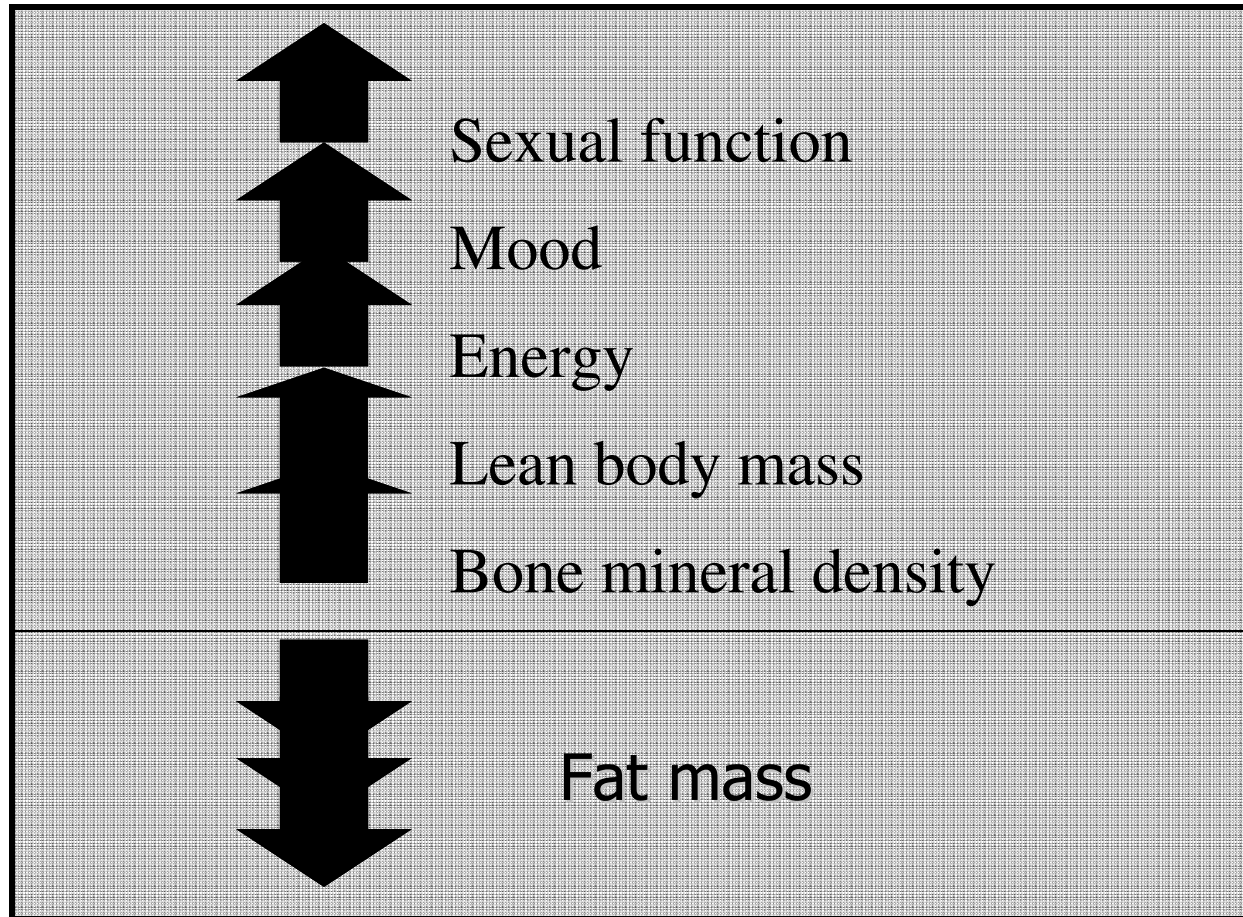
Modified from Nieschlag E, Swerdloff R, Behre HM et al. *The Aging Male* 2005;8(2):56-8.



mensHEALTH
INITIATIVE OF BC



Benefits of Testosterone Replacement: (in Hypogonadal men)



Wang C et al. *J Clin Endocrinol Metab* 2004;89:2085-2098.



mensHEALTH
INITIATIVE OF BC



Current Treatment Options

Intramuscular

- Depo-Testosterone (T cypionate)
- Delatestrel (T enanthate)

Oral

- Andriol / Testocaps (*T undecanoate*)

Testosterone patch

Androderm (Testosterone)

Testosterone gels

Androgel (Testosterone)

Testim (Testosterone)

Hypogonadism: Prevalence

HIM Study – Prevalence rate and odds ratio for hypogonadism by risk factors

<i>Risk factor/condition</i>	<i>Hypogonadism prevalence rate (95% CI)</i>	<i>Odds ratio (95% CI)</i>
Obesity	52.4 (47.9–56.9)	2.38 (1.93–2.93)
Diabetes	50.0 (45.5–54.5)	2.09 (1.70–2.58)
Hypertension	42.4 (39.6–45.2)	1.84 (1.53–2.22)
Rheumatoid arthritis	47.3 (34.1–60.5)	1.59 (0.92–2.72)
Hyperlipidaemia	40.4 (37.6–43.3)	1.47 (1.23–1.76)
Osteoporosis	44.4 (25.5–64.7)	1.41 (0.64–3.01)
Asthma/COPD	43.5 (36.8–50.3)	1.40 (1.04–1.86)
Prostatic disease/disorder	41.3 (36.4–46.2)	1.29 (1.03–1.62)
Chronic pain	38.8 (33.7–44.0)	1.13 (0.89–1.44)
Headaches (within last 2 weeks)	32.1 (25.3–38.8)	0.81 (0.58–1.11)

Mulligan T et al. *Int J Clin Pract* 2006;60:762-769.



Department of
UROLOGIC SCIENCES
UBC



mensHEALTH
INITIATIVE OF BC



Massachusetts Male Aging Study: Testosterone and Diabetes

Predictor	Increment	Odds Ratio*	95% CI	P
Free T	-1SD(3.9 ng/dl)	1.58	1.08-2.29	0.017

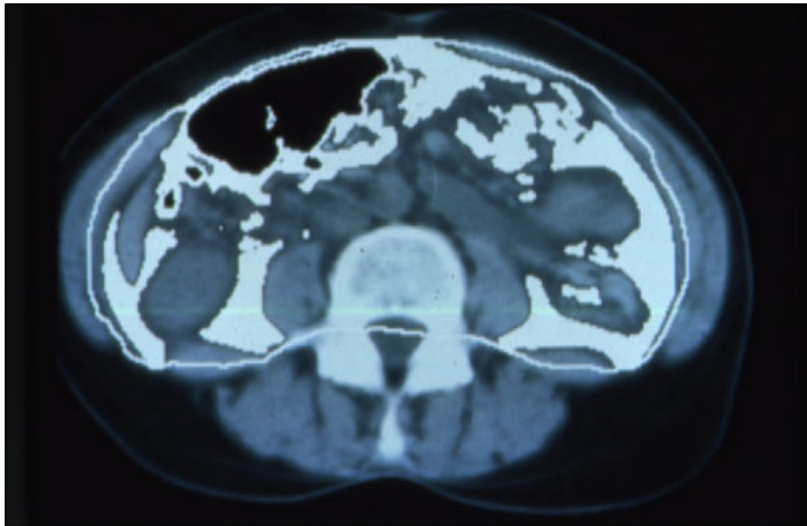
Stellato et al. Diabetes Care 23:490-4, 2000 From 1987 to 1989 with 9 yrs follow-up



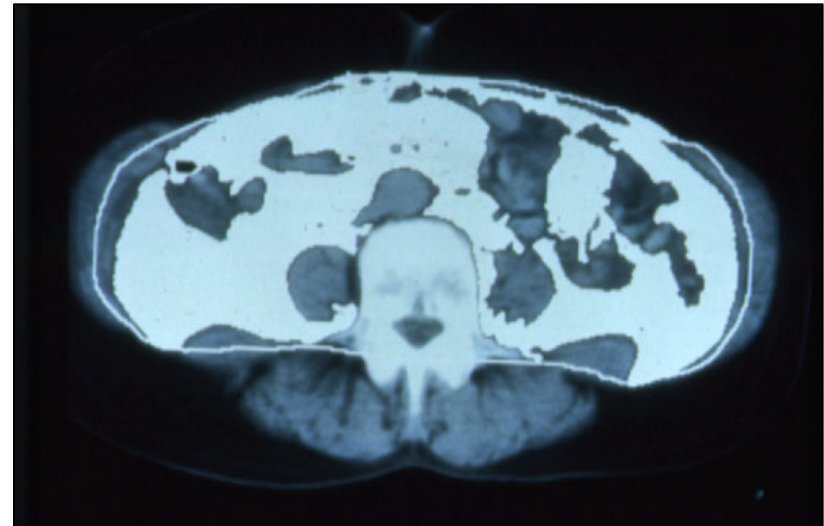
mensHEALTH
INITIATIVE OF BC



Visceral Fat Distribution:



Normal



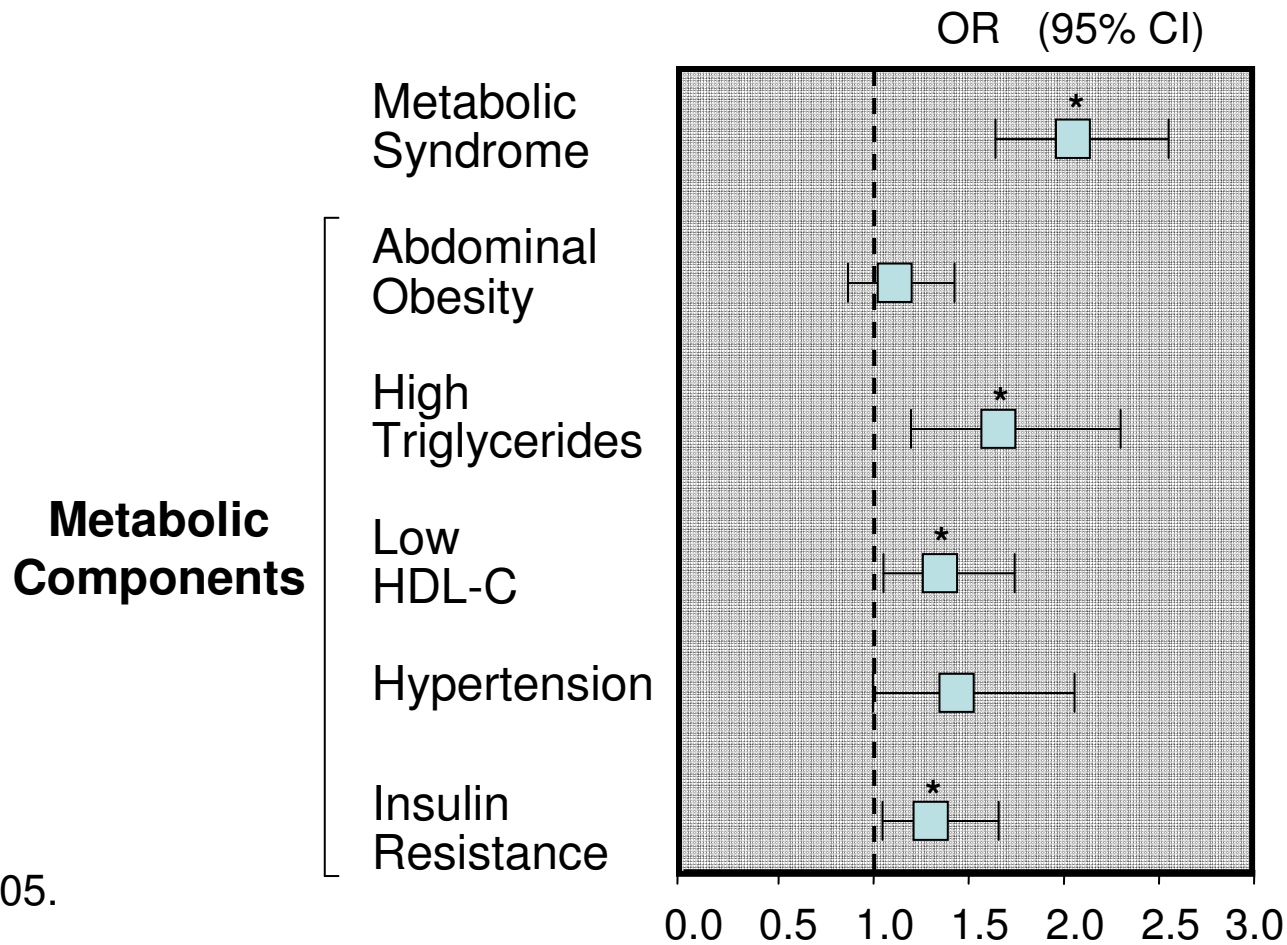
Increased Visceral Fat



mensHEALTH
INITIATIVE OF BC



Association of the Metabolic Syndrome With MI or Stroke (NHANES III Analysis)



Ninomiya JK, et al. *Circulation*. 2004;109:42-46.



mensHEALTH
INITIATIVE OF BC



Metabolic syndrome: Increased risk

Increased risk of cardiovascular events \approx 2-fold

Increased risk of type 2 diabetes \approx 5-fold

Grundy SM et al. *Circulation* 2005;112:2735-2752.



Department of
UROLOGIC SCIENCES
UBC



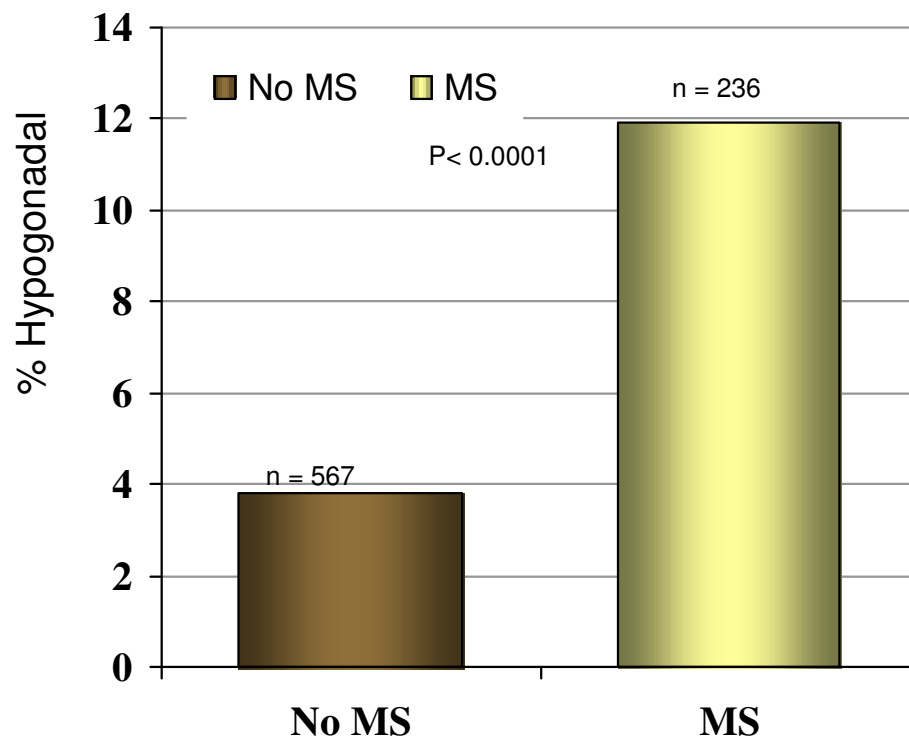
mensHEALTH
INITIATIVE OF BC

Vancouver
CoastalHealth
Promoting wellness. Ensuring care.



VGH&UBC
HOSPITAL FOUNDATION
Advancing world-class health care
for people in British Columbia

Prevalence of hypogonadism in the Metabolic syndrome



n = 803
All with sexual dysfunction

Metabolic syndrome (MS)
defined using NCEP-ATP III
criteria

Hypogonadism defined as
total testosterone <8 nmol/L

Corona G et al. Eur Urol 2006; 50:595-604



mensHEALTH
INITIATIVE OF BC



Low testosterone: Metabolic syndrome and mortality

Prospective study: 794 men, ages 50 – 90 years

3.05 fold (CI 1.88 – 4.95) increased prevalence of low testosterone in metabolic syndrome patients

1.33 (CI 1.10 – 1.62) risk of death for men with low testosterone

Laughlin G et al. Endocrine Society Annual Meeting 2007;OR55-2.



Department of
UROLOGIC SCIENCES
UBC



mensHEALTH
INITIATIVE OF BC

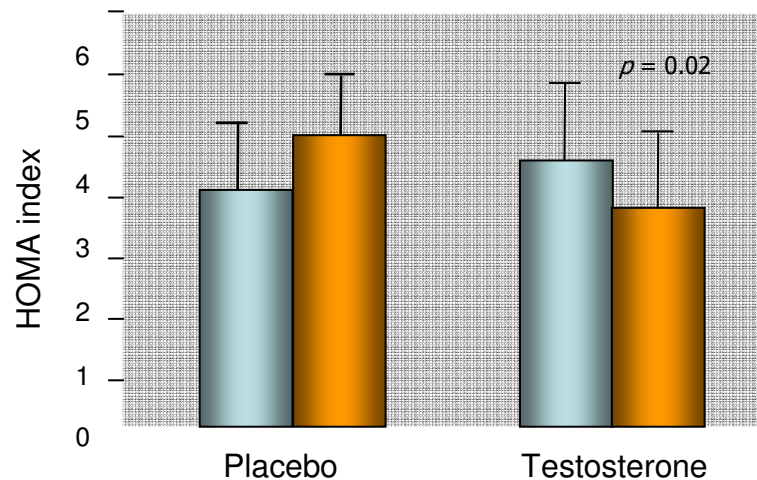
Vancouver
CoastalHealth
Promoting wellness. Ensuring care.



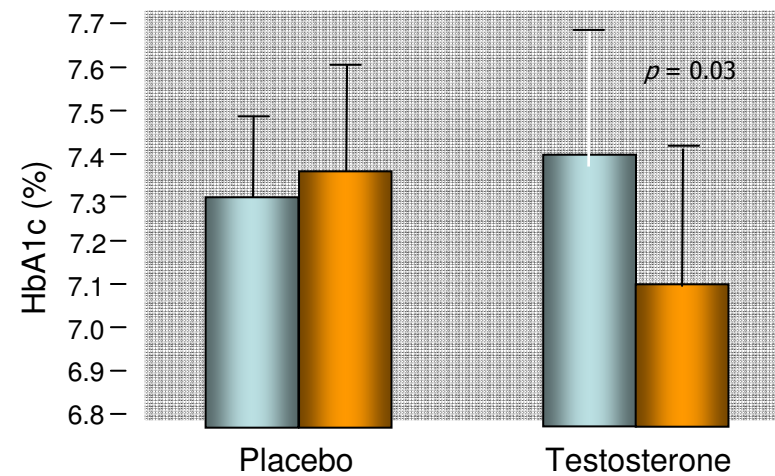
VGH&UBC
HOSPITAL FOUNDATION
Advancing world-class health care
for people in British Columbia

Benefits of Testosterone Replacement

Improves insulin resistance and blood sugar control in hypogonadal men with type 2 diabetes



24 men, RCT crossover
3 month treatment period with 1
month washout



■ Significant reduction in HOMA*
and HbA1c after 3 months of IM
testosterone therapy

■ Baseline ■ After 3 month treatment

* Homeostasis model assessment

Kapoor D et al. *Eur J Endocrinol* 2006;154: 899-906.

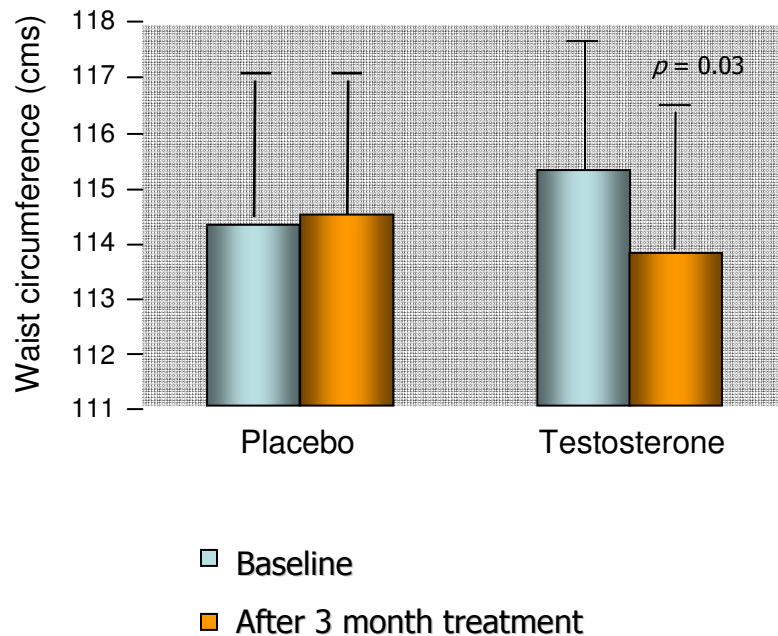


mensHEALTH
INITIATIVE OF BC



Benefits of TRT (continued)

Improves visceral adiposity & hypercholesterolemia in hypogonadal men with type 2 diabetes



Significant reduction in waist circumference after 3 months of IM testosterone therapy

Total cholesterol reduced from 5.11 mmol/L to 4.83 mmol/L with testosterone R_x (p=0.03 vs. placebo)

Kapoor D et al. *Eur J Endocrinol* 2006;154: 899-906.



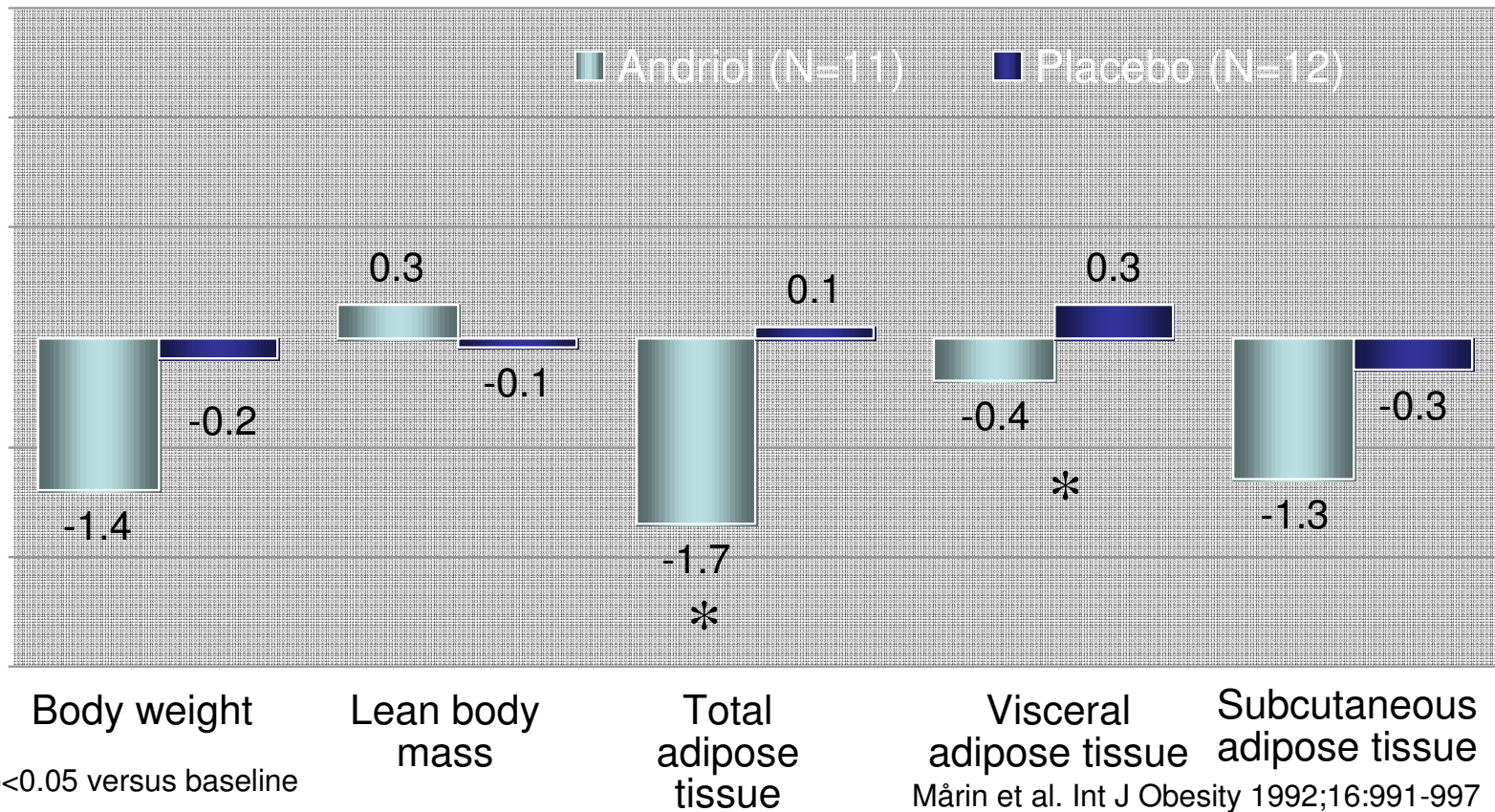
mensHEALTH
INITIATIVE OF BC



Effect of TU on body composition

8 Months TU 160 mg/d; >45 yrs; BMI >25 kg/m²; tT 16 nmol/L (9-21)

Change from baseline (kg)



mensHEALTH
INITIATIVE OF BC



Conclusions:

Hypogonadism is associated with type 2 Diabetes, obesity and the Metabolic Syndrome.

Presence of the Metabolic Syndrome is associated with an increased risk of vascular disease.

In both cross-sectional and prospective studies, low testosterone levels (TT and BioT) predict increased risk of Metabolic Syndrome or Diabetes developing.

Obesity and diabetes are associated with decreased TT and Bio-T.

Testosterone therapy can decrease body fat mass and in short term studies reduce insulin resistance in hypogonadal men.

Testosterone therapy can improve lipid parameters in hypogonadal men.



mensHEALTH
INITIATIVE OF BC



Patient monitoring Recommendations

Baseline

- testosterone measurement^{1,2}
- hematological assessment^{1,2}
- DRE^{1,2}
- PSA^{1,2}

Repeat q 3 months over first year, then annually^{1,2}

- maintain testosterone in lower to middle range expected in young adults^{1,2}

Bone mineral density every 2 years¹, especially if patient experienced a low-trauma fracture or osteoporosis²

1. Nieschlag E, Swerdloff R, Behre HM et al. *The Aging Male* 2005;8(2):56-8.
2. Bhasin S, Cunningham GR, Hayes FJ et al. *J Clin Endocrinol Metab* 2006;1995-2010.



Department of
UROLOGIC SCIENCES
UBC



mensHEALTH
INITIATIVE OF BC



VGH&UBC
HOSPITAL FOUNDATION
Advancing world-class health care
for people in British Columbia

Contra-indications to Testosterone Use

suspected or confirmed carcinoma of the prostate or breast^{1,2}
significant polycythemia (hematocrit>50%)^{1,2}
untreated sleep apnea^{1,2}
severe heart failure (eg, class III or IV)^{1,2}
severe symptoms of lower urinary tract obstruction^{1,2}
clinical evidence of bladder outflow obstruction¹
undiagnosed prostate nodule or induration²
unexplained elevation in PSA²

1. Nieschlag E, Swerdloff R, Behre HM et al. *The Aging Male* 2005;8(2):56-8.
2. Bhasin S, Cunningham GR, Hayes FJ et al. *J Clin Endocrinol Metab* 2006;1995-2010.



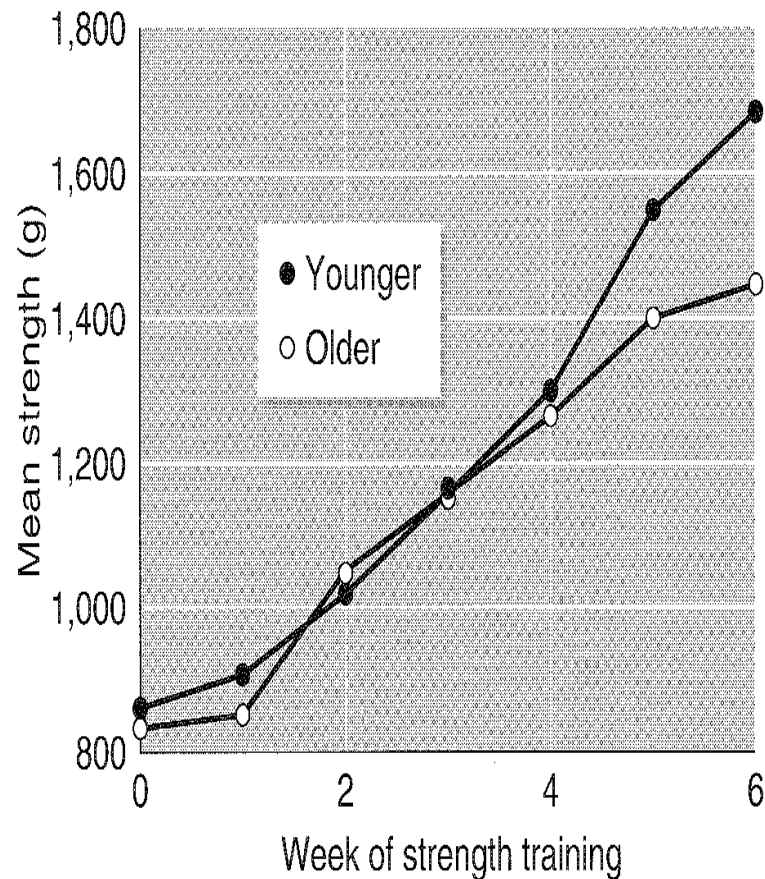
Department of
UROLOGIC SCIENCES
UBC



mensHEALTH
INITIATIVE OF BC



Effectiveness of Strength Training Programs in the Elderly



Strength training benefits adults of **any age**

Relative (%) strength gain is related to intensity and length of the strength-training program: **it is the same in older persons vs. younger persons**

Considerations

“Testosterone supplementation has the potential to counteract the signs, symptoms and health risks of late onset hypogonadism [and] entails the chance to maintain and improve the health status of elderly men.”

BUT...

Use in appropriate patients

Nieschlag E, Swerdloff R, Behre HM et al. *The Aging Male* 2005;8(2):59-74.



Department of
UROLOGIC SCIENCES
UBC

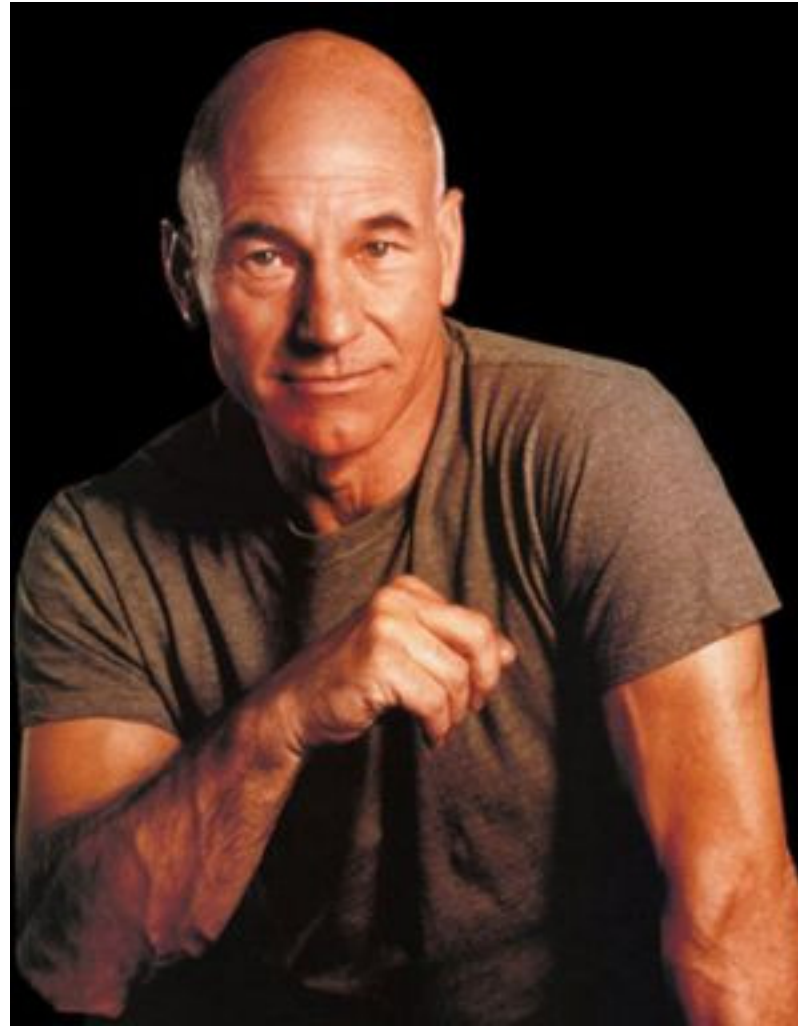


mensHEALTH
INITIATIVE OF BC

Vancouver
CoastalHealth
Promoting wellness. Ensuring care.



VGH&UBC
HOSPITAL FOUNDATION
Advancing world-class health care
for people in British Columbia



Department of
UROLOGIC SCIENCES
UBC



mensHEALTH
INITIATIVE OF BC

