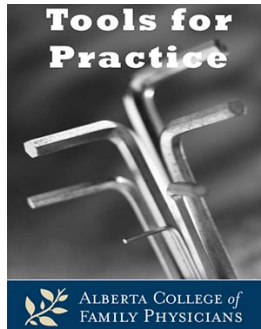


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Testosterone supplementation in men: Let's pause for a moment

Clinical Question: Is testosterone supplementation effective and safe for androgen decline in aging males?

Bottom-line: In older men, testosterone increases some muscle strength by 7%, with moderate improvements in erectile function and libido. There also appears to be an increase of adverse events, particularly cardiovascular in those with higher risk. Many results are inconsistent, at high risk of bias, and difficult to quantify in real world application.

Evidence:

- Main randomized, placebo-controlled trials in men with asymptomatic low testosterone:
 - 58 healthy men (age ≥ 60) followed 23 months.¹
 - No difference in quality of life, physical performance, or adverse effects.
 - 237 men (age 60-80) followed six months.²
 - No consistent difference in cognitive function, strength, quality of life, or adverse effects.
 - 209 men (age ≥ 65) with mobility issues (and higher cardiovascular risk) followed for six months.³
 - Improved leg and chest press strength, stair climb power with load by ~7%.
 - Stopped early for harm: All cardiovascular outcomes (hypertension to cardiovascular death), 22% testosterone vs. 5%.
- Meta-analyses (with up to 30 trials and 2,994 patients) found statistically significant increases:
 - Handgrip strength [standard mean difference (SMD)=0.30]⁴ and total body strength (SMD=0.54).⁵
 - Morning erections (SMD=0.65), libido (SMD=1.31), and sexual satisfaction (SMD \approx 1.2).^{6,7}
 - Cardiovascular disease (Odds ratio 1.61)^{8,9} and prostate complications [from increase symptom score to cancer] (Odds ratio 1.78).¹⁰

Context:

- Enthusiasm for any positive findings is tempered due to inconsistent results, small sample sizes, poor method description, lack of validated/useful endpoints, funding bias, and multiple outcome reporting.
 - Frequently do not specify if included symptomatic hypogonadism.
- Some suggest 0.8 SMD represents a large effect⁶ but this is estimation.
- FDA and the European Medicines Agency are reviewing testosterone safety due to cohort studies linking testosterone to cardiovascular events.¹¹⁻¹⁴
- “Normal” range of total AM testosterone 10-35 nmol/L.¹⁵
 - Varies with different labs, circadian rhythms, age, comorbidities, medications, and episodic secretion.
 - ~30% of mildly hypogonadal levels will normalize on retesting.^{15,16}
- Guidelines recommend testing testosterone levels and subsequent treatment only if symptomatic.^{16,17}

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Disclosure:

Adrienne J Lindblad, no conflicts to disclose. Andries Muller, speaker with honoraria (Abbott Laboratories) in the past two calendar years. Cheryl A Sadowski, sits on expert committee advising Alberta Ministry of Health on drug coverage; no other disclosures.

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