



Testosterone supplementation for cis-gender men: Let's (andro-)pause for a moment (Update)

CLINICAL QUESTION

What are the benefits and harms of testosterone supplementation in healthy cis-gender men or those with age-related low testosterone?

BOTTOM LINE

Compared to placebo, testosterone may increase lean body mass by ~1.6kg in older men but has no consistent, meaningful impact on sexual function, strength, fatigue, or cognition. Testosterone does not increase prostate events, myocardial infarction or stroke, but pulmonary embolism (0.9% versus 0.5% placebo) and atrial fibrillation (3.5% versus 2.4% placebo) may be increased.

EVIDENCE

- 16 systematic reviews from last five years¹⁻¹⁶ and main randomized, placebo-controlled trials (RCTs). Statistically significant unless indicated.
- Sexual function: Most comprehensive systematic review¹ (men ≥ 40 years with normal/low testosterone and sexual dysfunction). Highest quality RCTs:
 - Sexual function scale (range 6-30, higher=normal function): 6 RCTs, 2016 patients

- Mean difference: 2.4 at ≤12 months, not clinically different.
 - Others similar.²⁻⁴
- Strength: Most comprehensive review⁵ (11 RCTs, 814 men, 66-77 years old, normal/low testosterone). Over 3-12 months, highest quality RCTs:
 - Lean body mass: 1.6 kg higher with testosterone. Other reviews similar.⁶⁻¹⁰
 - Hand grip strength, physical performance tests: No difference.⁵
 - Leg strength: Inconsistent.⁵
- Fatigue: One systematic review with limitations.¹¹ Largest RCT: 464 patients, age 65+, low testosterone and self-reported “low vitality”:¹⁷
 - Proportion with clinical improvement on fatigue score: No difference.
- Cognition: Three systematic reviews with limited reporting.¹¹⁻¹³
 - Two largest RCTs: No difference.^{18,19}
- Quality of life: Best systematic review (7 RCTs, 1043 participants, most: testosterone <12nmol/L).¹¹
 - Symptom scale: Not clinically different.
 - Others similar.^{1,2,3,6}
- Harms: Largest RCT on cardiovascular effects of testosterone 1.62% gel in 5204 men, 55% with cardiovascular disease or at high risk.²⁰ Baseline testosterone=8nmol/L. At 33 months:
 - All-cause mortality, major cardiovascular events, prostate cancer, invasive prostatic procedures: No difference.
 - Atrial fibrillation: 3.5% versus 2.4% (placebo), number needed to harm=93.
 - Pulmonary embolism: 0.9% versus 0.5% (placebo) (no statistics provided).
 - Systematic reviews:^{1,14} Similar.

CONTEXT

- Low testosterone: < 10nmol/L.²¹
- Guidelines:^{21,22}
 - Asymptomatic: Not recommended.²²
 - Age-related low testosterone and sexual dysfunction: May discuss testosterone.²²
 - Best initial screening: Total testosterone (morning draw: 7-11am).²¹
- Best formulation is uncertain: Direct comparisons of different formulations lacking.¹

REFERENCES

1. Lee H, Hwang EC, Oh CK, *et al.* Cochrane Database Syst Rev. 2024; 1(1):CD013071.
2. Hudson J, Cruickshank M, Quinton R, *et al.* Lancet Healthy Longev. 2023; 4(10):e561-572.
3. Zhang Z, Kang D, Li H. BMC Endocr Disord. 2020; 20(1):33.
4. Taniguchi H, Shimada S, Kinoshita H, *et al.* Urol Int. 2022; 106(6): 539-552.
5. Parahiba SM, Ribeiro, ECT, Correa C, *et al.* Exp Gerontol. 2020; 142:111106.

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6. Mangolim AS, Brito LAR, Nunes-Nogueira VDS. *Euro J Endocrinol.* 2021; 186(1):123-35.
7. Correa C, Bieger P, Perry IS, *et al.* *Curr Pharm Des.* 2022; 28(7):586-594.
8. Lee TW, Kao PY, Chen YC, *et al.* *Gerontology.* 2023; 69(10):1157-1166.
9. Junjie W, Dongsheng H, Lei S, *et al.* *Curr Pharm Des.* 2019; 25(1); 73-84.
10. Burrato J, Kirk B, Phu S, *et al.* *Endocr Pract.* 2023; 29:727-34.
11. Diem SJ, Greer NL, MacDonald R, *et al.* *Ann Intern Med.* 2020; 172(2):105-18.
12. Buskbjerg CR, Gravholt CH, Dalby HR, *et al.* *J Endocr Soc.* 2019; 3(8):1465-84.
13. Tan S, Sohrabi HR, Weinborn M, *et al.* *Am J Geriatr Psychiatry.* 2019; 27(11):1232-46.
14. Sood A, Hosseinpour A, Sood A, *et al.* *Endocrin Pract.* 2024; 30(1):2-10.
15. Yang HJ, Kim KH, Kim DS, *et al.* *World J Mens Health.* 2023; 41(4):861-73.
16. Xu Z, Chen X, Zhou H, *et al.* *Front Endocrinol.* 2024; 15:335146.
17. Snyder PJ, Bhasin GR, Cunningham AM *et al.* *New Engl J Med.* 2016; 374:611-24.
18. Huang G, Wharton W, Bhasin S, *et al.* *Lancet Diabetes Endocrinol.* 2016; 4(8):657-665.
19. Resnick SM, Matsumoto AM, Stephens-Shields AJ, *et al.* *JAMA.* 2017; 317(7):717-27.
20. Lincoff AM, Bhasin S, Flevaris P, *et al.* *New Engl J Med.* 2023; 389(2):107-117.
21. Grober ED, Krakowsky Khera M, *et al.* *Can Urol Assoc J.* 2021; 15(5);E234-43.
22. Qaseem A, Horwitch CA, Vijan S, *et al.* *Ann Intern Med.* 2020; 172:126-133.

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