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Comments on the Food and Drug Administration Expert Panel on Testosterone Replacement Therapy for Men (FDA-2025-N-6743)

Public Citizen, a national nonprofit consumer advocacy organization with over one million members and supporters nationwide, submits the below comments on the Food and Drug Administration's (FDA's) Expert Panel on Testosterone Replacement Therapy for Men (FDA-2025-N-6743).

On December 10, 2025, the FDA convened an expert panel to explore the medical evidence and therapeutic uses of testosterone replacement therapy for men.[1] Public Citizen is concerned about the FDA's expert panel and the unsafe medical interventions it encouraged.

The process for selecting members of the FDA panel was not transparent, and several panelists have direct ties to pharmaceutical companies that manufacture testosterone products. The Testosterone Replacement Therapy for Assessment of Long-term Vascular Events and Efficacy Response in Hypogonadal Men (TRAVERSE) trial, for example, was funded by the pharmaceutical industry, and the FDA panel co-moderator, Dr. Mohit Khera, is an author of this trial.[2]

Although an FDA advisory committee meeting would typically include a robust discussion of all of the available evidence, the expert panel appeared to be looking only at data that supported the safety of testosterone replacement therapy. Moreover, the panel did not fully consider the evidence of minimal to no benefit other than for the approved indication.

Although testosterone replacement therapy is only FDA-approved for men with low testosterone levels (hypogonadism) from specific medical conditions, such as genetic issues, chemotherapy effects, or pituitary/hypothalamic injury,[3] many panelists appeared to favor expanding the indication. Several panelists, including Dr. Khera, the panel co-moderator, called for the elimination of the FDA's restriction

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[1] The Food and Drug Administration. FDA expert panel on testosterone replacement therapy for men. December 10, 2025. https://www.fda.gov/patients/fda-expert-panels/fda-expert-panel-testosterone-replacement-therapy-men-12102025. Accessed February 5, 2026.

[2] Lincoff, A. M., Bhasin, S., Flevaris, P., et al. Cardiovascular safety of testosterone-replacement therapy. *New England Journal of Medicine.* 2023*; 389*(2), 107–117. https://doi.org/10.1056/NEJMoa2215025.

[3] U.S. Food and Drug Administration. Testosterone Information. February 28, 2025. https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/testosterone-information#:~:text=FDA%20Drug%20Safety%20Communication:%20FDA,02/28/2025. Accessed February 5, 2026.

on using testosterone replacement therapy for age-related low testosterone.[4] Concerningly, the expert panel did not discuss the implications of potentially expanding the indication to a large population of older men with low or declining testosterone levels, or the health risks of testosterone replacement therapy in this population.

Public Citizen urges the FDA to require further independent studies of testosterone replacement therapy before considering approval for any additional indications, particularly for age-related testosterone deficiency. Public Citizen also urges the FDA to reinstate the boxed warning about increased cardiovascular risk, which was removed based on the results of the TRAVERSE trial.[5]

The path forward is for the FDA to refer this issue to a properly convened advisory committee, such as the Drug Safety and Risk Management Advisory Committee or the Endocrinology and Metabolic Drugs Advisory Committee, operating in full compliance with the Federal Advisory Committee Act.[6] Convening an advisory committee would foster accountability, transparency, and public trust in the agency's decision-making.

Testosterone Replacement Therapy Poses Serious Health Risks

Substantial evidence from peer-reviewed research has highlighted important concerns about the safety of testosterone replacement therapy, especially when this therapy is used by older men without clearly defined clinical indications. Well-designed studies have identified increased risks of adverse cardiovascular events (e.g. stroke, heart attack) as well as arrhythmias.

Evidence of cardiovascular harm associated with testosterone therapy has been particularly compelling. A 2013 retrospective cohort study by Vigen et al. evaluated over 8,700 men with low testosterone levels in the Department of Veterans Affairs system and found that those treated with testosterone replacement had a 29% higher risk of myocardial infarction, stroke, or death compared with untreated individuals, after adjustment for risk-related variables.[7]

Similarly, a 2014 study analyzed adverse cardiovascular events in a cohort of over 55,000 men newly starting testosterone therapy and found that men older than 65 years who received the therapy had more than a twofold increased risk of nonfatal myocardial infarction within 90 days compared with the 12 months prior to treatment.[8] These and other findings led the FDA in 2015 to mandate a boxed warning on testosterone replacement therapy products, emphasizing the potential risk for serious adverse cardiovascular events.

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[4] The Food and Drug Administration. FDA expert panel on testosterone replacement therapy for men. December 10, 2025. https://www.youtube.com/live/BdAawJmQ9Fs. Accessed February 5, 2026. Time stamps 29:20, 1:03:30.

[5] FDA recklessly removes boxed warning for risk of cardiovascular disease from testosterone labels. *Worst Pills, Best Pills News*. August 2025. https://www.worstpills.org/newsletters/view/1677. Accessed February 5, 2025.

[6] The Federal Advisory Committee Act (FACA): Overview and considerations for Congress. https://www.congress.gov/crs-product/R47984. February 5, 2026.

[7] Vigen R, O'Donnell, C.I, Baron AE, Grunwald GK, et al Association of testosterone therapy with mortality, myocardial infarction, and stroke in men with low testosterone levels. *JAMA*. 2013; 310(17), 1829–1836. https://doi.org/10.1001/jama.2013.280386.

[8] Finkle WD, Greenland S, Ridgeway G K, Adams JL, et al. Increased risk of non-fatal myocardial infarction following testosterone therapy prescription in men. *PLoS ONE*. 2014; 9(1), e85805. https://doi.org/10.1371/journal.pone.0085805.

Studies also have found an increased risk of cardiac arrhythmias associated with testosterone replacement therapy. A 2025 meta-analysis of randomized controlled trials in men aged 40 or older with testosterone deficiency found a more than 50% increase in the risk of arrhythmia for the treatment groups compared with the placebo groups; the study, however, found no increase in cardiovascular mortality, stroke, or myocardial infarction.[9] The TRAVERSE trial found that significantly more episodes of atrial fibrillation (3.5%) and nonfatal arrhythmias requiring intervention (5.2%) occurred in the testosterone group than in the placebo group (2.4% and 3.3%, respectively).[10] Testosterone replacement therapy requires rigorous safety evaluation before any expansion of its approved use.

Methodological Flaws With the TRAVERSE Trial

FDA expert panel members cited the TRAVERSE trial multiple times as evidence of the safety of testosterone replacement therapy. The study, however, has important methodological flaws.[11] The trial enrolled 5,246 men between 45 to 80 years of age with symptoms of hypogonadism, two fasting testosterone levels of less than 300 ng per deciliter, and existing (or a high risk of) cardiovascular disease. Most notably, the men randomized to the treatment arm were underdosed, with a reported median on-treatment serum testosterone level of just 350 ng/dL— barely above the clinical threshold for testosterone deficiency.[12] This level is also well below the therapeutic target testosterone range of 450–600 ng/dL recommended by the American Urological Association in their most recent (2024) clinical guidelines.[13]

TRAVERSE's protocol called for titration of study participants to the recommended therapeutic range of 350–750 ng/dL for transdermal 1.62% testosterone gel, but the observed median testosterone levels clustered at the very bottom of this therapeutic range for the four-years of the trial. As a result, the trial did not test the cardiovascular safety of full therapeutic testosterone replacement, but rather the effects of borderline or subtherapeutic dosing. This design flaw undermines the study's conclusions about the cardiovascular safety of testosterone replacement therapy.

The TRAVERSE trial exclusively evaluated transdermal testosterone gel, in spite of the fact that injectable testosterone — a popular form of testosterone therapy in the United States — has been associated with higher risks of cardiovascular events, including myocardial infarction and stroke.[14] Moreover, about 60% of participants in both study arms discontinued treatment before the end of the trial, biasing the results toward a null finding. In a noninferiority trial, this level of attrition by study participants severely limits the ability to detect real differences in risk.

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[9] Braga MA, Rivera A, Marinheiro G, Felix N, et al. Cardiovascular safety of testosterone-replacement therapy in middle-aged and older men: A meta-analysis of randomized controlled trials. *American Journal of Cardiovascular Drugs.* 2025; 25:767–777.

[10] Lincoff AM, Bhasin S, Flevaris P, et al. Cardiovascular safety of testosterone-replacement therapy. *New England Journal of Medicine.* 2023; 389(2), 107–117. https://doi.org/10.1056/NEJMoa2215025.

[11] FDA recklessly removes boxed warning for risk of cardiovascular disease from testosterone labels. *Worst Pills, Best Pills News*. August 2025. https://www.worstpills.org/newsletters/view/1677. Accessed February 5, 2025.

[12] Lincoff AM, Bhasin S, Flevaris P, et al. Cardiovascular safety of testosterone-replacement therapy. *New England Journal of Medicine.* 2023; 389(2), 107–117. https://doi.org/10.1056/NEJMoa2215025

[13] American Urological Association Guidelines, "Evaluation and Management of Testosterone Deficiency (2024)." https://www.auanet.org/guidelines-and-quality/guidelines/testosterone-deficiency-guideline. Accessed February 7, 2026.

[14] Layton JB, Meier CR, Sharpless JL, Stürmer T, et al. Comparative safety of testosterone dosage forms. *JAMA Internal Medicine.* 2015; 175(7), 1187–1196.

Limited Benefits of Testosterone Replacement Therapy in Men With Age-Related Low Testosterone
Although FDA panel members touted the desired effects of testosterone replacement therapy for age-related testosterone decline, evidence from high-quality studies reveals limited therapeutic benefits. A comprehensive systematic review and meta-analysis published in 2020 concluded that testosterone replacement therapy in older men with low testosterone and without medical conditions known to cause hypogonadism provided modest improvements in sexual function — about a 25% subjective reported improvement in erectile dysfunction over 58 weeks. However, there were no consistent benefits for physical function, energy, vitality, or cognitive performance.[15] These findings are consistent with a 2016 randomized trial of 790 older men with low serum testosterone, which found small to moderate gains in sexual desire and erectile function in the treatment group, but little to no benefit in walking distance or vitality after 12 months of treatment with testosterone gel or placebo.[16] The minimal clinical impact of testosterone replacement therapy on most domains—especially functional status and quality of life—raises concerns about the appropriateness of testosterone prescribing for men without clear, symptomatic hypogonadism. Furthermore, the modest benefits observed must be balanced against the significant cardiovascular risks.

Conclusion
Testosterone replacement therapy has significant and well-documented cardiovascular risks and unclear benefits for older men with age-related low testosterone. Public Citizen is concerned about the apparent endorsement of testosterone replacement therapy for age-related low testosterone by several FDA expert panel members without full consideration of the available evidence. Public Citizen is also concerned about the panel's composition and deliberative process, which lacked transparency and appropriate vetting of panel members for conflicts of interest

Public Citizen urges the FDA to require further independent studies of testosterone replacement therapy before considering approval for any additional indications, particularly for age-related testosterone deficiency. Public Citizen also urges the FDA to reinstate the boxed warning for increased cardiovascular risks on all testosterone products.

Thank you for your consideration of our comments regarding this important issue.

Sincerely,

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[15] Diem SJ, Greer NL, MacDonald R, McKenzie LG, et al. Efficacy and safety of testosterone treatment in men: An evidence report for a clinical practice guideline by the American College of Physicians. *Annals of Internal Medicine.* 2020; 172(2), 105–118.
[16] Snyder PJ, Bhasin S, Cunningham GR, Matsumoto AM, et al. *Effects of testosterone treatment in older men. The New England Journal of Medicine.* 2016; 374(7), 611–624.