Testosterone Therapy and Cardiovascular Risk in Postmenopausal Women: A Critical Appraisal of the TriNetX Analysis Presented at The Menopause Society 2026 Annual Meeting

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Subject of review: Jiang XD, et al. "Testosterone therapy and cardiovascular risk in postmenopausal women: a retrospective propensity-matched cohort study." Presented at the 2026 Annual Meeting of The Menopause Society, San Diego, October 20-24, 2026, and announced in the Society's press release "Testosterone Therapy May Increase Risk of Cardiovascular Disease in Postmenopausal Women" (October 20, 2026).

Purpose and scope

On October 20, 2026, The Menopause Society announced a study reporting that testosterone therapy in postmenopausal women was associated with an eight-fold increase in the hazard of cardiovascular disease. Because this message will reach clinicians and patients well before any peer-reviewed manuscript, I have reviewed it carefully and set it against the prospective, dose-documented literature.

My review is based on the Society's two-page press release, which is the only public description of the study at this time. I have limited every criticism to what the release states. Several of the most important questions (formulation, dose, route, duration of exposure, component-level outcomes, and how "initiation" was coded) cannot be answered from the release. That silence is itself a finding: a release announcing an eight-fold hazard should have been able to say what the women actually received.

For supporting evidence, I have relied only on prospective studies in which dosing, dispensing or administration is documented in the body of the paper. I have deliberately excluded retrospective and database studies, including those that favor my position, because the central weakness of the Jiang study is its retrospective database design.

Bottom line

This is a retrospective electronic health record (EHR) database association study. By design it cannot establish cause and effect, and the release concedes as much: the lead author describes the result as a "potentially important cardiovascular safety signal" that "warrants further prospective investigation." The headline, "Testosterone Therapy May Increase Risk of Cardiovascular Disease," runs ahead of the data. Exposure was never confirmed, no dose or serum level is reported, the effect size (HR 8.08) is difficult to reconcile with prospective, dose-documented data, the control event rate is unexpectedly low, and the composite outcome relies heavily on code-based diagnoses.

In my assessment, the study provides very low-quality evidence for causation, and an eight-fold hazard so far out of line with prospective, dose-documented data stretches credulity. The question the study raises is a fair one, however, it is far better answered by prospective, dose-documented interventional data, and those data do not show this signal.

What was presented

- Data source: TriNetX US Collaborative Network (a federated EHR database).
- Population: postmenopausal women aged 45 years and older who "initiated testosterone therapy," compared with women "without testosterone exposure"; more than 6,300 propensity-matched women in total.
- Washout: no testosterone exposure in the prior 12 months; prior cardiovascular disease excluded.
- Matching: 1:1 propensity matching on demographics, smoking, obesity, hysterectomy, surgical menopause, baseline menopausal hormone therapy, vaginal estrogen, vasomotor symptoms, premature ovarian insufficiency, diabetes, hypertension and dyslipidemia.
- Outcome: composite of coronary artery disease (angina, myocardial infarction, acute or chronic ischemic heart disease), cerebrovascular disease (ischemic stroke or arterial occlusive disease), or heart failure, from 30 days to 5 years after the index date.
- Follow-up: mean "nearly 3 years."
- Result: 3.8% vs 0.5%; HR 8.08 (95% CI 4.72 to 13.82). A sensitivity analysis comparing testosterone plus hormone therapy with hormone therapy alone was described as "consistent."

Study classification

- Prospective or retrospective: Retrospective. The presentation itself is titled "a retrospective propensity-matched cohort study."
- Study type: Observational analytic cohort using existing electronic health-record data, with 1:1 propensity-score matching. Not randomized; no intervention was assigned or controlled by the investigators.
- Oxford Centre for Evidence-Based Medicine (OCEBM) level: 2b at best (individual cohort study). Given unconfirmed exposure, unadjudicated outcomes and the absence of a peer-reviewed manuscript, its practical certainty is lower still. It is hypothesis-generating evidence and should not be weighed against prospective interventional data on equal terms.

Evaluation checklist

Question	Answer from the available report
1. Was it confirmed that testosterone was actually taken?	No. Women were identified as having "initiated" testosterone in TriNetX records. Filling, dispensing, continuation and use are not reported.
2. Was proper dose and administration confirmed?	No. No product, route, dose, frequency, duration, adherence or dose adjustment is reported.
3. Were serum testosterone levels measured?	Not reported.
4. Were serum levels followed over time?	Not reported.
5. What average serum levels were achieved on treatment?	Not available. No baseline, on-treatment, peak or serial levels are given, so it is unknown whether treated women were physiologic, above conventional female ranges, or barely exposed.
6. How were cardiovascular events measured?	Not stated. Given the TriNetX design, events were almost certainly identified from coded EHR diagnoses rather than direct clinical evaluation or adjudicated chart review. That is an inference; the release does not confirm the method.

In fairness, the study has real features worth acknowledging: a large matched cohort, exclusion of prevalent cardiovascular disease, a 12-month washout, and matching on major measured risk factors. None of these cure the problems that follow.

Principal flaws

1. Exposure was never confirmed

Nothing in the release establishes that any woman actually received testosterone, at what dose, by what route, or for how long. "Initiated testosterone therapy" in an EHR database typically means a prescription order or a medication-list entry. That does not confirm dispensing, utilization, adherence, or duration. There is no mention of serum testosterone levels. There is no dose-response analysis, and without one the study is missing a core criterion for causal inference.

This matters for clinical interpretation as well. No serum testosterone concentration has been validated as a threshold at which harm begins in women; population reference intervals describe untreated women and are not toxicity limits. Because the study has no information on dose or serum level, even if its association were real it could not say at what exposure any risk applies, and it cannot inform how a clinician should interpret a given level in a monitored patient.

Two additional problems follow:

- Compounded creams and pellets, which account for a large share of testosterone use in women in the United States, are frequently cash-pay and dispensed outside the systems that feed a database like TriNetX. The exposed cohort is therefore likely to be skewed toward whatever is captured in the record, which may include male-strength commercial products, and the "unexposed" cohort may contain treated women.
- A woman with a single prescription is counted as exposed for up to 5 years. The outcome window (30 days to 5 years) is not linked to any confirmed period of use.

2. The effect size is difficult to reconcile with dose-documented evidence

An eight-fold hazard is extraordinary for any drug. The release describes testosterone for women as prescribed "in very low doses," but the study itself reports no dose, route or serum level, and some women in clinical practice, particularly those treated with implants, are maintained at concentrations above conventional female reference ranges. My argument therefore does not depend on assuming the Jiang cohort received low doses. Whatever its members actually received, documented exposure at both ends of the range has not produced a signal of this kind.

Men receive far higher doses than women. In TRAVERSE (Lincoff et al., N Engl J Med 2023), the largest randomized cardiovascular safety trial of testosterone, 5,246 men aged 45 to 80 with preexisting cardiovascular disease or high cardiovascular risk received daily 1.62% testosterone gel, with the dose adjusted to keep serum testosterone between 350 and 750 ng/dL, or placebo. The primary endpoint (cardiovascular death, nonfatal MI or nonfatal stroke) occurred in 7.0% of the testosterone group vs 7.3% of the placebo group (HR 0.96, 95% CI 0.78 to 1.17), meeting the noninferiority criterion. These were high-risk men on monitored, full replacement doses, followed for a mean of 33 months, and there was no excess in major adverse cardiac events. Venous thromboembolism occurred in 1.7% vs 1.2% (HR 1.46, 95% CI 0.92 to 2.32), which was not statistically significant. TRAVERSE also listed several investigator-reported secondary safety findings, which were reported without adjustment for multiple comparisons and fall outside the Jiang composite.

A meta-analysis by Cannarella et al. (2023; 24 studies including 14 RCTs, more than 4,000 hypogonadal men) reported arterial thrombosis OR 1.27 (95% CI 0.47 to 3.43), stroke OR 1.34 (95% CI 0.09 to 18.97) and VTE OR 1.42 (95% CI 0.22 to 9.03), none statistically significant.

At the other end of the female exposure range, the Glaser implant cohorts maintained women at serum levels several-fold above endogenous values, with confirmed administration, and reported no adverse drug events attributed to testosterone other than androgenic effects. And in BLISS, the only randomized trial in women designed around cardiovascular outcomes, the pooled event rate in women selected for elevated cardiovascular risk was lower than anticipated (discussed below). If monitored full replacement doses in high-risk men, pharmacologic implant levels in women, and a randomized trial in at-risk women do not produce a clear arterial signal, an eight-fold arterial hazard in women is more consistent with bias than with biology.

3. The control event rate is unexpectedly low

The comparison group had a 0.5% cumulative event rate over nearly 3 years, roughly 0.17% per year, for a composite that includes angina, chronic ischemic heart disease, heart failure and arterial occlusive disease in women aged 45 and older with hypertension, diabetes and dyslipidemia present in the matched population. That is lower than would be expected.

Using the release's own figures (about 3,150 women per arm), the result rests on roughly 120 events in the testosterone group versus about 16 in the control group. A hazard ratio built on about 16 control events is fragile, which the wide confidence interval (4.72 to 13.82) reflects.

The likeliest explanation is ascertainment and surveillance bias, a well-known weakness of EHR network data:

- Women on testosterone are, by definition, engaged in ongoing care, with more visits, more labs and more opportunities for a diagnosis code to be entered.

- Comparator women "without testosterone exposure" may be sparsely captured in the network; an event that happens outside the network never appears.
- A diagnosis such as "angina" or "chronic ischemic heart disease" is often coded to justify a work-up, not because disease was confirmed.

4. The composite outcome is soft, unadjudicated and not broken down

The composite combines hard events (MI, ischemic stroke) with code-driven diagnoses (angina, chronic ischemic heart disease, arterial occlusive disease, heart failure). The release reports no component-level results, no adjudication, and no cardiovascular deaths. If the excess is driven by angina and chronic ischemic heart disease codes, the finding says more about coding behavior than about myocardial infarction or stroke. A responsible headline would wait for those components.

TRAVERSE offers a useful contrast. Heart failure hospitalization or urgent visit occurred in 2.1% of the testosterone group vs 1.9% of the placebo group, and hospitalization for unstable angina in 1.7% vs 2.3%. In a randomized trial with full-dose, monitored testosterone in high-risk men, the very categories that make up much of the Jiang composite showed no meaningful difference.

5. Propensity matching cannot fix what is not in the database

Matching balanced only coded variables. It cannot balance:

- why testosterone was prescribed (confounding by indication);
- the type of practice and prescriber, which differs systematically between women who receive testosterone and women who do not;
- actual BMI, blood pressure and lipid values (as opposed to the presence of a code), physical activity, family history, socioeconomic status, alcohol, and use of other prescribed or compounded hormones;
- the intensity of medical surveillance (Flaw 3).

Propensity scores make two cohorts look similar on paper. They do not convert a retrospective database into a randomized trial.

6. "Consistency" is not replication

The release relies on the finding being "consistent across multiple cohort definitions" and in a testosterone-plus-hormone-therapy vs hormone-therapy-alone comparison. Re-cutting the same database with the same exposure definition and the same outcome codes will reproduce the same biases. Consistency within one data source is not independent confirmation.

7. The headline outruns the authors' own caveats

The release concedes that "absolute event rates were low" and that the association "warrants further prospective investigation." Those are the statements of a hypothesis-generating abstract. The headline and the medical director's comment, which frames the results as a reminder to "carefully balance individualized risks," will be read by clinicians and patients as a demonstrated risk. That gap between data and message is my central concern with this release. The likely effect, whatever the intent, is to discourage appropriate testosterone therapy in women on the basis of an unconfirmed association.

8. A guideline target is not evidence of harm

The release, and in particular the medical director's comment, reflects the conservative guideline position. The 2019 Global Consensus Position Statement recommends avoiding preparations that produce supraphysiologic concentrations, and the 2021 ISSWSH guideline recommends keeping levels within the physiologic premenopausal range. I acknowledge that position. It is, however, a policy preference, not a demonstration that concentrations above that range cause harm. The International Expert Consensus on Testosterone Insufficiency and Treatment in Women reached materially different conclusions: optimal serum ranges in women have not been established, symptoms correlate poorly with serum levels, and treatment should be individualized to clinical response.

It is worth noting what the conservative guidelines themselves say about cardiovascular safety. The Global Consensus Position Statement found the data insufficient to assess the effect of testosterone on myocardial infarction or death. ISSWSH, after summarizing the sponsor-reported BLISS results, wrote: "Despite these reassuring outcomes, long-term (beyond 2 years) safety data, particularly regarding breast cancer and cardiovascular events (acute myocardial infarction, stroke, deep vein thrombosis, and death), are limited and inconclusive." In other words, the guideline bodies regard cardiovascular safety as unresolved and the best available trial data as reassuring. A single retrospective abstract does not resolve that question, and the release's headline should not have presented it as though it did.

What prospective, dose-documented evidence shows

The studies below meet the standard I set for this review: each is prospective, and dosing, dispensing or administration is documented in the body of the paper.

Source	Design	Dosing documented	Relevant finding
Shifren et al., N Engl J Med 2000;343:682-688	Randomized, placebo-controlled	Yes: transdermal testosterone 150 and 300 µg/day	Supraphysiologic free testosterone at the higher dose with negligible adverse reactions; greatest improvement in sexual function and well-being at 300 µg/day
Davis et al., Menopause 2006;13:387-396	Randomized, double-blind, placebo-controlled, 24 weeks; 77 surgically menopausal women	Yes: patch 300 µg/day	Adverse events similar in both groups; "no serious risks of therapy were observed"
Braunstein et al., Arch Intern Med 2005;165:1582-1589	Randomized, double-blind, placebo-controlled, 24 weeks; 447 women	Yes: patch 150, 300 or 450 µg/day	Adverse events similar in frequency across groups; no serious safety concerns observed

Source	Design	Dosing documented	Relevant finding
Davis et al. (APHRODITE), N Engl J Med 2008;359:2005-2017	Randomized, double-blind, placebo-controlled, 52 weeks; 814 women	Yes: patch 150 or 300 µg/day	Efficacy at 24 weeks, safety assessed at 52 weeks; androgenic effects (mainly unwanted hair) more common at 300 µg
Nachtigall et al., Gynecol Endocrinol 2011;27:39-48	Open-label extensions of two randomized trials, up to 4 years; 967 surgically menopausal women; 1,092 patient-years	Yes: patch 300 µg/day	No increase over time in adverse events, serious adverse events or withdrawals; no clinically meaningful changes in lipids, carbohydrate metabolism, liver or renal function, or coagulation parameters
Islam et al., Lancet Diabetes Endocrinol 2019;7:754-766	Systematic review and meta-analysis of 36 blinded RCTs (8,480 women), each at least 12 weeks	Yes, in the constituent RCTs	Neutral lipid profile with transdermal testosterone; acne and hair growth more likely; no serious adverse events recorded
BLISS (White et al., Am Heart J 2012;163:27-32)	Randomized, double-blind, placebo-controlled cardiovascular and breast safety trial; 3,656 women aged 50 and older with at least two cardiovascular risk factors	Yes: 1% testosterone gel, 300 µg/day	53 adjudicated cardiovascular events in more than 7,300 woman-years, a lower rate than anticipated (sponsor-reported; not peer-reviewed; arm-level data not released)
Glaser and Dimitrakakis, Maturitas 2013;76:342-349	5-year interim analysis of a 10-year, prospective, observational, IRB-approved study; 1,268 women; 5,642 person-years	Yes: in-office subcutaneous implants, 55-240 mg (about 2.0 to 2.5 mg/kg); serum T 299.36 ± 107.34 ng/dL at week 4 and 171.43 ± 73.01 ng/dL when symptoms returned	"Despite pharmacologic serum levels, there have been no reported adverse drug events attributed to T therapy other than expected androgenic side effects, which are reversible with lowering T dose"
Glaser, York and Dimitrakakis, BMC Cancer 2019;19:1271	10-year prospective cohort; 1,267 women with at least two implant insertions	Yes: mean dose 198.7 ± 55.8 mg; mean serum T 490 ± 210 ng/dL one week after implantation (n = 398); weekly research follow-up calls	No adverse events attributed to T therapy other than androgenic effects despite pharmacologic levels; invasive breast cancer 165 vs 271 per 100,000 person-years expected (SEER)

Source	Design	Dosing documented	Relevant finding
Glaser, Kalantaridou and Dimitrakakis, Maturitas 2013;74:179-184	Dosing study including a prospective pharmacokinetic group (12 previously untreated postmenopausal women, 100 mg implant)	Yes: mean dose 133.3 ± 26.8 mg (range 55-240 mg); serial serum T levels at baseline, 4 and 16 weeks	In patients treated for over one year, "there were no reported adverse drug events"
Glaser, York and Dimitrakakis, Maturitas 2011;68:355-361	Part of the same 10-year prospective IRB-approved study; 300 women, with follow-up data on 285	Yes: initial dose 75-160 mg; mean dose 133.3 ± 26.8 mg every 13.8 ± 3.8 weeks	"No adverse effects on blood sugar, insulin resistance, diabetes, or lipid profiles" (data not shown in the paper)
TRAVERSE (Lincoff et al., N Engl J Med 2023;389:107-117); 5,246 men	Randomized, double-blind, placebo-controlled	Yes: daily 1.62% gel titrated to serum T 350 to 750 ng/dL	MACE 7.0% vs 7.3%, HR 0.96 (0.78 to 1.17), noninferior; VTE 1.7% vs 1.2%, HR 1.46 (0.92 to 2.32), not significant
Cannarella et al., 2023; men	Meta-analysis, 14 RCTs within 24 studies	Yes, in the constituent RCTs	Arterial thrombosis, stroke, VTE and PE odds ratios all non-significant

The Glaser implant cohorts

The Glaser cohort is the mirror image of the Jiang study on every point that matters for exposure. Implants were inserted in the office, so administration is confirmed. Doses were weight-based and recorded at every insertion. Serum testosterone was measured on therapy and was several-fold above endogenous levels. Patients were followed with weekly research phone calls, and anyone not seen for 240 days was contacted. Over 5,642 person-years by 2013, at pharmacologic serum levels, no adverse drug events were attributed to testosterone other than expected androgenic effects. If testosterone in women carried an eight-fold cardiovascular hazard, a dose-confirmed cohort of this size with levels this high should have shown it. The cohort was designed around breast cancer incidence rather than adjudicated cardiovascular endpoints, but a population under active research follow-up for a decade would be expected to surface the myocardial infarctions, strokes and heart failure that an eight-fold hazard implies. None were attributed to testosterone.

BLISS: the randomized cardiovascular safety trial in women

The BioSante LibiGel Safety Study (BLISS; NCT00612742) is the only randomized trial in women designed around cardiovascular outcomes. It enrolled 3,656 postmenopausal women aged 50 and older, each with at least two cardiovascular risk factors, and randomized them to a once-daily 300 µg testosterone gel or placebo. The primary endpoint was an adjudicated composite of cardiovascular death, nonfatal MI, nonfatal stroke, coronary revascularization, hospitalized unstable angina and venous thromboembolism, with breast cancer as a co-primary endpoint. The FDA-agreed safety margin required the upper bound of the 97.2% confidence interval of the hazard ratio to be no higher than 2.0.

The final results were never published in a peer-reviewed journal, and I want to be clear about what is and is not known. Blinded interim reports presented in 2010 and 2011 described a pooled cardiovascular event rate of 0.55%, lower than predicted, and the Data Monitoring Committee

recommended continuing the trial unchanged after four unblinded reviews. The 2021 ISSWSH guideline reports that after 4 years and more than 7,300 woman-years of exposure, the sponsor "reported 53 adjudicated cardiovascular events, a lower than anticipated rate, with the number of breast cancers as anticipated based on subject ages," and notes that these results appeared in press releases but not in peer-reviewed publications. Event counts by treatment arm were never released.

Even with those limitations, BLISS is informative. Fifty-three events over more than 7,300 woman-years is about 0.73 per 100 woman-years, pooled across both arms, in women selected for elevated cardiovascular risk, with adjudicated outcomes and a confirmed dose. With roughly equal randomization, a true hazard ratio of 8 would split those 53 events about 47 on testosterone and 6 on placebo. A Data Monitoring Committee reviewing unblinded data repeatedly, against a safety margin of a hazard ratio of 2.0, would be very unlikely to miss an imbalance of that size. Because arm-level counts were never released, this is an inference rather than a measured result, but it is a strong one.

The comparison with Jiang is also instructive. The Jiang testosterone group's rate of 3.8% over nearly 3 years is roughly 1.27% per year, in women with prior cardiovascular disease excluded and no requirement for cardiovascular risk factors. That exceeds the pooled BLISS rate of about 0.73 per 100 woman-years in higher-risk women, using a BLISS composite that also counted revascularization and venous thromboembolism. The two composites are not identical, so I offer this as an illustration rather than a formal comparison, but it points in the same direction as everything else.

Long-term transdermal follow-up

Nachtigall et al. followed 967 surgically menopausal women on a 300 µg/day testosterone patch for up to 4 years in open-label extensions of two randomized trials, accumulating 1,092 patient-years. There was no increase over time in adverse events, serious adverse events or withdrawals, and no clinically meaningful changes in lipid profile, carbohydrate metabolism, renal and liver function, or coagulation parameters. This is the longest prospective follow-up of a defined testosterone regimen in women, and it shows no emerging cardiovascular or metabolic pattern.

Endogenous testosterone

Observational studies of endogenous testosterone point in the same direction. For example, American Journal of Epidemiology 2002 found the lowest risk of carotid atherosclerosis in postmenopausal women in the highest testosterone quartile (OR 0.43). These studies measure natural levels rather than treatment, so they support biological plausibility rather than serving as interventional evidence, but they are difficult to reconcile with the idea that testosterone is a potent cardiovascular hazard in women.

The remaining evidence gap

I want to state the remaining gap precisely. No adequately powered prospective trial in women has yet reported hard cardiovascular outcomes, by treatment arm, in a peer-reviewed publication. That gap is an argument for prospective, dose-documented research. It is not an argument for accepting a database association that lacks dose, level and outcome verification. The prospective data that do exist, in women and in men, show no signal of the kind or size claimed.

Overall assessment: study quality and how it should be received

Quality.

In my assessment, this study provides very low-quality evidence for any causal conclusion. It is a retrospective database association with unconfirmed exposure, no dose or serum level data, no dose-response analysis, no outcome adjudication, no component-level results, an unexpectedly low control event rate, and no peer-reviewed manuscript. Each of these is a recognized weakness on its own. Together, they leave the study unable to distinguish a drug effect from differences in who is prescribed testosterone, how closely those women are followed, and how their diagnoses are coded.

The size of the result.

A hazard ratio of 8 is, in my view, the single most telling feature of this study. An effect of that magnitude would be expected to surface in randomized trials and in prospective, dose-documented cohorts. It has not: not in TRAVERSE, with monitored full replacement doses in high-risk men; not in BLISS, with a confirmed dose in women at elevated cardiovascular risk; not in the randomized and long-term extension trials of transdermal testosterone in women; and not in the Glaser implant cohorts, with confirmed administration at serum levels several-fold above endogenous values. A result that is out of line with every prospective, dose-documented dataset stretches credulity, and is far more likely to reflect bias and confounding than a true effect of the hormone.

Framing.

In my opinion, the presentation reads as though the conclusion preceded the analysis. The headline states a risk; the body concedes that absolute rates were low, that the study is retrospective, and that prospective investigation is needed. The data support the body, not the headline. A release built around an eight-fold hazard, with no information on what the women actually received, is more likely to provoke alarm than to help clinicians and patients make treatment decisions.

How the medical community should receive it.

Clinicians should treat this abstract as a hypothesis-generating signal of low credibility, not as a basis for changing practice. It should not be used to stop or withhold testosterone in symptomatic women who are benefiting from monitored therapy, and it should not be cited in patient counseling as evidence of established risk. Reasonable responses are to request the full methods, component-level outcomes and exposure data; to wait for peer review; and to weigh the finding against the prospective, dose-documented literature, which does not support it. Clinicians who prescribe testosterone should continue to individualize therapy, monitor clinical response and androgenic effects, and document informed shared decision-making, as good practice already requires.

Questions for the authors

1. What formulations, doses and routes were used, and what share of exposed women had more than one prescription or a confirmed dispense?
2. Were serum testosterone levels available, and was there any dose-response or level-response relationship?
3. What were the component-level results, and how many events were MI, ischemic stroke or cardiovascular death?

4. How many encounters per patient-year did each cohort have, and does the association survive restriction to women with comparable follow-up intensity?
5. Did the authors run negative-control outcomes (conditions testosterone should not affect) to test for surveillance bias?
6. How were compounded and pellet therapies captured, if at all?

Conclusion

This presentation reports an association, not an effect. Its exposure is unconfirmed, it reports no dose or serum level, its effect size is difficult to reconcile with dose-documented evidence, its control event rate suggests under-ascertainment, its outcome is soft and undisclosed at the component level, and its "consistency" is internal to one database. The authors themselves call for prospective investigation.

Clinicians should treat the result as a hypothesis, not as a reason to withhold therapy from symptomatic women, and should weigh it against prospective, dose-documented interventional data, which do not show this signal. TRAVERSE found no excess in major adverse cardiac events with monitored, full-dose testosterone in high-risk men. BLISS, in women at elevated cardiovascular risk, reported a lower than anticipated event rate. The dose-confirmed Glaser implant cohorts reported no adverse drug events beyond androgenic effects at serum levels well above conventional female ranges. A serum testosterone value above a reference range is a clinical datum to be interpreted, not a diagnosis of harm, and this study offers no basis for treating it as one.

References

1. Jiang XD, et al. Testosterone therapy and cardiovascular risk in postmenopausal women: a retrospective propensity-matched cohort study. Presented at the 2026 Annual Meeting of The Menopause Society, San Diego, October 20-24, 2026. The Menopause Society press release, October 20, 2026.
2. Lincoff AM, Bhasin S, Flevaris P, et al. Cardiovascular safety of testosterone-replacement therapy (TRAVERSE). N Engl J Med 2023;389:107-117.
3. Cannarella R, et al. Meta-analysis of testosterone therapy and thrombotic outcomes in hypogonadal men. 2023.
4. Shifren JL, Braunstein GD, Simon JA, et al. Transdermal testosterone treatment in women with impaired sexual function after oophorectomy. N Engl J Med 2000;343:682-688.
5. Davis SR, van der Mooren MJ, van Lunsen RH, et al. Efficacy and safety of a testosterone patch for the treatment of hypoactive sexual desire disorder in surgically menopausal women: a randomized, placebo-controlled trial. Menopause 2006;13:387-396.
6. Braunstein GD, Sundwall DA, Katz M, et al. Safety and efficacy of a testosterone patch for the treatment of hypoactive sexual desire disorder in surgically menopausal women: a randomized, placebo-controlled trial. Arch Intern Med 2005;165:1582-1589.
7. Davis SR, Moreau M, Kroll R, et al. Testosterone for low libido in postmenopausal women not taking estrogen (APHRODITE). N Engl J Med 2008;359:2005-2017.
8. Nachtigall L, Casson P, Lucas J, Schofield V, Melson C, Simon JA. Safety and tolerability of testosterone patch therapy for up to 4 years in surgically menopausal women receiving oral or transdermal oestrogen. Gynecol Endocrinol 2011;27:39-48.
9. Islam RM, Bell RJ, Green S, Page MJ, Davis SR. Safety and efficacy of testosterone for women: a systematic review and meta-analysis of randomised controlled trial data. Lancet Diabetes Endocrinol 2019;7:754-766.
10. White WB, Grady D, Giudice LC, et al. A cardiovascular safety study of LibiGel (testosterone gel) in postmenopausal women with elevated cardiovascular risk and hypoactive sexual desire disorder. Am Heart J 2012;163:27-32.
11. BLISS blinded interim reports. Poster abstracts. J Womens Health 2010 and 2011.
12. Parish SJ, Simon JA, Davis SR, et al. International Society for the Study of Women's Sexual Health clinical practice guideline for the use of systemic testosterone for hypoactive sexual desire disorder in women. J Womens Health 2021;30:474-491 (also J Sex Med 2021;18:849-867).
13. Davis SR, Baber R, Panay N, et al. Global Consensus Position Statement on the Use of Testosterone Therapy for Women. J Clin Endocrinol Metab 2019;104:4660-4666.

14. Testosterone insufficiency and treatment in women: International Expert Consensus.
15. Glaser R, Dimitrakakis C. Reduced breast cancer incidence in women treated with subcutaneous testosterone, or testosterone with anastrozole: a prospective, observational study. Maturitas 2013;76:342-349.
16. Glaser RL, York AE, Dimitrakakis C. Incidence of invasive breast cancer in women treated with testosterone implants: a prospective 10-year cohort study. BMC Cancer 2019;19:1271.
17. Glaser R, Kalantaridou S, Dimitrakakis C. Testosterone implants in women: pharmacological dosing for a physiologic effect. Maturitas 2013;74:179-184.
18. Glaser R, York AE, Dimitrakakis C. Beneficial effects of testosterone therapy in women measured by the validated Menopause Rating Scale (MRS). Maturitas 2011;68:355-361.
19. Golden SH, et al. Endogenous postmenopausal hormones and carotid atherosclerosis: a case-control study of the Atherosclerosis Risk in Communities cohort. Am J Epidemiol 2002;155:437-445.

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