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Estradiol Today

The latest news from the **Estradiol Initiative**

Estradiol Initiative
A New Standard of Care

Welcome to the first issue of ***Estradiol Today***! Your comments and suggestions are appreciated, including topics you would like to see in future editions. Please email Bob Watson at **janebob99@lobo.net**.

The mission of the **Estradiol Initiative** non-profit organization is to educate patients and clinicians about the benefits and risks of using transdermal estradiol (tE2) for men receiving Androgen Deprivation Therapy (ADT) for prostate cancer. Our main goal is to secure FDA and NCCN approval for tE2 ADT (eADT) as a Standard of Care (SoC) for these patients.

In this first issue of ***Estradiol Today***, we offer four short essays from the lead researchers of the **Estradiol Initiative**. The essays are all short commentaries on the recent paper by Langley et al., published in the *New England Journal of Medicine* (2026). These essays share our diversity of perspectives on the *NEJM* paper, and they range from data rich summaries to personal perspectives on tE2 and PCa. We would be happy to get your feedback on any of these commentaries. Also, there is an Op-Ed piece about gynecomastia by Larry Schuller.

→ **Please visit our website at estradiolinitiative.org**

• *How much gynecomastia are men likely to experience using transdermal estradiol for ADT?*

Carly Sears and Larry Schuller

Langley et al. (2026)[1] make a strong case for using transdermal estradiol (tE2) for androgen deprivation therapy (ADT). However, gynecomastia is a common side effect of estradiol administration, which can be distressing for many men. While Langley et al. reported *subjective* measures of bother from gynecomastia, they did not report any *objective* measures of how much breast growth men actually experienced during the PATCH/STAMPEDE trials.

We reviewed three studies that measured the amount of breast growth experienced by 358 adult genetic males who used high-dose exogenous estradiol to purposefully induce breast growth (i.e., trans women).[2-4] Eighty-five percent of participants developed breasts that were less than or equal to an "A" cup size. Only 15% developed breasts of a "B" cup size or larger.

Prostate cancer patients considering using tE2 for ADT should not just be informed that estradiol induces gynecomastia. They should also be informed about the modest amount of breast growth they are likely to experience. Highly bothersome gynecomastia, however, can be addressed with surgical reduction.

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• *Transdermal Estradiol: a triple threat against prostate cancer, osteoporosis and financial toxicity*

Paul Schellhammer, MD

The PATCH/STAMPEDE trial[1] makes transdermal estradiol (tE2) a uniquely powerful agent to support the health of aging men. tE2 addresses the most frequently encountered male malignancy,[2] prostate cancer. ADT with tE2 is therapeutically equal to LHRH analogs (LHRHa), while mitigating many LHRHa-associated adverse events and thereby improving patients' QoL.[1,3] This can all be accomplished at a cost orders of magnitude less than current pharmaceutical regimes used to treat advanced prostate cancer.

Notably, the bone protective properties of tE2 can reduce the morbidity/mortality associated with osteoporotic fracture.[4] When androgen receptor inhibitors are combined with LHRHa to provide standard-of-care doublet therapy, bone loss accelerates and fracture risk rises.[5] In contrast, the use of tE2 limits the need for bone-protecting agents, thereby reducing overall costs of treatment and risks of adverse effects.[4]

In sum, tE2 ADT is a winning strategy for men since it can simultaneously control prostate cancer, avoid osteoporotic fractures, and do so at a lower cost than current ADT treatment protocols.

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• *Economic considerations of using transdermal estradiol for ADT*

Apoorv Dhir, MD and Bob Watson, PhD

Langley et al. (2026)[1] report that androgen deprivation therapy (ADT) with transdermal estradiol (tE2) provides equivalent safety and cancer control, with a better quality of life than LHRH agonists (LHRHa). However, Langley et al. restricted their economic considerations to countries with a National Healthcare System.

In the USA, tE2 ADT costs $1,900 per patient-year, assuming a median cost of $6 per patch[2] and dosing per the PATCH trial protocol.[1] In contrast, LHRHa ADT costs $4,800 per patient-year.[3] Assuming an estimated 200,000 men are currently on ADT,[4] the USA health system could save about $580 million per year in drug costs alone by switching to tE2 ADT.

Langley et al. reported that the incidence of fractures over 5-10 years was reduced by 50% by using tE2 ADT[1]. When considering the additional costs of bone-protective agents and costs of treating osteoporotic fractures, the annual cost savings of $580 million is likely a significant *underestimate* of the true cost savings. In summary, ADT with tE2 stands to result in significantly decreased costs for the USA health system.

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• *Transdermal Estradiol ADT from a prostate cancer patient's perspective*

Richard Wassersug, PhD

While Langley et al. (2026)[1] have documented that androgen deprivation therapy (ADT) with transdermal estradiol (tE2) provides equivalent prostate cancer (PCa) control and safety as LHRH agonists, their paper doesn't provide the **patient's perspective** on how tE2 improves their quality of life (QoL).

I was diagnosed with PCa at age 52 and had a radical prostatectomy, followed by salvage radiotherapy. Unfortunately, I immediately experienced biochemical progression. I then started on leuprolide for suppressing testosterone, but did not like the nocturnal hot flashes nor the physical and mental fatigue associated with it.[2–4] So, after two years, I switched to estradiol patches, which was before the PATCH trial began.

Now, without hot flashes, I sleep better and have less brain fog and daytime fatigue. Estradiol in castrated males improves REM sleep, which is cognitively protective.[5] I have talked to hundreds of PCa patients on standard ADT and I have yet to meet anyone who has had both the continuously good cancer control and QoL that I've had with over 22 years using tE2 for ADT.

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The Prostate Ribbon

by Larry Schuller

An editorial view, shining a light on prostate cancer. Because humor and having a positive attitude can also have vital therapeutic value.

While chest tissue growth is a potential side effect across all standard-of-care ADT agents, patient aversion to estradiol (E2) is strong. While it is true that E2 carries a higher incidence of gynecomastia than the other agents of ADT, the medical reality is that standard ADT treatments also cause the exact same side effect.

Furthermore, the hesitation to use E2 is frequently rooted in the misconception that it is exclusively a "female" hormone. In reality, estradiol is an essential hormone that males naturally require and normally produce (by converting their now-suppressed testosterone).

• **Please don't call them "Boobs"**

It just smacks of denigration, since the word's origins are: "*a stupid person, a bumbling oaf, or idiot*".

There is no shortage of nicknames, some funny and some disturbingly offensive, with everything in between. They (despite their utility in deflecting a man's embarrassment, which is an inappropriate reflex, after all) deserve a place in the vocabularic ash can.

My preferred choice is "*Bosoms*"; a friendly word, largely devoid of sexual or nutritional connotation. In any event, my bosoms are not a sign of lost manhood or developing femininity. They are simply cosmetic artifacts of my (successful) combat with prostate cancer.

I consider them a badge of honor and (if anyone asks or looks askance at them) an opportunity to proselytize about prostate cancer awareness and being a participatory, self-advocating patient.

Importantly, gynecomastia can also result from standard ADT treatments. So, avoiding estradiol ADT does not completely eliminate the risk of gynecomastia.

→ **Thank you for reading *Estradiol Today*. For more information, check out the Patient and Clinician FAQ's at: https://estradiolinitiative.org/.**