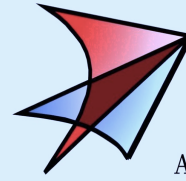


Estradiol Today

The latest news from the **Estradiol Initiative**



**Estradiol
Initiative**

A New Standard of Care

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

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

This issue of **Estradiol Today** focusses on the bothersome symptoms of **mastalgia** (breast and/or nipple pain) from using estradiol.

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→ Please visit our website at estradiolinitiative.org

Informal Survey of Mastalgia Symptoms

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September 12, 2026

Introduction

Gynecomastia (breast enlargement) commonly occurs in the months after starting transdermal estradiol (tE2) therapy for androgen deprivation therapy (ADT). Gynecomastia has been reported in 85% of men using tE2¹ and is commonly considered the predominant side effect of tE2. However, according to our survey results, about 50% of men also report experiencing bothersome symptoms of *mastalgia* (breast soreness and nipple pain). In contrast to gynecomastia, bothersome mastalgia have been anecdotally reported as occurring soon after starting tE2 therapy (i.e., in a few weeks). In some men, those symptoms can be severe enough to cause them to stop using tE2 after only a few weeks; believing that “*something must be wrong with my treatment.*”

In August of 2026, we informally surveyed 23 of the 68 members of our *E2 Users Group* about their use of tE2 products and their experience with mastalgia. Our two hypotheses about mastalgia symptoms were that they are: 1) **mild** and 2) **transient** (i.e., lasting only a few months), as the body adjusts to the higher serum estradiol levels.

Survey Results

Of the 23 men reporting on how much mastalgia bothered them, **Fig. 1** shows that 8% reported “none”; 48% reported “mild”; 22% reported “moderate”; and 22% reported “severe” bother (primarily from nipple pain). **Fig. 2** shows that 26% of men reported that their mastalgia symptoms lasted less than three months, while 61% reported that their symptoms lasted longer than 16 months.

Fig. 3 shows that 70% of men used patches, 26% used gel/cream, and 4% used Sub-Q injections (i.e., estradiol valerate). **Fig. 4** shows that the number of simultaneous patches ranged from 1 to 4, with a median of 3 simultaneous patches. 88% of patch users used 0.1 mg E2 patches. **Fig. 5** shows that 75% of men changed patches twice a week and 25% changed patches once a week. Eight different brands of patches were used by the n=16 patch users.

26% of men used E2 gel or cream (commercially available or compounded). The concentration of E2 in gels/creams ranged from 0.06% to 1.0%, with an average concentration of 0.4%. The most commonly used commercial brand of gel was *Estrogel™* (with a concentration of 0.06%). 78% of men consistently used the same dose of tE2, rather than increasing or decreasing the E2 dose over time.

Fig. 6 shows that 65% of men used tE2 for a duration shorter than 16 months and 35% used tE2 longer than 16 months (median duration = 12 months, range = 1-264 months). Three men reported using tE2 products for more than 20 years!

Discussion

Just over half of the men surveyed reported that their symptoms were either “none” or “mild”. Unfortunately, 44% reported that their symptoms were “moderate” to “severe” (primarily due to nipple pain). Anecdotally, we know of several men who stopped using tE2 after starting tE2 due to having severe nipple pain.

Our hypotheses that mastalgia symptoms were **mild** and **transient** (i.e., lasting less than 3 months) was **not supported** by this survey. While 26% of men did report that their symptoms disappeared in less than 3 months, 61% reported that their symptoms were continually “ongoing”. Therefore, mastalgia symptoms are neither “mild”, nor are they resolved in less than three months, for many men.

Fig. 7 shows results taken from a survey conducted in 2017 of n=727 men using 3-4 estradiol patches from the PATCH-II trial reported by Gilbert et al.⁵ **Fig. 7** shows that 63% reported “Not at all” or “A little bit” of discomfort. However, 37% reported “Quite a bit” or “Very much” discomfort. That compares favorably to the present survey’s results (shown in **Fig. 1**), which show that 44% of men reported “Moderate” or “Severe” discomfort.

There has not been much discussion in the literature of ways to prophylactically reduce or prevent bothersome symptoms of mastalgia. Prophylactic electron beam radiation has been reported to reduce the incidence of gynecomastia by as much as 50%.² But, it is not clear if there was a similar reduction in bothersome mastalgia.

It has been reported that NSAIDs reduce or eliminate breast and nipple pain.³ The most successful treatment was daily topical application of 1% diclofenac gel to the patients' breasts and nipples.^{3,4} Anecdotally, hot packs can also be used to help reduce this pain.

Appendix A lists the Survey questions and n=23 patients' responses. tE2 patches (0.1 mg strength, changed twice a week) are the most popular form of tE2. The number of simultaneous patches ranged from one to four at a time. 57% of respondents have been using tE2 for less than 13 months, while 13% have used tE2 products for more than 20 years.

We do not have enough data to show that certain tE2 products or dosages are associated with more or less bothersome symptoms.

Conclusions

56% of men reported that bothersome symptoms of mastalgia were either “None” or “Mild”. Unfortunately, 44% reported “Moderate” to “Severe” mastalgia (primarily due to nipple pain). These bothersome symptoms were anecdotally reported to occur soon after initiating tE2 treatment (typically within a few weeks), which can lead to patients to stopping their tE2 therapy. Daily topical use of 1% diclofenac gel can successfully manage mastalgia.

References

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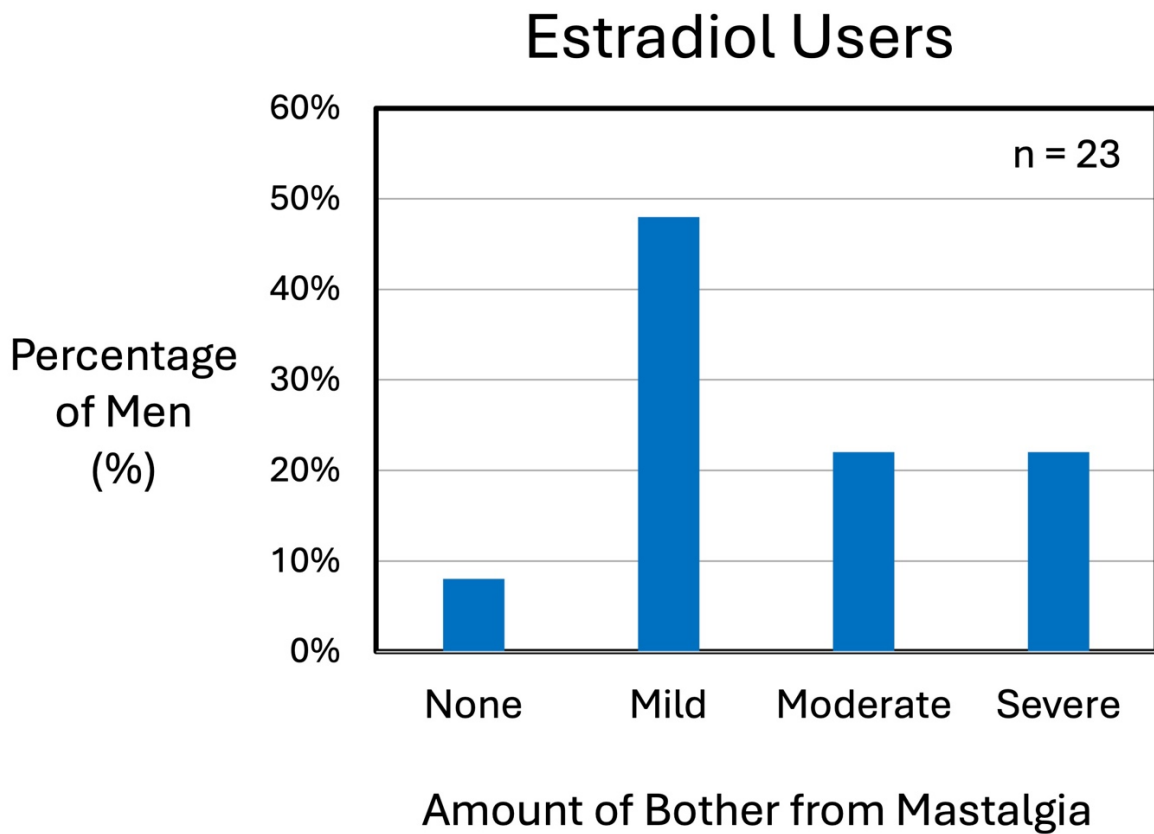


Fig. 1

E

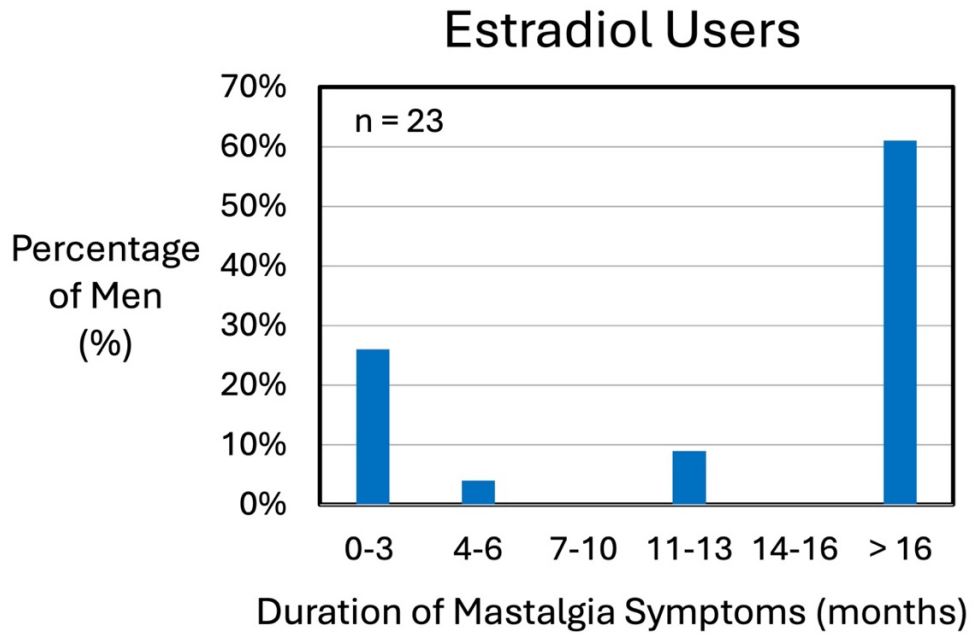


Fig. 2

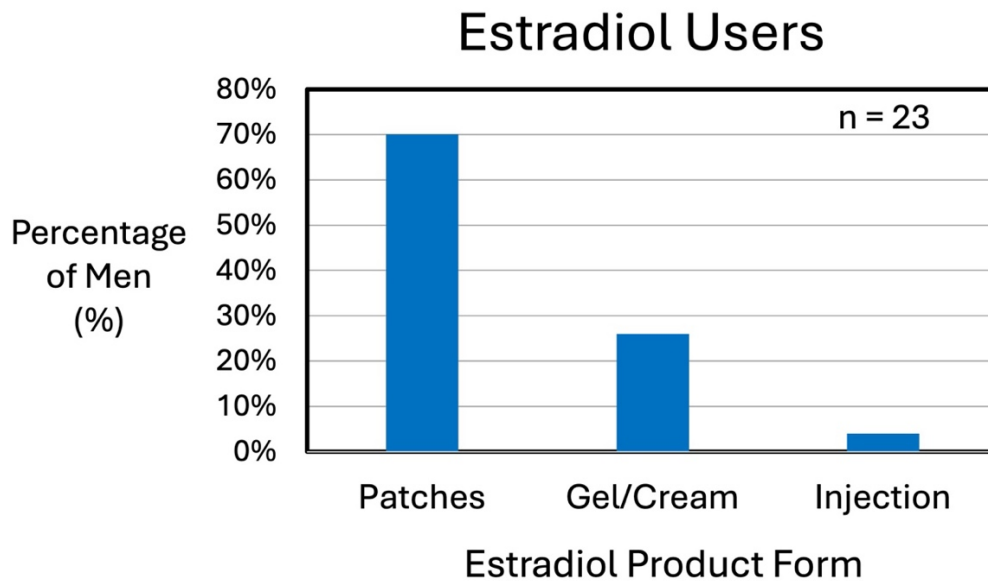


Fig. 3

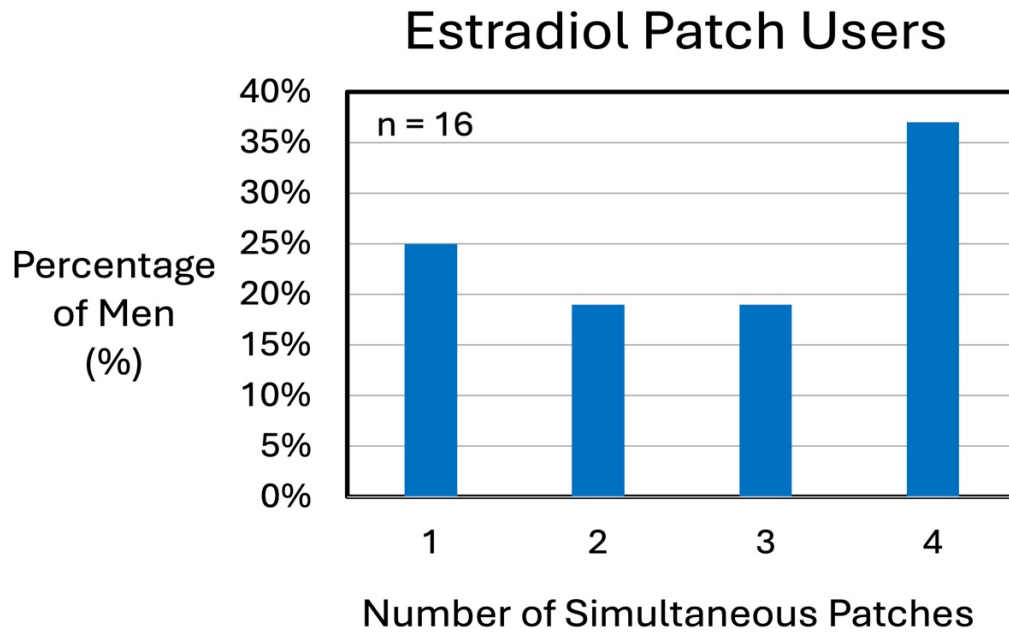


Fig. 4

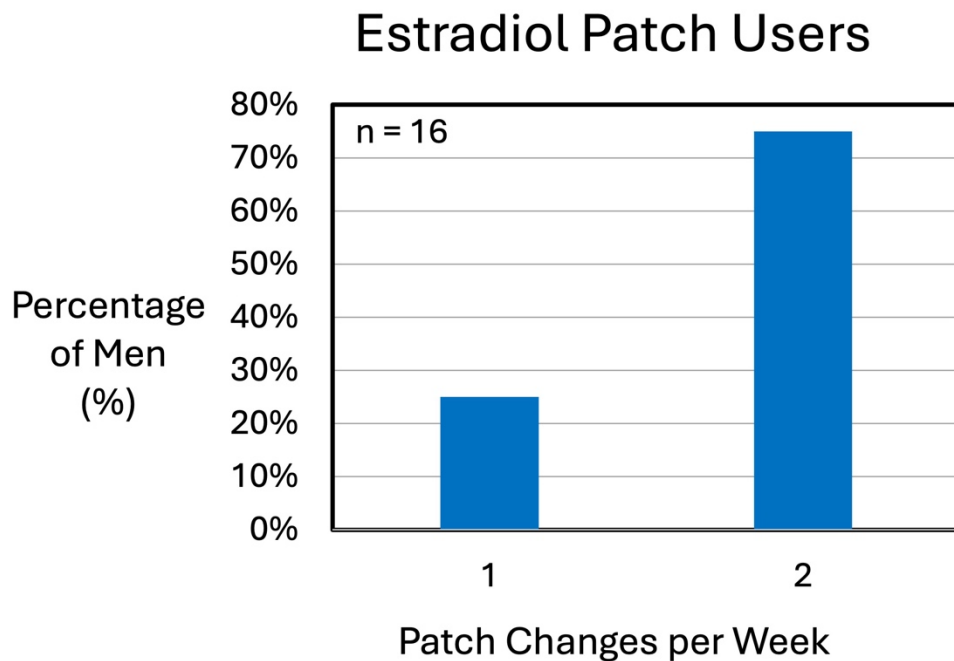


Fig. 5

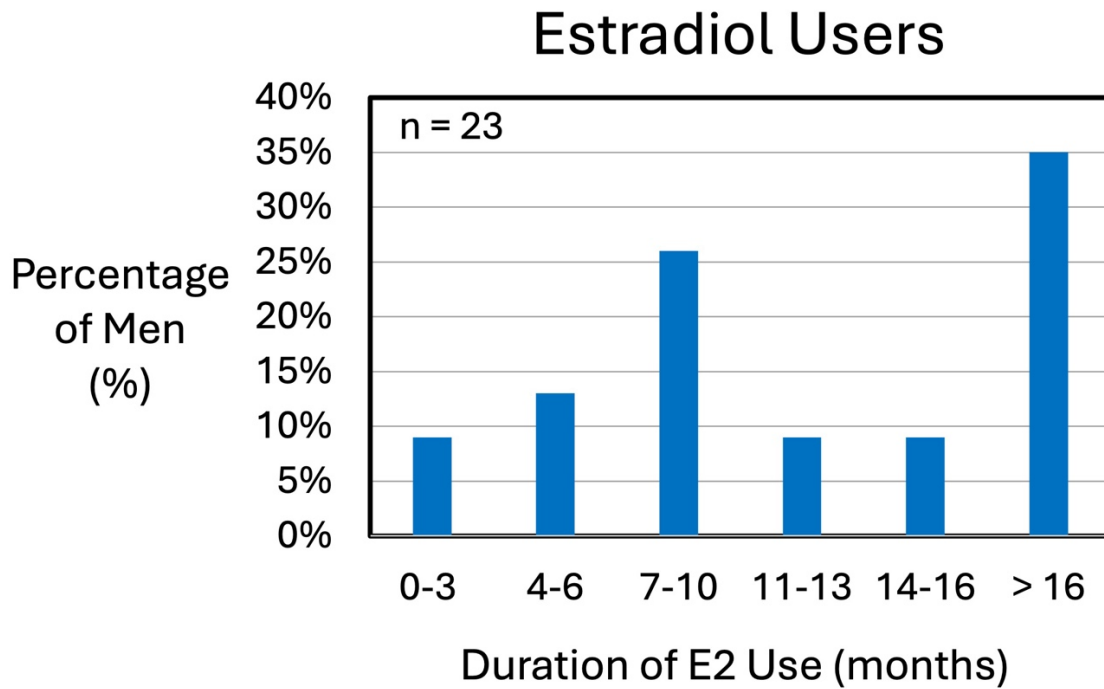


Fig. 6

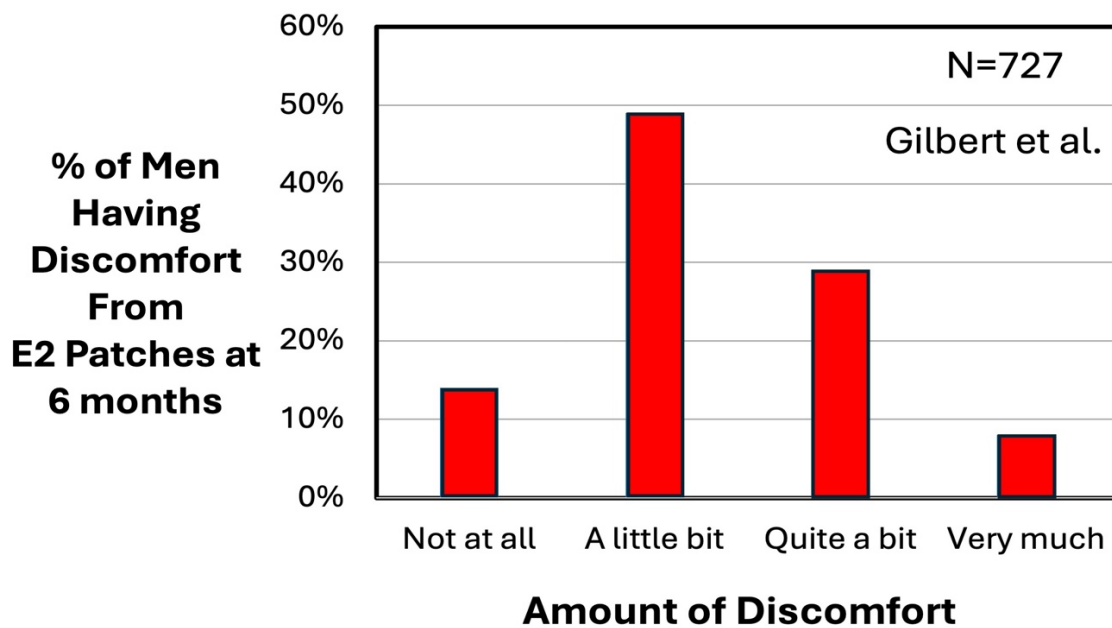


Fig. 7

APPENDIX A

Survey Questions and Responses

1. How is your estradiol delivered?

Patches	16 (70%)
Gel/Cream	6 (26%)
E2 Injection	1 (4%)
Total = 23 (100%)	

2. How many patches do you use?

1 patch	4 (25%)
2 patches	3 (19%)
3 patches	3 (19%)
4 patches	6 (37%)
Total = 16 (100%)	
Median = 3 patches (range = 1 – 4)	

3. How strong are the patches?

0.025 mg E2	1 (6%)
0.05 mg E2	1 (6%)
0.075 mg E2	0 (0%)
0.1 mg E2	14 (88%)
Total = 16 (100%)	
Median = 0.1 mg (range = 0.025 – 0.1 mg E2)	

4. How often are your patches changed?

Once a week	4 (25%)
Twice a week	12 (75%)
Total = 16 (100%)	

5. What concentration of E2 gel/cream did you use?

Average = 0.4% E2 (Range = 0.06% - 1.0%)

6. What commercial brand of gel/cream did you use?

EstroGel, Estrebet (India)

7. What E2 dosing protocol did you use?

Low-to-High 2 (9%)
 High-to-Low 3 (13%)
 Constant 18 (78%)
Total = 23 (100%)

8. What brand of patches did you use?

Evorel, Mylan, Climara, Minnevelle, Vivelle Dot, FEM7, Lyllana, Sandoz

9. How long have you used Estradiol?

0-3 months 2 (9%)
 4-6 months 3 (13%)
 7-10 months 6 (26%)
 11-13 months 2 (9%)
 14-16 months 2 (9%)
 > 16 months 8 (35%)
Total = 23 (100%)
Median = 12 months (Range = 1-264 months)

10. How bothersome was/is your mastalgia symptoms?

No Bother 2 (8%)
 Mild 11 (48%)
 Moderate 5 (22%)
 Severe 5 (22%)
Total = 23 (100%)

11. How long did your symptoms of mastalgia last?

0-3 months 6 (26%)
 4-6 months 1 (4%)
 7-10 months 0 (0%)
 11-13 months 2 (9%)
 14-16 months 0 (0%)
 Still Ongoing 14 (61%)
Total = 23 (100%)

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

→ Please consider making a tax-deductible donation to the *Estradiol Initiative*.

