Venous thromboembolism is a documented risk of some estradiol formulations, but evidence evaluating the perioperative risk of continuation of estradiol therapy is limited. This narrative review summarizes literature related to the perioperative venous thromboembolic risk of estradiol, with a focus on feminizing genitoplasty for trans people undergoing feminizing hormone therapy. Given the dearth of evidence underlying gender-affirming hormone therapy regimens, much of the risk is based on the menopausal hormone therapy literature. However, the doses used for trans people undergoing feminizing hormone therapy can be significantly higher than those used for menopausal hormone therapy and escalating estradiol dose is associated with an increased thrombotic risk. Transdermal formulations are not associated with an increased risk in postmenopausal people. Feminizing genitoplasty is associated with a low thromboembolic risk. However, many patients are instructed to cease estradiol therapy several weeks preoperatively based on reports of increased thrombotic risk in trans people undergoing feminizing hormone therapy and hemostatic changes with the oral contraceptive pill. This can result in psychological distress and vasomotor symptoms. There is insufficient evidence to support routine discontinuation of estradiol therapy in the perioperative period. There is a need for high-quality prospective trials evaluating the perioperative risk of estradiol therapy in trans people undergoing feminizing hormone therapy to formulate evidence-based recommendations.

INTRODUCTION

There have been significant increases in the number of transgender (trans) people (with a binary and/or non-binary gender) seeking healthcare worldwide [1]. Trans people undergoing feminizing hormone therapy are typically treated with estradiol with or without anti-androgen to increase serum estradiol concentration and decrease serum testosterone concentration into a range similar to cisgender females [2]. This results in development of feminine physical characteristics, including softening of skin, a decrease in facial and body hair growth, breast development, and changes in body composition including body fat redistribution and decreased muscle mass [3,4].

Venous thromboembolism (VTE) is a recognized side effect of some formulations of estradiol therapy and is the
most common side effect of feminizing hormone therapy [3]. However, estradiol formulations differ in their thrombotic risk and the incidence of VTE has decreased now that ethinyl estradiol is no longer recommended as part of the feminizing hormone therapy regimen [5].

Much of the evidence underlying the thrombotic risk of estradiol therapy is derived from the menopausal hormone therapy literature. Evidence suggests that oral but not transdermal formulations are associated with an increased VTE risk in post-menopausal people [6], potentially related to first-pass metabolism or the estradiol dose administered [7]. Escalating estradiol dose has been associated with increased VTE risk in some studies [8]. This is an important consideration, given that the estradiol doses administered as feminizing hormone therapy can be significantly higher than those used for menopausal hormone therapy.

Some trans people undergo gender-affirming surgery such as feminizing genitoplasty to align their physical characteristics with their gender identity. Due to the potential thrombotic complications of estradiol therapy and the increased risk of thrombosis perioperatively, guidelines including the Italian Society of Andrology and Sexual Medicine and National Observatory of Gender Identity recommend cessation of estradiol 2-4 weeks prior to feminizing genitoplasty or other major surgery [9-11]. However, these recommendations are based on evidence including estradiol formulations which are no longer used and many studies informing these recommendations were performed prior to introduction of routine VTE prophylaxis. Perioperative cessation of estradiol can result in psychological distress and vasomotor symptoms in trans people using feminizing hormone therapy [12].

Herein, we review the guidelines for feminizing hormone therapy, including the VTE risk of currently prescribed formulations. Next, we review the VTE risk and changes in hemostatic variables with different formulation of estradiol therapy. Finally, we discuss the thrombotic risk of estradiol therapy in the perioperative period, and implications for trans individuals undergoing feminizing genitoplasty. The material is based on peer-reviewed journals accessed within the PubMed database from January 1970 to 11 February 2020. The search terms “estradiol,” “estrogen,” “thrombosis,” “thromboembolism,” “surgery,” “perioperative” were used. We also searched the references listed in relevant publications. Original research articles, reviews, and societal guidelines were considered.

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### TABLE 1. Typical estradiol doses in trans and postmenopausal individuals.

| Formulation                  | Trans individuals   | Postmenopausal individuals |
|------------------------------|---------------------|---------------------------|
| Oral estradiol or estradiol valerate | 2-6mg daily         | 0.5-2mg daily             |
| Transdermal patch           | 100-150mcg daily   | 25-100mcg daily          |

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**FEMINIZING HORMONE THERAPY**

Several clinical guidelines provide protocols for commencement and monitoring of gender-affirming hormone therapy (GAHT) [3,13,14]. Feminizing hormone therapy involves estradiol treatment, often in combination with an anti-androgen (commonly cyproterone acetate 12.5-50mg daily or spironolactone 100-200mg daily) in individuals without orchidectomy. Estradiol is most commonly administered via the oral or transdermal route, with oral estradiol valerate or micronized estradiol the most commonly prescribed formulations [1]. Oral estradiol is more frequently prescribed in the United States due to differences in cost and insurance coverage [15]. Ethinyl estradiol and conjugated equine estrogens are no longer recommended given a higher thrombotic risk and inability to measure serum estradiol concentrations.

Serum estradiol concentration can be used for monitoring, and Endocrine Society Clinical Practice Guidelines recommend maintenance of serum estradiol and testosterone concentrations in the range for premenopausal females (367-734 pmol/L (100-200 pg/mL) and <1.7 nmol/L (50 ng/dL), respectively) [3]. Maintenance of estradiol concentrations within this range often requires significantly higher estradiol doses than those used for menopausal hormone therapy (Table 1) [1]. For instance, a recent retrospective analysis from Australia reported a median estradiol concentration of 290 pmol/L (79 pg/mL) on median oral estradiol valerate 6mg daily [16]. The exact role of monitoring estradiol concentration is unknown other than to avoid supraphysiological estradiol concentrations, and some clinicians instead monitor testosterone suppression to assess efficacy.

**RISK OF VENOUS THROMBOEMBOLISM IN TRANS INDIVIDUALS**

Observational studies have shown an increased VTE risk in trans people using feminizing hormone therapy [5,17,18], compared to both cisgender men and women [19]. However, the relative thrombotic risk differs between estradiol formulations [7,10,20]. Initial studies evaluating safety of GAHT documented a 45-fold increased risk of VTE (occurring in 6.3%) in trans people treated with ethinyl estradiol 100mcg daily and cyproterone acetate 100mg daily [21]. Due to this, ethinyl estradiol is no longer recommended for feminizing GAHT [3]. Conjugated equine estrogens have also been asso-
Table 2. Venous thromboembolism in trans individuals undergoing feminizing hormone therapy.

| Reference                  | Study type                  | Number of individuals | E2 regimen                                      | Number of VTE (%) | Perioperative VTE |
|----------------------------|-----------------------------|-----------------------|-------------------------------------------------|--------------------|------------------|
| Asscheman et al., 1989 [21]| Retrospective cohort       | 303                   | EE 100mcg                                        | 19 (6.3%)          | 4/235 (1.7%)     |
| Prior et al., 1989 [60]    | Prospective cohort         | 61                    | CEE 2.5 mg BD ¾ weeks                            | 0                  | N/A              |
| van Kesteren et al., 1997 [5]| Retrospective cohort    | 816                   | EE 100mcg Transdermal estradiol (n=138)          | 45 (5.5%)          | 5                |
| Schlatterer et al., 1998 [61]| Retrospective cohort     | 46                    | Intramuscular estradiol valerate 40-100mg every 2 weeks | 0                  | N/A              |
| Dittrich et al., 2005 [62] | Prospective cohort        | 60                    | Oral estradiol valerate + GnRHa                 | 1 (1.7%)           | Nil              |
| Wilson et al., 2009 [63]   | Prospective cohort        | 30                    | CEE (n=23) Transdermal estradiol (n=7)          | 0                  | N/A              |
| Ott et al., 2010 [27]      | Retrospective cohort      | 162                   | Estradiol valerate 100mcg/24hr                 | 0                  | N/A              |
| Seal et al., 2012 [22]     | Retrospective, controlled audit | 330                  | EE (n=133) CEE (n=36)                           | 4 (1.2%)           | Not reported     |
| Wierckx et al., 2012 [17]  | Cross-sectional study     | 50                    | Various transdermal preparations (n=25)         | 3 (6%)             | Nil              |
| Wierckx et al., 2013 [18]  | Cross-sectional study     | 214                   | Various transdermal preparations (n=105)        | 11 (5.1%)          | 3                |
| Wierckx et al., 2014 [26]  | Prospective cohort study  | 53                    | Oral estradiol valerate (n=40)                 | 0                  | N/A              |
| Arnold et al., 2016 [23]   | Retrospective cohort      | 676                   | Oral estradiol (n=676) CEE (n=42)               | 1 (0.15%)          | Nil              |
| Getahun et al., 2018 [25]  | Electronic medical record-based cohort study | 2842 | Not reported                                      | 61 (2.1%)          | Not reported     |
| Meyer et al., 2019 [24]    | Retrospective cohort study | 155                   | Transdermal preparations (n=82) Oral estradiol valerate or hemihydrate (n=73) | 3 (1.9%)           | 2                |

CEE, conjugated equine estrogens; EE, ethinyl estradiol; GnRHa, gonadotropin-releasing hormone agonist
associated with an increased VTE risk [22]. Modern GAHT regimens involving oral or transdermal estradiol have a lower risk of VTE; recent observational data suggests a risk between 0-2% [23-27]. A systematic review and meta-analysis found the overall risk approximates that of cisgender females prescribed estradiol [20]. Table 2 provides a summary of studies reporting VTE in trans people using feminizing hormone therapy.

**INFLUENCE OF ROUTE OF ADMINISTRATION AND DOSE**

The differential effects of VTE risk based on route of administration were first demonstrated in the EStrogen and THromboEmbolism Risk (ESTHER) study [28]. The case-control study enrolled 155 post-menopausal people with a first episode of VTE and 381 matched controls. Those treated with oral estradiol, compared to non-users, had a significantly higher estimated risk of VTE (odds ratio (OR) 3.5 (1.8–6.8)), whereas those treated with transdermal estradiol did not (OR 0.9 (0.5–1.6)) [28].

Following this, case-control [8,29,30] and cohort studies [31-34] in post-menopausal people have also documented an increased VTE risk with oral estradiol compared to transdermal estradiol (Table 3). Although the oral estradiol regimens differed between studies, with some reporting estradiol and/or conjugated equine estrogens, both preparations have independently been associated with an increased VTE risk.

Several studies in post-menopausal people have evaluated the influence of estrogen dose on VTE risk. High-dose (defined as >1mg estradiol [8,32], or >2mg estradiol or 0.625mg conjugated equine estrogens [30]) oral estradiol was associated with a higher risk of VTE in some studies [8,30] but not another [32]. There does not appear to be an increased VTE risk with high-dose (>50mcg/24hours) transdermal preparations [8,30,32]. However, one nested case-control study did suggest an increased risk of stroke in post-menopausal people treated with transdermal estradiol >50mcg/24hours compared to low-dose estradiol [35].

**CHANGES IN HEMOSTATIC VARIABLES WITH ESTRADIOL THERAPY**

**Ethinyl Estradiol**

Combined oral contraceptive agents are known to affect synthesis of coagulation factors. Levels of fibrinogen, factor VIII, von Willebrand factor, factor VII, factor X, and prothrombin increase while the level of protein S decreases [36]. Acquired resistance to activated protein C (APC) has also been reported [37]. Some parameters such as sex hormone-binding globulin increase in a dose-dependent manner, a potential biomarker of hepatic estradiol exposure [38]. Overall, these changes may result in a prothrombotic state and an increase in VTE risk.

The timeline of changes in these parameters has been evaluated in one study. Robinson et al. evaluated changes in hemostatic variables in 24 people following cessation of the combined oral contraceptive pill containing 30mcg ethinyl estradiol. After 6 months of treatment, there were statistically significant increases in fibrinogen and factor X, with a decrease in antithrombin III [39]. Following cessation, a “rebound” in concentrations of fibrinogen and antithrombin III was seen between weeks 2-6. The authors postulated that surgery should be undertaken at least 4 weeks following cessation of the OC, at which stage fibrinogen is low, antithrombin III is high, and factor X has returned to baseline. This has formed the basis for perioperative recommendations in trans people using feminizing hormone therapy.

**Menopausal Hormone Therapy**

Hemostatic variables differ between oral and transdermal estradiol preparations, theoretically due to first-pass metabolism in the liver and a resultant increased synthesis of pro-coagulant proteins following oral administration. A lower anti-thrombin III has been reported with oral but not transdermal formulations [40]. Several randomized controlled trials have also demonstrated that oral [41] but not transdermal estradiol [42,43] results in an acquired resistance to APC. Therefore, transdermal estradiol formulations at doses used for menopausal hormone therapy do not appear to have a significant effect on hemostasis.

**Studies in Trans People Undergoing Feminizing Hormone Therapy**

The influence of feminizing hormone regimens on hemostatic variables has also been evaluated in trans people. In an open-label randomized study, hemostatic parameters were measured prior to and 4 months after commencement of: ethinyl estradiol 100mcg daily and cyproterone acetate 100mg daily; oral estradiol 2mg twice daily and cyproterone acetate 100mg daily; transdermal estradiol 100mcg daily and cyproterone acetate 100mg daily, or; cyproterone acetate 100mg daily. The group treated with ethinyl estradiol had the largest change in hemostatic variables, with a large increase in APC resistance (1.2±0.8 to 4.1±1.0; p<0.001), a 9% increase in plasma protein C (p<0.012), and a 30% decrease in plasma protein S (p<0.005) [44]. In comparison, small changes were seen in all other groups [44].

More recently, the potential utility of global coagulation assays has been investigated in a cross-sectional study of trans individuals. Overall, trans individuals on estradiol demonstrated increased clot strength (max-
## Table 3. Studies evaluating VTE risk by estradiol formulation.

| Reference                | Study type        | Number of individuals | Hormone therapy use                                      | VTE risk                                                                 |
|--------------------------|-------------------|-----------------------|----------------------------------------------------------|--------------------------------------------------------------------------|
| Scarabin et al., 2003 [28]| Case-control      | 155 with VTE          | 62/155 (40%) VTE cases – 32 (51%) used oral E2           | OR oral E2 vs. non-users: 3.5 (1.8-6.8)                                   |
|                          |                   | 381 matched controls  | 120/381 (31%) controls – 27 (22%) used oral E2          | OR transdermal E2 vs. non-users: 0.9 (0.5-1.6)                             |
|                          |                   |                       |                                                          | OR oral E2 vs. transdermal E2: 4.0 (1.9-8.3)                              |
| Canonico et al., 2007 [29]| Case-control      | 271 with VTE          | 124/271 (45%) VTE cases – 57 (46%) used oral E2         | OR oral E2 vs. non-users: 4.2 (1.5-11.6)                                   |
|                          |                   | 610 matched controls  | 226/610 (37%) controls – 46 (20%) used oral E2         | OR transdermal E2 vs. non-users: 0.9 (0.4-2.1)                              |
| Renoux et al., 2010 [30] | Case-control      | 23505 with VTE        | 1004/23505 (4.3%) VTE cases – 729 (72%) used oral E2    | EE oral E2 vs. non-users: 1.49 (1.37-1.63)                                  |
|                          |                   | 231562 matched controls | 7851/231562 (3.4%) controls – 5105 (65%) used oral E2  | RR transdermal E2 vs. non-users: 1.01 (0.89-1.16)                             |
|                          |                   |                       |                                                          | VTE risk increased with increasing E2 dose                                |
| Canonico et al., 2010 [31]| Cohort study     | 98995 individuals     | 549 VTE cases                                          | HR oral E2 vs. non-users: 1.7 (1.1-2.8)                                   |
|                          |                   |                       | Oral E2 81 VTE                                         | HR transdermal E2 vs. non-users: 1.1 (0.8-1.8)                              |
|                          |                   |                       | Transdermal E2 174 E2                                   |                                                                          |
| Sweetland et al., 2012 [32]| Cohort study   | 1058259 individuals   | 2200 VTE cases                                         | RR oral E2 vs. non-users: 1.42 (1.22-1.66)                                  |
|                          |                   |                       | Oral E2 194/51853                                      | RR transdermal E2 vs. non-users: 0.82 (0.64-1.06)                             |
|                          |                   |                       | Transdermal E2 66/86250                                 |                                                                          |
| Simon et al., 2016 [33] | Matched cohort study | 2551 individuals treated with transdermal E2 matched to 2551 individuals treated with oral E2 | 13/2551 VTE events in transdermal E2 group                         | OR transdermal E2 vs. oral E2: 0.42 (0.19-0.96)                             |
| Laliberté et al., 2018 [34]| Matched cohort study | 27018 individuals treated with transdermal E2 matched to 27018 individuals treated with oral E2 | 115/27018 VTE events in transdermal E2 group | IRR transdermal E2 vs. oral E2: 0.67 (0.49-0.92)                             |
|                          |                   |                       |                                                          |                                                                          |
| Vinogradova et al., 2018 [8]| Case-control  | 80396 with VTE        | 5795/80396 (7.2%) VTE cases – 4915 (65%) used oral E2   | OR oral E2 vs. non-users: 1.58 (1.52-1.64)                                  |
|                          |                   | 391494 matched controls | 21670/391494 (5.5%) controls – 16938 (78%) used oral E2 | OR transdermal E2 vs. non-users: 0.93 (0.87-1.01)                             |
|                          |                   |                       |                                                          | OR oral E2 vs. transdermal E2: 1.70 (1.56-1.85)                              |
|                          |                   |                       |                                                          | OR oral E2 vs. CEE: 0.85 (0.76-0.95)                                       |
|                          |                   |                       |                                                          | VTE risk increased with increasing E2 dose                                |

CEE, conjugated equine estrogen; E2, estradiol; HR, hazard ratio; OR, odds ratio; IRR, incidence rate ratio; VTE, venous thromboembolism
Cessation of estradiol renders an individual prone to side effects including vasomotor symptoms and mood disturbance that can impact quality of life [12]. Due to the lack of data, there is variability in clinical practice and some surgeons continue estradiol therapy perioperatively.

**Rate of VTE with Feminizing Genitoplasty**

There are limited data evaluating VTE risk with feminizing genitoplasty though retrospective cohort studies have documented a low risk. In a retrospective analysis of outcomes in 233 individuals who underwent feminizing genitoplasty between 1994-2004, two individuals (0.9%) reported postoperative deep vein thrombosis (DVT), one of whom had non-fatal pulmonary embolism (PE) [56]. Guidelines at this center are to cease feminizing hormone therapy 6 weeks pre-operatively. Hormonal regimens and other VTE risk factors were not reported.

Similarly, there were no patient-reported VTE in another cohort of 232 individuals undergoing penile inversion vaginoplasty [12]. Patients were instructed to cease estradiol 3 weeks preoperatively. Two-hundred-and-fourteen (92%) patients ceased their feminizing hormones pre-operatively with a mean duration of abstinence of 22 days.

In a more recent retrospective analysis of 330 trans individuals who underwent penile inversion vaginoplasty between 2011-2015, there were no reported cases of DVT [57]. This was despite a perioperative estradiol regimen that involved continuation of estradiol tapered to 2mg at least 2 weeks prior to surgery. Similarly, there were no reports of DVT using a protocol in which those under 50 (n=49) continued estradiol until surgery, and people aged 50 years or older (n=10) discontinued estradiol 6 weeks preoperatively but could choose to continue transdermal estradiol until 2 weeks preoperatively [58].

**Patient-reported Outcomes of Preoperative Estradiol Cessation**

Cessation of estradiol 2 or 6 weeks preoperatively results in virilization with testosterone and estradiol concentrations near the male reference range [59]. There are limited data examining patient-reported outcomes of preoperative estradiol cessation. In a retrospective analysis, among participants who discontinued hormones preoperatively, 74 (35%) reported that this had been difficult [12]. The most common symptoms reported by participants who stopped taking hormones were hot flushes (43 participants, 20% of those who stopped), mood swings or irritability (42 participants, 20% of those who stopped), and increases in facial or body hair growth (12 participants, 6% of those who stopped) [12].
Table 4. Studies evaluating perioperative VTE risk with estradiol treatment.

| Reference          | Study type          | Hormone regimen                      | Population                                                                 | Findings                                                                 |
|--------------------|---------------------|--------------------------------------|-----------------------------------------------------------------------------|---------------------------------------------------------------------------|
| Vessey et al.,     | Case-control        | Oral contraceptives                  | 30 women with postoperative (various surgeries) VTE                         | 12/30 (40%) women used OC in month prior to surgery vs. 9/60 (15%) controls (p=0.01), RR: 3.8 |
| 1970 [47]          |                     |                                      | 60 matched controls without VTE                                            |                                                                           |
| Greene et al.,     | Case-control        | Oral contraceptives                  | 60 women with postoperative, post-infection or post-traumatic VTE           | 21/60 (35%) women used OC in month prior to admission vs. 10/60 (16.7%) controls |
| 1972 [48]          |                     |                                      | 60 matched controls without VTE                                            | RR (matched pair analysis): 6.5 (p=0.0074)                                  |
| Sagar et al.,      | Case-control        | Oral contraceptives                  | 31 women with postoperative (Emergency abdominal surgery) VTE detected by fibrinogen uptake | 6/31 (19%) women used OC (2 symptomatic and 4 asymptomatic) vs. 0/19 (0%) controls. (p<0.05) |
| 1976 [49]          |                     |                                      | 19 controls without VTE                                                   |                                                                           |
| Astedt et al.,     | Prospective cohort  | Ethinyl estradiol 50mcg or 200mcg    | 19 women aged >50 undergoing uterine prolapse surgery taking EE 50mcg (n=11) or 200mcg (n=8) | Fibrin deposits found in 6/11 women taking 50mcg EE; 4/8 women taking 200mcg EE; 18/157 controls (p<0.001) |
| 1980 [50]          |                     |                                      | 157 women in control group                                                |                                                                           |
| Bernstein et al.,  | Prospective cohort  | Estrogens, not otherwise specified   | 276 women aged >50 undergoing gynecological surgery                        | 12/31 (39%) women using estrogens vs. 35/245 (14%) those not using estrogens (p<0.01) |
| 1980 [64]          |                     |                                      | 31 of these treated with estrogen                                          |                                                                           |
| Gallus et al.,     | Prospective cohort  | Oral contraceptive                  | 221 women aged 21-49 undergoing abdominal or gynecological surgery         | 0/99 (0%) women taking OC vs. 1/122 (0.8%) women not taking OC             |
| 1984 [51]          |                     |                                      | 99 of these taking OC                                                     |                                                                           |
| Vessey et al.,     | Prospective cohort  | Oral contraceptive                  | 4359 not taking OC undergoing various surgeries                             | 12/1244 (0.96%) women taking OC in month prior to surgery vs. 22/4359 (0.5%) (p=NS) |
| 1986 [52]          |                     |                                      | 1244 women taking OC                                                       |                                                                           |
| Hurbanek et al.,   | Case-control        | Oral or transdermal estrogens        | 108 patients with postoperative VTE following hip or knee arthroplasty      | 18/108 (16.7%) women used estrogens vs. 49/210 (23.3%) controls: OR: 0.66 [95% CI, 0.35-1.18; p=0.17] |
| 2004 [53]          |                     |                                      | 210 matched controls                                                      |                                                                           |
| Barsoum et al.,    | Case-control        | Oral contraceptive, oral or transdermal estrogens | 726 women with VTE (302 hospitalized with or without surgery)              | OC OR: 3.29 [95% CI, 1.72-6.27; (p<0.001) Non-contraceptive estrogen and progesterin OR: 1.73 [95% CI, 1.04-2.87; p=0.03] |
| 2010 [65]          |                     |                                      | 830 controls (71 matched hospitalized controls)                           | Estrogen monotherapy OR: 1.32 [95% CI, 0.84-2.06; p=0.23]                  |
| Acuna et al.,      | Case-control        | Oral contraceptive (n=2)             | 31 women with VTE following trauma                                         | OC use vs. no use. OR: 0.70 [95% CI, 0.70-0.80]; p=0.41                     |
| 2011 [66]          |                     |                                      | 79 women without VTE                                                      |                                                                           |
| Schulte et al.,    | Retrospective cohort| Estrogens, not otherwise specified   | 1469 patients following spine surgery                                      | Estrogens vs. no estrogens. Univariate RR: 6.2 [95% CI, 1.4-26.1]; p<0.01; multivariate |
| 2013 [54]          |                     |                                      | 16 patients with postoperative VTE                                        | RR, 3.1 [95% CI, 3.5-128.8]; p<0.07                                      |
| Park et al.,       | Retrospective cohort| Estrogens, not otherwise specified   | 21261 patients who underwent spine surgery                                 | 10 patients treated with estrogens, none with VTE                         |
| 2019 [55]          |                     | (n=10)                               | 444 patients with postoperative VTE                                        | No patients with VTE were treated with estrogens                          |

EE, ethinyl estradiol; OC, oral contraceptives; OR, odds ratio; RR, relative risk; VTE, venous thromboembolism.
Future Directions

There is a need for prospective trials evaluating the perioperative risk of estradiol therapy in trans people. Based on safety in the menopausal hormone therapy literature, future research could give consideration to continuation of or transition to transdermal estradiol preparations in the perioperative period. Formal evaluation of the risks of cessation of estradiol on markers of quality of life, including vasomotor symptoms, mood disorders, and gender dysphoria should be undertaken.

CONCLUSION

There is currently limited evidence which supports routine cessation of estradiol regimens in the perioperative period in trans individuals at low thrombotic risk. Transdermal estradiol is not associated with VTE in postmenopausal women and could represent an alternative route of estradiol administration in the perioperative period although there is no supportive data. Future prospective trials should evaluate the safety of estradiol continuation in the perioperative period to enable evidence-based recommendations for this patient group.

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