

# PERIOPERATIVE CONSIDERATIONS FOR TRANSGENDER PATIENTS ON HORMONE THERAPY <sup>+</sup> <sub>○</sub> •

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# OBJECTIVES



At the completion of this educational session, learners will be able to:

1. Identify complications related to hormone therapy in transgender patients.
2. Recognize which transgender patients are at higher risk for complications during the perioperative period.
3. Advocate for preventive measures to improve patient outcomes in the transgender population.

# Terms

Gender Identity	Cisgender	Transgender	Gender Nonconformity	Gender Dysphoria
Internal sense of self and gender	Gender identity aligns with sex assigned at birth	Gender identity differs from sex assigned at birth 	Gender identity / role / expression diverges from cultural or societal norms	Distress caused by discrepancy between gender identity and the sex assigned at birth

# Gender-Affirming Hormone Therapy

<b>Transgender Women</b>	<b>Estrogen</b>  (PO, TD, IM)	<b>Anti-Androgens</b>  Spironolactone Bicalutamide Enzalutamide (PO)	<b>5<math>\alpha</math>- Reductase Inhibitor</b>  Finasteride Dutasteride (PO)	<b>Progesterone</b>  (PO)	<b>GnRH Agonist</b>  Leuprolide Triptorelin Goserelin Buserelin (IM,SC, IN)
<b>Transgender Men</b>	<b>Androgen</b> Testosterone (IM, SC, TD, PO)				

# Current Standard of Care

Conflicting information and lack of guidelines for gender-affirming hormone therapy (GAHT) in transgender patients

Unclear guidelines regarding preparation and care for this growing patient population



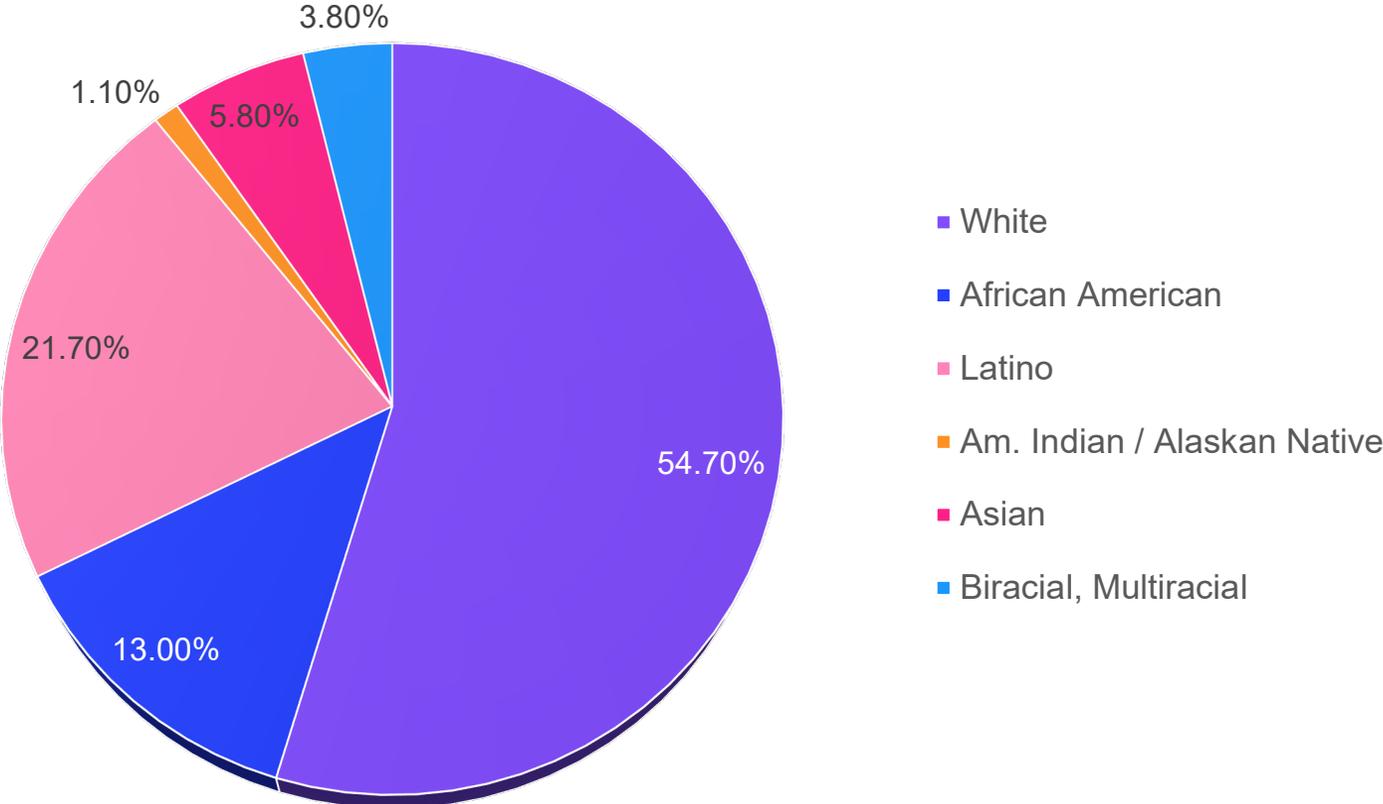
**WHY IS IT IMPORTANT  
TO OUR PRACTICE?**

# Why is it important?

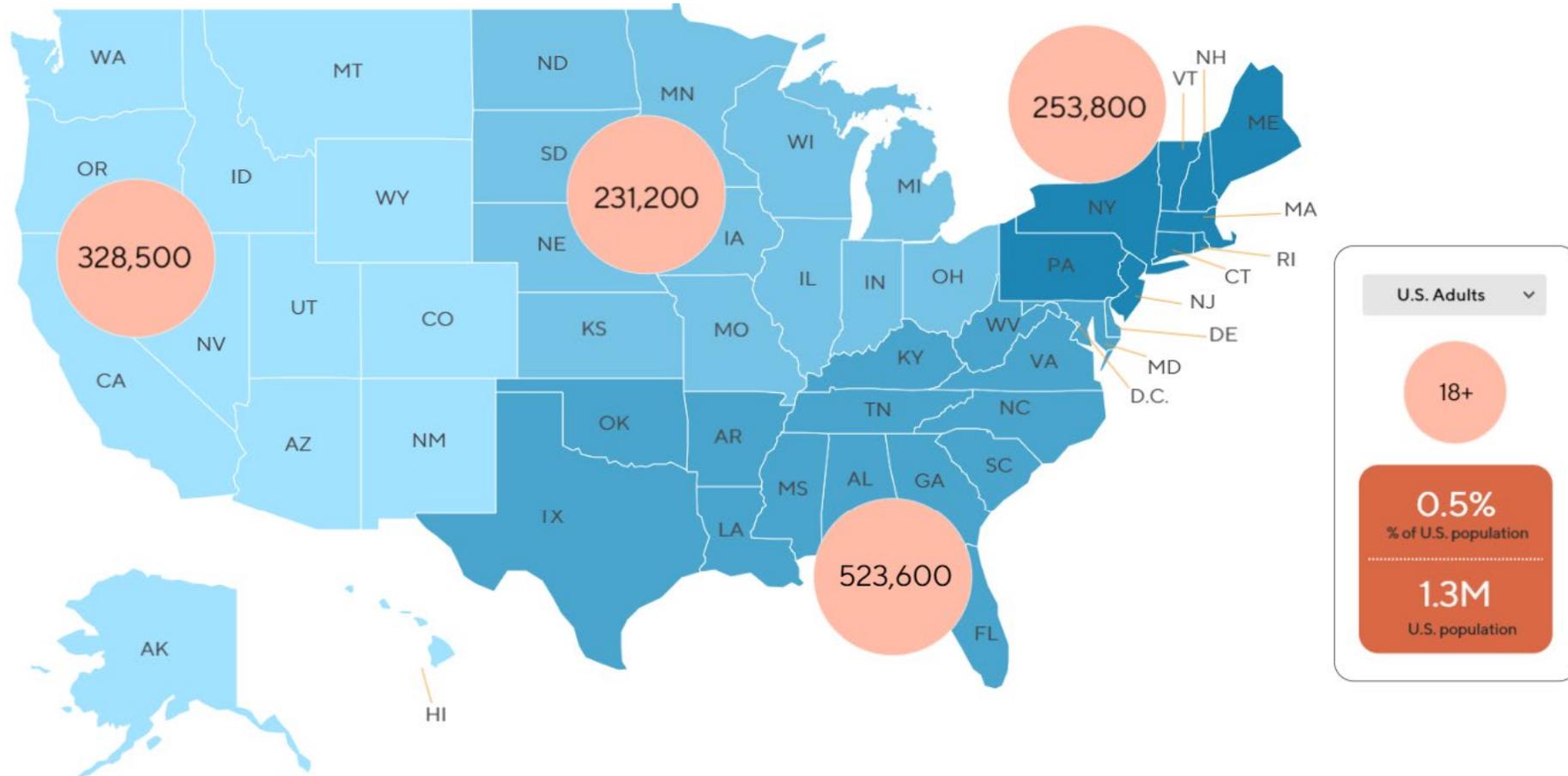
- USA - There are 1.6 million people over the age of 13 that identify as transgender
- Transgender patients are an underserved and marginalized population that continues to experience health disparities daily.
- It is imperative CRNAs understand how different hormone therapy treatments interact with our anesthetics
  - Complications
  - Transgender patients at highest risk
  - Preventative measures

# Statistics

Race/Ethnicity of Transgender Adults in the USA



# Geographical Distribution



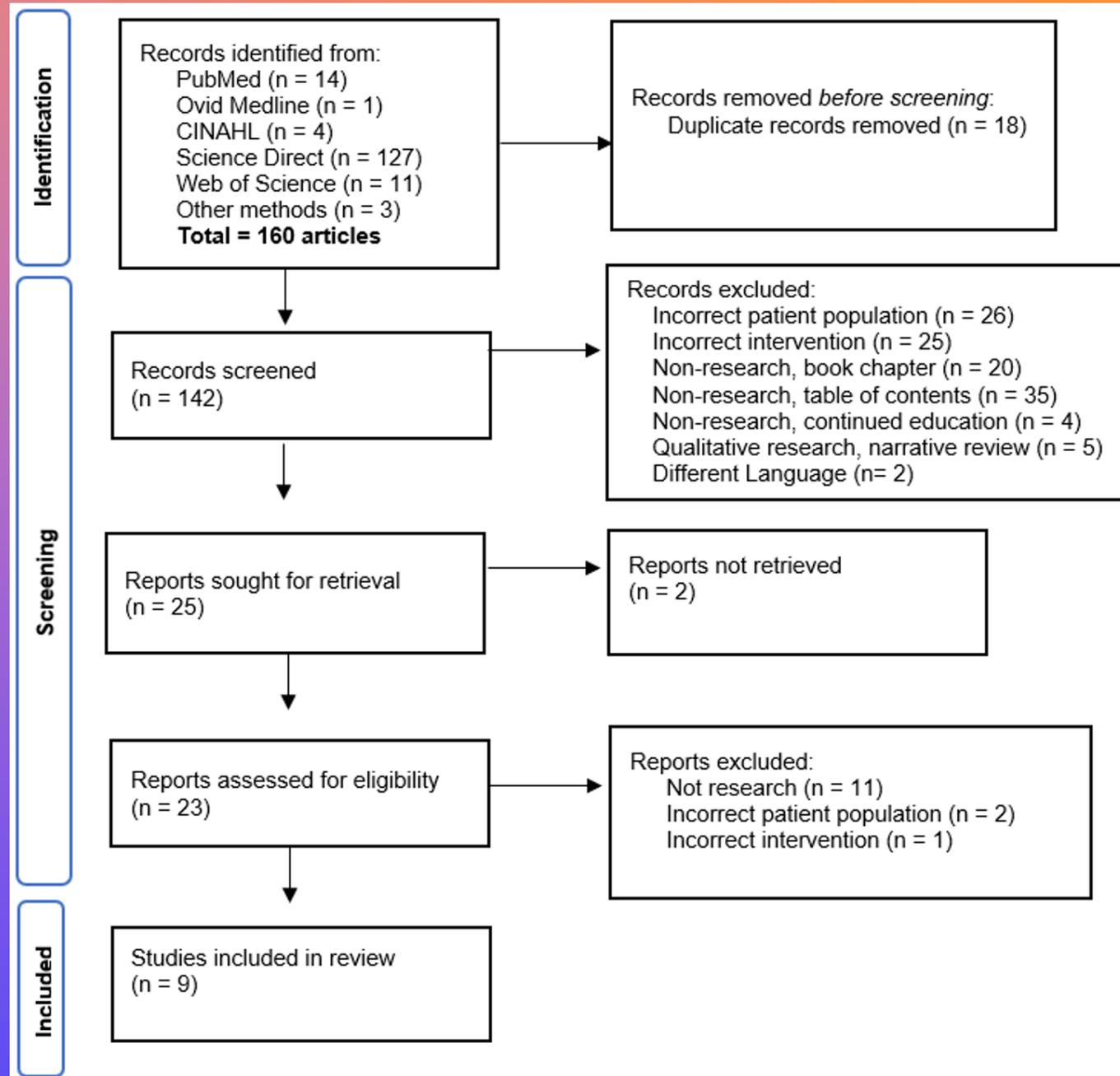


“The way to get started is to quit talking and begin doing.”

Walt Disney

# METHODS FOR RESEARCH

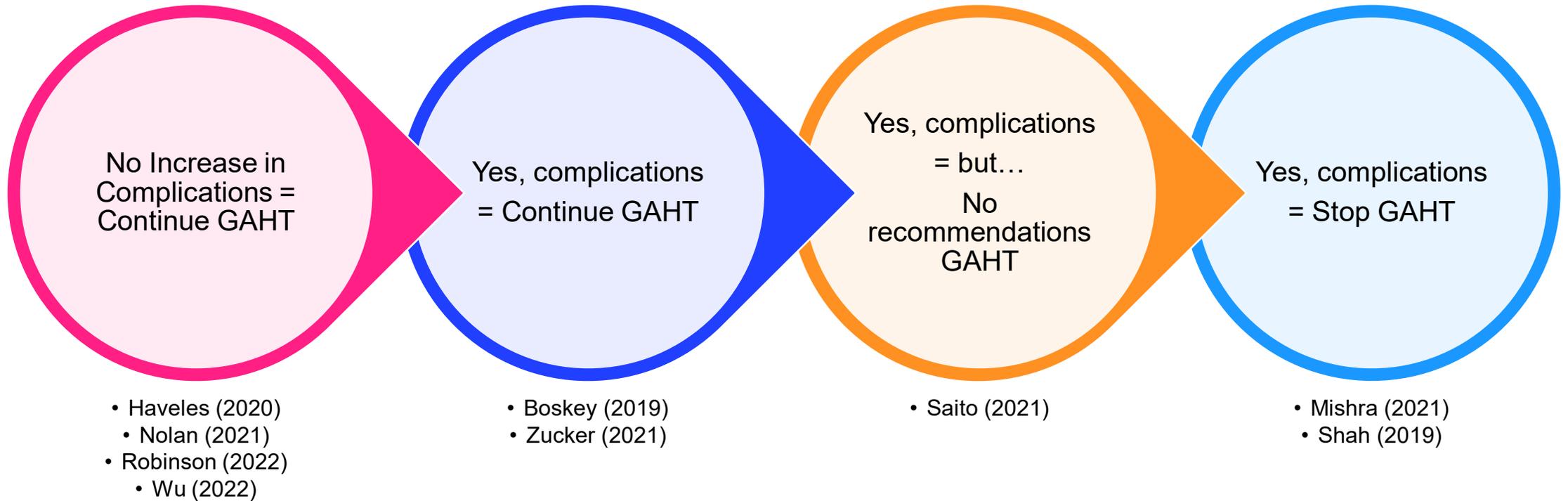
“AMONG TRANSGENDER PATIENTS, DOES HORMONE THERAPY INCREASE THE RISK FOR PERIOPERATIVE COMPLICATIONS?”



# 9 Included Studies

Study	Type	Results
Boskey (2019)	Systematic Review n = 18 articles	Preoperative testosterone does not affect mortality or cardiac outcome  Antiandrogens delay wound healing, ↑ infection, and fat necrosis. Stop before surgery.  Stop/restarting testosterone could ↑ risk of thrombosis
Haveles (2020)	Systematic Review n = 7 articles	Surgeries > 5hrs increased VTE risk if on HT It cannot be determined if continuing HT through perioperative period increased VTE risk
Mishra, Nath, Kaushal, Kain (2021)	Narrative Systematic Review n = 29 articles	Side effects of GAHT include: Dyslipidemia, VTE, PE, DM, HTN, stroke, liver dysfunction, PONV, migraine, postoperative delirium, altered wound healing Stop GAHT two to four weeks prior to surgery
Nolan IT, et al. (2021)	Cohort Study n = 178 patients	Rates of wound-healing, hematomas, wound breakdown, and skin graft loss, and VTE complications between the 2 groups were not statistically significant
Robinson IS, et al (2022)	Retrospective Study n = 490 patients	No difference in rates of VTE among all groups  No difference in hematoma or seroma requiring post-op surgical intervention between both groups
Saito N, et al (2021)	Correlational / Experimental Study n = 74 patients	Testosterone noted to increase risk for lethal ventricular arrhythmias  Estrogen ↑ risk for long QT interval syndrome in transgender females taking estrogen
Shah SB, et al (2019)	Narrative Systematic Review n = 32 articles	Estrogen therapy showed 20x increased risk for thrombosis in first 1 year of therapy in smokers  Higher risk for migraines and PONV  Testosterone ↑ risk of CVA/strokes d/t potential raise in Hgb/Hct up to 48%
Wu SS, et al (2022)	Retrospective Study n = 236 patients	No VTE complications found in either group. No evidence to support cessation of testosterone for "top surgeries"  Estrogen cessation found to be more important to prevent VTE d/t longer operative times and bedrest for "bottom surgeries" in transgender females
Zucker R, et al (2021)	Meta-Analysis n = 1170 RCT	Oral contraceptives ↑ risk of VTE when ethinyl estradiol content is > 50mcg/pill, vs estrogen alone  Transdermal estrogen has less thrombogenic events associated with it. VTE risk may ↑ with higher dosage, route, duration of regimen  No data to date to demonstrate benefit of withholding HT

# Results



# No increase in complications = Continue GAHT<sup>+</sup>

Haveles (2020)	Nolan (2021)	Robinson (2022)	Wu (2022)
“Effect of cross-sex HT on VTE risk in male-to-female gender-affirming surgery”	“Estrogen continuation and VTE in penile inversion vaginoplasty (PIV)”	“Perioperative Hormone Management in Gender-Affirming Mastectomy: Is Stopping Testosterone before Top Surgery Really Necessary?”	“The effect of preoperative GAHT use on perioperative adverse events in transmasculine individuals undergoing masculinizing chest surgery for gender affirmation”
GAHT: Estrogen, Testosterone, Spironolactone	GAHT: Estrogen	GAHT: Testosterone (TSTN)	GAHT: Testosterone (TSTN)
<p>Surgeries &gt; 5hrs had greater risk for VTE</p> <p>5/7 studies had VTE</p> <p>- No data to support ↑ risk for VTE and d/c of GAHT</p>	<p>Group A stopped for 2 wks before surgery and resumed 1 wk postop. Group B reduced estrogen dosages perioperatively</p> <p>- VTE complications not statistically significant.</p>	<p>3 groups: TSTN held, TSTN continued, TSTN never started</p> <p>- No difference in rates of VTE among all groups</p>	<p>2 groups : TSTN stopped &amp; TSNT continued</p> <p>No thromboembolic complications found in either group</p> <p>- No need to d/c TSTN in Top surgeries.</p>

# Yes, Complications = but, continue GAHT

Boskey (2019)	Zucker (2021)
“Association of Surgical Risk With Exogenous Hormone Use in Transgender Patients”	“Minimizing VTE in feminizing hormone therapy: applying lessons from cisgender women and previous data”
GAHT: Testosterone (TSTN), Estrogen, Progesterone, Anti-androgens	GAHT: Estrogen
<ul style="list-style-type: none"><li>- TSTN does NOT affect mortality or cardiac outcome</li><li>-PO ethinyl estradiol showed increased evidence for VTE risk</li><li>- Antiestrogens delay wound healing, ↑ infection, and fat necrosis. Consider stopping, if high risk</li></ul>	<ul style="list-style-type: none"><li>- VTE &gt; Stroke &gt; CV risk</li><li>- VTE risk ↑ with PO &gt; TD estrogen</li><li>- No data to date to demonstrate benefit of withholding HT .</li><li>- Small risk for VTE = encourage continued use of HT prior to vaginoplasty.</li><li>- Important to give SQ Heparin perioperatively</li></ul>

# Yes, Complications = No recommendations on GAHT

**Which drugs  
increase QT  
prolongation?**

## Saito (2021)

“Gender-affirming hormone treatment causes changes in gender phenotype in a 12-lead electrocardiogram”

GAHT: Testosterone (TSTN), Estrogen

- Transgender males had ↑ RBC count, Hgb, serum creatinine, t-wave amplitude, and significantly longer QRS duration
- Transgender females had ↓ BMI, RBC count, Hgb, serum creatinine, QRS and t-wave amplitude
- Testosterone noted to ↑ early-repolarization pattern, which could increase risk for lethal ventricular arrhythmias.
- Estrogen ↑ risk for long QT interval syndrome in transgender females

# Yes, Complications = but, continue GAHT

**Which drugs  
increase QT  
prolongation?**

- Methadone
- Sevo > Iso = Des
- Serotonin-3 Antagonist (Zofran, Granisetron, Palonosetron)
- Cardiac: Amiodarone, Sotalol, Quinidine, Procainamide
- Macrolide Antibiotics (Azithro/Erythro/Clarithromycin)
- Fluoroquinolones (-floxacin)
- Antifungals (Fluconazole)
- Psych: TCA, SSRI, Atypical/Typical antipsychotics
- HIV protease inhibitors (-navir)

# Yes, Complications = STOP GAHT

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Mishra (2021)	Shah (2019)
“Gender reassignment surgery – a narrative overview of anesthetic considerations and implications”	”Perioperative anaesthetic concerns in transgender patients: Indian perspective”
GAHT: Testosterone (TSTN), Estrogen, Progesterone, Anti-androgens	GAHT: Estrogen, Testosterone (TSTN)
<ul style="list-style-type: none"><li>- Found risk for VTE/DVT, cardiovascular risk, and stroke</li><li>- D/C GAHT 2-4 weeks prior to GRS</li><li>- Use low-dose ASA if risk for embolism and SQ Heparin if on estrogen.</li><li>- Adequate intraop hydration to avoid higher risk for stroke if on testosterone.</li></ul>	<ul style="list-style-type: none"><li>- VTE , Stroke , CV risk</li><li>- Exogenous estrogen therapy increases risk for venous thromboembolism and needs prophylaxis.</li><li>-Parenteral testosterone ↑ risk of CVA/strokes</li><li>-Suspension of HT preop for 2-4 weeks</li></ul>

# Adverse Effects of GAHT

- VTE (1-2%)
- Stroke
- Cardiovascular events (arrhythmias, MI)
- Coagulopathy (↓ ATIII, ↑ FIX, ↑fibrin, ↑ APC, ↑FVIII)
- Dyslipidemias
- Delayed wound healing
- ↑ Insulin resistance
- Liver dysfunction
- Infection
- PONV
- Migraine
- Post-operative delirium



# Risk of Discontinuing GAHT

- Rebound virilization
- Postoperative depression
- Psycho-emotional consequences
  - Mood lability
  - Fatigue
  - Anxiety
  - Suicide
- Myalgia
- Resumption of menses
- Hot flashes



# “AT-RISK” TRANSGENDER PATIENTS

- Prior history of VTE / PE / DVT<sup>+</sup> •
- Diabetes
- Smokers
- First two years of Estrogen therapy
- Obese
- CAD

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# Recommendations for Practice

- Of nine articles, six articles suggest continuation of GAHT prior to surgery, since GAHT's benefits outweigh the small risk for these complications.
- Based on the cumulative literature reviewed, anesthesia providers should consider continuing GAHT on a case-by-case basis with a team approach that includes the patient and other providers such as surgeon, endocrinologist, psychiatrist, and anesthesia.



# Recommendations for Practice

- Conduct a thorough pre-operative assessment
  - Assess the patient and allow ample time for questions
  - Evaluate labs based on biological sex unless on HT > 6 months
- Understand the risk factors associated with each complication.
- Anesthesia plan that includes prophylactic management
  - VTE prophylaxis: Early ambulation, SCDs
  - Use low-dose ASA and/or SQ Heparin if on estrogen.
  - Adequate intraop hydration if on testosterone
  - Consider intraop Hydrocortisone to avoid steroid withdrawal

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# Suggestions for Future Practice

- Further research should consider:
  - Large, randomized control trials
  - Different dosages, formulations, therapy lengths
  - GAHT classes
    - Estrogen, progesterone, testosterone, or antiandrogens
    - Unique risks with each drug class
- It is imperative to clarify the benefits versus the risks of continuing GAHT during the perioperative period

# Resources

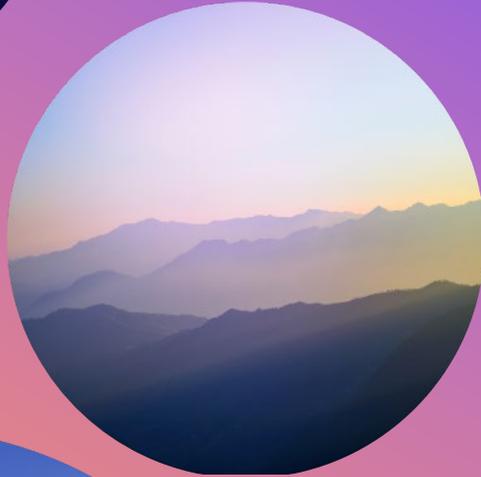
- Human Rights Campaign
  - [HRC.org](http://HRC.org)
- World Professional Association for Transgender Health
  - [WPATH.org](http://WPATH.org)
- Nurse Anesthesiology Pride Foundation
  - [CRNApride.com](http://CRNApride.com)



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# THANK YOU!

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References

