Gender care through the lifespan

Adam Foss, MD FAAP, FACP
He/Him/His
Internal Medicine-Pediatrics
Fairview Eagan

Objectives

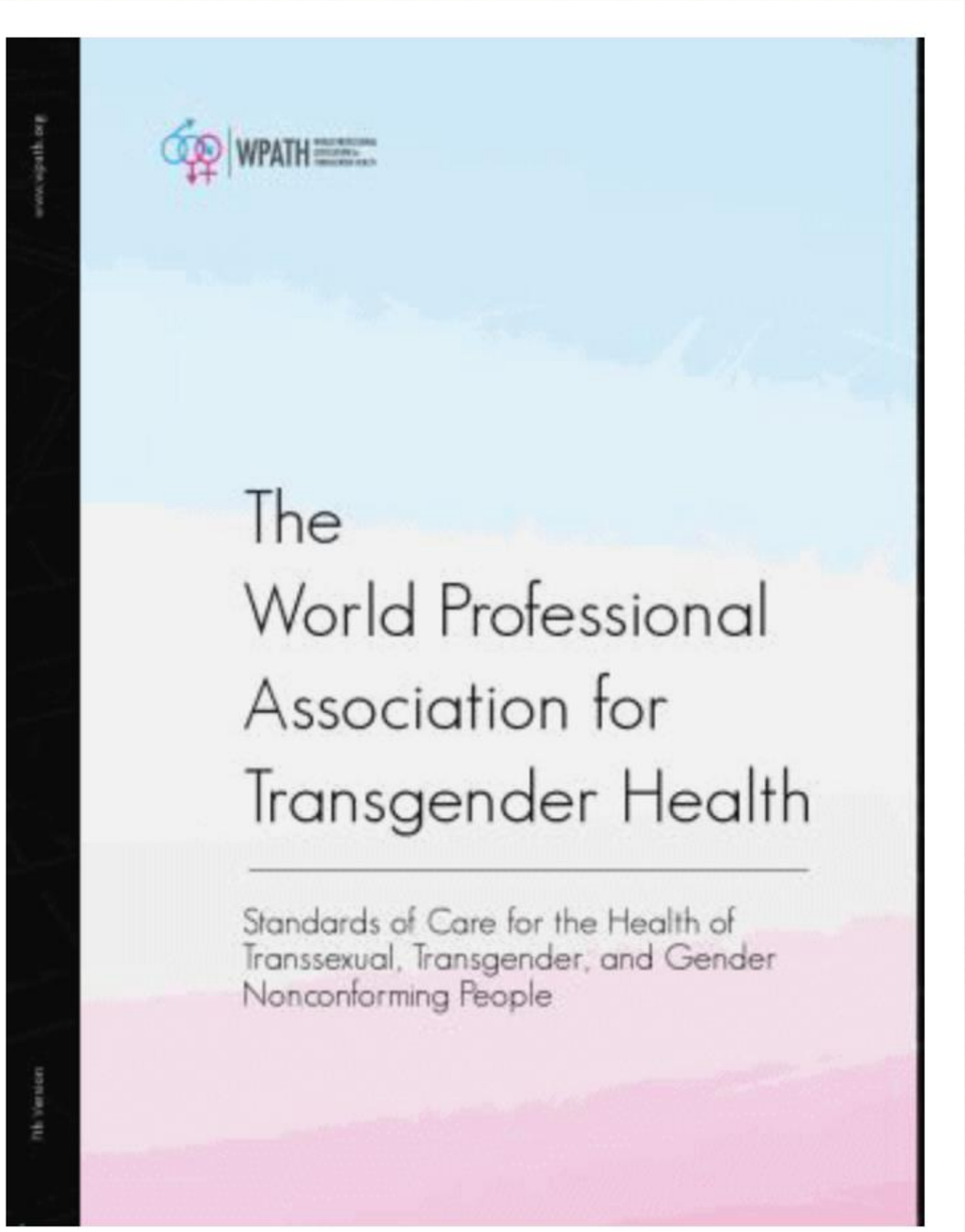
- Discuss timing for puberty blocking medications and informed consent
- Discuss approach to treatment with hormones in the adolescent patient
- Discuss the care for adult patients with medication management

Disclosures

- We will be discussing off label uses of medications
- We will be discussing best available standards of care
- I have no financial disclosures
- As I tell my patients, we are working together on this journey

Are there guidelines?

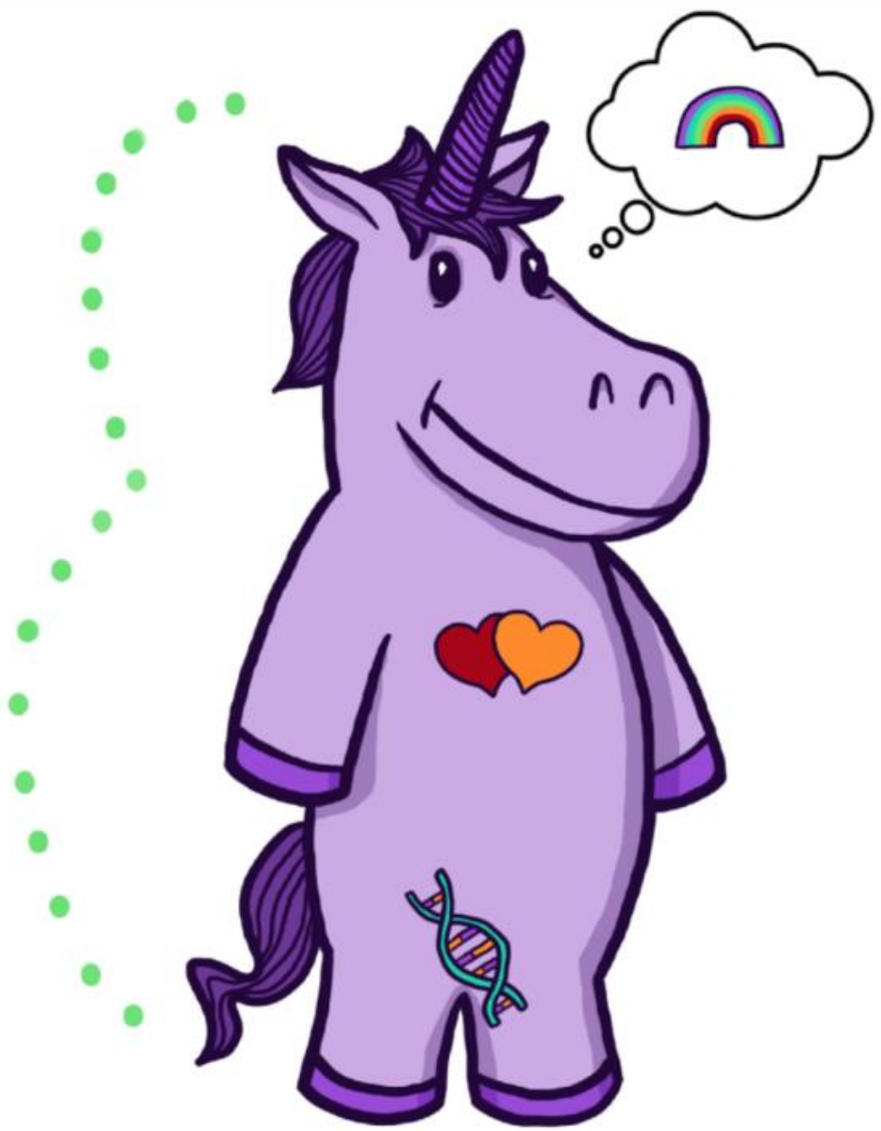
- WPATH- currently developing 8th version
- UCSF- June 2016
- Endocrine Society Guidelines- updated 2017



Gender Galaxy

http://www.canpreventgbv.ca/

Gender Unicorn



To learn more, go to:
www.transstudent.org/gender

Design by Landyn Pan and Anna Moore

Gender Identity

- Female / Woman / Girl
- Male / Man / Boy
- Other Gender(s)

Gender Expression

- Feminine
- Masculine
- Other

Sex Assigned at Birth

Female | Male | Other/Intersex

Physically Attracted to

- Women
- Men
- Other Gender(s)

Emotionally Attracted to

- Women
- Men
- Other Gender(s)

When does gender identity start?

Apples and Oranges

- Persisters: Children who have different gender identity other than what was assigned at birth for patient
- Desisters: Children who have diagnosis for gender treatment early in life but do not have this diagnosis by puberty
- Gender Identity: who I am (male, female, neither, etc)
- Gender expression: how I express who I am to the world (use of clothing, tools, etc)

Apples

- These are the persisters
- Respond to questioning with “I AM a ….”
- These are more likely to persist over time

Oranges

- These patients are more likely to respond as “I wish I were a …..”
- More likely to desist over time
- May be more likely to have different gender expression

Fruit Salads

- Combination of gender identity and gender expression
- “I am a ….” and “I express myself with ….”

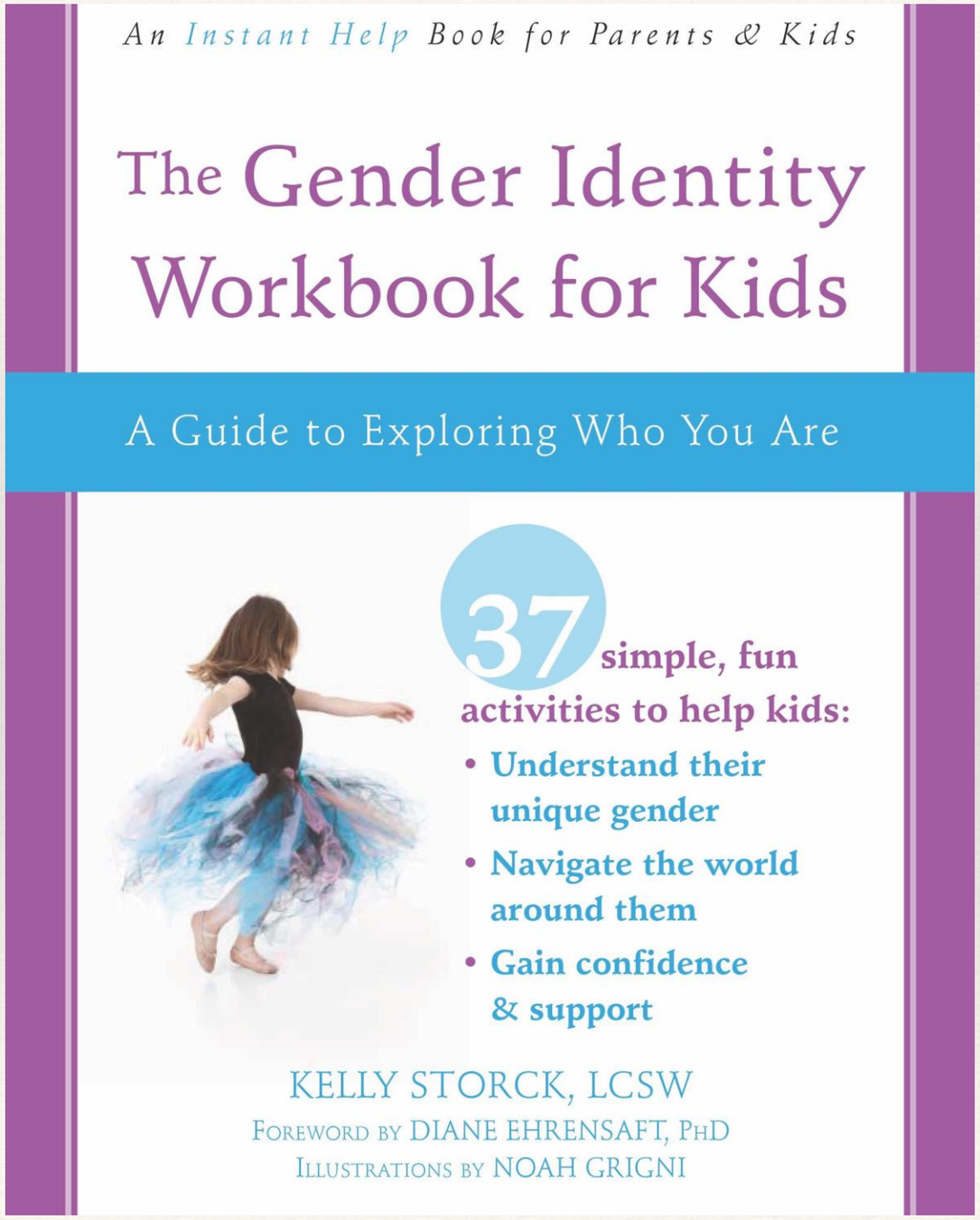
An Apple

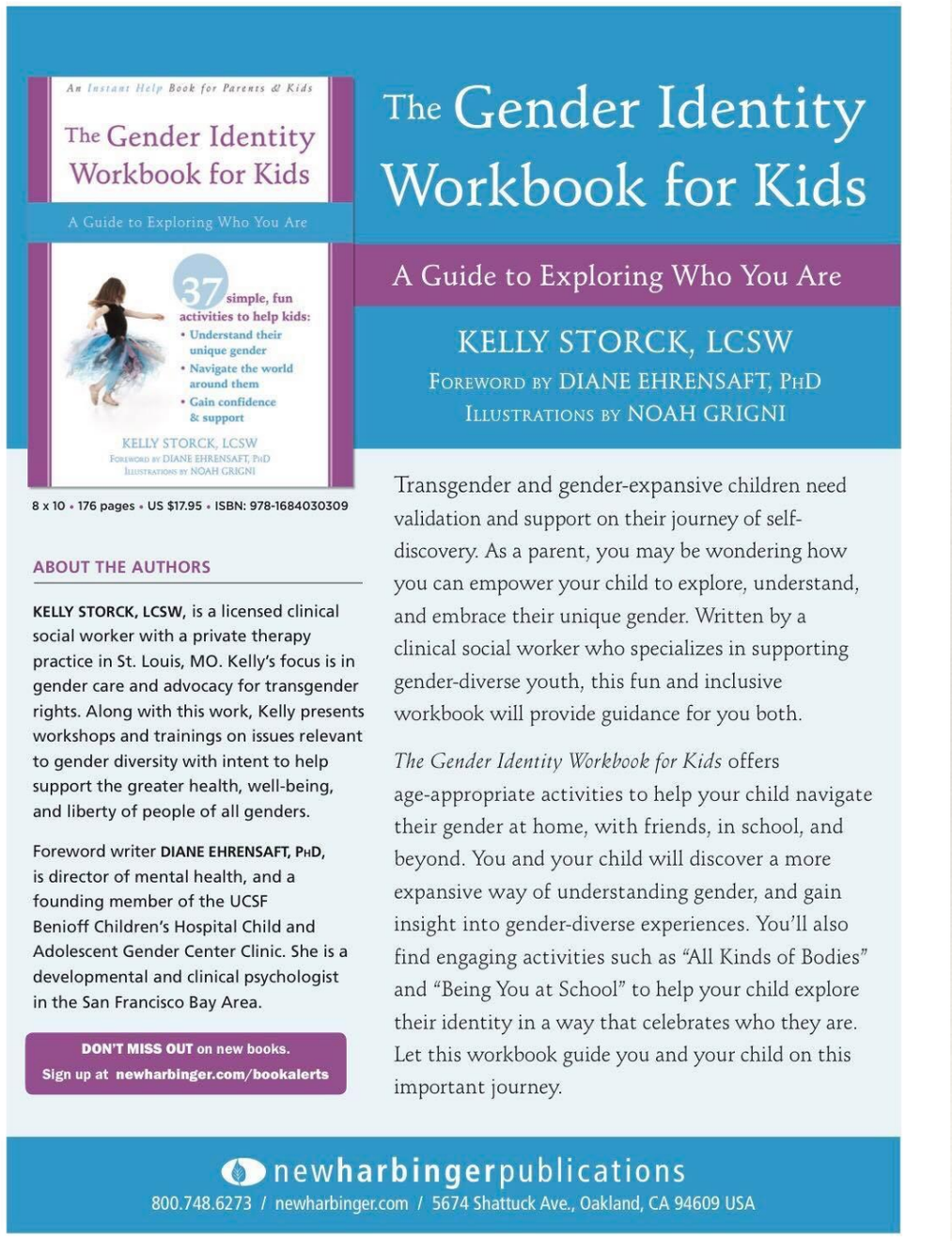
- https://youtu.be/d3M2kd_VmeM

How to approach treatment

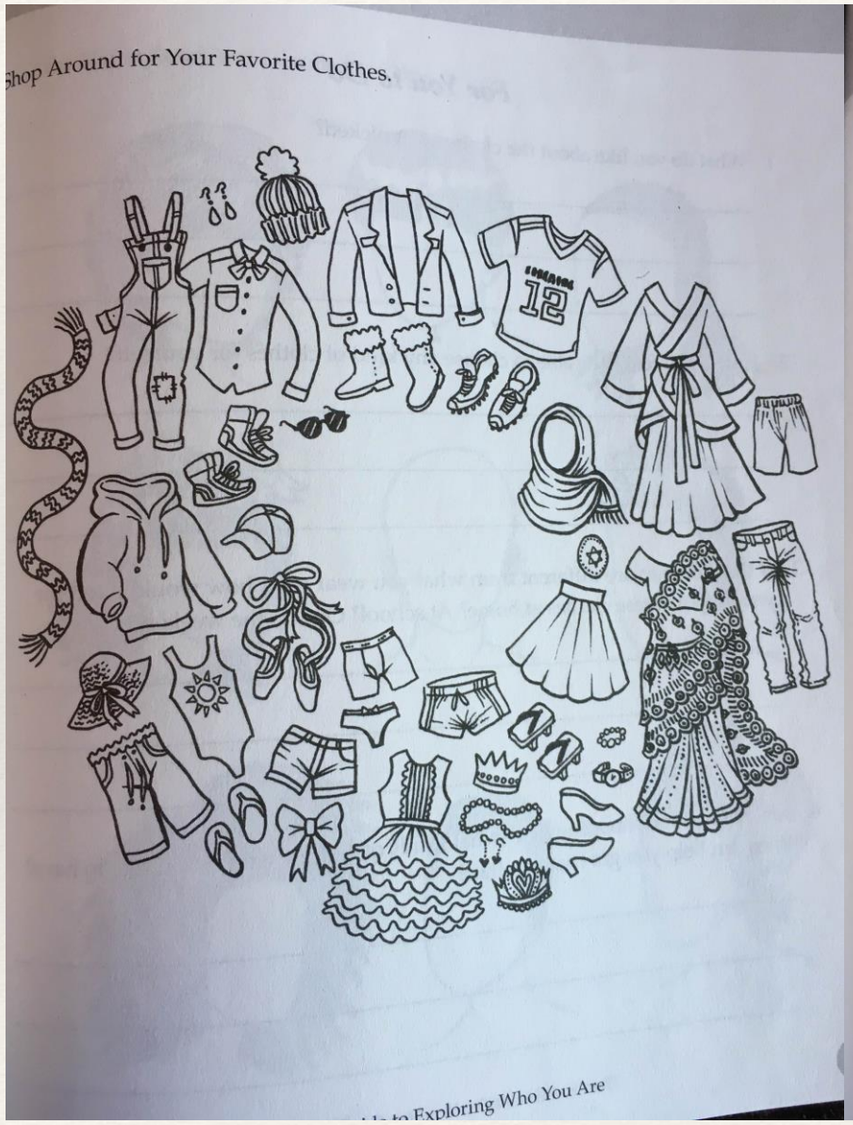
- Standards of care are in place
  - WPATH, Endocrine Society Guidelines, UCSF
- Gender centers have been becoming more common but not available in all areas
- Role for care team needs to be comprehensive
  - Include mental health support for family and patient
  - Full support from your team- RN, MA, desk staff, covering providers etc.

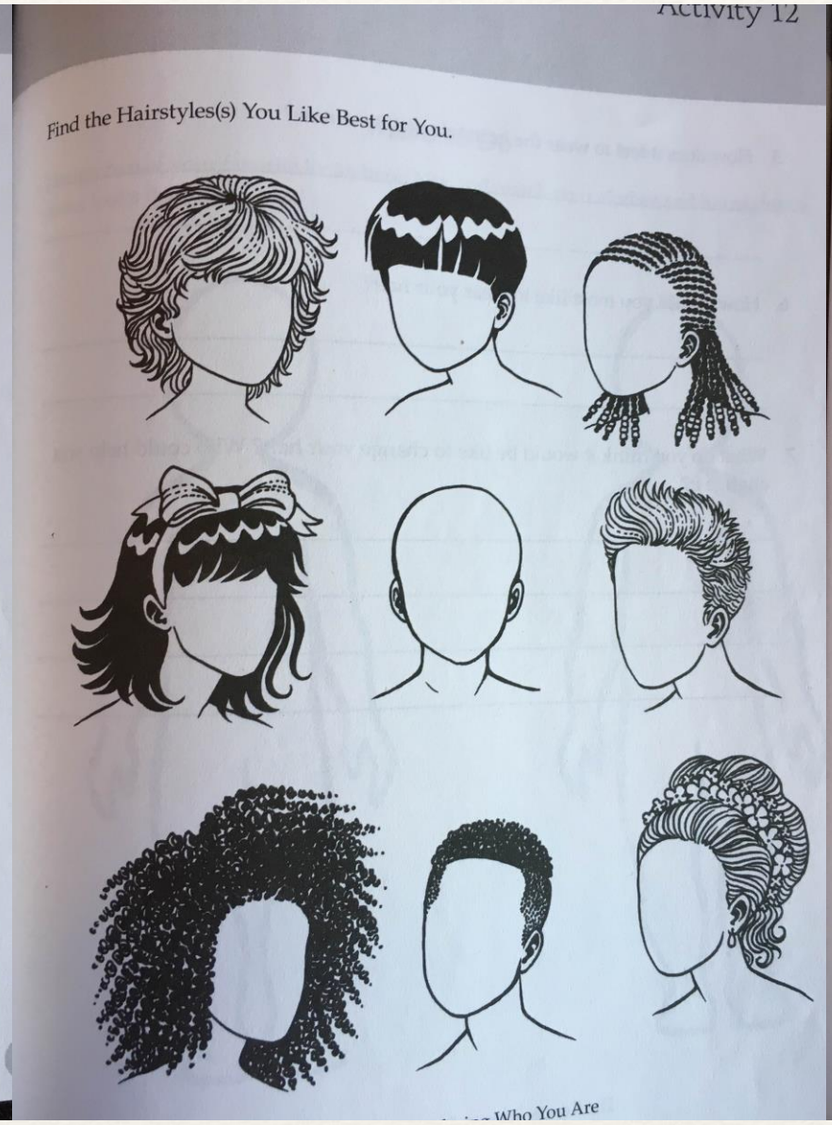
How to talk to kids about gender

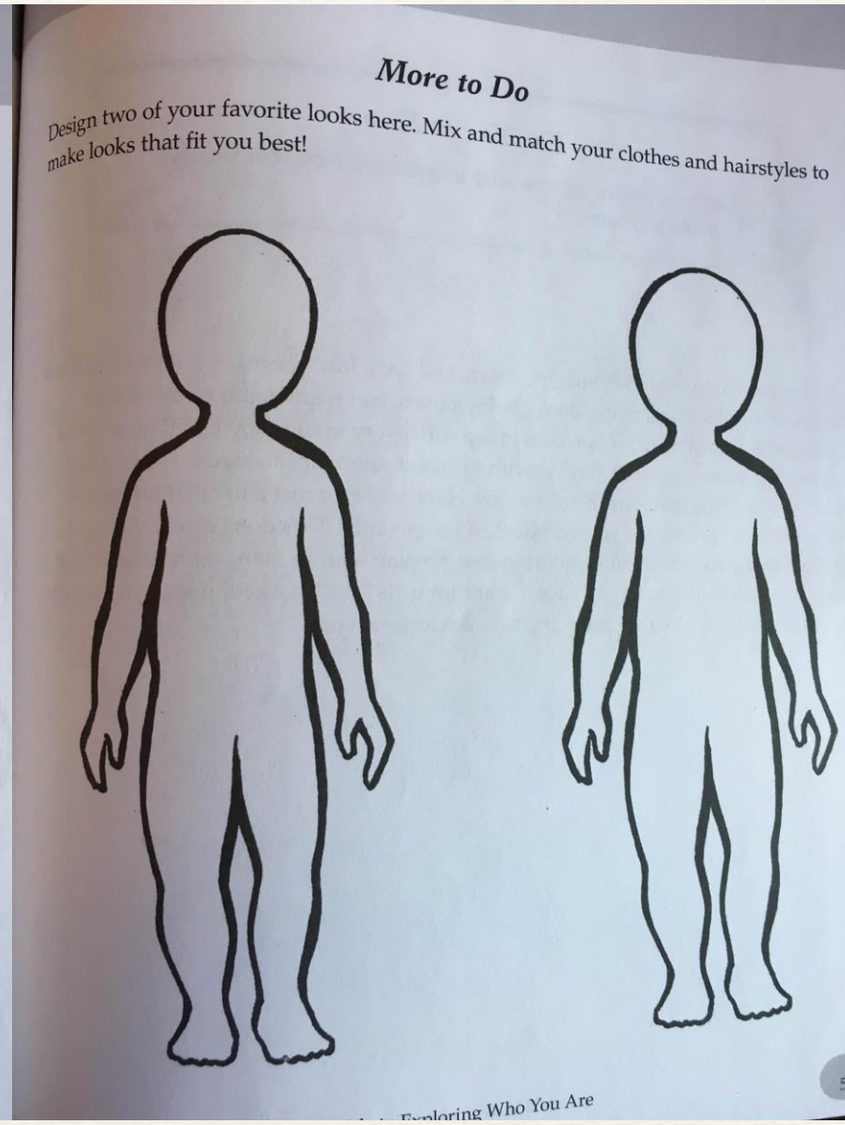




The gender unicorn





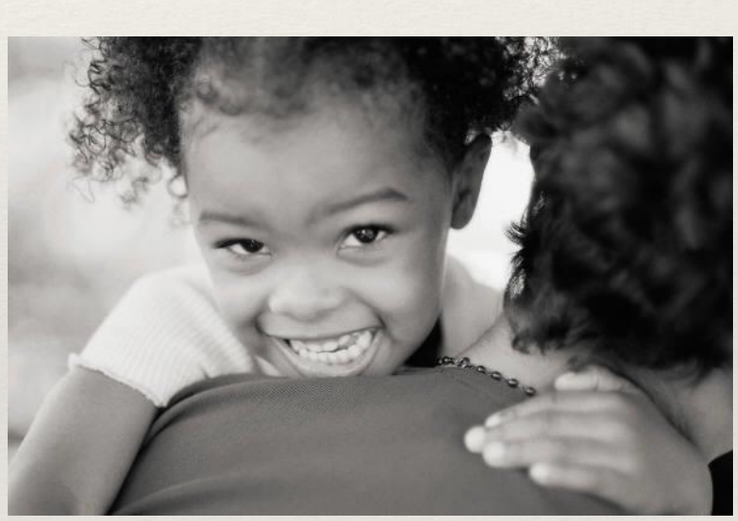


A Case

- Patient is a 15 yr old assigned female patient who presents as new patient for well child check
- Has been identifying and presenting self as male to family for several years but has not yet sought medical care
- Menstrual cycles are very dysphoric for patient
- Exam shows tanner stage IV development.

Pre-puberty

- Transition is the main consideration at this time
- No medication or surgical therapy
- Need to have a comprehensive team in place
  - Social work, psychology, medical



Medication Management

- Goal of therapy to start with is to allow pause in puberty
- Require patient to reach tanner stage II prior to initiation of therapy
- Needs to be in concert with mental health professionals for support for patient and family
  - Insurance will require documentation and meeting criteria for diagnosis before approval of medications

The Puberty Blocker- Leuprolide

- Gonadotropin releasing hormone (GnRH) agonist
- Injection or implantable devices can be used
- Need to have a clear and ongoing conversation about side effects, long term effects, fertility
  - Discuss this in concert with support system for patient
  - Typically 3 visits before giving medication
  - Monitor with labs and visits every 3 months at least

Why Puberty Blockers?

- They are completely reversible and allow time for gender exploration.
- However, longer term effects such as long term bone density changes are an ongoing consideration
  - Consideration of bone density testing, ensure adequate vitamin D and calcium intake
- Cross-Sex hormones are only partially reversible (some effects are long-term)

WPATH Criteria for Puberty Blockers

1. The adolescent has demonstrated a long-lasting and intense pattern of gender nonconformity or gender dysphoria (whether suppressed or expressed);

2. Gender dysphoria emerged or worsened with the onset of puberty;

3. Any co-existing psychological, medical, or social problems that could interfere with treatment (e.g., that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start treatment;

4. The adolescent has given informed consent and, particularly when the adolescent has not reached the age of medical consent, the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process.

WPATH Standards of Care 7th Edition

When to start cross-sex hormones

- Typical standards are to start at age 16
- Has been a push to start at younger age in certain circumstances
- Estrogen- used for feminizing effects
- Testosterone- masculinizing effects
- Goal is to mimic typical puberty

Table 8. Protocol Induction of Puberty

Induction of female puberty with oral 17β-estradiol, increasing the dose every 6 mo:
- 5 μg/kg/d
- 10 μg/kg/d
- 15 μg/kg/d
- 20 μg/kg/d
- Adult dose = 2–6 mg/d
- *In postpubertal transgender female adolescents, the dose of 17β-estradiol can be increased more rapidly:*
  - 1 mg/d for 6 mo
  - 2 mg/d

Induction of female puberty with transdermal 17β-estradiol, increasing the dose every 6 mo (new patch is placed every 3.5 d):
- 6.25–12.5 μg/24 h (cut 25-μg patch into quarters, then halves)
- 25 μg/24 h
- 37.5 μg/24 h
- Adult dose = 50–200 μg/24 h
- *For alternatives once at adult dose, see Table 11.*
- *Adjust maintenance dose to mimic physiological estradiol levels (see Table 15).*

Induction of male puberty with testosterone esters increasing the dose every 6 mo (IM or SC):
- 25 mg/m^2/2 wk (or alternatively, half this dose weekly, or double the dose every 4 wk)
- 50 mg/m^2/2 wk
- 75 mg/m^2/2 wk
- 100 mg/m^2/2 wk
- Adult dose = 100–200 mg every 2 wk
- *In postpubertal transgender male adolescents the dose of testosterone esters can be increased more rapidly:*
  - 75 mg/2 wk for 6 mo
  - 125 mg/2 wk
- *For alternatives once at adult dose, see Table 11.*
- *Adjust maintenance dose to mimic physiological testosterone levels (see Table 14).*

Adapted from Hembree *et al.* (118).

Abbreviations: IM, intramuscularly; SC, subcutaneously.

What about surgery for youth

- Standards generally recommend waiting until 18 for surgery per WPATH
- Some gender centers, surgery has been done in youth on a case by case basis.

Amenorrhea induction/Birth Control

- Discuss condom use and safe sex practices!
- Progesterone methods will not cause significant issues with cross-gender hormones
  - IUD
  - Nexplanon
  - Depo-provera

Follow-up on the case

- Had established mental health psychologist
- Leuprolide was started with cessation of menstruation after about 3 months
- Testosterone therapy started at age 16
- Now 17 and doing quite well on medication

Adult therapy

A Case

- 29 yr old assigned male presents to clinic for routine physical
- Confides in provider that has been working with psychologist about gender identity and would like to start medical therapy for transitioning to female identity

A Case

- What questions would you ask?

DSM-V Diagnostic Criteria

Table 2. DSM-5 Criteria for Gender Dysphoria in Adolescents and Adults

A. A marked incongruence between one's experienced/expressed gender and natal gender of at least 6 mo in duration, as manifested by at least two of the following:
   1. A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics)
   2. A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics)
   3. A strong desire for the primary and/or secondary sex characteristics of the other gender
   4. A strong desire to be of the other gender (or some alternative gender different from one's designated gender)
   5. A strong desire to be treated as the other gender (or some alternative gender different from one's designated gender)
   6. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's designated gender)

B. The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:
   1. The condition exists with a disorder of sex development.
   2. The condition is posttransitional, in that the individual has transitioned to full-time living in the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one sex-related medical procedure or treatment regimen—namely, regular sex hormone treatment or gender reassignment surgery confirming the desired gender (*e.g.*, penectomy, vaginoplasty in natal males; mastectomy or phalloplasty in natal females).

Reference: American Psychiatric Association (14).

Medication Mangement- Feminization

- Anti-androgens
  - Spironolactone
  - Finasteride
- Estrogens
  - Oral
  - Patch
  - Injectable
- Progesterone?
  - Role less clear, will get asked for it

Estrogen dosing

Estrogen				
Estradiol oral/sublingual	1mg/day	2-4mg/day	8mg/day	if >2mg recommend divided bid dosing
Estradiol transdermal	50mcg	100mcg	100-400 mcg	Max single patch dose available is 100mcg. Frequency of change is brand/product dependent. More than 2 patches at a time may be cumbersome for patients
Estradiol valerate IM[a]	<20mg IM q 2 wk	20mg IM q 2 wk	40mg IM q 2wk	May divide dose into weekly injections for cyclical symptoms
Estradiol cypionate IM	<2mg q 2wk	2mg IM q 2 wk	5mg IM q 2 wk	May divide dose into weekly injections for cyclical symptoms

UCSF Guidelines- 2016

Androgen Blockers

Androgen blocker			
Spironolactone	25mg qd	50mg bid	200mg bid
Finasteride	1mg qd		5mg qd
Dutasteride			0.5mg qd

UCSF Guidelines- 2016

Timeline for changes

TABLE 1B: EFFECTS AND EXPECTED TIME COURSE OF FEMINIZING HORMONES [A]

Effect	Expected Onset[B]	Expected Maximum Effect[B]
Body fat redistribution	3-6 months	2-5 years
Decreased muscle mass/ strength	3-6 months	1-2 years[C]
Softening of skin/decreased oiliness	3-6 months	unknown
Decreased libido	1-3 months	1-2 years
Decreased spontaneous erections	1-3 months	3-6 months
Male sexual dysfunction	variable	variable
Breast growth	3-6 months	2-3 years
Decreased testicular volume	3-6 months	2-3 years
Decreased sperm production	variable	variable
Thinning and slowed growth of body and facial hair	6-12 months	> 3 years[D]
Male pattern baldness	No regrowth, loss stops 1-3 months	1-2 years

[A] Adapted with permission from Hembree et al. (2009). *Copyright 2009, The Endocrine Society.*
[B] Estimates represent published and unpublished clinical observations.
[C] Significantly dependent on amount of exercise.
[D] Complete removal of male facial and body hair requires electrolysis, laser treatment, or both.

Endocrine Society Guidelines- 2017

Monitoring Estrogen therapy

Test	Comments	Baseline	3 months*	6 months*	12 months*	Yearly	PRN
BUN/Cr/K+	Only if spiro used	X	X	X	X	X	X
Lipids	No evidence to support monitoring at any time; use clinician discretion	Based on USPSTF guidelines					X
A1c or glucose	No evidence to support monitoring at any time; use clinician discretion	Based on USPSTF guidelines					
Estradiol			X	X			X
Total Testosterone			X	X	X		X
Sex Hormone Binding Globulin (SHBG)**			X	X	X		X
Albumin**			X	X	X		X
Prolactin	Only if symptoms of prolactinoma						X

UCSF Guidelines- 2016

Medication Mangement- Masculization

- Testosterone
- Topical (patch or gel)
- Never oral
- Subcutaneous or intramuscular

Testosterone dosing

Androgen	Initial - low dose[b]	Initial - typical	Maximum - typical[c]	Comment
Testosterone Cypionate[a]	20 mg/week IM/SQ	50mg/week IM/SQ	100mg/week IM/SQ	For q 2 wk dosing, double each dose
Testosterone Enthanate[a]	20mg/week IM/SQ	50mg/week IM/SQ	100mg/week IM/SQ	"
Testosterone topical gel 1%	12.5-25 mg Q AM	50mg Q AM	100mg Q AM	May come in pump or packet form
Testosterone topical gel 1.62%[d]	20.25mg Q AM	40.5 - 60.75mg Q AM	103.25mg Q AM	"
Testosterone patch	1-2mg Q PM	4mg Q PM	8mg Q PM	Patches come in 2mg and 4mg size. For lower doses, may cut patch
Testosterone cream[e]	10mg	50mg	100mg	
Testosterone axillary gel 2%	30mg Q AM	60mg Q AM	90-120mg Q AM	Comes in pump only, one pump = 30mg
Testosterone Undecanoate[f]	N/A	750mg IM, repeat in 4 weeks, then q 10 weeks ongoing	N/A	Requires participation in manufacturer monitored program[f]

- UCSF Guidelines- 2016

Timeline of Hormones

TABLE 1A: EFFECTS AND EXPECTED TIME COURSE OF MASCULINIZING HORMONES [A]

Effect	Expected Onset[B]	Expected Maximum Effect[B]
Skin oiliness/acne	1-6 months	1-2 years
Facial/body hair growth	3-6 months	3-5 years
Scalp hair loss	>12 months[C]	variable
Increased muscle mass/strength	6-12 months	2-5 years[D]
Body fat redistribution	3-6 months	2-5 years
Cessation of menses	2-6 months	n/a
Clitoral enlargement	3-6 months	1-2 years
Vaginal atrophy	3-6 months	1-2 years
Deepened voice	3-12 months	1-2 years

[A] Adapted with permission from Hembree et al.(2009). *Copyright 2009, The Endocrine Society.*
[B] Estimates represent published and unpublished clinical observations.
[C] Highly dependent on age and inheritance; may be minimal.
[D] Significantly dependent on amount of exercise.

Endocrine Society Guidelines- 2017

Monitoring testosterone therapy

Therapy	Comments	Baseline	3 months*	6 months*	12 months*	Yearly	PRN
Lipids	No evidence to support lipid monitoring at any time; use clinician discretion	Based on USPSTF guidelines					X
A1c or fasting glucose	No evidence to support lipid monitoring at any time; use clinician discretion	Based on USPSTF guidelines					X
Estradiol							X
Total Testosterone			X	X	X		X
Sex Hormone Binding Globulin (SHBG)**			X	X	X		X
Albumin**			X	X	X		X
Hemoglobin & Hematocrit		X	X	X	X	X	X

UCSF Guidelines- 2016

Medication Management

- It is all about finding the right fit for the right person.
- Do not get too into the binary with the medications
  - easy trap to fall into is assuming that everyone who desires masculinizing or feminizing hormones wants all effects of the medication

3rd Person Singular Subjective	3rd Person Singular Objective	3rd Person Singular Possessive	3rd Person Singular Reflexive
She	Her	Her	Herself
He	Him	His	Himself
They	Them	Their	Themselves
Ze	Zir	Zir/Zirs	Zirself
Xe	Xem	Xyr/Xyrself	Xemself
Ze	Hir	Hir/Hirs	Hirself
Per	Per	Per/Pers	Perself

Source: Adapted from the University of Alberta Student Union

Voice Therapy

- https://www.youtube.com/watch?v=2qFmNE1dxHs

Health Care Maintenance

- Sexually transmitted infections
- Consider PrEP (Pre-Exposure HIV prophylaxis)
- Test all anatomy involved
- HIV medications do not interfere or change treatment

Natal Male Predominant Cancers

- Still consider prostate cancer and testicular cancer in differential

Cervical Cancer Screening

- Make environment as comfortable as possible
- Careful use of speculum as vaginal mucosa can become atrophic from testosterone therapy
- Potential evidence of self collect being as effective as traditional collection

Breast Cancer Screening

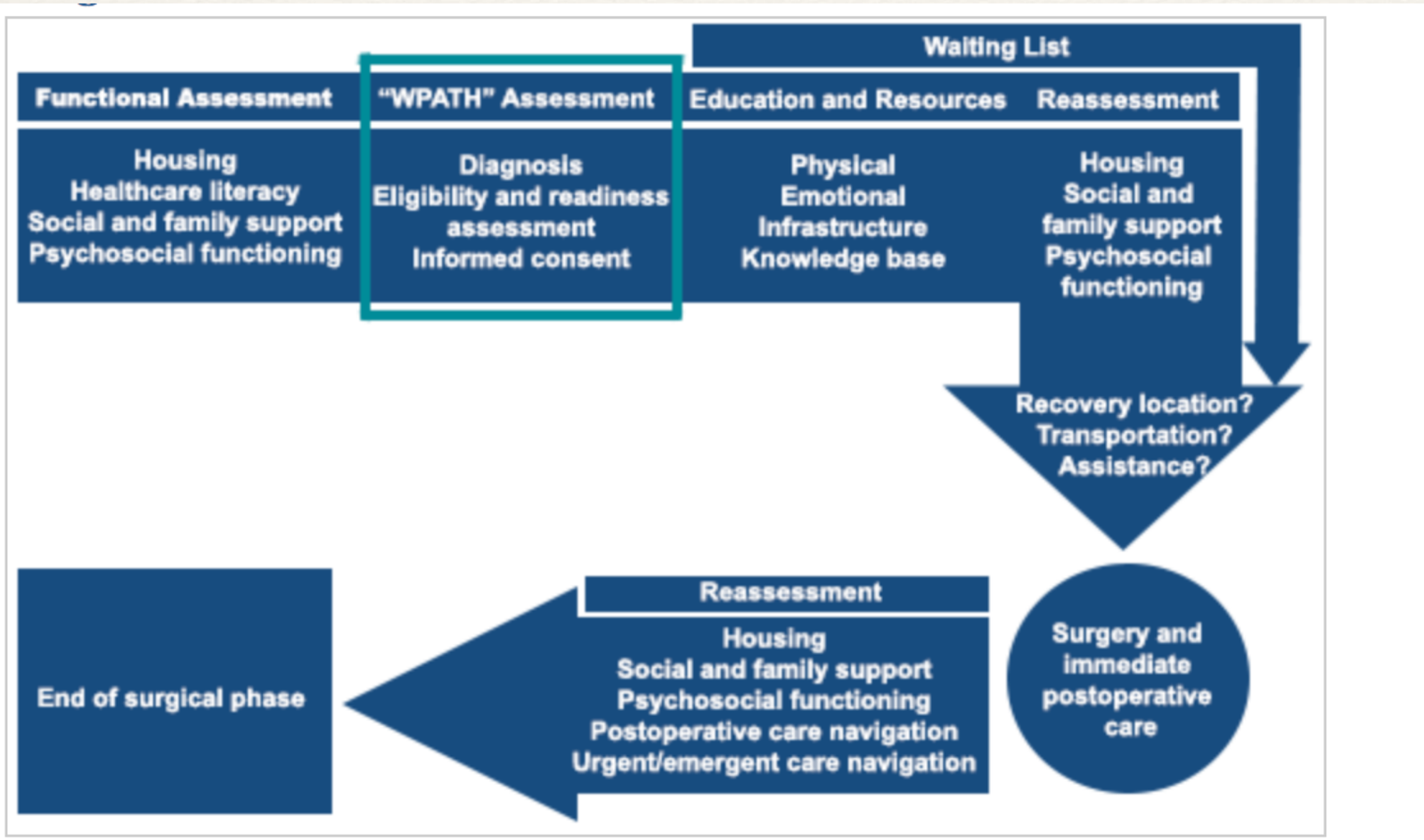
- Breast Cancer Screening
  - Transgender females- similar guidelines to natal assigned female
  - Transgender males- discussion about approach
    - have they had top surgery?

Osteoporosis

- Trangender people should all have screening starting at age 65
- Risk factors for osteoporosis considered under age 65 in the 50-64 age group
  - Hypogonadism (gonadectomy without hormone therapy)
  - Alcohol use (greater than 10 drinks per week)
  - Chronic steroid use
  - Smoking
  - Low BMI
  - Immobility
  - Vitamin D deficiency
  - HIV

Role of Primary Care before surgery

- Discuss support system, discuss ability to care for self after surgery, home life, smoking, etc



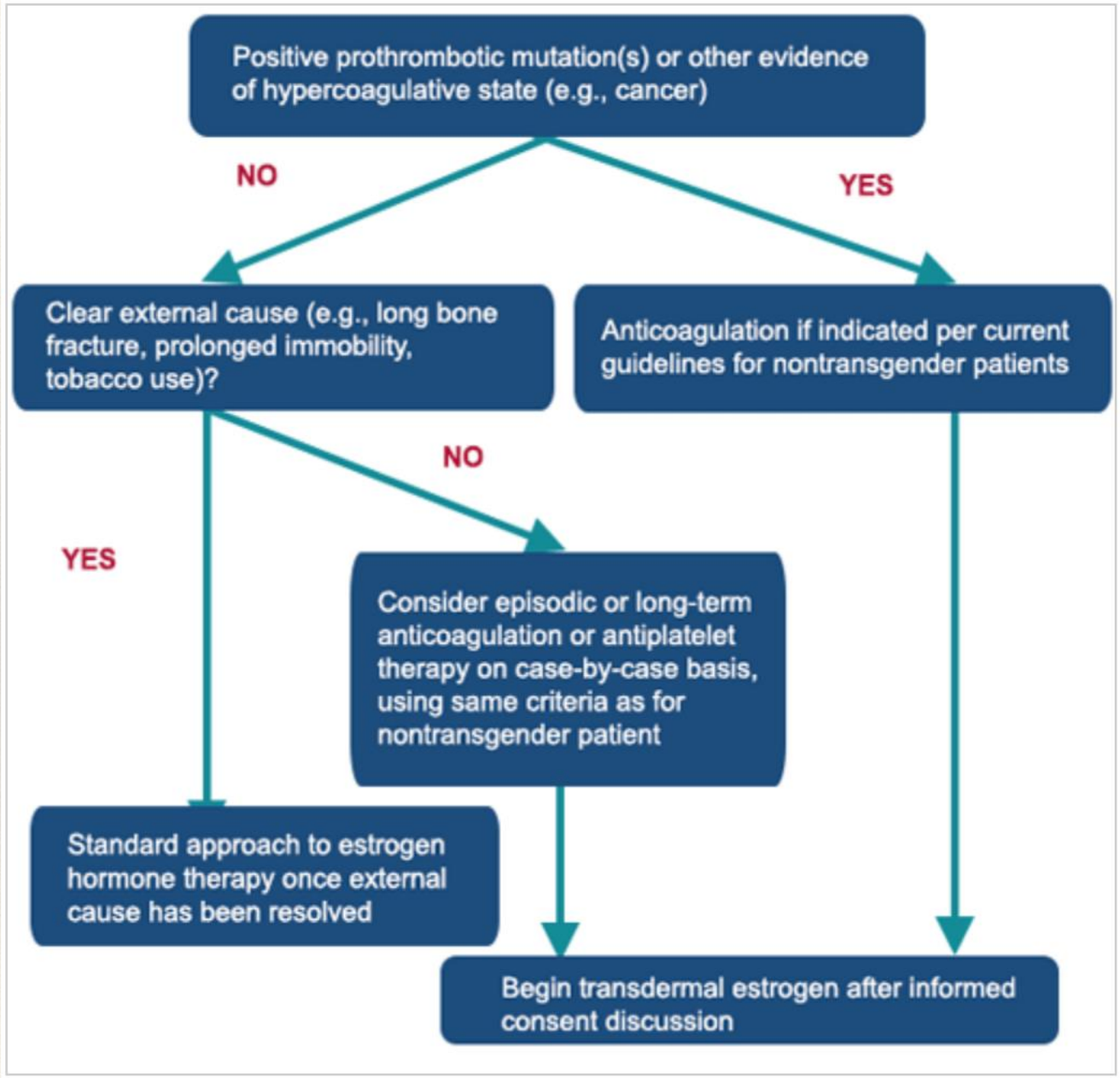
Adapted from: Deutsch MB. Gender-affirming Surgeries in the Era of Insurance Coverage: Developing a Framework for Psychosocial Support and Care Navigation in the Perioperative Period. J Health Care Poor Underserved; May 2016.

Thrombotic Risks of Estrogen

- Higher with oral estrogen versus transdermal
- Evidence of higher thrombosis comes from ethyl estrogens
  - However, smoking increases risk
- What to do with patients who develop a VTE?

Special Considerations with Estrogen

- Hypercoagulative state
- Migraine with Aura
- Smokers
- Estrogen positive cancers
- Perioperative use of estrogen



UCSF Guidelines- 2016

Fertility Preservation

- Transgender women: consider sperm banking prior to starting therapy
  - Concern for damage to spermatogenesis with estrogen
- Transgender men
  - Testosterone therapy may be held with trial of return to ovulation and resumption of menses
  - May consider Oocyte preservation
  - New studies in pediatrics looking at preservation of ovarian tissue with reproduction later

Geriatric Gender Care

- When and how to titrate hormones
- Consideration of physiologic phenomenon
  - Testosterone decline with age
  - Estrogen decrease with menopause

Questions?

foss0196@umn.edu

References

- UCSF Transgender Health Guidelines
  - last updated June 2016
  - http://transhealth.ucsf.edu/
- WPATH Standards of Care 7th Edition
  - 8th Edition in review
  - https://www.wpath.org/publications/soc
- Endocrine society guidelines- 2017
  - https://www.endocrine.org/guidelines-and-clinical-practice/clinical-practice-guidelines