Gender Affirming Care of the Adult Patient

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Financial Disclosure

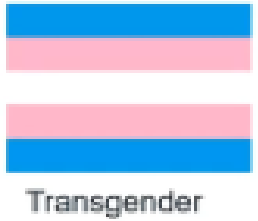
I have no financial disclosures or conflicts of interest

Outline

- Definitions
- Epidemiology
- Health Disparities
- Trans female and male therapy
    - Pharmacologic therapy
    - Metabolic Effects
    - Surgical therapy
    - Primary Care Consideration
- Reproductive Planning

Definitions

- Sex - assigned at birth as male or female based on biology, anatomy, chromosomes
- Gender identity: one’s sense of self as gendered or nongendered person (man, woman, both neither)



Gender identity different than assigned sex at birth

- Trans feminine: transgender women, trans women, trans female, transgender girls. Male assigned sex at birth
- Trans masculine: transgender men, trans men, trans male, transgender boys. Female assigned sex at birth
- Cultural variations: Hijra (South Asia), Travesti (Brazil), Waria (Indonesia), Two-spirit (North American)
- Gender minorities - National Institutes of Health Transgender, gender diverse, non-binary, gender fluid

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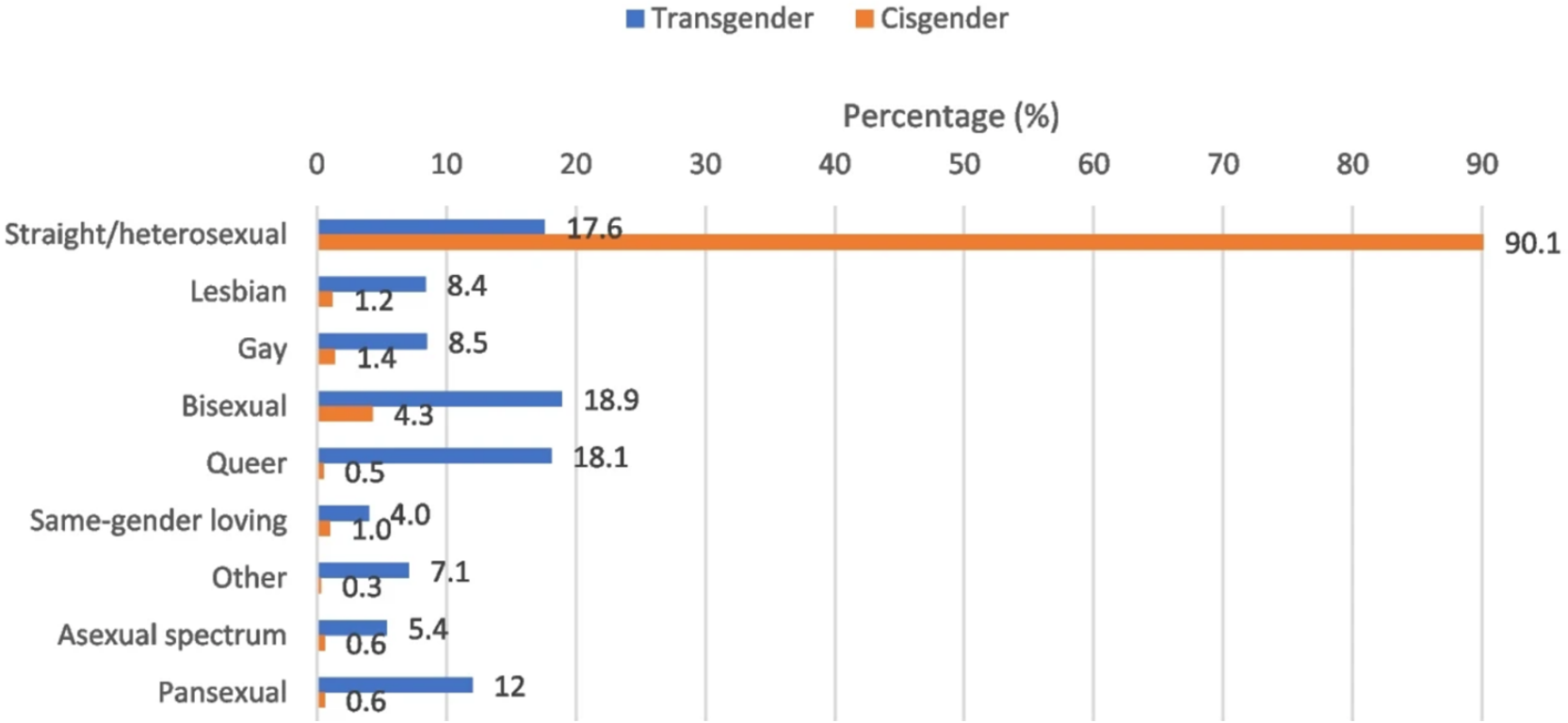
- Cisgender: Gender identity and assigned sex at birth same

Nonbinary

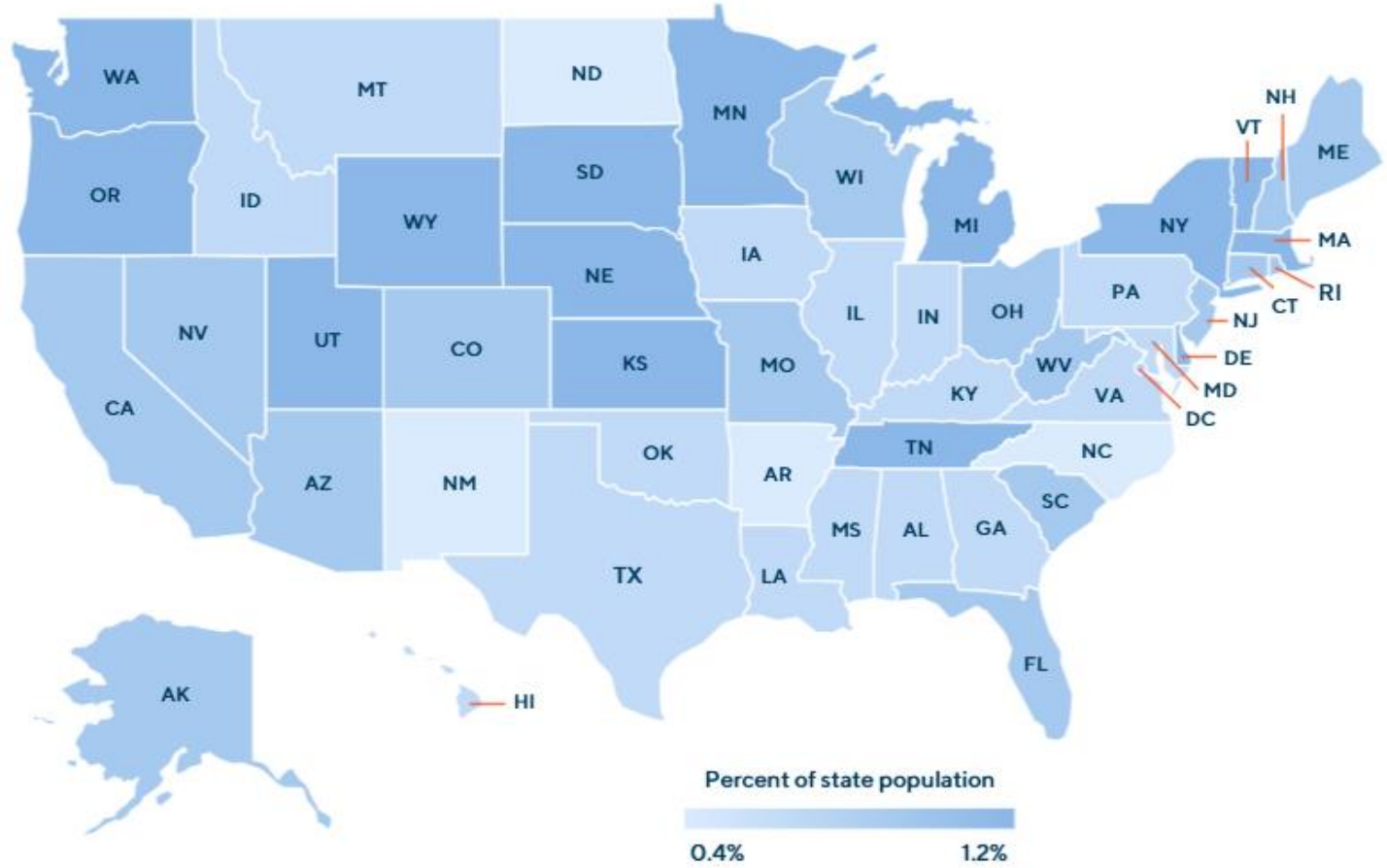
Gender identity or expression not exclusively male or female

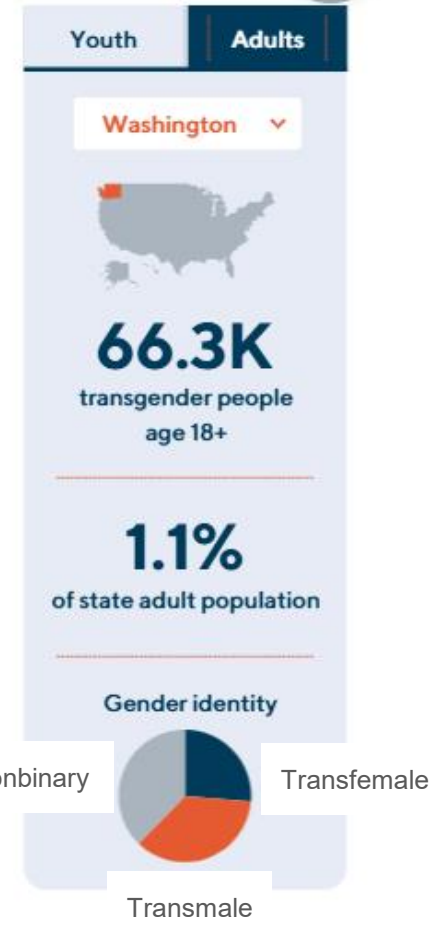
- Outside traditional male-female gender non-binary
- Genderqueer, gender fluid, gender expansive, agender, pangender
- Pronouns: They/them/their/Ze/hir/hirs

Gender Identity ≠ Sexual Orientation

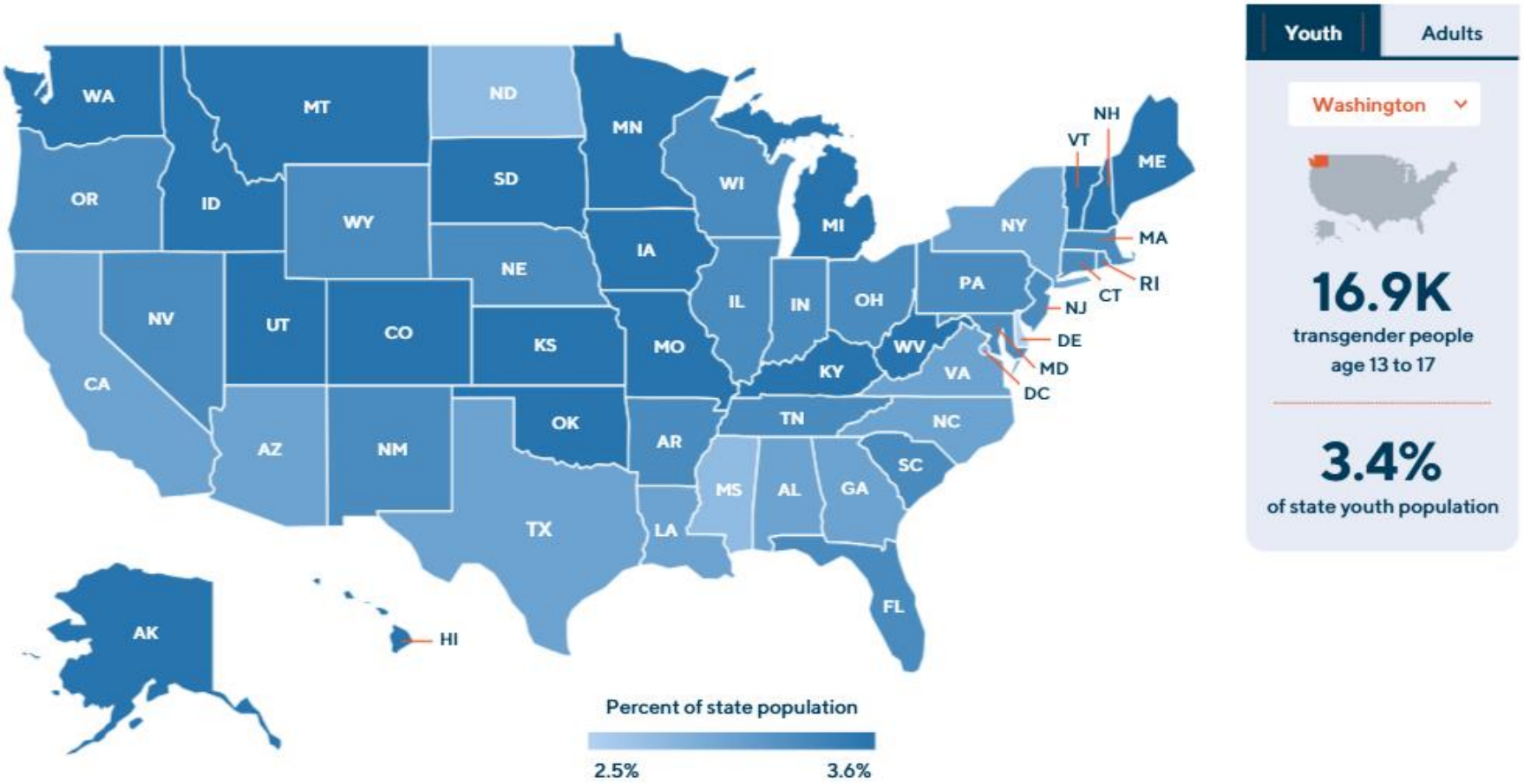


Reisner, S. L., Choi, S. K., Herman, J. L., Bockting, W., Krueger, E. A., & Meyer, I. H. (2023). Sexual orientation in transgender adults in the United States. *BMC Public Health,* 23(1), 1799.





https://williamsinstitute.law.ucla.edu/subpopulations/transgender-people/



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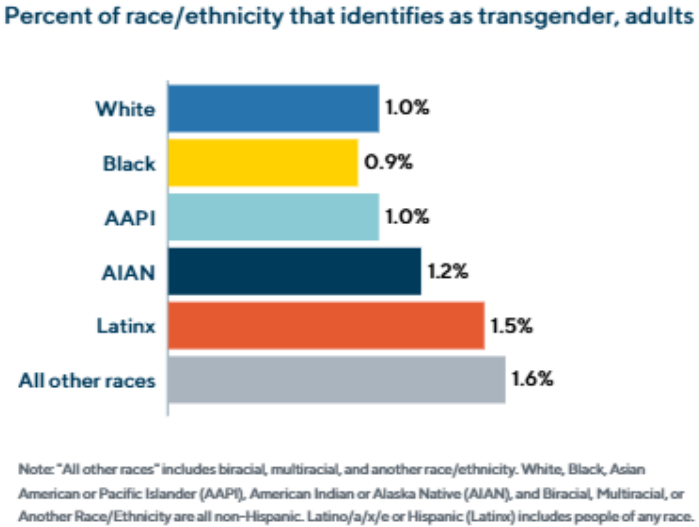
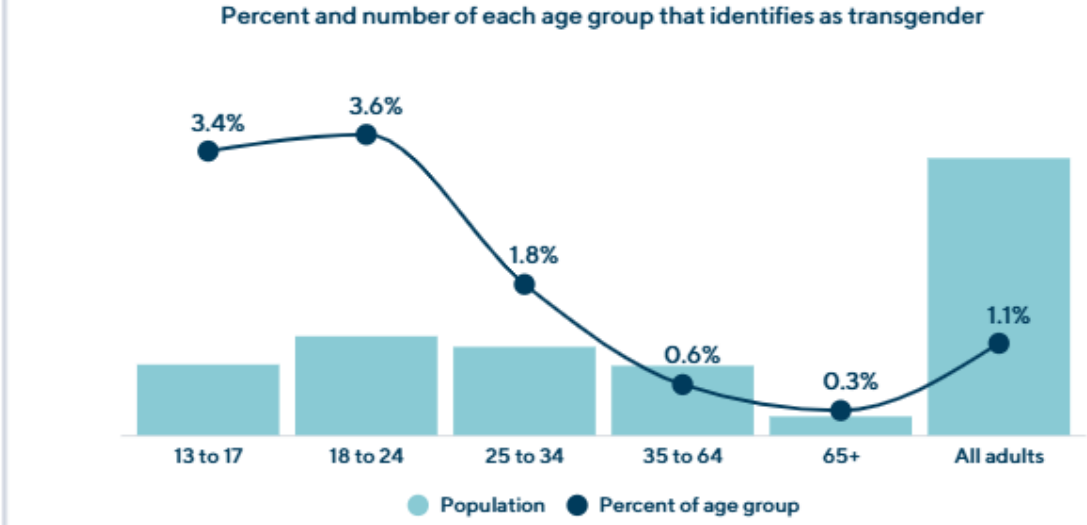
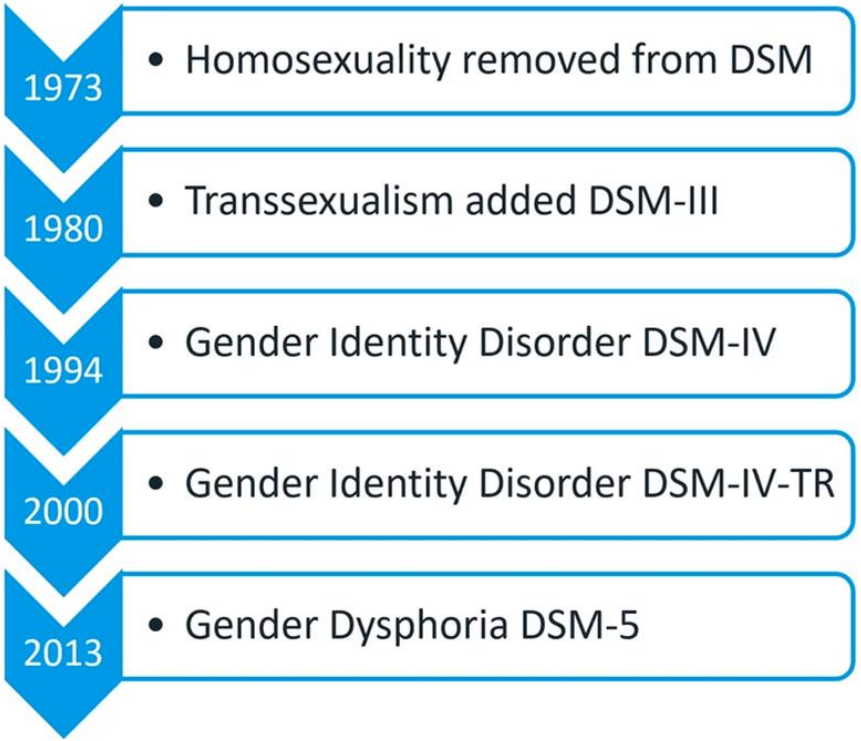




https://williamsinstitute.law.ucla.edu/subpopulations/transgender-people/

Diagnostic and Statistical Manual of Mental Disorders



Marked incongruence between one's experienced/expressed gender and their assigned gender, lasting at least 6 months with least two of the following:

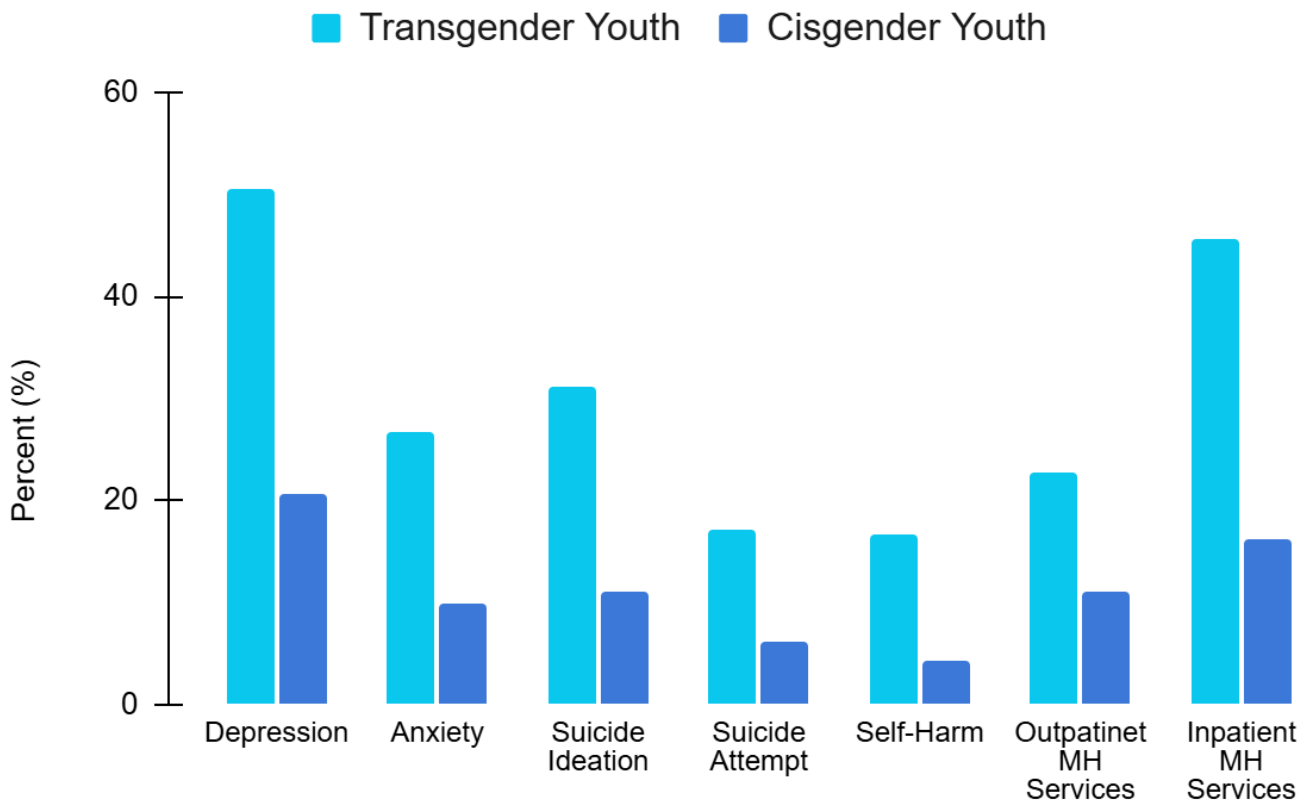
- A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics
- A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender
- A strong desire for the primary and/or secondary sex characteristics of the other gender
- A strong desire to be of the other gender (or some alternative gender different from one's assigned gender)
- A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender)
- A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender)

The condition must also be associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Transgender Health Inequities

- Increased Mortality
- Chronic Conditions and co-morbidities
- HIV and STIs
- Mental health and substance abuse
- Cancer related risks
- Violence Victimization
- Delays in preventative screening and treatment
- Lack of access to culturally responsive care

Mental Health Transgender Youth

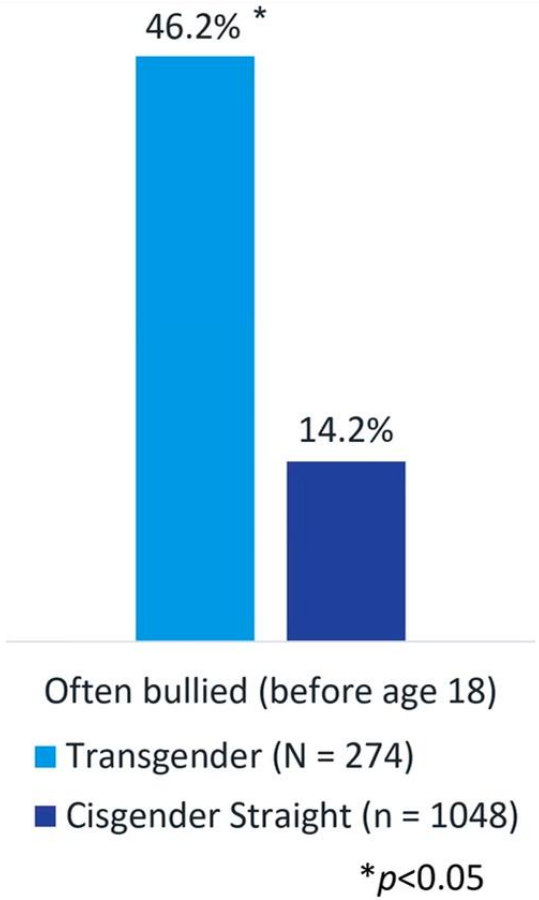


Reisner J Adolesc Health 2015

Suicidality by Gender Minority Status 2009-2014

Suicidality (suicide attempt, ideation or potenial attempt)	**OR GM versus NonGM (95% CI)**
Older adults	**2.10 (1.6 - 2.75)**
Disabled adults	**1.95 (1.82 - 2.09)**
Suicide attempt	
Older adults	4.37 (2.26 - 8.46)
Disabled adults	1.7 (1.5 - 1.94)
Suicidal ideation	
Older adults	2.61 (1.56 - 4.37)
Disabled adults	2.23 (2.05 - 2.43)
Potential suicide attempt	
Older adults	1.43 (1.71- 2.00).
DIsabled adults	1.36 (1.22 - 1.50)

Progovac AM Am J Prev Med 2020



Reasons for Bullying

	Transgender (n = 274)		Cisgender Straight (n = 1048)	
	Reason	%	Reason	%
1	Physical appearance	63.3	Physical appearance	46.3
2	Gender expression or appearance	46.4	Age	26.3
3	Sexual orientation	28.4	Sex (being female or male)	13.7

Meyer IH, Reisner SL, Herman J, Feldman J, Poteat T, Bockting W. Findings from a US transgender population study. USPATH 2019, Washington DC (Sept 2019 Plenary).

Associations Between Gender Identity and Cyberbullying Victimization in the Adolescent Brain Cognitive Development (ABCD) Study (Avg age 13)

	Adjusted	*P*
Transgender identification	OR (95% CI)	
No	Reference	--
Yes	**2.24 (1.22, 4.10)**	**0.009**
Maybe	**1.91 (1.05, 3.47)**	**0.035**
I do not understand this question	0.97 (0.58, 1.61)	0.900
Decline to answer	1.68 (0.68, 4.16)	0.259

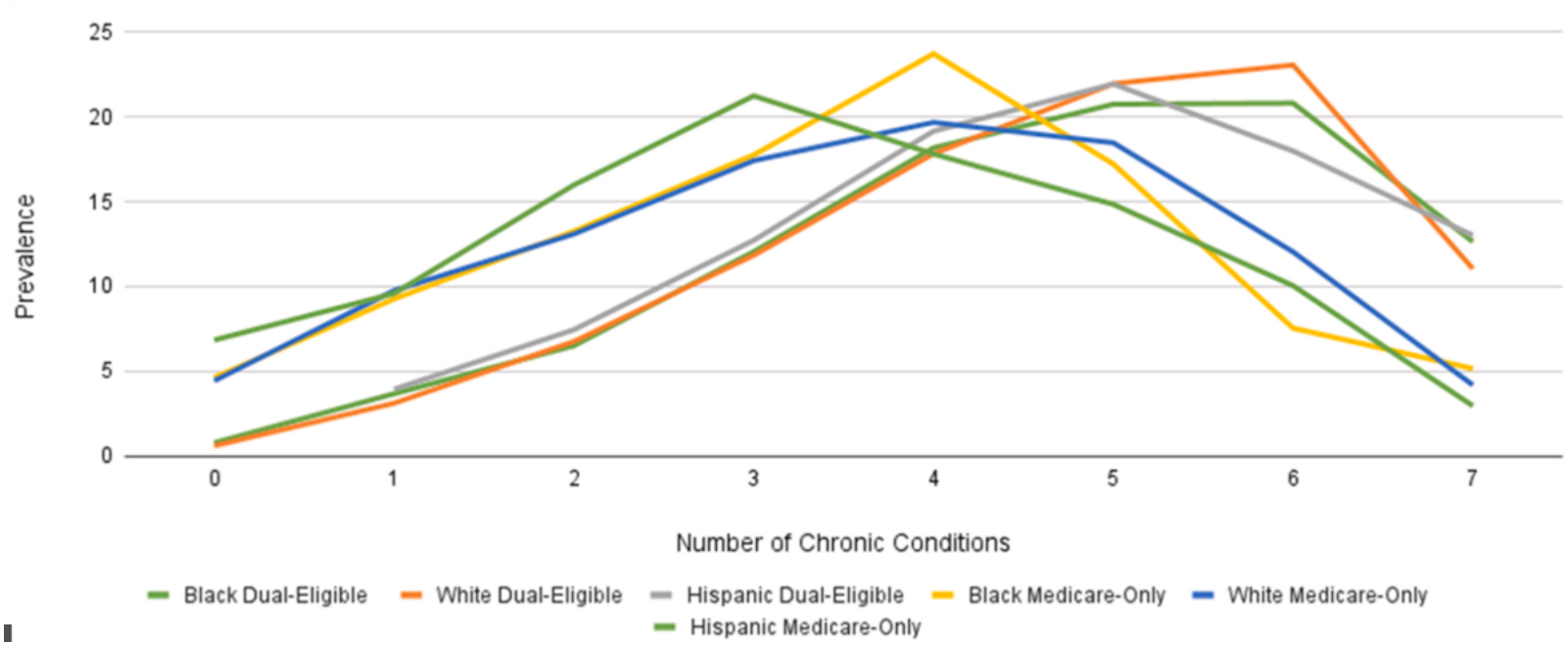
Nagata JM Academic Pediatrics, 2025

Privately Insured Trans and Cisgender Adults Chronic Conditions 2001-2019

	Transgender	Cisgender
Total morbidity score (mean)	**3.00**	**1.99**
Hypertension	27.27	32.64
Cardiac arrhythmia	17.25	12.56
Congestive heart failure	4.95	3.68
Hypothyroidism	19.13	12.90
Drug use disorder	8.12	3.21
Psychoses	5.81	1.44
Chronic pulmonary disease	26.29	18.13
Liver disease	9.22	5.97
Rheumatoid arthritis/collagen	7.88	5.30
AIDS/HIV	1.51	0.29

Poteat TC American Journal of Preventive Medicine. 2021

Concurrent Chronic Conditions Medicare/Medicaid patients by Race

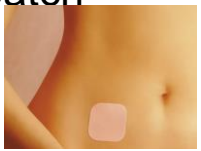


Progovac Am J Prev Med 2020

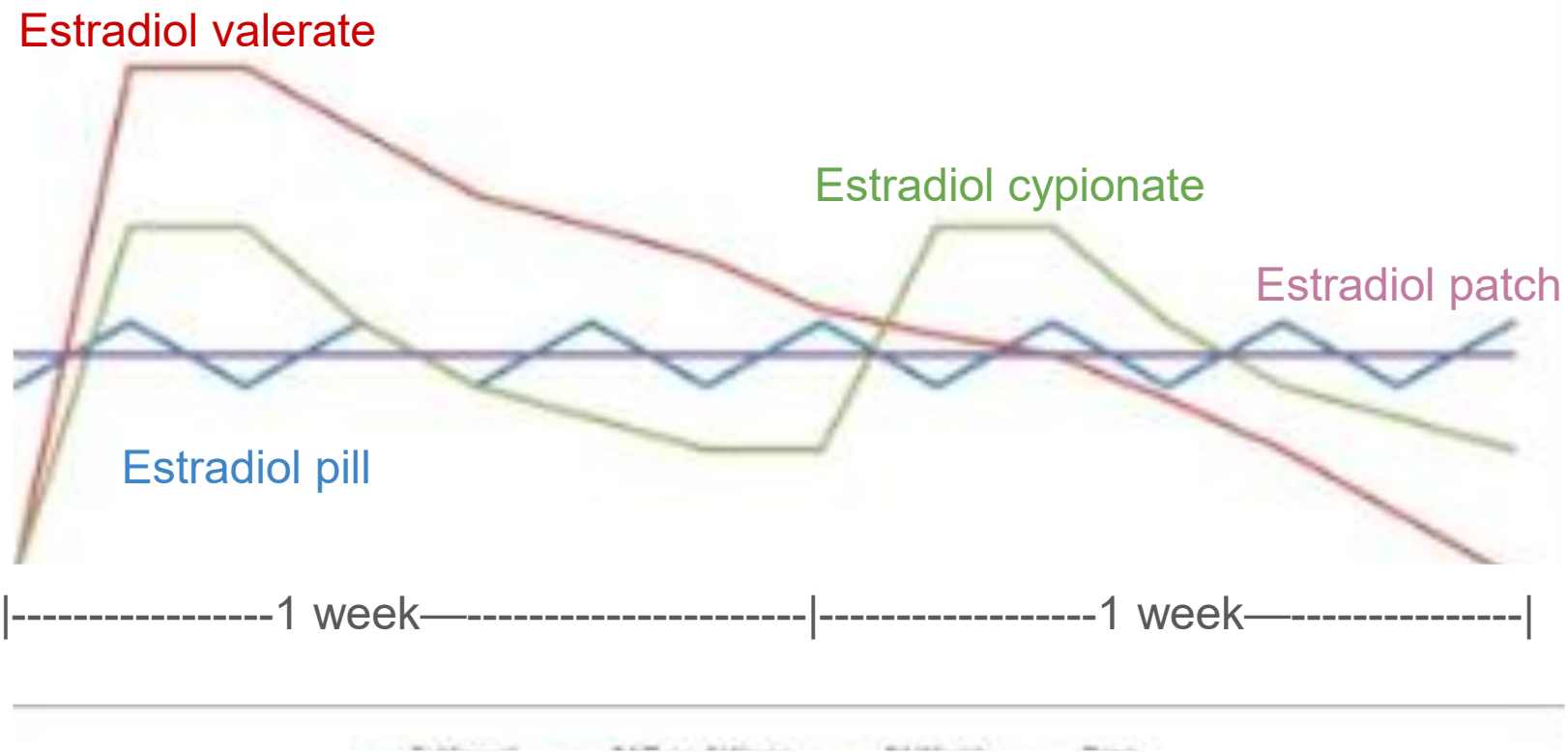
Chronic condition categories	Dual-Eligible Beneficiaries (n = 8041)			Medicare-Only Beneficiaries (n = 6237)		
	Non-Hispanic Black (n = 1519)	Non-Hispanic White (n = 5532)	Hispanic (n = 684)	Non-Hispanic Black (n = 755)	Non-Hispanic White (n = 4743)	Hispanic (n = 438)
Cancer	7.1 %	6.3 %	5.3 %	6.0 %	5.0 %	3.8 %
Cardiovascular	85.5 %	85.6 %	87.3 %	69.7 %	69.6 %	64.1 %
Developmental	8.3 %	15.0 %	8.2 %	2.6%	2.6 %	1.0 %
Infectious Disease	51.4 %	14.3 %	35.6 %	33.2 %	8.7 %	22.8 %
Lung Conditions	48.2 %	54.1 %	47.5 %	30.6 %	35.4 %	25.9 %
Physical Conditions	56.1 %	67.3 %	58.4 %	42.4 %	53.7 %	40.9 %
Mental Health	87.8 %	96.2 %	90.2 %	75.5 %	86.2 %	77.0 %
Sensory Conditions	50.2 %	47.9 %	44.3 %	31.9 %	32.3 %	33.5 %
Substance Use	8.3 %	14.2 %	14.3 %	4.5 %	7.6 %	5.5 %
Other Chronic Conditions	84.5 %	83.6 %	83.0 %	73.6 %	68.7 %	64.9 %

Progovac Am J Prev Med 2020

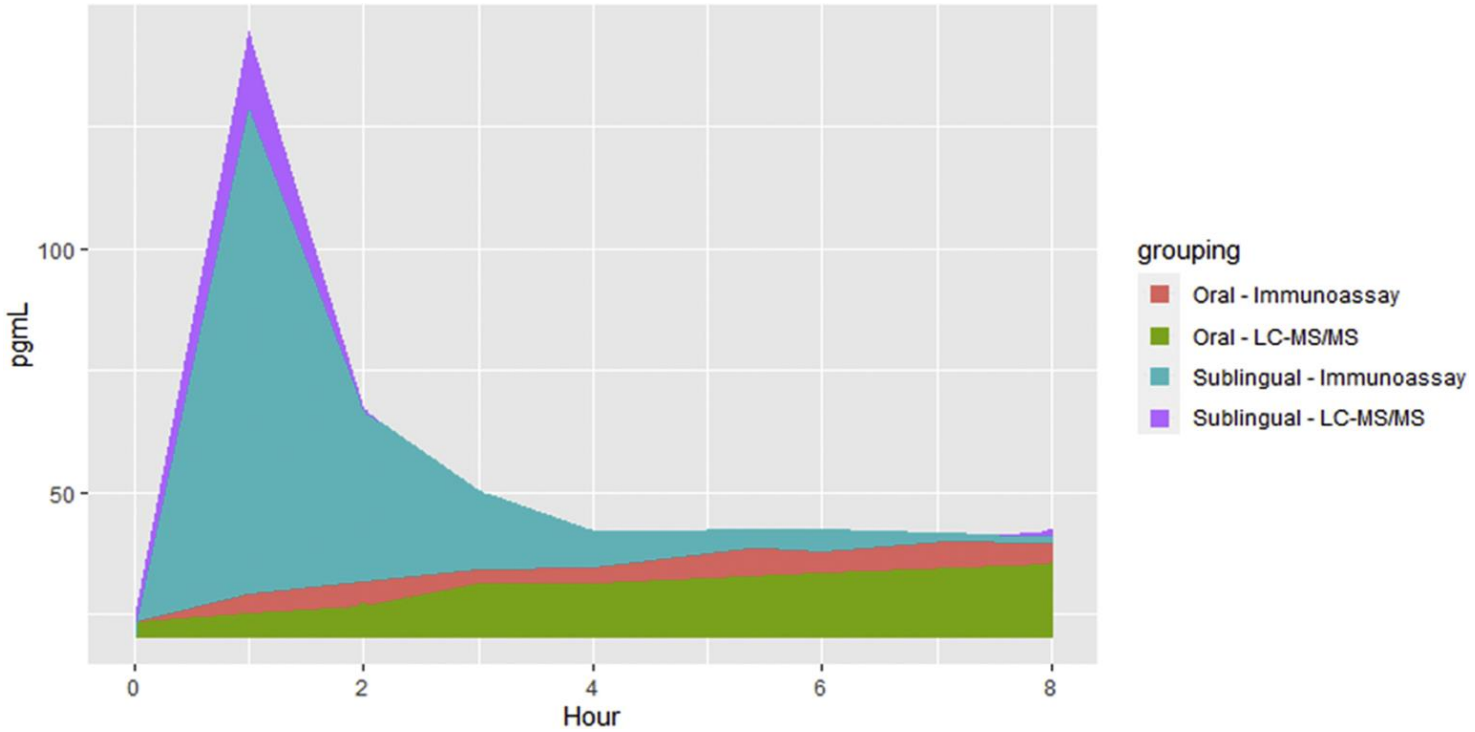
Trans female pharmacologic therapy

Estrogens		
Oral: estradiol (17-beta-estradiol valerate)	2 to 6 mg/day	Although some providers give higher doses of oral estradiol (greater than 6 mg/day), suggest that only doses less than or equal to 6 mg/day be used. Higher risk of thromboembolism
Transdermal estradiol patch  	0.025 to 0.2 mg per 24 hours, changed once or twice weekly, depending on specific preparation type	Lower risk of thromboembolism compared with oral estrogen preparations. May require several patches
Transdermal: estradiol gel 	0.25 to 1.25 mg applied once a day	Lower risk of thromboembolism compared with oral estrogen preparations.
Estradiol valerate	5 to 20 mg IM every 2 wks	Prolonged time to onset of effect and steady state, greater risk of accumulation and overdose. Intermittent shortages
Estradiol cypionate	2 to 10 mg IM every week	

Estradiol Pharmacokinetics

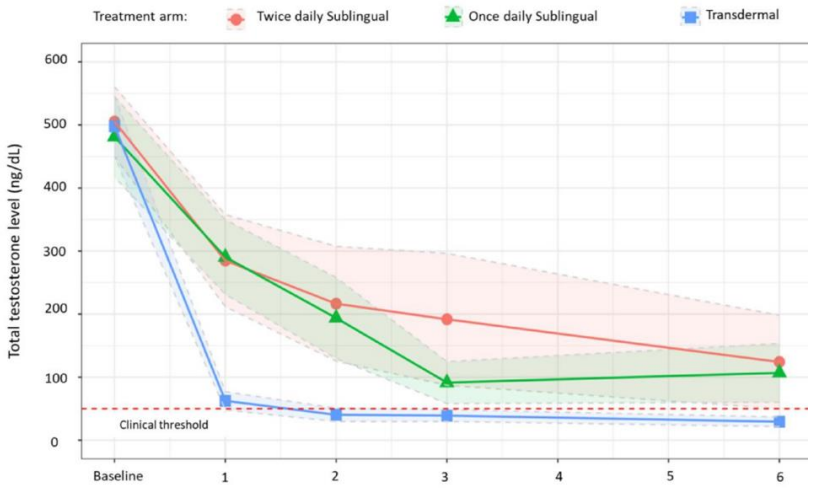


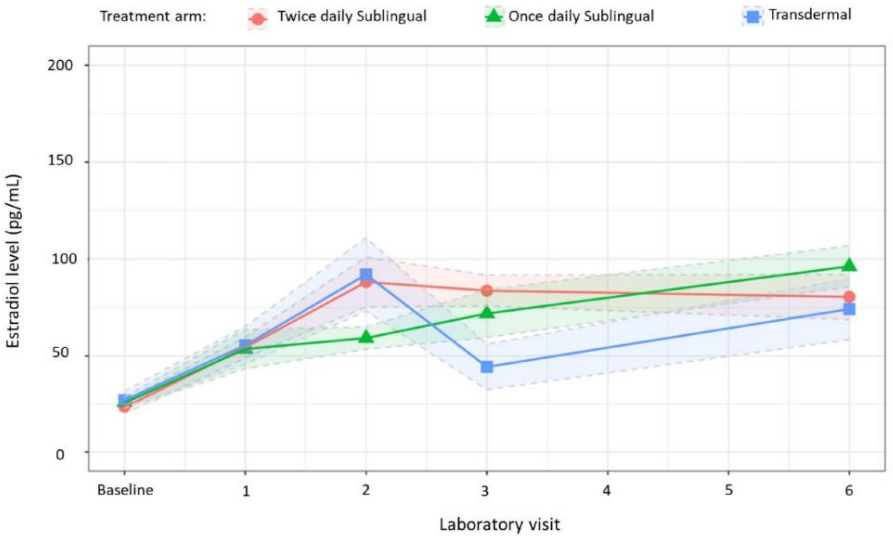
Pharmacokinetics of oral versus sublingual Estradiol



Doll E Endocrine Practice 2022,

Transdermal estradiol patches show greater testosterone suppression and lower estradiol levels with much lower total daily dose of estradiol compared to the total daily dose in the once-daily and twice-daily sublingual estradiol groups.





Cortez S, Journal of the Endocrine Society, 2024

Medication	Dosing	Comment
Anti Androgens		
Spironolactone	100 to 300 mg/day oral (classically max dosage of 100 mg twice daily)	Monitor blood pressure and electrolytes. Hyperkalemia (esp those at risk for volume depletion)
(Cyproterone acetate)	10 mg/day oral	10 mg daily for a maximal duration of 2 years is recommended. Cyproterone has been associated with uncommon episodes of fulminant hepatitis
GnRH agonists		
Leuprolide	3.75 to 7.5 mg IM depot monthly or 11.25 mg IM depot every 3 months	Inhibits gonadotropin secretion. Difficult insurance coverage
(Goserelin)	3.6 mg SQ implant monthly	Expensive. Difficult insurance coverage

Hormone	Initial	Maximum
((Medroxyprogesterone acetate (Provera)))	2.5mg qhs	5-10 mg qhs
Micronized progesterone	100 mg qhs	100-200 mg qhs

Test	Comments	Base line	3 mo	6 mo	12 mo	Yearly
BUN/Cr/K+	Only if spironolactone used	X	X	X	X	X
Estradiol	Goal mid range 100-200 pg/.ml Injections mid injection PO: 2+ hours after intake SL 4+ hours after intake		X	X	X	X
Total Testosterone	Endocrine society < 55 goal		X	X	X	X
Sex Hormone Binding Globulin /albumin	Used to calculate bioavailable testosterone monitoring/may help in complex cases		PRN			
Prolactin	Only if symptoms					

Effects of estrogen and anti-androgen therapy

Effect	Initial (mo)	Maximum (mo)
Decreased Libido	1-3	3-6
Breast Growth	3-6	24-36
Decreased Testicular Volume	3-6	24-36
Decreased Sperm Production	unknown	unknown
Redistribution of Body Fat	3-6	24-36
Decreased Muscle Mass	3-6	12-24
Softening of Skin	3-6	unknown
Decreased Terminal Hair	6-12	>36

Metabolic Effects of Trans female therapy

Metabolic effects of trans female therapy

	Standard Mean Difference	95% CI	*P* Value
LDL (mg/dL)	−0.05	−0.56 to 0.46	0.85
HDL (mg/dL)	0.25	−0.74 to 1.23	0.62
TG (mg/dL)	**0.64**	**0.01-1.27**	**0.05**
TC (mg/dL)	0.004	−0.18 to 0.18	0.96
SBP (mm Hg)	−0.51	−1.44 to 0.43	0.29
DBP (mm Hg)	−0.01	−0.81 to 0.79	0.97
BMI (kg/m^2)	0.38	−0.13 to 0.88	0.14

Rahman SU JACC Adv. 2024

With pharmacologic therapy risk of VTE is increased, CVA and MI not clear.

Event	Adjusted HR (95% CI)	
Transgender women	vs. cis gender men	vs.cis gender women
Transgender women overall cohort (n=2,842)		
VTE	**1.9 (1.4–2.7)**	**2.0 (1.4–2.8)**
Ischemic stroke	1.2 (0.9–1.7)	1.9 (1.3–2.6)
MI	0.9 (0.6–1.5)	1.8 (1.1–2.9)
Transgender women estrogen initiation cohort (n=853)		
VTE	**3.2 (1.5–6.5)**	**2.5 (1.2–5.0)**
At 0–2 years of follow-up	**1.5 (0.5–5.1)**	**1.7 (0.5–5.5)**
At >2 years of follow-up	**5.1 (2.1–12.6)**	**3.2 (1.3–7.6)**
Ischemic stroke	2.3 (1.2–4.3)	2.9 (1.5–5.5)
At 0–6 years of follow-up	1.3 (0.6–2.9)	2.3 (1.0–5.4)
At >6 years of follow-up	9.9 (3.0–33.1)	4.1 (1.5–11.4)
MI in the cohort overall	1.0 (0.3–3.2)	2.4 (0.6–9.4)

Masumori Circ Rep 2023

Circulation
Volume 144, Issue 6, 10 August 2021; Pages e136-e148
https://doi.org/10.1161/CIR.0000000000001003

AHA SCIENTIFIC STATEMENT

Assessing and Addressing Cardiovascular Health in People Who Are Transgender and Gender Diverse: A Scientific Statement From the American Heart Association

A growing body of research demonstrates that Transgender populations experience disproportionate risk for poor cardiovascular health across multiple behavioral and social determinants of health.

Metabolic Effects of Trans female therapy

Bone Health in Trans female

Prior to starting estrogen therapy, trans females had increased osteopenia and osteoporosis compared to cisgender man but BMD preserved compared to cisgender women. This may be due to reduced levels of physical activity, lower muscle mass and grips strength and lower levels of vitamin D. Van Caaengam 2013, Bone

Studies have shown lower, higher, and no change in bone density after initiating hormones. This could be due to heterogeneity in the both the type and duration of therapy

Surgical Trans female Therapy

Trans female Surgical Options

- Tracheal shave, face contouring, liposuction
- Top surgery - breast augmentation
- Bottom surgery

Orchiectomy - removal of testes

Vaginoplasty - surgical construction of a vagina most commonly involves use of penile and scrotal tissue using a penile inversion technique. Requires dilation of the vagina frequently after surgery with less frequent dilation over time.

http://brownsteincrane.com/mtf-surgery/

Primary Care for the Trans Female

Pelvic and breast considerations

No pap smears required

Pelvic exams to assess surgical site, acute genital infections

Neovaginal: granulation tissue

- Condyloma
- BV/yeast
- Chylamydia and gonorrhea have been reported

No indication for breast cancer screening

Trans Male Pharmacologic Therapy

Testosterone Pharmacotherapy

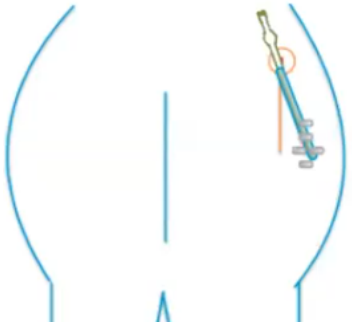
Androgen	Initial - typical	Maximum	Comment
Testosterone Cypionate	50mg/week IM/SQ	100mg/week IM/SQ	Q2week X double dose
Testosterone Enthanate	50mg/week IM/SQ	100mg/week IM/SQ	"
Testosterone topical gel 1%	50mg Q AM	100mg Q AM	Pump or packet form
Testosterone topical gel 1.62%	40.5 - 60.75mg Q AM	103.25mg Q AM	"
Testosterone axillary gel 2%	60mg Q AM	90-120mg Q AM	Comes in pump only, one pump = 30mg
Testosterone Undecanoate	750mg IM, repeat in 4 weeks, then q 10 weeks ongoing	N/A	Requires manufacturer monitored program

Other testosterone options

Jatenzo
Pro: Oral dosing
Con: Twice daily dosing with food, cost/coverage
Increased cost/coverage

Aveed
Pro: Less invasive, infrequent
Con: Specialty pharmacy
Administered in clinic
cost/coverage

Testosterone Pellet
Pro: Every 3 months
Con: Administered in clinic cost/coverage, person to person inconsistencies, insertion inconsistencies
soreness/infection rare



Effects of androgen therapy

Effect	Initial (mo)	Maximum (mo)
Skin oiliness/acne	1-6	12-24
Fat redistribution	1-6	24-60
Cessation of Menses	2-6	24-36
Clitoral enlargement	3-6	12-24
Vaginal atrophy	3-6	12-24
Deepening of voice	3-12	12-24
Scalp Hair Loss	6-12	
Increased Muscle Mass and Strength	6-12	24-60

Lesser used adjunctive therapy

- Estrogen cream locally for atrophy of frontal canal
  May also be used for inadequate pap smear tests

- Minoxidil or 5 alpha reductase inhibitors for androgenic hair loss

- Progesterone may aid in cessation of menses before or after starting testosterone therapy

Biochemical Monitoring

Therapy	Comments	Baseline	3 mo	6 mo	12 mo	Yearly
Estradiol	Goal < 50					
Total Testosterone	Mid range normal		X	X	X	
Sex Hormone Binding Globulin (SHBG) and albumin, optional	May be helpful in complex cases		PRN			
Hemoglobin & Hematocrit		X	X	X	X	X

Metabolic Effects of Trans Male Therapy

Metabolic Changes are seen in Trans Men

	Standard Mean Difference	95% CI	*P* Value
LDL (mg/dL)	**0.28**	**0.11-0.43**	**<0.01**
HDL (mg/dL)	**−0.50**	**−0.67 to −0.32**	**<0.01**
TG (mg/dL)	**0.42**	**0.25-0.60**	**<0.01**
TC (mg/dL)	**0.17**	**0.05-0.29**	**<0.01**
SBP (mm Hg)	−0.09	−0.61 to 0.42	0.72
DBP (mm Hg)	−0.27	−0.76 to −0.21	0.27
BMI (kg/m^2)	**0.24**	**0.11-0.38**	**<0.01**

Rahman SU JACC Adv. 2024

With pharmacologic therapy risk of VTE, CVA and MI not clearly increased

Event	Adjusted HR (95% CI)	
Transgender men	vs. cis gender men	vs.cis gender women
Transgender men overall cohort (n=2,118)		
VTE	1.6 (0.9–2.9)	1.1 (0.6–2.1)
Ischemic stroke	1.1 (0.6–2.0)	1.3 (0.7–2.5)
MI	0.7 (0.3–1.8)	1.3 (0.5–3.9)
Testosterone initiation cohort (n=585)		
VTE	2.7 (0.6–12.1)	1.5 (0.4–5.6)
Ischemic stroke	Not calculated	Not calculated
MI	–	–

Masumori Circ Rep 2023

Bone Health

- Testosterone is overall considered protect to bone density
  This may be due to increased muscle mass/mechanical loading
  Role of aromatization of testosterone to estrogen

- Recommendations: Insufficient evidence to guide recommendations.

- Consider screening bone density age > 65 or > 5 years off of hormone therapy and post gonadectomy

Surgical Therapy

Trans male Surgery

- Top surgery: Removal of breasts/mastectomy or reduction
- Bottom surgery

  Hysterectomy: Not required but a frequency used surgery. Patient may also have oophorectomy but needs HRT until age 50 for bone and vaginal protection

  Metoidioplasty - clitoral enlargement and separation. Cutting ligaments around the clitorus to lengthen the clitorus which is called a neophallus. This is often accompanied by lengthening of the urethra to allow urination upon standing

  Phalloplasty - surgical construction of a penis, tissue is commonly taken from a skin graft from the latissimus dorsi or radial forearm to construct a penis. The urethra also needs to be lengthened in this procedure to allow urination upon standing.

Trans male Surgery

Physical exam after Metoidoplasty or Phalloplasty

Urethral strictures, granulation tissue

Be aware of changes in libido and orgasm following surgery

Primary Care for Trans Male

Cervical Pap Smear

- All individuals with a cervix share same recommendations for screening
- Testosterone can cause atrophy of the cervical epithelium mimicking dysplasia
- Increase in “unsatisfactory” samples seen: 10.8% (10 times higher than in cisgender women)
- Individuals on testosterone are found to have reduced screening rates and long latency to follow up testing
- Recommend making a note on lab acquisition form that the patient is on testosterone and amenorrheic
- Talk to patients about abnormal/unsatisfactory paps prior to exam
- Review importance of follow up

Recommend consider mammogram at age 40-50 with or past or current hormone use equal or greater than 5 years for a person of average risk

Variables	Observed cases	Expected cases	Standardised incidence ratio (95% CI)	Expected cases	Standardised incidence ratio (95% CI)
		Reference: incidence ratio in cisgender men		Reference: incidence ratio in cisgender women	
Trans men (n=1229)					
Invasive	4	0.07	58.9 (18.7 to 142.2)	18.54	0.2 (0.1 to 0.5)
Age					
<30	0	0.00	-	0.14	-
30-50	2	0.01	282.3 (47.3 to 932.5)	4.78	0.4 (0.1 to 1.4)
>50	2	0.06	32.9 (5.5 to 108.8)	13.62	0.2 (0.0 to 0.5)
Non-invasive	0	0.01	-	3.55	-

de Blok CJ BMJ 2019

Contraception

Testosterone does not reliably prevent ovulation

Consider non-estrogen containing contraception

- Mirena IUD, Nexplanon
- Norethindrone acetate, Depo-Provera

STD Screening

Gonorrhea and Chlamydia

- Frontal Canal:

  Screen during pap smear

  Urine screening

Extragenital testing (rectum and throat)

Syphillis

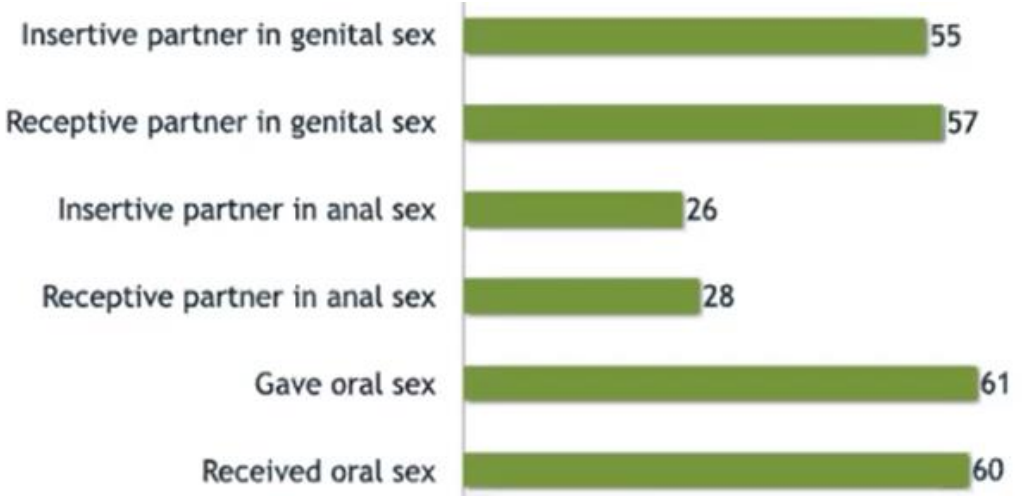
  Blood test, visual exam

  (rash, LAD, chancre)

HIV

  Offer PEP, discuss Prep

Sexual Behaviors of Transgender patients, Trans Pulse project last year %



Bauer BMC Public 2012

Reproductive Planning

- Recommend sperm and oocyte planning prior to pharmacologic therapy
- Gender affirming treatments affect gonads and gametes

  Estrogen may decrease sperm concentration and motility

  Androgens long terms may accelerate loss of ovarian reserve, may be associated with polycystic appearing ovaries

- Spontaneous conception can occur with both trans men and trans women
- Reproductive assistance can be successful with trans men, including 2 case reports of continuation of testosterone therapy in the setting of IVF.

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Transgender Health

Our goal is to provide transgender and non-binary patients with transgender health care services that are evidence-based and have an individualized approach to meet our patient's personal goals and needs. Virginia Mason Franciscan Health is proud to provide skilled and compassionate health care services with our multidisciplinary team in a welcoming and supportive environment.

We respect how individualized and private gender transition is and that many patients have questions about approaches or the elements of gender transition. Our team utilizes the World Professional Association for Transgender Health Guidelines (WPATH) as well as clinical guidelines within each specialty to work together to help achieve optimal health and well-being for our patients.

Thank you