Transgender Demographics & Gender Affirming Hormone Therapy for Adults

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Women’s Health Primary Care
National Center of Excellence in Women’s Health

Dimensions LGBTQ Youth Clinic
San Francisco Department of Public Health
Identity & Orientation

• Gender Identity
  – How one self-identifies in the way they live and move through the world
  – Mind
  – Female? Male? Something else?

• Gender Expression
  – How one “does” gender
  – Feminine? Masculine? Androgynous?

• Sexual Orientation
Trans* Terminology

- Trans Man / Trans-masculine
  - Female-to-Male/FTM
  - “Female Assigned at Birth (FAAB)”
- MTF / Trans Woman / Trans-feminine
  - “Male-to-Female/MTF”
  - Male Assigned at Birth (MAAB)
- Genderqueer/non-binary/non-conforming
  - Range of identities which lie outside binary M/F
Trans* Terminology

• Lesbian transgender woman
  – Female identity, attracted to women

• Gay transgender man
  – Male identity, attracted to men

• Cisgender = non-transgender
Collecting Sexual Orientation and Gender Identity (SOGI) Data

Preferred Name: Click here to enter text.

Legal Name, if differs: Click here to enter text.

Date of Birth: Click here to enter a date.

Gender Identity: Female □ Male □ Transgender Female □ Transgender Male

□ Genderqueer/Gender Nonconforming/Nonbinary/Neither Male Nor Female

□ Gender Identity Not Listed Here (specify): Click here to enter text.

Birth Assigned Sex: □ Female □ Male

Sexual Orientation (optional): □ Lesbian/Gay/Homosexual □ Straight/Heterosexual

□ Bisexual/Pansexual/Queer □ Sexual Orientation Not Listed Here (specify): Click here to enter text.
<table>
<thead>
<tr>
<th></th>
<th>1-Step</th>
<th>2-Step</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Trans</td>
<td>99.16%</td>
<td>98.35%</td>
</tr>
<tr>
<td>Trans</td>
<td>0.84%</td>
<td>1.65%</td>
</tr>
</tbody>
</table>

P < 0.00004

**Figure 1.** Framework for studies of population size in transgender and gender non-conforming populations. An ideal study would include all constructs within each of the four structural domains.

### Sampling

- Population based

### Methods

- Participants are given clear definitions of the terms “transgender” and “gender nonconforming”, or locally equivalent and appropriate terminology

### Measurement

- Use of two-step methodology
- Gender identity choices include the ability to capture non-binary identities and those who have not sought medical interventions
- Engage community stakeholders to ensure local language and terminology considerations are incorporated into list of gender identity choices

### Reporting

- Clearly state that the reported data may lack generalizability to other populations
- Recognize that some transgender and gender nonconforming people may be hesitant to disclose their gender identity, resulting in underestimation
- Data should be reported based on identified gender or gender spectrum, rather than based on sex assigned at birth
- Survey instrument, or list of choices for gender identity and sex assigned at birth are included in the report/manuscript
Transgender prevalence studies – clinic based

<table>
<thead>
<tr>
<th>Author</th>
<th>Year pub.</th>
<th>Country</th>
<th>Age</th>
<th>Years covered</th>
<th>Number overall (per 100,000)</th>
<th>Number TM (per 100,000)</th>
<th>Number TF (per 100,000)</th>
<th>Method for calculating numerator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tsoi11</td>
<td>1988</td>
<td>Singapore</td>
<td>&gt;15</td>
<td>1986</td>
<td>23.6</td>
<td>12</td>
<td>35.2</td>
<td>Number who underwent genital surgery</td>
</tr>
<tr>
<td>Van Kesteren et al.12</td>
<td>1996</td>
<td>Netherlands</td>
<td>&gt;15</td>
<td>1975-1992</td>
<td>8.05</td>
<td>4.3</td>
<td>12.1</td>
<td>Number treated at a single gender clinic with hormones</td>
</tr>
<tr>
<td>Gomez-Gil et al.13</td>
<td>2006</td>
<td>Spain</td>
<td>&gt;15</td>
<td>1996-2004</td>
<td>3.88</td>
<td>2.07</td>
<td>4.75</td>
<td>Number referred to a single gender clinic</td>
</tr>
<tr>
<td>De Cuypere et al.14</td>
<td>2007</td>
<td>Belgium</td>
<td>&gt;15</td>
<td>1985-2006</td>
<td>4.28</td>
<td>2.95</td>
<td>7.75</td>
<td>Number who underwent genital surgery using national data</td>
</tr>
<tr>
<td>Vujovic et al.15</td>
<td>2009</td>
<td>Serbia</td>
<td>&gt;18</td>
<td>1987-2006</td>
<td>2.25</td>
<td>2.27</td>
<td>2.23</td>
<td>Number referred to a single gender clinic</td>
</tr>
<tr>
<td>Baba et al.16</td>
<td>2011</td>
<td>Japan</td>
<td>13-56</td>
<td>2003-2010</td>
<td>-----</td>
<td>8.2</td>
<td>3.97</td>
<td>Number referred to a single gender clinic</td>
</tr>
<tr>
<td>Blosnich et al.17</td>
<td>2013</td>
<td>USA</td>
<td>-----</td>
<td>2000-2011</td>
<td>22.9</td>
<td>-----</td>
<td>-----</td>
<td>Nationwide chart review for all patients at a military veteran health system with one of two ICD-9 diagnostic codes for Gender Identity Disorder</td>
</tr>
</tbody>
</table>

“-----” indicates data level not reported.

TM: Transgender man/ trans-masculine spectrum.

TF: Transgender woman / trans-feminine spectrum.
### Transgender prevalence studies – population based

Table 2. Selected studies of the size of the transgender and gender nonconforming population in population-based samples (*methodology 2*).

<table>
<thead>
<tr>
<th>Author</th>
<th>Year pub.</th>
<th>Country</th>
<th>Age</th>
<th>Years covered</th>
<th>Number overall (per 100,000)</th>
<th>Number TM (per 100,000)</th>
<th>Number TF (per 100,000)</th>
<th>Method for calculating numerator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Almeida et al.</td>
<td>2009</td>
<td>USA</td>
<td>13-19</td>
<td>2006</td>
<td>1647</td>
<td>-----</td>
<td>-----</td>
<td>Stratified random sample of 1,032 high school students in city of Boston, USA who were asked a “yes/no” question regarding transgender status</td>
</tr>
<tr>
<td>Conron et al.</td>
<td>2012</td>
<td>USA</td>
<td>18-64</td>
<td>2007-2009</td>
<td>457</td>
<td>-----</td>
<td>-----</td>
<td>Number who responded “yes” when asked if they are transgender (with definition given) in a random-digit-dialing telephone sample of 28,662 residents of the US State of Massachusetts</td>
</tr>
<tr>
<td>Clark et al.</td>
<td>2014</td>
<td>New Zealand</td>
<td>In high school</td>
<td>2012</td>
<td>1175</td>
<td>-----</td>
<td>-----</td>
<td>Nationally representative sample of New Zealand high school students who were asked a “yes/no” question regarding transgender status</td>
</tr>
</tbody>
</table>

“-----” indicates data level not reported.

TM: Transgender man/ trans-masculine spectrum.

TF: Transgender woman / trans-feminine spectrum.

Deutsch MB. Making it Count: Improving Estimates of the Size of the Transgender and Gender Nonconforming Populations. LGBT Health; In Press
Gender ID of trans respondents in Statewide CA sample

<table>
<thead>
<tr>
<th>Gender Identity</th>
<th>Approximate %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Man/boy</td>
<td>9%</td>
</tr>
<tr>
<td>Woman/girl</td>
<td>7%</td>
</tr>
<tr>
<td>Androgynous</td>
<td>24%</td>
</tr>
<tr>
<td>Genderqueer</td>
<td>32%</td>
</tr>
<tr>
<td>Transgender</td>
<td>11%</td>
</tr>
<tr>
<td>Transman</td>
<td>11%</td>
</tr>
<tr>
<td>Transwoman</td>
<td>6%</td>
</tr>
</tbody>
</table>
Sexual orientation among trans respondents in a statewide CA survey

<table>
<thead>
<tr>
<th>Sexual Orientation</th>
<th>Approximate %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesbian</td>
<td>25%</td>
</tr>
<tr>
<td>Gay</td>
<td>9%</td>
</tr>
<tr>
<td>Bisexual/Pansexual</td>
<td>22%</td>
</tr>
<tr>
<td>Queer</td>
<td>32%</td>
</tr>
<tr>
<td>Questioning their sexual orientation</td>
<td>1%</td>
</tr>
<tr>
<td>Heterosexual/Straight</td>
<td>10%</td>
</tr>
</tbody>
</table>
Health Disparities

During the spring and summer of 2008 the Transgender Law Center (TLC) conducted a study of the economic health of the transgender community in California. We gathered 646 responses from transgender adults living in the state, and found alarmingly high rates of discrimination in employment, housing and healthcare.

**Health Care Access**
Transgender Californians report alarmingly high rates of denial of basic health care services.

- 33% were denied surgery
- 27% were denied hormones
- 21% were denied counseling and mental health services
- 15% were denied gender-specific care (such as pap smears for transmen and prostate exams for transwomen)
- 10% were denied primary health care

Some 30% of the community reports that they postponed care for illness or preventive care due to disrespect or discrimination from doctors or other health care providers. Forty-two percent of respondents delayed seeking care because they could not afford it. Twenty-six percent report health conditions that have worsened because they postponed care.
INJUSTICE AT EVERY TURN:
A REPORT OF THE NATIONAL
TRANSGENDER DISCRIMINATION
SURVEY, EXECUTIVE SUMMARY

Grant, Jaime M., Lisa A. Mottet, Justin Tanis, Jack Harrison, Jody L. Herman, and Mara Keisling.

• Health outcomes for all categories of respondents show the appalling effects of social and economic marginalization, including much higher rates of HIV infection, smoking, drug and alcohol use and suicide attempts than the general population.

• Refusal of care: **19% of our sample reported being refused medical care** due to their transgender or gender non-conforming status, with even higher numbers among people of color in the survey.

• Uninformed doctors: **50% of the sample reported having to teach their medical providers about transgender care.**

• High HIV rates: Respondents reported **over four times the national average of HIV infection, with rates higher among transgender people of color.**

• Postponed care: Survey participants reported that when they were sick or injured, **many postponed medical care due to discrimination (28%) or inability to afford it (48%).**
Figure 1. Percentage of Medical Schools Teaching LGBT-Related Topics in the Required Curriculum

Subject

- Sexual Orientation
- HIV
- Gender Identity
- STI
- Safer Sex
- DSD/Intersex
- Barriers to Care
- Mental Health Issues
- LGBT Adolescents
- Coming Out
- Unhealthy Relationships/IPV
- Substance Use
- Chronic Disease Risk
- SRS
- Body Image
- Transitioning

Schools Teaching LGBT-Related Subjects, %

75% response rate
<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>HIV prevalence in transgender women (95% CI)</th>
<th>Odds ratio (95% CI)</th>
<th>HIV prevalence in reproductive-age adults</th>
<th>HIV prevalence in reproductive-age males</th>
<th>Proportion of total HIV infections in men</th>
<th>Income level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina</td>
<td>931</td>
<td>33.5% (28.3–38.8)</td>
<td>92.4 (80.6–105.8)</td>
<td>0.54%</td>
<td>0.73%</td>
<td>67.3%</td>
<td>M</td>
</tr>
<tr>
<td>Brazil</td>
<td>638</td>
<td>33.1% (26.7–39.4)</td>
<td>85.3 (72.3–100.6)</td>
<td>0.58%</td>
<td>0.68%</td>
<td>59.2%</td>
<td>M</td>
</tr>
<tr>
<td>El Salvador</td>
<td>67</td>
<td>19.4% (0.0–40.9)</td>
<td>23.2 (12.7–42.5)</td>
<td>1.03%</td>
<td>1.42%</td>
<td>65.6%</td>
<td>M</td>
</tr>
<tr>
<td>Peru</td>
<td>450</td>
<td>28.9% (21.1–36.7)</td>
<td>84.7 (69.1–103.9)</td>
<td>0.48%</td>
<td>0.73%</td>
<td>75.3%</td>
<td>M</td>
</tr>
<tr>
<td>Uruguay</td>
<td>260</td>
<td>18.8% (7.9–29.8)</td>
<td>38.3 (28.1–52.3)</td>
<td>0.60%</td>
<td>0.82%</td>
<td>67.7%</td>
<td>M</td>
</tr>
<tr>
<td>Australia</td>
<td>133</td>
<td>4.5% (0.0–21.1)</td>
<td>24.9 (11.0–56.5)</td>
<td>0.19%</td>
<td>0.26%</td>
<td>69.0%</td>
<td>H</td>
</tr>
<tr>
<td>India</td>
<td>135</td>
<td>43.7% (31.0–56.4)</td>
<td>208.0 (148.0–292.3)</td>
<td>0.37%</td>
<td>0.44%</td>
<td>61.7%</td>
<td>M</td>
</tr>
<tr>
<td>Indonesia</td>
<td>1384</td>
<td>26.1% (21.6–30.6)</td>
<td>180.3 (159.9–203.3)</td>
<td>0.20%</td>
<td>0.32%</td>
<td>70.7%</td>
<td>M</td>
</tr>
<tr>
<td>Pakistan</td>
<td>2643</td>
<td>2.2% (0.0–6.0)</td>
<td>21.9 (16.9–28.4)</td>
<td>0.10%</td>
<td>0.14%</td>
<td>70.5%</td>
<td>M</td>
</tr>
<tr>
<td>Thailand</td>
<td>614</td>
<td>12.5% (5.1–19.9)</td>
<td>9.9 (7.8–12.6)</td>
<td>1.43%</td>
<td>1.71%</td>
<td>59.6%</td>
<td>M</td>
</tr>
<tr>
<td>Vietnam</td>
<td>75</td>
<td>6.7% (0.0–28.5)</td>
<td>15.6 (6.3–38.8)</td>
<td>0.45%</td>
<td>0.73%</td>
<td>70.0%</td>
<td>M</td>
</tr>
<tr>
<td>Italy</td>
<td>826</td>
<td>24.5% (18.5–30.4)</td>
<td>65.8 (56.1–77.1)</td>
<td>0.49%</td>
<td>0.65%</td>
<td>65.7%</td>
<td>M</td>
</tr>
<tr>
<td>Netherlands</td>
<td>69</td>
<td>18.8% (0.0–40.1)</td>
<td>81.8 (44.7–149.5)</td>
<td>0.28%</td>
<td>0.39%</td>
<td>68.6%</td>
<td>H</td>
</tr>
<tr>
<td>Spain</td>
<td>136</td>
<td>18.4% (3.2–33.6)</td>
<td>40.9 (26.5–63.1)</td>
<td>0.55%</td>
<td>0.81%</td>
<td>75.4%</td>
<td>H</td>
</tr>
<tr>
<td>USA</td>
<td>2705</td>
<td>21.7% (18.4–25.1)</td>
<td>34.2 (31.2–37.5)</td>
<td>0.81%</td>
<td>1.18%</td>
<td>74.2%</td>
<td>H</td>
</tr>
<tr>
<td>Pooled estimate</td>
<td>11,066</td>
<td>19.1% (17.4–20.7)</td>
<td>48.8 (31.2–76.3)</td>
<td>0.44%</td>
<td>0.58%</td>
<td>..</td>
<td>..</td>
</tr>
</tbody>
</table>

*Degrees of freedom=14, heterogeneity $\chi^2=914.7, I^2=98.5\%$, test of odds ratio=1, $z=16.21$, $p=0.0001$. Income level: M=middle-income; H=high-income.

Table 1: Meta-analyses of aggregated country data for HIV prevalence in transgender women versus all reproductive age adults, 2000–11

Worldwide burden of HIV in transgender women: a systematic review and meta-analysis

Stefan D Baral, Tonia Poteat, Susanne Strömdahl, Andrea I. Wirtz, Thomas E Guadamuz, Chris Beyrer

States that prohibit discrimination based on sexual orientation only (2 states): New Hampshire, Wisconsin

States that prohibit discrimination against public employees based on sexual orientation and gender identity (6 states): Indiana, Kentucky, Michigan, Montana, Pennsylvania, Virginia

States that prohibit discrimination against public employees based on sexual orientation only (4 states): Alaska, Arizona, Missouri, Ohio

*State courts, commissions, agencies, or attorney general have interpreted the existing law to include some protection against discrimination against transgender individuals in Florida and New York.
**States that prohibit housing discrimination based on sexual orientation and gender identity** (20 states & D.C.): California, Colorado, Connecticut, Delaware, District of Columbia, Hawaii, Illinois, Iowa, Maine, Maryland, Massachusetts, Minnesota, Nevada, New Jersey, New Mexico, New York, Oregon, Rhode Island, Utah, Vermont, Washington

**States that prohibit housing discrimination based on sexual orientation only** (2 states): New Hampshire, Wisconsin

Federal Requirements: The Department of Housing and Urban Development (HUD) requires grantees and participants of HUD programs to comply with local and state non-discrimination laws that include sexual orientation and gender identity. HUD also prohibits inquiries regarding the sexual orientation or gender identity of a prospective tenant or applicant for assisted housing in every state.
HIV pre-exposure prophylaxis in transgender women: a subgroup analysis of the iPrEx trial.

Deutsch MB, Glidden DV, Sevelius J, Keatley J, McMahan V, Guanira J, Kallas EG, Chariyalertsak S, Grant RM; iPrEx investigators.
Research Funded by the National Institutes of Health on the Health of Lesbian, Gay, Bisexual, and Transgender Populations

Robert W. S. Coulter, MPH, Karey S. Kenst, MPH, Deborah J. Bowen, PhD, and Scout, PhD

Evidence for providing a respectful and appropriate transgender care setting

• Improved patient satisfaction
• Improved patient retention
• Patient safety
• Improved care
  – Patients may be more comfortable with sensitive exams when they feel their identity is being respected
  – Patients may be more likely to come in for other needed preventive and primary care, if they feel the clinic offers an accepting and gender affirming environment

What is A Respectful and Culturally Appropriate Care Setting?

• Bathrooms – what bathrooms are transgender people allowed to use? Are there safety issues (for example, transgender women in the men’s room may be at risk of assault)

• Waiting room materials and atmosphere – are there any pamphlets, posters etc... which make transgender people feel comfortable?

• Medical Records, including Electronic Medical Records – is there a way to note patient’s chosen name and pronoun, if they differ from that on legal documents?

BMC Pediatr. 2015; 15: 187. Improving transgender health by building safe clinical environments that promote existing resilience: Results from a qualitative analysis of providers

What is A Respectful and Culturally Appropriate Care Setting?

• Front desk, nurse and provider staff –
  – are clinic staff trained in basic transgender cultural competency?
  – Do they understand the importance of using the chosen name and pronoun, even if they differ from that which is on legal ID?
  – Do they understand how to record and access this information in the medical record?

• Engage the community both in the development of clinical services oriented towards transgender people, as well as for dissemination of awareness about the services.
Gender Affirming Treatments and Procedures

• Hormone therapy
• Surgery
• Other procedures
  – Hair removal
    • Transgender women -> facial and/or body hair removal
    • Transgender men -> Hair removal at graft site for phalloplasty
  – Speech therapy for voice feminization or masculinization
    • Role of voice surgery is evolving
Gender Affirming Interventions – Non Medical

• Chest binding - > use of a tight bra or elastic bandage to flatten breasts and give a male chest contour

• Packing -> Use of an external penile prosthesis to give a male genital contour

• Tucking -> Displacement of the testicles into the inguinal canal, movement of the penis posteriorly into the perineum, and use of a tight undergarment to give a female genital contour

• Scalp hair replacement procedures – hairpiece, wig, hair transplants
Common Surgeries

• Hysterectomy / oopherectomy
• Vaginoplasty
• Phalloplasty
• Metaoidioplasty
• Breast augmentation
• Mastectomy
• Orchietomy
• Facial feminization
• Tracheal shaving
• Other “cosmetic” procedures
  – Cosmetic in quotes, since many of these procedures are not at all cosmetic, but instead therapeutic in transgender people
Why offer gender affirming care?

• Hormone therapy reduces anxiety, depression and improves social functioning & QOL

• Surgery improves global functioning, sexual functioning, family and interpersonal relationships, body image, and quality of life
Why offer gender affirming care?

- Regret relating to surgery is very rare (1% or less), and generally relates to surgical complications.

- Note that studies have been conducted in a variety of country/language settings.

- Bundling of hormones and other gender affirming procedures may improve participation in other important health care, such as HIV care or smoking cessation.

- Gender affirming procedures, including hormone therapy, genital, chest, and facial surgery, voice procedures, and hair removal are defined as medically necessary by WPATH SOCv7.
Is transition care coverage cost effective?

- $8655/QALY savings
- Cost of coverage is $0.016 per-member per-month

*Societal Implications of Health Insurance Coverage for Medically Necessary Services in the U.S. Transgender Population: A Cost-Effectiveness Analysis*

William V. Padula, PhD MS MSc¹, Shiona Heru, JD², and Jonathan D. Campbell, PhD³

J Gen Intern Med
DOI: 10.1007/s11606-015-3529-6
© Society of General Internal Medicine 2015
Transgender Youth

• Benefits of early identification
  – Avoid irreversible hormonal changes
  – Avoid trauma of undesired puberty
  – Gain socialization benefits of age-appropriate, felt-gender transition
Transgender Youth - Outcomes

• Transgender kids who transition have better mental health outcomes than those who do not

• Transgender kids who transition have mental health outcomes similar to non-transgender kids

Pediatrics
March 2016

Mental Health of Transgender Children Who Are Supported in Their Identities
Kristina R. Olson, Lily Durwood, Madeleine DeMeules, Katie A. McLaughlin
Feminizing Hormones - Goals

• Development of feminine secondary sex characteristics

• Suppression/minimization of masculine secondary sex characteristics
Feminizing hormones – physical effects

- Breast development

- Feminine redistribution of subcutaneous facial and body fat.

- Reduced muscle mass

- Reduced body and (to a lesser extent) facial hair

- Changes in perspiration and odors

- Arrest (and possible reversal) of scalp hair loss
Feminizing hormones – other effects

• Reduced libido and erectile function

• Reduced size of testes, reduced or absent ejaculatory fluid and sperm count

• Changes in emotional and social functioning
  – Effects vary from person to person
  – Avoid projecting stereotypes
Feminizing hormones –
general approach

• Estrogen plus:

• Androgen blocker plus:

• (Sometimes) progestagen
Estrogens: 17-beta estradiol

• “Bio-identical” = identical to the estrogen secreted from a human ovary)

• Patch, tablet, injected (valerate or cypionate ester) forms most commonly used in transgender care

• Gels, creams, sprays exist for menopausal use, but tend to not deliver high enough dose for feminization
Estrogens – side effects

• Migraines

• Mood swings

• Weight gain

• Hot flashes
Spironolactone

• Potassium sparing diuretic with properties that block both testosterone synthesis and receptor activity. (9)
  – May cause orthostasis or polyuria
  – Monitor renal function and potassium
  – Use caution with ACE-inhibitors or angiotensin 2 receptor blockers
Progestagens

- Medroxyprogesterone, micronized progesterone are potential agents.

- No data to guide use or role of progestagens in feminizing hormone therapy.

- Anecdotal improvement in (7,8):
  - Breast/areaolar development
  - Mood and libido

- May be helpful if having difficulty with full androgen suppression.

- Take an individualized approach.
Progestagens - risks

• Some evidence from the US based Women’s Health Initiative suggests increased risk of cardiac events or breast cancer when used as part of a menopausal regimen (9)

  – Study has numerous confounders
  – Effect size is very small
  – Findings may not apply to transgender care

  – Norpregnane derived progestagens (norethindrone, norgestrel) may have increased thrombogenicity compared to medroxyprogesterone or cyproterone (10)
### Hormone dosing table

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Initial–low&lt;sup&gt;#&lt;/sup&gt;</th>
<th>Initial</th>
<th>Maximum *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol oral/sublingual</td>
<td>1mg</td>
<td>2-4mg/day</td>
<td>8mg/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estradiol transdermal</td>
<td>50mcg</td>
<td>100mcg</td>
<td>100-400 mcg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estradiol valerate IM</td>
<td>&lt;20mg</td>
<td>20mg IM q 2 wk</td>
<td>40mg IM q 2wk</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estradiol cypionate IM</td>
<td>&lt;2mg</td>
<td>2mg IM q 2 wk</td>
<td>5mg IM q 2 wk</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progestagen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medroxyprogesterone</td>
<td>2.5mg</td>
<td></td>
<td>5-10mg qhs</td>
</tr>
<tr>
<td>acetate (Provera)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Micronized progesterone</td>
<td></td>
<td></td>
<td>100-200 mg qhs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Androgen blocker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spironolactone</td>
<td>25mg qd</td>
<td>50mg bid</td>
<td>200mg bid</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Finasteride</td>
<td>1mg qd</td>
<td></td>
<td>5mg qd</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dutasteride</td>
<td></td>
<td></td>
<td>0.5mg qd</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyproterone</td>
<td>100mg/day</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Maximum dosing does not mean maximal effect, and do not necessarily represent a target or ideal dose. Dose increases should be based on patient response and (if done) monitored hormone levels.

# Initial-low dosing for those who desire (or require due to medical history) a low dose or slow upward titration.
## Lab monitoring

<table>
<thead>
<tr>
<th>Comments</th>
<th>Baseline</th>
<th>3 months *</th>
<th>6 months*</th>
<th>12 months*</th>
<th>Yearly</th>
<th>PRN</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN/Cr/K+</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Only if spiro used</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipids</td>
<td>X if clinically indicated</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>A1c or glucose</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estradiol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Total Testosterone</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin **</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prolactin</td>
<td>Only if symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
</tr>
</tbody>
</table>

* In first year of therapy only
Monitoring therapy

• If hormone level testing is not feasible or available, monitor clinical progress
  – Reduced erections and ejaculatory fluid
  – Reduced body hair

• No evidence that supraphysiologic estrogen levels result in further feminization
  – May increase risk of thromboembolism
  – Maximal effects can take 2-5 years (13)

• Estradiol assays will not accurately measure levels in patients using equine estrogens or ethinyl estradiol
  – In these cases, consider using a “total estrogen” assay
Expected effects and time frames

• Factors which predict both extent of and length of time to achieve feminizing effects:
  – Age at start
  – Genetics
  – Body habitus/shape

• Results are individualized and patients should avoid making comparisons to others
  – Hormone level monitoring may reassure patient

• Maintain reasonable expectations
  – Actual results may not meet desired effects
Monitoring “sex specific” labs

• Hemoglobin/hematocrit (“H&H”)
• Creatinine
• Alkaline phosphatase

• All may vary depending on sex hormone milieu
• Transgender women:
  – May retain elevated muscle mass (Creatinine)
  – May retain higher bone mass (Alkaline phosphatase)
  – Do not menstruate (hemoglobin/hematocrit)
  – Modify reference ranges accordingly (see table) (9)
Sex-specific reference ranges for non-hormone labs

<table>
<thead>
<tr>
<th>Lab measure</th>
<th>Lower Limit of normal</th>
<th>Upper Limit of normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>?</td>
<td>Male value</td>
</tr>
<tr>
<td>H&amp;H</td>
<td>Female value</td>
<td>Male value</td>
</tr>
<tr>
<td>Alk Phos</td>
<td>?</td>
<td>Male value</td>
</tr>
</tbody>
</table>
Pituitary adenoma

• Several cases have been reported in transgender women (19)

• However, Endocrine Society guidelines recommend watchful waiting only in cases of asymptomatic prolactinomas (20)

• Therefore in the absence of visual disturbances, galactorrhea, or headache syndromes, routine monitoring of prolactin not likely of clinical value
Venous thromboembolism – data from menopause literature

- Menopausal studies suggest no increased risk when transdermal estradiol used (29)

- Menopausal data on oral 17-beta estradiol is mixed, with risks as high as 2.5-4x increase (10,29)
  - With a background rate of 1:1,000 to 1:10,000 in general population, absolute increase is small (4)
Venous thromboembolism – data in transgender women

• Studies > 10 years old showing 20 to 40 fold increase involved use of up to 200mcg/day of ethinyl estradiol, and did not control for tobacco use (30,31)
  – These studies are not applicable to modern 17-beta estradiol regimens used in an average risk, non-smoking population

• No increased risk has been observed in a large retrospective sample of Dutch transgender women using 17-beta estradiol (5)
Primary and secondary prevention of VTE

• Insufficient evidence to guide the use of estrogen therapy, anticoagulation, or antiplatelet therapy in transgender women with risk factors or personal history of DVT

• Case series of 11 transgender women with activated protein C resistance using transdermal estradiol without anticoagulation or antiplatelet therapy found no VTE after mean 64 months (32)
Primary and secondary prevention of VTE - scenarios

• Role of episodic (i.e. airplane flights) or long term anticoagulation/antiplatelet therapy should be considered in the context of risks of GI or intracranial hemorrhage

• Routine VTE prophylaxis with ASA in unselected transgender patients not recommended

• Routine screening for prothrombotic mutations not recommended in the absence of risk factors (32)

• Estrogen therapy should not be administered in patients with risk factors for or history of VTE who continue to smoke tobacco
Masculinizing Hormones
Goals of therapy

• Development/emphasis of masculine secondary sex characteristics

• Elimination/minimization of feminine secondary sex characteristics
Masculinizing hormones – physical effects

- Development of facial and body hair
- Redistribution of body fat
- Increased muscle mass
- Deepened/masculine voice
- Increased perspiration, change in urine and body odors
- Frontal and temporal hairline recession, possible male-pattern baldness/crown recession
- Clitoral growth
Masculinizing hormones – other effects

- Increased libido
- Vaginal dryness and atrophy
- Cessation of menses
- Infertility/anovulatory state
- Possible changes in emotional and social functioning
Masculinizing hormones –
general approach

• Use of one of several forms of parenteral testosterone

• Other adjuncts may include progestagens, 5-alpha reductase inhibitors or aromatase inhibitors
Testosterone

• Bio-identical testosterone = chemically equivalent to the testosterone secreted from the human testicle

• Oral methyltestosterone no longer used
  – This is the origin of the perception that testosterone can present risk of liver damage

• May require higher doses than in non-transgender men, since transgender men require complete replacement, rather than supplementation
# Testosterone dosing

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

a: Available as standard U.S. Pharmacopia (USP) as well as compounded products.

b: Initial – low dose recommended for genderqueer and nonbinary dosing.
Intramuscular vs. subcutaneous routes

• Many providers have administered testosterone using the subcutaneous route with good efficacy and patient satisfaction, and without complications.
  – Non-inferior to IM in 2 small studies (3,4)

• Benefits of subcutaneous administration (3,4) :
  – Smaller and less painful needle,
  – May avoid scarring or fibrosis from long term (possibly > 50 years) intramuscular therapy.
Management after gonadectomy

• Avoid routinely reducing testosterone dose after gonadectomy

  – Testosterone is dosed for complete replacement
  – Unless pt desires lower dose after oopherectomy, maintaining effects will require maintaining physiologic dosing
Erythrocytosis / polycythemia

- May avoid risk by changing to a lower dose/more frequent dosing schedule with lower peak levels, or transdermal routes (8)

- Phlebotomy or donation of blood may be appropriate short term solution

- Pathologic erythrocytosis should be ruled out in all cases
  - Obesity related sleep apnea
  - Tobacco use
  - Neoplasm

- Be sure to use male range values
Coexisting metabolic disorders

- PCOS has been found to be more prevalent in transgender men pre-testosterone than in non-transgender women (21)
  - 60% in a Japanese study

- PCOS is not a contraindication to testosterone therapy
  - Do maintain higher index of suspicion for hyperlipidemia and diabetes

- Amenorrhea in the presence of testosterone generally indicates endometrial atrophy (18,19) rather than hyperplasia
Coexisting metabolic disorders

• Psychosocial benefits of testosterone may include positive lifestyle changes which can reduce obesity and glucose and lipid disorders

• These benefits likely outweigh any potential increased metabolic risks
Acne

• Approach is similar to that in non-transgender people

• Acne tends to peak in 1\textsuperscript{st} year of therapy, then declines (20)

• Avoiding supraphysiologic levels, and avoiding excessive peaks associated with prolong (2-4 week) dosing intervals may help minimize acne
Health outcomes?
Table 2. Baseline and 6-Month Biometrics for Transgender Women (n=16)

<table>
<thead>
<tr>
<th>Biometric</th>
<th>Baseline</th>
<th>6-mo</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>172.5 (12)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>69.4 (17.9)</td>
<td>68.8 (20.2)</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.8 (4.3)</td>
<td>23 (4.5)</td>
<td>NS</td>
</tr>
<tr>
<td>BP (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>130.5 (11.5)</td>
<td>120.5 (15.5)</td>
<td>.006</td>
</tr>
<tr>
<td>Diastolic</td>
<td>78 (21)</td>
<td>67 (12)</td>
<td>.001</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>171 (50)</td>
<td>176.5 (42)</td>
<td>NS</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>58.5 (16)</td>
<td>66.5 (25.5)</td>
<td>.049</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>97 (42)</td>
<td>89.5 (20.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>71.5 (37.5)</td>
<td>94 (65.5)</td>
<td>.013</td>
</tr>
</tbody>
</table>

NS, nonsignificant; BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Data are median (interquartile range) unless otherwise specified. All statistical analysis used the Wilcoxon signed-rank test for paired samples.

Table 3. Baseline and 6-Month Biometrics for Transgender Men (n=31)

<table>
<thead>
<tr>
<th>Biometric</th>
<th>Baseline</th>
<th>6-mo</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>164 (9)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78 (45.4)</td>
<td>79.4 (36.2)</td>
<td>.024</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.1 (11.2)</td>
<td>30.0 (11.4)</td>
<td>.024</td>
</tr>
<tr>
<td>BP (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>120 (23)</td>
<td>123 (14)</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic</td>
<td>72 (16)</td>
<td>70 (16)</td>
<td>NS</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>177 (38)</td>
<td>178 (42)</td>
<td>NS</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td>58 (22)</td>
<td>56 (29)</td>
<td>.006</td>
</tr>
<tr>
<td>LDL (mg/dL)</td>
<td>93 (33)</td>
<td>97 (38)</td>
<td>NS</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>75 (56)</td>
<td>73 (69)</td>
<td>NS</td>
</tr>
</tbody>
</table>

BMI, body mass index; BP, blood pressure; NS, nonsignificant; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Data are median (interquartile range) unless otherwise specified. All statistical analysis used the Wilcoxon signed-rank test for paired samples.

Effects of Cross-Sex Hormone Treatment on Transgender Women and Men

Madeline B. Deutsch, MD, Vipra Bhakri, MS, MPH, and Katrina Kubicek, MS

(Obstet Gynecol 2015;
Post-HRT Characteristics - FTM

Cross-Sex Hormone Therapy Alters the Serum Lipid Profile: A Retrospective Cohort Study in 169 Transsexuals

J Sex Med 2011;8:2361–2369
Post-HRT Characteristics - MTF

Cross-Sex Hormone Therapy Alters the Serum Lipid Profile: A Retrospective Cohort Study in 169 Transsexuals

Johannes Ott, MD,* Stefanie Aust, MD,* Regina Promberger, MD,† Johannes C. Huber, MD, PhD,* and Ulrike Kaufmann, MD

*Department of Gynecological Endocrinology and Reproductive Medicine—Medical University of Vienna, Vienna, Austria
†Department of Surgery—Medical University of Vienna, Vienna, Austria

J Sex Med 2011;8:2361–2369
Table 2: SMR adjusted for age and period of follow-up on hormone treatment by biological sex in 1331 male-to-female and female-to-male transsexual subjects.

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Male-to-female transsexuals</th>
<th>Female-to-male transsexuals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Observed cases</td>
<td>SMR (95% CI)</td>
</tr>
<tr>
<td>Malignant neoplasm</td>
<td>28</td>
<td>0.98 (0.88–1.08)</td>
</tr>
<tr>
<td>Lung</td>
<td>13</td>
<td>1.35 (1.14–1.58)</td>
</tr>
<tr>
<td>Digestive tract</td>
<td>3</td>
<td>0.42 (0.28–0.60)</td>
</tr>
<tr>
<td>Hematological</td>
<td>6</td>
<td>2.58 (1.97–3.30)</td>
</tr>
<tr>
<td>Brain</td>
<td>2</td>
<td>1.59 (0.95–2.46)</td>
</tr>
<tr>
<td>Other: kidney, melanoma, bone, and prostate in MTF. In FTM: leiomyosarcoma</td>
<td>4</td>
<td>0.79 (0.57–1.07)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>18</td>
<td>1.64 (1.43–1.87)</td>
</tr>
<tr>
<td>Cerebrovascular accidents</td>
<td>5</td>
<td>1.26 (0.93–1.64)</td>
</tr>
<tr>
<td>AIDS</td>
<td>16</td>
<td>30.20 (26.0–34.7)</td>
</tr>
<tr>
<td>Endocrine/diabetes</td>
<td>2</td>
<td>0.85 (0.41–1.32)</td>
</tr>
<tr>
<td>Respiratory system diseases</td>
<td>4</td>
<td>0.85 (0.61–1.14)</td>
</tr>
<tr>
<td>Digestive system diseases</td>
<td>3</td>
<td>1.01 (0.68–1.45)</td>
</tr>
<tr>
<td>Genitourinary system disease (ESRD)</td>
<td>1</td>
<td>1.21 (0.58–2.17)</td>
</tr>
<tr>
<td>Nervous system disease (MS)</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>External causes</td>
<td>24</td>
<td>7.67 (6.84–8.56)</td>
</tr>
<tr>
<td>Illicit drugs use</td>
<td>5</td>
<td>13.20 (9.70–17.6)</td>
</tr>
<tr>
<td>Suicide</td>
<td>17</td>
<td>5.70 (4.93–6.54)</td>
</tr>
<tr>
<td>Unknown/ill-defined symptoms</td>
<td>21</td>
<td>4.00 (3.52–4.51)</td>
</tr>
<tr>
<td>Total</td>
<td>122</td>
<td>1.51 (1.47–1.55)</td>
</tr>
</tbody>
</table>

CLINICAL STUDY

A long-term follow-up study of mortality in transsexuals receiving treatment with cross-sex hormones

Henk Asscheman1, Erik J Giltay2, Jos A J Megens2, W (Pim) de Ronde1, Michael A A van Trotsenburg2 and Louis J G Gooren1
Acknowledging Gender and Sex

This course is best viewed in full-screen mode. Click F11 on your PC keyboard to enter or exit full screen at any time. Does not apply to iPads® or other mobile devices.
The UCSF Transgender Care Navigation Program is a collaboration between The Center of Excellence for Transgender Health and the National Center of Excellence in Women's Health. Both Centers work together with partner providers and clinics to assist transgender, gender nonconforming, and nonbinary people seeking general healthcare or gender affirming medical care at UCSF.


33. Single-Dose Pharmacokinetics of Sublingual Versus Oral Administration of Micronized 17β-Estradiol

34. Estrogen Deficiency in Severe Postpartum Depression: Successful Treatment With Sublingual Physiologic 17β-Estradiol: A Preliminary Study

Antti Ahokas, M.D., Ph.D.; Jutta Kaukoranta, M.D.; Kristian Wahlbeck, M.D., Ph.D.; and Marjatta Aito, M.D.
Bibliography – Masculinizing Hormones


Bibliography – Masculinizing Hormones


21. Association between polycystic ovary syndrome and female-to-male transsexuality

Tsuyoshi Baba1,5, Toshiaki Endo1, Hiroyuki Honma1, Yoshimitsu Kitajima1, Takuhiro Hayashi1, Hiroshi Ikeda2, Naoya Masumori1, Hirofumi Kamiya4, Osamu Moriwaka4 and Tsuyoshi Saito1