# Management of Transgender Youth

Jorge De Jesús MD FACE

#### Disclosures:

- Dr Jorge De Jesús has no formal training or experience in treating transgender individuals
- This presentation is a summary of my opinions based on current clinical guidelines and most recent published medical literature
- I have no conflict of interests with the content of the presentation to be offered
- I have received honorariums as speaker from pharmaceutical companies as : Janssen; Sanofi-Aventis- Merck



### Objectives:

Role of prenatal brain organization in gender dysphoria/gender incongruence

Genes, hormones and environment seem to influence gender development

Gender identity is not a binary phenomenon

Increasing demand for health care services at very young ages

Need of health care providers to become competent in transgender care

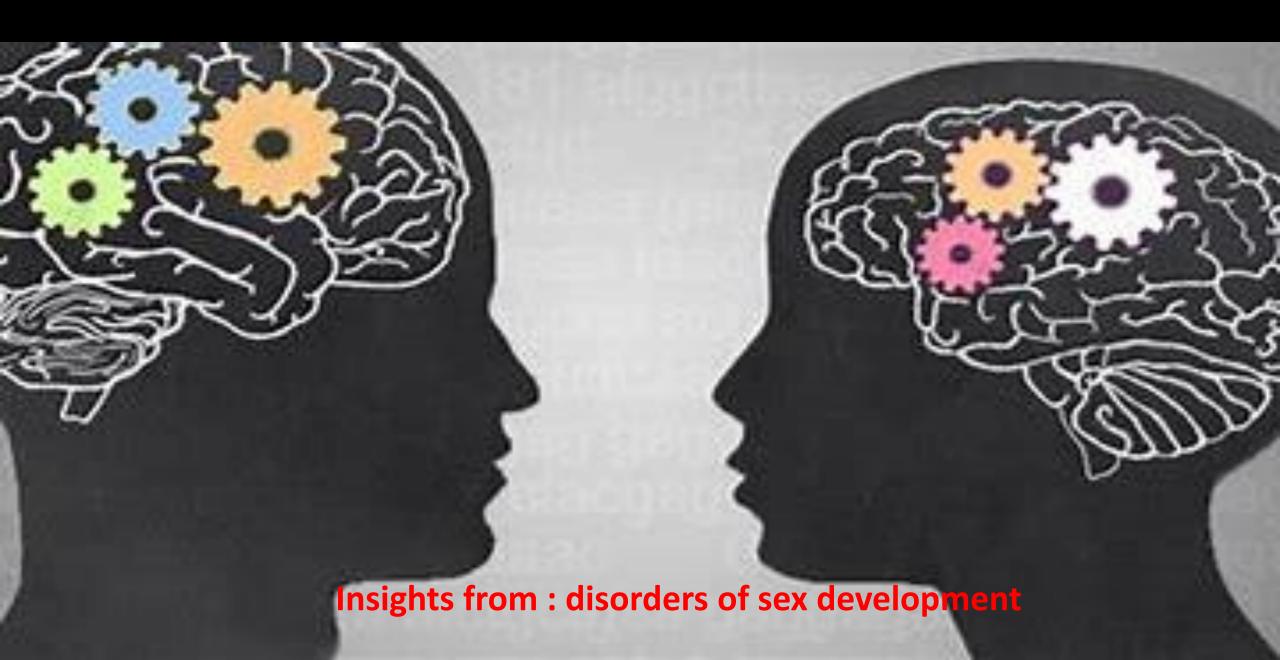
### Epidemiology: Transgender Individuals

#### **Dutch Population**

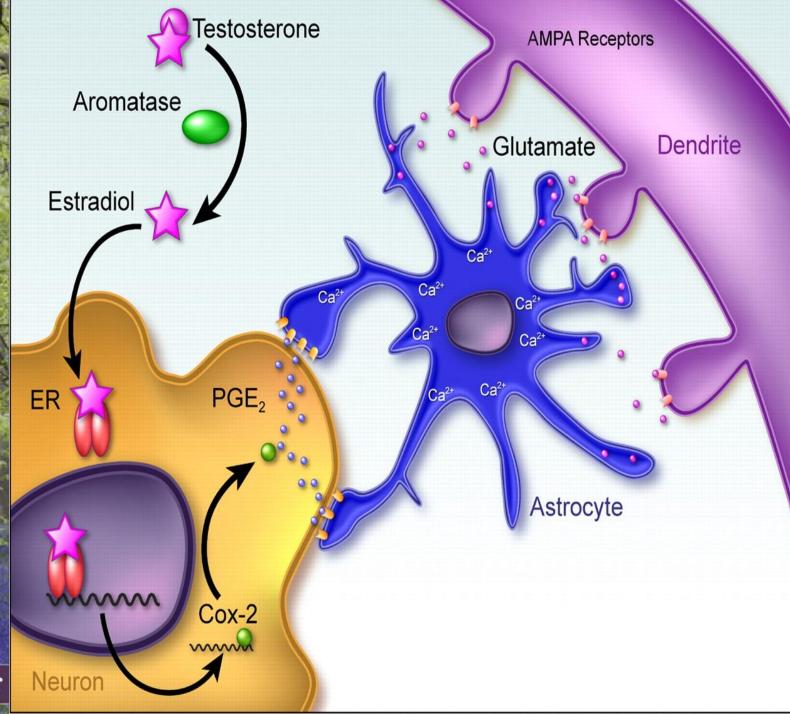
- The Amsterdam Gender Dysphoria Clinic
- Prevalence 1 in 10,000 assigned males
- 1-30,000 assigned females
- (four decades study)
- Archives of Sexual Behavior Netherlands

#### Meta-analysis overall population

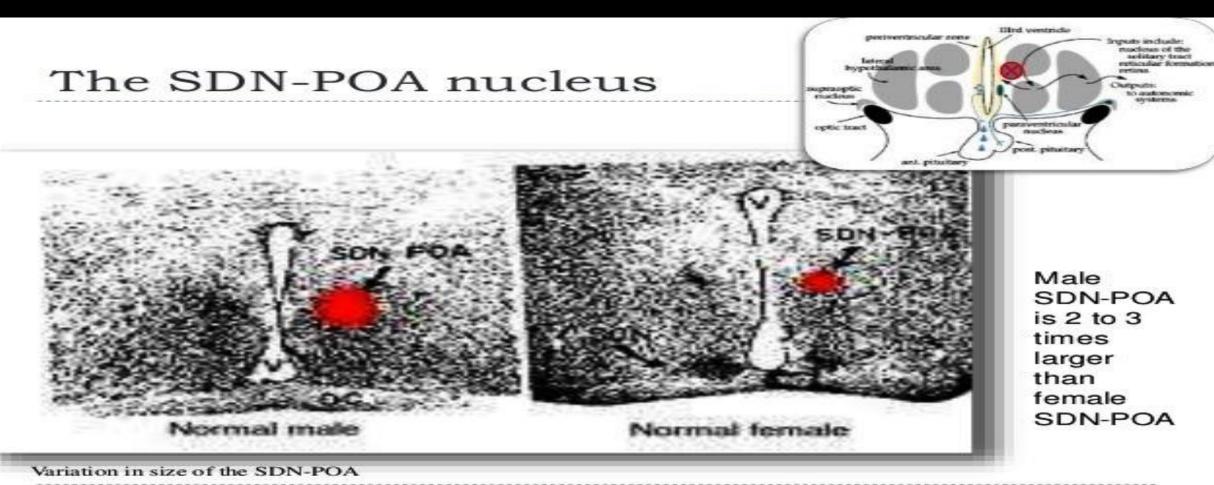
- Overall population:
- 1-20,000 individuals
- 1-15,000 transwomen
- 1-40,000 transmen
- Arcelus et al (Eur Psychiatry 2015)



"Scientists hypothesize that a combination of genetic, hormonal and social factors determine sexual orientation. These factors [...] include genes, prenatal hormones, and brain structure." whisper



# Comparative brain structures pre-optic area: three times larger in males than in females



The Sdn-poa Area In The Human Brain: A Comparative Morphometric Study, Michel A. Hofman And Dick F. Swaab

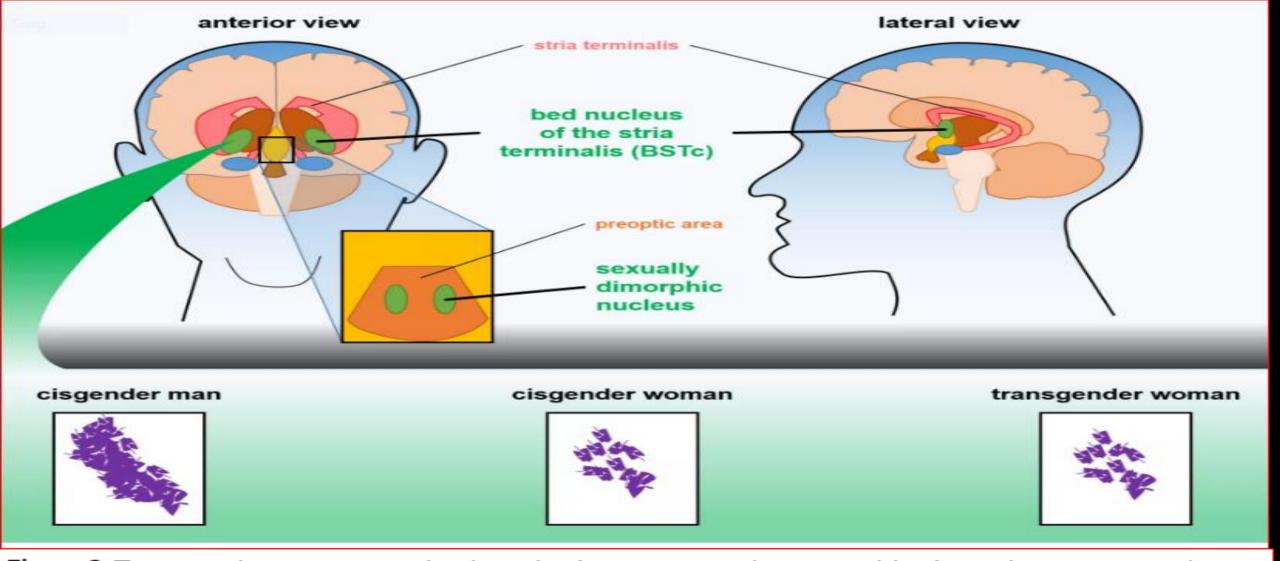


Figure 2: Transgender women tend to have brain structures that resemble cisgender women, rather than cisgender men. Two sexually dimorphic (differing between men and women) areas of the brain are often compared between men and women. The bed nucleus of the stria terminalus (BSTc) and sexually dimorphic nucleus of transgender women are more similar to those of cisgender woman than to those of cisgender men, suggesting that the general brain structure of these women is in keeping with their gender identity.

#### Sexual dimorphism in olfactory signaling

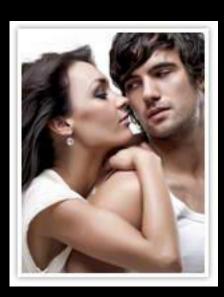
Lisa Stowers<sup>a</sup> and Darren W Logan<sup>b</sup>

<u>Author information</u> ► Copyright and License information ►

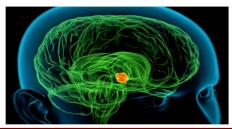
AND\*



\*14,16 androstandien 3 one Male sweat; saliva; semen EST
Estrogen dervirative
from urine in
pregnant women



#### Kisspeptin Expression in the Human Infundibular Nucleus in Relation to Sex, Gender Identity, and Sexual Orientation



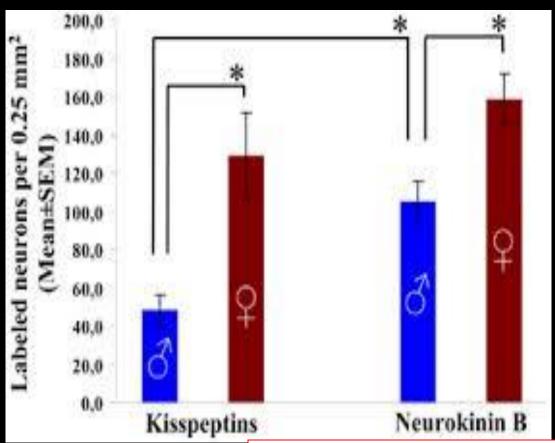
#### 09/06/2016

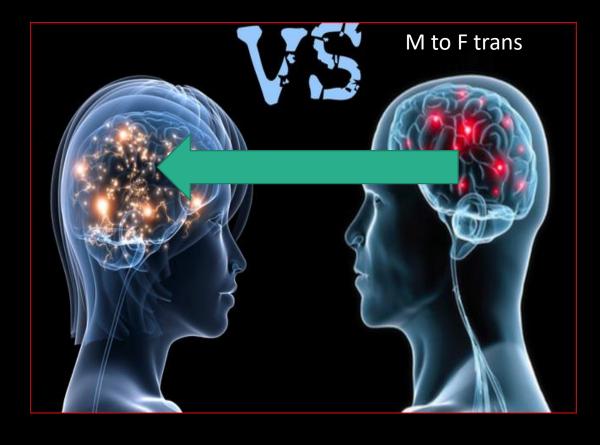
#### CONTEXT:

Since the discovery of its central role in reproduction, our functional neuroanatomical knowledge of the hypothalamic kisspeptin system is predominantly based on animal studies. Although sex differences in kisspeptin expression have been shown in humans in adulthood, the developmental origin of this sex difference is unknown.

#### OBJECTIVES:

Our objectives were to determine the following: 1) when during development the sex difference in kisspeptin expression in the infundibular nucleus would emerge and 2) whether this sex difference is related to sexual orientation or transsexuality.





CONCLUSIONS: These findings suggest that infundibular kisspeptin neurons are sensitive to circulating sex steroid hormones throughout life and that the sex reversal observed in MTF transsexuals might reflect, at least partially, an atypical brain sexual differentiation.

Journal of Clinical Endocrinology & Metabolism

# Genetic Link Between Gender Dysphoria and Sex Hormone Signaling

Madeleine Foreman; Lauren Hare; Kate York; Kara Balakrishnan; Francisco J. Sánchez; Fintan Harte; Jaco Erasmus; Eric Vilain; Vincent R. Harley

DISCLOSURES | J Clin Endocrinol Metab. 2019;104(2):390-396.

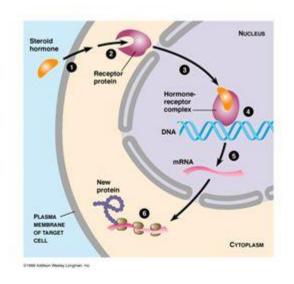
**Main Outcome Measured:** Genomic DNA was genotyped for repeat length polymorphisms or single nucleotide polymorphisms.

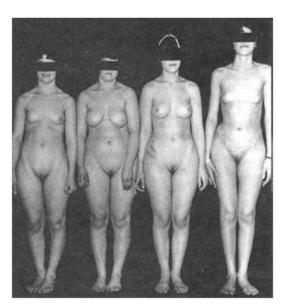
**Results:** A significant association was identified between gender dysphoria and *ERα*, *SRD5A2*, and *STS* alleles, as well as *ERα* and *SULT2A1* genotypes. Several allele combinations were also overrepresented in transgender women, most involving *AR* (namely, *AR-ERβ*, *AR-PGR*, *AR-COMT*, *CYP17-SRD5A2*). Overrepresented alleles and genotypes are proposed to undermasculinize/feminize on the basis of their reported effects in other disease contexts.

**Conclusion:** Gender dysphoria may have an oligogenic component, with several genes involved in sex hormone—signaling contributing.

# Androgen Insensitivity

- Incidence about 1 in 20,000 births
- Used to be called "testicular feminization". 46,XY with normal (undescended) testes. The testes secrete testosterone, but the cells lack a receptor for it. No receptor = no response to the hormone. Complete androgen insensitivity, CAIS.
- As a result, the male ducts (vas deferens, epididymus, seminal vesicles)
  are not present. However, the testes secrete MIS, which causes the
  female ducts (uterus, fallopian tubes, upper vagina) to degenerate.
- External genitalia develop as male if DHT is present, but testosterone and DHT use the same receptor. So, female external genitalia, including the lower 2/3 of the vagina.
- At puberty, the testes again secrete testosterone. The enzyme aromatase converts it into estradiol. Thus, female secondary sexual characteristics develop. Often "voluptuously feminine". No menstruation of course: no ovaries and no uterus. Pubic and armpit hair is usually scant or absent.
  - Occasionally, the undescended testes can become cancerous, so they are often surgically removed after puberty is complete (so as to get normal female development).





Complete Androgen
Insensitivity Syndrome
2-5/100,000
tends to be sexually oriented
toward men despite XY
karyotype

**Role of Androgen Receptor** 

#### 5 alpha reductase deficiency



Guevodoces

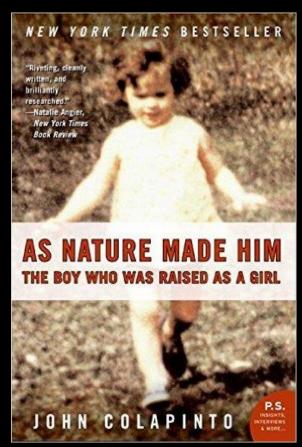
XY karyotype
Usually a baby girl with a large
clitoris

At puberty, clitoris enhances, testes descend, develops masculine features. Even when raised as girls, more than 60% become heterosexual males

This would tend to indicate that **testosteron**e more than DHT is responsible for the organizational brain

# Gender Identity is Programmed at Birth

Case of John –Johan-John (XY)



Feeling male, as he was born, transitioned back to male at age 14
Attempted marriage. Failed . Suicide at age 38

Lost penis at 8 months and raised as a girl

# Conceptualization gender identity

Gender identity (gender experience) is not a binary

ENDE

phenomenon

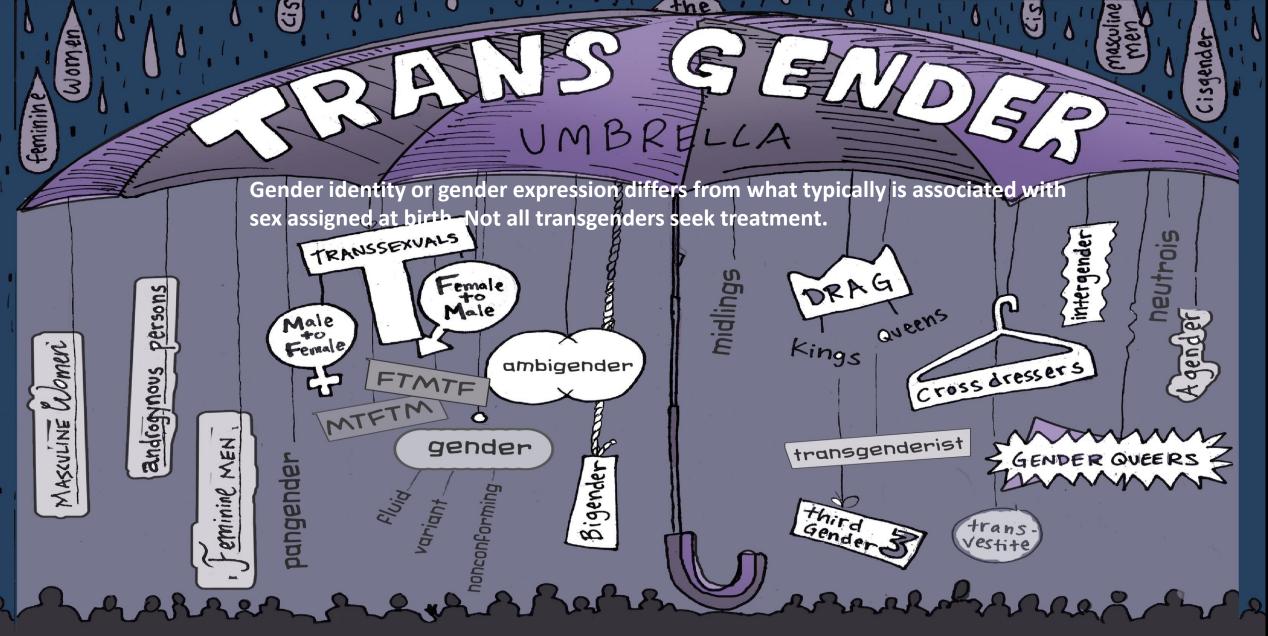
Male

- Female
- In-between

 Outside the male female continuum (gender queer, bigender, a-gender)

(Kuyper & Wijssen 2014; Van Caenegem et al. 2015)



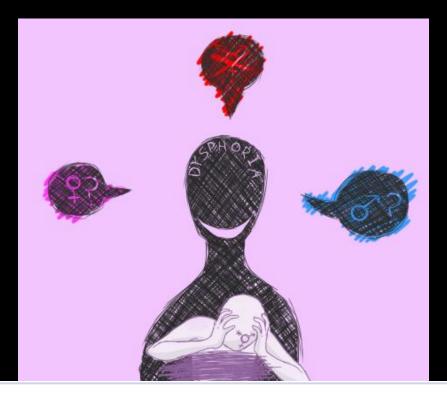


What does transgender mean? What do all these different identities have in common?

An element of crossing over or challenging binary gender roles or expectations.

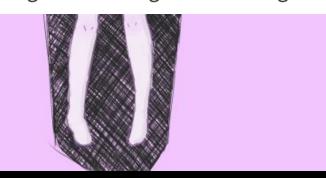
## Gender Dysphoria:\*

Distress and discontent experienced if gender identity and designated gender are not congruent



Condition is associated with clinically significant distress impairment in social, occupational, and other important areas of functioning

Gender incongruence: This is an umbrella term used when the gender identity and/or gender expression differs from what is typically associated with the designated gender. Gender incongruence is also the proposed name of the gender identity–related diagnoses in ICD-11. Not all individuals with gender incongruence have gender dysphoria or seek treatment.



Endocrine Treatment of Gender-Dysphoric/ Gender-Incongruent Persons: An Endocrine Society\* Clinical Practice Guideline

Wylie C. Hembree, <sup>1</sup> Peggy T. Cohen-Kettenis, <sup>2</sup> Louis Gooren, <sup>3</sup> Sabine E. Hannema, <sup>4</sup> Walter J. Meyer, <sup>5</sup> M. Hassan Murad, <sup>6</sup> Stephen M. Rosenthal, <sup>7</sup> Joshua D. Safer, <sup>8</sup> Vin Tangpricha, <sup>9</sup> and Guy G. T'Sjoen <sup>10</sup>

#### 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 m at least two of the following:
  - A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex character young adolescents, the anticipated secondary sex characteristics)
  - A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary 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 gen
  - A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender di one's designated gender)
- B. The condition is associated with clinically significant distress or impairment in social, occupational, or other important functioning.

Specify if:

- 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 legalization of gender change) and has undergone (or is preparing to have) at least one sex-related medical procedure or regimen—namely, regular sex hormone treatment or gender reassignment surgery confirming the desired gender (penectomy, vaginoplasty in natal males; mastectomy or phalloplasty in natal females).

Reference: American Psychiatric Association (14).

#### Table 3. ICD-10 Criteria for Transsexualism

#### Transsexualism (F64.0) has three criteria:

- The desire to live and be accepted as a member of the opposite sex, usually accompanied by the wish to make his or her body as congruent as possible with the preferred sex through surgery and hormone treatments.
- 2. The transsexual identity has been present persistently for at least 2 y.
- 3. The disorder is not a symptom of another mental disorder or a genetic, DSD, or chromosomal abnormality.

Gender identity
that is inconsistent
with the
individual's
assigned sex

A desire to transition permanently to the gender with which he/she identifies



Persistent presence of tranidentity for at least 2 years

Usually early in adolescence

Not a symptom of another mental disorder (schizophrenia)

Not associated with chromosomal / receptor defects abnormalities

Emphasis that this is not a disease

# 2. Conceptualization diagnostic category (1)

No longer 2 categories: "transsexual" or "non-transsexual" Instead: GD/gender incongruence can be:

- Extreme or mild
- Vary in associated distress
- Fluctuating or permanent
- More or less associated with anatomic dysphoria
- Accompanied by wish for complete or partial social transition



# 2. Conceptualization diagnostic category (2.1)

#### Mental disorder?

American Psychiatric Association has kept the diagnosis in Diagnostic and Statistical Manual of Mental Disorders (DSM-5)

#### → Yes

Removal may block access to reimbursed care

Transgender advocates: classifying GD/gender incongruence as a diagnosis pathologizes a normal variant of human gender identity





# 2. Conceptualization diagnostic category (2.2)

World Health Organization will likely put the diagnosis in a chapter on Sexual and Gender Health, separate from mental health in the next version International Classification of Disease (ICD-11)

#### $\rightarrow$ NO

Diagnosis is needed for reimbursed care, but not necessarily a psychiatric diagnosis

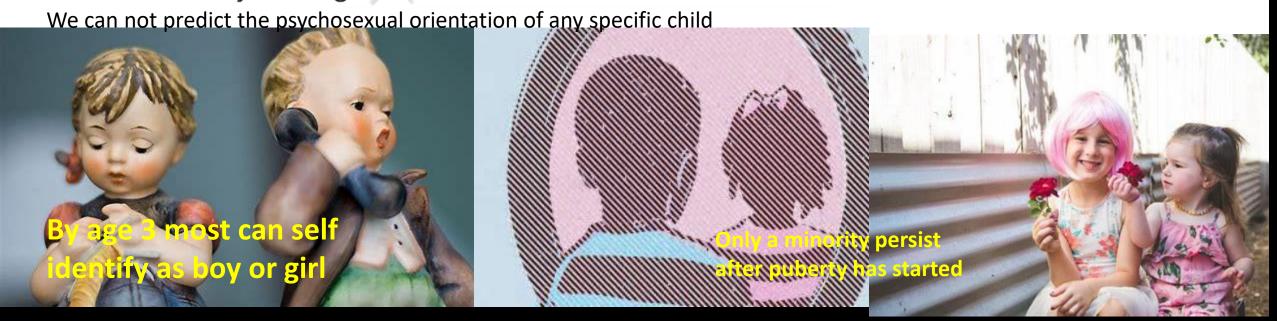


# Caring for Transgender Kids: Is Clinical Practice Outpacing the Science?

Becky McCall, BSc, MSc; Lisa Nainggolan

DISCLOSURES | August 28, 2018

In the year leading up to March 2018, the Tavistock Centre—the United Kingdom's only National Health Service (NHS)—funded clinic to treat gender dysphoria in children—received a record number of referrals: 2500, a 25% increase from the previous year and a 50-fold increase from 12 years ago.<sup>[1]</sup>





Should this transgender girl have received endocrine treatment when she first presented at age 9 years? Is treatment indicated now at the start of puberty? What is the best treatment option, and which side effects need to be discussed? What monitoring is necessary during treatment?

#### **Evaluation of a Transgender Child**

A child, assigned male at birth, first visited the gender clinic at age 9 years for gender dysphoria. She liked to wear dresses and make-up but did so only at home because of feelings of shame. She mainly played with girls and recently announced that she was a girl. Upon physical examination, she was prepubertal. She was diagnosed with gender dysphoria by the gender team psychologist and child psychiatrist. The patient started puberty at 11 years of age (Tanner stage was G2; testicular volume of 5 mL). She found the prospect of puberty distressing and wished to start suppression treatment. Although her parents were supportive, she did not yet present herself as a girl in public. The psychologist concluded that the gender dysphoria had persisted, no psychosocial problems were present that might interfere with treatment, and she was capable of giving informed consent.

1.4. We recommend against puberty blocking and gender-affirming hormone treatment in prepubertal children with GD/gender incongruence. (1 l⊕⊕○○)

#### Endocrine Treatment of Gender-Dysphoric/ Gender-Incongruent Persons: An Endocrine Society\* Clinical Practice Guideline

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A patient should have entered puberty before starting any intervention because gender dysphoria may resolve once puberty starts. This has been shown to happen in 73% to 88% of children who attend clinic.



The Tavistock and Portman NHS Foundation Trust. GIDS referrals increase in 2017/18. Source Accessed August 14, 2018.

### Case Discussion

Endocrine Treatment of Gender-Dysphoric/ Gender-Incongruent Persons: An Endocrine Society\* Clinical Practice Guideline

Wylie C. Hembree, <sup>1</sup> Peggy T. Cohen-Kettenis, <sup>2</sup> Louis Gooren, <sup>3</sup> Sabine E. Hannema, <sup>4</sup> Walter J. Meyer, <sup>5</sup> M. Hassan Murad, <sup>6</sup> Stephen M. Rosenthal, <sup>7</sup> Joshua D. Safer, <sup>8</sup> Vin Tangpricha, <sup>9</sup> and Guy G. T'Sjoen <sup>10</sup>

Gender dysphoria may manifest at an early age

It may not persist into adolescence and adulthood in the majority of cases

Gender clinic may help families understand the child's feeling and behavior

The guidelines recommend against puberty blocking agents or gender affirming hormone treatment in prepubertal children

Gender dysphoria should be re-assessed once the child enters puberty

Worsening of gender dysphoria at the onset of puberty must be present to consider puberty suppression.

Informed consent (parents/guardian) if child has no legal age for consenting treatment.







Child should have the mental capacity to give informed consent

Experienced professional should assist child and family with decisions regarding social transitioning

In case the child has not the legal age to give the informed consent-parent/guardian consent is required.

# GnRH agonist concerns:







**FERTILITY ISSUES** 



BRAIN: ??

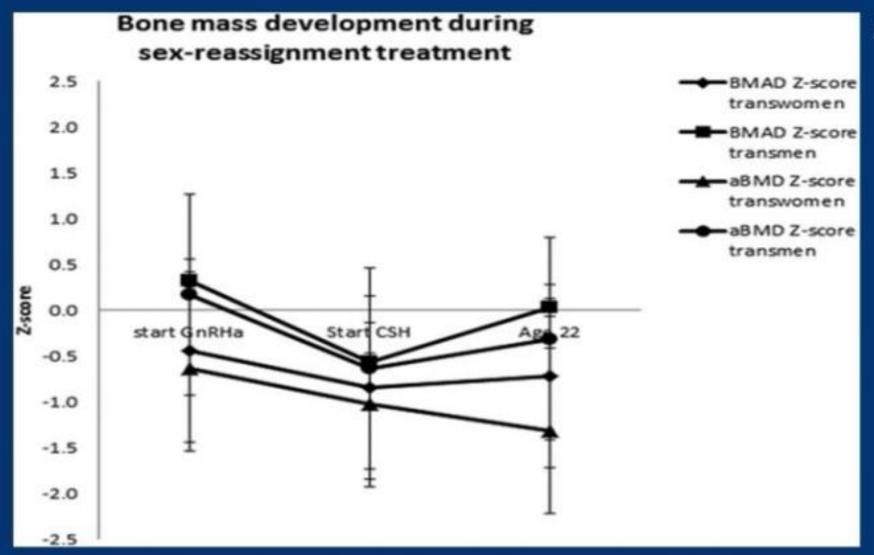


ARTERIAL
HYPERTENSION IN
GIRLS: BP MONITORING



HOT FLASHES; FATIGUE; MOOD ALTERATIONS

# Current Treatment Model: 6 Year Follow-Up Bone Mineral Density: Lumbar Spine



Klink D et al. JCEM, 2015



# Baseline and Follow-up During Suppression of Puberty

#### Table 7. Baseline and Follow-Up Protocol During Suppression of Puberty

Every 3–6 mo
Anthropometry: height, weight, sitting height, blood pressure, Tanner stages
Every 6–12 mo
Laboratory: LH, FSH, E2/T, 25OH vitamin D

Every 1–2 y

Bone density using DXA

Bone age on X-ray of the left hand (if clinically indicated)

Adapted from Hembree et al. (118).

# GnRH Agonists & Fertility in GD/Gender Incongruent Youth

- Blocking puberty at Tanner 2
  - Compromised oocyte maturation
  - Compromised spermatogenesis
- Parental dilemmas
- Preservation of fertility: desired option



# GnRH Agonists & Brain Effects in GD/Gender Incongruent Youth

#### Does GnRHa effect "Executive Functioning"?

- Working memory
- Reasoning
- Problem solving
- Planning and execution
- Pre-frontal activation
- Significant development during puberty

#### Study

- MTF (N = 18): Rx'd (8), 1.6 +/- 1 (SD) yr
- FTM (N = 22): Rx'd (12), 1.6 +/- 1 (SD) yr

#### Results

No detrimental effect on Executive functioning



### Evaluation of Gender dysphoria and Initiation of Hormone Therapy in a Transgender Adolescent

An adolescent assigned female at birth, preferred stereotypical societal masculine behaviors as a child and realized he was a transgender boy at age 14.

After evaluation by qualified mental health professional persistent gender dysphoria was diagnosed

He started with GnRH analogue to suppress puberty at age 15.

At this time breast development was at Tanner 3 and menarche had not yet occurred. Endocrine evaluation was unremarkable prior to GnRH

GnRH well tolerated improved mood; regular evaluations by gender team and pediatric endocrinologist were performed

At age 16 dysphoria persisted and wished to start testosterone treatment. Wanted a more masculine voice

Family was supportive

Which issues need to be addressed before testosterone treatment is started?

What investigations are needed?

What medication and dose?



# Discussion female to male adolescent



Before initiating testosterone therapy a mental health professional should confirm that the gender dysphoria is



No psychological or social problems are present that could



And that adolescent is mentally capable of giving informed



Inform the reversible and irreversible effect of T treatment (



Ovarian function and fertility issues



Contraception: T is not an effective form of contraception!!!!



Sexually transmitted diseases!!!!

# Discussion continued (T Treatment in F-M)

- Assess contraindications for T treatment
- Monitor Hct; lipids; bone age; bone mineral density
- If endogenous puberty has not been completed: start with low dose 25 mg/m2 q 2 weeks, and increase gradually to the adult dose over 2 years.
- In those that have undergone puberty and reached adult height, T can be started at higher dose 75 mg q 2 weeks and increased more rapidly
- Breast surgery: timing depends on the physical and health status of individual.



## Table 9. Baseline and Follow-up Protocol During Induction of Puberty

Every 3–6 mo

Anthropometry: height, weight, sitting height, blood pressure, Tanner stages

Every 6–12 mo

- •In transgender males: hemoglobin/hematocrit, lipids, testosterone, 25OH vitamin D
- •In transgender females: prolactin, estradiol, 250H vitamin D

Every 1–2 y

- BMD using DXA
- •Bone age on X-ray of the left hand (if clinically indicated)

BMD should be monitored into adulthood (until the age of 25–30 y or until peak bone mass has been reached). For recommendations on monitoring once pubertal induction has been completed, see Tables 14 and 15.

Adapted from Hembree et al. (118).

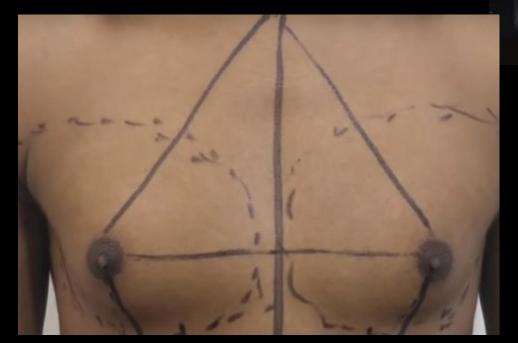
# 21 y/o college graduate assigned male gender at birth

- Presents to your office with desire to transition to female gender
- Asking about removal of male genitalia and vagina formation
- Concerned about prominent "Adams apple"
- She was wearing gender neutral clothing
- Works at pharmaceutical company in a large metropolitan territory
- Presents as male at work but as female when at home and nights out.
- Supportive family and friends
- Started estrogen therapy (2months) and went to surgeon
- Surgeon consults endocrinology service









These surgeries do not affect sexual functioning or fertility; so have less stringent criteria for approval

## Gender Affirming Surgery?

- We need a well supported diagnosis and prior hormone treatment before gender affirming surgery
- Gender affirming surgery is often needed for the patient to relieve gender dysphoria
- Removal of gonads and penis is the most regulated of transfeminine genital surgeries
- Expert surgeon can achieve genitalia almost identical to those of affirmed gender but:
- Guidelines recommend that prior to genital surgery, complete one year of gender affirming hormones and live full time in the new gender role prior to receiving gender affirming genital surgery.

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Need to understand expected results!!

#### Possible complications

Cost, length of hospitalization

Surgical rehabilitation

Neovaginal dilatations

Time consuming and uncomfortable

## Penis into a vagina



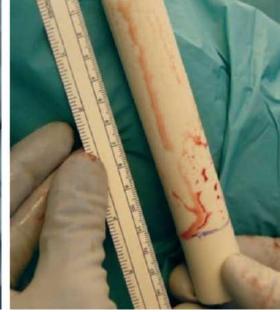
Preserve neurovascular bundle Retain newly formed clitoris Plastic Reconstructive Surgery-Global Open (PRS Global Open)

#### Solely Penile Skin for Neovaginal Construction in Sex Reassignment Surgery

Hannes Sigurjonsson, MD; Johan Rinder, MD, PhD; Ebba K. Lindqvist, MD; Filip Farnebo, MD, PhDl T. Kalle Lundgren, MD, PhD

DISCLOSURES | Plast Reconstr Surg Glob Open. 2016;4(6):e767







## Fertility Desires and Reproductive Needs of Transgender People

Clinical Endocrinology, 2019-06-29

Transgender people assume parental roles in the manner of their selfidentified gender identities; nevertheless, concerns regarding incongruence between the nature of conserved gametes and the gender identity may be raised.<sup>[93]</sup> According to a recent public opinion webbased study<sup>[94]</sup> including a representative sample of 1111 US residents (age range 18-75 years), the majority (76%) of the respondents considered that healthcare providers should help transgender persons to have their biological children, more than 60% of the participants agreed that gamete preservation should be offered to transgender people before hormonal treatment, and 60% declared that healthcare practitioners should help transgender men carry pregnancies.

#### Table 1. Fertility preservation options for transgender people

Age group	Transgender men (assigned female at birth)	Transgender women (assigned male at birth)
Pre- pubertal	Ovarian tissue cryopreservation <sup>†</sup>	Testicular tissue cryopreservation†
Post- pubertal	Oocyte cryopreservation	Sperm cryopreservation
	Embryo cryopreservation (with partner's or donor's sperm)	Embryo cryopreservation (with partner's or donor's egg)
	Uterus preservation	Uterus transplantation <sup>‡</sup>

<sup>†,</sup> experimental; ‡, theoretical.

Translational Andrology and Urology

#### Fertility Concerns of the Transgender Patient

# TRANSGENDER RIGHTS TOOLKIT: A LEGAL GUIDE FOR TRANS PEOPLE AND THEIR ADVOCATES

According to international guidelines, [22,23] fertility preservation should thus be discussed with transgender youth before pubertal suppression, keeping in mind that techniques for the in vitro maturation of immature germ cells are still mostly experimental.<sup>[57]</sup> For more information, the reader is redirected to one of the recent reviews on this topic. [25,58]

Transgender female: estrogen

Very high risk of adverse outcomes:

Thromboembolic disease

Moderate risk of adverse outcomes:

- Macroprolactinoma
- Breast cancer
- Coronary artery disease
- Cerebrovascular disease
- Cholelithiasis
- Hypertriglyceridemia

Transgender male: testosterone

Very high risk of adverse outcomes:

• Erythrocytosis (hematocrit > 50%)

Moderate risk of adverse outcomes:

- Severe liver dysfunction (transaminases > threefold upper limit of normal)
- Coronary artery disease
- Cerebrovascular disease

Downgraded in new 2017 guidelines

downgraded

## Downgrading Of Prolactin Measurements

- From "recommend" to "suggest"
- Data from European cohorts suggest that cyproterone may be the anti-androgen causing prolactin elevations; whereas in the U.S.A, very few prolactinomas have been reported using GnrH agonists or spironolactone



## Removed Recommendation To Serially Measure Liver Function Tests

 Routine measurement of LFTs have been removed from both transmasculine and transfeminine recommendations due to no evidence suggesting that hormone therapy results in adverse liver function



#### Table 15. Monitoring of Transgender Persons on Gender-Affirming Hormone Therapy: Transgender Female

- 1. Evaluate patient every 3 mo in the first year and then one to two times per year to monitor for appropriate signs of feminization and for development of adverse reactions.
- 2. Measure serum testosterone and estradiol every 3 mo.
- a. Serum testosterone levels should be <50 ng/dL.
- b. Serum estradiol should not exceed the peak physiologic range: 100–200 pg/mL.
- 3. For individuals on spironolactone, serum electrolytes, particularly potassium, should be monitored every 3 mo in the first year and annually thereafter.
- 4. Routine cancer screening is recommended, as in nontransgender individuals (all tissues present).
- 5. Consider BMD testing at baseline (160). In individuals at low risk, screening for osteoporosis should be conducted at age 60 years or in those who are not compliant with hormone therapy.

This table presents strong recommendations and does not include lower level recommendations.

## Key Issue: maintain estrogen levels within physiologic range

DVT; liver dysfunction; hypertension Avoid ethinyl estradiol or conjugated estrogens

#### Table 14. Monitoring of Transgender Persons on Gender-Affirming Hormone Therapy: Transgender Male

- 1. Evaluate patient every 3 mo in the first year and then one to two times per year to monitor for appropriate signs of virilization and for development of adverse reactions.
- 2. Measure serum testosterone every 3 mo until levels are in the normal physiologic male range:<sup>a</sup>
- a. For testosterone enanthate/cypionate injections, the testosterone level should be measured midway between injections. The target level is 400–700 ng/dL to 400 ng/dL. Alternatively, measure peak and trough levels to ensure levels remain in the normal male range.
- b. For parenteral testosterone undecanoate, testosterone should be measured just before the following injection. If the level is <400 ng/dL, adjust dosing interval.
- c. For transdermal testosterone, the testosterone level can be measured no sooner than after 1 wk of daily application (at least 2 h after application).
- 3. Measure hematocrit or hemoglobin at baseline and every 3 mo for the first year and then one to two times a year. Monitor weight, blood pressure, and lipids at regular intervals.
- 4. Screening for osteoporosis should be conducted in those who stop testosterone treatment, are not compliant with hormone therapy, or who develop risks for bone loss.
- 5. If cervical tissue is present, monitoring as recommended by the American College of Obstetricians and Gynecologists.
- 6. Ovariectomy can be considered after completion of hormone transition.
- 7. Conduct sub- and periareolar annual breast examinations if mastectomy performed. If mastectomy is not performed, then consider mammograms as recommended by the American Cancer Society.

#### Key Issue: maintain T levels at physiologic range

Excess T: erythrocytosis; sleep apnea; hypertension; weight increase; salt retention; lipid changes; cystic acne

<sup>&</sup>lt;sup>a</sup>Adapted from Lapauw et al. (154) and Ott et al. (159).

- Venous thromboembolism
  - In the Dutch cohorts, rates of 2.6% annually in first year, falling to 0.4% thereafter, with 1-2% risk of death from PE
    - BUT all but 1 of these patients was using oral ethinyl estradiol
    - Similar to CVD rates seen on controlled natal females using OCPs with high dose (50mcg) ethinyl estradiol
  - Belgian cohorts also showed increased incidence of VT (6-8%), but ONLY in patients treated with ethinyl estradiol

# Estrogen and testicular cancer (m-to-f)

Journal of Medical Case Reports

## Exogenous Estrogen Therapy, Testicular Cancer, and the Male to Female Transgender Population

A Case Report

Gursimran Chandhoke; Bobby Shayegan; Sebastien J. Hotte DISCLOSURES | J Med Case Reports. 2019;12(373)

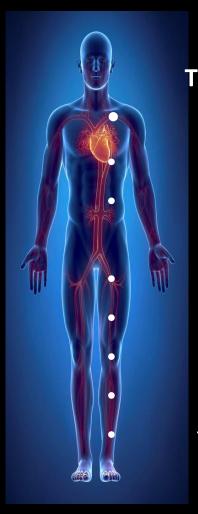
#### **Estrogens and TC**

Over the course of the last few decades, the overall incidence of TC has increased and has doubled over the last 40 years in many regions in the world.<sup>[5]</sup> One theory that looks to explain this phenomenon is TDS, which suggests that the increased incidence of impaired spermatogenesis, reproductive tract abnormalities (for example, cryptorchidism), and TC, all share a common etiology related to errors in gonocyte development.<sup>[6]</sup> The earliest signs of TC can be found during embryogenesis, in which excessive levels of estrogen during early pregnancy can lead to a disturbance in the development of primordial germ cells destined to form spermatogonia. This results in premalignant cells which may become carcinoma in situ after birth. These cells remain dormant until there is a change in their local microenvironment, attributable to changes in (1) androgen levels, (2) excessive estrogens, or (3) exogenous hormonal imbalance.<sup>[7]</sup> These can be manifested as the hormonal changes of puberty, through exogenous hormonal administration, and from exposure to occupational and environmental estrogenic chemicals.

## Cardiovascular risk of gender affirming hormonal therapy

**Trans-males** Lower HDL; higher TG and LDL Long term studies: no evidence of increased cardiovascular mortality **Data insufficient** 

Manage cardiovascular risk factors as in general population



#### **Trans-female**

Favorable in lipids increase in weight & BP; increased insulin resistance

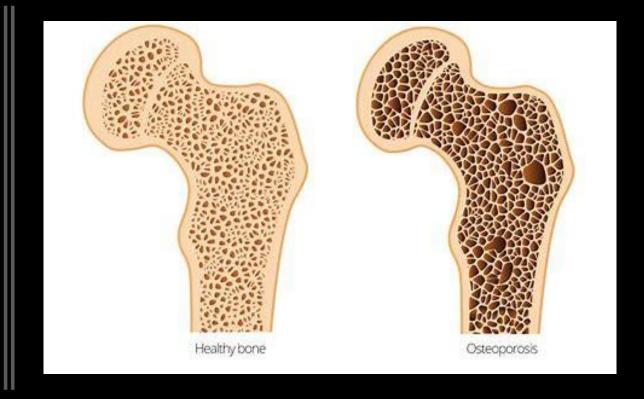
Long term studies: no increased cardiovascular mortality (avoid use of ethinyl estradiol) follow guidelines cisgender population

## Bone Density

#### Monitor LH levels in transgender males

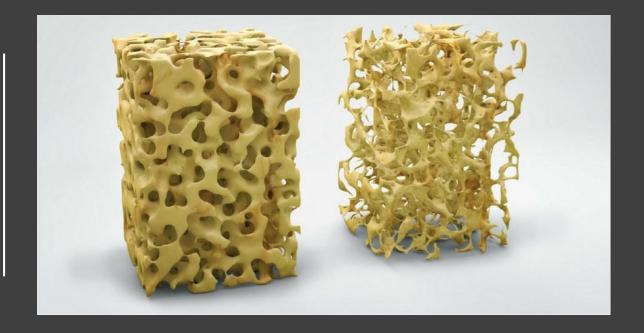
#### Transgender males

Baseline bone mineral measurements in transgender males are generally in the expected range for their pretreatment gender (188). However, adequate dosing of testosterone is important to maintain bone mass in transgender males (189, 190). In one study (190), serum LH levels were inversely related to BMD, suggesting that low levels of sex hormones were associated with bone loss. Thus, LH levels in the normal range may serve as an indicator of the adequacy of sex steroid administration to preserve bone mass. The protective effect of testosterone may be mediated by peripheral conversion to estradiol, both systemically and locally in the bone.



#### Transgender females

A baseline study of BMD reported T scores less than -2.5 in 16% of transgender females (191). In aging males, studies suggest that serum estradiol more positively correlates with BMD than does testosterone (192, 193) and is more important for peak bone mass (194). Estrogen preserves BMD in transgender females who continue on estrogen and antiandrogen therapies (188, 190, 191, 195, 196).



## Bone density trans-females

Do BMD at baseline; then at age 60 if low risk; more frequent in non-compliant patients

\*Transman (Female to Male): assigned female sex (XX)at birth who identifies as male

Ivonne: 2007 best female vaulter in Germany

Balian after gender reassignment surgery 2008



<sup>\*</sup>American Society for Clinical Pathology 2016 Medscape



## Transsexual, 44, elects to die by euthanasia after botched sex-change operation turned him into a 'monster'

- Nathan Verhelst, 44, born Nancy, was disappointed with sex-change results
- · His life was ended by the same doctor who euthanised deaf twins last year
- · Comes after Belgian euthanasia cases jumped 25 per cent in one year
- It is now the cause of nearly one in 50 deaths in the country



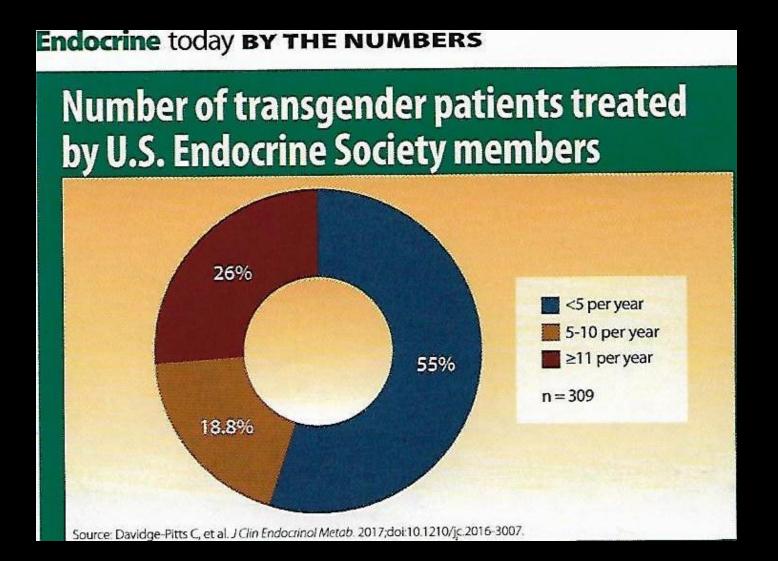
# Morbidity and Mortality in the Transgender Community

- Significant increase in mortality is seen amongst transgender individuals compared to the general population
- Most of the increase in mortality was due to higher rates of AIDS, suicide, drug-related deaths
- Asschermann's 2011 review of Dutch patient cohort:
   50% higher mortality rate in MTF patients

# Many Healthcare Providers Fail Transgender People (National Center for Transgender Equality)

- US survey on transgender people 2015( NCTE)
- Anonymous on- line survey 27,000 adults
- 1:5 reported that their healthcare professional tried to stop them from being transgender
- Those who had negative experiences more likely to suffer distress; attempt suicide; run away from home; homelessness; and engage in sex work than their counterparts that did not have negative experiences.
- Need to improve how medical professionals respond to transgender patients.

## Training Needed in Transgender Care



Survey conducted by Davidge-Pitts
Assess transgender status of healthcare in
U.S. Endocrinology Training Programs
Only 22 programs provided comprehensive
transgender –oriented sexual and social
history taking
14 provided education on systemic physical

13 provided education on psychosocial and legal issues

Lack of interest Lack of training Lack of funding

examination

Need for providers to become competent in the area of transgender medicine.



# PROJECT TO A TRANS-CENTRIC ACHIEVABLE PRIMARY CARE MODEL IN THE CAPIRREAN

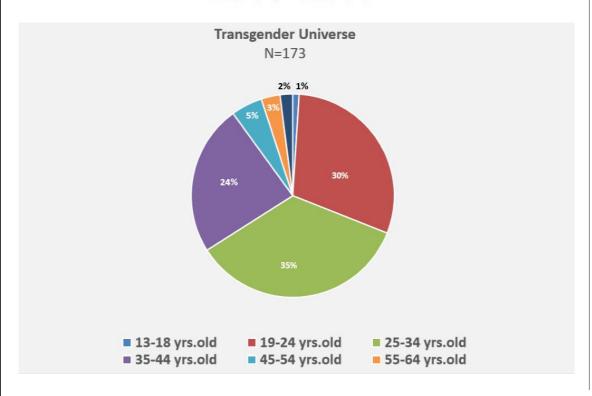
This project, named **Translucent**, combined culturally-competent, well-trained health care professionals sensitive to concerns that affect the Transgender population.

As a pilot project, Translucent started with twenty (20) Trans females and was successfully accepted by the Trans community.

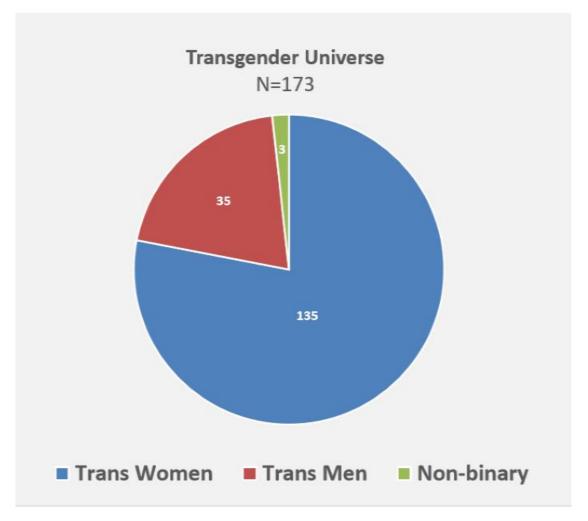
#### References

Vazquez-Rivera, M. & Ortiz-Calderón, J.C. (2017). Espacios seguros: Modalidades grupales para personas de experiencia trans (Safe spaces: Group modalities for persons of trans experiences). Boletín Diversidad, 8(1). Retrieved from http://www.boletindiversidad.org

## Translucent Clinic 2016-2019



#### 2016-2019



#### **THANKS!** Macevedo@centroararat.org (787) 496-0818



Representa la inclusión, solidaridad y el respeto a la diferencia. Los colores simbolizan pasión, vitalidad, amor y fuerza.



#### Consejo Asesor del Gobernador en Asuntos LGBTT is at Colegio de Medicos Cirujanos de Puerto Rico.

39 mins · San Juan, Puerto Rico · 🚱

Ayer presentamos oficialmente la Carta Normativa de ASES 19-305 a todas los planes médicos y aseguradoras de P.R. sobre cero discrimen por orientación sexual, identidad y expresión de género. Puerto Rico se mueve a paso firme a la plena igualdad en la salud. E ¡Enhorabuena!



#### **Conclusions:**

- 1. Endocrinologists play an important role in Gender Affirmation
- 2. Treatment helps develop physical characteristics of the Affirmed Gender
- 3. Endocrine regimens should:
  - a. Suppress endogenous sex hormone levels, and
  - b. Maintain normal sex hormone levels of person's affirmed gender

### Conclusions

- No hormone treatment for pre-pubertal persons with GD/Gender Incongruence
- Adolescent treatment should include knowledgeable Mental Health Practitioners and fertility discussion
- Suppress puberty at Tanner Stage G2/B2 adolescents (informed consent)
- Gender affirming hormone at age 16 or earlier if compelling reasons





## Conclusions

- Treat adults to attain physiologic levels of gender-appropriate steroids
- Removal of natal gonads may be required to avoid high dose steroids
- Hormone treatment must be monitored for adverse effects and during hormone surgery



#### "Primum Non Nocere"

- Our mission as physicians is to help others
- Even one word could have negative impact in the individual that is seeking help
- Be non-judgemental
- Improve curriculum of training programs to at least sensitize the health care professionals to improve understanding of the transgender patient and optimize the resources available to help them
- If we do not lead, these individuals will fall into unconscionable individuals with no heart, who are cold blooded, and delinquents







" mejor prender un fosforito que maldecir la oscuridad"

