Gender-Affirming Endocrine Care of Transgender People

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Transgender Infopunt

Melanie Verbeke Judith Van Schuylenbergh Joz Motmans

Gender affirming endocrine care

GENDER NON BINARY

Female to male =

TRANS MAN

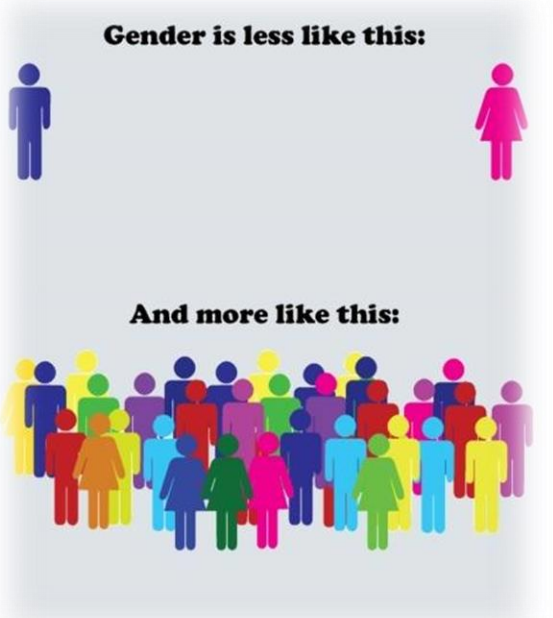
TRANSGENDER MAN

Male to female =

TRANS WOMAN

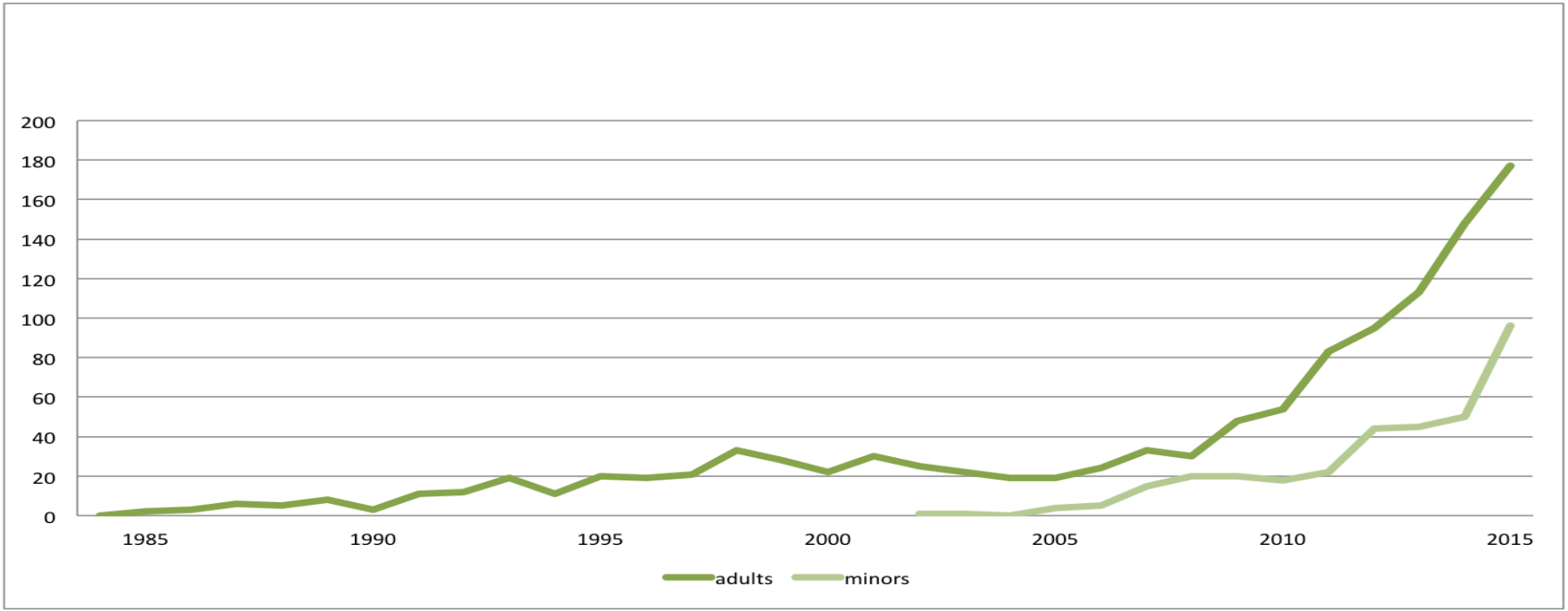
TRANSGENDER WOMAN

The challenge



Transgender research in the 21th century: a selective critical review from a neurocognitive perspective. Mueller S, De Cuypere G, T'Sjoen G. *Am. J. Psychiatry* 2017, 1; 174(12):1155-1162

New per year (Belgium)



Prevalence

0.5 – 1.3% for birth-assigned males

0.4- 1.2% for birth-assigned females

Table.
Population studies yielding prevalence data for transgender people

	Sample	Measure	Prevalence of transgender people by birth-assigned sex		
			Male	Female	All
Conron et al (2012), USA14	28176 adults	Identification as transgender	0·5%*	0·4%*	0·5%
Glen and Hurrell (2012), UK15	9950 adults	Identification as other gender or in another way	0·6%†	0·4%†	0·5%†
Clark et al (2014), New Zealand16	7729 high-school students	Identification as transgender	1·3%‡	1·2%‡	1·2%
Kuyper and Wijsen (2014), Netherlands17	8064 adults	Identification on gender spectrum	1·1%	0·8%	0·9%¶
Van Caenegem et al (2015), Belgium18	1832 adults	Identification on gender spectrum	0·7%	0·6%	0·6%

* Extrapolated from table 1 in article.

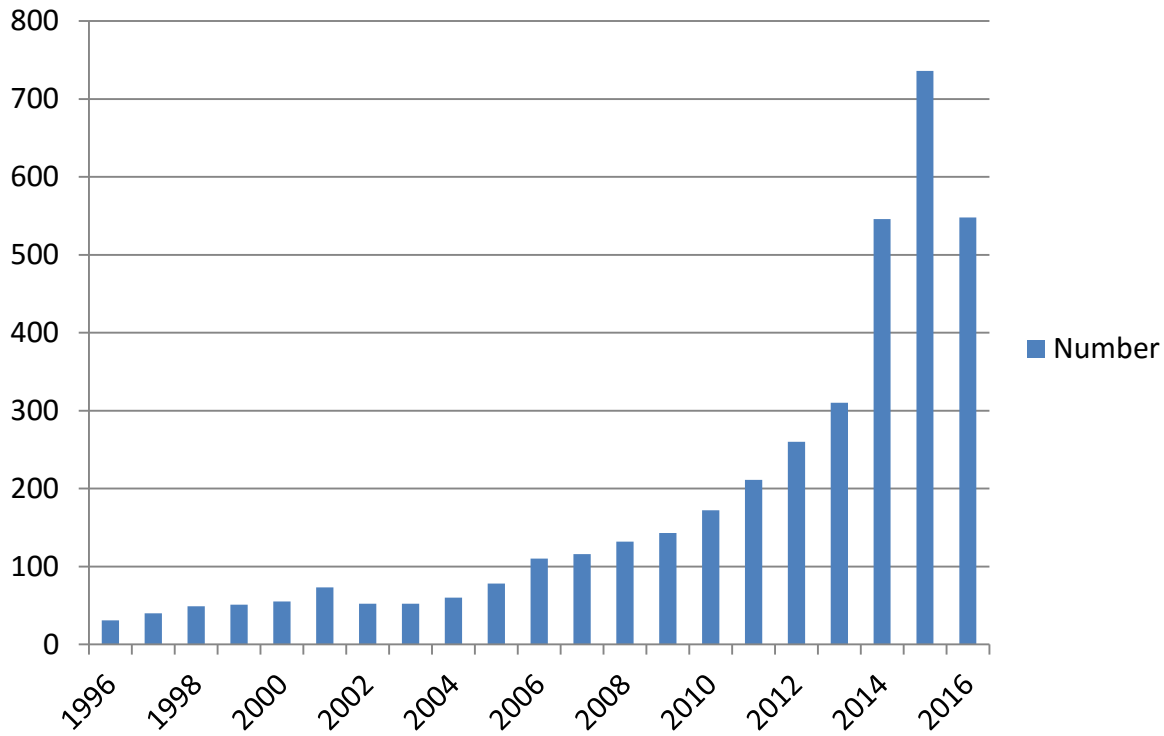
† Extrapolated from annex B in paper.

‡ Extrapolated from table 1 in paper.

¶ Extrapolated from table 3 in article.

Transgender people: health at the margins of society. Sam Winter, Milton Diamond, Jamison Green, Dan Karasic, Terry Reed, Stephen Whittle, Kevan Wylie. *Lancet* 2016; 388: 390–400

Scientific output in 1996 - 2016



PubMed

SEARCH: gender dysphoria OR gender incongruence OR transgender OR transsexual OR gender identity disorder

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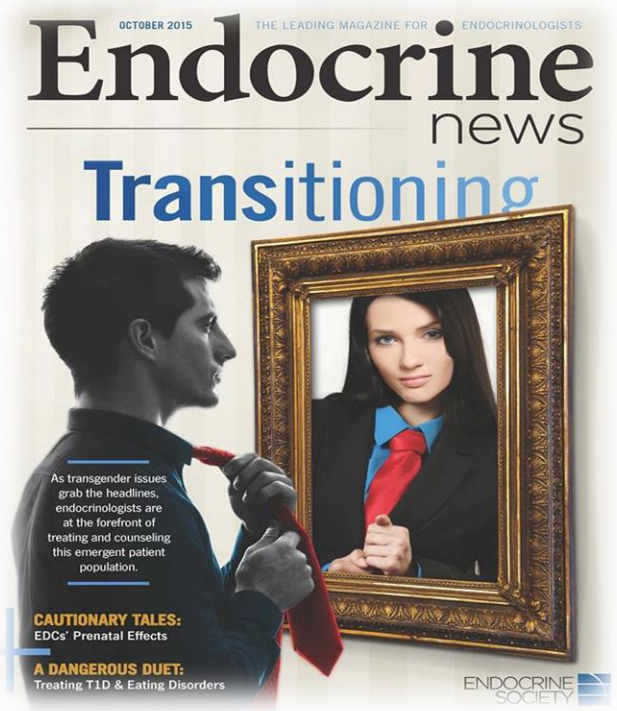

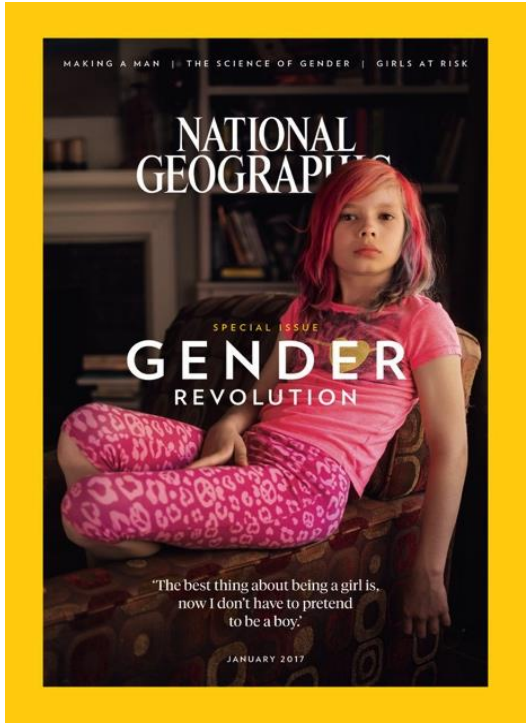

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US & Canada

Transgender toilet use: US schools 'must respect gender identity'

13 May 2016 | US & Canada

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The White House says gender identity is a civil rights issue

The Obama administration has told schools to let transgender pupils use toilets matching their gender identity.

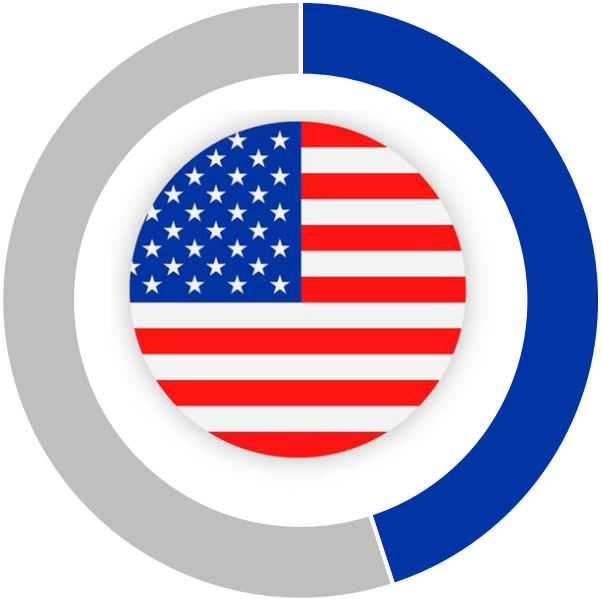
Attorney General Loretta Lynch said schools that don't comply may face lawsuits or lose federal aid if

US transgender debate

Why toilets matter to trans rights

Suicide attempt rates life-time

38,7%



45,0%

Hormones and Mental Health

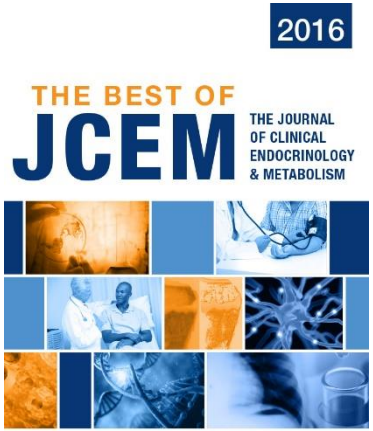
Table 2 Mean SCL-90-scores of "treated population" vs. "general population"

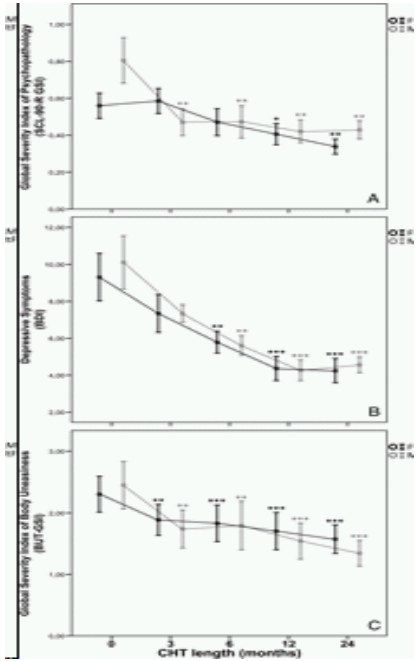
		Study group					
SCL-90 subscale	General population (SD)	Baseline (SD) n = 56	*P*	After hormone therapy (SD) n = 47	*P*	After SRS (SD) n = 42	*P*
ANG [10–50]	12.8 (4.4)	17.0 (6.4)	<0.001	12.4 (5.1)	0.220	13.5 (4.2)	0.286
AGO [7–35]	7.9 (2.3)	9.5 (4.2)		8.1 (1.8)	0.402	8.2 (2.0)	0.264
DEP [16–80]	21.6 (7.6)	34.7 (14.3)	<0.001	23.8 (9.0)	0.090	24.4 (9.2)	0.086
SOM [12–60]	16.7 (5.3)	18.6 (6.7)		15.2 (2.7)	<0.001	17.1 (6.2)	0.453
IN [9–45]	12.6 (4.3)	16.6 (7.0)	<0.001	12.8 (4.4)	0.359	15.1 (6.7)	0.051
SEN [18–90]	24.1 (7.6)	31.8 (11.7)	<0.001	24.6 (7.9)	0.277	25.8 (7.1)	0.097
HOS [6–30]	7.2 (2.1)	8.2 (3.0)	<0.001	7.4 (2.0)	0.181	7.2 (1.8)	0.237
SLA [3–15]	4.5 (2.2)	5.8 (3.2)	<0.001	4.4 (1.7)	0.192	5.2 (3.4)	0.*033*
NEUR [90–450]	**118.3 (32.4)**	**157.7 (49.8)**	**<0.001**	**119.7 (32.1)**	**0.359**	**127.9 (37.2)**	**0.082**

P values show differences between "treated population" and "general population."
AGO = agoraphobia; ANG = anxiety; DEP = depression; HOS = hostility; IN = paranoid ideation/psychoticism; NEUR = overall psychoneurotic distress; SCL-90 = Symptom Checklist-90; SD = standard deviation; SEN = interpersonal sensitivity; SLA = sleeping problems; SOM = somatization

Effects of different steps in gender reassignment therapy on psychopathology: a prospective study of persons with a gender identity disorder. Heylens, Verroken, De Cock, T'Sjoen, De Cuypere. *Journal of Sexual Medicine* 2014,11:119-126

Hormones and Mental health





Psychopathology

Depressive Symptoms

Body Uneasiness

Cross-sex hormone treatment and psychobiological changes in transsexual persons: two-year follow-up data. Fisher, Castellini, Ristori, Casale, Cassioli, et al. *Journal of Clinical Endocrinology and Metabolism* 2016, 101(11):4260-4269

Conclusion 1

- The need for transgender health care is much higher than expected.

Conclusion 1

- The need for transgender health care is much higher than expected.
- Endocrinologists definitely have a role to play.

Gender affirming therapy

Standards of Care for the Health of Transsexual, Transgender, and Gender-Nonconforming People, Version 7. Coleman E, Bockting W, Botzer M, Cohen-Kettenis P, De Cuypere G, Feldman J, et al. *Int J Transgenderism* [Internet]. 2011;13(4):165–232.

Gender affirming therapy

Self- diagnosis

* Informed consent, decisions about gamete storage

Standards of Care for the Health of Transsexual, Transgender, and Gender-Nonconforming People, Version 7. Coleman E, Bockting W, Botzer M, Cohen-Kettenis P, De Cuypere G, Feldman J, et al. *Int J Transgenderism* [Internet]. 2011;13(4):165–232.

Endocrine treatment in adults

Trans men

Suppression of menses

GnRH analogues

IM Medroxyprogesteroneacetate 150mg/3months

or

Lynestrenol 5mg daily

Testosterone (T)

Intramuscular

T undecanoate IM 1000mg/12w

T esters IM 250mg/2w

Transdermal: gel daily

Gender non binary?

Trans women

Anti-androgens

GnRH analogues

Cyproterone acetate 25-50mg OD

Spironolactone 200-400mg

Estrogens

Oral estradiol

Estradiol valerate 4mg daily

Transdermal estradiol

Gel 3mg daily

Patch 100µg/72h

Treatment in adolescents

Self- diagnosis

Diagnostic phase*

Hormonal phase

B2-3/ G3-4

GnRH analogue

Surgery

16 yrs

GnRH analogue + gender affirming hormones

Hormones continued

18 yrs

Surgery + gender affirming hormones

Female puberty with 17-beta-oestradiol, increasing the dose every 6 months 5 – 10 – 15 - 20 ùg/kg/day

Male puberty with testosterone esters, increasing the dose every 6 months 25 – 50 – 75 - 100 mg/m^2/2 weeks IM

Early medical intervention in adolescents with gender dysphoria. Delemarre-van de Waal, H. In *Gender Dysphoria and Disorders of Sex Development. Progress in Care and Knowledge*. 2013 Springer 193-204

Anti-androgen and estrogen treatment in trans women

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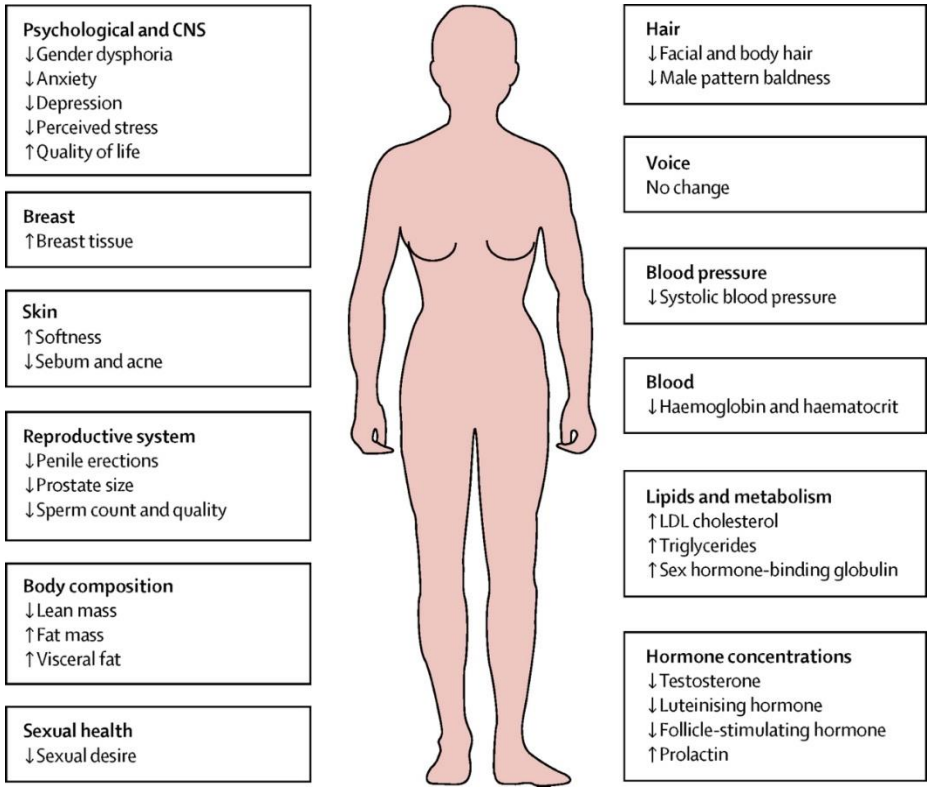

Oestrogen and anti-androgen therapy for transgender women. Tangpricha V, Den Heijer M. *The Lancet Diabetes and Endocrinology.* 2016

Anti-androgen and estrogen treatment in trans women

Effects

Breast growth (T2-3)

🡻Body hair

Softening of the skin

Reduction of muscle mass

🡻Testicular size

Changes in emotional function

Redistribution of fat

(Little effect on facial hair)

Oestrogen and anti-androgen therapy for transgender women. Tangpricha V, Den Heijer M. *The Lancet Diabetes and Endocrinology.* 2016

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Reduction of muscle mass

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Changes in emotional function

Redistribution of fat

(Little effect on facial hair)

Side effects

↑Risk for thromboembolism

↑Risk of depression

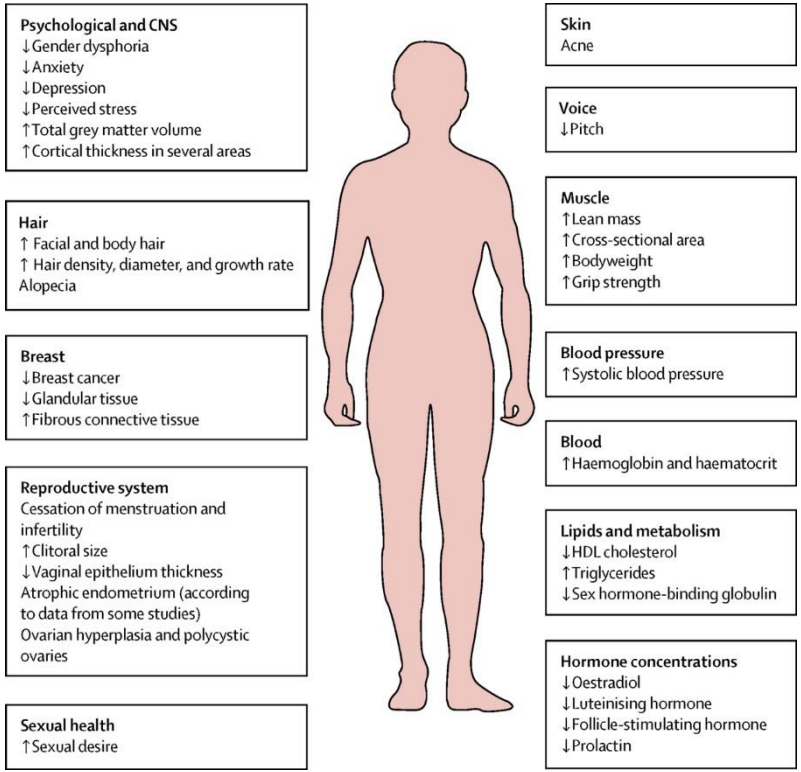
↑Risk of osteoporosis

Changes in sexual desire

↓Fertility

Oestrogen and anti-androgen therapy for transgender women. Tangpricha V, Den Heijer M. *The Lancet Diabetes and Endocrinology.* 2016

Testosteron treatment in trans men



Testosterone therapy for transgender men. Irwig MS. *The Lancet Diabetes and Endocrinology.* 2016

Testosteron treatment in trans men

Effects

Deepening of voice

Facial and body hair

Clitoral growth

Cessation of menses

↑Muscle mass and strength

↓Fat mass

↑Sexual desire

Testosterone therapy for transgender men. Irwig MS. *The Lancet Diabetes and Endocrinology.* 2016

Testosteron treatment in trans men

Effects

Deepening of voice

Facial and body hair

Clitoral growth

Cessation of menses

↑Muscle mass and strength

↓Fat mass

↑Sexual desire

Side effects

Acne

Frontal and temporal hairline recession

↓Fertility

Testosterone therapy for transgender men. Irwig MS. *The Lancet Diabetes and Endocrinology.* 2016

WITHOUT DATA

you're just another person with an opinion

W. Edwards Deming

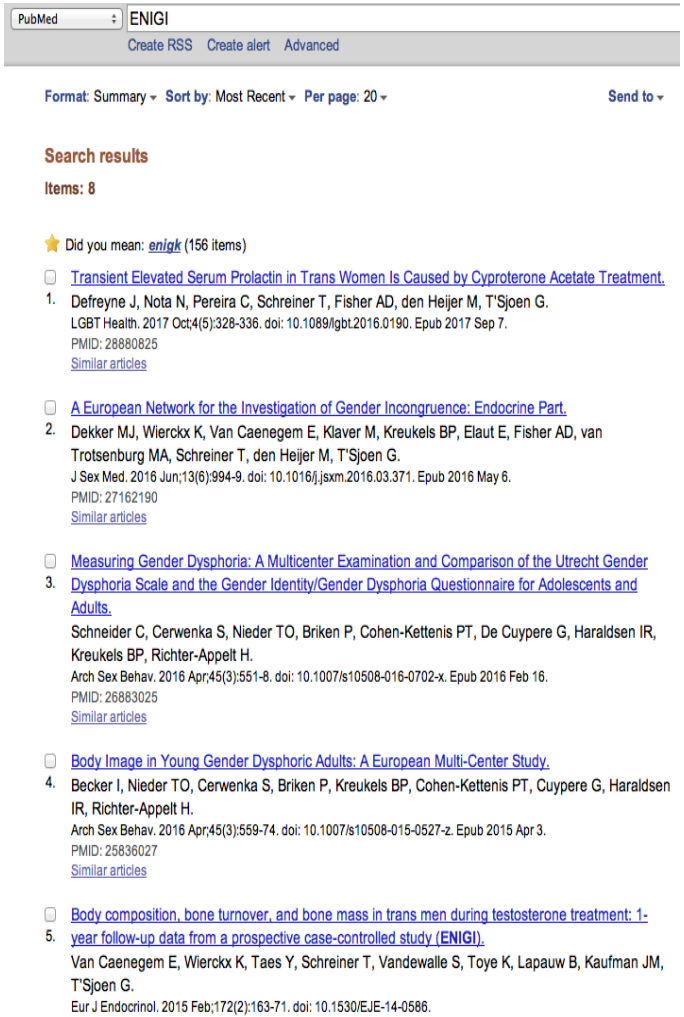
ENIGI

European Network for the Investigation of Gender Incongruence

Amsterdam Florence Ghent Hamburg* Oslo

* only mental health

Search: ENIGI



MORE COMING SOON!

stay tuned...

ENIGI: effects of hormone treatment (1)

Trans men (T)

Effective

No major adverse events

Less favourable lipid profile

↑total body weight (+3%)

Frequent symptoms:

- Voice instability
- High sexual desire
- Decrease in emotionality
- Clitoral pain

Trans women (CPA + E2)

Effective

No major adverse events

Favourable lipid profile

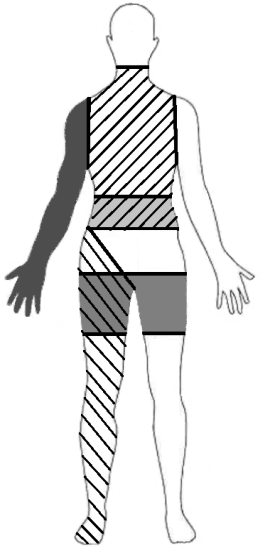
↑total body weight (+ 3%)

Frequent symptoms:

- Breast tenderness
- Low sexual desire
- Increase in emotionality
- Hot flashes

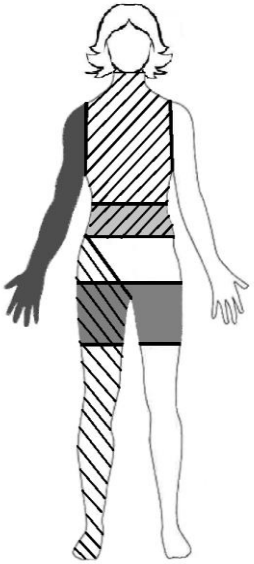
A European Network for the Investigation of Gender Incongruence: Endocrine Part. Dekker, Wierckx, Van Caenegem, Klaver, Kreukels, Elaut, Fisher, van Trotsenburg, Schreiner, T'Sjoen *Journal of Sexual Medicine* 2016 13:994-999

Trans men



	Body fat	Lean body mass
Arm region	-10% (-13%;-8%)	+19% (18%;21%)
Trunk region	-3% (-6%;0%)	+9% (8%;10%)
Android region	+1% (-3%;5%)	+10% (8%:12%)
Gynoid region	-14% (-16%;-12%)	+11% (10%;13%)
Leg region	-16% (-19%;-14%)	+12% (10%;13%)

Trans women



	Body fat	Lean body mass
Arm region	+33% (29%;37%)	-6% (-7%;-5%)
Trunk region	+21% (16%;25%)	-2% (-2%;-1%)
Android region	+18% (13%;23%)	0% (-1%;2%)
Gynoid region	+34% (29%;38%)	-3% (-4%;-2%)
Leg region	+42% (37%;46%)	-3% (-4%;-3%)

Feminization and masculinization of regional body parts and effects on body shape during the first year of cross-sex hormonal therapy: results from a multi-center prospective study. Klaver M, de Blok C, Wiepjes C, Nota N, Dekker M, de Mutsert R, Schreiner T, Fisher A, T'Sjoen G, den Heijer M. *European Journal of Endocrinology* 2017

ENIGI: effects of hormone treatment (2)

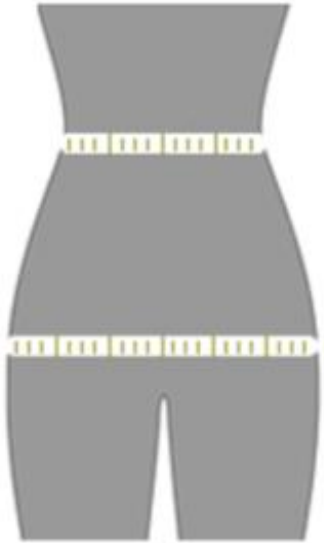
Transwomen

Mean change (95% confidence interval)

Waist: -0.6 cm (-1.7;0.4)
-0.7 cm (-1.7;0.3) *

Hip: +3.2 cm (2.3;4.0)
+3.2 cm (2.3;4.0) *

WHR: -0.03 (-0.04;-0.02)
-0.03 (-0.04;-0.02) *



Transmen

Mean change (95% confidence interval)

Waist: -0.4 cm (-1.7;0.9)
-0.3 cm (-1.6;0.9) *

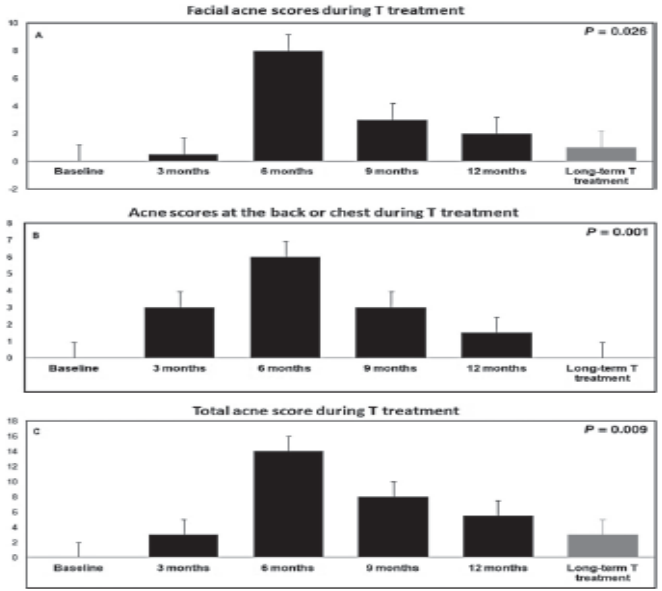
Hip: -1.9 cm (-3.0;-0.8)
-1.9 cm (-3.1;-0.7) *

WHR: 0.01 (0.0;0.02)
0.01 (0.0;0.02) *

Feminization and masculinization of regional body parts and effects on body shape during the first year of cross-sex hormonal therapy: results from a multi-center prospective study. Klaver M, de Blok C, Wiepjes C, Nota N, Dekker M, de Mutsert R, Schreiner T, Fisher A, T'Sjoen G, den Heijer M. *European Journal of Endocrinology* 2017

ENIGI: Acne & Body hair growth

Acne



Body hair

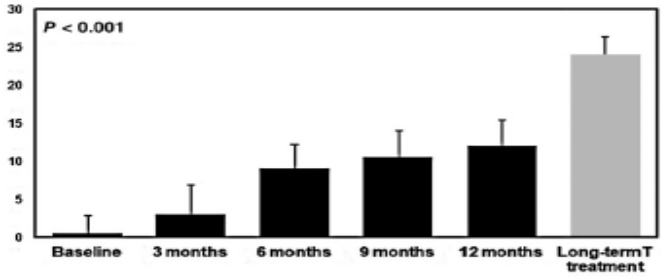


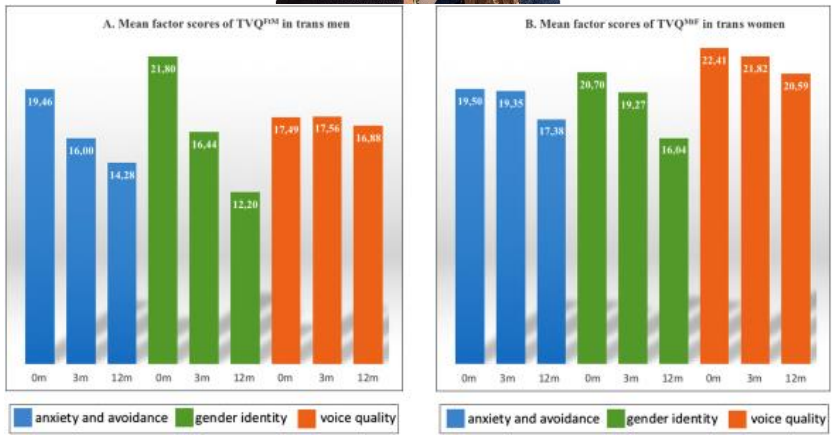
Figure 1 Ferriman and Gallwey (F&G) scores during T treatment. Data are presented as the median F&G score; error bars represent 95% confidence intervals. Long-term T treatment represents median F&G scores from the cross-sectional study. *P* value results from ANOVA repeated measures analyses.

Short-and long-term clinical skin effects of testosterone treatment in trans men. Wierckx, Van de Peer, Verhaeghe, Dedecker, Van Caenegem, Toye, Kaufman, T'Sjoen. *Journal of Sexual Medicine* 2014 11(1):222-9

ENIGI: self-perception of voice

Trans men (n = 80)

Trans women (n = 103)



Self-perception of voice in transgender persons during cross-sex hormone therapy. Bultynck, Pas, Defreyne, Cosyns, den Heijer, T'Sjoen. *The Laryngoscope* 2017

Recent addition to the literature: Associations between Transsexual Voice Questionnaire (TVQMtF) and self-report of voice femininity and acoustic voice measures. Dacakis, Oates, Douglas. *Int J Lang Commun Disord* 2017

Debate: which testosterone in trans men is preferred?

	Groups	Baseline	Week 54	GLM analysis	
			Posttreatment	*P* value vs. posttreatment	*P* value vs. group
LH (IU/L)	TD	7.3 (3.5–11.2)	5.1 (1.9–8.3)	*P* = 0.289	*P* = 0.160
	T-gel	12.8 (6.6–39.8)	9.2 (4.5–13.9)		
	TU	5.8 (2.1–9.5)	5.1 (2.0–8.1)		
FSH (IU/L)	TD	6.2 (4.3–8.1)	5.1 (3.8–6.4)	*P* = 0.700	*P* = 0.538
	T-gel	6.1 (3.4–8.9)	5.6 (3.7–7.5)		
	TU	4.6 (2.8–6–4)	5.3 (4.1–6.6)		
E (pg/mL)	TD	102.9 (61.4–144.5)	70.6 (28.0–113.2)	*P* = 0.002	*P* = 0.502
	T-gel	167.3 (124.0–210.5)	81.9 (37.6–126.2)		
	TU	190.9 (92.2–169.6)	72.3 (32.6–111.9)		
PRL (ng/mL)	TD	18.2 (13.1–23.3)	9.8 (6.4–13.3)	*P* = 0.026	*P* = 0.260
	T-gel	17.0 (11.7–22.3)	15.6 (11.9–19.2)		
	TU	15.7 (11.4–20.1)	13.1 (10.2–16.1)		
T (ng/mL)	TD	0.54 (0.43–0.65)	7.39 (5.33–9.46)	*P* < 0.0005	n.s.
	T-gel	0.45 (0.35–0.55)	5.89 (4.01–7.78)		
	TU	0.44 (0.35–0.54)	6.14 (4.39–7.89)		
SHBG (nmol/L)	TD	65.4 (49.4–82.4)	31.8 (22.3–41.4)	*P* = 0.000	*P* = 0.587
	T-gel	65.2 (48.9–81.4)	31.6 (22.5–40.7)		
	TU	60.3 (44.0–76.5)	34.3 (25.2–43.4)		
cFT (nmol/L)	TD	0.01 (0.01–0.02)	0.31 (0.09–0.54)	*P* = 0.000	*P* = 0.910
	T-gel	0.01 (0.00–0.01)	0.34 (0.12–0.57)		
	TU	0.01 (0.00–0.01)	0.28 (0.06–0.49)		

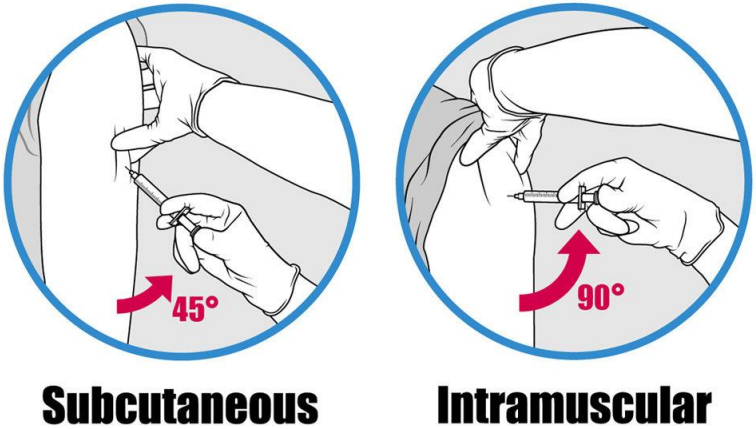
Data are expressed as mean (95% CI)
cFT = calculated free testosterone; CI = confidence interval; E = estradiol; FSH = follicle-stimulating hormone; GLM = general linear model; LH = lutainizin hormone; n.s. = not significant; PRL = prolactin; SHBG = sex hormone-binding globulin; T = testosterone; TD = testoviron depot; T-gel = testosterone gel; TU = testosterone undecanoate

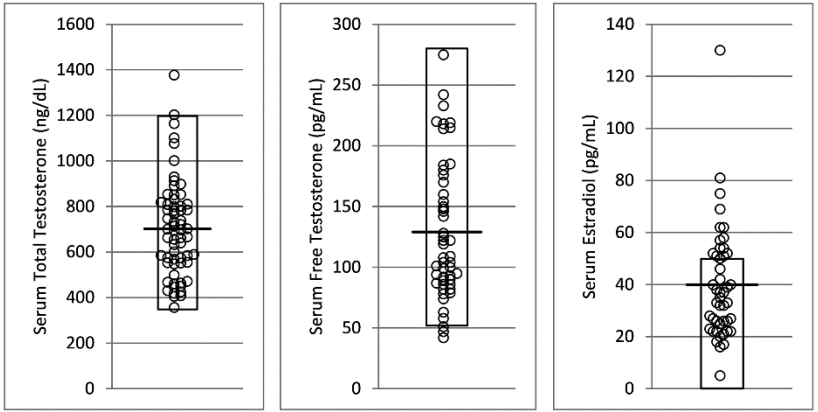
	Groups	Baseline	Week 30	Week 54	GLM analysis	
			Posttreatment	Posttreatment	*P* value vs. posttreatment	*P* value vs. groups
Glucose (mg/dL)	TD	87.3 (82.2–92.4)	81.2 (75.6–86.7)	82.0 (76.9–87.0)	*P* = 0.019	*P* = 0.749
	T-gel	84.0 (78.7–89.3)	81.5 (75.7–87.3)	80.0 (74.7–85.3)		
	TU	83.1 (77.9–88.2)	81.7 (76.1–87.2)	80.1 (75.0–85.1)		
Insulin (mcu/mL)	TD	6.04 (4.88–7.18)	5.52 (4.14–6.91)	5.21 (3.93–6.49)	*P* = 0.917	*P* = 0.41
	T-gel	5.71 (4.44–6.98)	6.61 (5.08–8.14)	6.10 (4.68–7.52)		
	TU	5.82 (46.68–6.98)	4.84 (3.45–6.22)	5.86 (4.58–7.15)		
HOMA-IR	TD	1.26 (1.03–1.49)	1.09 (0.83–1.35)	0.92 (0.68–1.16)	*P* = 0.62	*P* = 0.28
	T-gel	1.12 (0.87–1.37)	1.26 (0.97–1.55)	1.21 (0.94–1.47)		
	TU	1.18 (0.96–1.41)	0.98 (0.72–1.25)	1.14 (0.90–1.38)		
Waist circumference (cm)	TD	73.1 (68.23–78.0)	76.7 (71.70–81.7)	77.5 (723.7–82.2)	*P* = 0.256	*P* = 0.317
	T-gel	82.7 (73.2–92.1)	81.3 (71.8–90.9)	84.0 (74.9–93.1)		
	TU	81.5 (74.2–88.8)	79.6 (72.2–87.0)	80.6 (73.5–87.7)		
Hip circumference (cm)	TD	94.4 (90.6–98.2)	96.0 (92.0–99.9)	96.0 (91.9–100.1)	*P* = 0.089	*P* = 0.206
	T-gel	98.7 (91.4–105.9)	100.7 (93.1–108.3)	98.0 (90.2–105.8)		
	TU	97.2 (91.6–102.8)	98.28 (92.3–104.1)	101.8 (95.7–107.9)		
WHR	TD	0.77 (0.72–0.82)	0.80 (0.76–0.84)	0.81 (0.77–0.85)	*P* = 0.322	*P* = 0.072
	T-gel	0.84 (0.74–0.93)	0.80 (0.73–0.88)	0.85 (0.78–0.93)		
	TU	0.84 (0.77–0.92)	0.81 (0.75–0.87)	0.79 (0.73–0.85)		
Body weight (kg)	TD	57.8 (51.2–64.4)	61.8 (55.2–68.5)	61.3 (55.0–67.5)	*P* < 0.0005	*P* = 0.063
	T-gel	67.3 (59.7–74.9)	69.6 (61.9–77.2)	68.7 (61.5–75.9)		
	TU	59.6 (52.3–66.8)	60.0 (52.7–67.3)	60.5 (53.7–67.4)		
BMI (kg/m²)	TD	22.3 (19.9–24.6)	23.8 (21.5–26.1)	23.6 (21.4–25.8)	*P* < 0.0005	*P* = 0.058
	T-gel	23.9 (21.2–26.6)	24.6 (21.9–27.3)	24.3 (21.8–26.9)		
	TU	22.1 (19.5–24.6)	22.2 (19.7–24.8)	22.4 (20.0–24.8)		

No differences between
intramuscular **T-undecanoate, T-enanthate**, or **transdermal T**
with regard to anthropometric or biochemical variables.

Effects of three different testosterone formulations in female-to-male transsexual persons. Pelusi, Constantino, Martelli, Lambertini, Bazzocchi, Ponti, Battista, Venturoli, Meriggiola. *Journal of Sexual Medicine* 2014 11(12):3002-11

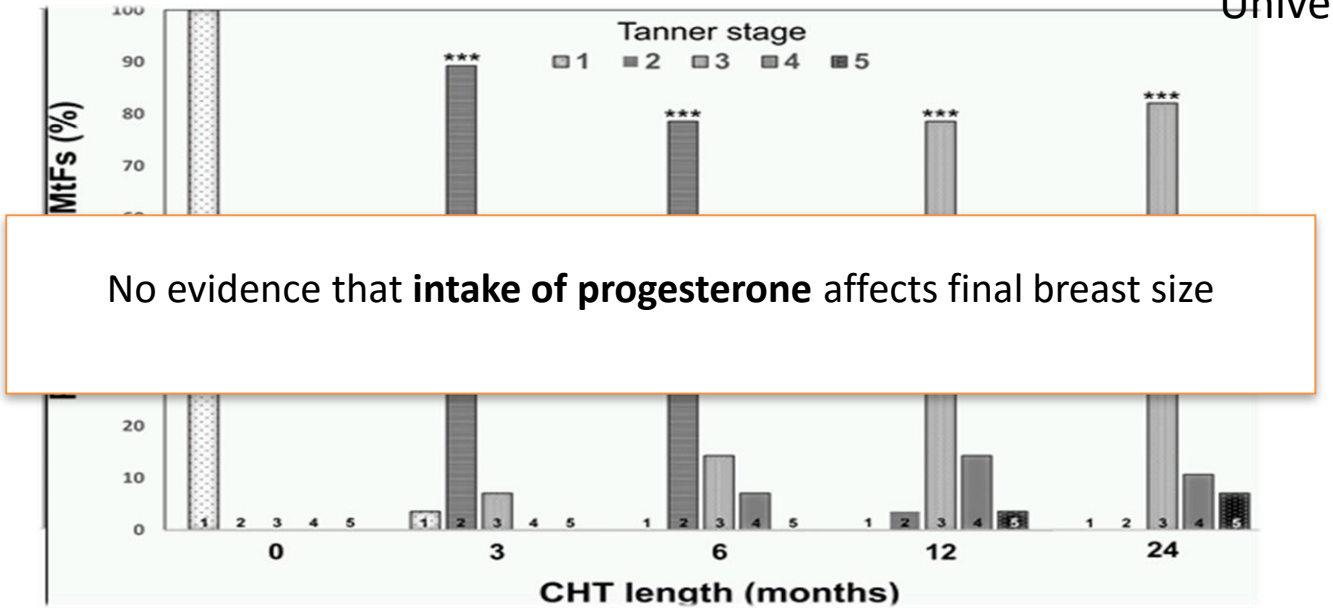
Debate: sc injection of testosterone?





Subcutaneaous injection of testosterone is an effective and preferred alternative to intramuscular injection: demonstration in female-to-male transgender patients. Spratt, Stewart, Savage, Craig, Spack et al. *Journal of Clinical Endocrinology and Metabolism*, 2017, 102(7):2349-2355.

Debate: Progesterone for trans women- Yes or no?



No evidence that **intake of progesterone** affects final breast size

Cross-sex hormone treatment and psychobiological changes in transsexual persons: two-year follow-up data. Fisher, Castellini, Ristori, Casale, Cassioli, et al. *Journal of Clinical Endocrinology and Metabolism* 2016, 101(11):4260-4269

Clinical Review: Breast development in trans women receiving cross-sex hormones. Wierckx K, Gooren L, T'Sjoen G. *Journal of Sexual Medicine* 2014 11(5):1240-7.

Breast development- data from ENIGI (n = 229)

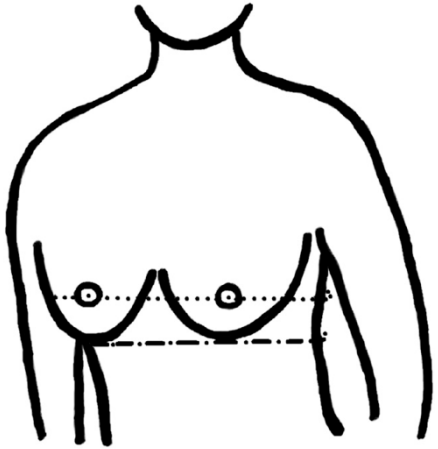


Figure 1. Placement of the tape measure for circumference measurements. For breast circumference measurement, the tape measure was placed around the thorax over the fullest part of the breast (dotted line) and for chest circumference measurement in the inframammary fold (dashed-dotted line).

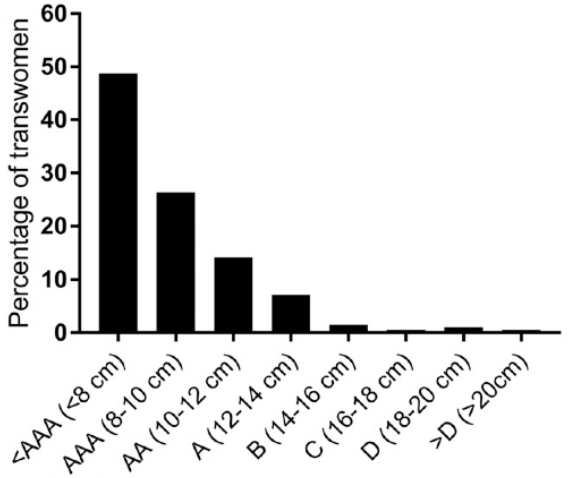


Figure 4. Gained bra cup sizes in 197 transwomen after 1 year of CHT. Data are shown as percentage of transwomen per cup size.

Breast Development in Transwomen After One Year of Cross-sex Hormone Therapy: Results of A Prospective Multicenter Study
Christel de Blok, Maartje Klaver, Chantal Wiepjes, Nienke Nota, Annemieke Heijboer, Alessandra Fisher, Thomas Schreiner, Guy T'Sjoen, Martin den Heijer, *The Journal of Clinical Endocrinology & Metabolism*, jc.2017-01927

Short term data

Mid term data

Long term data

Mid-term morbidity and mortality

Trans men

safe

no increased overall and cancer morbidity

Trans women

Mortality and morbidity in transsexual subjects treated with cross-sex hormones. Van Kesteren P, Asscheman H, Megens J, Gooren LJ. *Clinical Endocrinology* 1997; 47: 337-343

A long-term evaluation of cross-sex hormone treatment in transsexual persons. Wierckx K, Mueller S, Weyers S, Van Caenegem E, Roef G, Heylens G, T'Sjoen G. *Journal of Sexual Medicine* 2012; 9:2641-51

Mid-term morbidity and mortality

Trans men

safe

no increased overall and cancer morbidity

no increased overall + CV mortality

Trans women

venous thrombosis (6-8% incidence with ethinyl estradiol)

cardio- and cerebrovascular disease (MI and stroke)

?

depression

osteoporosis

no increased cancer morbidity

no increased overall + CV mortality

Mortality and morbidity in transsexual subjects treated with cross-sex hormones. Van Kesteren P, Asscheman H, Megens J, Gooren LJ. *Clinical Endocrinology* 1997; 47: 337-343

A long-term evaluation of cross-sex hormone treatment in transsexual persons. Wierckx K, Mueller S, Weyers S, Van Caenegem E, Roef G, Heylens G, T'Sjoen G. *Journal of Sexual Medicine* 2012; 9: 2641-51

Cardiovascular risk factors

Trans men

Trans women

Table 3 Short-term changes in metabolic and cardiovascular risk factors in FtoM transsexual persons.

Outcome variable	Observed changes	References	Effect on cardiovascular morbidity
Body composition			
Weight/BMI	No effect/increase	(28)/(40, 45, 66)	↑
Visceral fat	Slight increase	(66)	↑
Total body fat	No effect/increase	(28)/(66)	↑
Insulin metabolism			
Fasting glucose	Decrease	(28, 40)	↓
Fasting insulin	No effect	(28, 40, 66)	–
Insulin sensitivity	No effect/slight decrease	(28)/(66)	–/↑
Lipid spectrum			
Total cholesterol	No effect	(28, 48, 66)	–
LDL cholesterol	No effect	(28, 40, 48, 66)	–
HDL cholesterol	Decrease	(28, 40, 66)	↑
VLDL cholesterol	No effect	(28)	–
Triglycerides	Increase	(40, 66)	↑
Fish fatty acid (DHA)	Decrease	(66)	↑
Other CVD risk factors			
Heart rate	–	(40)	–
Diastolic blood pressure	No effect	(28, 40, 66)	–
Systolic blood pressure	No effect/increase	(28, 40)/(66)	–/↑
Arterial stiffness	No effect	(40)	–
Hemostasis/fibrinolysis	No effect	(22, 45)	–
Total homocysteine	Increase	(48)	↑
Inflammation markers	Increase	(66)	↑

Table 2 Short-term changes in metabolic and cardiovascular risk factors in MtoF transsexual persons.

Outcome variable	Observed changes	References	Effect on cardiovascular morbidity
Body composition			
Weight	Increase	(28, 40, 45, 66)	↑
Visceral fat	Increase	(45)	↑
Total body fat	Increase	(28, 66)	↑
Insulin metabolism			
Fasting glucose	No effect	(28, 40)	–
Fasting insulin	Increase	(28, 40, 66)	↑
Insulin sensitivity	Decrease	(28, 66)	↑
Lipid spectrum			
Total cholesterol	No effect	(28, 45, 66)	–
LDL cholesterol	No effect/increase	(28)/(66)	–/↓
HDL cholesterol	Increase	(28, 66)	↓
VLDL cholesterol	No effect	(28)	–
Triglycerides	Increase?	(40, 45)	↑
Fish fatty acid (DHA)	Increase	(66)	↓
Other CVD risk factors			
Heart rate	No effect	(40)	–
Diastolic blood pressure	No effect/increase	(28)/(40)	–/↑
Systolic blood pressure	No effect/increase	(28)/(40)	–/↑
Arterial stiffness	No effect	(40)	–
Hemostasis/fibrinolysis	Increase	(22, 45)	↑
Total homocysteine	Decrease	(48)	↓
Inflammation markers	No effect/increase	(48)/(66)	–/↑

Cardiovascular disease in transsexual persons treated with cross-sex hormones: reversal of the traditional sex difference in cardiovascular disease pattern. Gooren, Wierckx, Giltay. *European Journal of Endocrinology* 2014 70(6):809-19

Cardiovascular endpoints

Table 5 Studies on cardiovascular endpoints in FtoM transsexuals compared with general population or control population.

Reference	n	Follow-up	Treatment regimen	Outcome
(16)	122	Median duration HRT of 4.4 years[a]	Test e u	
(15)	293	Mean duration HRT of 8.2 years	Test e u	
(14)	365	Median duration HRT of 18.5 years[a]	Test e u	
(17)	133	Median time since SRS was 9.1 years[a]	Not	
(56)	37	Mean duration HRT of 4.9±4.6 years	Different testosterone preparations	No difference in cardiovascular morbidity compared with control men and women
(27)	138	Median duration HRT of 6 years	Different testosterone preparations	No difference in cardiovascular morbidity compared with control men and women

Table 4 Studies on cardiovascular endpoints in MtoF transsexuals compared with general population or control group.

Reference	n	Follow-up	Treatment regimen	Outcome
(16)	303	Median duration HRT	Ethinyl estradiol 100 μg/day and	45-fold increase in VT and/or PE
				No increased cardiovascular morbidity and mortality 20-fold increase in venous thrombosis and/or pulmonary embolism
				No increased cardiovascular morbidity or mortality rate Higher mortality due to ischemic heart disease; SMR 1.64 (1.43–1.87)
		of 9.1 years*		Higher mortality due to CVD; SMR 2.11 (1.32–3.21) in age group 40–64 years Higher mortality due to cardiovascular disease compared with controls Lower cardiovascular morbidity compared with control male and female population
(56)	58	Mean duration HRT of 6.5±7.9 years	Different estrogen regimens and cyproterone acetate 50 mg/day	Higher number of AMI compared with control women Higher number of CVD compared with control men and women
(27)	214	Median duration HRT of 6 years	Different estrogen regimens and cyproterone acetate 50 mg/day	

Discordant change in classical **cardiometabolic risk factors** and actual **cardiovascular risk**

Cardiovascular disease in transsexual persons treated with cross-sex hormones: reversal of the traditional sex difference in cardiovascular disease pattern. Gooren, Wierckx, Giltay. *European Journal of Endocrinology* 2014 70(6):809-19

Incidence of venous thromboembolism in transgender women receiving oral estradiol. Arnold, Sarkodie, Coleman, Goldstein. *Journal of Sexual Medicine* 2016 13-173-1777


LOW
NORMAL
HIGH
ALARMING
CHOLESTEROL
Level

Systematic review on lipids

29 studies
No increase in CV morbidity

Trans men (n = 1503)

Triglycerides
at 3-6 months (+9 mg/dl)
at ≥ 24 months (+21.4)

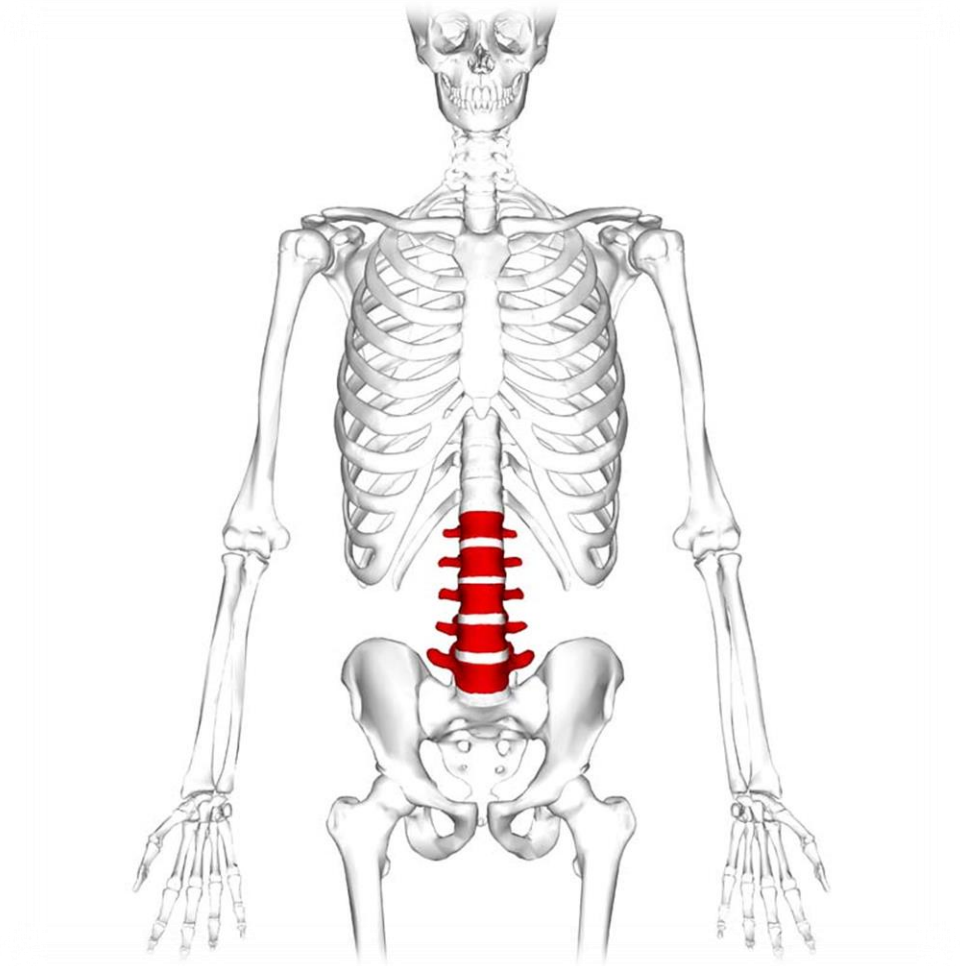
LDL-C levels
at 12 months (+11.3)
≥ 24 months (+17.8).

HDL-C levels decreased
(highest at ≥ 24 months, -8.5).

Trans women (n = 3238)

- Triglycerides were higher at ≥ 24 months (+ 31,9)
- No change in other parameters

Effects of sex steroids on lipids, venous thromboembolism, cardiovascular disease and mortality in transgender individuals: a systematic review and meta-analysis. Maraka S, Ospina N, Rodriguez-Gutierrez R, Davidge-Pitts C, Nippoldt T, Murad MH. *Journal of Clinical Endocrinology and Metabolism* 2017



Systematic review in bone

13 studies
no fracture data available

Trans men

Baseline measurements: normal

No significant changes

Trans women

T- score <2,5 in 16% at baseline

Lumbar spine BMD
at 12 months +0.044 g/cm^2
at 24 months +0.057 g/cm^2

Effect of sex steroids on the bone health of transgender individuals: a systematic review and meta-analysis. Ospina N, Maraka S, Rodriguez-Gutierrez R, Davidge-Pitts C, Nippoldt T, Murad M.H. *The Journal of Endocrinology and Metabolism* 2017

Preservation of volumetric bone density and geometry in trans women during cross-sex hormonal therapy: a prospective observational study. Van Caenegem E, Wierckx K, Taes Y, Schreiner T, Vandewalle S, Toye K, Kaufman JM, T'Sjoen G. *Osteoporos Int.* 2015 Jan;26(1):35-47.

Breast cancer risk?

Breast Cancer Res Treat
DOI 10.1007/s10549-014-3213-2

EPIDEMIOLOGY

Incidence of breast cancer in a cohort of 5,135 transgender veterans

George R. Brown · Kenneth T. Jones

Breast cancer risk?

Breast Cancer Res Treat
DOI 10.1007/s10549-014-3213-2

EPIDEMIOLOGY

Incidence of breast cancer in a cohort of 5,135 transgender veterans

George R. Brown · Kenneth T. Jones

N = 3,556 (trans women), N = 1,579 (trans men)

Cases of breast-Ca. trans men: 7 and trans women: 3

Incidence 20.0/100,000 patient years

No difference in comparison to an age – (birth) sex-matched general population

Incidence of breast cancer in a cohort of 5,135 transgender veterans. Brown G & Jones K. *Breast Cancer Res Treat* 2015 149(1):191-8

Breast cancer risk?

ORIGINAL RESEARCH—ONCOLOGY

Breast Cancer Development in Transsexual Subjects Receiving Cross-Sex Hormone Treatment

Louis J. Gooren, MD, PhD,*† Michael A.A. van Trotsenburg, MD, PhD,‡ Erik J. Giltay, MD, PhD,§ and Paul J. van Diest, MD, PhD¶

*Emeritus VU University Medical Center, Amsterdam, The Netherlands; †Androconsult, Chiang Mai, Thailand; ‡VU University Medical Center, Amsterdam, The Netherlands; §Department of Psychiatry, LUMC, Leiden, The Netherlands; ¶Department of Pathology, University Medical Center, Utrecht, The Netherlands

DOI: 10.1111/jsm.12319

n = 2,307 (trans women), n = 795 (trans men)

Cases of breastCA trans men: 2 and trans women: 1

Trans women: Incidence 4.1 / 100,000 patient years

No difference in comparison to age – (birth) sex-matched general population

Incidence 5.9 / 100,000 patient years

Lower incidence than age-matched women, same incidence as age-matched men

No evidence for **increase in breast cancer risk** under CHT in **trans men or trans women**

Breast cancer development in transsexual subjects receiving cross-sex hormone treatment. Gooren, van Trotsenburg, Giltay, van Diest *Journal of Sexual Medicine* 2013 10(12): 3129-34

Short term data

Mid term data

Long term data

Conclusion 2

- Gender affirming hormone treatment is easy
- Gender affirming hormone therapy is safe

Conclusion 2

- Gender affirming hormone treatment is easy
- Gender affirming hormone therapy is safe
- It saves lifes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