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KINDERKLINIKEN
Bern

Entwicklungspsychopharmakologie:

Pharmakologische Hormonbehandlung bei Geschlechtsidentitätsstörungen im Kindes- und Jugendalter

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Acknowledgment:

Trans Versorgungs-Team Kinder- und Jugendmedizin Bern

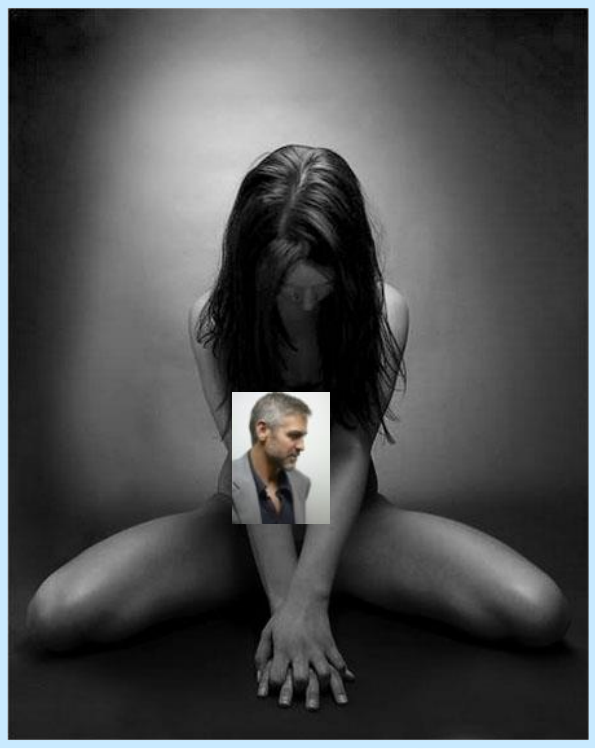
Psychosomatik
MB KiJu

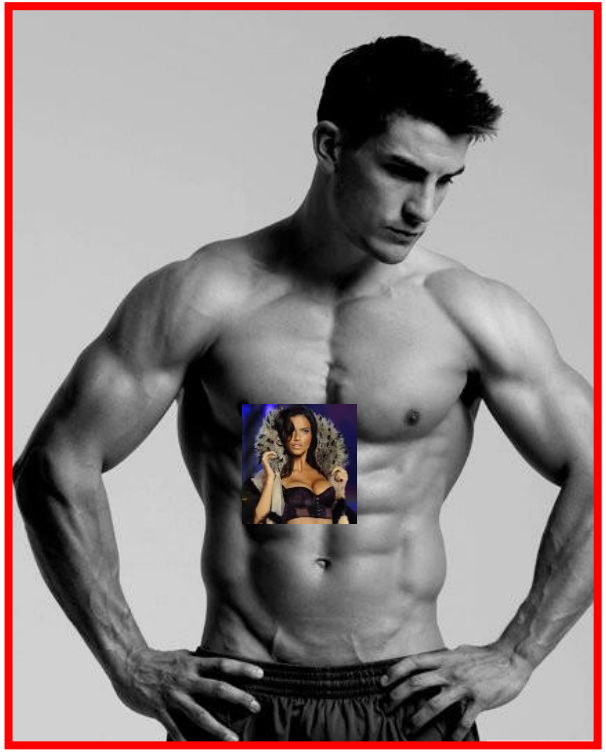
Pädiatrische
Endokrinologie

Kinder- und
Jugendpsychiatrie

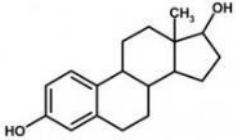
Inhalt

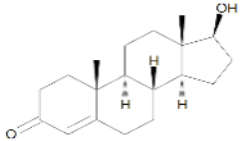
- Grundlagen der menschlichen Sexualentwicklung
- Somatische Transgender Medizin heute (Handlungsrichtlinien des Endokrinologen)
- Wirkungen, Nebenwirkungen und Langzeitfolgen von hormonellen Therapien
- Ein paar Studien
- Die Berner Erfahrung
- Perspektive





Estrogen



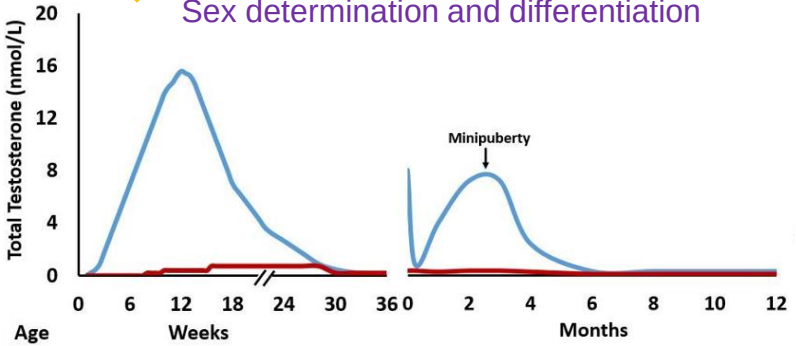


Testosterone

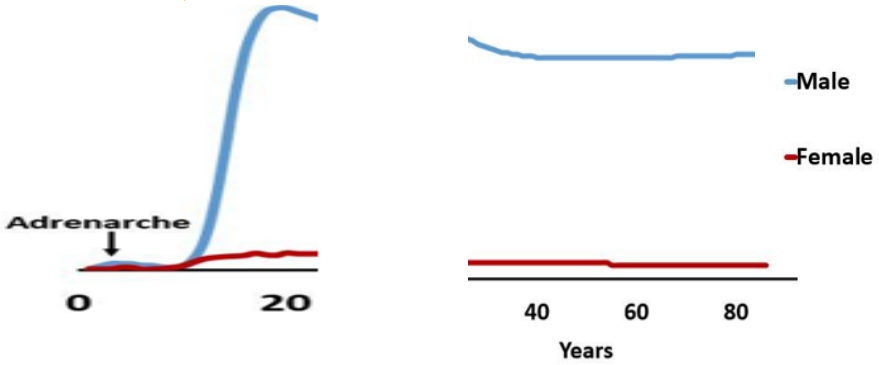
Phasen der sexuelle Entwicklung

→DSD:

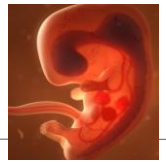
Sex determination and differentiation



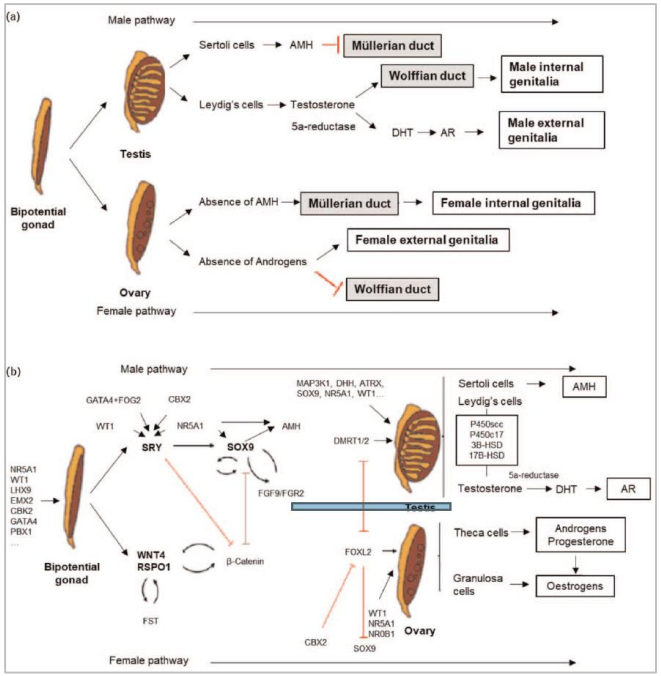
→DSD →Infertility

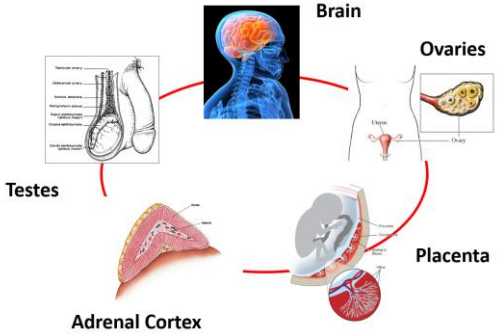


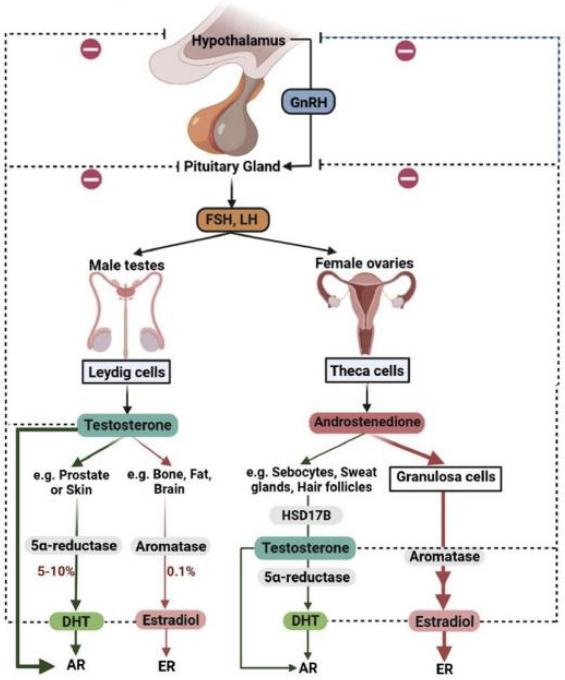
Prenatal → Infancy → Childhood → **Puberty** → **Adulthood**



Entwicklung der Sexualorgane und deren Regulation







Martinez and Flück co-pediatrics 2021

Naamneh Elzenaty, du Toit, Flück BPRCEM 2022

Gender Dysphorie und die Somatische Transgender Medizin

„Transgeschlechtliche Personen berichten, ihre körperlichen Geschlechtsmerkmale als nicht passend zu ihrem geschlechtlichen Selbsterleben zu empfinden, d.h. nicht passend zu ihrer *Geschlechtsidentität*. In diesem Sinne entsteht ein Gefühl, im falschen Körper zu leben: Dabei ist der *Geschlechtskörper* gemeint. Daher streben viele transgeschlechtliche Menschen *körpermedizinische Behandlungen* (z.B. durch Hormone oder Operationen) an, um ihren Körper ihrem geschlechtlichen Erleben anzugleichen.

Das Leiden, das aus der Unstimmigkeit von Geschlechtskörper und Geschlechtsidentität entsteht, nennt man *Geschlechtsdysphorie*.“

Becker, Brunner und Preuss: Inter- und Transgeschlechtlichkeit im Vergleich, in: Schweizer und Vogler: Die Schönheiten des Geschlechts. Intersex im Dialog. Campus Verlag, Hamburg/New York 2018

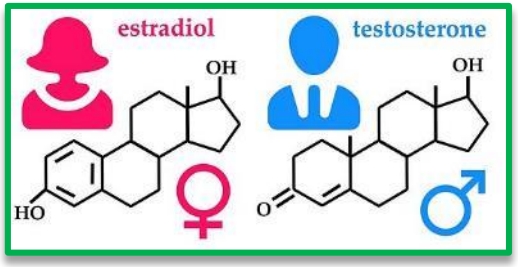
Körpermedizinische Umbaumöglichkeiten eines typisch männlichen oder weiblichen biologischen Systems

Medizinische Massnahmen Stufe 1-3

Blockade

GAHT

Chirurgie



Hormonelle Therapien (Stufe 1 und 2)

Step 1

Step 2

Table 1. Hormonal interventions for transgender adolescents (All currently off-label for gender nonconforming/transgender youth)

A. Inhibitors of gonadal sex steroid secretion or action
1. GnRH analogues: Inhibition of the hypothalamic-pituitary-gonadal (HPG) axis (FTM and MTF)
a. Leuprolide acetate IM (1- or 3-month preparations) or SC (1-, 3-, 4-, or 6-month preparations) at dose sufficient to suppress pituitary gonadotropins and gonadal sex steroids
b. Histrelin acetate SC implant (once-yearly dosing, though may have longer effectiveness)
c. Other options: goserelin acetate SC implant (4- or 12-week preparations); nafarelin acetate Intranasal (multiple daily doses) also available, but no reported use in this population
2. Alternative approaches
a. Medroxyprogesterone acetate orally (up to 40 mg/day) or IM (150 mg q 3 months): Inhibition of HPG axis and direct inhibition of gonadal steroidogenesis (FTM an MTF)
b. Spironolactone (25 to 50 mg/day with gradual increase to 100–300 mg/day orally, divided into BID dosing): Inhibition of testosterone synthesis and action (MTF)
c. Cyproterone acetate (gradual increase up to 100 mg/day orally; not available in U.S.): Inhibition of testosterone synthesis and action (MTF)
d. Finasteride (2.5–5 mg/day orally) Inhibition of type II 5 α-reductase, blocking conversion of testosterone to 5 α-dihydrotestosterone (MTF)
B. Cross-sex hormones
1. MTF: Estrogen: 17 β-estradiol
a. Transdermal: twice weekly patches (6.25 mcg [achieved by cutting a 25 mcg patch] with gradual increase to full adult dose)
b. Oral/sublingual: daily (0.25 mg with gradual increase to full adult dose of 2–6 mg/day)
c. Parenteral IM (synthetic esters of 17 β-estradiol): estradiol valerate (5–20 mg up to 30–40 mg q 2 weeks) or estradiol cypionate (2–10 mg q 1 week)
2. FTM: Testosterone
a. Parenteral IM or SC (synthetic esters of testosterone): testosterone cypionate or enanthate (12.5 mg q week or 25 mg q 2 weeks, with gradual increase to 50–100 mg q week or 100–200 mg q 2 weeks)
b. Transdermal (consider once full adult testosterone dose has been achieved parenterally): patch (2.5–7.5 mg/day) or 1% gel (2.5–10 grams/day of gel = 25–100 mg/day of testosterone)

GnRH, gonadotropin releasing hormone; IM, intramuscular; SC, subcutaneous; FTM: female-to-male; MTF, male-to-female; q, every.
Adapted from Rosenthal SM. J Clin Endocrinol Metab 2014;99:4379-89, with permission of .the Endocrine Society[16].

Rosenthal apem 2016

Wirkorte/-mechanismen Stufe 1 Medikamente

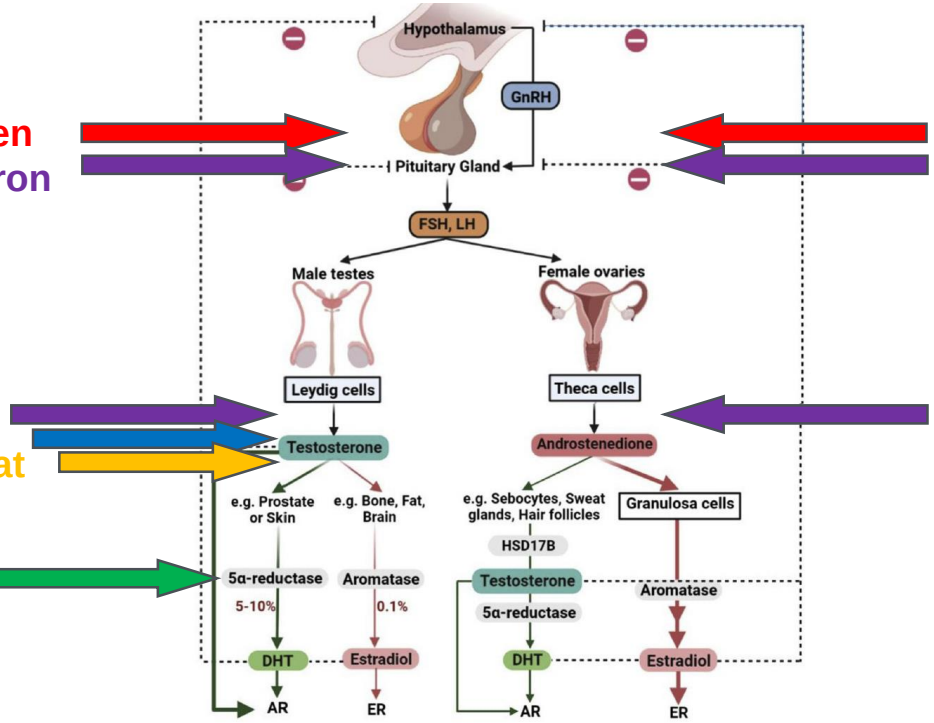
MtF

FtM

GnRH Antagonisten
Medroxyprogesteron Acetat

Spironolactone
Cyproterone Acetat

Finasteride



Ziel: HPG Achse inaktivieren, Sexualhormonproduktion stoppen, in präpubertären Zustand zurückversetzen

Stufe 1: GnRH Analoga: Lucrin, Decapeptyl Depot sc/im

- synthetisch hergestellte Derivate des natürlichen Hormons Gonadotropin-Releasing-Hormon (GnRH, LHRH)
- hemmen bei einer längerfristigen Verabreichung die Sekretion von LH und FSH durch Down- Regulation der Rezeptoren; senken dadurch die Östrogen- und Androgen-konzentrationen
- Cave: Bei einer kurzfristigen Anwendung steigen die Hormonspiegel

Nebenwirkungen

- Folgen des Östrogen- oder Androgenentzugs
- Weitere: Kopfschmerzen, Stimmungsveränderungen, Depressionen, Verminderung der Libido, erektile Dysfunktion und lokale Reaktionen an der Injektionsstelle

FtM & MtF

Stufe 1: Medroxyprogesterone Acetat po/im

- Derivat des natürlichen Gestagens Progesteron
- gestagen, androgen, antiöstrogen, antigonadotrop und adrenokortikoid
- metabolisiert über CYP3A

Interaktionen:

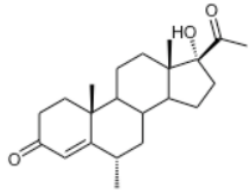
- Mit Medis, die CYP3A beeinflussen, z.B. Antiepileptika, Barbiturate

Nebenwirkungen:

- Gewichtszunahme, Kopfschmerzen, Nervosität, Verringerung der Knochenmineraldichte, Thromboembolismus

Kontraindikationen:

- Risiko für Thrombosen, Leberfunktionsstörungen und Porphyrie



FtM & MtF

Stufe 1: Spironolactone po

- Aldosteron-Antagonist und Anti-Androgen
- Schwach diuretisch, antihypertensiv und antiandrogen

Nebenwirkungen:

- Hyperkaliämie, Herzrhythmusstörungen, Gynäkomastie
- Kopfschmerzen, Schwindel, Verwirrung, Gangstörungen, Magen-Darm-Störungen, Hautausschläge, vermehrte Behaarung oder Haarausfall

Interaktionen

- ACE Hemmer, Furosemid, NSAR u.a.

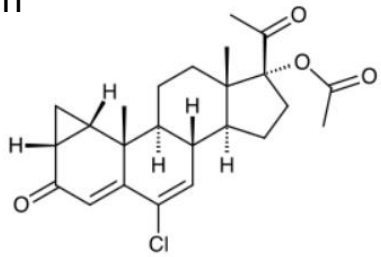
Kontraindikationen:

- Überempfindlichkeit, akutes Nierenversagen, schwere Niereninsuffizienz, Anurie, Morbus Addison, Hyperkaliämie, Hyponatriämie

MtF

Stufe 1: Cyproterone Acetate po

- Wirkstoff aus der Gruppe der Antiandrogene mit gestagenen und antiandrogenen Eigenschaften
- Metabolisiert über CYP3A4



Interaktionen:

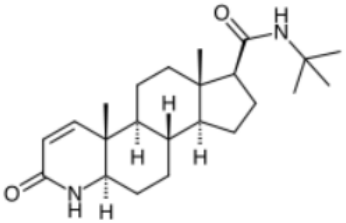
- CYP-Inhibitoren und –Induktoren; Antibiotika

Nebenwirkungen:

- Gewichtszunahme, Hautausschlag, Kopfschmerzen, Spannungsgefühl in der Brust, Brustschmerzen, depressive Verstimmung, Übelkeit und Verdauungsbeschwerden
- selten schwere Herz-Kreislauf-Erkrankungen wie eine venöse Thrombose, eine Lungenembolie, ein Schlaganfall und ein Herzinfarkt

MtF

Stufe 1: Finasterid po



- selektiver und kompetitiver Inhibitor der 5alpha-Reduktase
- Blockiert die Synthese von Dihydrotestosterone aus Testosterone
- Metabolisiert über CYP3A4

Interaktionen mit:

- Hemmern und Induktoren des Isoenzyms CYP3A4

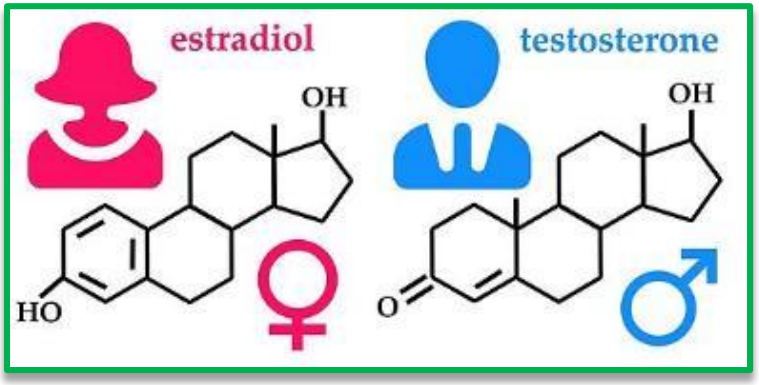
Nebenwirkungen:

- verminderte Libido, Impotenz, Erektionsstörungen, Ejakulationsstörungen, Berührungsempfindlichkeit der Brust, Brustvergrösserung und Hautausschlag

MtF

Stufe 2: Gegengeschlechts Hormon Therapie (GAHT)

GAHT



Gender Affirming Hormone Therapy

Stufe 2: Physiologische Effekte von Oestrogenen

Female:

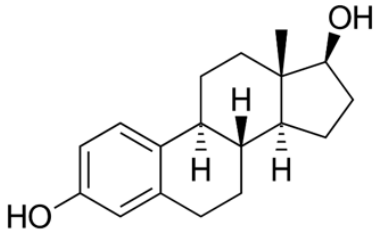
- Sexual development
- Sexual desire
- Menstrual cycle, fertility and reproduction

Male:

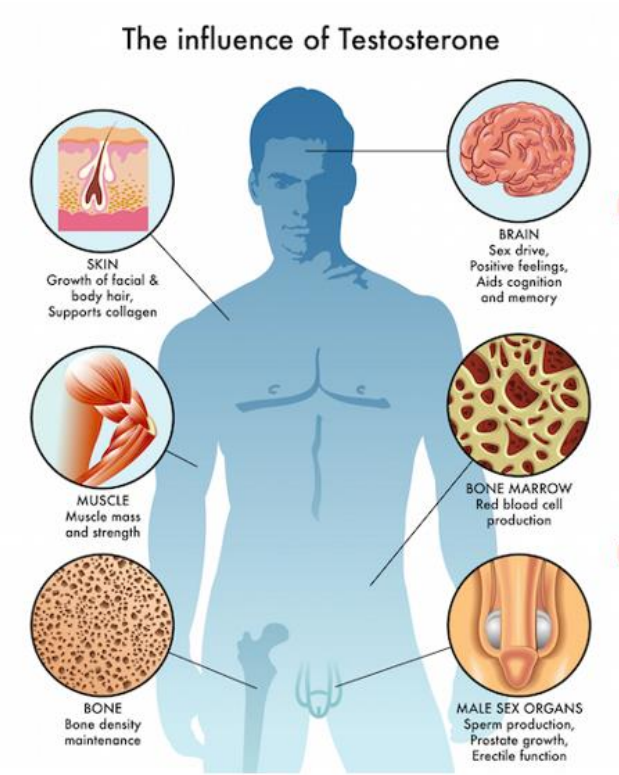
- Sexual desire
- Erectile function

Both sexes:

- Growth and body composition
- Lipid metabolism
- Brain function
- Bone health
- Skin health



Stufe 2: Physiologische Effekte von Testosteron



Effekt der hormonellen Therapien bei Trans (Stufe2)

Psychological and CNS
↓Gender dysphoria
↓Anxiety
↓Depression
↓Perceived stress
↑Quality of life

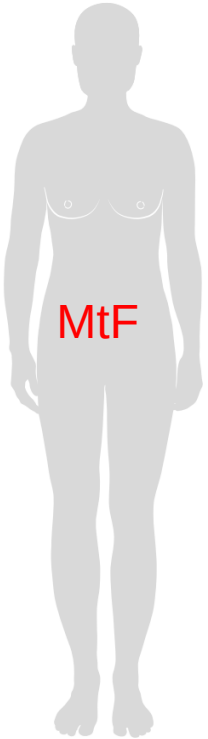
Breast
↑Breast tissue

Skin
↑Softness
↓Sebum and acne

Reproductive system
↓Penile erections
↓Prostate size
↓Sperm count and quality

Body composition
↓Lean mass
↑Fat mass
↑Visceral fat

Sexual health
↓Sexual desire



Hair
↓Facial and body hair
↓Male pattern baldness

Voice
No change

Blood pressure
↓Systolic blood pressure

Blood
↓Hemoglobin and hematocrit

Lipids and metabolism
↑LDL cholesterol
↑Triglycerides
↑Sex hormone-binding globulin

Hormone concentrations
↓Testosterone
↓Luteinising hormone
↓Follicle-stimulating hormone
↑Prolactin

Oestrogene und Antiandrogene

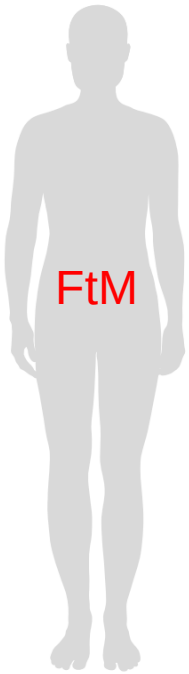
Psychological and CNS
↓Gender dysphoria
↓Anxiety
↓Depression
↓Perceived stress
↑Total grey matter volume
↑Cortical thickness in several areas

Hair
↑Facial and body hair
↑Hair density, diameter, and growth rate
Alopecia

Breast
↓Breast cancer
↓Glandular tissue
↑Fibrous connective tissue

Reproductive system
Cessation of menstruation and infertility
↑Clitoral size
↓Vaginal epithelium thickness
Atrophic endometrium (according to data from some studies)
Ovarian hyperplasia and polycystic ovaries

Body composition
↑Sexual desire



Skin
Acne

Voice
↓Pitch

Muscle
↑Lean mass
↑Cross-sectional area
↑Bodyweight
↑Grip strength

Blood pressure
↑Systolic blood pressure

Blood
↑Hemoglobin and hematocrit

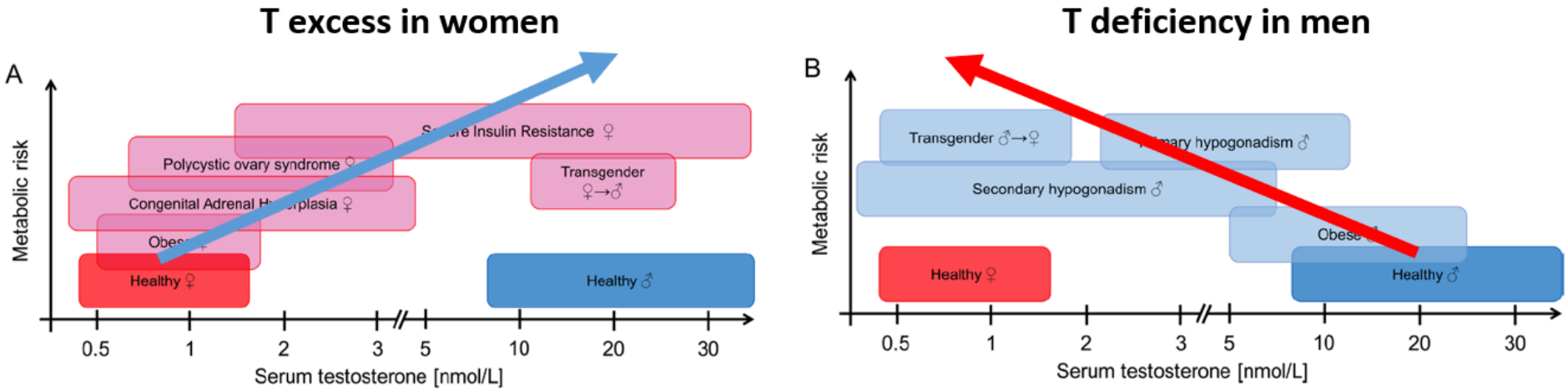
Lipids and metabolism
↓HDL cholesterol
↑Triglycerides
↓Sex hormone-binding globulin

Hormone concentrations
↓Estradiol
↓Luteinising hormone
↓Follicle-stimulating hormone
↓Prolactin

Testosteron

T'Sjoen et al Endocr Rev 2019

Stufe 2: Testosteron und Metabolismus



Sexually dimorphic associations between circulating testosterone levels and increasing metabolic risk. The estimated metabolic risk for different populations suffering from female androgen excess (Panel A) or male androgen deficiency (Panel B) is shown in relation to testosterone levels. Serum testosterone concentrations of women with androgen excess and men with androgen deficiency overlap and are associated with severe adverse metabolic consequences
Schiffer et al. EJE 2017

Erwartete Wirkungen der Stufe 2 Hormontherapien

MtF

Effect of oestrogen	Onset	Maximum	Reversibility
Redistribution of body fat	3-6 months	2-3 years	Likely
Decrease in muscle mass and strength	3-6 months	1-2 years	Likely
Softening of skin and decreased oiliness	3-6 months	unknown	Likely
Decreased libido	1-3 months	3-6 months	Likely
Decreased spontaneous erections	1-3 months	3-6 months	Likely
Breast growth	3-6 months	2-3 years	Not possible
Decreased testicular volume	3-6 months	2-3 years	Unknown
Decreased sperm production	Unknown	> 3 years	Unknown
Decreased terminal hair growth	6-12 months	>3 years	Possible
Scalp hair	Variable		
Voice changes	None		

FtM

Effect of testosterone	Onset	Maximum	Reversibility
Skin oiliness and acne	1-6 months	1-2 years	Likely
Facial and body hair growth	6-12 months	4-5 years	Unlikely
Scalp hair loss	6-12 months		Unlikely
Increased muscle mass and strength	6-12 months	2-5 years	Likely
Fat redistribution	1-6 months	2-5 years	Likely
Cessation of menses	1-6 months		Likely
Clitoral enlargement	1-6 months	1-2 years	Unknown
Vaginal atrophy	1-6 months	1-2 years	Unknown
Deepening of voice	6-12 months	1-2 years	Not possible

Empfohlene Kontrollen von Hormontherapien (Stufe 1 und 2)

Table 2. Monitoring during pubertal suppression and during cross-sex hormone treatment*

A. Pubertal suppression	
Measure	Frequency
1. Physical exam: height, weight, Tanner staging	T 0 & q 3 mo
2. Hormonal studies: ultrasensitive LH, FSH, estradiol/testosterone	T 0 & q 3 mo
3. Metabolic: Ca, phos, alk phos, 25-OH vitamin D (see also ref. 3)	T 0 & q 1 yr
4. Bone density: DEXA	T 0 & q 1 yr
5. Bone age	T 0 & q 1 yr
B. Cross-sex hormone treatment in previously suppressed patients or in late pubertal patients not previously suppressed	
Measure	Frequency
1. Physical exam: height, weight, Tanner staging, BP (for FTM, in particular); monitor for adverse reactions	T 0 & q 3 mo**
2. Hormonal studies: ultrasensitive LH, FSH, estradiol/testosterone	T 0 & q 3 mo**
If MTF: Also monitor prolactin	T 0 & q 1 yr
3. Metabolic: Ca, phos, alk phos, 25-OH vitamin D, complete blood count, renal & liver function, fasting lipids, glucose, insulin, glycosylated hemoglobin	T 0 & q 3 mo**
If MTF on spironolactone: serum electrolytes (potassium)	T 0 & q 3 mo**
4. Bone density: DEXA (if puberty previously suppressed)	T 0 & q 1 yr***
5. Bone age (if puberty previously suppressed)	T 0 & q 1 yr***

LH, luteinizing hormone; FSH, follicle stimulating hormone; DEXA, dual-energy X-ray Absorptiometry; BP, blood pressure; FTM: female-to-male; MTF, male-to-female; q, every.
*Modified from reference 4; **q 3–12 months after 1st year; ***Until puberty is completed.
Adapted from Rosenthal SM. J Clin Endocrinol Metab 2014;99:4379-89, with permission of .the Endocrine Society[16].

Rosenthal apem 2016

Transgender Medizin und Chirurgie (Stufe 3)

- Vaginalplastik, Clitoris OPs
- Phalloplastik, Skrotum Plastik
- Brust /Thorax Formung
- Mastektomie
- Feminisierende Gesichtseingriffe
- Trachea Shaving
- Hysterektomie, Oovorektomie, Vaginectomy
- Orchiectomy
- Etc.

Nicht <18 Jahren (in Bern)

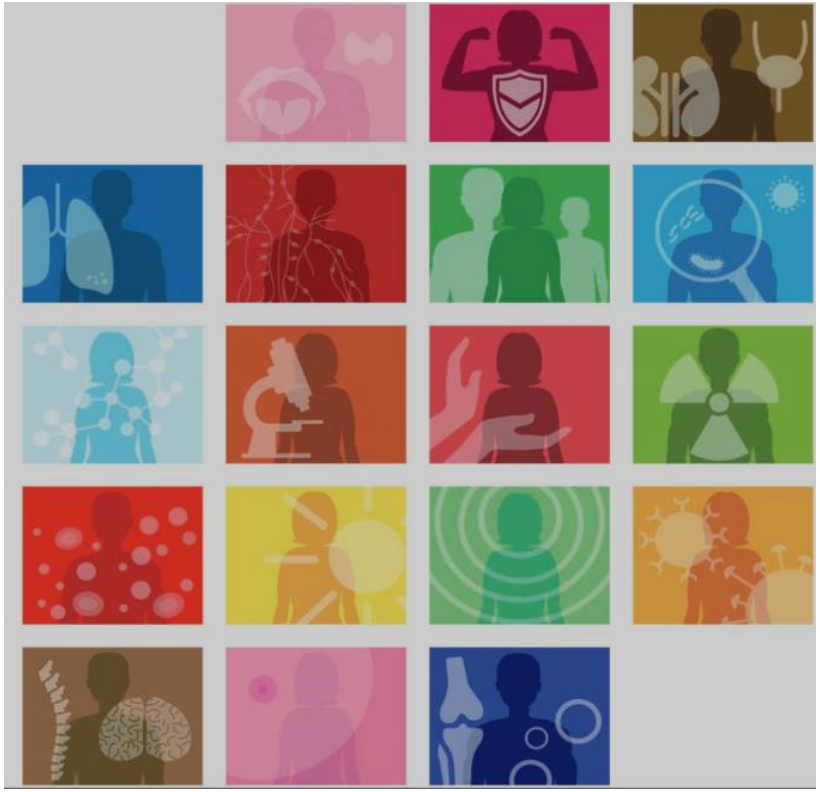
Cave: IRREVERSIBEL

Nebenwirkungen und Langzeitfolgen

- Hormonentzugssymptome (Flush, Stimmungsschwankungen)
- Wachstumsbeeinflussung (Länge, Gewicht, BMI, Body Composition und Body Shape)
- Beeinflussung der Pubertätsentwicklung und der Fertilität
- Beeinflussung der Hirnentwicklung in der Adoleszenz mit psychologischen und psychosozialen Folgen
- Wirkung auf das Skelett
- Auswirkungen auf Blutdruck, Gerinnung, Lipide und die kardiovaskuläre Gesundheit
- Tumor Risiko Profil
- UND? - Vieles ist noch unklar, v.a. Langzeitfolgen

PRIMUM NON NOCERE

Ein paar Studien



GAHT Ameliorates Depression and Suicid Risk

Journal of Adolescent Health 70 (2022) 643–649

ELSEVIER

JOURNAL OF ADOLESCENT HEALTH
www.jahonline.org

Original article

Association of Gender-Affirming Hormone Therapy With Depression, Thoughts of Suicide, and Attempted Suicide Among Transgender and Nonbinary Youth

Amy E. Green, Ph.D. *, Jonah P. DeChants, Ph.D., Myeshia N. Price, Ph.D., and Carrie K. Davis, M.S.W.
The Trevor Project, West Hollywood, California

- Online Umfrage in US
- Oktober bis Dezember 2020
- LGBTQ Gruppe, Alter 13-24 Jahre
- N=11’914 Trans und Nonbinary

Resultate:

14% erhielten GAHT

50% wollten GAHT, erhielten sie nicht

36% wollten keine GAHT

Multivariate adjusted logistic regression of gender-affirming hormone therapy on depression and suicidality among transgender and nonbinary youth

	Overall sample		Ages 13–17	
	aOR (95% CI)	*p*-value	aOR (95% CI)	*p*-value
Depression	0.73 (0.61–0.88)	<.001	0.61 (0.43–0.86)	<.01
Seriously considered suicide	0.74 (0.62–0.88)	<.001	0.74 (0.52–1.03)	.08
Attempted suicide	0.84 (0.66–1.07)	.16	0.62 (0.40–0.97)	.04

Adjusted for age, socioeconomic status, census region, gender identity, sexual orientation, race/ethnicity, parent support for gender identity, gender identity-based victimization, gender identity conversion efforts, and history of puberty blocker use.
aOR = adjusted odds ratio; CI = confidence interval.

Psychosocial outcome after 2 years GAH therapy

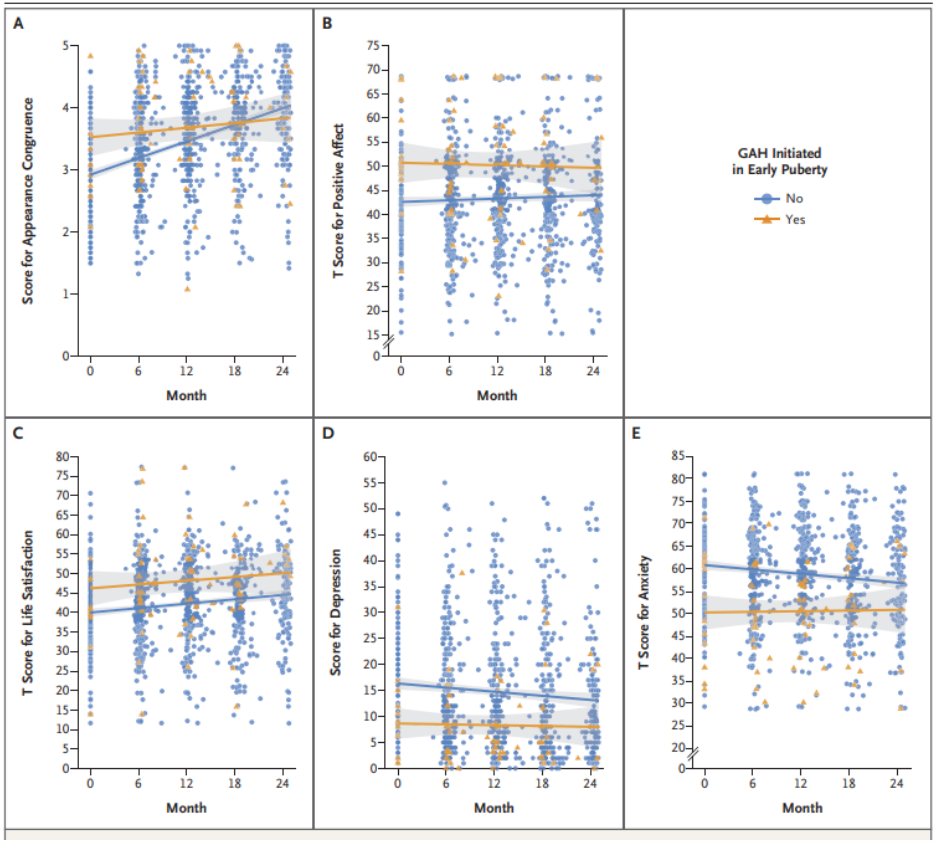


Table 2. Adverse Events.

Event	No. of Events in Sample
Any event	15
Death by suicide	2
Suicidal ideation reported during study visit	11
Severe anxiety triggered by study visit	2

Early puberty: Tanner 2 and 3
Late puberty: Tanner 4 and 5

Conclusion: …. despite improvement across psychosocial outcomes on average, there was *substantial variability* around the mean trajectory of change. Some participants continued to report high levels of depression and anxiety and low positive affect and life satisfaction, despite the use of GAH.

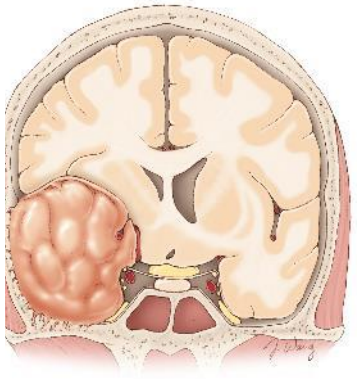
Chen et al. NEJM Jan 2023

Use of high dose cyproterone acetate increases the risk of intracranial mengioma in women: cohort study

Weill et al. BMJ 2021 (Retrospective study)

Take home message:

- A strong dose-effect relation was observed between use of cyproterone acetate and risk of intracranial meningiomas; typically located in the anterior and middle skull base.
- Analysis of transgender participants showed a high risk of meningioma
- A noticeable reduction in risk was observed after discontinuation of treatment.



Background and results

Background:

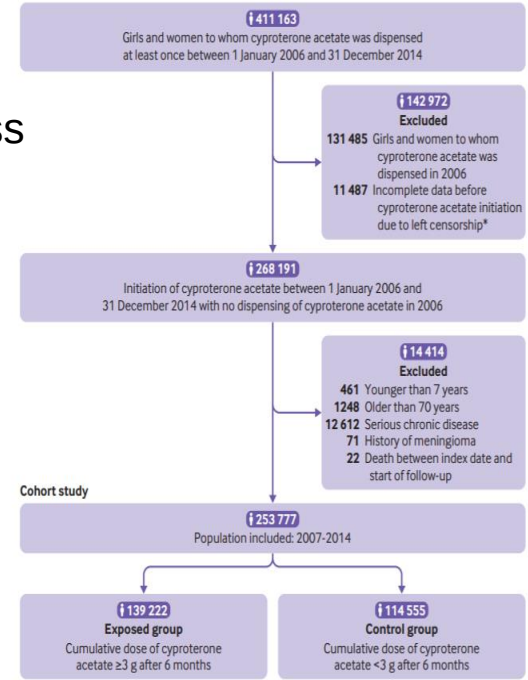
Cyproterone (C) acetate is a synthetic progestogen with strong antiandrogen and anti-gonadotrophin effects. Meningiomas express progesterone receptors. High doses of C may be used in MtF transgender persons for long(er) periods.

Results:

Table 3 | Incidence, relative risk, and adjusted hazard ratio of meningioma according to exposure to cyproterone acetate (main cohort, 2007-14; n=253 777)

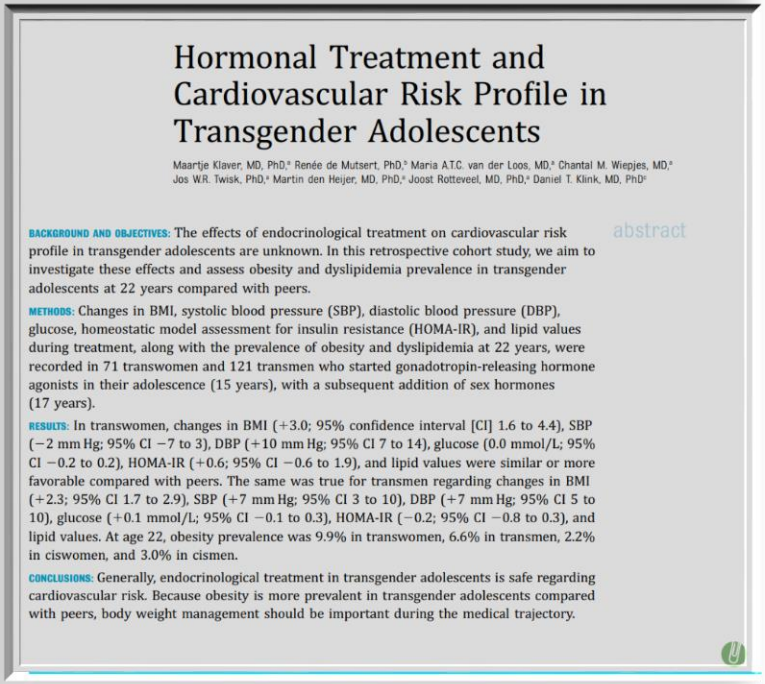
Drug use	Person years	No of meningiomas	Incidence per 100 000 person years	Relative risk (95% CI)	Adjusted hazard ratio (95% CI)*
Control group (<3 g)	439 949	20	4.5	Reference	Reference
Exposed (≥3 g)	289 544	69	23.8 ⬇ x5	5.2 (3.2 to 8.6)	6.6 (4.0 to 11.1)
Cumulative dose (g):					
≥3 to <6	53 744	2	3.7	0.8 (0.2 to 3.5)	1.1 (0.3 to 4.9)
≥6 to <12	79 202	6	7.6	1.7 (0.7 to 4.1)	2.2 (0.9 to 5.6)
≥12 to <36	115 594	30	26.0	5.7 (3.2 to 10.1)	6.4 (3.6 to 11.5)
≥36 to <60	29 390	16	54.4	12.0 (6.2 to 23.1)	11.3 (5.8 to 22.2)
≥60	11 615	15	129.1	28.4 (14.5 to 55.5)	21.7 (10.8 to 43.5)

*Adjustment for age as time dependent variable and oestrogens as binary variable on inclusion.



Weill et al. BMJ 2021

Late Effects of Hormonal Treatment on CV Outcome



Hormonal Treatment and Cardiovascular Risk Profile in Transgender Adolescents

Maartje Klaver, MD, PhD,[a] Renée de Mutsert, PhD,[b] Maria A.T.C. van der Loos, MD,[a] Chantal M. Wiepjes, MD,[a] Jos W.R. Twisk, PhD,[a] Martin den Heijer, MD, PhD,[a] Joost Rotteveel, MD, PhD,[a] Daniel T. Klink, MD, PhD[c]

abstract

BACKGROUND AND OBJECTIVES: The effects of endocrinological treatment on cardiovascular risk profile in transgender adolescents are unknown. In this retrospective cohort study, we aim to investigate these effects and assess obesity and dyslipidemia prevalence in transgender adolescents at 22 years compared with peers.

METHODS: Changes in BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), glucose, homeostatic model assessment for insulin resistance (HOMA-IR), and lipid values during treatment, along with the prevalence of obesity and dyslipidemia at 22 years, were recorded in 71 transwomen and 121 transmen who started gonadotropin-releasing hormone agonists in their adolescence (15 years), with a subsequent addition of sex hormones (17 years).

RESULTS: In transwomen, changes in BMI (+3.0; 95% confidence interval [CI] 1.6 to 4.4), SBP (−2 mm Hg; 95% CI −7 to 3), DBP (+10 mm Hg; 95% CI 7 to 14), glucose (0.0 mmol/L; 95% CI −0.2 to 0.2), HOMA-IR (+0.6; 95% CI −0.6 to 1.9), and lipid values were similar or more favorable compared with peers. The same was true for transmen regarding changes in BMI (+2.3; 95% CI 1.7 to 2.9), SBP (+7 mm Hg; 95% CI 3 to 10), DBP (+7 mm Hg; 95% CI 5 to 10), glucose (+0.1 mmol/L; 95% CI −0.1 to 0.3), HOMA-IR (−0.2; 95% CI −0.8 to 0.3), and lipid values. At age 22, obesity prevalence was 9.9% in transwomen, 6.6% in transmen, 2.2% in ciswomen, and 3.0% in cismen.

CONCLUSIONS: Generally, endocrinological treatment in transgender adolescents is safe regarding cardiovascular risk. Because obesity is more prevalent in transgender adolescents compared with peers, body weight management should be important during the medical trajectory.

PEDIATRICS Volume 145 (3), 2020:e20190741

(1) Body Composition and Markers of Cardiometabolic Health in Transgender Youth Compared With Cisgender Youth. Nokoff NJ, Scarbro SL, Moreau KL, Zeitler P, Nadeau KJ, Juarez-Colunga E, Kelsey MM. J Clin Endocrinol Metab. 2020, Mar 1; 105: e704-14; DOI 10.1210/clinem/dgz029, PMID 31544944.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7112978/

(2) Cardiometabolic Effects of Testosterone in Transmen and Estrogen Plus Cyproterone Acetate in Transwomen.van Velzen DM, Paldino A, Klaver M, Nota NM, Defreyne J, Hovingh GK, Thijs A, Simsek S, T'Sjoen G, den Heijer M. J Clin Endocrinol Metab. 2019, Jun 1; 104: 1937-47; DOI 10.1210/jc.2018-02138, PMID 30602016.
https://www.ncbi.nlm.nih.gov/pubmed/30602016

(3) Cardiovascular Disease Risk Factors and Myocardial Infarction in the Transgender Population. Alzahrani T, Nguyen T, Ryan A, Dwairy A, McCaffrey J, Yunus R, Forgione J, Krepp J, Nagy C, Mazhari R, Reiner J. Circ Cardiovasc Qual Outcomes. 2019, Apr; 12: e005597; DOI 10.1161/CIRCOUTCOMES.119.005597, PMID 30950651.
https://www.ncbi.nlm.nih.gov/pubmed/30950651

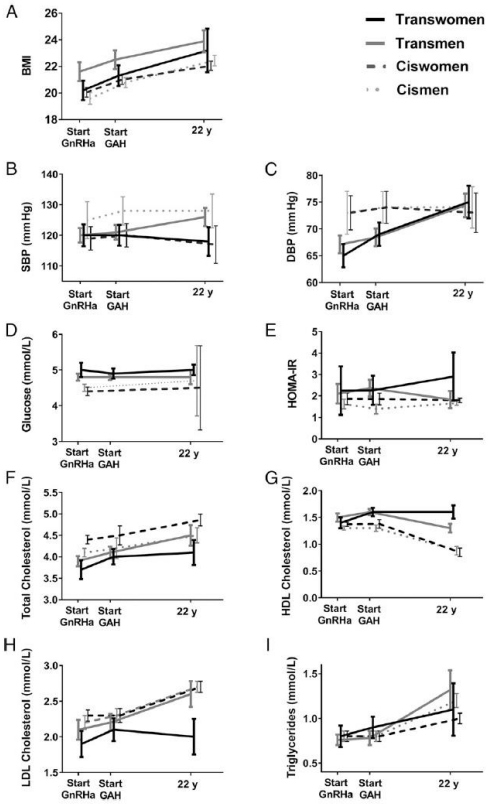
(4) Compromised endothelial function in transgender men taking testosterone. Gulanski BI, Flannery CA, Peter PR, Leone CA, Stachenfeld NS. Clin Endocrinol (Oxf). 2020, Feb; 92: 138-44; DOI 10.1111/cen.14132, PMID 31765022.
https://www.ncbi.nlm.nih.gov/pubmed/31765022

Study Subject Characteristics and Results: Cave Obesity

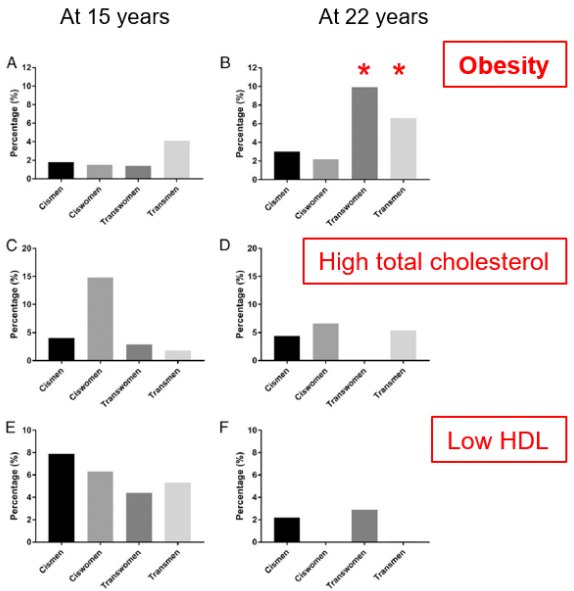
	Transwomen	Transmen
No.	71	121
Age at start of GnRHa treatment, y, mean (SD)	14.6 (1.8)	15.2 (2.0)
Age at start of GAH treatment, y, mean (SD)	16.4 (1.1)	16.9 (0.9)
Ethnicity white, %	98	94
Tanner stage at start, No.[a]		
T1	0	0
T2	6	3
T3	21	8
T4	6	26
T5	34	79
Menarche, %	—	84
Duration of GnRHa monotherapy, y, median (IQR)	2.1 (1.0–2.7)	1.0 (0.5–2.9)
Duration of GnRHa + GAH, y, median (IQR)	3.1 (2.5–3.6)	2.3 (1.8–2.8)
Duration GAH monotherapy, y, median (IQR)	2.2 (1.1–3.1)	2.9 (1.7–3.4)
E2 level at start of GnRHa treatment, pmol/L, median (IQR)	57 (36–81)	112 (64–219)
E2 level at start of GAH treatment, pmol/L, median (IQR)	25 (20–30)	28 (23–36)
E2 level at 22 y of age, pmol/L, median (IQR)	121 (81–154)	70 (43–135)
Testosterone Level at start of GnRHa treatment, nmol/L, median (IQR)	9.1 (3.7–14.0)	1.0 (1.0–1.3)
Testosterone Level at start of GAH treatment, nmol/L, median (IQR)	1.0 (1.0–1.0)	1.0 (1.0–1.0)
Testosterone Level at 22 y of age, nmol/L median (IQR)	1.0 (0.8–1.0)	16.0 (8.8–37.0)

IQR, interquartile range; —, not applicable.
[a] For 4 transwomen and 5 transmen, the Tanner stage at start was unknown.

MtF n=71
Ftm n=121
Total n=192



Age adjusted pravelence of:



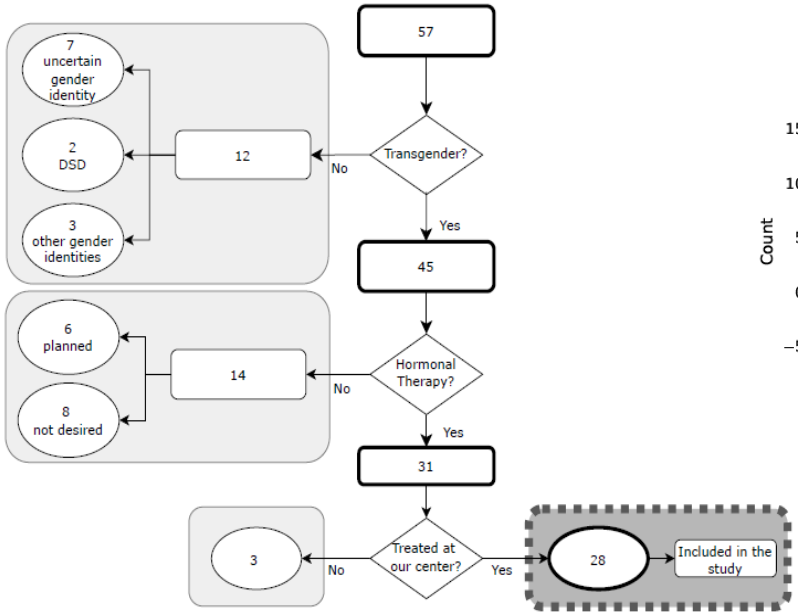
PEDIATRICS Volume 145 (3), 2020:e20190741

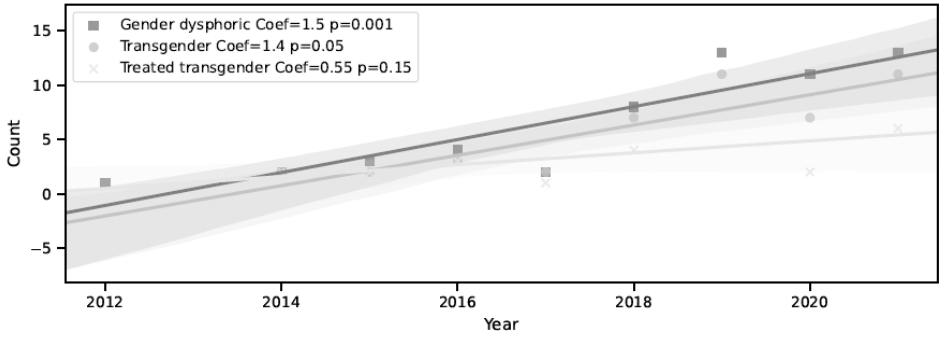
Overall Conclusion: GAHT Increases CV Risk

- ✓ Klaver et al show that puberty suppression and hormonal treatment in 192 Dutch transgender adolescents had no effect over time on blood pressure, insulin resistance and lipid profile, but young transgender persons were **more often obese** than cisgender peers.
- ✓ Findings from Nokoff et al (1) support these results showing that **body fat and lean tissue** of both 19 transgender male and 13 transgender female adolescents **under sex-affirming hormone treatment lies in between those of cisgender controls**.
- ✓ In transgender adults, **cardiovascular risk seems to increase mainly in transgender men undergoing testosterone treatment**: A prospective European multicenter study found unfavorable lipid profiles in 188 transmen after one year of hormone treatment (2), but not in transwomen. Endothelial function was impaired in 11 testosterone-treated US American transgender men, However transwomen were not studied (3). Finally, a cross-sectional study with a large random sample obtained from the US Centers for Disease Control and prevention (CDC) found that transgender women and men had a 2 and 4-fold increased odds for myocardial infarction compared to cisgender peers, after adjusting for age, race, chronic diseases and health behaviors (4).
- ✓ **Therefore, good weight management to lower obesity in the transgender adolescent population seems essential to improve cardiovascular health later in life; in particular in transgender men, who seem to be especially vulnerable to cardiovascular problems.**

Berner Erfahrungen der letzten 10 Jahre

Zuweisung wegen GD





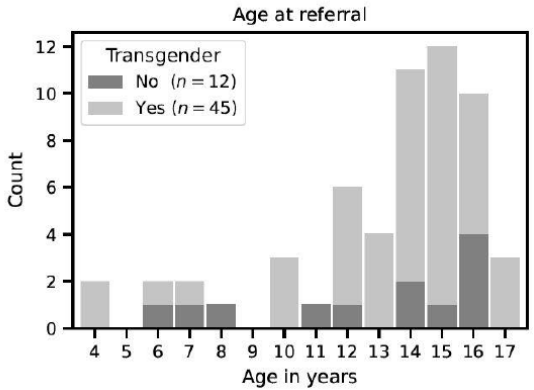
Diagnose durch Psych Team

Retrospektive, deskriptive Arbeit

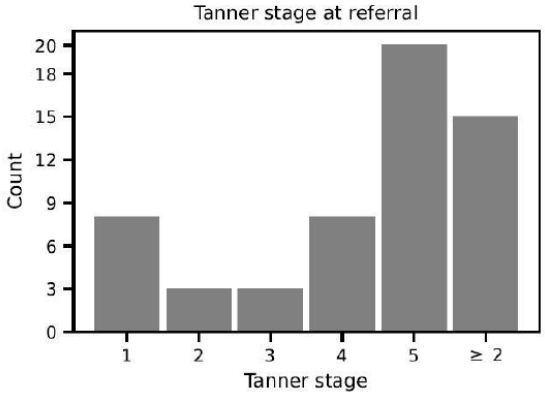
Mazzi et al. *In Revision*

Charakteristika der GD Gruppe

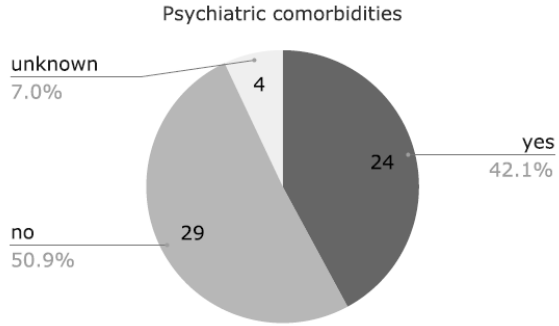
A.



B.

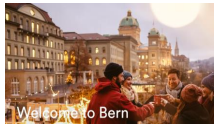


C.

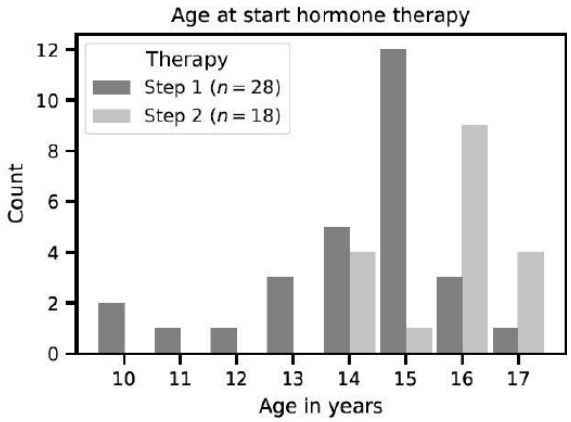


Mazzi et al. *In Revision*

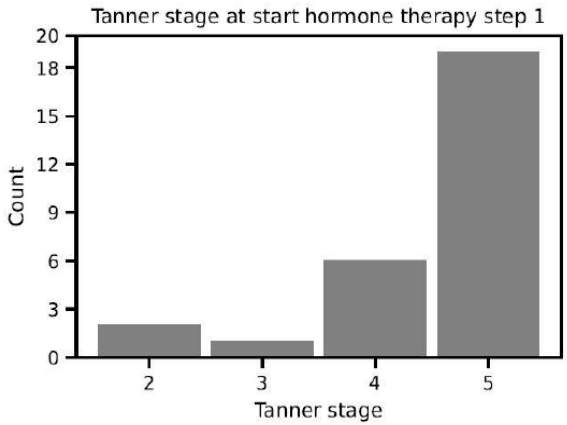
Charakteristika der hormonell therapierten Transgender



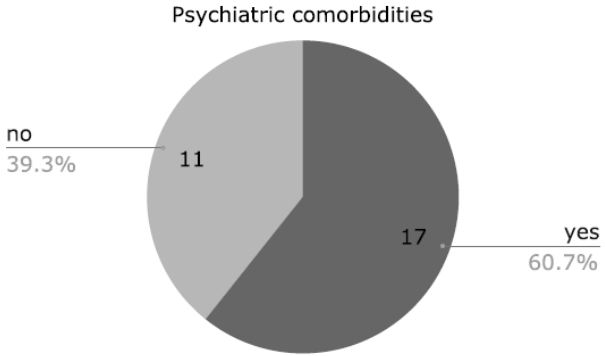
D.



E.



F.



- Our study confirms the trending rise of transgender youth seeking specialist care for the past decade.
- Offering hormonal treatments only under mental health care supervision, we found a high prevalence of psychiatric comorbidities that needed additional treatments.
- Therefore, we agree with current guidelines that hormonal treatments should only be offered to transgender youth after proper evaluation by specialized mental health care professionals.

Mazzi et al. *In Revision*

Aktuelle Probleme und Bedürfnisse

- Limitierte Langzeitdaten
- Fehlende Daten für frühe Interventionsgruppe (Tanner 2-3) und non-binäre Menschen
- Meist kleine Kohorten, cross-section Design

Es braucht deshalb ….

- Netzwerke unter Einbezug von Betroffenen
- Innovative und Patienten-zentrierte Langzeitstudien, randomisiert und kontrolliert

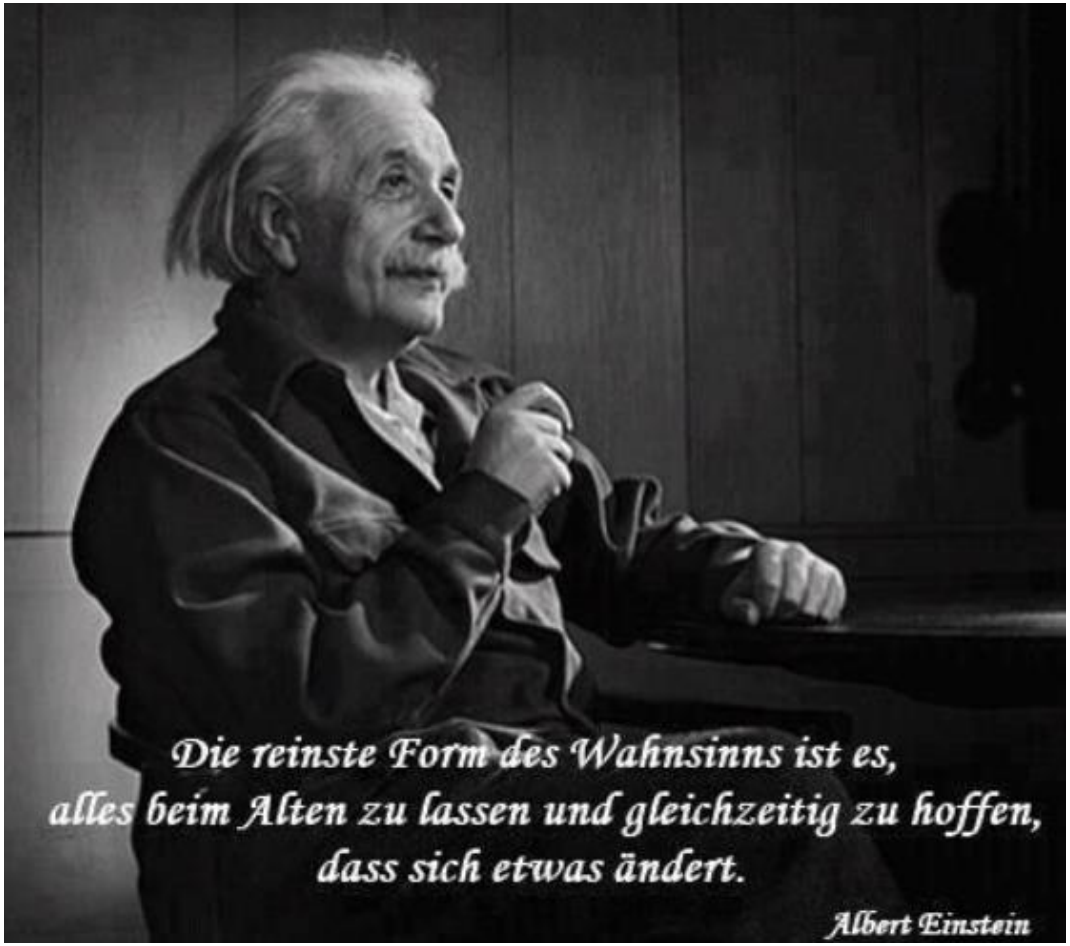
Ziel muss sein, Daten zur Sicherheit und Effizienz von hormonellen Therapien zu sammeln

Primum non nocere

Suizidalität
QoL

Somatische
Gesundheit

Body and Soul


Die reinste Form des Wahnsinns ist es,
alles beim Alten zu lassen und gleichzeitig zu hoffen,
dass sich etwas ändert.
Albert Einstein

(Why) is the indicence of gender dysphoria (GD) increasing?

Parent reports of adolescents and young adults perceived to show signs of a rapid onset of gender dysphoria

Lisa Littman *

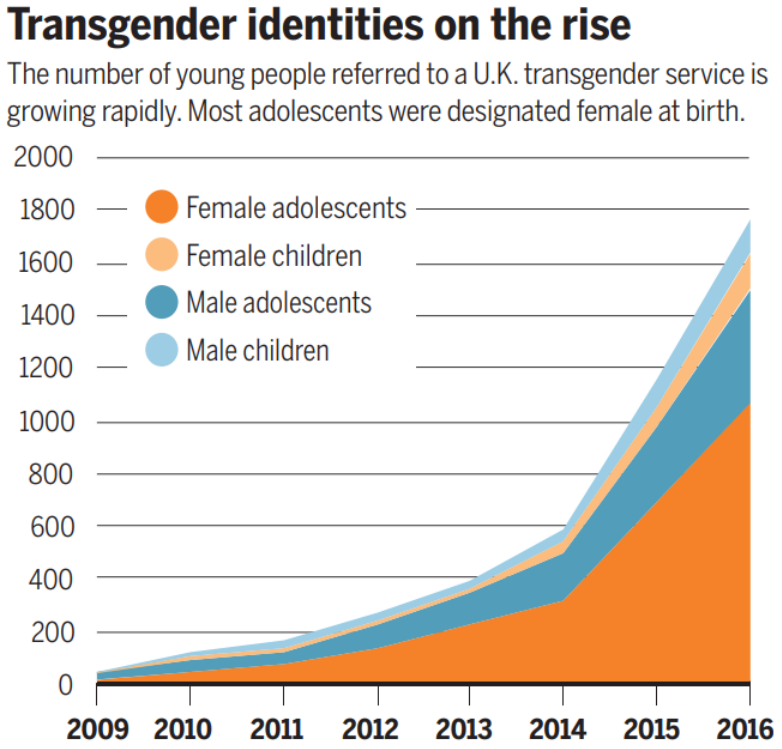
Department of Behavioral and Social Sciences, Brown University School of Public Health, Providence, Rhode Island, United States of America

Fact: A sharp and unexplained rise in GD has been observed woldwide in adolescents, especially in natal girls. Causes and outcome remain unknown.

Q: To find an explanation for the increase in sudden, rapid-onset GD in pubertal and postpubertal adolescents.

Web-based questionnaire for parents.
n=256

pone 2018



Rapid Onset Gender Dysphoria – a Hype?

Findings:

- Predominantly F (86%)
- Mean age at announcement of trans* identity: 15 years
- 40% mentioned before a non-heterosexual sex orientation
- 62% had at least one (1-7) mental health diagnosis or a neurodevelopmental disability
- 36% had trans* friends
- Parents reported a decline in parent-child relationship (57%) and mental health (42%) with the «coming out»
- Trans-identification went parallel to increased media/internet use and/or trans-identification of a peer group friend.

Littman's conclusions:

1) Not all young people presenting at these vulnerable ages are correct in their self-assessment of the cause of their GD symptoms.

2) Some young people may be seeking gender transition to escape other emotional difficulties.

SurveyMonkey

Table 1. **Characteristics of the identified Transgender subjects hormonally treated at our center** (n = 28) including information on their psychiatric comorbidities, if present (n=17). Age at hormonal treatment step 1 and 2 and anthropometric data of all 28 individuals are given in a summary list.

Mazzi et al. *submitted*

ID	Gender	Age 1st contact	Step 1							Step 2						Psychiatric comorbidities
			Age year	Tanner	Height cm	Height SDS	Weight kg	BMI kg/m²	BMI SDS	Age year	Height cm	Height SDS	Weight kg	BMI kg/m²	BMI SDS	
1	Transmale	15.7	15.7	5	160.4	-0.29	49.4	19.2	-0.52	17.43	161.1	-0.28	44.1	16.99	-1.93	D
2	Transfemale	12.9	11.8*	2	145.5	-1.26	33.9	16.01	-1.2	14.31	150.5	-1.78	37.7	16.64	-0.87	no
3	Transfemale	14.2	14.3	4	170.5	0.62	48.5	16.7	-1.24	14.96	171.5	0.22	53	18	-0.79	no
4	Transmale	12.8	12.9	5	161.5	0.95	62.9	24.1	1.48	n/a						no
5	Transmale	15.2	15.2	5	171.8	1.5	49.6	16.8	-1.59	17.08	173	1.56	54.4	18.2	-1.21	D, M
6	Transfemale	15.6	15.6	4	169.6	-0.22	85.4	29.7	2.17	n/a						no
7	Transmale	16.8	16.8	5	168.1	0.81	95.2	33.7	2.81	n/a						D
8	Transmale	14.8	15.0	5	167	0.88	54.4	19.5	-0.23	n/a						no
9	Transmale	14.1	14.1	5	162.5	0.38	48	18.2	-0.6	n/a						D
10	Transmale	10.0	10.4	2	143	0.44	40.5	19.8	0.92	14.04	160.4	-0.01	59	22.9	0.95	no
11	Transmale	14.6	14.7	5	169.5	1.23	57.5	20	0.1	16.1	169.7	1.1	63.6	22.1	0.48	D
12	Transfemale	14.5	14.5	4	166	0	53.95	19.6	0.02	n/a						no
13	Transmale	15.7	15.7	5	-		55	-	-	16.4	169.7	1.07	60.45	21	0.11	Asperger
14	Transmale	15.0	15.0	5	154.2	-1.14	43.3	18.2	-0.65	16.1	155.5	-1.09	55.6	23	0.69	D
15	Transmale	13.5	13.6	5	161.7	0.53	54.75	20.9	0.59	16.1	168.4	0.9	59.45	21	0.08	no
16	Transmale	14.9	15.1	4	161.9	0.07	45.8	17.5	-1.1	n/a						D
17	Transfemale	16.0	15.5*	5	186.6	1.94	55.2	15.9	-2.41	16.47	187.4	1.98	57	16.2	-2.26	Asperger
18	Transmale	10.3	10.3	3	153	1.82	39	16.7	-0.05	14.08	167	1.12	53.7	19.3	-0.12	ADHD
19	Transmale	15.0	15.0	5	161.2	-0.1	57	21.9	0.57	16.52	161.7	-0.16	56.9	21.8	0.34	D
20	Transmale	14.9	14.2*	5	160.7	-0.19	97.4	37.7	3.19	n/a						D
21	Transmale	13.2	13.4	5	157.1	-0.15	73.5	29.8	2	15.59	159	-0.51	74.85	29.6	1.76	D
22	Transfemale	15.5	15.7	4	181.5	1.09	48.3	14.6	-3.67	16.58	181.5	0.94	51	15.5	-3.08	Asperger
23	Transmale	13.8	13.9	4	144	-2.42	35.9	17.3	-0.78	16.68	151	-1.83	46.6	20.4	-0.14	D, M
24	Transmale	15.2	16.0	5	161.2	-0.2	67.55	26	1.45	17.55	161	-0.3	71.9	27.7	1.87	no
25	Transmale	17.2	17.2	5	180.5	2.7	71.4	21.9	0.27	n/a						no
26	Transmale	14.9	15.1	5	160.4	-0.17	48.3	18.8	-0.53	15.84	161.3	-0.15	46.7	17.9	-1.04	no
27	Transmale	15.5	15.6	5	167.9	0.88	85.45	30.3	2.28	17.4			97.1			D
28	Transmale	16.2	16.4	5	169.6	1.06	62.55	21.7	0.29	n/a						D

Transfemale (n = 6)	Median	15.0	15.0	4	170.0	0.3	51.2	16.3	-1.2	15.7	176.5	0.58	52.0	16.4	-1.56
	Range	(12.9;16.0)	(11.8;15.7)	(2;5)	(145.5;186.6)	(-1.26;1.94)	(33.9;85.4)	(14.6;29.7)	(-3.67;2.17)	(14.3;16.6)	(150.5;187.4)	(-1.78;1.98)	(37.7;57)	(15.5;18)	(-3.08;-0.79)
Transmale (n = 22)	Median	14.9	15.0	5	161.5	0.4	54.9	20.0	0.27	16.2	161.3	-0.15	57.9	21.0	0.11
	Range	(10.0;17.2)	(10.3;17.2)	(2;5)	(143;180.5)	(-2.42;2.7)	(35.9;97.4)	(16.7;37.7)	(-1.59;3.19)	(14.0;17.5)	(151;173)	(-1.83;1-56)	(44.1;97.1)	(17;29.6)	(-1.93;1.87)

* Therapy started external
Psychiatric comorbidities: 3 main categories: D: Depressions/Suicidal/Self-harm, A: ADHD/Asperger; M: mental disorders (ID 5 dissociative disorders, ID 23 unclear diagnosis)
SDS: standard deviations, calculated based on biological sex.
n/a: not applicable