



The year in review

ENDOCRINOLOGY

Defreyne Justine, MD, PhD
Ghent University Hospital, Belgium



11-13 AUGUST 2021
GOTHENBURG, SWEDEN

Topics

- Changes in physical features
- Changes in the lab
- Adverse events, side effects, safety
- Genetics
- Fertility
- Long(er) term results

Changes in physical features

- Anticipated changes
- Body composition
- Vaginal bleeding

Original Article: Clinical Investigation

What is the most anticipated change induced by treatment using gender-affirming hormones in individuals with gender incongruence?

Naoya Masumori,¹ Tsuyoshi Baba,² Teruo Abe³ and Koji Niwa⁴

Departments of ¹Urology and ²Obstetrics and Gynecology, Sapporo Medical University School of Medicine, Sapporo, ³Abe Mental Clinic, Urayasu, and ⁴Nagumo Clinic Osaka, Osaka, Japan

- Objectives: To identify **the most eagerly anticipated change** resulting from hormone therapy using gender-affirming hormones for patients with gender incongruence undergoing a clinical trial.
- Methods:
 - Transgender people seen at three institutions in Japan at the start of gender-affirming hormones
 - Question: what is the most anticipated change due to gender-affirming hormone (between giving informed consent and the first administration)
- Results:
 - 336 transgender men who were administered androgens and 48 transgender women who received estrogens
 - **Transgender men: cessation of menses** (52.7%) followed by a deepened voice (32.4%)
 - **Transgender women: breast development** (35.4%), followed by **gynoid fat deposition** (29.2%).
- Conclusions: **Cessation of menses** in transgender men and **breast development/gynoid fat deposition** in transgender women might represent primary end-points in clinical trials evaluating the efficacy of hormonal treatment in these patients.

Variation in sensitivity and rate of change in body composition: steps toward individualizing transgender care

Daan M van Velzen¹, **Nienke M Nota¹**, **Suat Simsek^{1,2}**, **Elfi B Conemans¹**,
Guy T'Sjoen^{3,4} and **Martin den Heijer¹**

¹Division of Endocrinology, Department of Internal Medicine, Amsterdam University Medical Center, Amsterdam, The Netherlands, ²Northwest Clinics, Department of Endocrinology, Alkmaar, The Netherlands, ³Department of Endocrinology, and ⁴Center for Sexology and Gender, Ghent University Hospital, Ghent, Belgium

Correspondence
should be addressed
to M den Heijer

Email
m.denheijer@vumc.nl

- Objective: To identify the **characteristics of a group of transgender individuals who report a lack of physical change during HT**
- Design and methods:
 - ENIGI
 - Body composition measures
 - 323 transmen and 288 transwomen
 - Absence of change was defined as transmen with a decrease in lean body mass or transwomen with a decrease in fat percentage.
- Results:
 - 19 of 94 (20.2%) transmen and in 9 of 96 (9.4%) transwomen had no change after 24 months
 - **TM: related to lower testosterone levels and less suppression of LH**
 - **TW: no association** with serum levels of sex steroids
- Conclusions:
 - The results provide a rationale for **individualizing hormone therapy** in transmen, by considering individual effects rather than solely relying on a standardized dosage of hormone therapy



Relationships between body mass index with oral estradiol dose and serum estradiol concentration in transgender adults undergoing feminising hormone therapy

Brendan J. Nolan, Adam Brownhill, Ingrid Bretherton, Peggy Wong, Susan Fox, Peter Locke, Nicholas Russell, Mathis Grossmann, Jeffrey D. Zajac and Ada S. Cheung 

- Aim: to assess if body mass index (BMI) correlated with estradiol dose/concentration and assess the correlation between estradiol dose and estradiol concentrations.
- Methods:
 - Retrospective cross-sectional study: transgender individuals attending a primary or secondary care clinic in Melbourne, Australia who were **prescribed oral estradiol valerate for at least 6 months** and had estradiol dose and concentration available.
 - Outcomes were the correlation between estradiol dose and BMI, and estradiol dose and estradiol concentration.
- Results:
 - 259 individuals {median age 25.8 [interquartile range (IQR) 21.9, 33.5] years}.
 - Median duration of estradiol therapy 24 (15, 33) months.
 - Median estradiol concentration 328 (238, 434) pmol/l [89 (65, 118) pg/ml] on 6 (4, 8) mg estradiol valerate.
 - Median BMI 24.7 (21.8, 28.6) kg/m².
 - **Weak positive correlation between estradiol dose and estradiol concentration ($r=0.156$, $p=0.012$).**

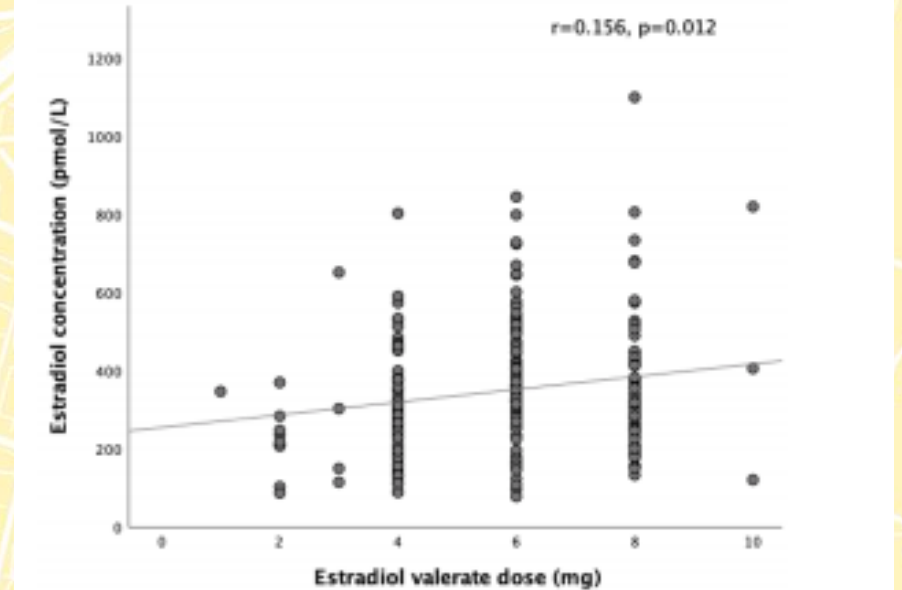


Figure 1. Correlation between estradiol valerate dose and estradiol concentration. BMI, body mass index.

- Results:

- **No correlation between BMI and estradiol concentration** achieved ($r = -0.063$, $p=0.413$) or **BMI and estradiol dose** ($r=0.048$, $p=0.536$).

- Conclusion:

- Estradiol dose weakly correlated with estradiol concentration, suggesting **significant interindividual variability**.
- Prescription of **estradiol dose should not be based upon an individual's BMI**

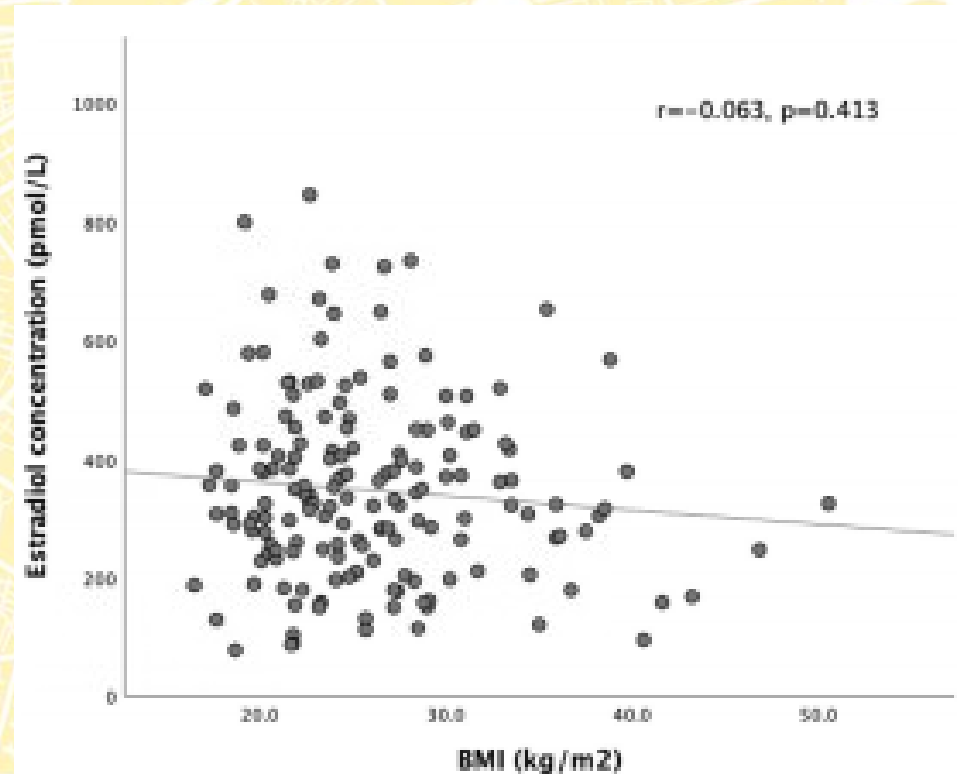
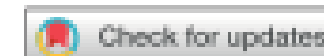


Figure 2. Lack of correlation between BMI and estradiol concentration.
BMI, body mass index.



Vaginal bleeding and spotting in transgender men after initiation of testosterone therapy: A prospective cohort study (ENIGI)

Justine Defreyne^{a*} , Yuran Vanwonderghem^{a*} , Sarah Collet^a, Sean J. Iwamoto^b , Chantal M. Wiepjes^c, Alessandra D. Fisher^d, Thomas Schreiner^e, Martin Den Heijer^f and Guy T'Sjoen^g

^aDepartment of Endocrinology, Ghent University Hospital, Ghent, Belgium; ^bDivision of Endocrinology, Metabolism & Diabetes, Department of Medicine, University of Colorado School of Medicine and Rocky Mountain Regional VA Medical Center, Aurora, Colorado, USA; ^cDepartment of Endocrinology and Center of Expertise on Gender Dysphoria, Amsterdam University Medical Center, VUmc, Amsterdam, The Netherlands; ^dDepartment of Experimental, Clinical and Biomedical Sciences, Andrology, Women's Endocrinology and Gender Incongruence Unit, University of Florence, Florence, Italy; ^eDepartment of Endocrinology, Oslo University Hospital, Oslo, Norway; ^fDepartment of Endocrinology and Center of Expertise on Gender Dysphoria, Amsterdam University Medical Center, VUmc, Amsterdam, The Netherlands; ^gDepartment of Endocrinology, Center for Sexology and Gender, Ghent University Hospital, Ghent, Belgium



11-13 AUGUST 2021
GOTHENBURG, SWEDEN

- Aim: To investigate the clinical effects of various testosterone preparations on vaginal bleeding and spotting in transgender men.
- Methods:
 - Prospective cohort study (ENIGI)
 - Data on the persistence and intensity of vaginal bleeding and spotting, serum sex steroid levels and body
 - 267 transgender men
 - Three-year follow-up period, starting at the initiation of various testosterone preparations.
- Results:
 - After three months of testosterone, **17.9% of transgender men reported persistent vaginal bleeding and 26.8% reported spotting.**
 - After twelve months: bleeding 4.7% and spotting 6.9%
 - **No participants reported vaginal bleeding or spotting after 18 months of testosterone.**

Changes in the lab

- Coagulation assays
- Liver enzymes



Volume 105, Issue 7
July 2020

Global Coagulation Assays in Transgender Women on Oral and Transdermal Estradiol Therapy

Hui Yin Lim ✉, Shalem Y Leemaqz, Niloufar Torkamani, Mathis Grossmann, Jeffrey D Zajac, Harshal Nandurkar, Prahlad Ho, Ada S Cheung






The Journal of Clinical Endocrinology & Metabolism, Volume 105, Issue 7, July 2020, Pages e2369–e2377, <https://doi.org/10.1210/clinem/dgaa262>

Published: 15 May 2020 **Article history ▼**

- Objective: To assess the global coagulation assay (GCA) profiles of transgender women in comparison to cisgender controls and to compare how GCA differ between routes of estradiol therapy in transgender women.
- Methods:
 - Cross-sectional case-control study.
 - Transgender women, cisgender male and cisgender female controls.
 - Citrated blood samples were analyzed for
 - (i) whole blood thromboelastography (TEG®5000)
 - (ii) platelet-poor plasma thrombin generation (calibrated automated thrombogram)
 - (iii) platelet-poor plasma fibrin generation (overall hemostatic potential assay)
- Results:
 - Twenty-six transgender women (16 oral estradiol, 10 transdermal estradiol) compared with 98 cisgender women and 55 cisgender men.
 - No differences in serum estradiol concentration ($P = 0.929$) and duration of therapy ($P = 0.496$) between formulations
 - **Transgender women vs cisgender men**
 - hypercoagulable parameters on both thromboelastography (maximum amplitude + 6.94 mm (3.55, 10.33); $P < 0.001$) and
 - increased overall fibrinolytic potential (+4.89% (0.52, 9.25); $P = 0.024$)
 - **Transgender women vs cisgender women**
 - No significant changes
 - Route of estradiol delivery or duration of use did not influence the GCA parameters.
- Conclusion: Transgender women on estradiol therapy demonstrated hypercoagulable GCA parameters compared with cisgender men with a shift towards cisgender female parameters. Route of estradiol delivery did not influence the GCA parameters.

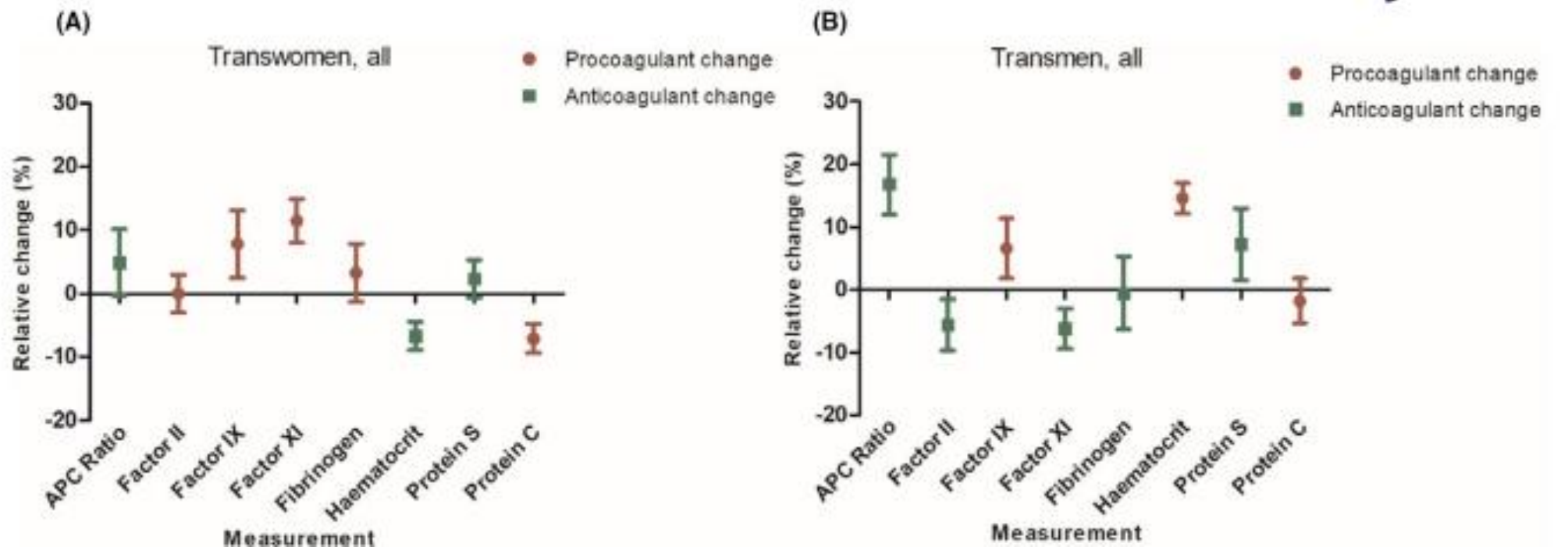
ORIGINAL ARTICLE

Effect of gender-affirming hormone use on coagulation profiles in transmen and transwomen

Luuk J.J. Scheres^{1,2}  | Nienke L.D. Selier^{3,4}  | Nienke M. Nota^{3,4}  |
Jeske J.K. van Diemen⁵ | Suzanne C. Cannegieter^{1,6}  | Martin den Heijer^{1,3,4} 

- Aims: To examine the effect of GAHT on coagulation parameters associated with venous thromboembolism (VTE) risk.
- Methods:
 - Factor (F)II, FIX, FXI, protein (p)C and free pS, fibrinogen, hematocrit, sex hormone-binding globulin, and normalized activated protein C ratio
 - 98 transwomen and 100 transmen before and after 12 months of GAHT (oral or transdermal estradiol and anti-androgens in transwomen, transdermal or intramuscular testosterone in transmen).

- Results:



- TW:
 - **More procoagulant profiles after GAHT** (increase in FIX: 9.6 IU/dL (95% CI 3.1–16.0) and FXI: 13.5 IU/dL (95% CI 9.5–17.5), and a decrease in pC: -7.7 IU/dL (95% CI -10.1 to -5.2))
 - **Influenced by route of administration (oral vs. transdermal) and age**
 - Higher sex-hormone binding globulin level after 12 months was associated with a lower activated protein C resistance
- TM:
 - changes were not procoagulant overall and were influenced by age
- **Conclusions:** GAHT in transmen was not associated with apparent procoagulant changes, which provides some reassurance regarding VTE risk. In transwomen, GAHT resulted in procoagulant changes, which likely contributes to the observed increased VTE risk.

Is there a need for liver enzyme monitoring in people using gender-affirming hormone therapy?

Theresa A Stangl¹, **Chantal M Wiepjes**¹, **Justine Defreyne**², **Elfi Conemans**¹,
Alessandra D Fisher³, **Thomas Schreiner**⁴, **Guy T'Sjoen**² and **Martin den Heijer**¹

¹Department of Internal Medicine, Division of Endocrinology, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands, ²Department of Endocrinology, Centre for Sexology and Gender, Ghent University Hospital, Ghent, Belgium, ³Department of Experimental, Clinical and Biomedical Sciences, Sexual Medicine and Andrology Unit, University of Florence, Florence, Italy, and ⁴Department of Endocrinology, Oslo University Hospital, Oslo, Norway

Correspondence
should be addressed
to M den Heijer

Email
[m.denheijer@
amsterdamumc.nl](mailto:m.denheijer@amsterdamumc.nl)


- Context: Different guidelines mention a severe risk of liver injury within the first months after the start of treatment with anabolic androgenic steroids, anti-androgens, and oral contraceptives, which is potentially fatal.
- Objective: **The incidence of liver injury** in a transgender population using gender-affirming hormone therapy.
- Methods:
 - Multicentre prospective study with 1933 transgender individuals, who started with hormone therapy between 2010 and 2020.
 - Analyses before hormone therapy, after 3 months, and after 12 months of hormone therapy
 - **Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyltransferase (GGT)**
 - Both male and female reference values were considered.
 - Liver injury was defined as either an elevation of 2× upper limit of normal (ULN) of ALP, 3× ULN of ALT, or 3× ULN of AST.

- Results:
 - 889 transgender women and 1044 transgender men
 - Liver injury incidence within 12 months after the start of hormone therapy (without attribution to alcohol abuse, medical history, or comedication):
 - TW 0.1% and 0.0% (F and M reference intervals respectively)
 - TM 0.6 and 0.4% (F and M reference intervals respectively)
- Conclusion: **The incidence of liver injury is found to be very low.** We, therefore, conclude that liver enzyme monitoring within the frame of the risk of liver injury due to hormone therapy is not necessary for a transgender population.

Adverse events, side effects, safety

- Insulin resistance
- Cardiovascular risk

Effects of Gender-Affirming Hormone Therapy on Insulin Sensitivity and Incretin Responses in Transgender People

Samyah Shadid¹ , Kessewa Abosi-Appadu¹, Anne-Sophie De Maertelaere¹, Justine Defreyne¹, Laurens Veldeman¹, Jens J. Holst³, Bruno Lapauw¹, Tina Vilsbøll⁴ **and** Guy T'Sjoen^{1,2}

 Author Affiliations

Corresponding author: Samyah Shadid, samyah.shadid@uzgent.be

K.A.-A. and A.-S.D.M. contributed equally to this work.

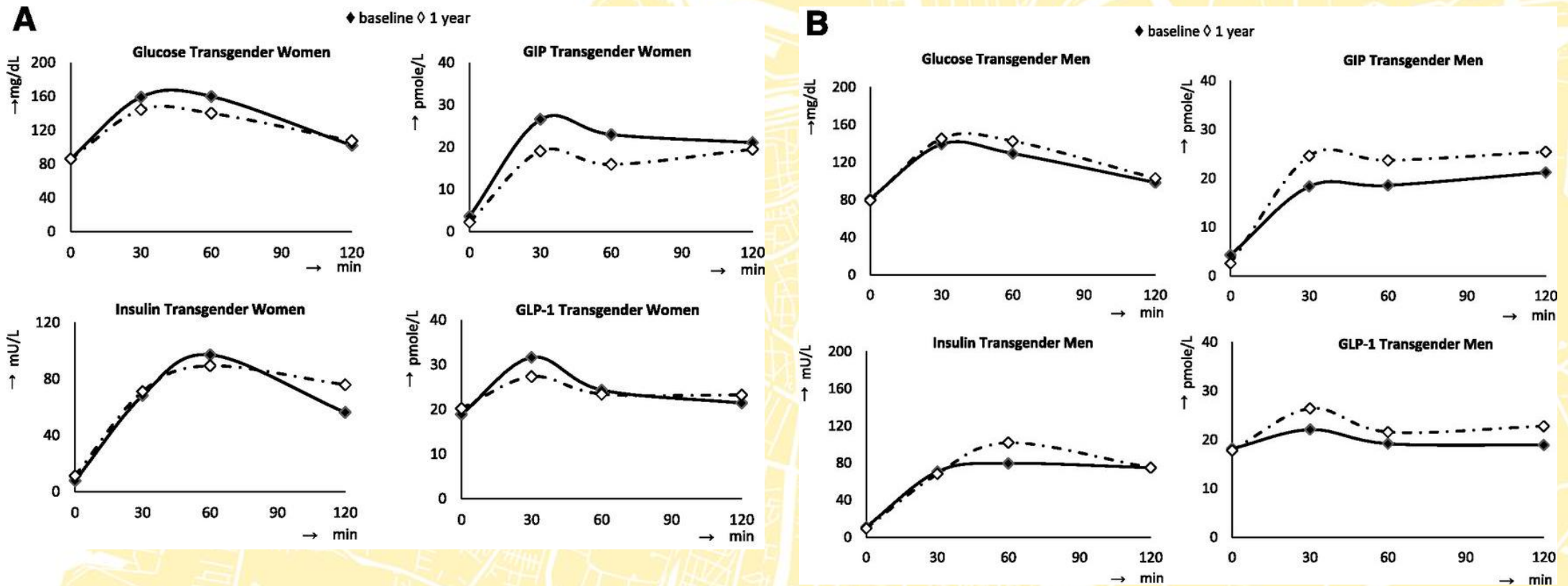
Diabetes Care 2020 Feb; 43(2): 411-417.

<https://doi.org/10.2337/dc19-1061>



Check for updates

- Aim: To assess long-term influences of sex hormone administration on insulin sensitivity and incretin hormones.
- Methods:
 - Prospective cohort: 35 transgender men (TM) and 55 transgender women (TW) before and after 1 year of gender-affirming hormone therapy
 - European Network for the Investigation of Gender Incongruence (ENIGI) study.
 - Body composition and oral glucose tolerance tests (OGTTs)
- Results:
 - TM
 - **Increased body weight (2.8 ± 1.0 kg; $P < 0.01$), fat-free mass (FFM) (3.1 ± 0.9 kg; $P < 0.01$), and waist-to-hip ratio (-0.03 ± 0.01 ; $P < 0.01$)**
 - Changes in glucose metabolism cfr next slide
 - TW
 - **Increased body weight (1.4 ± 0.8 kg; $P = 0.07$) with decreasing FFM (-2.3 ± 0.4 kg; $P < 0.01$) and waist-to-hip ratio (-0.03 ± 0.01 ; $P < 0.01$).**



CONCLUSIONS In this cohort of transgender persons, insulin sensitivity but also post-OGTT incretin responses tend to increase with masculinization and to decrease with feminization.



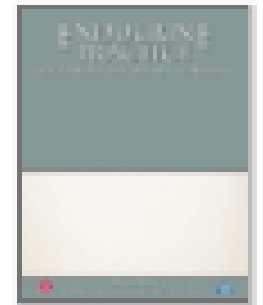
Access through UGent

[Purchase PDF](#)




Endocrine Practice

Volume 26, Issue 8, August 2020, Pages 883-890



Original Articles

Differential Endocrine and Metabolic Effects of Testosterone Suppressive Agents in Transgender Women

Yael Sofer MD ^{1, 2}, Iris Yaish MD ¹, Marianna Yaron MD ¹, Michal Yacobi Bach MD ¹, Naftali Stern MD ^{1, 2}, Yona Greenman MD ^{1, 2}  

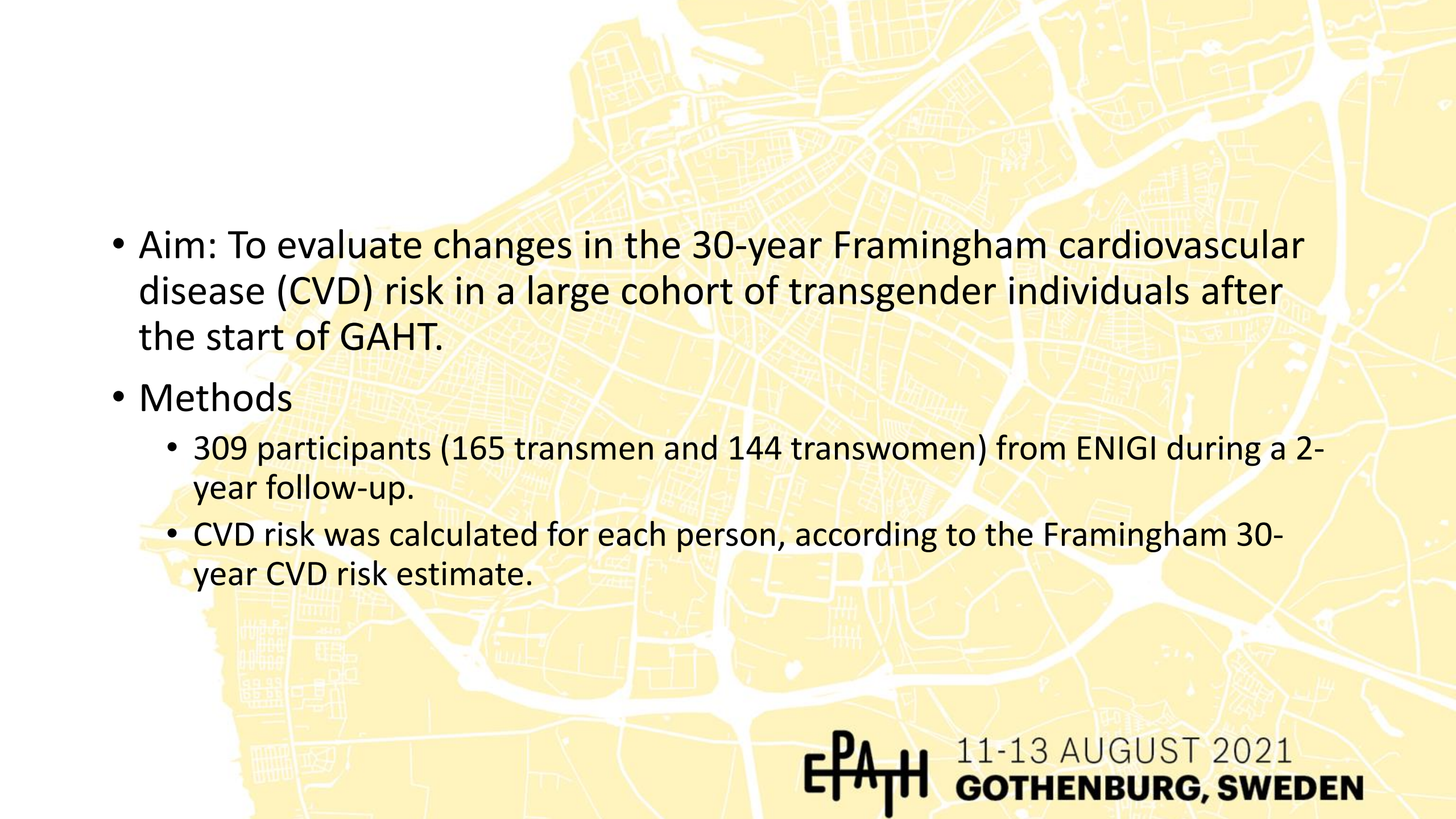
- Aim: to characterize possible differential effects of these compounds on metabolic and endocrine variables.
- Methods:
 - Historic cohort study of transgender people treated in a tertiary referral center.
 - A longitudinal analysis and a cross-sectional analysis at the last visit was carried out.
- Results:
 - 126 transgender women (75 treatment-naïve)
 - CPA was the predominant androgen suppressive therapy (70%), followed by spironolactone (17.6%), and GA (10.2%).
 - **Larger increase in serum prolactin levels after three months in those on CPA (compared to spironolactone or GA)**
 - **CPA: worse metabolic profile than with spironolactone or GA: lower HDL, higher BMI, systolic and diastolic BP**
- Conclusion: Treatment of transgender women with CPA was associated with **hyperprolactinemia and a worse cardiovascular risk profile** than treatment with spironolactone or GA.

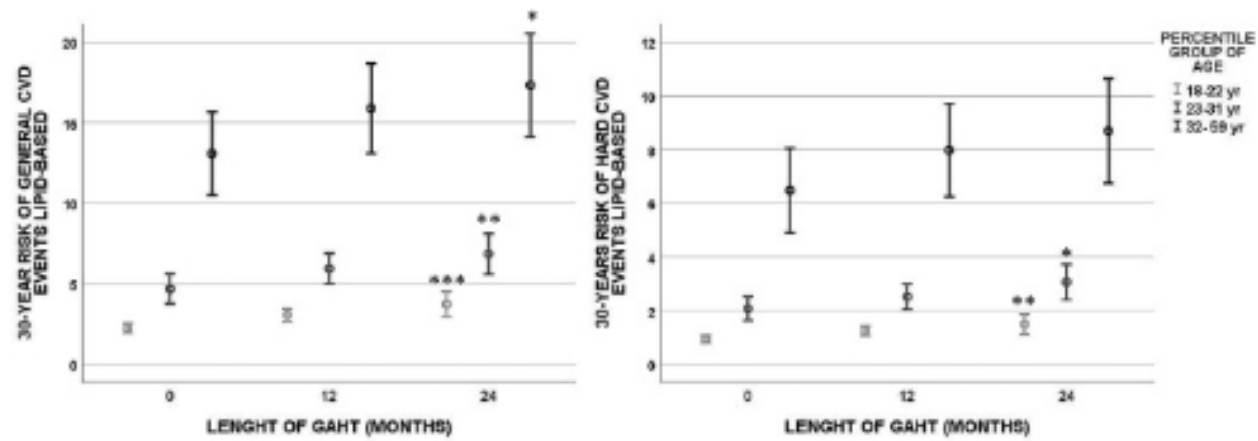
Original Research & Reviews

Transgender Health

Does Gender-Affirming Hormonal Treatment Affect 30-Year Cardiovascular Risk in Transgender Persons? A Two-Year Prospective European Study (ENIGI)

Carlotta Cocchetti MD¹, Giovanni Castellini MD, PhD², Davide Iacuanello MD³, Alessia Romani MD¹, Mario Maggi MD, PhD⁴, Linda Vignozzi MD, PhD¹, Thomas Schreiner MD⁵, Martin den Heijer MD, PhD⁶, Guy T'Sjoen MD, PhD⁷, Alessandra Daphne Fisher MD, PhD¹ ✉

- 
- A faint, yellow-toned map of Gothenburg, Sweden, serves as the background for the slide. It shows the city's layout with streets, water bodies, and green spaces.
- Aim: To evaluate changes in the 30-year Framingham cardiovascular disease (CVD) risk in a large cohort of transgender individuals after the start of GAHT.
 - Methods
 - 309 participants (165 transmen and 144 transwomen) from ENIGI during a 2-year follow-up.
 - CVD risk was calculated for each person, according to the Framingham 30-year CVD risk estimate.



Download : [Download high-res image \(259KB\)](#)

Download : [Download full-size image](#)

Figure 2. Changes in 30-years lipid-based risk of general and hard CVD events stratified for age in transmen, after the start of gender affirming hormonal treatment (GAHT). Transmen were stratified in tertiles according to age (N = 67 aged 18–22 years, N = 54 aged 23–31 years, N = 54 aged 32–59 years). *P < .05, **P < .005, ***P < .0001 across time.

• Results

• TW:

- A significant **decrease in triglycerides, total cholesterol and LDL-cholesterol** was observed during the 2-year follow-up
- No significant changes in general and hard CVD risk based on lipid profile were observed in transwomen over time.

• TM:

- **Increased total cholesterol, triglycerides, and LDL cholesterol** levels and decreased HDL cholesterol levels
- an increase in the risk of general and hard CVD events based on lipid profile over time

- **Conclusions:** unfavorable lipid changes in transmen after the start of GAHT even during a longer follow-up, empathizing the potential clinical impact of these modifications on individual long-term CVD risk.

The effect of transgender hormonal treatment on high density lipoprotein cholesterol efflux capacity

Daan M. van Velzen ^{a, 1}, Maria Pia Adorni ^{b, 1}, Francesca Zimetti ^c, Arianna Strazzella ^d, Suat Simsek ^{a, e}, Cesare R. Sirtori ^f, Martin den Heijer ^{a, 2}, Massimiliano Ruscica ^{f, 2}

- Aims:
 - Study the **ability of HDL to remove cholesterol** from arterial wall macrophages (cholesterol efflux capacity (CEC)),
 - Study the serum capacity to load macrophages with cholesterol (cholesterol loading capacity, CLC) = index of pro-atherogenic potential
- Methods
 - 15 TM, 15 TW at baseline and after 12 months of HT
 - In human THP-1 macrophages:
 - Total HDL-CEC from macrophages
 - ATP-binding cassette transporters (ABC): A1 and ABCG1 HDL-CEC
 - HDL-CEC by aqueous diffusion

- Results

- TW:

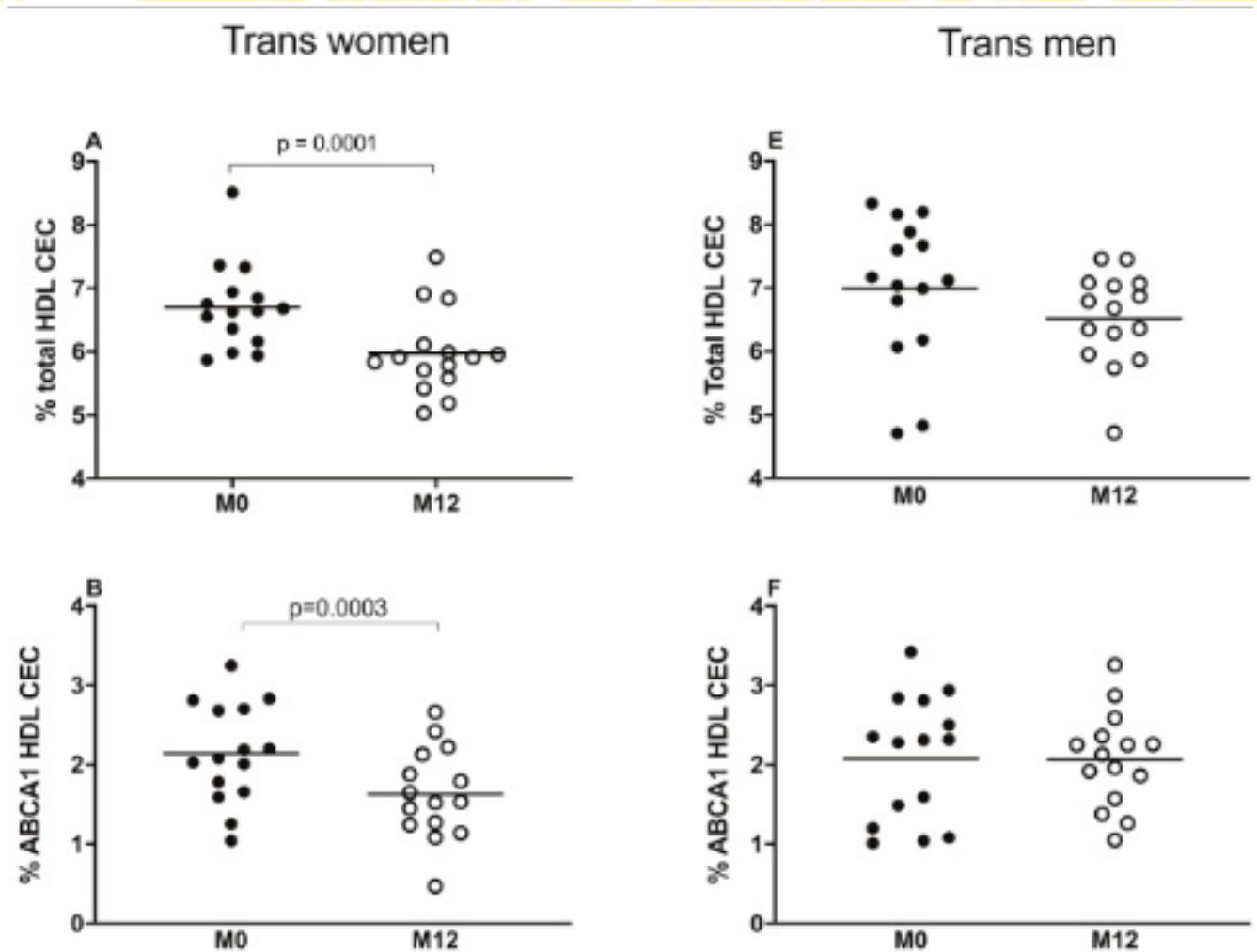
- Decrease in total HDL-CEC, ABCA1 HDL-CEC and aqueous diffusion HDL-CEC

- TM:

- Decrease in aqueous diffusion HDL-CEC
 - No change in ABCG1 HDL-CEC

- Conclusions:

Total HDL-CEC decreased during HT in trans women, with a specific reduction in ABCA1 CEC. **This finding might contribute to a higher CVD risk.**



Genetics





11-13 AUGUST 2021
GOTHENBURG, SWEDEN

Original Research & Reviews

Transgender Health

Gender-Affirming Hormone Therapy Modifies the CpG Methylation Pattern of the ESR1 Gene Promoter After Six Months of Treatment in Transmen

Rosa Fernández PhD^{1, 2}  , Karla Ramírez^{1, 2}, Esther Gómez-Gil MD³, Joselyn Cortés-Cortés PhD^{1, 2}, Mireia Mora MD⁴, Gloria Aranda MD⁴, Enrique Delgado Zayas^{1, 2}, Isabel Esteva MD⁵, Mari Cruz Almaraz MD⁵, Antonio Guillamon MD⁶, Eduardo Pásaro PhD^{1, 2}

- Aim: To analyze whether the **methylation of region III (RIII) of the ESR1 promoter** is involved in the biological basis of gender dysphoria.
- Methods
 - prospective study of the CpG methylation profile of RIII (–1,188 to –790 bp) of the ESR1 promoter
 - cisgender population (10 men and 10 women) and transgender population (10 trans men and 10 trans women), before and after 6 months of gender-affirming hormone treatment.
- Results
 - Sex differences in RIII methylation profiles in cisgender and transgender populations:
 - **Cismen showed a higher methylation degree than ciswomen** at CpG sites 297, 306, 509, and at the total fragment
 - Transmen showed a lower methylation level than trans women at sites 306, 372, and at the total fragment
 - Before the hormone treatment, transmen showed the lowest methylation level with respect to cisgender and transgender populations, whereas transwomen reached an intermediate methylation level between both the cisgender groups.
 - **After the hormone treatment, transmen showed a statistically significant methylation increase, whereas transwomen showed a non-significant methylation decrease.**
 - After the hormone treatment, the RIII methylation differences between transmen and transwomen disappeared, and **both transgender groups reached an intermediate methylation level between both the cisgender groups.**
- Conclusions
 - Sex differences in RIII methylation patterns in cisgender and transgender populations before the hormone treatment.
 - Hormonal treatment modified RIII methylation in trans populations, which are now more similar to their gender.
 - **Our results suggest that the methylation of RIII could be involved in gender dysphoria.**

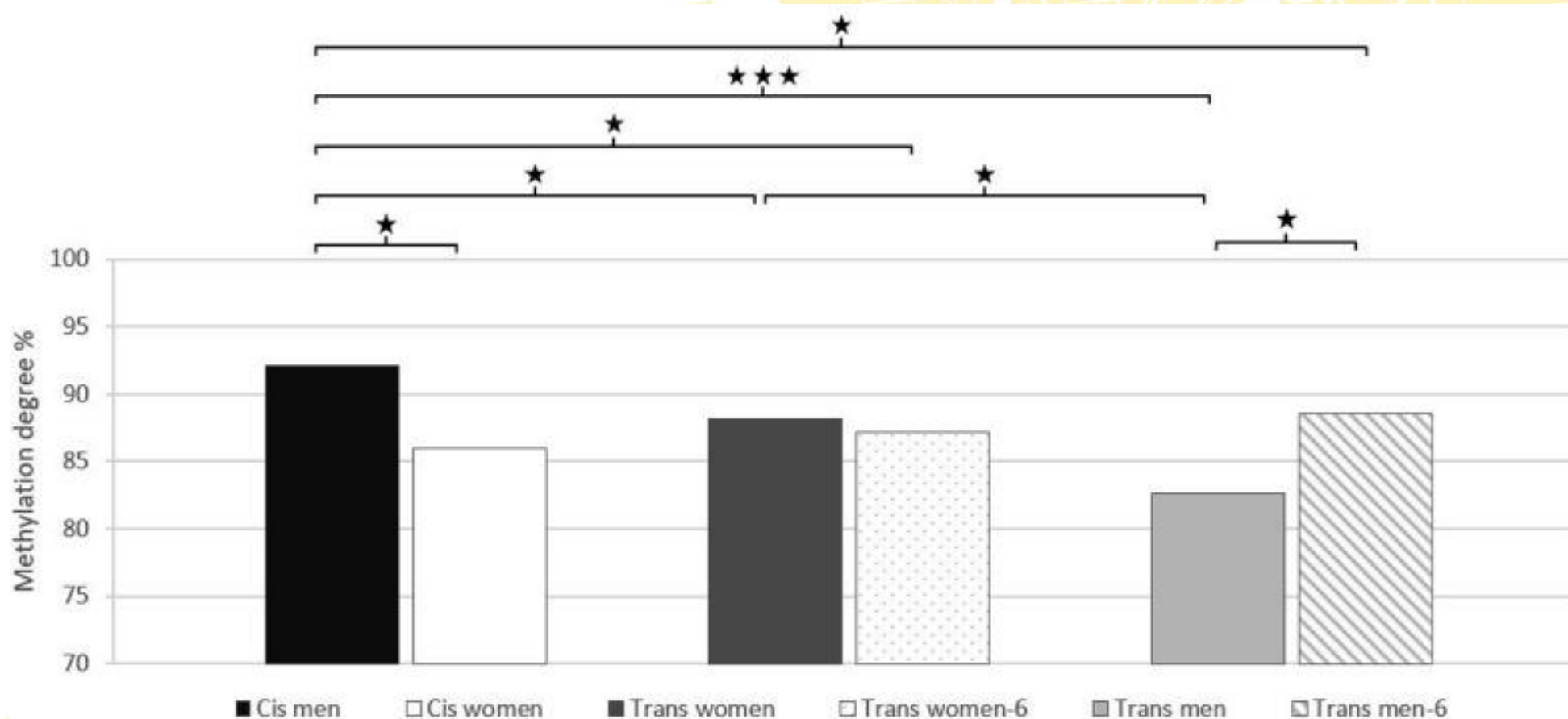






Figure 1. Global RIII methylation degree in the cisgender and transgender populations before and after gender-affirming hormone treatment.

Fertility

- Masculinizing HT
- Feminizing HT

ORIGINAL ARTICLE |  Open Access |   

Sperm quality in transgender women before or after gender affirming hormone therapy—A prospective cohort study

Kenny A. Rodriguez-Wallberg , Jakob Häljestig, Stefan Arver, Anna L. V. Johansson, Frida E. Lundberg

First published: 08 March 2021 | <https://doi.org/10.1111/andr.12999>

- Aim:
 - To assess sperm quality parameters of semen samples provided for FP by transgender women before or after GAHT
 - to compare sperm quality with a reference population of unscreened men defined by the World Health Organization (WHO)
 - to describe referral patterns over calendar time and estimate time from referral to semen cryopreservation.
- Methods:
 - Prospective cohort study of 212 transgender women referred for FP to the Reproductive Medicine Clinic of Karolinska University Hospital, Sweden, between 2013 and 2018.
 - Among 177 individuals that provided semen samples for cryopreservation, 16 had previously received GAHT.
- Results
 - Individuals **with previous GAHT presented with significantly lower total sperm count** than individuals without
 - Higher proportions of sperm abnormalities were also noted among individuals who had not undergone previous GAHT, compared to the WHO reference population ($p < 0.001$).
 - Referrals of transgender women for FP increased over time.
 - The median time from referral to semen cryopreservation was 27 days.
- Conclusions: A **high occurrence of sperm abnormalities** was found in transgender women, especially among individuals who had previously received GAHT. The results underline the importance of thoroughly discussing parenthood options and FP with patients early after diagnosis and referring the patients for semen banking preferably before starting GAHT.

Impaired semen quality in trans women: prevalence and determinants

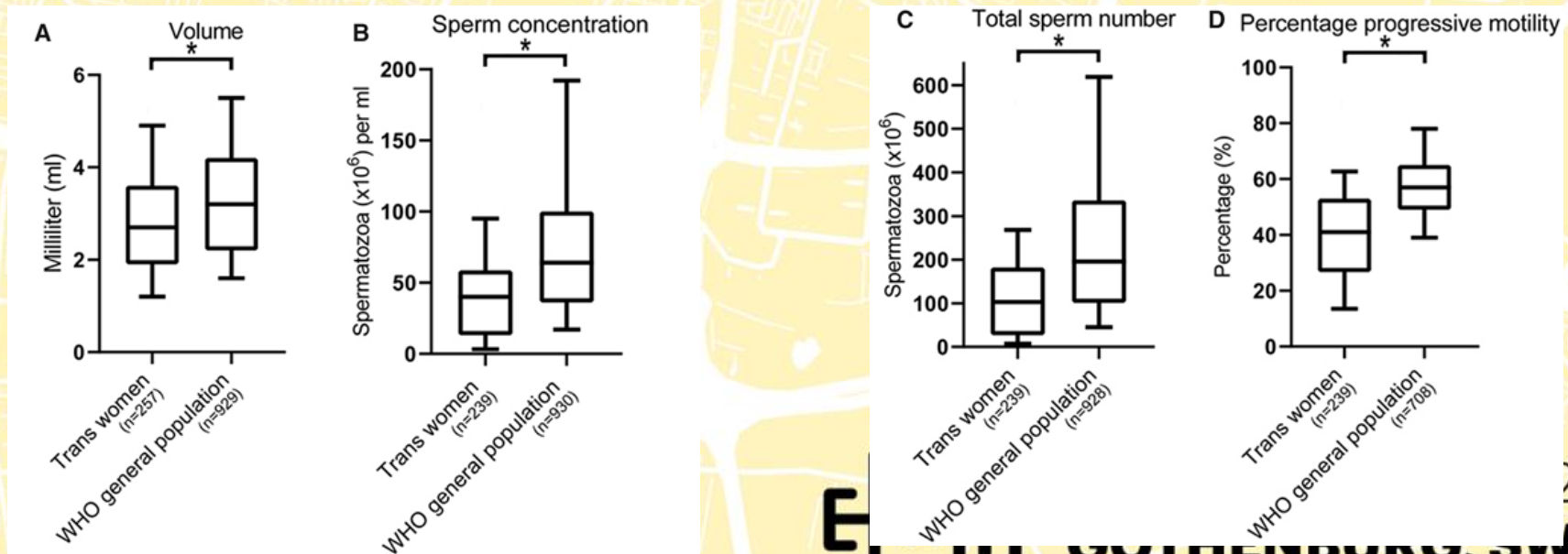
I de Nie , A Meißner, E H Kostelijk, A T Soufan, I A C Voorn-de Warem, M den Heijer, J Huirne, N M van Mello

Human Reproduction, Volume 35, Issue 7, July 2020, Pages 1529–1536,
<https://doi.org/10.1093/humrep/deaa133>

Published: 02 July 2020 **Article history** ▼

- Aim: What is the semen quality in trans women at time of fertility preservation, prior to the start of gender-affirming hormone treatment?
- Methods:
 - A retrospective cohort study was performed including 260 TW
 - Preserved semen in trans women, prior to their medical transition, who visited our gender clinic.
 - Semen parameters, age, alcohol consumption, smoking, cannabis use, BMI, previous use of estrogens or anti-androgens and endocrine laboratory results.
 - Semen parameters were categorized using reference values for human semen of the World Health Organization (WHO) and compared with data from the general population.

- Results:
 - **Semen quality in trans women was significantly decreased** compared to WHO data from the general population.
 - In total, 21 trans women had an azoospermia
 - No correlation was found between previous gender-affirming hormone use and decreased semen parameters.
 - In only 26.4% of thawed semen samples was the quality adequate for a minimally invasive IUI.
- Conclusions: **Semen quality in trans women was decreased compared to the general population**, which could not be explained by known risk factors. Since low pre-freeze semen quality results in an even lower post-thaw semen quality, the majority of trans women and their female partner or surrogate may need an invasive and burdensome treatment to establish a pregnancy.



Characterisation of testicular function and spermatogenesis in transgender women

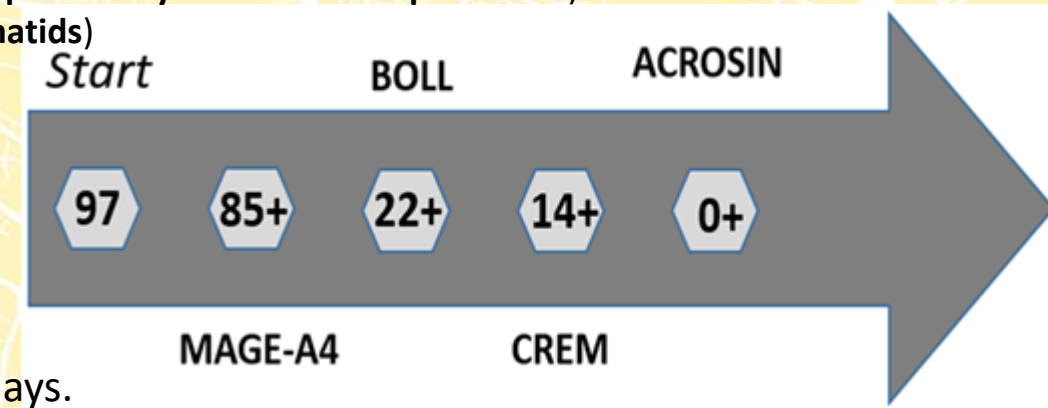
Gertjan Vereecke, Justine Defreyne ✉, Dorien Van Saen, Sarah Collet, Jo Van Dorpe, Guy T'Sjoen, Ellen Goossens [Author Notes](#)

Human Reproduction, Volume 36, Issue 1, January 2021, Pages 5–15,

<https://doi.org/10.1093/humrep/deaa254>

Published: 30 November 2020 **Article history ▼**

- Aim: Does gender-affirming treatment prevent full spermatogenesis in transgender women (TW)?
- Methods:
 - prospective cohort study part of ENIGI, subsample from Ghent
 - 97 TW who initiated HT with cyproterone acetate (CPA) plus oestrogens and proceeded with gonadectomy at the Ghent University Hospital
 - Testicular tissue retrieved during gonadectomy was processed and stained for four different germ cell markers:
 - melanoma-associated antigen A4 (MAGE-A4, marker **for spermatogonia and early spermatocytes**)
 - boule homologue, RNA-binding protein (BOLL, marker **for secondary spermatocytes and round spermatids**)
 - cAMP-responsive element modulator (CREM, marker **for round spermatids**)
 - acrosin (marker for **acrosome visualization**)
 - Serum levels of sex steroids were measured prior to surgery.
- Results:
 - Suppressed testosterone levels (<50 ng/dl) were found in 92% of the participants prior to surgery
 - The mean time between initiation of HT and surgery was 685 days.
 - In 88% (85/97) of the sections, MAGE-A4 staining was positive.
 - Further staining could not reveal complete spermatogenesis in any participant.
- Conclusions:
 - **HT leads to complete suppression of spermatogenesis in most TW**
 - **Serum testosterone levels are associated with the sperm maturation rate.**
 - **It is important to discuss sperm preservation before the start of hormone therapy.**





Original article




Low feasibility of in vitro matured oocytes originating from cumulus complexes found during ovarian tissue preparation at the moment of gender confirmation surgery and during testosterone treatment for fertility preservation in transgender men

Sylvia Lierman B.M.L.S.^a, Annelies Tolpe M.B.S.^a, Ilse De Croo M.B.S.^a, Stefanie De Gheselle M.B.^a, Justine Defreyne M.D., Ph.D.^b, Machteld Beetens M.B.S.^c, Annelies Dheedene Ph.D.^c, Roos Colman Ph.D.^d, Björn Menten Ph.D.^e, Guy T'Sjoen M.D.^b, Petra De Sutter M.D.^a, Kelly Tilleman Ph.D.^a 

- Aim: the feasibility of in vitro maturation of **ovarian tissue oocytes for fertility preservation in transgender men on testosterone treatment.**
- Methods:
 - Cross-sectional study, 83 transgender men presenting for gonadectomy at the Ghent University Hospital
 - In vitro maturation of cumulus-oocyte complexes (COCs) harvested at the time gonadectomy, and fertilization through ICSI.
- Result(s):
 - All participants were on testosterone treatment for a median of 83 (64[Quartile 1]; 113.2[Quartile 2]) weeks.
 - A total of 1,903 COCs (mean per participant, 23 ± 15.8) were collected.
 - The in vitro maturation rate was 23.8%
 - Vitrification rate was 21.5%
 - Survival rate after warming was 72.6% (n = 151)
 - **After ICSI, the rate of normal fertilized oocytes was 34.5%, and 25 (52.1%) embryos reached day 3. One blastocyst was achieved on day 5.**
 - A normal genetic pattern was seen in 42% embryos.
- Conclusion(s): Ovarian tissue oocytes matured in vitro show **low developmental capacity in transgender men, when collected under testosterone treatment.**

Long(er) term results

- Bone health
- Suicide risk

Original Article |  Open Access |  

Fracture Risk in Trans Women and Trans Men Using Long-Term Gender-Affirming Hormonal Treatment: A Nationwide Cohort Study

Chantal M Wiepjes, Christel JM de Blok, Annemieke S Staphorsius, Nienke M Nota, Mariska C Vlot, Renate T de Jongh, Martin den Heijer 

First published: 05 September 2019 | <https://doi.org/10.1002/jbmr.3862> | Citations: 12

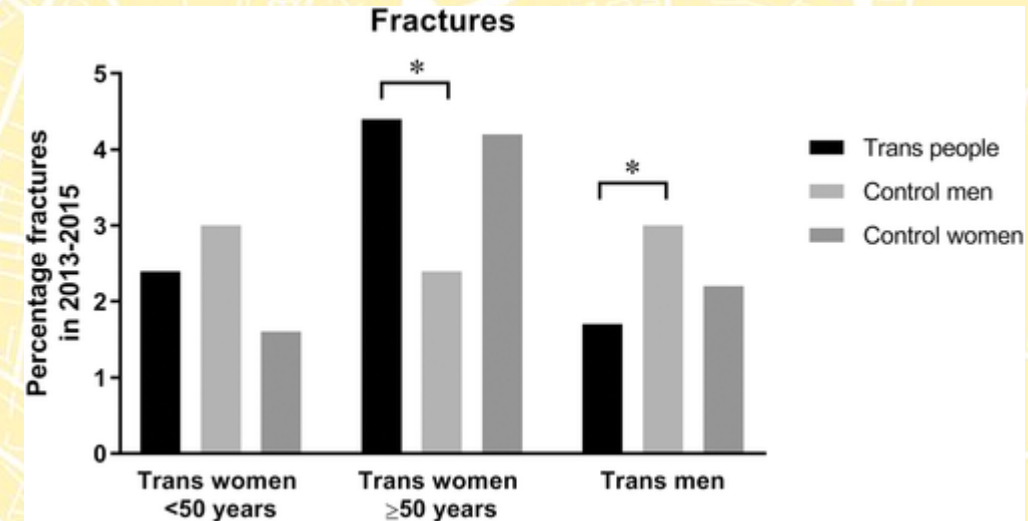
- Aim: to compare the fracture incidence in transgender people using long-term HT with an age-matched reference population.

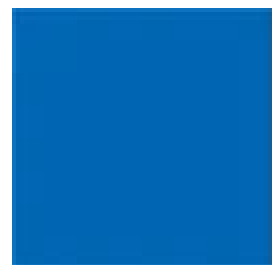
- Methods:


- Retrospective cohort study: all adult transgender people who started HT before 2016
 - linked to a random population-based sample of 5 age-matched reference men and 5 age-matched reference women per person
 - Fracture incidence was determined using diagnoses from visits to hospital emergency rooms nationwide between 2013 and 2015.

- Results:


- 1089 trans women aged <50 years, 934 trans women aged ≥50 years using HT for median 8 and 19 years, respectively, were included.). A total of 1036 trans men using HT for median 9 years were included.
 - 2,4% of TW <50 years had a fracture, 3.0% of the age-matched reference men (odds ratio [OR] = 0.78, 95% confidence interval [CI] 0.51–1.19) and 1.6% of the age-matched reference women (OR = 1.49, 95% CI 0.96–2.32) experienced a fracture.
 - **4.4% of TW >50 years had a fracture compared with 2.4% of the age-matched reference men (OR = 1.90, 95% CI 1.32–2.74), and 4.2% of the age-matched reference women (OR = 1.05, 95% CI 0.75–1.49)**
 - **Fractures occurred in 1.7% of the trans men, 3.0% of the age-matched reference men (OR = 0.57, 95% CI 0.35–0.94), and 2.2% of the age-matched reference women (OR = 0.79, 95% CI 0.48–1.30).**
- Conclusion: fracture risk was higher in older trans women compared with age-matched reference men. In young trans women, fracture risk tended to be increased compared with age-matched reference women. Fracture risk was not increased in young trans men.





Original Article |  Open Access |  

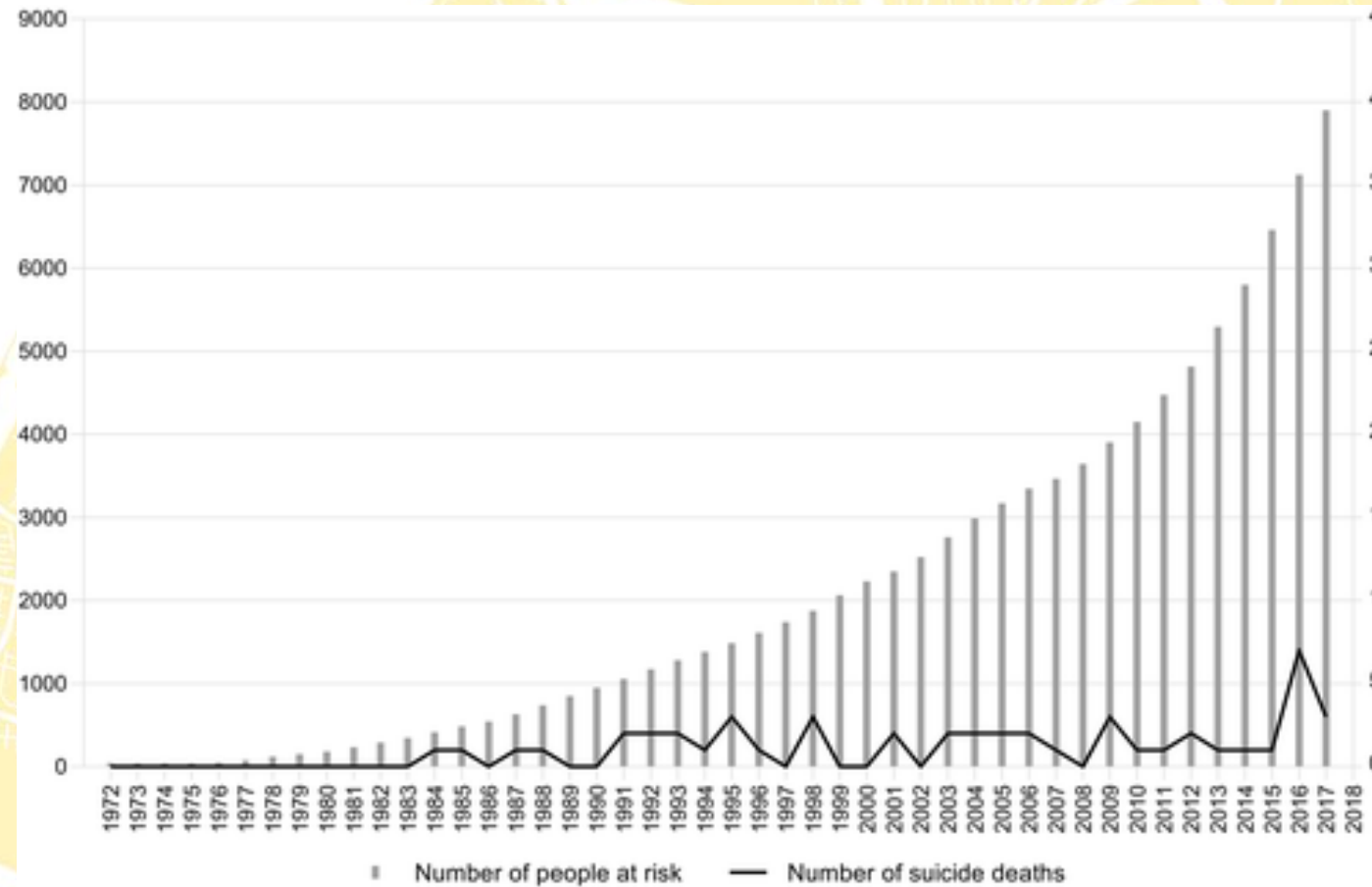
Trends in suicide death risk in transgender people: results from the Amsterdam Cohort of Gender Dysphoria study (1972–2017)

C. M. Wiepjes, M. den Heijer, M. A. Bremmer, N. M. Nota, C. J. M. de Blok, B. J. G. Coumou, T. D. Steensma 

First published: 18 February 2020 | <https://doi.org/10.1111/acps.13164> | Citations: 6

[Go here for SFX](#)

- Objective: To explore the overall suicide death rate, the incidence over time, and the stage in transition where suicide deaths were observed in transgender people.
- Methods:
 - A chart study with all 8263 referrals to our clinic since 1972.
 - Information on death occurrence, time, and cause of death was obtained from multiple sources.
- Results:
 - 5107 trans women (median age at first visit 28 years, median follow-up time 10 years) and 3156 trans men (median age at first visit 20 years, median follow-up time 5 years)
 - **41 trans women and 8 trans men died by suicide**
 - In trans women, suicide deaths decreased over time, while it did not change in trans men.
 - Of all suicide deaths, 14 people were no longer in treatment, 35 were in treatment in the previous two years.
 - **The mean number of suicides in the years 2013–2017 was higher in the trans population compared with the Dutch population.**



Conclusions: We observed **no increase in suicide death risk over time and even a decrease in suicide death risk in trans women**. However, the suicide risk in transgender people is higher than in the general population and seems to occur **during every stage of transitioning**. It is important to have specific attention for suicide risk in the counseling of this population and in providing suicide prevention programs.

Conclusion

