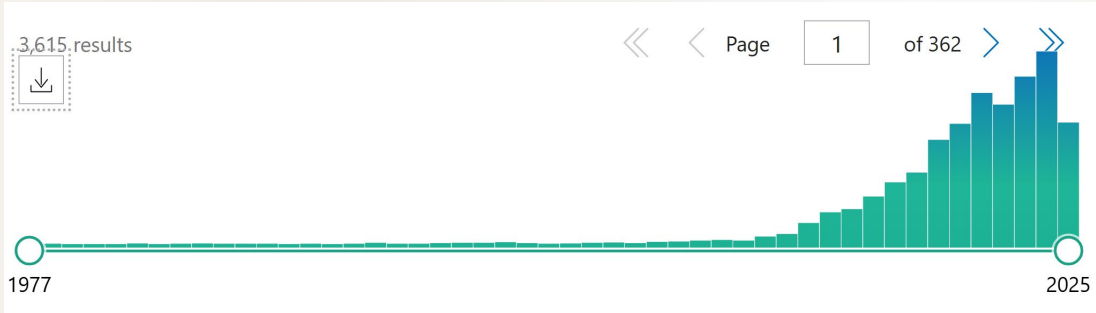
The Year in Review Endocrinology

Sabine Hannema, paediatric endocrinologist

Amsterdam UMC, the Netherlands

EPATH 4-6 SEPTEMBER 2025
HAMBURG, GERMANY

Literature review



Pubmed search

- **transgender OR "gender dysphor*" OR "gender incongru*" OR "gender diverse"**

AND

- **androgen OR estrogen OR testosterone OR estradiol OR hormon* OR "GnRH analog*" OR "puberty suppres*"**
- Published between 1st May 2023 and 1st July 2025

1140 results (14 RCT, 292 reviews)

Topics

- Efficacy of hormone treatment
- GAHT and the immune system
- GAHT and the heart
- GAHT and the kidney
- Longer term outcomes of GnRHa/GAHT in adolescents
  - GAHT continuation
  - GnRHa & GAHT and bone
  - GnRHa & GAHT and sexual function

Efficacy of hormone treatment

Randomised trials

EPATH 4-6 SEPTEMBER 2025
HAMBURG, GERMANY

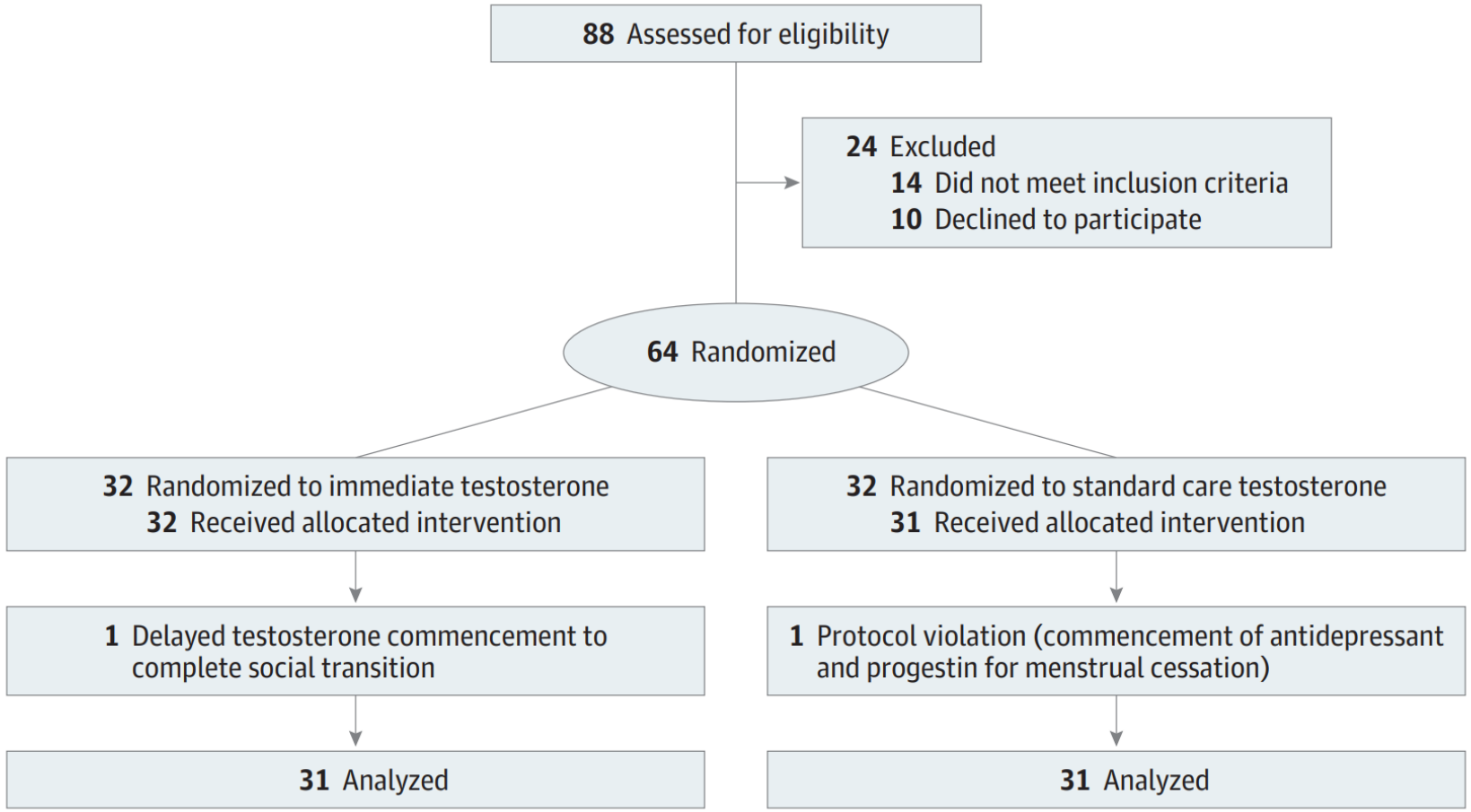
Original Investigation | Diabetes and Endocrinology

Early Access to Testosterone Therapy in Transgender and Gender-Diverse Adults Seeking Masculinization

A Randomized Clinical Trial

Brendan J. Nolan, MBBS; Sav Zwickl, PhD; Peter Locke; Jeffrey D. Zajac, PhD; Ada S. Cheung, MBBS, PhD

- Open label



Nolan et al. JAMA Netw Open 2023; 6(9):e2331919

Table 2. Change From Baseline to Month 3 in Individuals Receiving Immediate Commencement Testosterone Compared With Those Receiving Standard Care

Parameter		Mean (SD)		
		Intervention (n = 31)	Standard care (n = 31)	Mean difference (95% CI)[a]
0 mo	GPSQ	46.2 (6.0)	44.0 (6.8)	
3 mo		38.0 (6.2)	43.4 (7.9)	−7.2 (−8.3 to −6.1)
0 mo	PHQ-9	15.2 (4.7)	14.1 (6.0)	
3 mo		8.6 (5.2)	13.4 (6.3)	−5.6 (−6.8 to −4.4)
0 mo	SIDAS	12.0 (8.5)	11.6 (10.0)	
3 mo		5.6 (7.3)	11.8 (11.9)	−6.5 (−8.2 to −4.8)

Conclusion:
Testosterone therapy significantly decreases gender dysphoria, depression, and suicidality in transgender and gender-diverse individuals desiring testosterone therapy.

Nolan et al. JAMA Netw Open 2023; 6(9):e2331919

A Randomized Controlled Trial Comparing Testosterone Enanthate and Testosterone Undecanoate as a Gender Affirming Hormonal Therapy in Trans Males

Sankar Sinju[1] | Subbiah Sridhar[1] | Palaniyappan Sreenivasan[1] | Sureshkumar Paramasivam[2] | Geethaanjali Varadarajan[3] | Nattanmai Krishnan Mahalakshmi[4] | Thangavel Gnanasekharan[5] | Vasanthiy Natarajan[1]

- 58 transgender males randomised
  - 29 T enanthate 100 mg/2 wk for 3 mo, then 250 mg/3 wk
  - 29 T undecanoate 1000 mg at 0-6-12 wk, then every 12 wk
  - Three dropped out of each arm (discontinued T or lost to follow-up)

Clinical outcome	T enanthate	T undecanoate	p
Cessation of menses	2.8 ± 1.1	1.7 ± 0.57	0.01
Facial & body hair (mFGS>8)	2.5 ± 1	1.8 ± 0.6	0.003
Acne (GAGS>1)	4.5 ± 0.9	4.1 ± 0.85	0.1
Voice change	2.3 ± 0.6	2.15 ± 0.3	0.24
Clitoromegaly (clitoral index>35mm2)	1.8 ± 0.6	2.0 ± 0.6	0.15

- At 1 year no differences in clinical or biochemical outcomes

Conclusion: both options effective and safe

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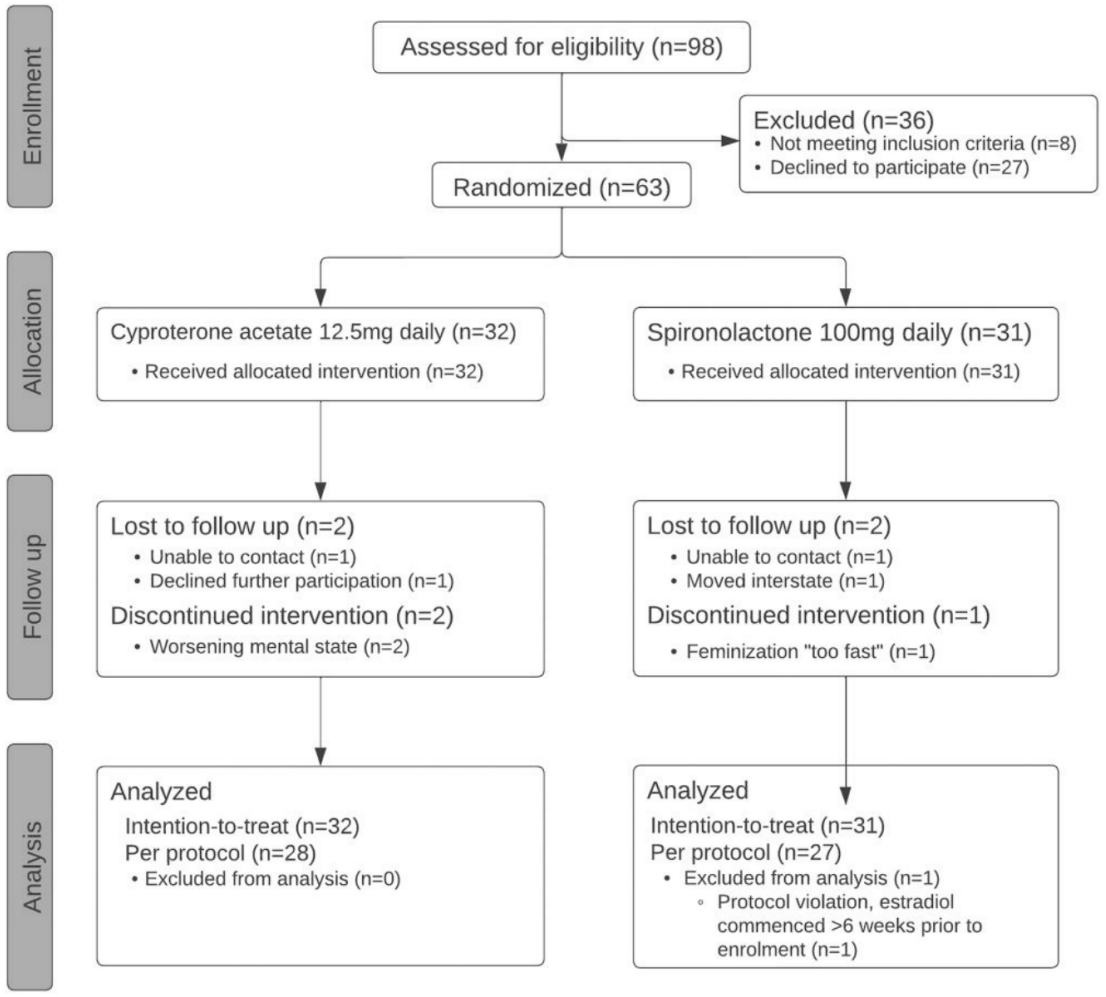
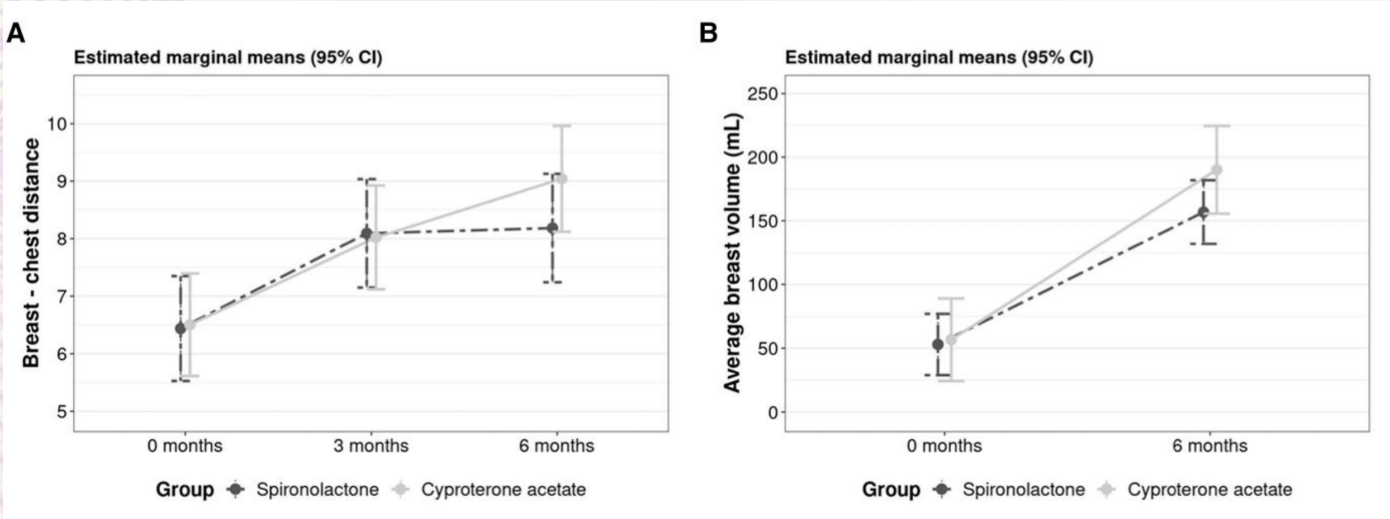
Sinju et al. Clin Endocrinol 2025; 103(1):89-96

The Journal of Clinical Endocrinology & Metabolism, 2025, **110**, e1874–e1884
https://doi.org/10.1210/clinem/dgae650
Advance access publication 17 September 2024
Clinical Research Article

Effect of Spironolactone and Cyproterone Acetate on Breast Growth in Transgender People: A Randomized Clinical Trial

Lachlan M. Angus,[1,2] Shalem Y. Leemaqz,[3] Anna K. Kasielska-Trojan,[4] Maksym Mikołajczyk,[4] James C. G. Doery,[5,6] Jeffrey D. Zajac,[1,2] and Ada S. Cheung[1,2]





Conclusion:
No difference in breast development.
Shared decision making, considering side effects.

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Angus et al. J Clin Endocrinol Metab 2025;110(6):e1874-84.

GAHT and the immune system

4-6 SEPTEMBER 2025
HAMBURG, GERMANY

Article

Immune system adaptation during gender-affirming testosterone treatment

https://doi.org/10.1038/s41586-024-07789-z

Received: 6 April 2023

Accepted: 4 July 2024

Published online: 4 September 2024

Open access

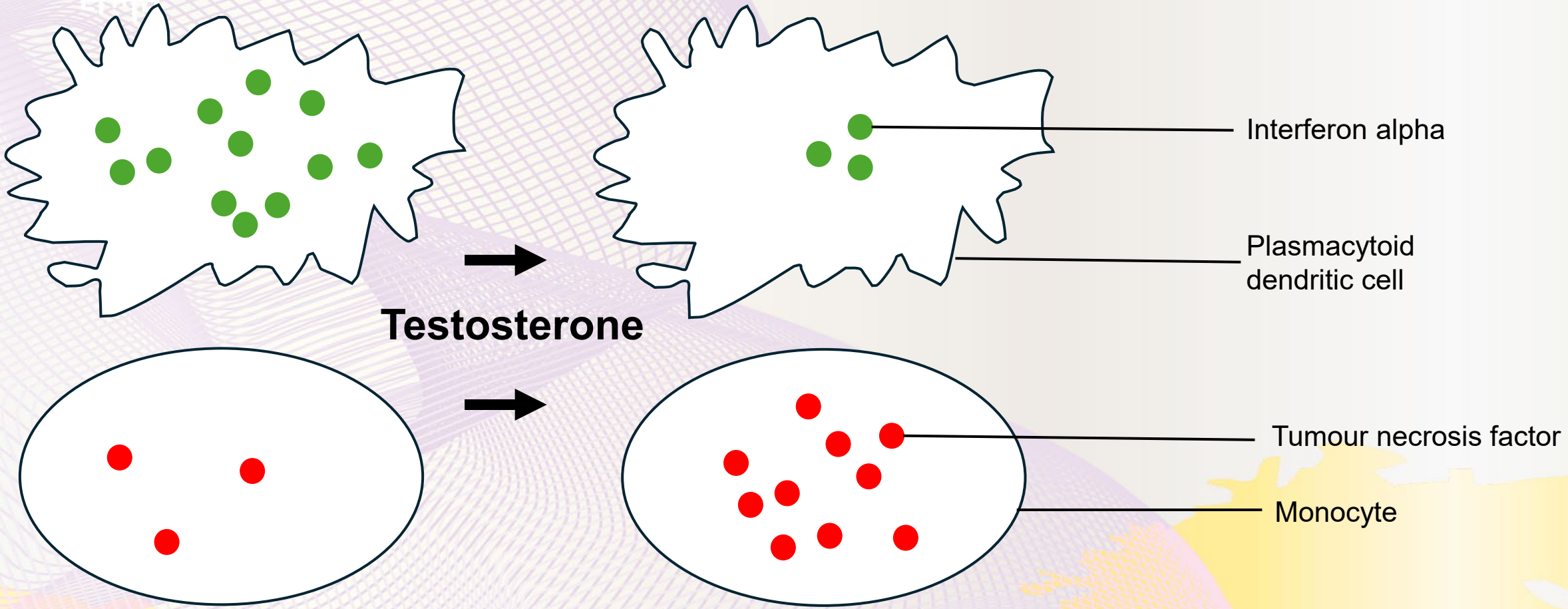
Tadepally Lakshmikanth[1,17], Camila Consiglio[1,2,17], Fabian Sardh[3,4], Rikard Forlin[1], Jun Wang[1], Ziyang Tan[1], Hugo Barcenilla[1], Lucie Rodriguez[1], Jamie Sugrue[5], Peri Noori[3], Margarita Ivanchenko[1], Laura Piñero Páez[1], Laura Gonzalez[1], Constantin Habimana Mugabo[1], Anette Johnsson[1], Henrik Ryberg[6,7], Åsa Hallgren[3], Christian Pou[1], Yang Chen[1], Jaromír Mikeš[1], Anna James[1], Per Dahlqvist[8], Jeanette Wahlberg[9], Anders Hagelin[10,11], Mats Holmberg[10,11], Marie Degerblad[10,12], Magnus Isaksson[13], Darragh Duffy[5], Olle Kämpe[3,14], Nils Landegren[3,4,17] ✉ & Petter Brodin[1,15,16,17] ✉

Study population:

- 23 adult transgender individuals starting nebido (750-1000 mg/12 weeks).
- Normal sex hormone concentrations.
- No autoimmune diseases, immunodeficiencies or signs of continuing infection/inflammation.

- Blood samples at 0 – 3 – 12 months of treatment.
- Immune cell phenotypes and functional immune cell responses in vitro a.o.

Lakshmikanth et al. Nature 2024; 633(8028):155-164



Changes in line with sex-divergent responses in public datasets

Lakshmikanth et al. Nature 2024; 633(8028):155-164
McCarthy. Nature. 2024;633(8028):38-40

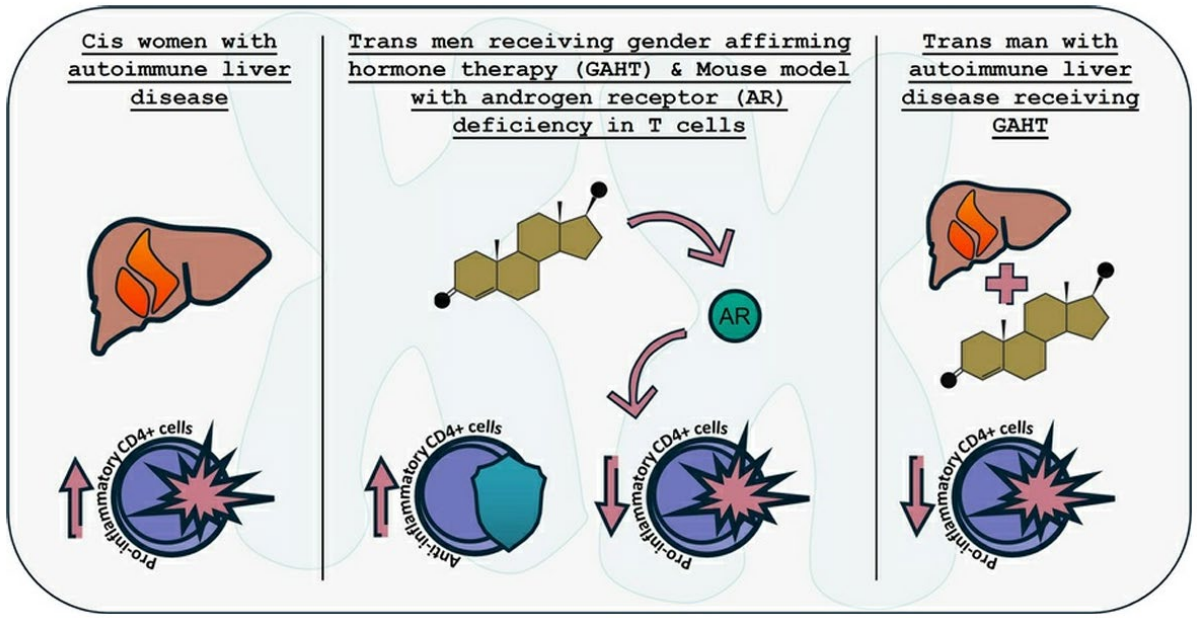
Conclusion:
Testosterone induces changes in the immune system which may have health implications.

JCI insight

RESEARCH ARTICLE

Testosterone affects female CD4+ T cells in healthy individuals and autoimmune liver diseases

Lara Henze,[1] Nico Will,[1] Dakyung Lee,[1] Victor Haas,[1] Christian Casar,[1,2] Jasper Meyer,[1] Stephanie Stein,[1] Franziska Mangler,[1] Silja Steinmann,[1] Tobias Poch,[1] Jenny Krause,[1] Johannes Fuss,[3] Johanna Schröder,[4] Alexandra E. Kulle,[5] Paul-Martin Holterhus,[5] Stefan Bonn,[6,7] Marcus Altfeld,[8] Samuel Huber,[1,9] Ansgar W. Lohse,[1,9] Dorothee Schwinge,[1] and Christoph Schramm[1,9,10]



Henze et al. JCI Insight. 2025;10(8):e184544

European Journal of Endocrinology, 2025, **192**, 408–417
https://doi.org/10.1093/ejendo/lvaf051
Advance access publication 15 March 2025
Original Research

EJE

Autoimmune diseases in 3812 Danish transgender persons and 38 120 cisgender controls before and after transgender care: a register-based cohort study

Dorte Glintborg,[1,2,*] Jens-Jakob Kjer Møller,[3] Katrine Hass Rubin,[3,4] Louise Lehmann Christensen,[1,2] and Marianne Skovsager Andersen[1,2]

Glintborg et al. Eur J Endocrinol 2025;192(4):408-417

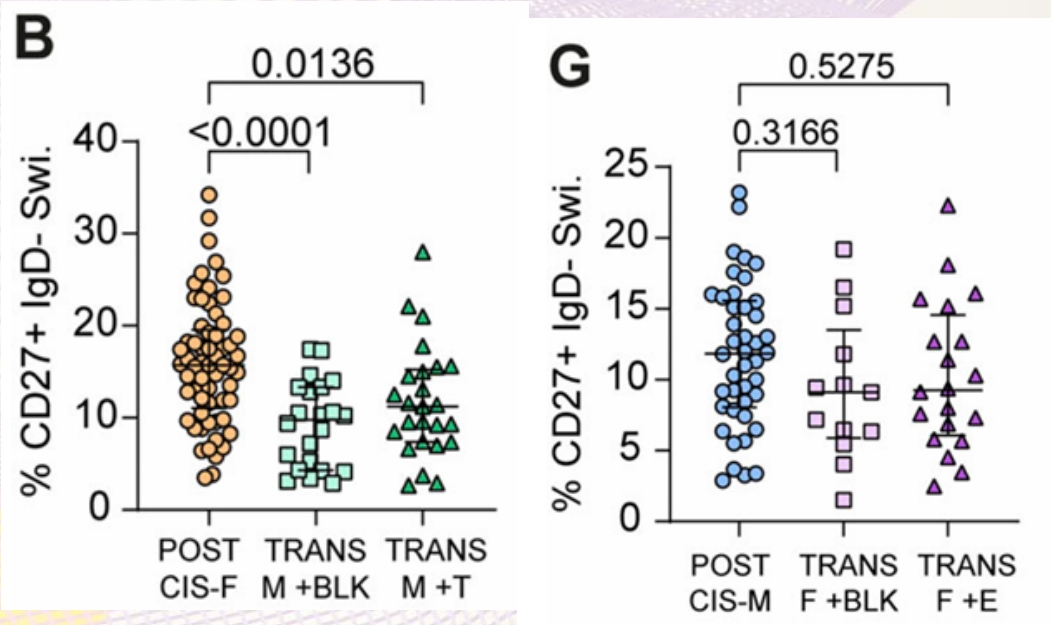
EPATH 4-6 SEPTEMBER 2025 HAMBURG, GERMANY

JEM Journal of Experimental Medicine

BRIEF DEFINITIVE REPORT

Estrogen influences class-switched memory B cell frequency only in humans with two X chromosomes

Hannah Peckham[1,2,3], Anna Radziszewska[1,2], Justyna Sikora[7], Nina M. de Gruijter[1,2], Restuadi Restuadi[1,3], Melissa Kartawinata[1,3], Lucia Martin-Gutierrez[1,2], George A. Robinson[1,2], Claire T. Deakin[1,3,5,6], Lucy R. Wedderburn[1,3,5], Elizabeth C. Jury[1,2], Gary Butler[3,4], Emma S. Chambers[7], Elizabeth C. Rosser[1,2*], and Coziana Ciurtin[1,2,4*]



Peckham et al. J Exp Med;2025;222(4):e20241253

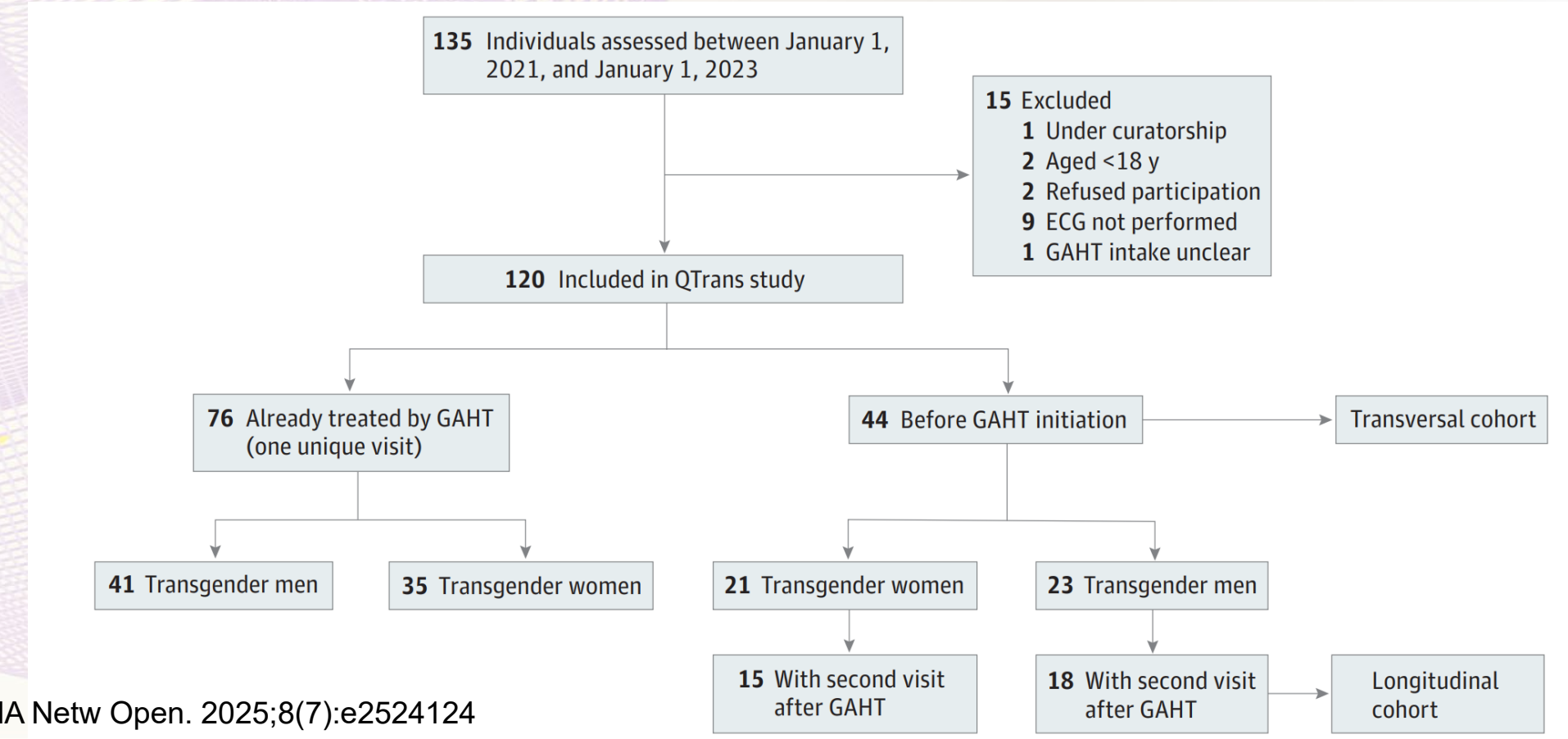
GAHT and the heart

JAMA Network Open™

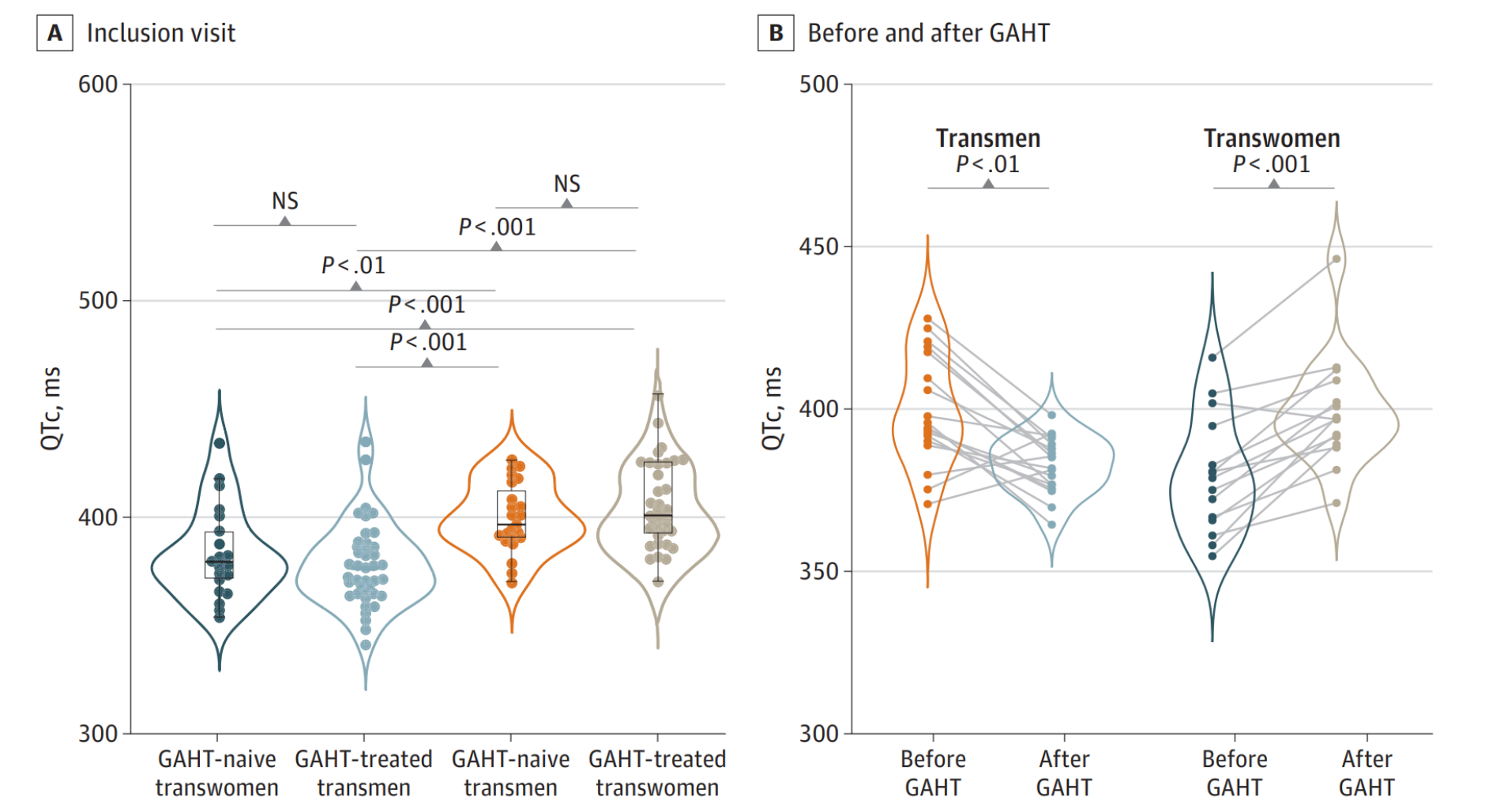
Original Investigation | Cardiology

Transgender-Affirming Hormone Therapies, QT Prolongation, and Cardiac Repolarization

Virginie Grouthier, MD; Marie Matamala, MD; Antoine Tabarin, MD, PhD; Amandine Galioot; Thierry Couffinhal, MD, PhD; Martino Vaglio, PhD; Fabio Badilini, PhD; Edi Prifti, PhD; Joe-Elie Salem, MD, PhD



Grouthier et al. JAMA Netw Open. 2025;8(7):e2524124



Conclusion:
GAHT induces changes in QTc corresponding to the known QTc sexual dimorphism in adults.

EPATH 4-6 SEPTEMBER 2025 HAMBURG, GERMANY

Grouthier et al. JAMA Netw Open. 2025;8(7):e2524124

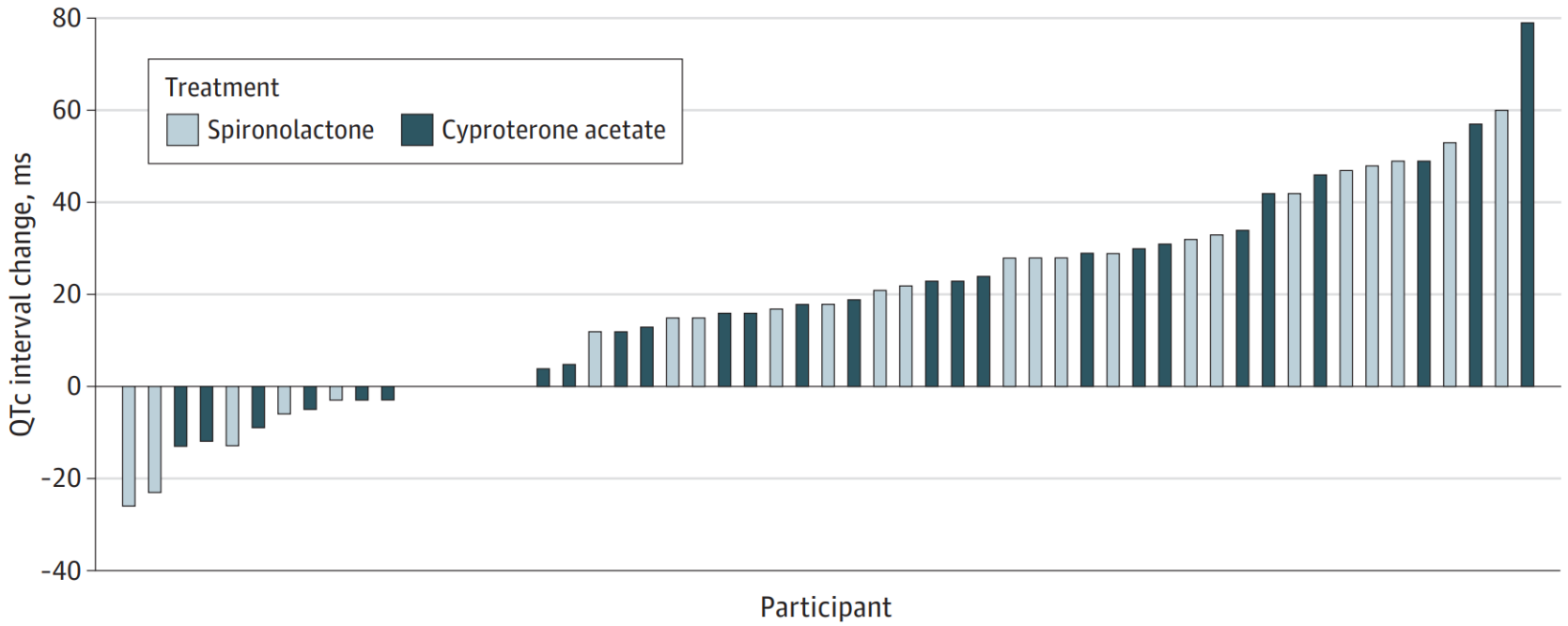
JAMA Network Open

Research Letter | Cardiology

Effect of Feminizing Hormone Therapy on QTc Interval
A Secondary Analysis of a Randomized Clinical Trial

Lachlan M. Angus, MBBS; Tina Lin, MBBS; Shalem Y. Leemaqz, PhD; Ada S. Cheung, PhD

Figure. Waterfall Plot of QTc Interval Change Over 6 mo by Participant



BER 2025
GERMANY

Angus et al. JAMA Netw Open. 2024;7(3):e243994.

GAHT and the kidney

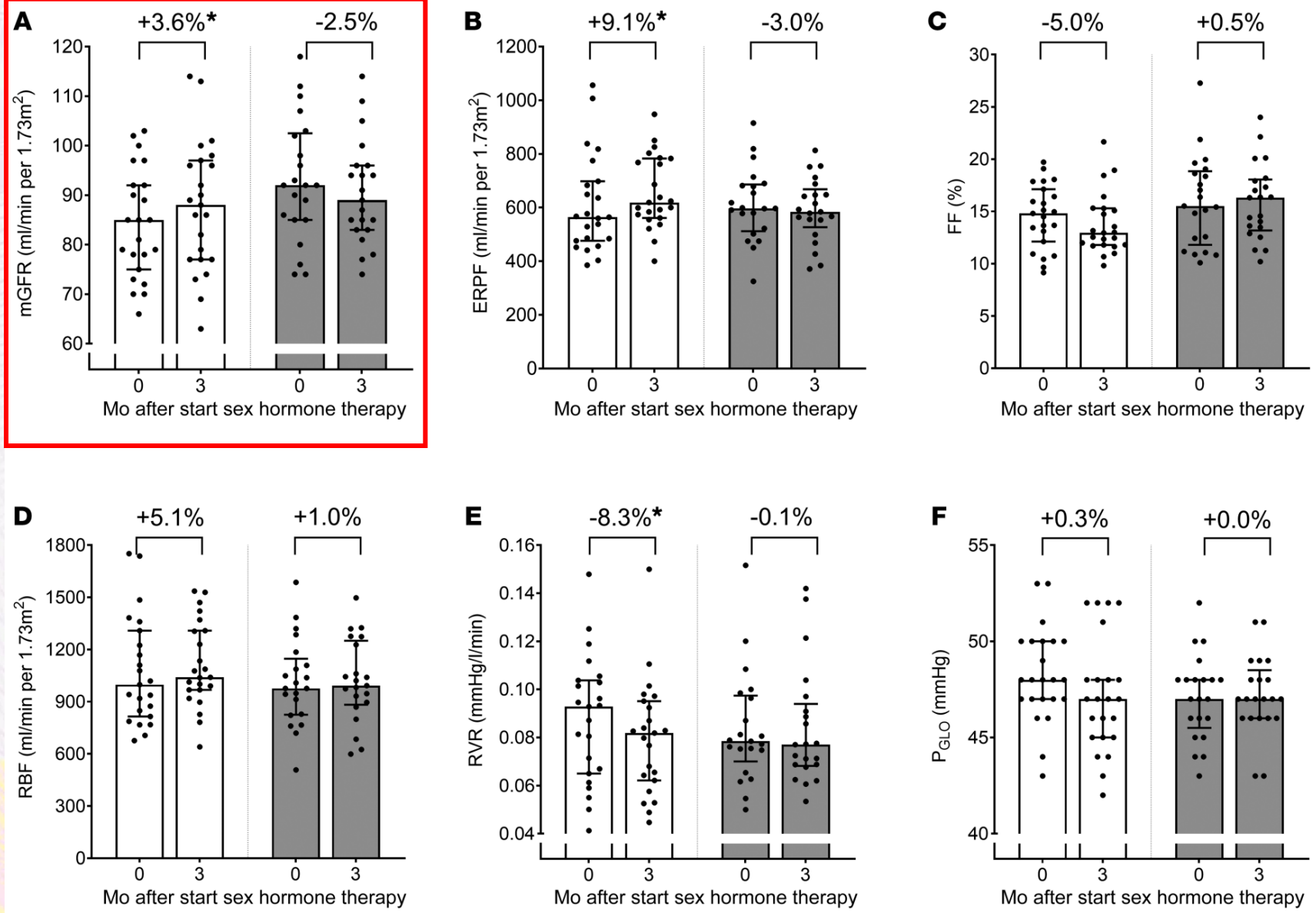
The Journal of Clinical Investigation CLINICAL RESEARCH AND PUBLIC HEALTH

Unveiling mechanisms underlying kidney function changes during sex hormone therapy

Sarah A. van Eeghen,[1,2,3] Laura Pyle,[4,5] Phoom Narongkiatikhun,[4,6] Ye Ji Choi,[4,5] Wassim Obeid,[7] Chirag R. Parikh,[7] Taryn G. Vosters,[8] Irene G.M. van Valkengoed,[8] Merle M. Krebber,[9] Daan J. Touw,[10] Martin den Heijer,[1,2,3] Petter Bjornstad,[4] Daniël H. van Raalte,[3,11,12] and Natalie J. Nokoff[5]

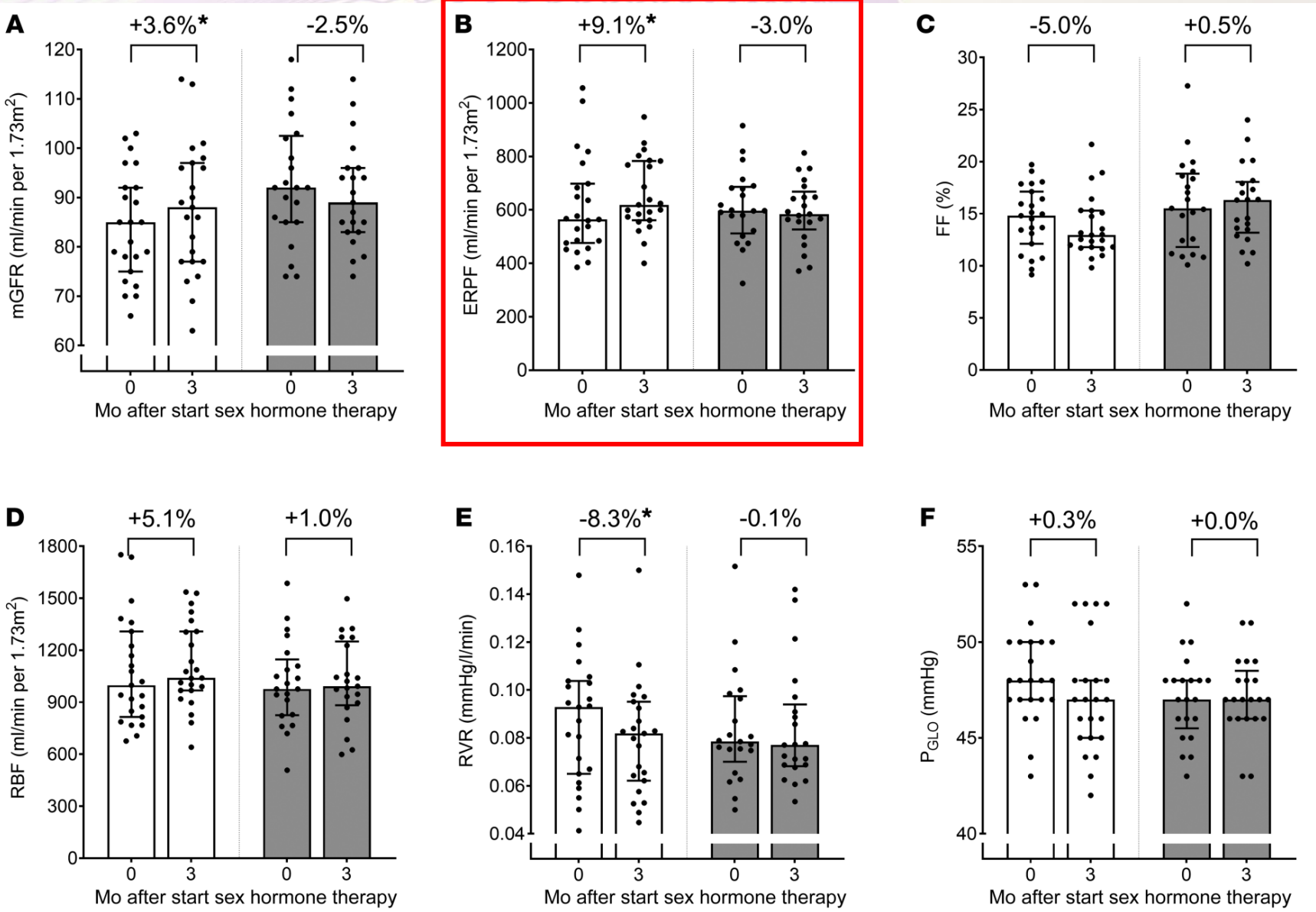
- Prospective observational cohort study
- 23 transgender women and 21 transgender men aged 17-40 yr
- Assessed before and 3 months after initiating GAHT
- Measured GFR determined using plasma iohexol clearance
- Effective renal plasma flow (ERPF) determined using plasma PAH clearance

Van Eeghen et al. J Clin Invest. 2025;135(9):e190850

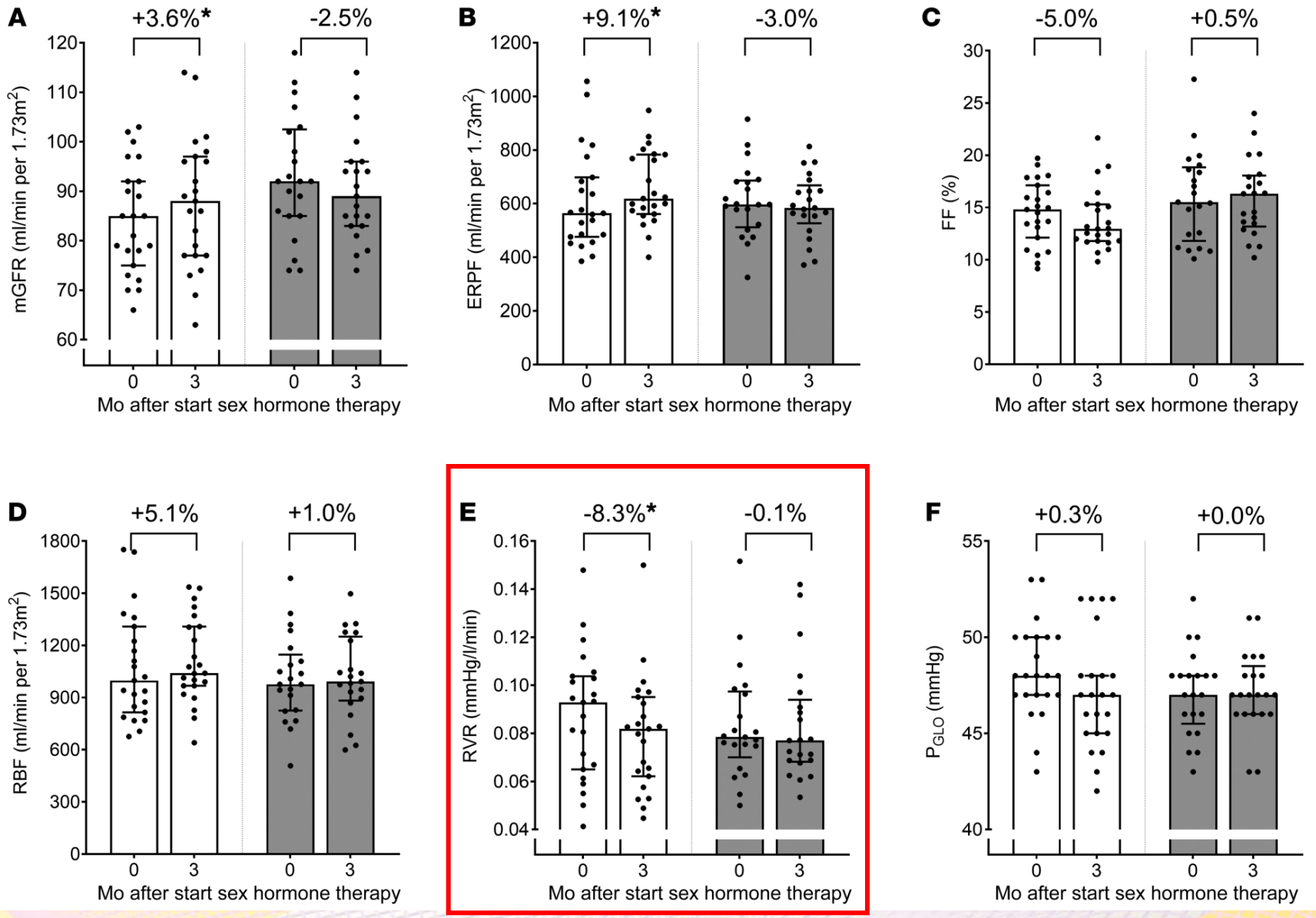


EPATH 4-6 SEPTEMBER 2025 HAMBURG, GERMANY

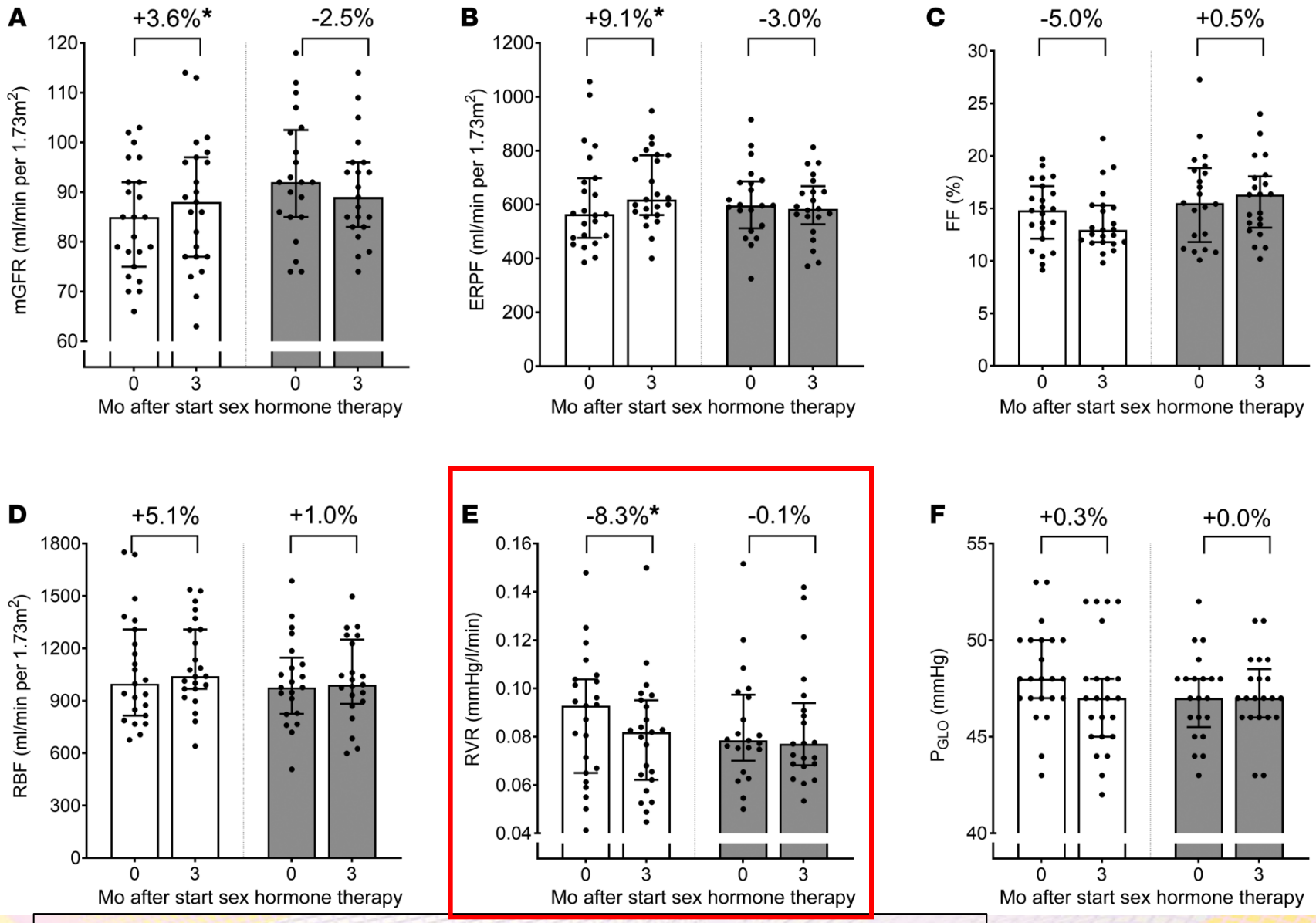
Van Eeghen et al. J Clin Invest. 2025;135(9):e190850



Van Eeghen et al. J Clin Invest. 2025;135(9):e190850



Van Eeghen et al. J Clin Invest. 2025;135(9):e190850



Conclusion:
Estradiol shows protective effects on glomerular and tubular function, while testosterone predominantly exerts opposing effects.

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Van Eeghen et al. J Clin Invest. 2025;135(9):e190850

Longer term outcomes of GnRHa/GAHT in adolescents

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HAMBURG, GERMANY

GAHT discontinuation

1st Author	Country	n	Age at start GAHT	Follow-up duration	Discontin.	Restarted	Reident. sex RAB
Boskey	USA	1050	16.8 ± 1.9	Min. 6 mo	57 (6%)	20 (2%)	5 (0.5%)
Gupta	USA	264 adults 121 <18 yr	32 15	Med 32 mo (IQR 15-73)	5 (1.9%) 4 (3.3%)	2 (0.8%)	1 (0.4%) 1 (0.8%)
Kaltiala	Finland	1359	25.6 ± 9.3	Med 44.5 mo	107 (7.9%)		
Cavve	Australia	132			1 (0.8%)		1 (0.8%)
Nyquist	Norway	469 adults 314 <18 yr	18.1 ± 2.2		18 (2.3%)		11 (1.4%)
Olson	USA	182	13.25 ± 0.97	Mean 3.40 y ±1.96	3 or 4 (1.6-2.2%)		

Boskey et al. J Adolesc Health. 2025;76:584-91
Gupta et al. J Clin Endocrinol Metab. 2023;108:e1236-44
Kaltiala et al. BMC Psychiatry 2024; 24:566
Cavve et al. JAMA Pediatr 2024;178:446-53
Nyquist et al. Acta Paediatr 2025; 114:1006-14
Olson et al. JAMA Pediatr 2024; 178:1354-61

Conclusion:
Several studies show that 0.8-7.9% of adolescents/young adults discontinue GAHT, some of whom reidentify with sex registered at birth

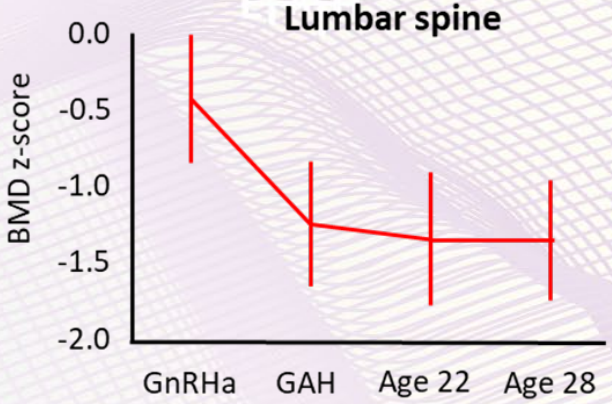
JAMA Pediatrics | Original Investigation

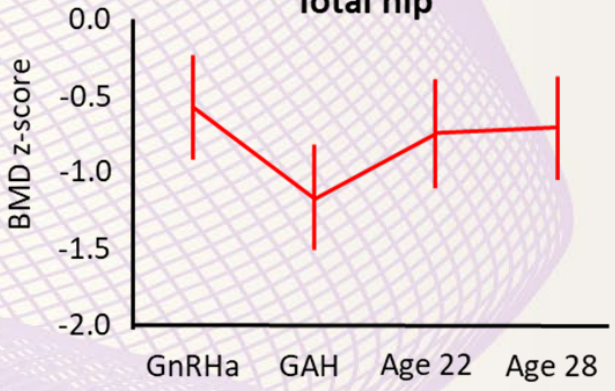
Bone Mineral Density in Transgender Adolescents Treated With Puberty Suppression and Subsequent Gender-Affirming Hormones

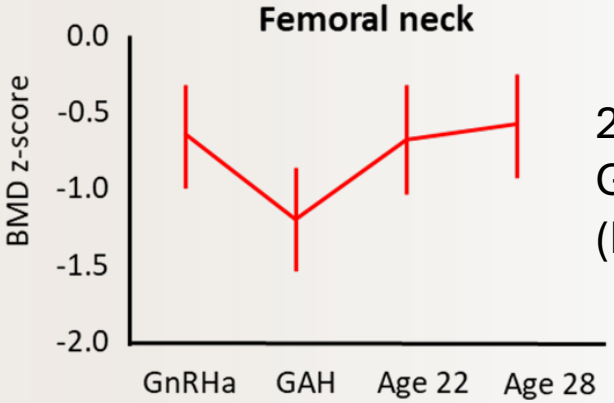
Maria Anna Theodora Catharina van der Loos, MD; Mariska Caroline Vlot, MD, PhD; Daniel Tatting Klink, MD, PhD; Sabine Elisabeth Hannema, MD, PhD; Martin den Heijer, MD, PhD; Chantal Maria Wiepjes, MD, PhD

- Prospective study
- 25 transgender women and 50 transgender men
  - puberty suppression before age 18 years
  - at least 9 years of GAHT
- Median age 28.2 years
- Bone mineral density assessed using DXA scan
- Prior scans
  - At start GnRHa – median age 14.5 / 14.9
  - At start GAHT - median age 16.0 / 16.1
  - Around age 22 y

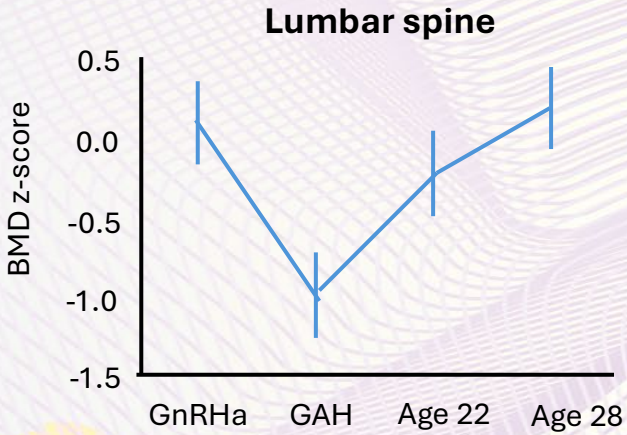
van der Loos et al. JAMA Pediatr 2023;177(12):1332-1341

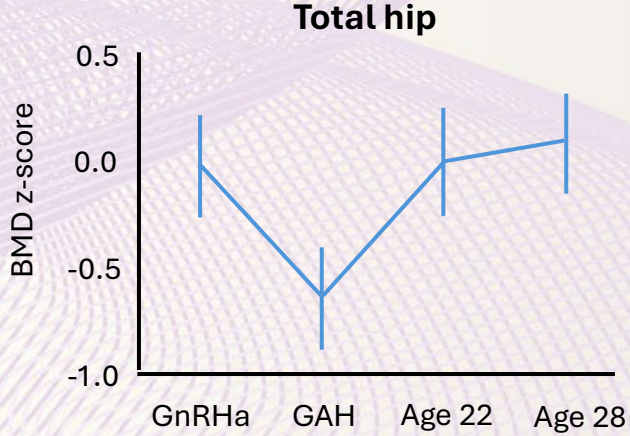


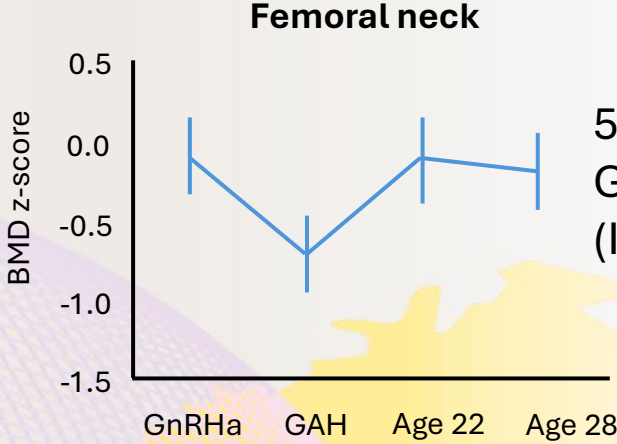




25 TF
GAHT for 11.6 y
(IQR 10.1-14.7)







50 TM
GAHT for 11.9 y
(IQR 10.2-13.8)

van der Loos et al. JAMA Pediatr 2023;177(12):1332-1341

Conclusion:
BMD z-scores decline during GnRHa treatment with complete catch-up at the hip and femoral neck but not the lumbar spine in transgender women and at all sites in transgender men.

The Journal of Sexual Medicine, 2025, **22**, 196–204
https://doi.org/10.1093/jsxmed/qdae152
Advance access publication date 6 November 2024
Original Research

Timing of puberty suppression in transgender adolescents and sexual functioning after vaginoplasty

Isabelle S. van der Meulen, MD*, Sara L. Bungener, MD, Anna I.R. van der Miesen, MD, PhD, Sabine E. Hannema, MD, PhD, Baudewijntje P.C. Kreukels, PhD, Thomas D. Steensma, PhD, Mark-Bram Bouman, MD, PhD, Annelou L.C. de Vries, MD, PhD

- Retrospective cohort study
- 37 Transfeminine individuals who received PS, GAHT and genital surgery
  - 16 PS from Tanner stage G2/G3
  - 21 PS from Tanner stage G4/G5
- 21-item questionnaire adapted from a large Dutch sexual health study among youth in the general population, asking about sexual and romantic relationship experiences at different time points across GAMT.

van der Meulen et al. J Sex Med 2025;22(1):196-204

Variable	All participants (*N* = 37) *N (%)*	Early PS (n = 16) n (%)	Late PS (n = 21) n (%)	Significance, *P,*	Effect size,[d]
Sexual desire					
Before surgery[a]	30 (91)	14 (88)	16 (94)	0.60	0.12
After surgery[a]	31 (91)	16 (100)	15 (83)	0.23	−.29
Sexual arousal					
Before surgery[a]	26 (70)	8 (50)	18 (86)	*0.03*	0.39
After surgery[a]	32 (89)	15 (94)	17 (85)	0.61	−.14
Ability to orgasm					
Before surgery[be]	14 (40)	3 (18)	11 (58)	*0.02*	−.40
After surgery[a]	28 (78)	13 (87)	15 (71)	0.42	0.18

van der Meulen et al. J Sex Med 2025;22(1):196-204

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Before surgery[be]	14 (40)	3 (18)	11 (58)	*0.02*	−.40
After surgery[a]	28 (78)	13 (87)	15 (71)	0.42	0.18

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Variable	All participants (*N* = 37) *N (%)*	Early PS (n = 16) n (%)	Late PS (n = 21) n (%)	Significance, *P,*	Effect size,[d]
Sexual desire					
Before surgery[a]	30 (91)	14 (88)	16 (94)	0.60	0.12
After surgery[a]	31 (91)	16 (100)	15 (83)	0.23	−.29
Sexual arousal					
Before surgery[a]	26 (70)	8 (50)	18 (86)	*0.03*	0.39
After surgery[a]	32 (89)	15 (94)	17 (85)	0.61	−.14
Ability to orgasm					
Before surgery[be]	14 (40)	3 (18)	11 (58)	*0.02*	−.40
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Conclusion:
Post-vaginoplasty most transgender women after early or late suppression of puberty have the ability to experience sexual desire and arousal, and to achieve orgasms. Outcomes are comparable to previous findings after treatment started in adulthood.

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Conclusions

- Increasing evidence on the efficacy of GAHT and of specific regimens.
- GAHT induce changes in many organs.
- Research on longer-term outcomes of treatment in adolescence suggests
  - Delayed development with GnRHa
  - Catch-up after GAHT
  - Great majority continues to use GAHT
- New questions raised!

Thank you

EPATH 4-6 SEPTEMBER 2025
HAMBURG, GERMANY