

23rd Post-ENDO Symposium: Transgender Healthcare

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Agenda

- Changes in kidney function with gender affirming hormone treatment
- Hot topic progesterone
- Comparison of Antiandrogens in breast development
- Breast cancer screening in gender diverse individuals
- Incidence and reasons for discontinuing gender affirming medical treatment

Changes in kidney function with gender affirming hormone treatment

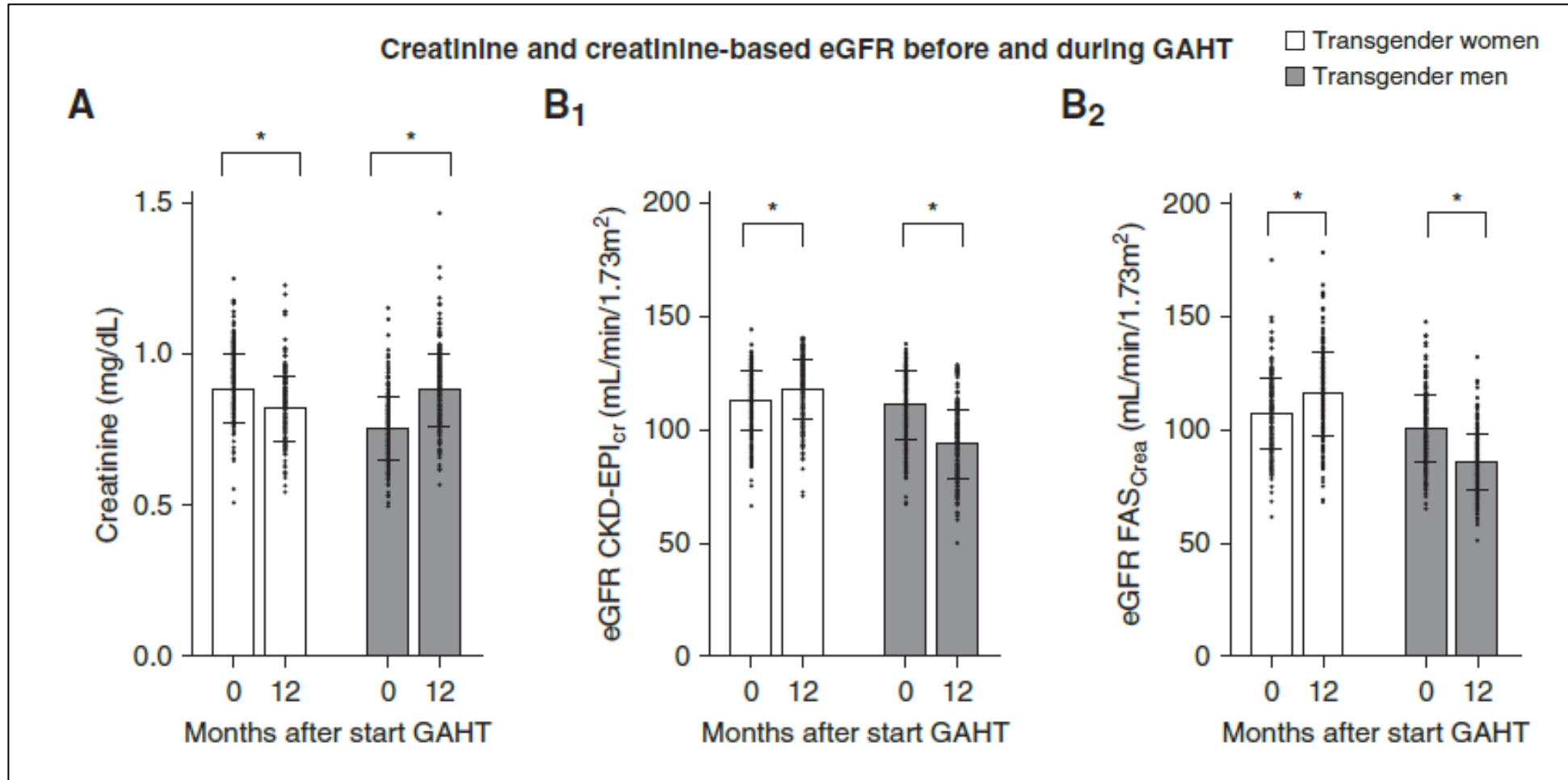
- Background:

- Faster decline in kidney function in cis men with CKD compared to cis women – possibly due to sex hormones?
- No data on trans individuals
- Challenging interpretation
Testosterone → Muscle mass ↑ → Creatinine ↑

- Methods:

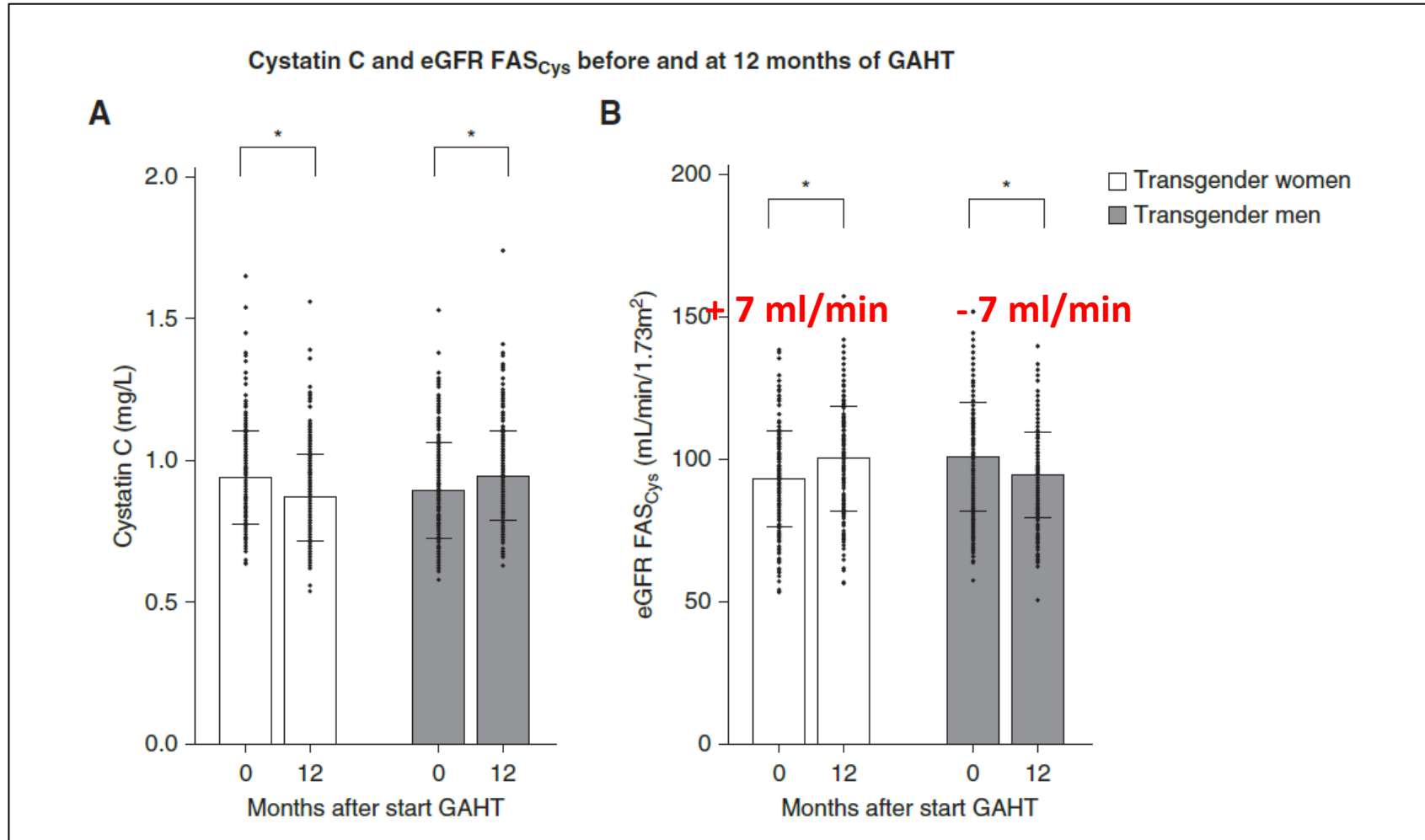
- 260 transfem., 258 trans masc. Persons
- Measurement of Creatinine and Cystatin C at baseline and at 12 mo after initiation of hormone treatment

Changes in creatinine (clearance)



van Eeghen S et al. Cystatin C-Based eGFR Changes during Gender-Affirming Hormone Therapy in Transgender Individuals. Clin J Am Soc Nephrol. 2023

Changes in Cystatin C (clearance)



Conclusion

- Sex hormones do affect kidney function!
- Changes of kidney function are minor, but...
- Take into account in individuals with already impaired kidney function!

Short-term effects of micronised progesterone

- Background: Poor sleep quality common in trans persons; progesterone improved sleep-quality in postmenopausal women
- 8-week randomised placebo controlled trial: mProgesterone vs. placebo
- 28 persons, median age 26 y
- Outcomes: Sleep-Quality and Kessler psychological distress scale

→ Improvement of sleep quality
No effect on psychological distress

Hot topic Progesterone

- Larger studies on efficacy and safety are lacking!
 - Systematic Review 2022:
 - 10 studies (1 RCT, 4 prospective, 5 retrospective/observational)
 - Overall 4041 persons
 - Including Cyproterone Acetate as «progesterone» (7/10 studies!)
- No improvement in breast development or quality of life
- Increased risk for venous thromboembolism (?), decrease in HDL

Hot topic Progesterone

- Larger studies for efficacy and safety are lacking!
- Systematic Review 2022:
 - No improvement in breast development or quality of life
 - Increased risk for venous thromboembolism (?), decrease in HDL
- ONE planned study
 - Addition of progesterone to feminizing gender-affirming hormone therapy in transgender individuals for breast development: a randomized controlled trial
 - Non-blinded RCT
 - Plan: 90 tf persons after gonadectomy
 - Randomized to different doses of E2 and Progesterone
 - Outcome: breast volume measured by 3D imaging, baseline + 12 months

Hot topic Progesterone

- Larger studies for efficacy and safety are lacking!
- Review 2022:
 - No improvement

Insufficient Data to recommend routine use of Progesterone!

- **Effect of adding gender-affirming hormone therapy in individuals for breast development: a randomized controlled trial**
 - Non-blinded RCT
 - Plan to include 90 persons, randomized to different doses of E2 and Progesterone

Antiandrogenic drugs and breast development

- E2 + Cyproterone acetate 12.5 mg vs. E2 + Spironolactone 100 mg
- Double-blind RCT, 55 persons, 6 months duration
- Prim. Outcome: Breast-chest-distance
- Sec. Outcome: Estimated volume with AI-based estimation

→ No significant difference in breast development between groups
→ Significant inter-individual variation

Risk for breast cancer in trans women



MTP Session: Sean Iwamoto (Colorado); Tamar Reisman (Weill Cornell Medicine): Challenging cases for Gender-Diverse Individuals
de Blok CJM, et al. Breast cancer risk in transgender people receiving hormone treatment: nationwide cohort study in the Netherlands. BMJ. 2019

Screening recommendations

Population	Guideline (Society)
<i>Transgender woman (male to female)</i>	
Hormones < 5 y, average risk	No screening
Hormones ≥ 5 y, average risk	Biennial, start at age 50 (UCSF)
	Annual, start at age 50 (Fenway)
	Same as natal females (Endocrine)
	Screening “may be appropriate” (ACR)
Hormones < 5 y, high risk*	Screening “may be appropriate” (ACR)
Hormones ≥ 5 y, high risk*	Annual screening starting age 25-30 (ACR)
<i>Transgender man (female to male)</i>	
Breasts present	Age/risk guidelines for natal females
Breasts absent	No screening
	Educate on risk of residual breast tissue
* High risk: personal history breast cancer, chest wall radiation age 10-30, <u>gene mutation</u> , history of breast or ovarian cancer.	

Screening recommendations

Population	Guideline (Society)
<i>Transgender woman (male to female)</i>	

Transfeminine (>5 y of E2-treatment) and transmasculine persons:

Screening analogue cis women:

Biennial mammography >50 y w/o risk factors

Annual mammography >25-30 y w risk factors

*

High risk: personal history breast cancer, chest wall radiation age 10-30, [gene mutation](#), history of breast or ovarian cancer.

Prevalence of and reasons for discontinuing gender affirming-medical treatments

- Detransition = stopping or reversing some or all aspects of gender-affirming social, legal, and/or medical interventions
- Numbers of gender diverse adolescents and young adults are constantly increasing
 - Gender diversity diagnosis in 6-17 yo: 15 k in 2017 → 42 k in 2021
 - Similar increases in all age groups and around the world
- Limited data on prevalence and predictive factors for detransition

Respaut R, Terhune C. Number of transgender children seeking treatment surges in U.S. Reuters. 2022

MacKinnon KR, et al. Discontinuation of Gender-Affirming Medical Treatments: Prevalence and Associated Features in a Nonprobabilistic Sample of Transgender and Gender-Diverse Adolescents and Young Adults in Canada and the United States. J Adolesc Health. 2024

Methods / Study population

- Age 15-29 y
- Online questionnaire, cross-sectional
 - Frequency of detransition
 - Reasons for detransition
 - Associated factors for detransition
- 720 persons – ever started gender affirming medical treatment

General population data

Mackinnon KR, et al. Discontinuation of Gender-Affirming Medical Treatments: Prevalence and Associated Features in a Nonprobabilistic Sample of Transgender and Gender-Diverse Adolescents and Young Adults in Canada and the United States. *J Adolesc Health*. 2024

Results 1: Frequency of detransition (??)

16.8 % (121 / 720) indicated «having ever stopped/reversed treatment»

- 45/121 (37.2%) «Yes, but I wish I hadn't»
 - No indication about re-treatment
 - No data about length of hormone treatment
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- «Discontinuation rate» comparable to other US data
 - Way higher than in the Netherlands (16.8 vs. 2%!)
 - NL: stringent criteria, extended mental health assessment, stepwise approach (Screening -> Puberty blockers -> Hormone treatment)

MacKinnon KR, et al. Discontinuation of Gender-Affirming Medical Treatments: Prevalence and Associated Features in a Nonprobabilistic Sample of Transgender and Gender-Diverse Adolescents and Young Adults in Canada and the United States. *J Adolesc Health*. 2024

van der Loos MATC et al. Continuation of gender-affirming hormones in transgender people starting puberty suppression in adolescence: a cohort study in the Netherlands. *Lancet Child Adolesc Health*. 2022

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Results 2: Reasons for detransition

75/121
Answered!

Reason	n (%)
Health reasons	28 (37.3%)
Change in gender identity	24 (32.0%)
Cost	12 (16.0%)
Lack of availability of medical services/treatment	9 (12.0%)
Healthcare provider/therapist(s) encouraged me to explore other ways to deal with gender dysphoria	5 (6.7%)
Partner(s) encouraged me to explore other ways to deal with gender dysphoria	4 (5.3%)
For reproductive/fertility considerations	4 (5.3%)
Friend(s) encouraged me to explore other ways to deal with gender dysphoria	3 (4.0%)
Employment	2 (2.7%)
Something else; please describe:	35 (46.7%)

Mackinnon KR, et al. Discontinuation of Gender-Affirming Medical Treatments: Prevalence and Associated Features in a Nonprobabilistic Sample of Transgender and Gender-Diverse Adolescents and Young Adults in Canada and the United States. J Adolesc Health. 2024

Results 3: Factors associated with detransition

- Positive correlation:
 - Greater age
 - Nonbinary identity
 - Diagnosis of Schizophrenia
 - Christian religion / religious families
- Inverse correlation:
 - Trans male identity
 - High income
 - Being areligious
 - Support from family, friends and healthcare providers

Discussion

- Results preliminary, contributing to other literature on discontinuation
- Prevalence of 16.8% is higher than in European studies!
→ Mostly due to the very liberal definition of detransition in this questionnaire
- **Real-life detransition rates much lower!**
 - **No official detransition-rates for Switzerland available**

Thank you for your attention!

