A year in review- Endocrinology

Matthias Auer
Max Planck Institute of Psychiatry
RG Clinical Neuroendocrinology
Munich, Germany
mauer@psych.mpg.de

Hormone therapy in trans men

Max-Planck-Institut für Psychiatrie

Effects of Three Different Testosterone Formulations in Female-to-Male Transsexual Persons

Carla Pelusi, MD,* Antonietta Costantino, PhD,† Valentina Martelli, MD,† Martina Lambertini, MD,† Alberto Bazzocchi, MD, PhD,‡§ Federico Ponti, MD,§ Giuseppe Battista, MD,§ Stefano Venturoli, MD,† and Maria C. Meriggiola, MD, PhD†

	Groups	Baseline	Week 54 Posttreatment	GLM analysis *P* value vs. posttreatment	GLM analysis *P* value vs. group
LH (IU/L)	TD	7.3 (3.5–11.2)	5.1 (1.9–8.3)	*P* = 0.289	*P* = 0.160
	T-gel	12.8 (6.6–39.8)	9.2 (4.5–13.9)		
	TU	5.8 (2.1–9.5)	5.1 (2.0–8.1)		
FSH (IU/L)	TD	6.2 (4.3–8.1)	5.1 (3.8–6.4)	*P* = 0.700	*P* = 0.538
	T-gel	6.1 (3.4–8.9)	5.6 (3.7–7.5)		
	TU	4.6 (2.8–6–4)	5.3 (4.1–6.6)		
E (pg/mL)	TD	102.9 (61.4–144.5)	70.6 (28.0–113.2)	*P* = 0.002	*P* = 0.502
	T-gel	167			
	TU	130			
PRL (ng/mL)	TD	18			
	T-gel	17			
	TU	15			
T (ng/mL)	TD	0.5			
	T-gel	0.4			
	TU	0.4			
SHBG (nmol/L)	TD	65			
	T-gel	65			
	TU	60			
cFT (nmol/L)	TD	0.0			
	T-gel	0.01 (0.00–0.01)	0.34 (0.12–0.57)		
	TU	0.01 (0.00–0.01)	0.28 (0.06–0.49)		

	Groups	Baseline	Week 30 Posttreatment	Week 54 Posttreatment	GLM analysis *P* value vs. posttreatment	GLM analysis *P* value vs. groups
Glucose (mg/dL)	TD	87.3 (82.2–92.4)	81.2 (75.6–86.7)	82.0 (76.9–87.0)	*P* = 0.019	*P* = 0.749
	T-gel	84.0 (78.7–89.3)	81.5 (75.7–87.3)	80.0 (74.7–85.3)		
	TU	83.1 (77.9–88.2)	81.7 (76.1–87.2)	80.1 (75.0–85.1)		
Insulin (mcu/mL)	TD	6.04 (4.88–7.18)	5.52 (4.14–6.91)	5.21 (3.93–6.49)	*P* = 0.917	*P* = 0.41
	T-gel	5.71 (4.44–6.98)	6.61 (5.08–8.14)	6.10 (4.68–7.52)		
	TU	5.82 (46.68–6.98)	4.84 (3.45–6.22)	5.86 (4.58–7.15)		
				–1.16)	*P* = 0.62	*P* = 0.28
				–1.47)		
				–1.38)		
				–82.2)	*P* = 0.256	*P* = 0.317
				–93.1)		
				–87.7)		
				–100.1)	*P* = 0.089	*P* = 0.206
				–105.8)		
				–107.9)		
				–0.85)	*P* = 0.322	*P* = 0.072
				–0.93)		
				–0.85)		
Body weight (kg)	TD	57.8 (51.2–64.4)	61.8 (55.2–68.5)	61.3 (55.0–67.5)	*P* < 0.0005	*P* = 0.063
	T-gel	67.3 (59.7–74.9)	69.6 (61.9–77.2)	68.7 (61.5–75.9)		
	TU	59.6 (52.3–66.8)	60.0 (52.7–67.3)	60.5 (53.7–67.4)		
BMI (kg/m²)	TD	22.3 (19.9–24.6)	23.8 (21.5–26.1)	23.6 (21.4–25.8)	*P* < 0.0005	*P* = 0.058
	T-gel	23.9 (21.2–26.6)	24.6 (21.9–27.3)	24.3 (21.8–26.9)		
	TU	22.1 (19.5–24.6)	22.2 (19.7–24.8)	22.4 (20.0–24.8)		

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

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

J Sex Med. 2014

Acne & Body hair growth

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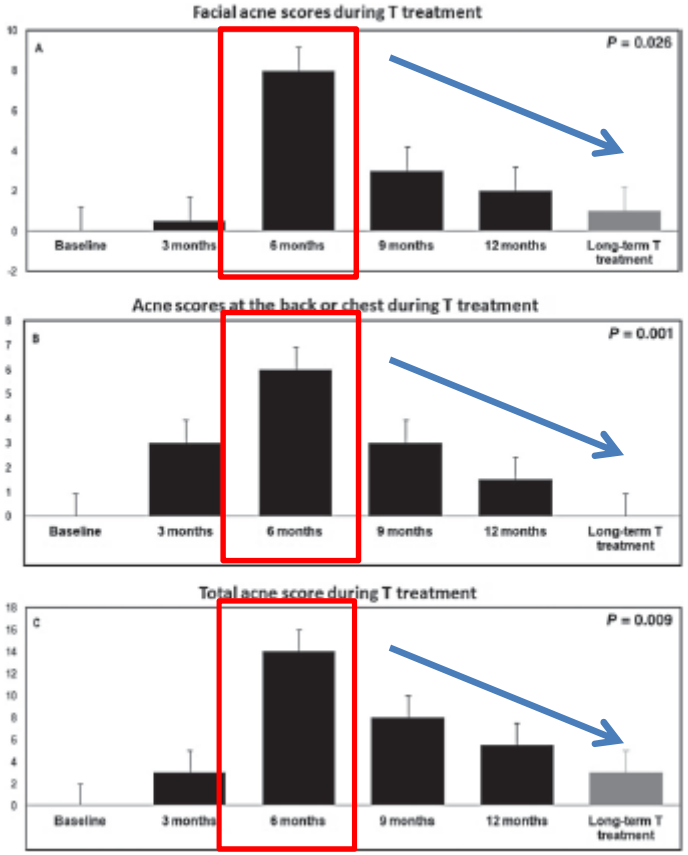
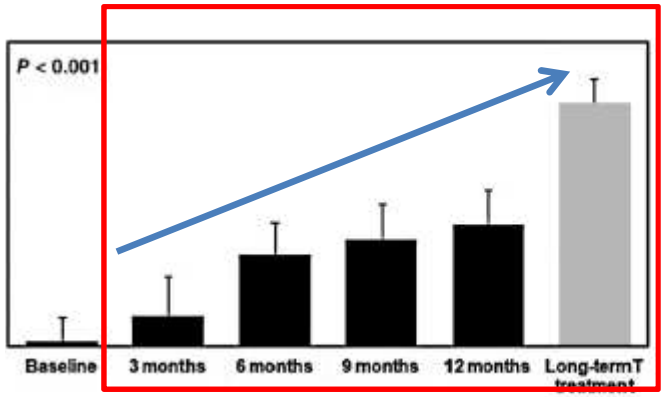
Short- and Long-Term Clinical Skin Effects of Testosterone Treatment in Trans Men

Katrien Wierckx, MD,[1*] Fleur Van de Peer,[1*] Evelien Verhaeghe, MD, PhD,[†] David Dedecker,[*] Eva Van Caenegem, MD,[*] Kaatje Toye,[*] Jean Marc Kaufman, MD, PhD,[*] and Guy T'Sjoen, MD, PhD[*‡]

[*]Department of Endocrinology, Ghent University Hospital, Ghent, Belgium; [†]Department of Dermatology, Ghent University Hospital, Ghent, Belgium; [‡]Department of Sexology and Gender Problems, Ghent University Hospital, Ghent, Belgium

Acne





Body hair

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

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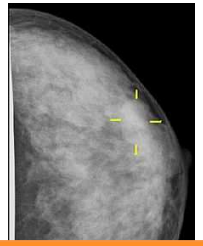
Breast cancer risk?

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

EPIDEMIOLOGY

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

George R. Brown · Kenneth T. Jones



- **N = 3,556 (MtF), N = 1,579 (FtM)**
- Cases of breast-Ca. **FTM: 7** and **MTF: 3**
- Incidence **20.0/100,000** patient years
- **No difference in comparison** to age – (birth) sex-matched general population

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

ORIGINAL RESEARCH—ONCO

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

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

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

DOI: 10.1111/jsm.12319

- **N = 2,307 (MtF), N = 795 (FtM)**
- Cases of breast-Ca. **FTM: 2** und **MTF: 1**
- **MtF:** Incidence **4.1 / 100,000** patient years
- **No difference in comparison** to age – (birth) sex-matched general population
- **Incidence 5.9 / 100,000** patient years
- **Lower incidence** than age-matched **women, same incidence** as age matched **men**

Familial breast cancer?

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ORIGINAL RESEARCH—TRANSGENDER AND GENDER NONCONFORMANCE

Hormonal and Surgical Treatment in Trans-Women with BRCA1 Mutations: A Controversial Topic

Britt Colebunders MD,* Guy T'Sjoen MD, PhD,†‡ Steven Weyers MD, PhD§ and Stan Monstrey MD, PhD*

- **So far no published case of BRCA1 positivity and breast cancer** in gender dysphoria
- **Men who are BRCA1-carriers** have a **5.8% risk** of developing breast cancer before the age of 70 (General population **0.1%**)
- There is also a **higher risk for developing prostate-cancer**
- Women with BRCA1 mutations have a **78.3%** risk to develop breast cancer before the age of 70 (General population **0.1%**)
- Commonly **hormone-receptor-negative**

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Central effects of cross-sex hormone treatment

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OPEN ACCESS Freely available online PLOS | ONE

Effects of Androgen Deprivation on Cerebral Morphometry in Prostate Cancer Patients – An Exploratory Study

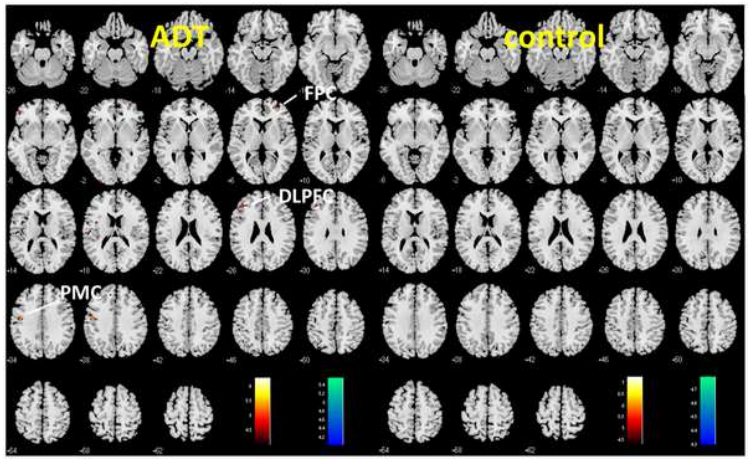
Herta H. Chao[1,2*], Sien Hu[3], Jaime S. Ide[4], Edward Uchio[5], Sheng Zhang[3], Michal Rose[1,2], John Concato[1,2,6], Chiang-shan R. Li[3,7,8]

Shrinkage of brain volume in men treated with androgen deprivation for prostate cancer

European Journal of Endocrinology (2006) **155** S107–S114 ISSN 0804-4643

Changing your sex changes your brain: influences of testosterone and estrogen on adult human brain structure

Hilleke E Hulshoff Pol, Peggy T Cohen-Kettenis[1], Neeltje E M Van Haren, Jiska S Peper, Rachel G H Brans, Wiepke Cahn, Hugo G Schnack, Louis J G Gooren[2] and René S Kahn



Decrease in brain volume in trans women following CSH
Increase in brain volume in trans men following CSH

BDNF in transwomen

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SHORT COMMUNICATION

Cross-sex hormone treatment in male-to-female transsexual persons reduces serum brain-derived neurotrophic factor (BDNF)

Johannes Fuss[a,*], Rainer Hellweg[b], Eva Van Caenegem[c], Peer Briken[a], Günter K. Stalla[d], Guy T'Sjoen[c], Matthias K. Auer[d]

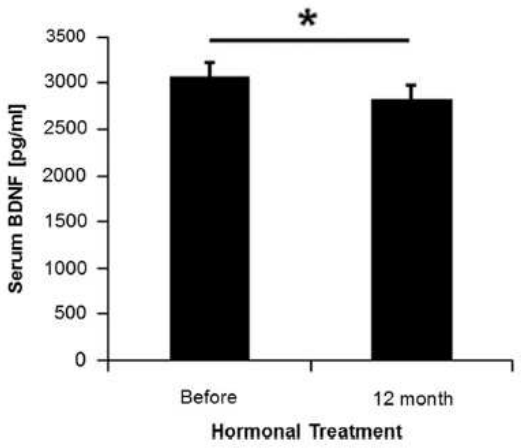

Fig. 1 Serum BDNF is significantly lower after 12 month of cross-sex hormone treatment.

Decrease in BDNF-levels in trans women following 12 months of CSH independent of lifestyle and changes in anthropometry.
-> Direct effect on **BDNF**-release from **thrombocytes?**

Eur Neuropsychopharmacol. 2014

Breast development

ORIGINAL RESEARCH—TRANSGENDER AND GENDER NONCONFORMANCE

Clinical Review: Breast Development in Trans Women Receiving Cross-Sex Hormones

Katrien Wierckx, MD,* Louis Gooren, MD, PhD,† and Guy T'Sjoen, MD, PhD*‡

- **Breast growth starts 2-3 months** following initiation of CRH **and progresses up to 2 years**
- **35%** achieve **A-cups** **less than A cups** fol continuous CSH
- **No differences between GnRH –analogues** or **antiandrogens**
- **Progesterone** does not induce **proliferation (volume)** of breast tissue but differentiation.

No evidence that **high doses of E2** or **intake of progesterone** affects final breast size

Table 1 Studies concerning the effect of cross-sex hormone treatment on breast size in trans women

Center	Study design	Hormone treatment	N	Outcome
Department of Dermatology, New York University, New York [15]	Case reports	Various estrogen treatments	5	Breast development
Gender Clinic, University of Texas, Medical Branch, Galveston, Texas [16]	Cross- sectional	EE 0.05–10 mg OD or conjugated equine estrogens (1.25–5 mg OD)	39	Effect of EE vs. conjugated equine estrogens on breast hemicircumference Effect of estrogen dose on breast hemicircumference
Gender Clinic, University of Texas, Medical Branch, Galveston, Texas [17]	Prospective	EE 0.05–10 mg OD or conjugated equine estrogens (1.25–10 mg OD) 15% oral progestin (mostly MPA 10 mg OD)	60	Time course of breast growth (breast hemicircumference) Effect of ethinyl estradiol vs. conjugated equine estrogens on breast hemicircumference Effect of estrogen dose on breast hemicircumference Effect of progestin on breast hemicircumference
Department of Plastic and Reconstructive Surgery, Academic Hospital Vrije Universiteit, Amsterdam, Netherlands [21]	Retrospective	EE 100 μg OD and CPA 100 mg OD	359	Percentage of trans persons that underwent augmentation mammoplasty
Department of Medicine University of Seville Seville, Spain	Cross sectional	Various cross-sex hormone treatments	27	Tanner stage
Department of Obstetrics and Gynaecology, Erlangen University Hospital, Germany [22]	Prospective (24 months)	Subcutaneous injection of GnRH every 4 weeks and estradiol valerate 6 mg OD	60	Cup size Percentage of trans persons that planned to undergo augmentation mammoplasty
Department of Sexology and Gender Problems, University Hospital Ghent, Belgium [23]	Cross-sectional	CPA 50–100 mg OD; various estrogen treatments	32	Percentage of trans persons that underwent augmentation mammoplasty
Department of Medicine, St George's hospital, London, United Kingdom [13]	Retrospective	Various estrogen and anti-androgen treatments	165	Predictive markers for mammoplasty Type of estrogen and type of anti-androgen

CPA = cyproterone acetate; EE = ethinyl estradiol; MPA = medroxyprogesterone acetate; OD = once daily

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Cardiovascular risk factors

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Cardiovascular disease in transsexual persons treated with cross-sex hormones: reversal of the traditional sex difference in cardiovascular disease pattern

Louis J Gooren[†], Katrien Wierckx[1] and Erik J Giltay[2]

Trans women

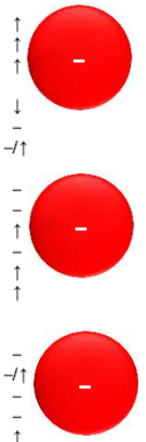
Table 2 Short-term changes in metabolic and cardiovascular risk factors in MtoF transsexual persons.

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

Trans men

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

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



Mortality

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Trans women

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

Reference	n	Follow-up	Treatment regimen	Outcome
(16)	303	Median duration HRT of 4.4 years	Ethinyl estradiol 100 μg/day and cyproterone acetate 100 mg/day	45-fold increase in VT and/or PE No increased cardiovascular morbidity and mortality
(15)	816	Mean duration HRT of 9.5 years	Ethinyl estradiol 100 μg/day or transdermal 17β-estradiol 100 μg/twice a week and cyproterone acetate 100 mg/day	20-fold increase in venous thrombosis and/or pulmonary embolism No increased cardiovascular morbidity or mortality rate
(14)	966	Median duration HRT of 18.5 years*	Ethinyl estradiol 100 μg/day or transdermal 17β-estradiol 100 μg/twice a week and cyproterone acetate 100 mg/day	Higher mortality due to ischemic heart disease; SMR 1.64 (1.43–1.87)
(17)	191	Median time since SRS of 9.1 years*	Not specified	Higher mortality due to CVD; SMR 2.11 (1.32–3.21) in age group 40–64 years Higher mortality due to cardiovascular disease compared with controls
(56)	58			orbidity ol male and
(27)	214			compared with compared with men

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

Table 5 Studies on ... ol population.

Reference	n	Follow-up	Treatment regimen	Outcome
(16)	122	Median duration HRT of 4.4 years[a]	Testosterone esters 250 mg i.m. every 2 weeks or testosterone undecanoate 120–160 mg/day	No increased cardiovascular morbidity
(15)	293	Mean duration HRT of 8.2 years	Testosterone esters 250 mg i.m. every 2 weeks or testosterone undecanoate 160 mg/day	No increased cardiovascular morbidity or mortality rate
(14)	365	Median duration HRT of 18.5 years[a]	Testosterone esters 250 mg i.m. every 2 weeks or testosterone undecanoate 160 mg/day	No increased cardiovascular mortality rate
(17)	133	Median time since SRS was 9.1 years[a]	Not specified	Higher mortality due to cardiovascular disease compared with controls
(56)	37	Mean duration HRT of 4.9±4.6 years	Different testosterone preparations	No difference in cardiovascular morbidity compared with control men and women
(27)	138	Median duration HRT of 6 years	Different testosterone preparations	No difference in cardiovascular morbidity compared with control men and women

Trans men

Mortality

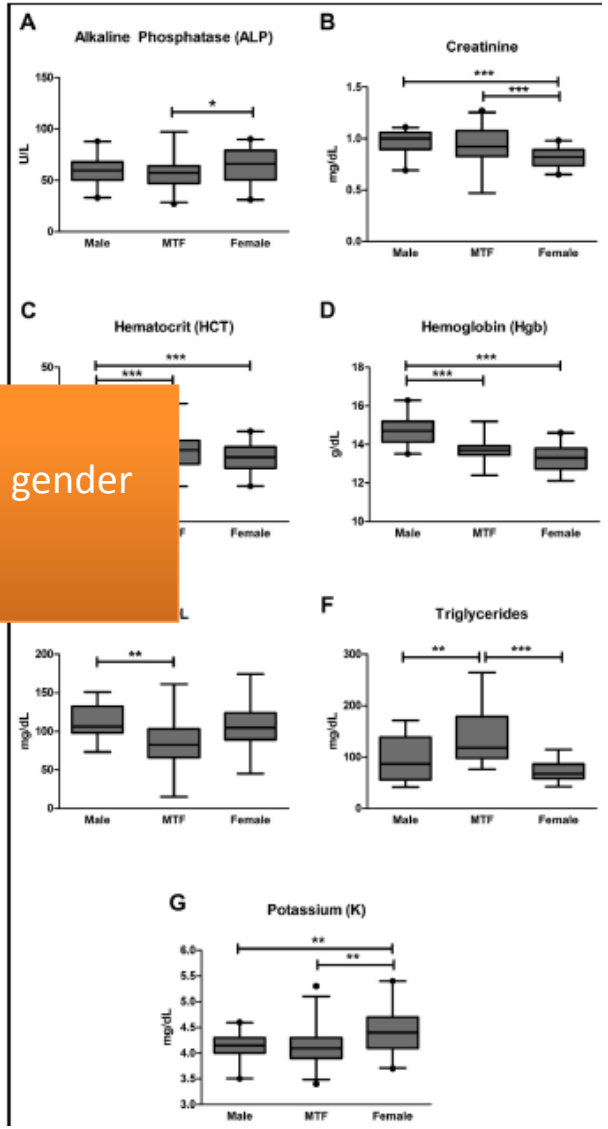
Interpreting Laboratory Results in Trans Hormone Therapy

Tiffany K. Roberts, PhD,[a] Colleen S. Kraft, MD,[a] Deborah French, PhD,[b] Wuyang
Vin Tangpricha, MD, PhD,[d] Corinne R. Fantz, PhD[a]

METHODS: Laboratory dat
from the medical records
patients on **hormone ther**
with **20 male** and **20 fema**
subjects.

CONCLUSIONS: Preliminary data suggest that **new reference intervals** need to be established?

What is a **"normal" lab value** in gender dysphoria with CSH?



Thank you!