

Transforming Your Clinical Practice: An Exploration of Transgender Bone Health

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Pronouns: She/Her

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Medicine
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Endocrinology & Metabolism

LAND ACKNOWLEDGEMENT

I acknowledge that I am giving this lecture on the traditional territory of many nations including the Mississaugas of the Credit, the Anishnabeg, the Chippewa, the Haudenosaunee and the Wendat peoples.

These nations lived and thrived in these spaces for millennia, and today, are still home to many diverse First Nations, Inuit and Métis peoples.

These lands are unceded and traditional to these nations, and we must work to recognize and address ongoing colonial harms.

DISCLOSURES

I do not have a relationship with a for-profit and/or a not-for-profit organization to disclose.

OBJECTIVES

- 1. Understand why Transgender health is an important and rapidly growing field in medicine**
- 2. Describe the physiology of sexual dimorphism in bone health and how this relates to Transgender bone health**
- 3. Learn current guidelines and emerging research in Transgender bone health**
 - highlight important differences for adolescents and adults**

OUTLINE

1. **Why is transgender health important for clinicians?**
2. **Sexual dimorphism in bone health**
3. **Bone mineral density changes in trans-adolescents**
4. **Review Endocrine Society Transgender Health Guidelines pertaining to bone health in adults**
5. **Discuss the latest recommendations for trans-adult bone health screening**

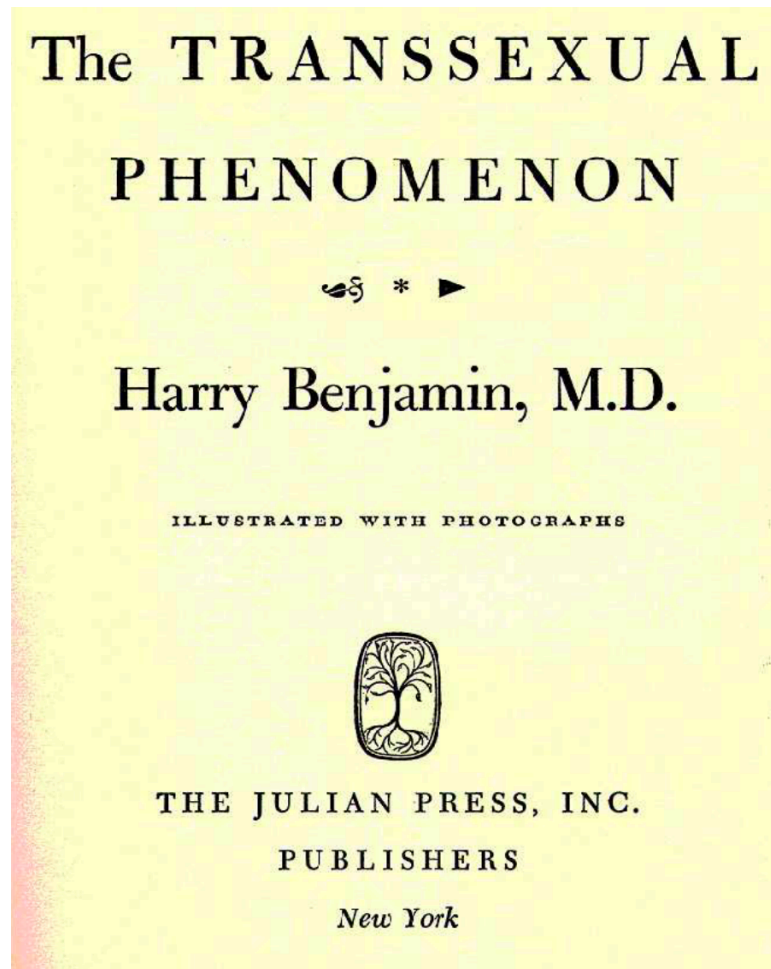
LET'S START WITH SOME DEFINITIONS

- **Transgender:** A person whose gender identity differs from their sex assigned at birth
- **Cisgender:** A person whose gender identity is the same as their sex assigned at birth
- **Sex (AFAB/AMAB):** The natal sex assigned at birth, based on external genitalia, as well as chromosomes and gonads
 - Assigned female at birth or designated female at birth
 - Assigned male at birth or designated male at birth
- **Gender identity:** A person's internal sense of self and how they fit into the world, from the perspective of gender

LET'S START WITH SOME DEFINITIONS

- **Transsexual:** A clinical term which had historically been used to describe those transgender people who sought medical intervention (hormones, surgery) for gender affirmation (**term is no longer used!**)
- **Gender Affirming Hormone Therapy (GAHT):** using hormones to reduce characteristics of their natal sex and induce characteristics reflective of their gender identity
- **Areal Bone Mineral Density (aBMD):** measured by DEXA scan; is the amount of bone mineral divided by the bone scanned area
- **Bone Mineral Apparent Density (BMAD):** is a calculation from the DEXA scan to estimate volumetric bone mineral density (often used in children/adolescents)

BUT FIRST...WHO IS THIS MAN?



Endocrinologist: Dr. Harry Benjamin

Publishes “The Transsexual Phenomenon” in 1966.

- Argues against psychotherapy as a “cure” for *transsexuals
(*since antiquated term)
- Used gender-affirming hormone therapy to treat patients

FATHER OF TRANS CARE IN ENDOCRINOLOGY



Volume 102, Issue 11

1 November 2017

Article Contents

Abstract

EDITOR'S CHOICE

Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society* Clinical Practice Guideline FREE

Wylie C Hembree, Peggy T Cohen-Kettenis, Louis Gooren, Sabine E Hannema, Walter J Meyer, M Hassan Murad, Stephen M Rosenthal, Joshua D Safer, Vin Tangpricha, Guy G T'Sjoen **Author Notes**

The Journal of Clinical Endocrinology & Metabolism, Volume 102, Issue 11, 1 November 2017, Pages 3869–3903, <https://doi.org/10.1210/jc.2017-01658>

Published: 13 September 2017 **Article history** ▼

Hembree et al. 2017

Endocrinology & Metabolism

SIMILAR DISCOURSE OCCURS TODAY...

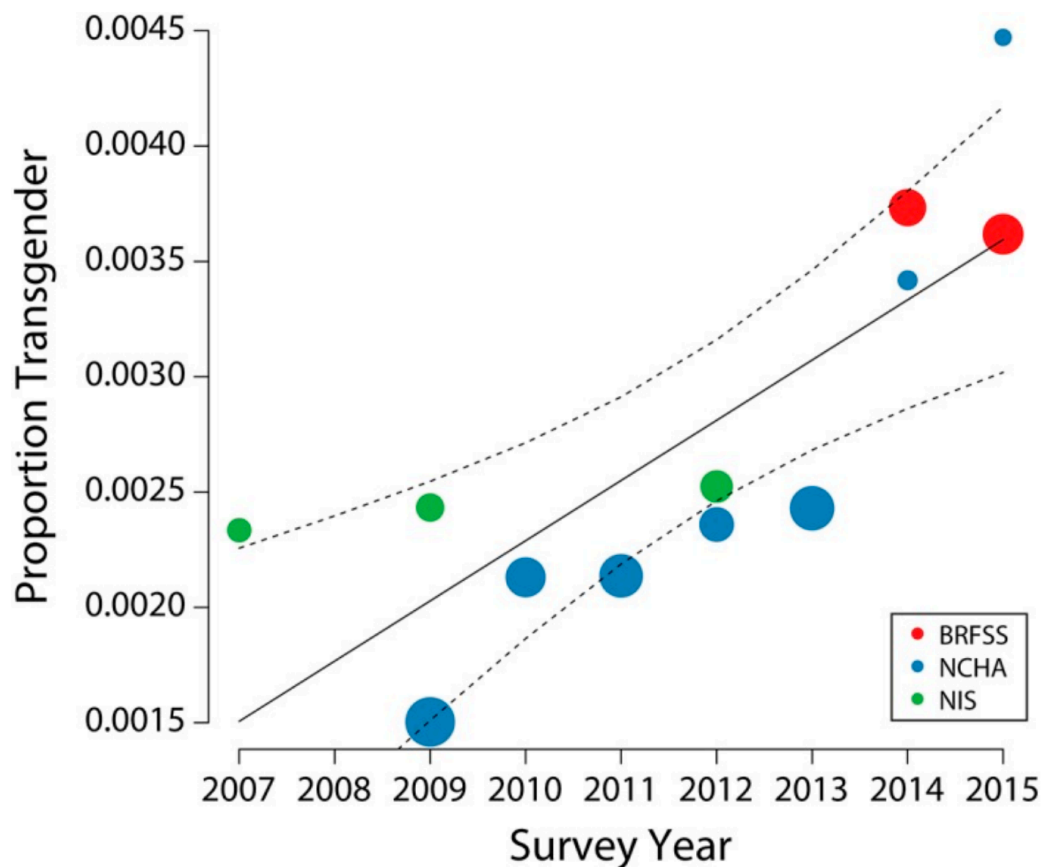
Response to Letter to the Editor: “Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline”

Stephen M Rosenthal, Wylie C Hembree, Peggy T Cohen-Kettenis, Louis Gooren, Sabine E Hannema, Walter J Meyer, M Hassan Murad, Joshua D Safer, Vin Tangpricha, Guy G T’Sjoen

The Journal of Clinical Endocrinology & Metabolism, Volume 104, Issue 11, November 2019, Pages 5102–5103, <https://doi.org/10.1210/jc.2019-00930>

Published: 02 May 2019 **Article history** ▼

EPIDEMIOLOGY – PREVALENCE IN U.S.A.



1 in every 250
Americans

~ 1.4 million
Americans

WHY ARE WE TALKING ABOUT THIS NOW?

Trans Individuals in Ontario

- 75% of trans people indicated they need to transition medically.
- In 2013, an estimated 43.0% of trans Ontarians were currently using hormones.
- 11% had obtained hormones from nonmedical sources.

Bauer G et al. Trans PULSE e-Bulletin, (2010);
Rotondi et al. *American journal of public health* (2013)

WHY ARE WE TALKING ABOUT THIS NOW?

- Barriers to adequate care of this population include little or no formal training in addressing the needs of transgender patients.
- Confidence or comfort level in providing care to transgender patients has been reported to be low among practicing endocrinologists.
- ~80% have treated a transgender patient, **yet** ~80% have never received training on care of transgender patients.

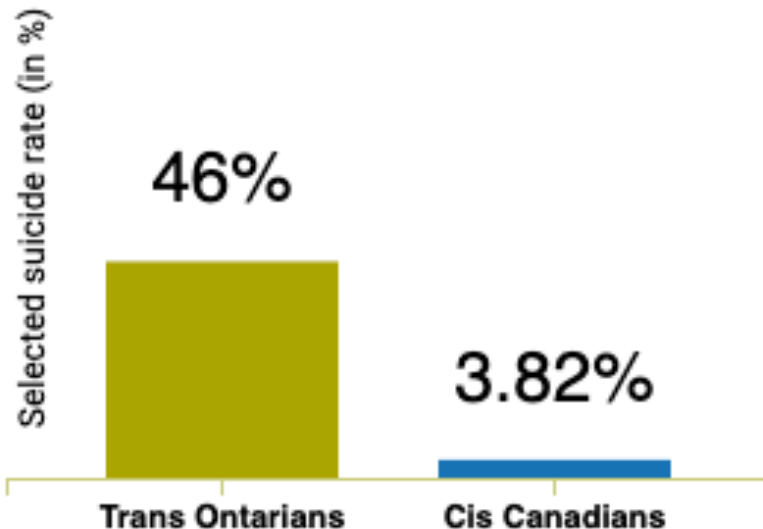
Irwig MS. Endocr Pract. 2016;
Davidge-Pitts et al. JCEM 2017



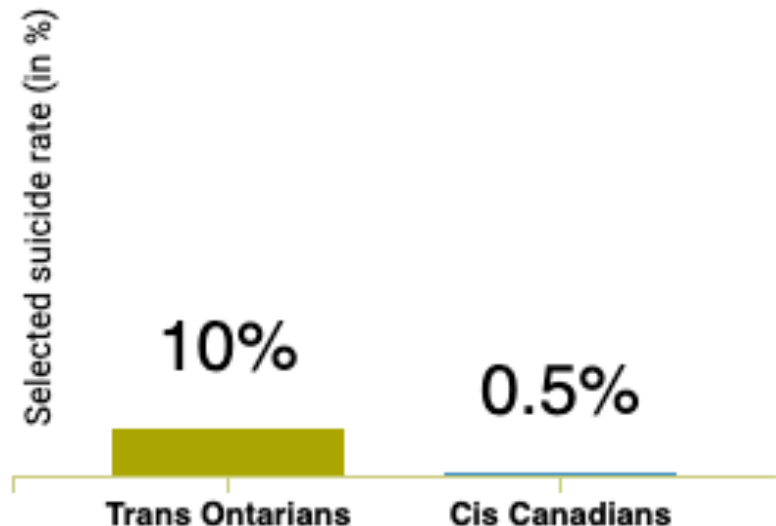
RATES OF SUICIDE ATTEMPT IN TRANS VS. CIS ONTARIANS

Compare rates between *trans* and *cis* people:

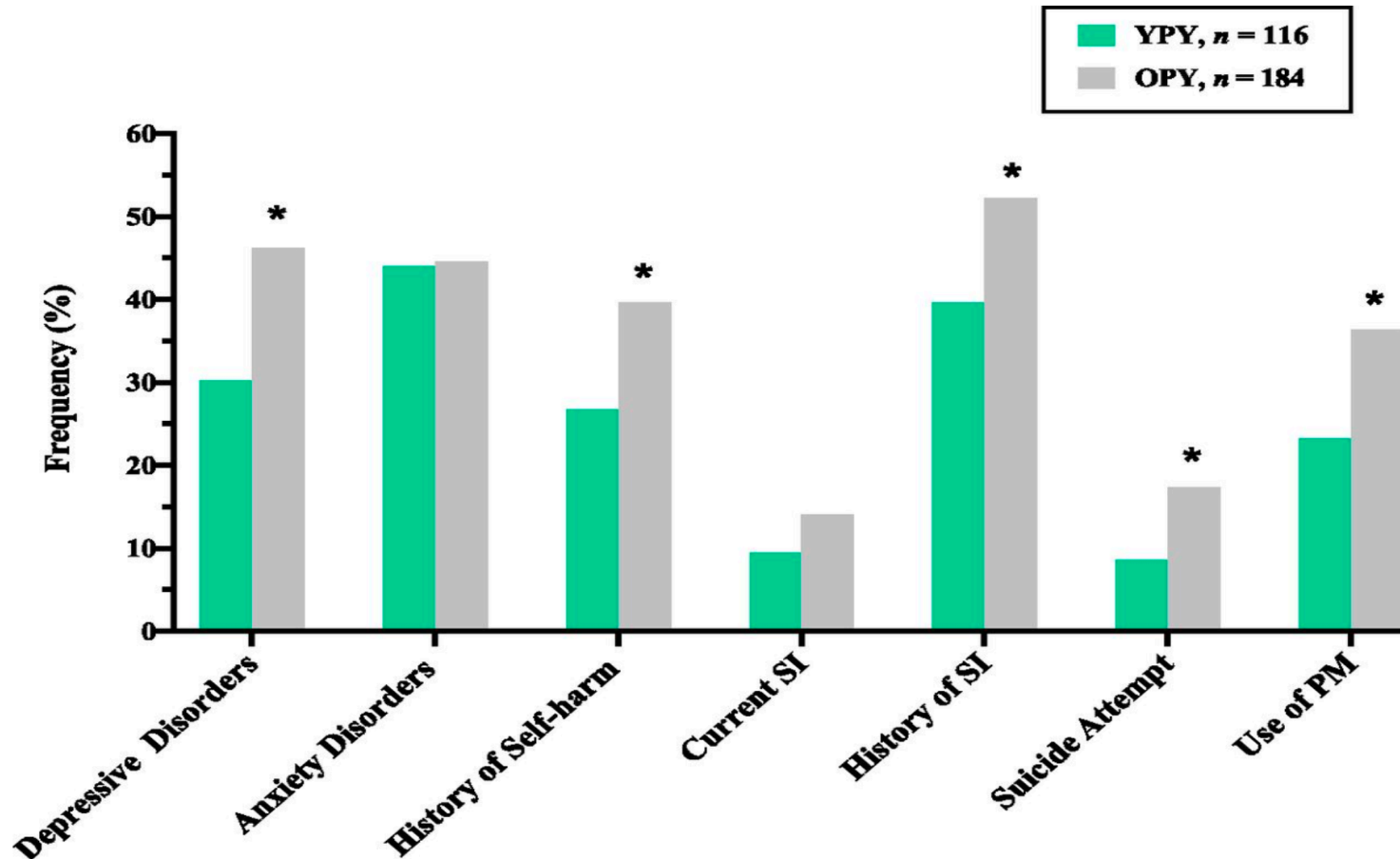
SUICIDE ATTEMPT (ACROSS LIFESPAN) ▼



SUICIDE ATTEMPT (PAST YEAR) ▼



TRANS-YOUTH AND MENTAL HEALTH



- YPY = younger presenting youth <15 yo
- OPY = older presenting youth ≥ 15 yo

Sorbara et al. Paediatrics 2020



DYSPHORIA RELIEVED IN YOUTH AFTER GAHT

- 55 young adults (22 transwomen and 33 transmen)
- Gender Dysphoria assessed before puberty blockers, during cross-hormone tx, after affirmation tx

	N ^a	T0	T1	T2	T0-T2
		Mean (SD)	Mean (SD)	Mean (SD)	t test
					P
UGDS	33	53.51 (8.29)	54.39 (7.70)	15.81 (2.78)	<.001
MtF	11	47.07 (11.05)	48.95 (10.80)	17.27 (2.57)	<.001
FtM	22	56.74 (3.74)	57.11 (3.40)	15.08 (2.64)	<.001
Body Image (BIS)					
Primary sex characteristics	45	4.13 (0.59)	4.05 (0.60)	2.59 (0.82)	<.001
MtF	17	4.03 (0.68)	3.82 (0.56)	2.07 (0.74)	<.001
FtM	28	4.18 (0.53)	4.13 (0.60)	2.89 (0.71)	<.001
Secondary sex characteristics	45	2.73 (0.72)	2.86 (0.67)	2.27 (0.56)	<.001
MtF	17	2.63 (0.60)	2.34 (0.68)	1.93 (0.63)	<.001
FtM	28	2.80 (0.72)	3.18 (0.43)	2.48 (0.40)	.05

De Vries et al. Paediatrics 2014

TAKE HOME POINTS

- Gender Identity \neq Sex (assigned at birth)
- The first transgender health guidelines were published 42 years ago in 1979
- Clinical competence for Transcare needs to improve among healthcare providers
- Suicidality was highest with those who were planning to transition, but who had not yet begun

OUTLINE

- ~~1. Why is transgender health important for clinicians?~~
- 2. Sexual dimorphism in bone health**
- 3. Bone mineral density changes in trans-adolescents**
- 4. Review Endocrine Society Transgender Health Guidelines pertaining to bone health in adults**
- 5. Discuss the latest recommendations for trans-adult bone health screening**

DETERMINANTS OF BONE HEALTH

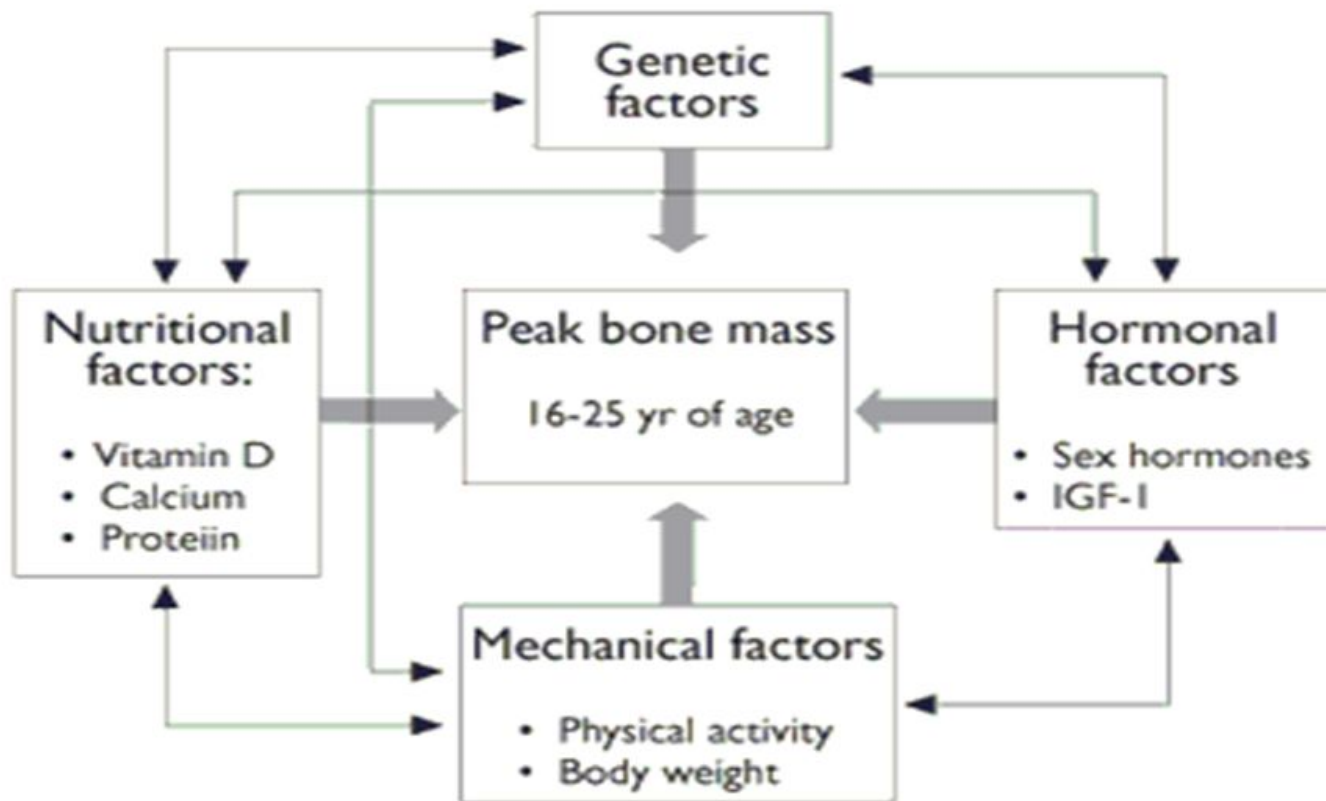
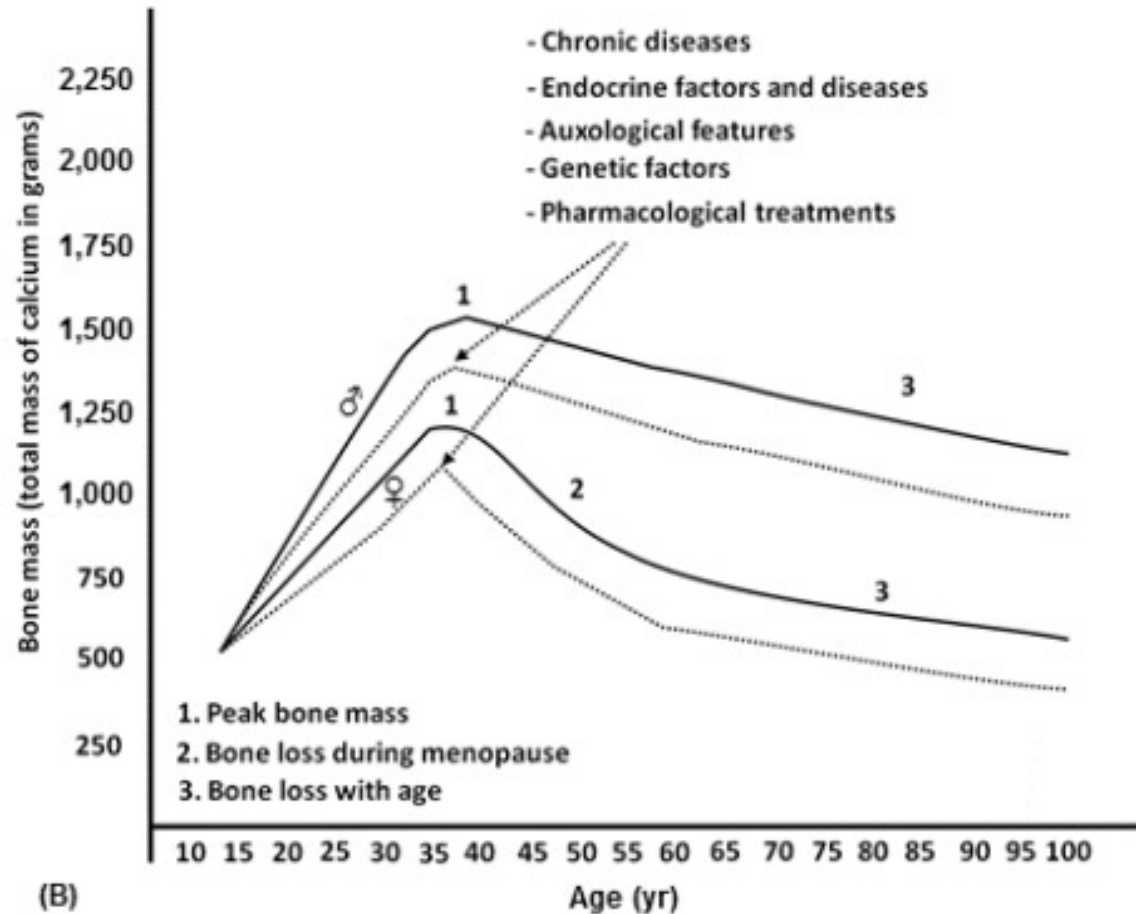
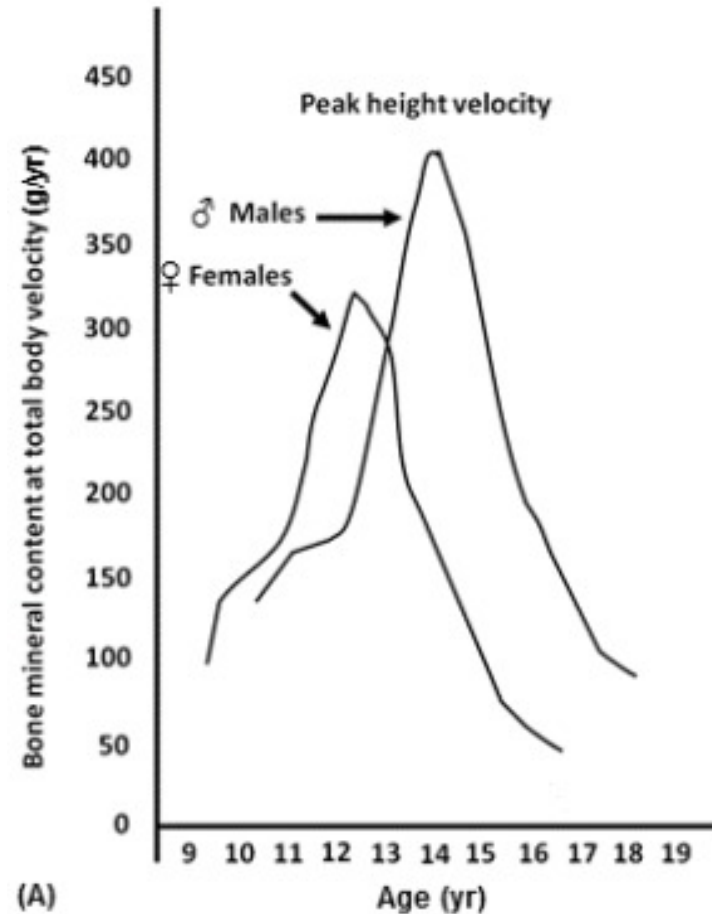


Figure from Bonjour JP et al. 2009

ACQUISITION OF PEAK BONE MASS



Pre puberty

Puberty
(Early – late)

Post puberty

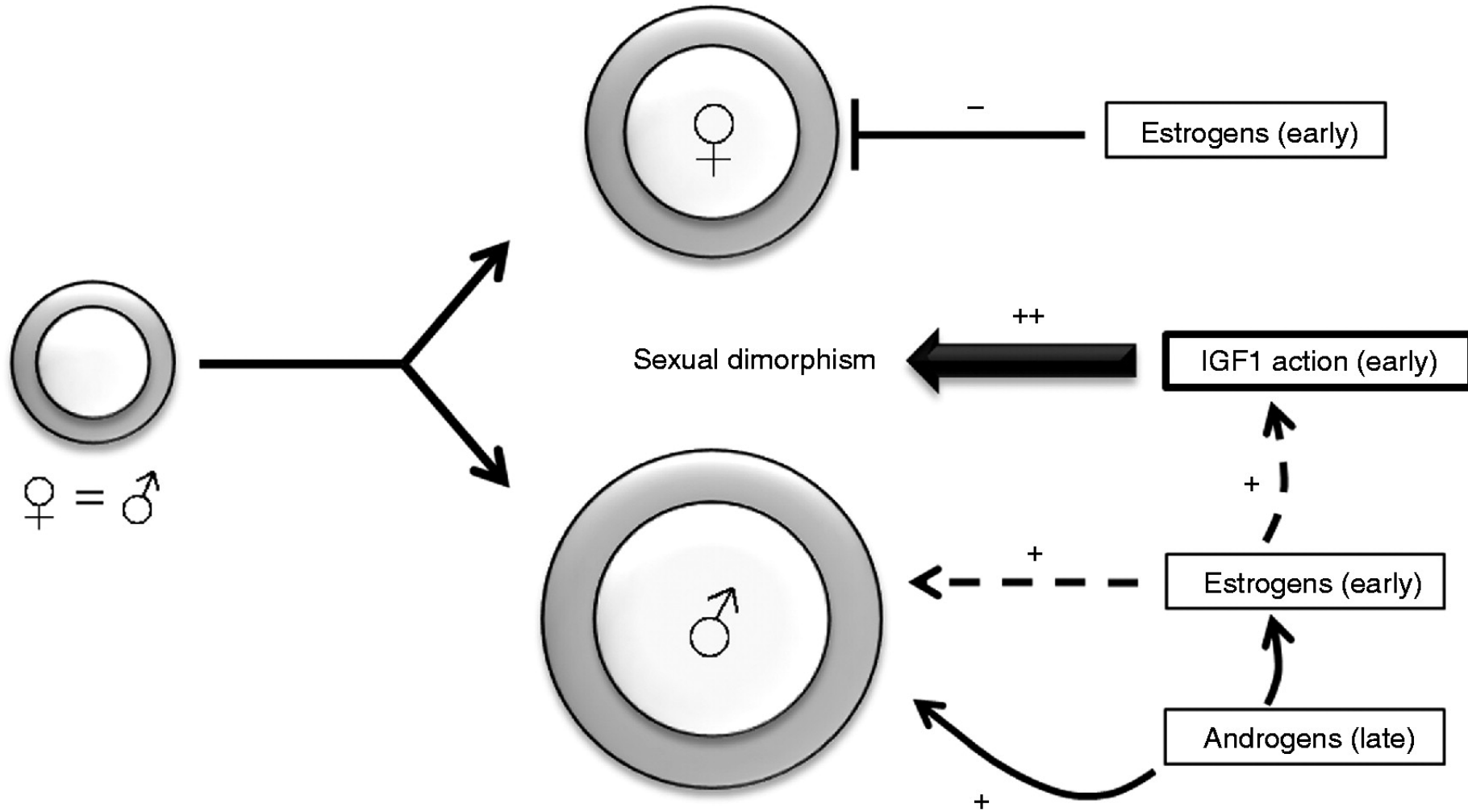
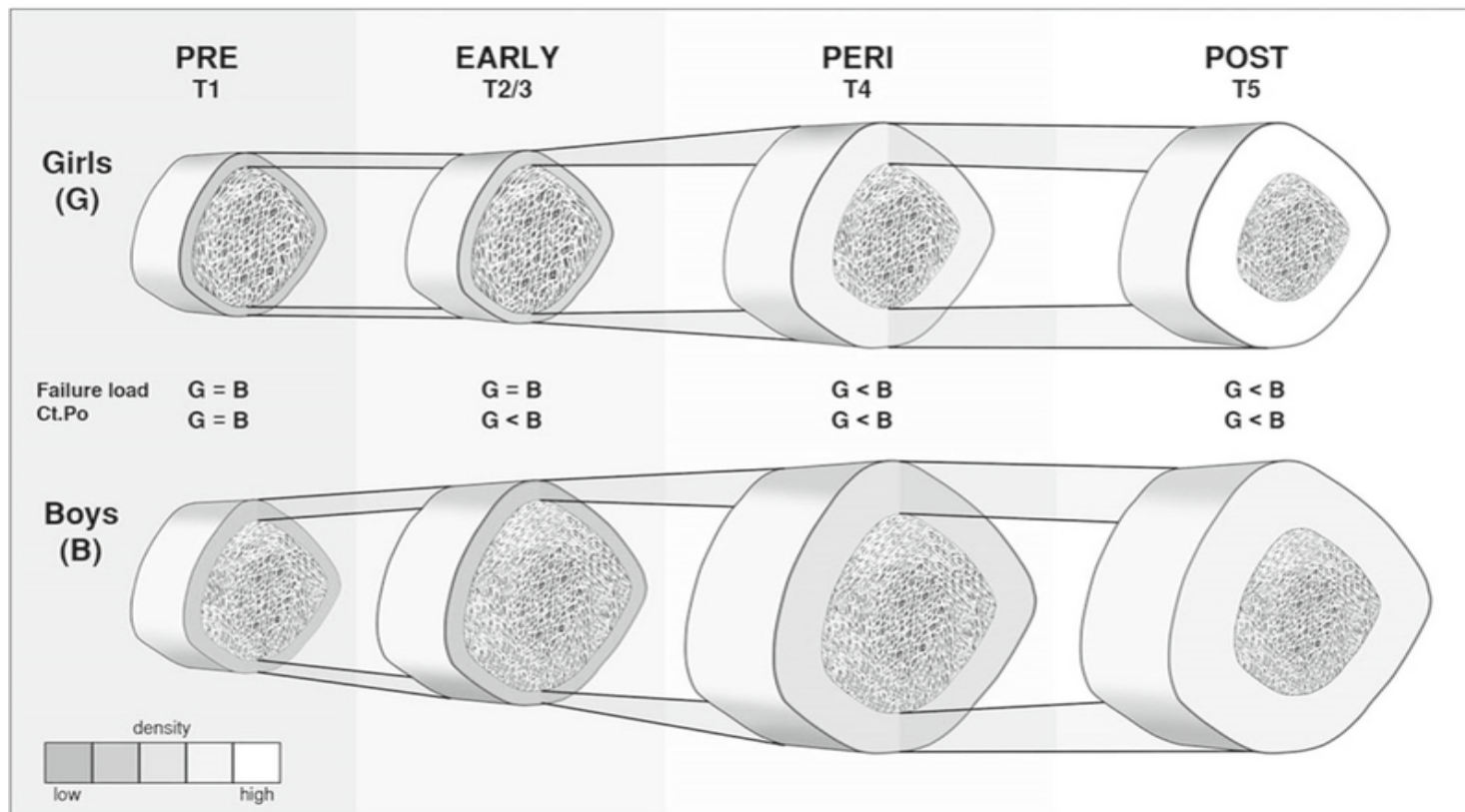


Figure from Callewaert et al. 2010 Journal of Endocrinology 207, 2; [10.1677/JOE-10-0209](https://doi.org/10.1677/JOE-10-0209)

Endocrinology & Metabolism

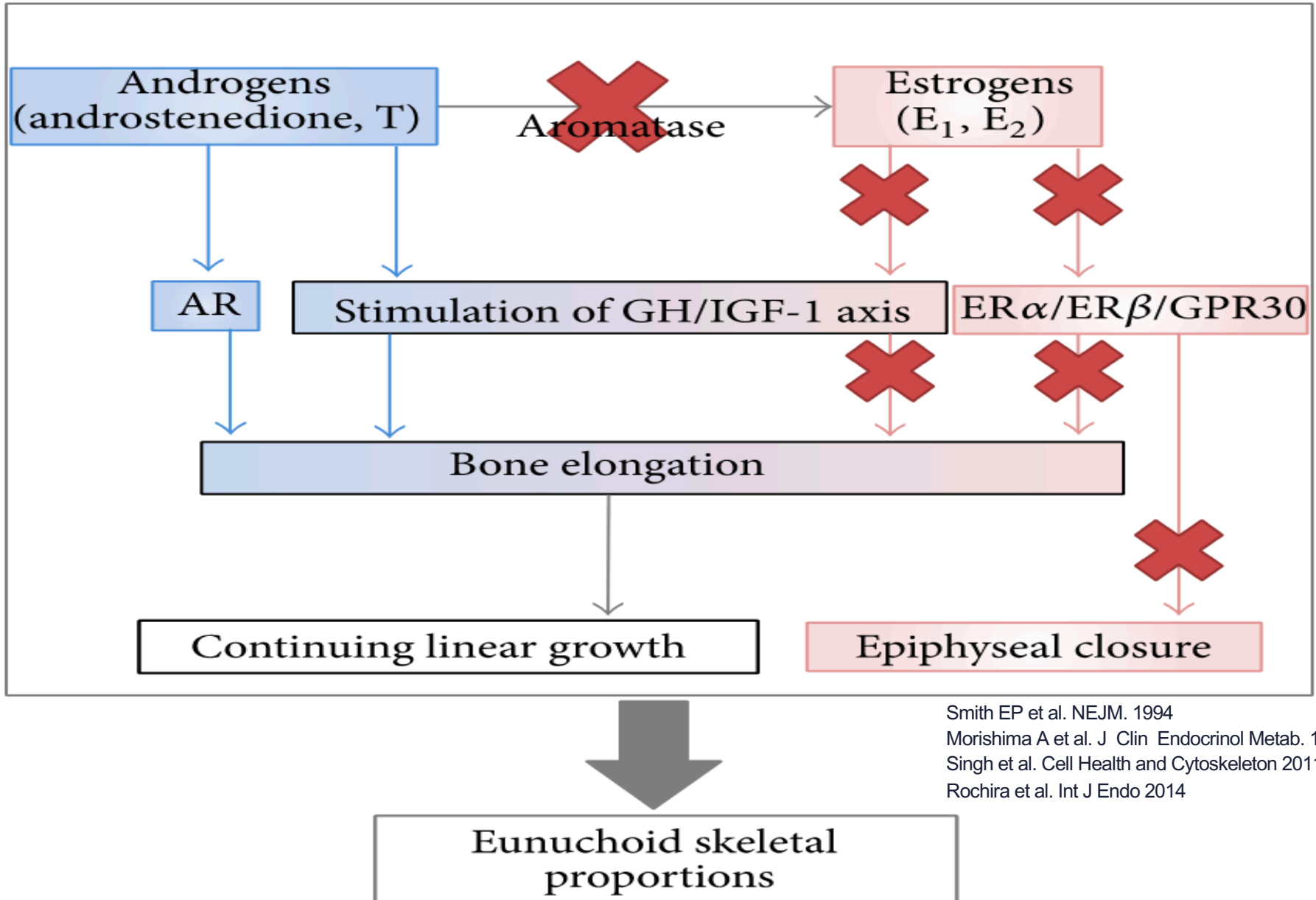
ENDOSTEAL VS. PERIOSTEAL APPPOSITION

Total Bone Size and Cortical Bone Density Across Natal Puberty



Nishiyama et al Journal of Bone and Mineral Research, Volume: 27, Issue 2, Pages: 273–282, First published: 25 October 2011

EFFECT OF ESTROGEN ON PUBERTAL BONE



Smith EP et al. NEJM. 1994

Morishima A et al. J Clin Endocrinol Metab. 1995

Singh et al. Cell Health and Cytoskeleton 2011

Rochira et al. Int J Endo 2014

TAKE HOME POINTS

- Peak bone mass (PBM) is well known as a key determinant of the lifetime risk of osteoporosis.
- Adolescence is a critical time for peak bone accrual.
- Bone growth is sexually dimorphic.
- Cis-men/boys = wider bones.
- Cis-women/girls = more endosteal growth.
- Estrogen plays a KEY role in epiphyseal fusion and in maintenance of bone health in BOTH anatomical sexes.

OUTLINE

- ~~1. Why is transgender health important for clinicians?~~
- ~~2. Sexual dimorphism in bone health~~
- 3. Bone mineral density changes in trans-adolescents**
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- 5. Discuss the latest recommendations for trans-adult bone health screening**

ENDOSOCIETY TRANS CARE RECOMMENDATIONS IN ADOLESCENTS

2.2. We suggest that clinicians begin pubertal hormone suppression after girls and boys first exhibit physical changes of puberty. (2 | ⊕⊕○○)

2.3. We recommend that, where indicated, GnRH analogues are used to suppress pubertal hormones. (1 | ⊕⊕○○)

2.4. In adolescents who request sex hormone treatment (given this is a partly irreversible treatment), we recommend initiating treatment using a gradually increasing dose schedule after a multidisciplinary team of medical and MHPs has confirmed the persistence of GD/gender incongruence and sufficient mental capacity to give informed consent, which most adolescents have by age 16 years. (1 | ⊕⊕○○).

ENDOSOCIETY TRASCARE MONITORING IN ADOLESCENTS (*Pubertal Suppression*)

Table 7. Baseline and Follow-Up Protocol During Suppression of Puberty

Every 3–6 mo

Anthropometry: height, weight, sitting height, blood pressure, Tanner stages

Every 6–12 mo

Laboratory: LH, FSH, E2/T, 25OH vitamin D

Every 1–2 y

Bone density using DXA

Bone age on X-ray of the left hand (if clinically indicated)

Adapted from Hembree et al. (118).

Abbreviations: DXA, dual-energy X-ray absorptiometry; E2, estradiol; FSH, follicle stimulating hormone; LH, luteinizing hormone; T, testosterone;



ENDOSOCIETY TRASCARE MONITORING IN ADOLESCENTS (*Induction of Puberty*)

Table 9. Baseline and Follow-up Protocol During Induction of Puberty

Every 3–6 mo

- Anthropometry: height, weight, sitting height, blood pressure, Tanner stages

Every 6–12 mo

- In transgender males: hemoglobin/hematocrit, lipids, testosterone, 25OH vitamin D
- In transgender females: prolactin, estradiol, 25OH vitamin D

Every 1–2 y

- BMD using DXA
- Bone age on X-ray of the left hand (if clinically indicated)

BMD should be monitored into adulthood (until the age of 25–30 y or until peak bone mass has been reached).



Z-SCORES WITH GnRHa FOLLOWED BY GAHT

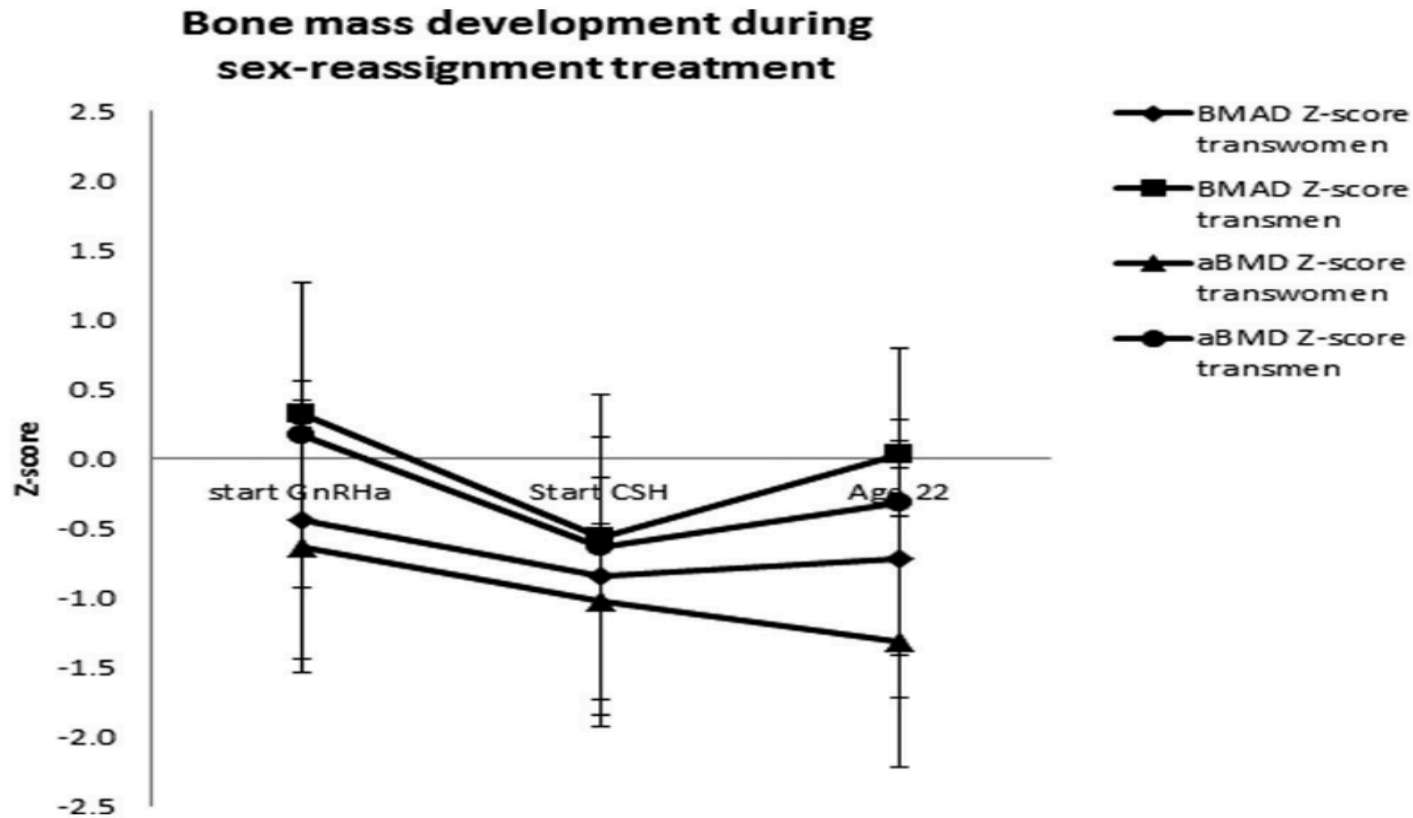


Figure 1. Longitudinal z-score (mean \pm SD) development of the LS from start medical treatment until the age of 22 years in transmen and transwomen.

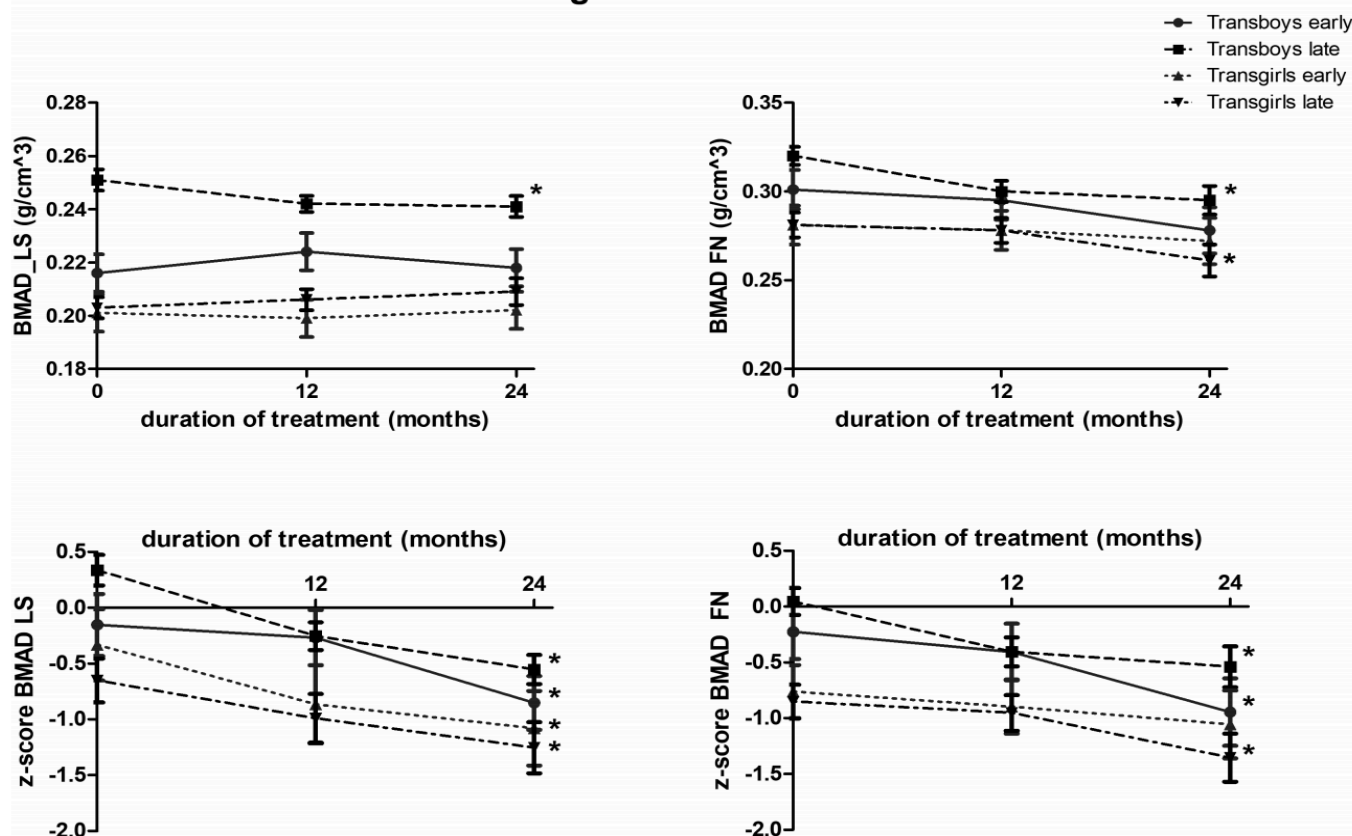
GnRH IMPACT ON BMD, BMAD and BTMs

- **Case report:** normal BMD z scores at age 35 years in transman who used GnRH analogs from age 13.7 years until age 18.6 years
(before initiating sex hormone treatment)
- **Retrospective study:** 22 Transwomen and 34 transmen: GnRHa leads to a decrease of bone turnover markers (BTMs) in both transwomen and transmen transgender adolescents.
- BMAD and BMAD Z-scores increase predominantly in the LS as a result of treatment with GAHT.

GnRH IMPACT ON BMAD

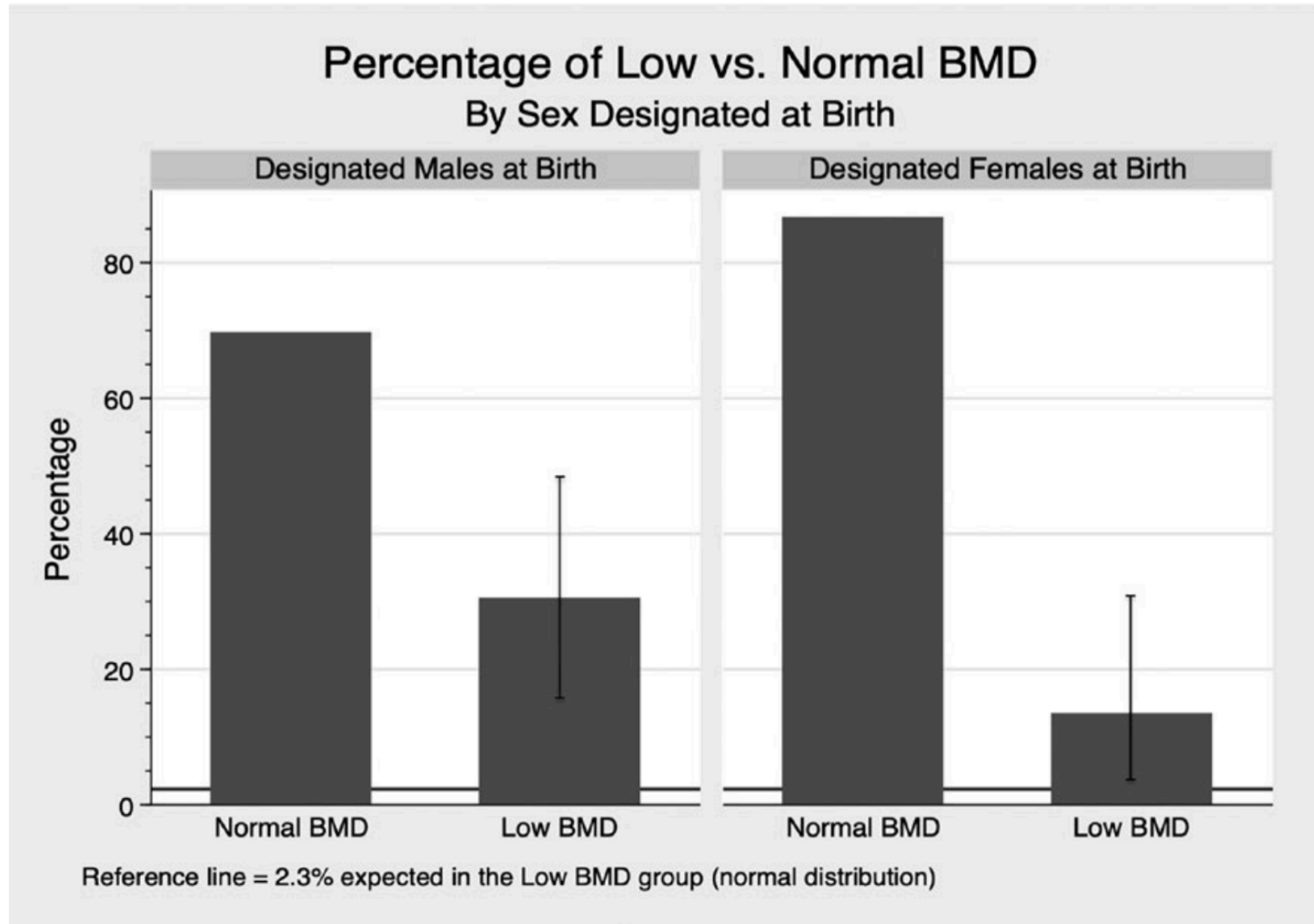
- EP - 51 transgirls and 70 transboys receiving GnRHa
- LP - 36 transgirls and 42 transboys receiving GnRHa

BMAD and BMAD z-scores during GnRHa



Schagen SEE et al. JCEM 2020

% LOW vs. NORMAL BMD IN TRANS-YOUTH



TAKE HOME POINTS

- **DXA scans are recommended both in suppression of puberty and pubertal induction...but they may not be necessary.**
- **Transgirls had lower BMAD PRIOR to starting any GAHT.**
- **Z-scores normalized in transboys but remained below zero in transgirls after GAHT.**
- **Whether low aBMD or BMAD translates into increased fracture risk remains left for discovery.**



OUTLINE

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ENDOSOCIETY TRANS CARE RECOMMENDATIONS IN ADULTS

- 4.4. We recommend that clinicians **obtain BMD measurements when risk factors for osteoporosis exist**, specifically in those who **stop sex hormone therapy after gonadectomy**.
- **TRANSMEN:**
Screening for osteoporosis should be conducted in those who:
 - a) Stop testosterone
 - b) Are not compliant with hormone therapy
 - c) Who develop risks for bone loss

ENDOSOCIETY TRANS CARE RECOMMENDATIONS IN ADULTS

- 4.4. We recommend that clinicians **obtain BMD measurements when risk factors for osteoporosis exist**, specifically in those who **stop sex hormone therapy after gonadectomy**.
- **TRANSWOMEN:**
Consider BMD testing at baseline.
 - a) Screening for osteoporosis should be conducted at age 60 years
 - b) In those who are not compliant with hormone therapy

BASELINE BMD – TRANS INDIVIDUALS

- Several investigators have described lower bone mass and smaller bone sizes in Transwomen prior to starting GAHT
- Lifestyle factors (physical activity, smoking, vitamin D status) thought to be potential contributors
- Prior to initiation of GAHT, BMD in Transmen are similar to that reported among cis-women controls

Lapauw et al. *Bone* 2008; Van Caenegem et al. *JCEM* 2012; Van Caenegem et al. *Bone* 2013;
Van Caenegem et al. *Eur J Endocrin* 2015; Wiepjes et al *JBMR* 2018

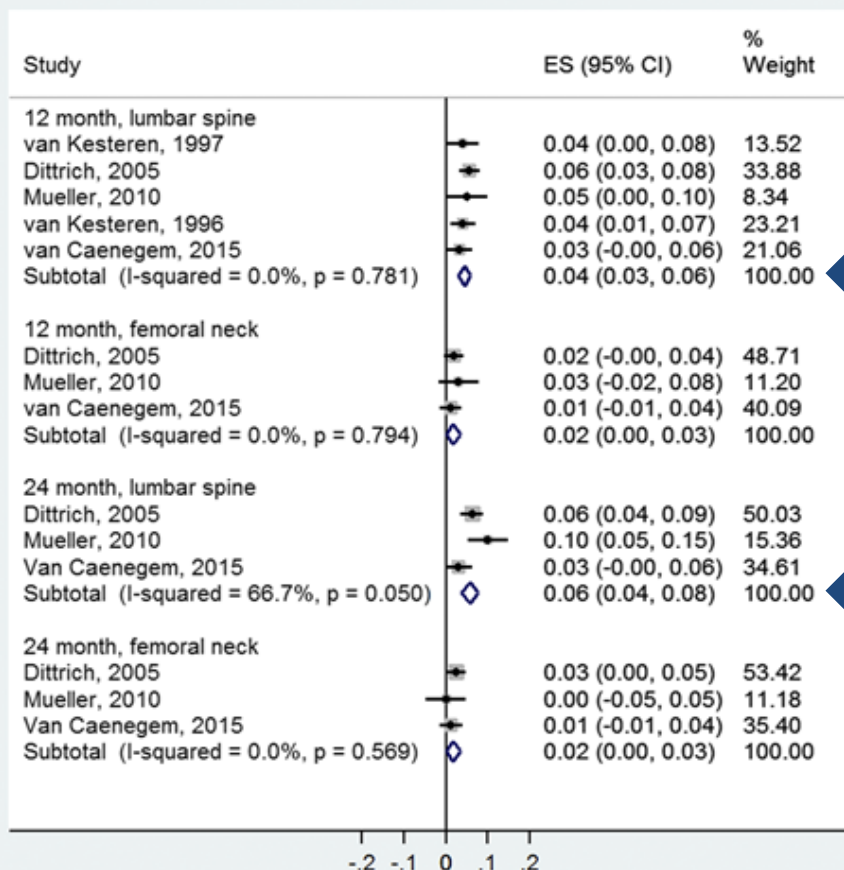
BMD FOLLOWING GAHT METANALYSIS

- 392 Transwomen (9 studies) and 247 Transmen (8 studies).
- Different routes of hormone administration and doses were used.
- Twelve studies evaluated changes in BMD, and only one study evaluated fracture rates.
- BMD outcome assessment was performed at baseline (pre-GAHT), 12 and 24 months.

BMD FOLLOWING GAHT METANALYSIS

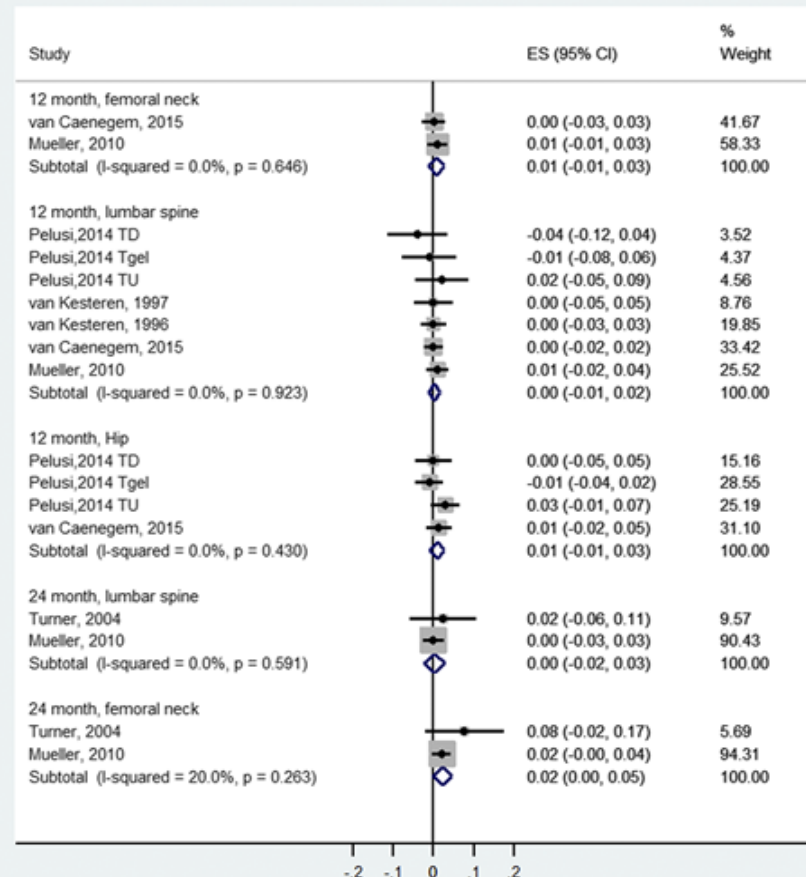
TRANSWOMEN

Male to Female



TRANSMEN

Female to Male



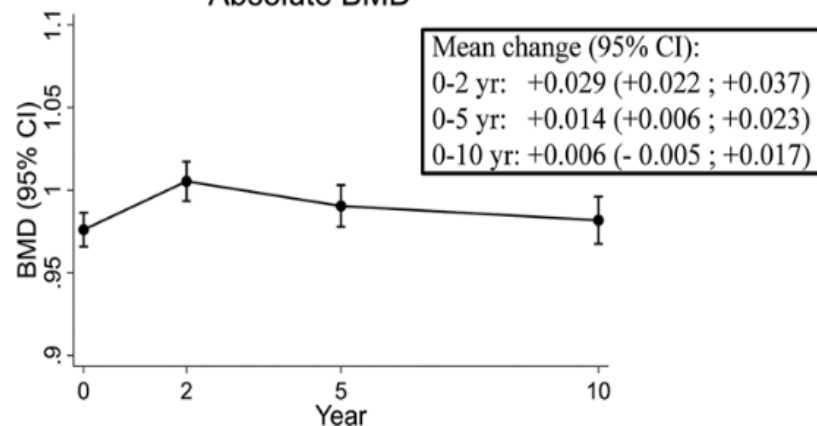
BMD BASELINE, 12–24 Months FOLLOW-UP DURING GAHT WITH NO GONADECTOMY

Hormone preparation	Parameter	GAHT administration route		
		Oral	Transdermal (or percutaneous)	Intramuscular
BMD				
17β-estradiol	Femoral neck	↑ ^a	No data	↔
	Lumbar spine	↑	↔	↑
	Total body	No data	↔	No data
Testosterone	Femoral neck	No data	No data	↔
	Lumbar spine	No data	↔	↔
	Total body	No data	↔	↔

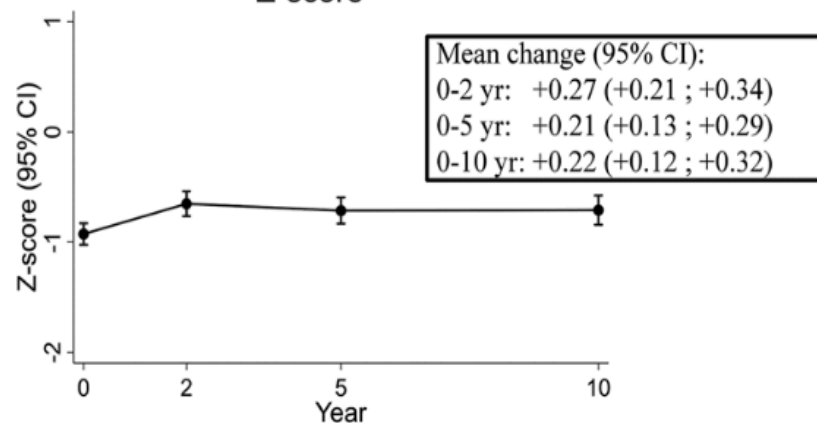
Bone Safety During the First Ten Years of GAHT

Transwomen

Absolute BMD

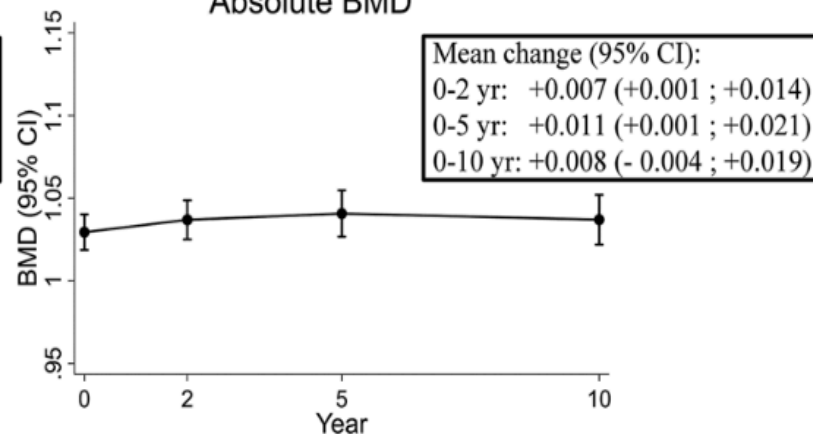


Z-score

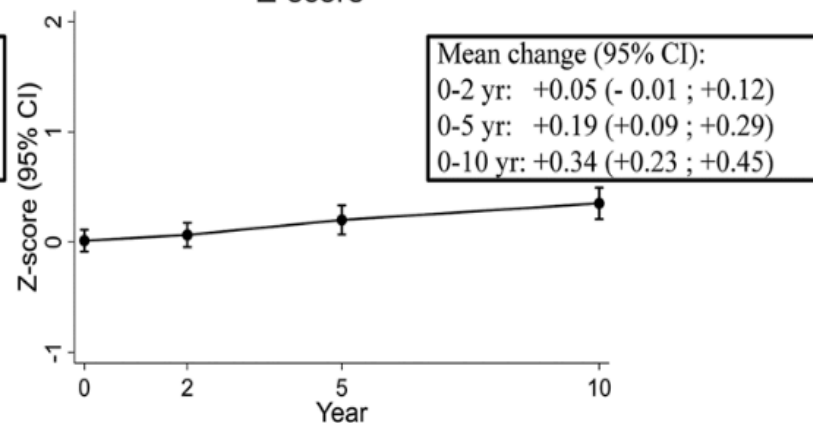


Transmen

Absolute BMD



Z-score



TAKE HOME POINTS

- Similar to paediatric literature, adult transwomen also demonstrate lower baseline BMDs prior to GAHT
- BMD changes at 1, 2, 5, and 10-years on GAHT demonstrate either maintenance of BMD or increase in BMD at the Lumbar Spine for both transwomen and transmen
- No obvious signals for harm on bone health with GAHT in adults

What is the fracture incidence in a large cohort of adult transgender people using GAHT?

Table 1. Characteristics of the Study Population

	Trans women aged < 50 years	Trans women aged ≥ 50 years	Trans men
No. of people	1089	934	1,036
Age (years) in 2015	38 (9)	60 (8)	40 (14)
Age (years) at start HT	26 (22–33)	40 (31–48)	25 (21–33)
Duration HT (years)	8 (3–16)	19 (11–29)	9 (2–22)
BMI (kg/m ²) (<i>n</i> = 2756)	23.9 (4.2)	25.7 (4.6)	25.8 (4.9)
Smoking, % yes (<i>n</i> = 2614)	44.7	49.0	47.8
Gonadectomy, % yes	57.8	80.9	69.8
T-score lumbar spine	−1.13 (1.23)	−0.91 (1.33)	−0.18 (1.19)
T-score total hip	−0.77 (0.85)	−0.67 (0.88)	+0.04 (0.98)
T-score femoral neck	−0.99 (0.94)	−1.19 (0.88)	−0.30 (1.05)
Laboratory			
Estradiol (pmol/L)	211 (132–308)	241 (138–391)	147 (102–205)
Testosterone (nmol/L)	1.2 (0.7–1.4)	1.3 (1.0–1.3)	25.0 (17.1–36.5)
LH (IU/L)	2.2 (0.2–9.7)	3.2 (0.3–8.4)	3.6 (0.9–11.5)

HT = hormonal treatment; BMI = body mass index; LH = luteinizing hormone. Characteristics are shown as mean with standard deviation, median with interquartile range, or percentage. Associations are shown as odds ratios (OR) with 95% confidence intervals (CI).

Laboratory measurements were available for 66% of the trans women and 72% of the trans men.

What is the fracture incidence in a large cohort of adult transgender people using GAHT?

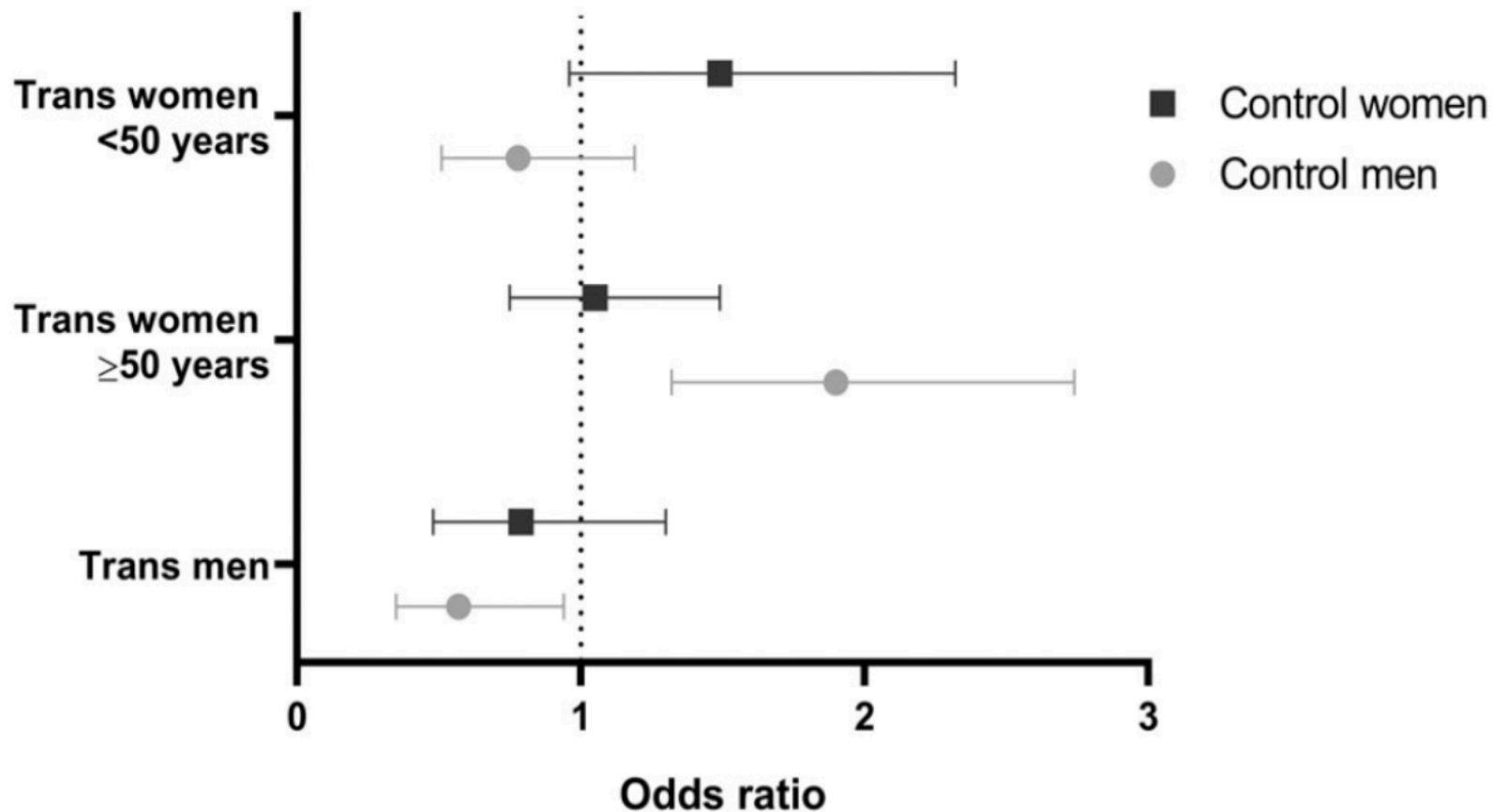
Table 2. Differences in Characteristics in the Transgender Population With and Without Fractures

	Trans women		<i>p</i> Value	Trans men		<i>p</i> value
	No fracture	Fracture		No fracture	Fracture	
No. of people	1,956	67		1,018	18	
Age (years) in 2015	48 (14)	55 (13)	0.001	40 (14)	45 (14)	0.449
Age (years) at start HT	31 (24–41)	33 (26–45)	0.190	25 (21–33)	25 (21–34)	0.985
BMI (kg/m ²) (<i>n</i> = 1785)	24.6 (4.4)	25.8 (5.1)	0.265	25.8 (4.9)	24.4 (3.5)	0.257
Smoking, % yes (<i>n</i> = 1714)	46	63	0.087	48	56	0.519
<i>T</i> -score lumbar spine	−1.02 (1.28)	−1.34 (1.40)	0.021	−0.17 (1.19)	−0.43 (1.04)	0.973
<i>T</i> -score total hip	−0.73 (0.86)	−0.94 (0.97)	0.175	+0.05 (0.98)	−0.35 (0.81)	0.204
<i>T</i> -score femoral neck	−1.06 (0.92)	−1.36 (1.04)	0.073	−0.30 (1.05)	−0.79 (0.60)	0.138
Laboratory						
Estradiol (pmol/L)	220 (135–337)	172 (116–299)	0.585	148 (103–206)	84 (65–133)	0.030
Testosterone (nmol/L)	1.3 (0.8–1.3)	1.3 (0.9–2.2)	0.446	25 (17–37)	22 (17–29)	0.265
LH (IU/L)	2.5 (0.3–9.3)	2.8 (0.7–9.6)	0.808	3.6 (0.9–11.4)	10.1 (2.2–15.2)	0.231

HT = hormonal treatment; BMI = body mass index; LH = luteinizing hormone. Characteristics are shown as mean with standard deviation, median with interquartile range, or percentage.

Laboratory measurements were available for 66% of the trans women and 72% of the trans men.

What is the fracture incidence in a large cohort of adult transgender people using GAHT?



POINTS OF CONTENTION OF THIS STUDY

- Many European studies tend to use Cyproterone acetate as androgen blockade; in Canada, spironolactone is often used.
- Study does not have the numbers to look at the subgroup of those who had gonadectomy.
- Unknown co-morbid status of trans-patients and their 10 age matched references
- Not all the important confounding factors were addressed:

Wiepjes et al. J Bone Miner Res 2019

CAROC*	FRAX®†
<u>Risk Factors:</u> <ul style="list-style-type: none">• Sex 😊• Age 😊• BMD 😊• Fragility fracture after 40• Systemic glucocorticoid use (≥ 3 months)†	<u>Additional Risk Factors:</u> <ul style="list-style-type: none">• Low BMI• Parental history of fracture (especially hip)• Current smoking 😊• Alcohol intake ≥ 3 units/day• Rheumatoid arthritis, or other secondary causes of osteoporosis

LONG-TERM MONITORING OF TRANS-PATIENTS

Which reference range should we use for transgender and gender diverse patients?

Michael S Irwig 

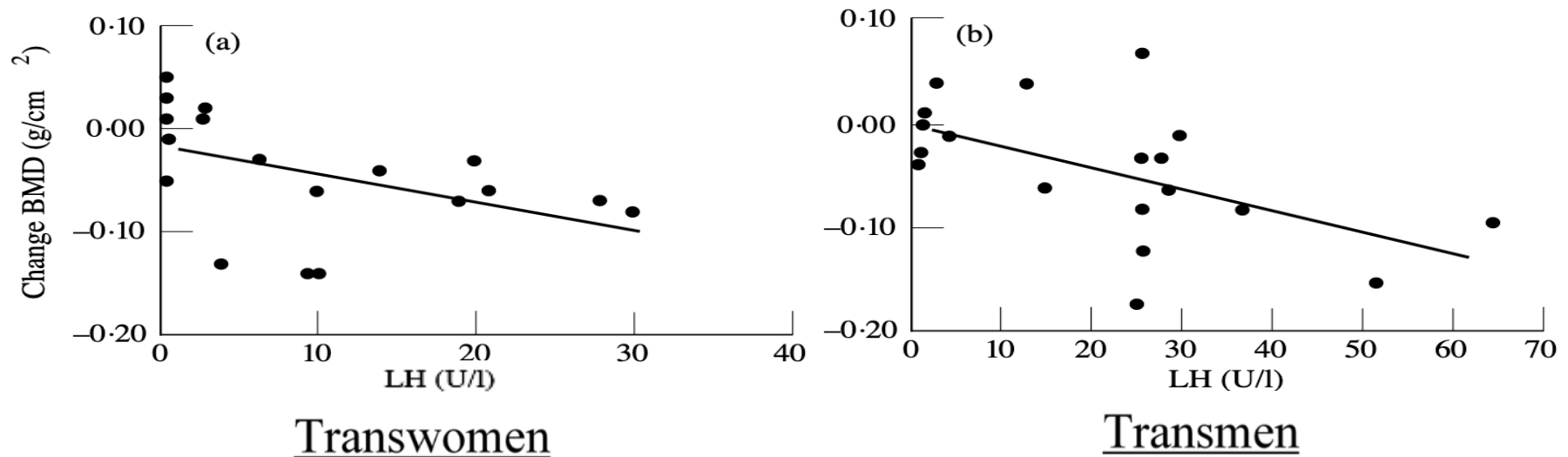
The Journal of Clinical Endocrinology & Metabolism, dgaa671, <https://doi.org/10.1210/clinem/dgaa671>

Published: 18 September 2020 **Article history** ▼

TAKE HOME POINTS

- Transwomen **aged <50 years did not** have an increased fracture risk **compared with age-matched reference men** aged <50 years
- Transwomen **aged ≥ 50 years** had a **similar fracture risk** compared with **age-matched reference women** aged ≥ 50 years but an *increased* fracture risk **compared with age matched reference men** aged ≥ 50 years
- Transmen fracture risk being **similar to age-matched reference women**; but *lower* fracture risk to **age-matched reference men**

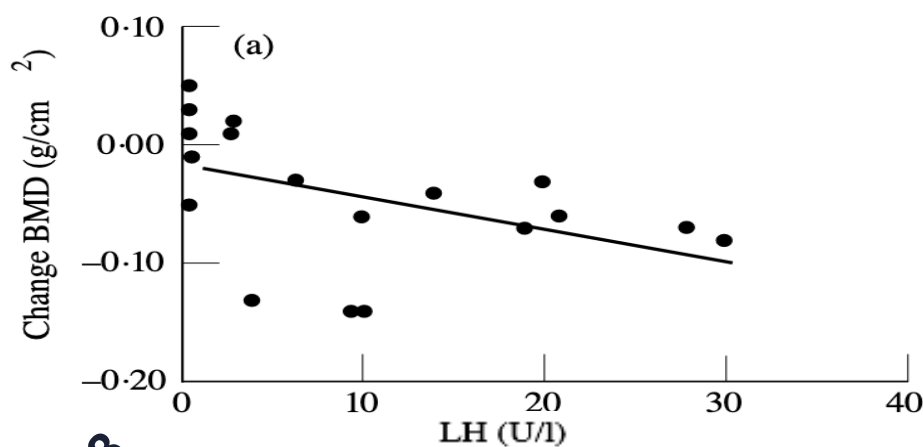
ADULT TRANS- HORMONE MARKERS AND BMD



- “In **one** study, serum LH levels were inversely related to BMD, suggesting that low levels of sex hormones were associated with bone loss.”
- “**Thus, LH levels in the normal range may serve as an indicator of the adequacy of sex steroid administration to preserve bone mass.**”

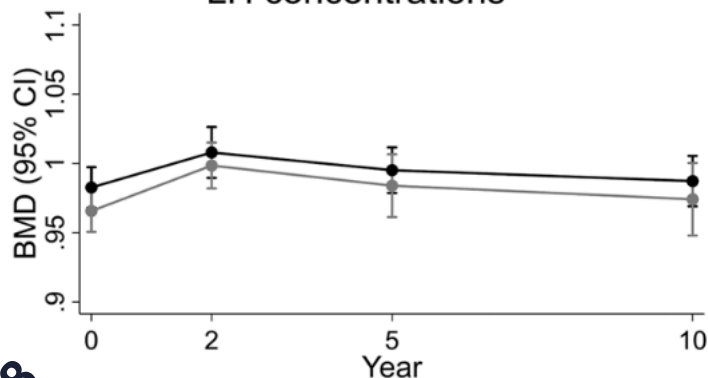


ADULT TRANS- HORMONE MARKERS AND BMD

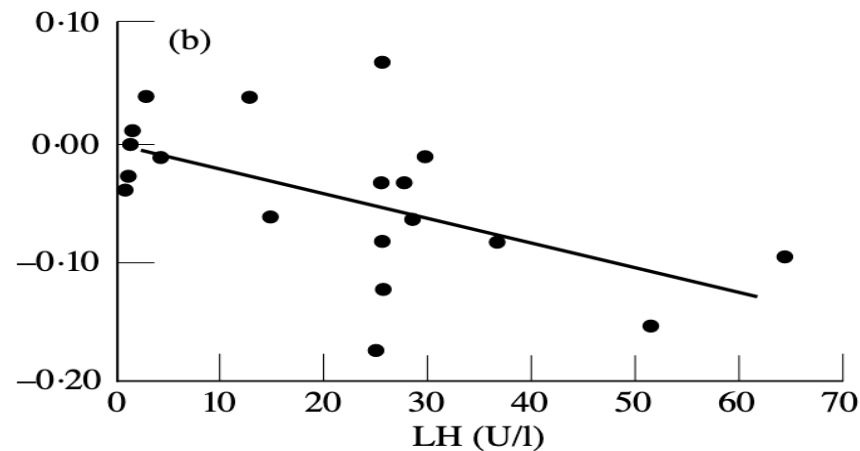


Transwomen

LH concentrations

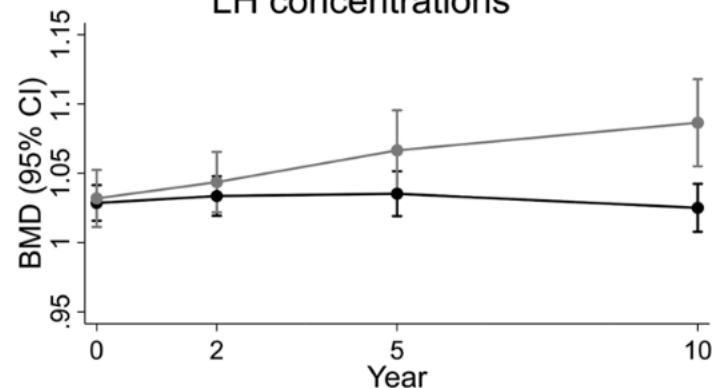


—●— >1 (1-58) U/L (n=353): +0.005 (-0.008 ; +0.017)
 —●— <1 (0.1-1) U/L (n=330): +0.008 (-0.014 ; +0.031)



Transmen

LH concentrations



—●— >1 (1-82) U/L (n=384): -0.004 (-0.016 ; +0.009)
 —●— <1 (0.1-1) U/L (n=150): +0.055 (+0.029 ; +0.080)



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Van Kesteren et al. *Clinical Endocrinology* 1998

Endocrinology & Metabolism

Wiepjes et al. *JBMR* 2018

ADULT TRANS-HORMONE MARKERS AND BMD

- Wiepjes et al. (2018) go on to show no differences in change in LS BMD were observed between different age groups of transmen and transwomen
- Transwomen with higher estradiol concentrations during GAHT had an increase in LS BMD, whereas low estradiol concentrations were associated with a decrease in LS BMD. Testosterone concentrations in transwomen were not associated with the change in LSBMD.
- Therefore, postulating that estradiol levels are more useful indicators of adequate GAHT dosing in Transwomen.
- In transmen, neither estradiol and testosterone concentrations were not associated with change in LS BMD.



TAKE HOME POINTS

- Although LH was shown to be inversely proportional to BMD in one study circa 1998 – this has **not** been re-demonstrated
- LH concentrations may be considered in evaluation of the adequacy of testosterone dosing for bone health in transmen
- Estradiol levels are more useful indicators of adequate GAHT dosing for bone health in transwomen

OUTLINE

- ~~1. Why is transgender health important for clinicians?~~
- ~~2. Sexual dimorphism in bone health~~
- ~~3. Bone mineral density changes in trans-adolescents~~
- ~~4. Review Endocrine Society Transgender Health Guidelines pertaining to bone health in adults~~
- 5. Discuss the latest recommendations for trans-adult bone health screening**

Bone Densitometry in Transgender and Gender Non-Conforming (TGNC) Individuals 2019:

International Society for Clinical
Densitometry (ISCD) Official Position

ISCD POSITION #1: SCREENING

Indications for Baseline BMD in TGNC Individuals

- History of gonadectomy or therapy that lowers endogenous gonadal steroid levels prior to initiation of GAHT
- Hypogonadism with no plans to take GAHT
- Existing ISCD indications for BMD testing (glucocorticoid use, hyperparathyroidism etc.)

ISCD POSITION #2: FOLLOW UP

Indications for Follow-Up BMD in TGNC Individuals

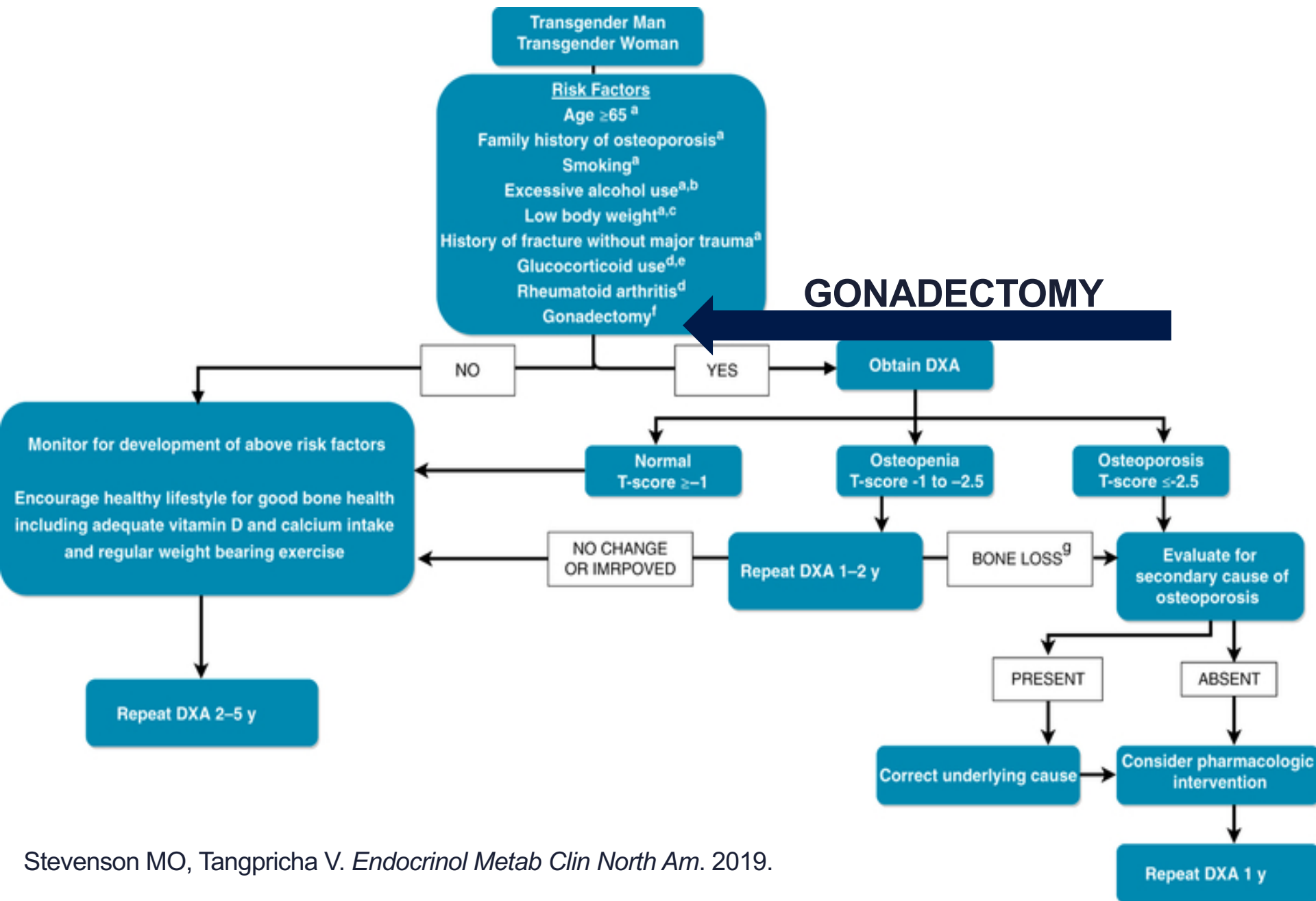
- Testing should be done when the results are likely to influence management:
- Pre-existing low BMD
- Individuals taking GnRH analogs
- Nonadherence (or inadequate dosing) of GAHT
- Plans to discontinue GAHT
- Other risk factors for bone loss or fragility fracture

ISCD POSITION #3: Z-SCORE & T-SCORE

Calculation of T-Score in TGNC Individuals

- T-scores should always be calculated using 'Caucasian' (non-race) adjusted female normative database for all trans-individuals regardless of ethnic group
- T-score of <-2.5 is used for diagnosis of osteoporosis in all trans-individuals age 50 or older, regardless of hormone status
- Z-scores should be calculated using the normative database that matches the gender identity of the individual

TRANS-PATIENT BONE HEALTH SCREENING ALGORITHM



TAKE HOME POINTS

- As long as a TGNC individual is on standard GAHT, BMD should remain stable to increasing, so **there is no indication to monitor** for bone loss or osteoporosis strictly on the basis of TGNC status
- TGNC individuals who experience substantial periods of hypogonadism (>1 yr) might experience bone loss or failure of bone accrual during that time and should be considered for baseline measurement of BMD
- There are no data to support that TGNC individuals have a fracture risk different from that of cisgender individuals
- The Z-score in transgender individuals should be calculated using the reference data (mean and standard deviation) of the gender conforming with the individual's gender identity

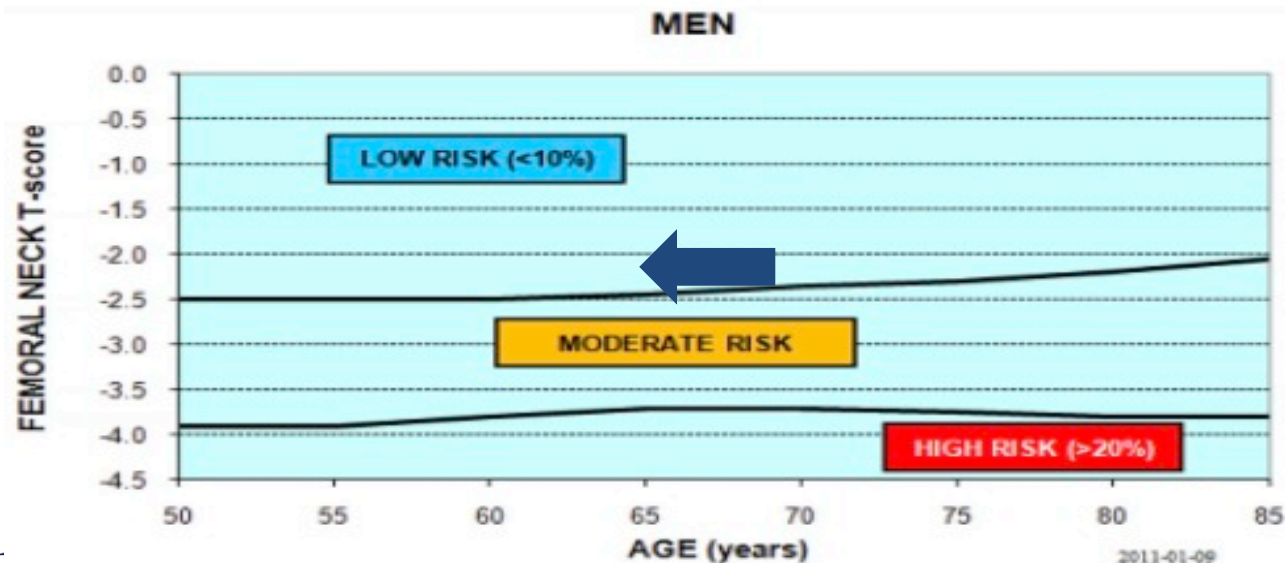
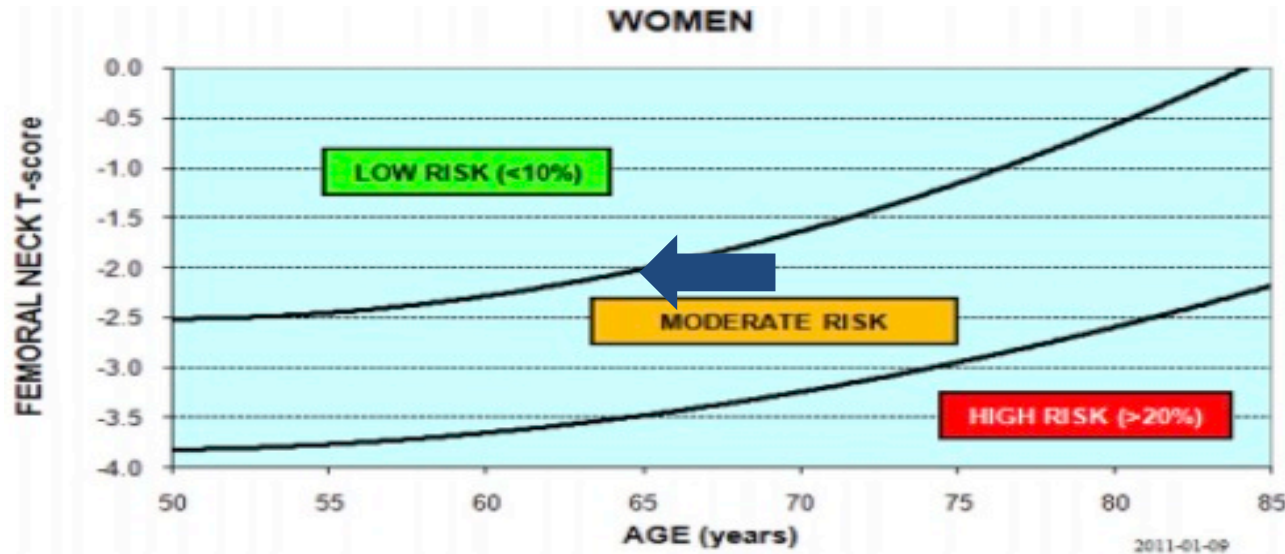
CASE EXAMPLE

65yo white Canadian transgender woman presenting to your practice with questions about her bone health.

- No known family history of osteoporotic fractures.
- She consumes dairy products ~2x/day and takes a vitamin D.
- She is a current smoker. No EtOH use.
- She has been on GAHT since age 25.
- She underwent orchiectomy at age 35. No BMD baseline.
- Wt. 70kg, Ht 175cm.
- Her current estradiol level is within normal cis-woman limits; her testosterone is appropriately suppressed.
- Her DXA shows left femoral neck T-score -2.1; left total hip of -2.1; spine (L1-L4) T-score -1.8 (compared to cis-woman ref range)
- **How do we best risk stratify and treat?**



CAROC EXAMPLE



FRAX SCORE EXAMPLE

Transwoman - “Assigned Female” on FRAX

Country: **Canada**

Name/ID:

[About the risk factors](#)

Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth

Age:

Date of Birth:

Y:

M:

D:

2. Sex



Male



Female

3. Weight (kg)

4. Height (cm)

5. Previous Fracture



No



Yes

6. Parent Fractured Hip



No



Yes

7. Current Smoking



No



Yes

8. Glucocorticoids



No



Yes

9. Rheumatoid arthritis



No



Yes

10. Secondary osteoporosis



No



Yes

11. Alcohol 3 or more units/day



No



Yes

12. Femoral neck BMD (g/cm²)

T-Score



-2.1

[Clear](#)

[Calculate](#)

BMI: 22.9

The ten year probability of fracture (%)



with BMD

Major osteoporotic

9.8

Hip Fracture

2.7

If you have a TBS value, click here:

[Adjust with TBS](#)



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FRAX SCORE EXAMPLE

Transwoman - “Assigned Male” on FRAX

Country: **Canada**

Name/ID:

[About the risk factors](#)

Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth

Age:

Date of Birth:

Y:

M:

D:

2. Sex



Male



Female

3. Weight (kg)

4. Height (cm)

5. Previous Fracture



No



Yes

6. Parent Fractured Hip



No



Yes

7. Current Smoking



No



Yes

8. Glucocorticoids



No



Yes

9. Rheumatoid arthritis



No



Yes

10. Secondary osteoporosis



No



Yes

11. Alcohol 3 or more units/day



No



Yes

12. Femoral neck BMD (g/cm²)

T-Score



BMI: 22.9

The ten year probability of fracture (%)



with BMD

Major osteoporotic

8.0

Hip Fracture

3.3



If you have a TBS value, click here:

[Adjust with TBS](#)



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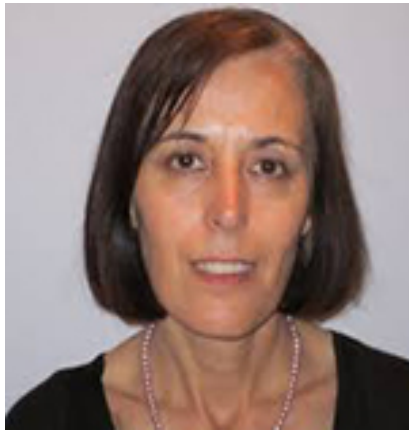
TAKE HOME POINTS

- DEXA scans are recommended q 2 years but may not be needed in TransYouth
- Bone turnover markers seem to have limited utility
- There is some BMD recovery once GAHT is started
- Transgirls have lower pre-treatment BMDs at baseline
- 10-year BMD studies in adult transwomen and transmen show LS BMD increase or maintenance
- LH does not appear to be inversely related to BMD
- BMD are not necessary in adult trans-populations without existing risk factors (as long as GAHT adherent, but get baseline BMD if gonadectomy)



TAKE HOME POINTS

- **Diversity, equity and inclusion:**
“you cannot find that which you are not looking for”
- **More studies, research and advocacy are needed to better understand the impacts of GAHT on bone health – this will allow us to safely titrate and optimize GAHT**



Dr. Rowena Ridout



Dr. Sandra Kim



Dr. Raymond Fung

Thank You to My Endocrine Mentors!



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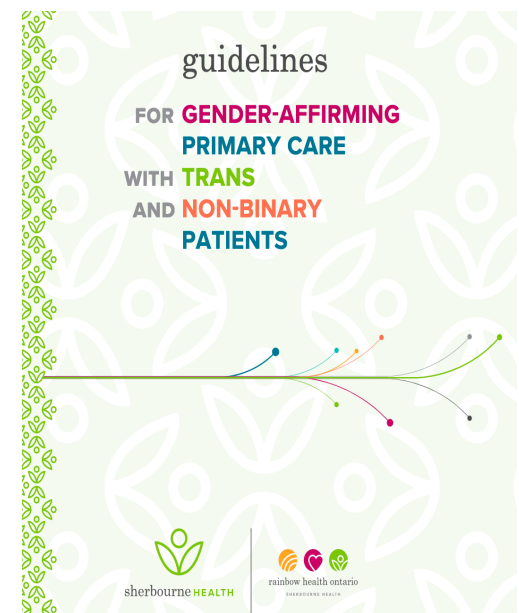
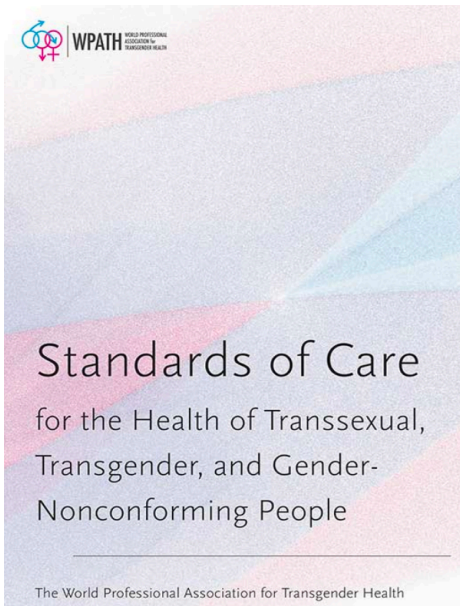
Endocrinology & Metabolism

OUTLINE

1. Why is transgender health important for clinicians?
2. Sexual dimorphism in bone health
3. Bone mineral density changes in trans-adolescents
4. Review Endocrine Society Transgender Health Guidelines pertaining to bone health in adults
5. Discuss the latest recommendations for trans-adult bone health screening

OBJECTIVES

- 1. Understand why Transgender health is an important and rapidly growing field in medicine**
- 2. Describe the physiology of sexual dimorphism in bone health and how this relates to Transgender bone health**
- 3. Learn current guidelines and emerging research in Transgender bone health**
 - highlight important differences for adolescents and adults**



Thank You!



Volume 102, Issue 11
1 November 2017

EDITOR'S CHOICE

Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society* Clinical Practice Guideline FREE

Wylie C Hembree, Peggy T Cohen-Kettenis, Louis Gooren, Sabine E Hannema, Walter J Meyer, M Hassan Murad, Stephen M Rosenthal, Joshua D Safer, Vin Tangpricha, Guy G T'Sjoen Author Notes

The Journal of Clinical Endocrinology & Metabolism, Volume 102, Issue 11, 1 November

Questions?/Discussion

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EXTRA SLIDES

YOUTH SERUM BONE MARKERS DURING GnRHA Tx

- 51 transgirls and 70 transboys receiving GnRHa
- 36 transgirls and 42 transboys receiving GnRHa

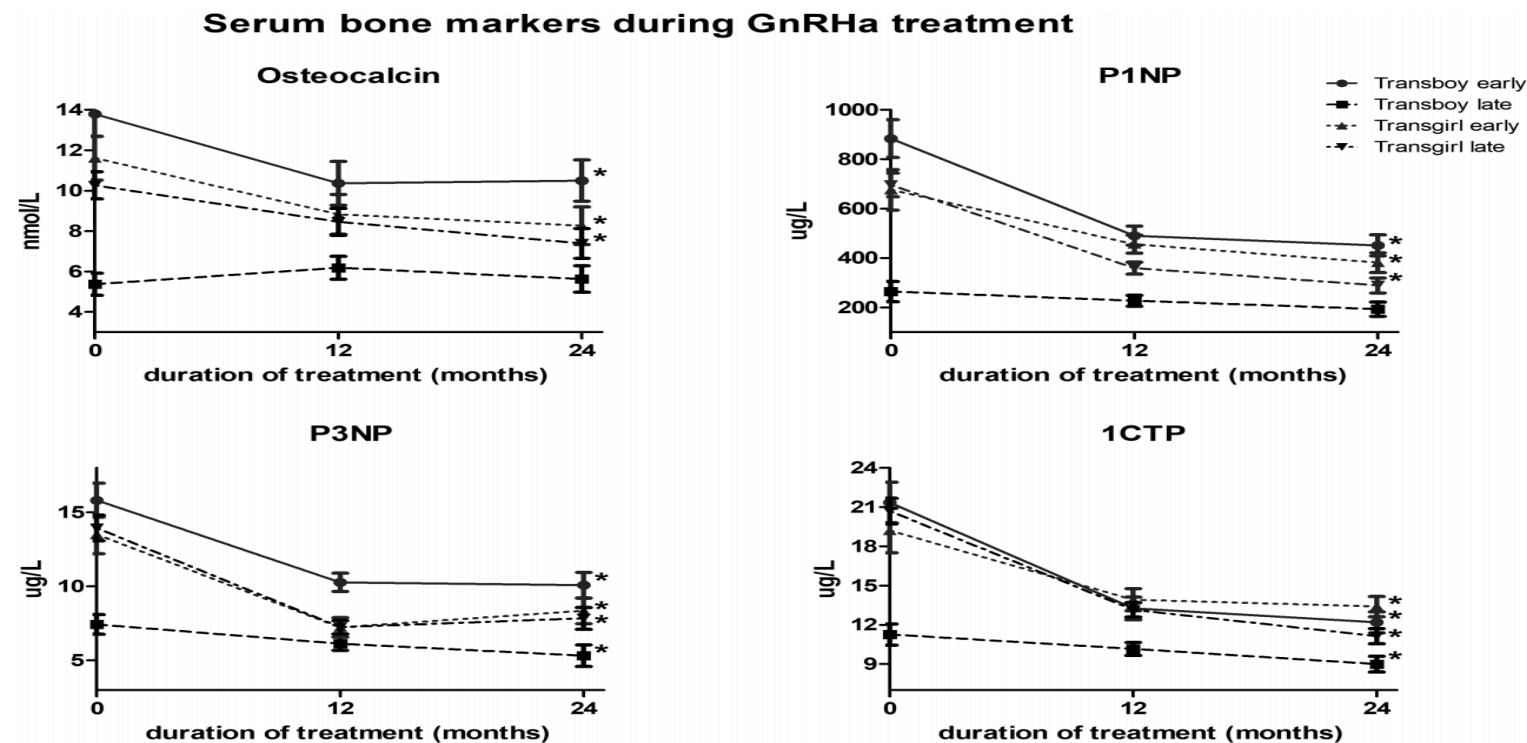
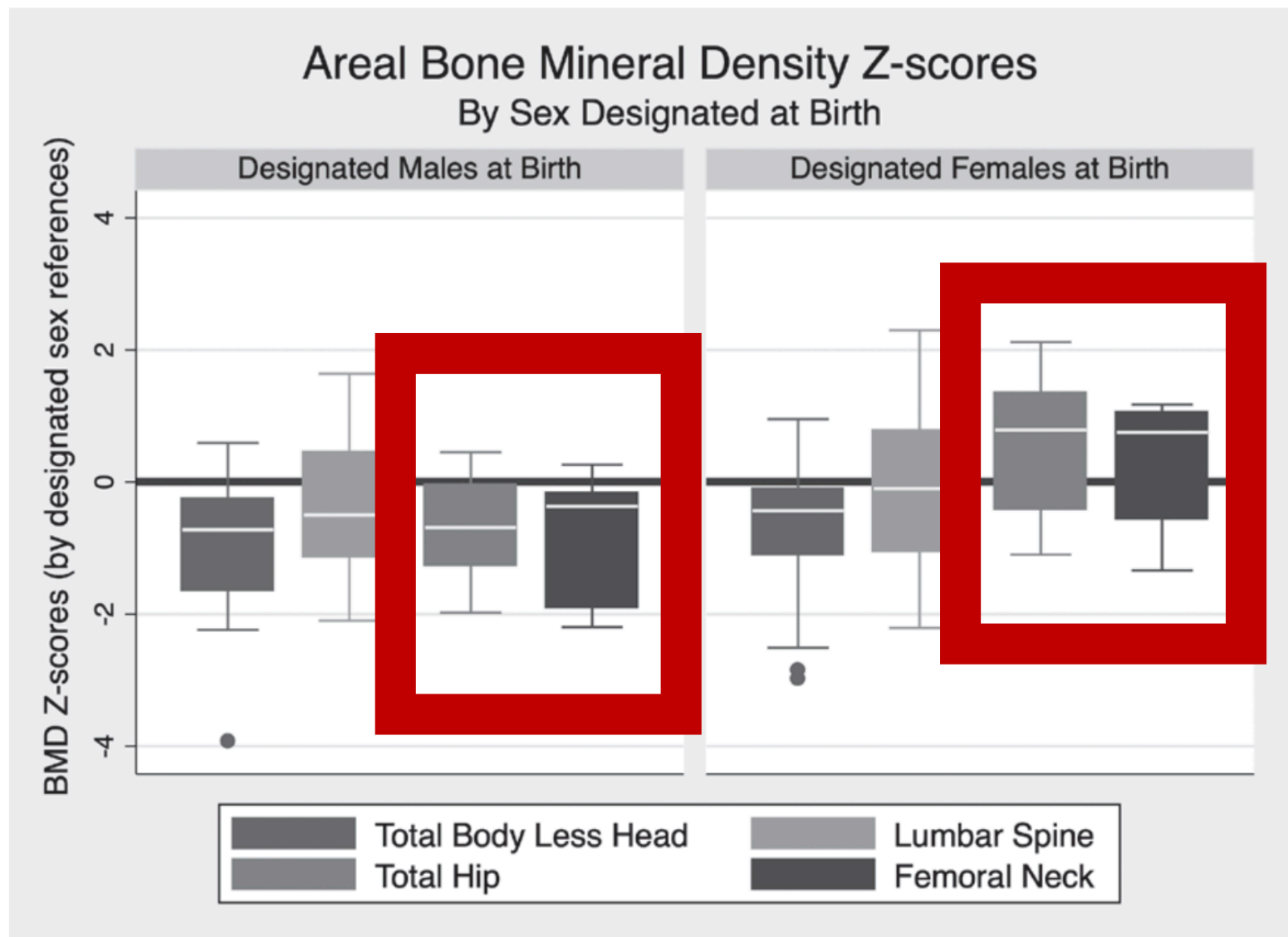


Figure 2. Estimated marginal means and negative standard error of the mean of osteocalcin, P1NP, P3NP, and 1CTP prior to and during 2 years of GnRHa administration in transgirls and transboys. Significant changes during the 2 years of GnRHa administration are indicated by asterisk.

aBMD IN TRANS-YOUTH *BEFORE* GnRH_a



aBMD BASELINE, 12–24 Months FOLLOW-UP DURING GAHT WITH *NO GONADECTOMY*

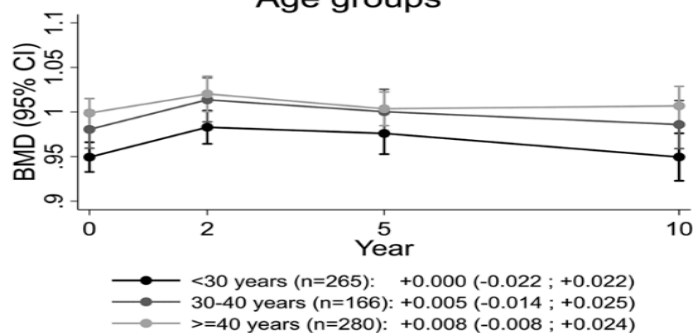
Hormone preparation	Parameter	GAHT administration route		
		Oral	Transdermal (or percutaneous)	Intramuscular
BMD				
17β-estradiol	Femoral neck	↑ ^a	No data	↔
	Lumbar spine	↑	↔	↑
	Total body	No data	↔	No data
Testosterone	Femoral neck	No data	No data	↔
	Lumbar spine	No data	↔	↔
	Total body	No data	↔	↔

	Oral tablet	Transdermal/percutaneous preparations	Intramuscular injection
Serum-binding proteins			
SHBG	↑ during estradiol ^{**} ; no oral testosterone data available.	↔ during estradiol; ↓ during testosterone [*]	↑ during estradiol ^{**} ; ↓ during testosterone (undecanoate and esters) ^{**}

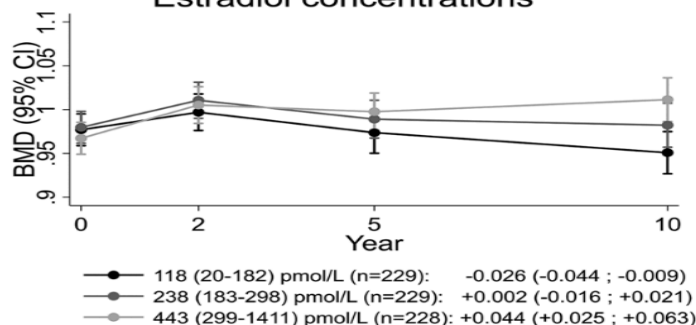
HORMONE MARKERS AND BMD IN ADULTS

Transwomen

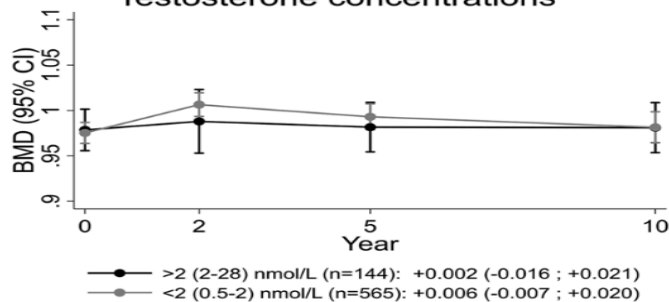
Age groups



Estradiol concentrations

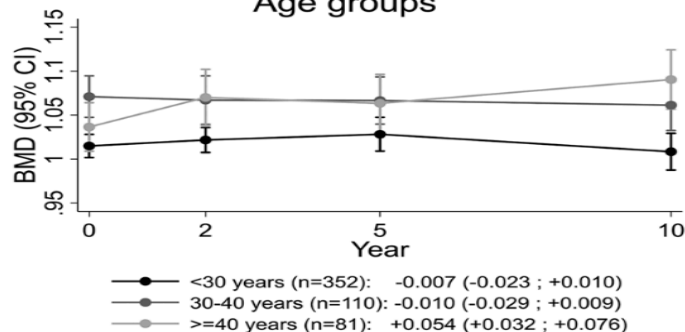


Testosterone concentrations

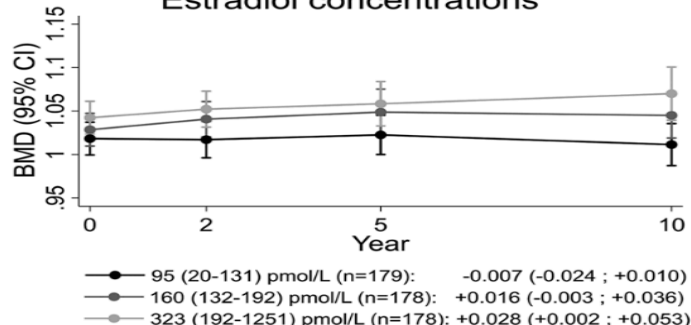


Transmen

Age groups



Estradiol concentrations



Testosterone concentrations

