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| Medical treatment - Tables by Outcome | November 2024 |

# Summary of anthropometry outcomes

| **No** | **Study** | **Analysis** | **Baseline** | **12 months** | **24 months** | **At GAHT** | **Comment** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| 1 | (Boogers. et al., 2022)  N’lands | Bone age – Chronological age (BA-CA), Mean ± SD    Growth velocity (GV cm per year), mean (95% CI)    Height SDS, mean (95% CI) | AMAB only  BA – CA = -0.2 ± 0.9 years | GV = 5.3 ± 2.2 cm/year | GV = 3.5 ± 1.3 cm/year | BA – CA = 1.6 ± 0.8  BA – CA = mean -0.5 years/year of PS 95% CI ± -0.8 to -0.2)        Height SDS = -0.37/year, 95%CI -0.47 to -0.27 | Significant decrease in Bone age vs Chronological age. |
| 2 | (Boogers et al., 2023)  N’lands | Height SDS, mean ± SD    BMI SDS, median (IQR) | AMAB only  Height SDS = 0.04 ± 1.00    BMI SDS = 0.63 ± -0.41 to 1.39 |  |  | Height SDS = -0.42 ± 1.1    BMI-SDS = 0.43 (-0.41 to 1.51) | No sig change in BMI in AMAB adolescents.  Decrease in Height SDS. Significance not analysed. |
| 3 | (Carmichael et al., 2021)  UK | Height Z-score, Mean (95%CI)  Weight Z-score, Mean (95%CI)  BMI Z-score, Mean (95%CI)    BMD Z-score, Mean (95%CI) | AMAB & AFAB combined  Height z-score 0.4 (0.1 0.7  Weight z-score 0.8 (0.4, 1.3)  BMI z-score 0.7 (0.2 1.1)    BMD z-score -0.5 (-0.8, -0.1) All n=44  BMD z-score -0.4 (-0.8, -0.1)  Baseline n = 43  BMD z-score -0.7 (-1.2, -0.1)  Baseline n=24  BMD z-score -0.2 (-1.0, 0.6)  Baseline n=12 | Height z-score 0.2 (-0.1, 0.4)  Weight z score 0.8 (0.3, 1.3)  BMI z-score 0.7 (0.2, 1.2)      BMD z-score -1.0 (-1.3. -0.6)  FU 12 months n = 43 | Height z-score 0.0 (-0.4, 0.4)  Weight z-score 0.6 (-0.1, 1.3)  BMI z-score 0.6 (-0.1, 1.3)            BMD z-score -1.3 (-1.9, -0.7)  FU 24 months, n = 24 | Height z-score 0.0 (-0.5, 0.5)  Weight z-score 1.0 (0.1, 1.9)  BMI z-score 1.1 (0.3, 1.9)  Follow up at 36 months              BMD z-score -1.5 (-2.2, -0.8)  FU 36 months, n = 12 | Significant decrease in Height Z-score  Increase in BMI Z-score at 36 months  Significant decrease of BMD-z-scores at 12 and 24 months. No further change at 36 months |
| 4 | (Ciancia et al., 2022)  Belgium | Height Z-score Mean ± SD | AMAB  Height Z-score = -0.46 ± 1.11      AFAB  Height Z-score = -0.32 ± 0.34 |  |  | AMAB  Height gain = 12.67 cm ± 5.73  Height Z score = -0.90 ± 1.02, p < 0.001)    AFAB  Height gain = 10.17 cm ± 2.96  Height Z-score = -0.43 ± 0.56 | AMAB: Good correlation between duration of treatment and height gain  AFAB: Weak correlation between duration of PS and height gain    For AMAB & AFAB Total height based on gender assigned at birth is the best predictor for final height |
| 5 | (Ghelani et al., 2020)  UK | Height SDS, change SDS score from reference  Weight SDS, mean ± SDS  BMI SDSs, mean ± SDS  Lean Mass ± SDS  Results expressed as change in SDS scores from reference population at baseline and 12 months. | AMAB, (change in SDS score)  Δ Height SDS = -0.88  Δ Weight SDS = -0.05  Δ BMI SDS = 0.63  Δ Lean Mass SDS = -0.68  AFAB  Δ Height SDS = -0.09  Δ Weight SDS = 0.88  Δ BMI SDS = 1.04  Δ Lean Mass SDS = 0.15 | AMAB  Δ Height = -1.05, p<0.05  Δ Weight = -0.303, p=ns  Δ BMI = 0.56, p=ns  Δ Lean Mass= -1.11, p=0.002  AFAB  Δ Height = -0.05, p=ns,  Δ Weight = -0.14, p=ns  Δ BMI = 1.14, p= ns  Δ Lean Mass = -0.08, p=ns |  |  | AMAB: a significant decrease in  height and lean mass SDSs over 12-months GnRHa treatment period  AFAB: no apparent effect  on body composition from the parameters measured for transboys. |
| 6 | (Joseph et al., 2019)  UK | Height, mean (SD)  Weight, mean (SD)  BMI, mean (SD) | AMAB, n = 10  Height = 160.3 (5.4)  Weight = 66.4 (14.6)  BMI = 25.8 (5.3)    AFAB, n = 21  Height = 159.0 (35.8)  Weight = 49.8 (17.1)  BMI = 19.4 (5.3) | AMAB, n= 10  Height = 163.4 (5.7)  Weight = 76.1 (19.4)  BMI = 28.2 (7.1)    AFAB, n = 21  Height = 160.3 (36.7)  Weight = 66.4 (14.6)  BMI = 20.7 (7.9) | AMAB, n=10  Height = 165.1 (5.7)  Weight = 82.9 (30.5)  BMI = 30.5 (8.6)    AFAB, n = 21  Height = 160.3 (37.5)  Weight = 66.4 (14.6)  BMI = 20.9 (6.6) | - | An increase in height and weight with transgirls (AMAB) having a larger increase in BMI, and transboys (AFAB) a greater increase in height. |
| 8 | (Klink. et al., 2015)  N’Lands | Height, mean ± SDS  BMI, mean ± SDS | AMAB, n=15  Height SDS = 0.14 ± 1.3  BMI SDS = 0.17 ± 0.90    AFAB, n = 19  Height SDS = -0.06  BMI SDS = 0.3 ± 1.0 |  |  | AMAB  Height SDS = -0.97 ± 1.3, p<0.001  BMI SDS =0.07 ± 1.11, p = ns    AFAB  Height SDS = -0.1 ± 1.3, p = ns  BMI SDS = 0.5 ± 1.2, p = ns | No significant change in BMI in either AMAB or AFAB during GnRHa treatment.  A significant decrease in height SDS in AMAB compared to cisgender reference group |
| 9 | (Navabi et al., 2021)  Canada | BMI z-score (mean (SD)  Lean body mass (LBM) z-score  Total Body Fat, (TBF) z-score %    z-scores calculated from sex assigned at birth | AMAB n = 51  BMI z-score = 0.62 (1.67)  LBM z-score = -1.19 (1.45)  TBF z-score = 1.42 (1.02)    AFAB n = 119  BMI z-score = 0.89 (1.25)  LBM z-score = -1.03 (1.22)  TBF z-score =1.68 (0.96) |  |  | AMAB n = 36  BMI z-score = 0.45 (1.69), p=0.475  LBM z-score = -1.99 (1.58), p<0.001  TBF z-score = 2.46 (0.51), p<0.001    AFAB n = 80  BMI z-score = 0.99 (1.30), p = 0.083  LBM z-score = -1.01 (1.28), p< 0.89  TBF z-score = 1.78 (0.90), p=0.053 | No evidence of change in BMI z-score for AMAB or AFAB during GnRHa treatment.  Significant decrease in LBM and increase in TBF for AMAB.  Non-significant trend for increase in TBF for AFAB. |
| 10 | (Nokoff et al., 2021a)  USA | BMI percentile  GD compared to cis-gender controls |  |  |  | AMAB  GD (n=8) vs Cisgender (n=17)  BMI percentile  44 ± 39 vs 45 ± 38, p=ns    AFAB  GD (n=9) vs cisgender (n=14)  BMI percentile  62 ± 32 vs 67 ± 29, p = ns | No significant difference in BMI between AMAB or AFAB GD adolescents compared to cisgender controls |
| 11 | (Perl et al., 2021)Israel | BMI-SDS | AFAB (n=15)  BMI SDS = 0.2 ± 0.9 |  |  | AFAB (n = 15)  BMI SDS = 0.4± 0.9, p=0.198 | No significant change in BMI after GnRHa treatment in AFAB adolescents. |
| 12 | (Schagen et al., 2016) | Height (Ht) SDS, (mean (SD))  BMI SDS  Total body fat percent (Fat%)  Lean body mass percent (LBM%) | AMAB  Ht SD S =0.20 (1.0), n=36  BMI SDS = 0.82 (1.1), n=36  Fat % = 22.4 (6.9), n=26  LBM% = 74.6 (6.4), n=26    AFAB  Ht SD S = -0.10 (1.1), n41  BMI SDS = 0.68 (1.2), n=41  Fat % = 25.0 (6.9), n=26  LBM% = 71.5 (6.7) | AMAB  Ht SDS, -0.04 (1.0), p<0.001  BMI SDS 0.89 (1.2), p=ns  Fat% = 26.8 (6.6), p<0.001  LBM% = 70.9 (7.3), p=0.001    AFAB  Ht SDS, -0.25 (1.1), p<0.001  BMI SDS 0.84 (1.2), p=0.01  Fat% = 29.5 (7.3), p<0.001  LBM% = 67.7 (6.7), p<0.001 |  |  | In AMAB adolescents, significant decrease in height SDS and Fat% and significant decrease in LBM%. No significant change in BMI SDS.      In AFAB significant decrease in height SDS and LBM% and sign increase in BMI SDS and Fat%. |
| 13 | (Schagen et al., 2020)  N’lands | Height  Weight  BMI |  |  |  |  | Descriptive data provided but no comparisons of centiles before and after GnRHa provided |
| 14 | (Schulmeister et al., 2022)  USA | BMI z score  Height velocity (HV)  centimetres per year (cm/yr) median (IQR)  Tanner stage 2,3,4 (T2, T3,T4) | AMAB, n = 26  BMI z score =0.46 (0.89)    AFAB, n = 29  BMI z-score = 0.38 (0.94) | AMAB  BMI Z score = 0.66 (0.97)  HV T2 = 5.6 (4.7 – 5.7), n = 21  HV T3 = 4.2 (2.3 – 6.4), n = 3  HV T4 = 1.6 (1.5 – 2.9), n= 2    AFAB  BMI-z-score = 0.63 (0.95)  HV T2 = 5.0 (4.2 – 5.4), n = 13  HV T3 = 4.4 (4.0 – 5.5), n = 13  HV T4 = 2.9 (1.5 – 3.5), n = 3 |  |  | Tanner stage had a significant impact on HV.  HV was also negatively associated with age at GnRHa start  even when Tanner stage at start was included as a covariate,  demonstrating that some but not all of the effect of age was  mediated by Tanner stage (R2 = 0.3, p = 0.02). |
| 16 | (Stoffers et al., 2019)  N’lands | Height (Ht) SDS  BMI SDS  Using both male (transgender) and female (sex assigned at birth) reference range | AFAB n = 62  Ht SDS male = -1.3 ± 1.2  Ht SDS female = -0.1 ± 1.0  BMI SDS male = 0.68 ± 1.0  BMI SDS female = 0.47 ± 1.0 |  |  | AFAB n = 62  Ht SDS male = -1.7 ± 09  Ht SDS female = -0.2 ± 1.0  BMI SDS male = 0.58 ± 1.1  BMI SDS female = 0.40 ± 1.0 | No significant change in height SDS or BMI SDS using reference ranges for either identified gender or sex assigned at birth. |
| 19 | (Vlot et al., 2017)  N’Lands | Height  Weight |  |  |  |  | Descriptive data provided but no comparisons of centiles before and after GnRHa provided |
| 20 | (Willemsen et al., 2023)  N’lands | Height (Ht) SDS  Pubertal (P) and post-pubertal (PP) comparison of growth using female reference range | AFAB n = 61  P-Ht SDS = 0.1 ± 1.5  PP -Ht SDS -0.1 ± 1.0 |  |  | AFAB n = 61  P-Ht SDS = -0.2 ± 1.0  PP -Ht SDS -0.2 ± 1.1 | Transgender boys with BA >12 years at start PS declined more in height SDS during PS compared with transgender boys with BA ≤12 years (difference between groups −0.6; 95% CI, −0.7 to −0.4). |

AFAB = Assigned female at birth, AMAB = Assigned male at birth, BMI = Body mass index, BA = bone age, CA = chronological age, GD = Gender dysphoria, GV = growth velocity, Ht = height, IQR = interquartile range, LBM = lean body mass, N’lands = Netherlands, SDS = standard deviation, TBF = Total body fat, UK = United Kingdom, USA = United States of America, Wt = weight

# Appendix 5 Summary of lumbar spine bone mineralisation outcomes

| **No** | **Study** | **Analysis** | **BMD Z-scores Lumbar Spine** | | | |
| --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **Baseline** | **12 months** | **24 months** | **At GAHT** |
| **2** | **(Boogers et al., 2023)**  **N ’lands** | **BMD-HAZ-scores**  **Regular dose oestradiol (2 mg)**  **High dose oestradiol (6 mg)**  **Ethinyl oestradiol** |  |  |  | **Data not provided for changes in BMD during PS alone. However, BMD HAZ-score decreased for all three groups.** |
| 3 | (Carmichael et al., 2021)  UK | AMAB and AFAB combined  BMD Z-score (Mean (95%CI)) | BMD z-score -0.5 (-0.8, -0.1) All n=44    BMD z-score -0.4 (-0.8, -0.1)  Baseline n = 43    BMD z-score -0.7 (-1.2, -0.1)  Baseline n=24    BMD z-score -0.2 (-1.0, 0.6)  Baseline n=24 | BMD z-score -1.0 (-1.3. -0.6)  FU 12 months n = 43 | BMD z-score -1.3 (-1.9, -0.7)  FU 24 months, n = 24 | BMD z-score -1.5 (-2.2, -0.8)  FU 36 months, n = 12 |
| **6** | **(Joseph et al., 2019)**  **UK** | **BMAD Z-scores**  Mean (SD)  P1 baseline to 12 months  P2 baseline to 24 months  P3 12 to 24 months | AMAB 3 scans, n=10, 0.13 (0.972)    AMAB 2 scans, n=31: 0.859 (0.154)      AFAB 3 scans, n=21: -0.715 (1.406)    AFAB 2 scans, n=39: -0.186 (1.230) | AMAB 3 scans, n=10: -6.50 (1.182)  p1 < 0.001  AMAB 2 scans, n=31: -0.228 (1.027)  P1 <0.000    AFAB 3 scans, n=21: -1.610 (1.462), p1<0.000  AMAB 2 scans, n=39; -0.541 (1.396  P1 < 0.006 | AMAB 3 scans, n=10 -0.890 (1.075),  p2 < 0.000.  p3 = 0.203      AFAB 3 scans, n=21: -2.000 (1.384),  p2 <0.000.  P3 = 0.035 | - |
| **8** | **(Klink. et al., 2015)**  **N’Lands** | **BMAD z-scores**  **Mean (SD)**  **P1 baseline to start of GAHT** | AMAB, n=11, -0.44 (1.10)    AFAB, n=18, 0.28 (0,90) | - | - | AMAB, n=11, -0.90 (0.80) p1 = NS    AFAB, n=18, -0.50 (0.81) p1 = 0.004 |
| **9** | **(Navabi et al., 2021)**  **Canada** | **BMAD Z-scores**  **Baseline; mean (SD)**  **Prior to GAHT, mean (95% CI)**  **p1 AMAB to AFAB**  **p2 Baseline to GAHT** | AMAB, n = 51: -0.22 (1.41)      AFAB, n=119: -0.10 (1.00)  P1 < 0.001 | - | - | AMAB: n = 36, BMAD Z-score -0.76 (1.48) change -0.37 (-0.61 to -0.14)  p2= NS    AFAB: n = 80, BMD Z-score -0.76 (0.93) change -0.59,  P2 <0.001 |
| **13** | **(Schagen et al., 2020)**  **N’lands** | **BMAD Z scores mean (SD)**  **p1 baseline to 24 months early puberty**  **p2 baseline to 24 months late puberty** | AMAB early puberty, -0.33 (0.33)    AMAB late puberty, -0.65 (0.20)    AFAB early puberty, -0.15 (0.29)    AFAB late puberty, 0.33 (0.14) | - | AMAB Early puberty, -1.10 (0.34)  p1 <0.05  AMAB late puberty, -0.15 (0.29)  p2 <0.05  AFAB early puberty, -0.86 (0.30)  p1 <0.05  AFAB late puberty, -0.56 (0.17)  p2 <0.05 | - |
| **16** | **(Stoffers et al., 2019)**  **N’lands** | **BMD Z-score**  **Mean (SD)** | AFAB: n = 62, 0.02 (1.00) |  |  | AFAB, -0.81 (1.02), P <0.001 |
| **19** | **(Vlot et al., 2017)**  **N’Lands** | **BMAD Z-score**  **Mean (range)**  **p1 comparison baseline young AMAB & AFAB**  **p2 comparison baseline old AMAB & AFAB**  **p3 comparison young AMAB baseline to GAHT**  **p4 comparison old AMAB baseline to GAHT**  **p5 comparison young AFAB baseline to GAHT**  **p6 comparison old AFAB baseline to GAHT** | AMAB young n = 15, -0.2 (-1.82 to 1.18)  AMAB old, n= 5, -1.18 (-1.78 to 1.09)  p1 = 0.003  p2 = NS  AFAB young n= 11, -0.05 (-0.78 to 2.94)  AFAB old n=23, 0.27 (-1.6 to 1.8) |  |  | AMAB young, -1.52 (-2.36 to 0.42)  AMAB old, -1.15 (-2.21 to 0.08)  p3 = NS  p4 NS  AFAB young, -0.84 (-2.2 to 0.87)  AFAB old, 0.29 (-2.28 to 0.90)  p5 < 0.01  p6 <0.01 |

AMAB = assigned male at birth (transgirls), AFAB = assigned female at birth (transboys), At GAHT = at the commencement of gender affirming hormone treatment. Baseline = prior to initiation of GAHT, BMAD z-score = Bone Mineral Apparent Density z-score. CI = confidence intervals. N’lands = Netherlands, NS = not significant, UK = United Kingdom

2. Insufficient data provided to assess BMD-z-scores

3. AMAB and AFAB analysed as a single group. Height adjusted BMD z scores. Statistical analyses not performed for Z-scores. 44 cases assessed at baseline, 43 assessed at 12 months, 24 assessed at 24 months and n=12 assessed at 36 months (data not shown. BMD z-score data at 36 months (n= 12) (-1.5 (-2.2 to -0.8); baseline -0.2 (-1.0 to 0.6) 36 months. A decrease in HA BMD-Z score was identified from baseline to 12 months 24 months but no further decrease from 24 to 36 months.

6. Mean BMD Z-scores decreased from baseline to 12 months for AMAB and AFAB adolescents. In the subgroup with a DEXA scan at 24 months there was a significant decrease in BMAD z-scores in AFAD from 12 to 24 months, but not AMAD adolescents.

8. Mean BMAD z-scores did not significantly decrease for AMAB adolescents from commencement of GnRHa therapy to commencement of GAHT, but significant decrease for AFAB adolescents.

9. Mean BMAD z-score significantly less in AMAB adolescents than AFAB but did not significantly change in AMAB but did significantly change in AFAB.

13. Early puberty defined as Tanner 2/3, late puberty defined as Tanner 4/5. At baseline, mean BMD z-score higher in AFAB than AMAB adolescents. The BMAD z-score of all groups significantly decreased by 24 months of treatment with GnRHa

16. Mean BMD z-scores decreased from baseline to treatment with GAHT in transboys (AFAB adolescents)

19. Young and old based on bone age. Young AFAB bone age < 14 years, young AMAB <15 years. At baseline, the young transgirls (AMAB) had a lower mean BMAD Z-score than the young transmen (p=0.003). There was no difference at baseline between young and old transmen, young and old transwomen, or between old transmen and old transwomen. Suppression of puberty resulted in a decrease of BMAD of the old transmen.

# Appendix 6 Summary of cardiometabolic outcomes

| **No** | **Study** | **Analysis** | **Baseline** | **12 months** | **24 months** | **At GAHT** | **Comment** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| 2 | (Boogers et al., 2023)  N’lands | Height SDS  Mean ± SD    BMI SDS, median (IQR) | AMAB only  Height SDS = 0.04 ± 1.00    BMI SDS = 0.63 ± -0.41 to 1.39 |  |  | Height SDS = -0.42 ± 1.1    BMISDS = 0.43 (-0.41 to 1.51) | No sig change in BMI in AMAB adolescents.  Decrease in Height SDS. Significance not analysed. |
| 3 | (Carmichael et al., 2021)  UK | Height Z-score (Mean (95%CI))  Weight Z-score (Mean (95%CI))  BMI Z-score (Mean (95%CI))    BMD Z-score (Mean (95%CI)) | AMAB & AFAB combined  Height z-score 0.4 (0.1 0.7  Weight z-score 0.8 (0.4, 1.3)  BMI z-score 0.7 (0.2 1.1)    BMD z-score -0.5 (-0.8, -0.1) All n=44  BMD z-score -0.4 (-0.8, -0.1)  Baseline n = 43  BMD z-score -0.7 (-1.2, -0.1)  Baseline n=24  BMD z-score -0.2 (-1.0, 0.6)  Baseline n=24 | Height z-score 0.2 (-0.1, 0.4)  Weight z score 0.8 (0.3, 1.3)  BMI z-score 0.7 (0.2, 1.2)        BMD z-score -1.0 (-1.3. -0.6)  FU 12 months n = 43 | Height z-score 0.0 (-0.4, 0.4)  Weight z-score 0.6 (-0.1, 1.3)  BMI z-score 0.6 (-0.1, 1.3)            BMD z-score -1.3 (-1.9, -0.7)  FU 24 months, n = 24 | Height z-score0.0 (-0.5, 0.5)  Weight z-score 1.0 (0.1, 1.9)  BMI z-score 1.1 (0.3, 1.9)  Follow up at 36 months              BMD z-score -1.5 (-2.2, -0.8)  FU 36 months, n = 12 | Significant decrease in Height Z-score  Increase in BMI Z-score at 36 months  Significant decrease of BMD-z-scores at 12 and 24 months. No further change at 36 months |
| 5 | (Ghelani et al., 2020)  UK | Height ± SDS  Weight ± SDS  BMI ± SDS  Lean Mass ± SDS | AMAB,  Height = -0.88  Weight = -0.05  BMI = 0.63  Lean Mass = -0.68  AFAB  Height = -0.09  Weight = 0.88  BMI = 1.04  Lean Mass = 0.15 | AMAB  Height = -1.05, p<0.05  Weight = -0.303, p=ns  BMI = 0.56, p=ns  Lean Mass = -1.11, p=0.002  AFAB  Height = -0.05, p=ns,  Weight = -0.14, p=ns  BMI = 1.14, p= ns  Lean Mass = -0.08, p=ns |  |  | AMAB: a significant decrease in  height and lean mass SDSs over 12-months GnRHa treatment period  AFAB: no apparent effect  on body composition from the parameters measured for  transboys. |
| 6 | (Joseph et al., 2019)  UK | Height ± SD  Weight ± SD  BMI ± SD | AMAB, n = 10  Height = 160.3 (5.4)  Weight = 66.4 (14.6)  BMI = 25.8 (5.3)    AFAB, n = 21  Height = 159.0 (35.8)  Weight = 49.8 (17.1)  BMI = 19.4 (5.3) | AMAB, n= 10  Height = 163.4 (5.7)  Weight = 76.1 (19.4)  BMI = 28.2 (7.1)    AFAB, n = 21  Height = 160.3 (36.7)  Weight = 66.4 (14.6)  BMI = 20.7 (7.9) | AMAB, n=10  Height = 165.1 (5.7)  Weight = 82.9 (30.5)  BMI = 30.5 (8.6)    AFAB, n = 21  Height = 160.3 (37.5)  Weight = 66.4 (14.6)  BMI = 20.9 (6.6) | - | An increase in height and weight  with transgirls (AMAB) having a larger increase in BMI, and transboys (AFAB) a greater increase in height. |
| 8 | (Klink. et al., 2015)  N’Lands | Height SDS  BMI SDS    Height velocity | AMAB, n=15  Height SDS = 0.14 ± 1.3  BMI SDS = 0.17 ± 0.90    AFAB  Height SDS = -0.06 HV was also negatively associated with age at GnRHa start  even when Tanner stage at start was included as a covariate,  demonstrating that some but not all of the effect of age was  mediated by Tanner stage (R2 ¼ .3, p ¼ .02). 1.2  BMI SDS = 0.3 ± 1.0 |  |  | AMAB  Height SDS = -0.97 ± 1.3, p<0.001  BMI SDS =0.07 ± 1.11, p = ns    AFAB  Height SDS = -0.1 ± 1.3, p = ns  BMI SDS = 0.5 ± 1.2, p = ns | No significant change in BMI in either AMAB or AFAB during GnRHa treatment.  A significant decrease in height SDS in AMAB compared to cisgender reference group |
| 9 | (Navabi et al., 2021)  Canada | BMI z-score (mean (SD)  Lean body mass(LBM) z-score  Total Body Fat,(TBF) z-score %    z-scores calculated from sex assigned at birth | AMAB n = 51  BMI z-score = 0.62 (1.67)  LBM z-score = -1.19 (1.45)  TBF z-score = 1.42 (1.02)    AFAB n = 119  BMI z-score = 0.89 (1.25)  LBM z-score = -1.03 (1.22)  TBF z-score =1.68 (0.96) |  |  | AMAB n = 36  BMI z-score = 0.45 (1.69), p=0.475  LBM z-score = -1.99 (1.58), p<0.001  TBF z-score = 2.46 (0.51), p<0.001    AFAB n = 80  BMI z-score = 0.99 (1.30), p = 0.083  LBM z-score = -1.01 (1.28), p< 0.89  TBF z-score = 1.78 (0.90), p=0.053 | No evidence of change in BMI z-score for AMAB or AFAB during GnRHa treatment.  Significant decrease in LBM and increase in TBF for AMAB.  Non-significant trend for increase in TBF for AFAB. |
| 10 | (Nokoff et al., 2021a)  USA | BMI percentile  GD compared to cis-gender controls |  |  |  | AMAB  GD (n=8) vs Cisgender (n=17)  BMI percentile  44 ± 39 vs 45 ± 38, p=ns    AFAB  GD (n=9) vs cisgender (n=14)  BMI percentile  62 ± 32 vs 67 ± 29, p = ns | No significant difference in BMI between AMAB or AFAB GD adolescents compared to cisgender controls |
| 11 | (Perl et al., 2021)  Israel | BMI SDS | AFAB (n=15)  BMI SDS = 0.2 ± 0.9 |  |  | AFAB (n = 15)  BMI SDS = 0.4± 0.9, p=0.198 | No significant change in BMI after GnRHa treatment in AFAB adolescents. |
| 12 | (Schagen et al., 2016)  N’lands | Height (Ht) SDS (mean (SD))  BMI SDS  Fat percent (Fat%)  Lean body mass percent (LBM%) | AMAB  Ht SD S =0.20 (1.0), n=36  BMI SDS = 0.82 (1.1), n=36  Fat % = 22.4 (6.9), n=26  LBM% = 74.6 (6.4), n=26    AFAB  Ht SD S = -0.10 (1.1), n41  BMI SDS = 0.68 (1.2), n=41  Fat % = 25.0 (6.9), n=26  LBM% = 71.5 (6.7) | AMAB  Ht SDS,-0.04 (1.0) ,p<.001  BMI SDS 0.89 (1.2), p=ns  Fat% = 26.8 (6.6), p<0.001  LBM% = 70.9 (7.3), p=0.001    AFAB  Ht SDS,-0.25 (1.1) ,p<.001  BMI SDS 0.84 (1.2), p=0.01  Fat% = 29.5 (7.3), p<0.001  LBM% = 67.7 (6.7), p<0.001 |  |  | In AMAB adolescents, significant decrease in height SDS and Fat% and significant decrease in LBM%. No significant change in BMI SDS.      In AFAB significant decrease in height SDS and LBM% and sign increase in BMI SDS and Fat%. |
| 13 | (Schagen et al., 2020)  N’lands | Height  Weight  BMI |  |  |  |  | Descriptive data provided but no comparisons of centiles before and after GnRHa provided |
| 14 | (Schulmeister et al., 2022)  USA | BMI z score  Height velocity (HV)  centimetres per year (cm/yr) median (IQR)  Tanner stage 2,3,4 (T2, T3,T4) | AMAB, n = 26  BMI z score =0.46 (0.89)    AFAB, n = 29  BMI z-score = 0.38 (0.94) | AMAB  BMI Z score = 0.66 (0.97)  HV T2 = 5.6 (4.7 – 5.7), n = 21  HV T3 = 4.2 (2.3 – 6.4), n = 3  HV T4 = 1.6 (1.5 – 2.9), n= 2    AFAB  BMI-z-score = 0.63 (0.95)  HV T2 = 5.0 (4.2 – 5.4), n = 13  HV T3 = 4.4 (4.0 – 5.5), n = 13  HV T4 = 2.9 (1.5 – 3.5), n = 3 |  |  | Tanner stage had a significant impact on HV.  HV was also negatively associated with age at GnRHa start  even when Tanner stage at start was included as a covariate,  demonstrating that some but not all of the effect of age was  mediated by Tanner stage (R2 = 0.3, p = 0.02). |
| 16 | (Stoffers et al., 2019)  N’lands | Height (Ht) SDS  BMI SDS  Using both male (transgender) and female (sex assigned at birth) reference range | AFAB n = 62  Ht SDS male = -1.3 ± 1.2  Ht SDS female = -0.1 ± 1.0  BMI SDS male = 0.68 ± 1.0  BMI SDS female = 0.47 ± 1.0 |  |  | AFAB n = 62  Ht SDS male = -1.7 ± 09  Ht SDS female = -0.2 ± 1.0  BMI SDS male = 0.58 ± 1.1  BMI SDS female = 0.40 ± 1.0 | No significant change in height SDS or BMI SDS using reference ranges for either identified gender or sex assigned at birth. |
| 19 | (Vlot et al., 2017)  N’Lands | Height  Weight |  |  |  |  | Descriptive data provided but no comparisons of centiles before and after GnRHa provided |

Boogers, L. S., van der Loos, M. A. T. C., Wiepjes, C. M., van Trotsenburg, A. S. P., den Heijer, M., & Hannema, S. E. (2023). The dose-dependent effect of estrogen on bone mineral density in trans girls. *European Journal of Endocrinology*. [**https://doi.org/https://dx.doi.org/10.1093/ejendo/lvad116**](https://doi.org/https://dx.doi.org/10.1093/ejendo/lvad116)

Boogers., L. S., Wiepjes, C. M., Klink, D. T., Hellinga, I., van Trotsenburg, A. S. P., den Heijer, M., & Hannema, S. E. (2022). Transgender Girls Grow Tall: Adult Height Is Unaffected by GnRH Analogue and Estradiol Treatment. *The Journal of clinical endocrinology and metabolism*, *107*(9), e3805-e3815. [**https://doi.org/https://dx.doi.org/10.1210/clinem/dgac349**](https://doi.org/https://dx.doi.org/10.1210/clinem/dgac349)

Ciancia, S., Dubois, V., Claessens, F., Craen, M., Doms, S., El Kharraz, S., Kim, N. R., Klink, D., Vanderschueren, D., & Cools, M. (2022). Long-term GnRHa use and bone health in transgender adolescents: can a mouse model inform clinical practice?

Ghelani, R., Lim, C., Brain, C., Fewtrell, M., & Butler, G. (2020). Sudden sex hormone withdrawal and the effects on body composition in late pubertal adolescents with gender dysphoria [Article]. *Journal of Pediatric Endocrinology and Metabolism*, *33*(1), 107-112. [**https://doi.org/10.1515/jpem-2019-0045**](https://doi.org/10.1515/jpem-2019-0045)

Perl, L., Elkon-Tamir, E., Segev-Becker, A., Israeli, G., Brener, A., & Oren, A. (2021). Blood pressure dynamics after pubertal suppression with gonadotropin-releasing hormone analogs followed by estradiol treatment in transgender female adolescents: a pilot study. *Journal of pediatric endocrinology & metabolism : JPEM*, *34*(6), 741-745. [**https://doi.org/https://dx.doi.org/10.1515/jpem-2021-0172**](https://doi.org/https://dx.doi.org/10.1515/jpem-2021-0172)

Schagen, S. E., Cohen-Kettenis, P. T., Delemarre-van de Waal, H. A., & Hannema, S. E. (2016). Efficacy and Safety of Gonadotropin-Releasing Hormone Agonist Treatment to Suppress Puberty in Gender Dysphoric Adolescents. *J Sex Med*, *13*(7), 1125-1132. [**https://doi.org/10.1016/j.jsxm.2016.05.004**](https://doi.org/10.1016/j.jsxm.2016.05.004)

Schagen, S. E. E., Wouters, F. M., Cohen-Kettenis, P. T., Gooren, L. J., & Hannema, S. E. (2020). Bone Development in Transgender Adolescents Treated With GnRH Analogues and Subsequent Gender-Affirming Hormones. *Journal of Clinical Endocrinology & Metabolism*, *105*(12), e4252-4263. [**https://doi.org/10.1210/clinem/dgaa604**](https://doi.org/10.1210/clinem/dgaa604)

Stoffers, I. E., de Vries, M. C., & Hannema, S. E. (2019). Physical changes, laboratory parameters, and bone mineral density during testosterone treatment in adolescents with gender dysphoria. *J Sex Med*, *16*(9), 1459-1468. [**https://doi.org/10.1016/j.jsxm.2019.06.014**](https://doi.org/10.1016/j.jsxm.2019.06.014)

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