Bilaga till rapport

Hormonbehandling vid könsdysfori-vuxna / Hormone treatment of adults with gender dysphoria,
rapport 348, 2022

Bilaga 4.Sammanfattning av de systematiska översikter som ingår i rapporten

Appendix 4.Summary of systematic reviews on gender confirming hormonal treatment. All with PRISMA methodology and low or moderate risk of bias (AMSTAR).

Innehåll/ Contents

Psychosocial effects

Article End of search	Endpoints (improvement)	N included articles reporting on different psychosocial outcomes. Period published	Number of trans persons	Evidence synthesis	Authors' conclusions
White-Hughto et al. 2016 (1) November 2014	Psychological functioning quality of life	2 on phycological function 1 on quality of life (included in Baker 2021) All 3 from 2014	247 (154 of depression, 107 on quality of life))	Narrative	Low quality evidence suggests that hormone therapy may lead to improvements in psychological functioning
Rowniak et al. 2019 (2) September 2017	Depression Anxiety Quality of life,	5 on depression (1 in Baker 2021) 2 on anxiety (1 in Baker 2021) 3 on quality of life (2 included in Baker 2021) 2008-2017	552 (404 on depression, 164 on anxiety, 211 on quality of life)	Narrative	However, because the certainty of this evidence was very low to low, recommendations for hormone use to improve quality of life, depression and anxiety could not be made
Nobili et al. 2018 (3) July 20176	Quality of life	29 on quality of life (3 included in Baker 2021) 2006-2017	Not reported	Narrative 14 in meta-analysis	Evidence suggests that transgender people have lower QoL than the general population. Some evidence suggests that QoL improves post-treatment.
Baker et al. 2021 (4) June 2020	Depression Anxiety quality of life fatal suicide	15 on depression ¨ 10 on anxiety 8 on quality of life 4 on suicide 1976-2020	Not reported	Narrative	Hormone therapy was associated with increased QOL, decreased depression, and decreased anxiety. Associations were similar across gender identity and age. Certainty in this conclusion is limited by high risk of bias in study designs, small sample sizes, and confounding with other interventions. We could not draw any conclusions about death by suicide.
Karalexi et al. 2020 (5) June 2019	Cognition	10 1995–2016	384	Meta analysis	Current evidence does not support an adverse impact of hormone therapy on cognitive function, whereas a statistically significant enhancing effect on visuospatial ability was

					shown in aF (assigned female (FtM))

Tumour development

Article End of search	Endpoints (improvement)	N included articles reporting on different psychosocial outcomes. Period published	Number of trans persons	Evidence synthesis	Authors' conclusions
McFarlane et al. 2018 (6) April 2018	Cancer incidence	9 (7 case-reports) on breast cancer 8 (6 case-reports) on prostate cancer 6 case report on meningioma 6 case-reports on prolactinoma 2 on other tumours 7 cohorts 2 cross-sectional 34 case-reports 1989-2017	Not reported	Narrative	Retrospective cohort studies suggest no increase in risk of tumour development in transgender individuals receiving GAHT compared to the general population. Notably, the mean ages of cohorts were young and were treated with GAHT for insufficient durations to assess tumour risk. Case reports raise potential associations between high-dose oestradiol and anti-androgen therapy with prolactinoma and meningioma, respectively.

Bone health

Article End of search	Endpoints	N included articles reporting on different psychosocial outcomes. Period published	Number of trans persons	Evidence synthesis	Authors' conclusions
Delgado Ruiz et al. 2019 (7) December 2018	Bone mineral density Bone metabolism Bone turnover	9 on bone mineral density 3 on bone metabolism	Not reported	Narrative	Considering the limitations of this systematic review, it was concluded that long-term cross-sex pharmacotherapy for transwomen and transmen transgender patients does

		5 on bone turnover 1998-2018			not alter the calcium, phosphate, alkaline phosphatase, and osteocalcin levels, and will slightly increase the bone formation in both transwomen and transmen patients. Furthermore, long-term pharmacotherapy reduces the BMD in transwomen patients.
Sing-Ospina et al. 2017 (8) April 2015	Bone mineral density	13 on bone mineral density (1 included in Delagado-Ruiz 2018) 1996-2015	639	Meta-analysis	In FTM individuals and compared with baseline values before initiation of masculinizing hormone therapy, there was no statistically significant difference in the lumbar spine, femoral neck, or total hip bone mineral density (BMD) when assessed at 12 and 24 months. In MTF individuals and compared with baseline values before initiation of feminizing hormone therapy, there was a statistically significant increase Fracture rates were evaluated in a single cohort of 53 MTF and 53 FTM individuals, with no events at 12 months. The body of evidence is derived mostly from observational studies at moderate risk of bias.

Cardiovascular effects

Article End of search	Endpoints	N included articles reporting on different psychosocial outcomes. Period published	Number of trans persons	Evidence synthesis	Authors' conclusions
Ignacio et al. 2022 (9) November 2020	Stroke	14 narrative and of these five in meta-analysis 1978-2019	Not reported	14 narratives Subset of 5 in meta-analysis	Hormonal therapy in male to female (MTF) transgenders may confer cardiovascular risks in this population. However, more population-based studies that include clinical characteristics

					and outcomes of chronic health diseases in MTF transgenders are warranted.
Connelly et al. 2021 (10) January 2020	Blood pressure	14 1989-2019	1309	Narrative	There is currently insufficient data to advise the impact of GHT on BP in transgender individuals.
Velho et al. 2017 (11) March 2017	Body mass index Blood pressure Lipid profiles Liver enzymes	11 on body mass index 7 on blood pressure (5 included in Connelly 2022) 13 on lipid profiles 6 on liver enzymes	Not reported	Narrative	Slight but significant increases in BMI were reported (from 1.3 to 11.4%). Three out of seven studies assessing the impact of different testosterone formulations on blood pressure detected modest increases or clinically irrelevant changes in this variable. In another study, however, two patients developed hypertension, which was resolved after cessation of testosterone therapy. Decreases in HDL-cholesterol and increases in LDL-cholesterol were consistently observed. Six studies assessing liver function showed slight or no changes. Overall, the quality of evidence was low,
Kahn et al. 2019 (12) April 2018	Depp venous thrombosis (incidence)	12		Narrative	Our study estimated the incidence rate of venous thromboembolism in transgender women pre-scribed oestrogen to be 2.3 per 1000 person-years, but because of heterogeneity this estimate cannot be reliably applied to transgender women as a group. There are insufficient data in the literature to partition by subgroup for subgroup prohibiting

					the analysis to control for tobacco use, age, and obesity, w
Defreyne et al. 2019 (13) June 2018	Cardiometabolic risk factors Thromboembolism	4 on cardiovascular mortality, 12 on cardiovascular morbidity, 12 on blood pressure, 25 on lipids, 24 on body composition 19 on markers of increased thrombosis. 1986-2018		Narrative	Studies describing a higher risk for cardiometabolic and thromboembolic morbidity and/or mortality in transgender women (but not transgender men) mainly covered data on transgender women using the now obsolete ethinyl oestradiol and, therefore, are no longer valid. Currently, most of the available literature on transgender people adhering to standard treatment regimens consists of retrospective cohort studies of insufficient follow-up duration. When assessing markers of cardiometabolic disease, the available literature is inconclusive, which may be ascribed to relatively short follow-up duration and small sample size.
Totaro et al. 2021 (14) April 2021	Risk of venous thromboembolism (VTE)	18 1989-2021	11 542 assigned males at birth	Meta analysis and meta regression	The overall rate of VTE in AMAB trans people undergoing gender affirming hormone therapy was 2%. In AMAB population with <37.5 years undergoing estrogen therapy for less than 53 months, the risk of VTE appears to be negligible.
Spanos et al. 2020 (15) March 2019	Insulin resistance	26 1997-2019	1 440	Narrative	Evidence in transgender men suggests that testosterone therapy increases lean mass, decreases fat mass, and has no impact on insulin resistance. Evidence in transgender women suggests that feminising hormone therapy (estradiol, with or without anti-androgen agents)

					decreases lean mass, increases fat mass, and may worsen insulin resistance

AMAB = assigned male at birth
AFAB = assigned female at birth
MtF = male to female
FtM = female to male
GHT = gender confirming hormone therapy
QOL = quality of life

References

1. White Hughto JM, Reisner SL. A Systematic Review of the Effects of Hormone Therapy on Psychological Functioning and Quality of Life in Transgender Individuals. Transgend Health. 2016;1(1):21-31.

2. Rowniak S, Bolt L, Sharifi C. Effect of cross-sex hormones on the quality of life, depression and anxiety of transgender individuals: A quantitative systematic review. JBI Database of Systematic Reviews and Implementation Reports. 2019;17(9):1826-54.

3. Nobili A, Glazebrook C, Arcelus J. Quality of life of treatment-seeking transgender adults: A systematic review and meta-analysis. Reviews in Endocrine and Metabolic Disorders. 2018;19(3):199-220.

4. Baker KE, Wilson LM, Sharma R, Dukhanin V, McArthur K, Robinson KA. Hormone Therapy, Mental Health, and Quality of Life Among Transgender People: A Systematic Review. J Endocr Soc. 2021;5(4):bvab011.

5. Karalexi MA, Georgakis MK, Dimitriou NG, Vichos T, Katsimpris A, Petridou ET, et al. Gender-affirming hormone treatment and cognitive function in transgender young adults: a systematic review and meta-analysis. Psychoneuroendocrinology. 2020;119:104721.

6. McFarlane T, Zajac JD, Cheung AS. Gender-affirming hormone therapy and the risk of sex hormone-dependent tumours in transgender individuals—A systematic review. Clinical Endocrinology. 2018;89(6):700-11.

7. Delgado-Ruiz R, Swanson P, Romanos G. Systematic review of the long-term effects of transgender hormone therapy on bone markers and bone mineral density and their potential effects in implant therapy. Journal of Clinical Medicine. 2019;8(6).

8. Singh-Ospina N, Maraka S, Rodriguez-Gutierrez R, Davidge-Pitts C, Nippoldt TB, Prokop LJ, et al. Effect of Sex Steroids on the Bone Health of Transgender Individuals: A Systematic Review and Meta-Analysis. J Clin Endocrinol Metab. 2017;102(11):3904-13.

9. Ignacio KHD, Diestro JDB, Espiritu AI, Pineda-Franks MC. Stroke in Male-to-Female Transgenders: A Systematic Review and Meta-Analysis. Can J Neurol Sci. 2022;49(1):76-83.

10. Connelly PJ, Clark A, Touyz RM, Delles C. Transgender adults, gender-affirming hormone therapy and blood pressure: a systematic review. J Hypertens. 2021;39(2):223-30.

11. Velho I, Fighera TM, Ziegelmann PK, Spritzer PM. Effects of testosterone therapy on BMI, blood pressure, and laboratory profile of transgender men: a systematic review. Andrology. 2017;5(5):881-8.

12. Khan J, Schmidt RL, Spittal MJ, Goldstein Z, Smock KJ, Greene DN. Venous Thrombotic Risk in Transgender Women Undergoing Estrogen Therapy: A Systematic Review and Metaanalysis. Clinical Chemistry. 2019;65(1):57-66.

13. Defreyne J, Van de Bruaene LDL, Rietzschel E, Van Schuylenbergh J, T'Sjoen GGR. Effects of Gender-Affirming Hormones on Lipid, Metabolic, and Cardiac Surrogate Blood Markers in Transgender Persons. Clinical Chemistry. 2019;65(1):119-34.

14. Totaro M, Palazzi S, Castellini C, Parisi A, D'Amato F, Tienforti D, et al. Risk of Venous Thromboembolism in Transgender People Undergoing Hormone Feminizing Therapy: A Prevalence Meta-Analysis and Meta-Regression Study. Front Endocrinol (Lausanne). 2021;12:741866.

15. Spanos C, Bretherton I, Zajac JD, Cheung AS. Effects of gender-affirming hormone therapy on insulin resistance and body composition in transgender individuals: A systematic review. World journal of diabetes. 2020;11(3):66-77.