Transgender Health
Volume 8, Number 1, 2023

DOI: 10.1089/trgh.2020.0094

REVIEW

The Effect of Gender-Affirming Hormones on Gender Dysphoria, Quality of Life, and Psychological Functioning in Transgender Individuals: A Systematic Review

Taylah R. van Leerdam,[1] Jeffrey D. Zajac,[1,2] and Ada S. Cheung[1,2,*]

Abstract

Gender-affirming hormone therapy (GAHT) is an essential part of gender affirmation for many transgender (including people with binary and nonbinary identities) individuals and although controlled studies are unethical, there remains limited evidence on the impact of GAHT on gender dysphoria, quality of life (QoL), and psychological functioning. Some clinicians and policy makers use the lack of evidence to argue against providing gender-affirming care. The aim of this review is to systematically and critically assess the available literature on the influence of GAHT on improving gender- and body-related dysphoria, psychological well-being, and QoL. Using Preferred Reporting Items for Systematic Review and Meta-analysis guidelines, we searched Ovid MEDLINE®, Embase®, and Ovid PsycINFO® from inception to March 6, 2019 to assess the influence of GAHT on (1) gender dysphoria, (2) body uneasiness, (3) body satisfaction, (4) psychological well-being, (5) QoL, (6) interpersonal and global functioning, and (7) self-esteem. Our search strategy found no randomized controlled trials. Ten longitudinal cohort studies, 25 cross-sectional studies, and 3 articles reporting both cross-sectional and longitudinal data were identified. While results are mixed, the majority of studies demonstrate that GAHT reduces gender dysphoria, body dissatisfaction, and uneasiness, subsequently improving psychological well-being and QoL in transgender individuals. However, all current researches are of low to moderate quality comprising longitudinal cohort studies and cross-sectional studies, making it difficult to draw clear conclusions and do not reflect external social factors unaffected by GAHT, which significantly impact on dysphoria, well-being, and QoL.

Keywords: gender-affirming hormone therapy; gender dysphoria; gender identity; mental health; quality of life; transgender

Introduction

Gender-affirming hormone therapy (GAHT) plays an important role in gender affirmation for many transgender (including people with binary and nonbinary identities) individuals.[1] Testosterone, the mainstay of masculinizing hormone therapy, aims to induce masculine secondary sex characteristics, as well as suppress/minimize feminine characteristics. Estrogens are the primary class of medications used to feminize.[1] Antiandrogens are an adjunct to estrogens, which suppress testosterone and include cyproterone acetate, spironolactone, and gonadotrophin-releasing hormone agonists.[2] By better aligning an individual's physical appearance with their gender identity, GAHT aims to reduce body and gender dysphoria, subsequently improving psychological well-being and quality of life (QoL).[2]

Awareness around the unique health care issues transgender people experience is on the rise, but there are still significant gaps in the research considering an

[1]Department of Medicine (Austin Health), The University of Melbourne, Heidelberg, Australia.
[2]Department of Endocrinology, Austin Health, Heidelberg, Australia.

*Address correspondence to: Ada S. Cheung, MBBS (Hons), PhD, Department of Endocrinology, Austin Health, 145 Studley Road, Heidelberg 3084, Victoria, Australia, E-mail: adac@unimelb.edu.au

estimated 0.3–0.5% of the population identify as transgender.[3] Transgender, including gender diverse and nonbinary people, experience many barriers to accessing health care, including difficulty in finding providers, discrimination, and the limited evidence to support gender-affirming treatments.[4] Gender-affirming treatments have been deemed medically necessary for many individuals,[5] but there is still limited evidence in the efficacy and long-term effects of these treatments.[6] Some clinicians and policy makers use the limit in outcome data to argue against providing gender-affirming care.[7] These factors compound the mental and physical health outcomes of transgender people.[4] It should be noted that untreated control group of transgender people is unethical and therefore cannot be the gold standard as evidence for this population. However, this should not preclude more robust longitudinal research, which would be of significant benefit and necessary to improve health care outcomes in transgender people. As such, the aim of this review is to systematically and critically assess the available literature on the influence of GAHT on improving gender- and body-related dysphoria, psychological well-being, and QoL.

Methods

This systematic review utilized the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) guidelines.[8]

Eligibility criteria

Observational studies (i.e., cross-sectional and longitudinal studies) were included, provided they were in English and in a peer-reviewed journal. Case reports and qualitative studies were excluded. Studies were eligible for inclusion provided they were assessing a transgender population on GAHT. This review did not exclude articles where no official diagnosis of gender dysphoria/gender identity disorder had been made according to the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*) or equivalent. The review accepted all types, dosages, administrations, and durations of GAHT, self, or physician prescribed. Studies where the primary intervention was either gender-affirming surgeries or puberty blockers, or where the primary population was people with disorders of sexual development were excluded. All ages were included. We did not specifically exclude studies that included adolescents, but the youngest reported participant was 15 years.

To assess the efficacy of GAHT in improving gender- and body-related dysphoria, as well as psychological well-being and QoL, this review included both cross-sectional and longitudinal studies assessing the influence of GAHT on (1) gender dysphoria, (2) body uneasiness, (3) body satisfaction, (4) psychological well-being, (5) QoL, (6) interpersonal and global functioning, and (7) self-esteem.

Information sources and search strategy

The first author consulted an expert reference librarian for advice in conducting the electronic database search with input from the last author. Eligible studies were identified using Ovid MEDLINE®, Embase®, and Ovid PsycINFO®, from inception to March 6, 2019. The search used controlled vocabulary and keywords to outline the population (transgender individuals), intervention (GAHT), and outcomes (gender dysphoria, body uneasiness, body satisfaction, mental health, QoL, interpersonal and global functioning, and self-esteem).

The bibliographies of all relevant studies were used to uncover further articles.

Results

Search of the databases Ovid MEDLINE, Embase, and Ovid PsycINFO identified 1193 articles. Duplicates were removed, leaving 973. After abstract and title screening, 904 articles were excluded, leaving 69 for full-text screening. After full-text screening, 32 articles were identified. Six articles were sourced from the bibliographies of articles from the original search, giving a total of 38 (Fig. 1). All studies were observational; 10 were longitudinally designed (Table 1), 25 cross-sectional (Table 2), and 3 utilized both (Table 3). No randomized control trials were identified.

The influence of gender-affirming hormones on gender dysphoria

A dual design study (Table 3) first completed cross-sectional analysis of 359 transgender individuals (167 on GAHT, 192 not on GAHT), with unexpectedly higher reported levels of self-reported global gender dysphoria in people using masculinizing or feminizing GAHT.[9] When the questionnaire was broken into domains of subjective, social, sociolegal, and somatic indicators of gender identity, different patterns emerged for transgender people using feminizing and masculinizing hormone therapy. People using feminizing GAHT reported lower subjective, but higher levels of gender dysphoria related to social indicators of gender

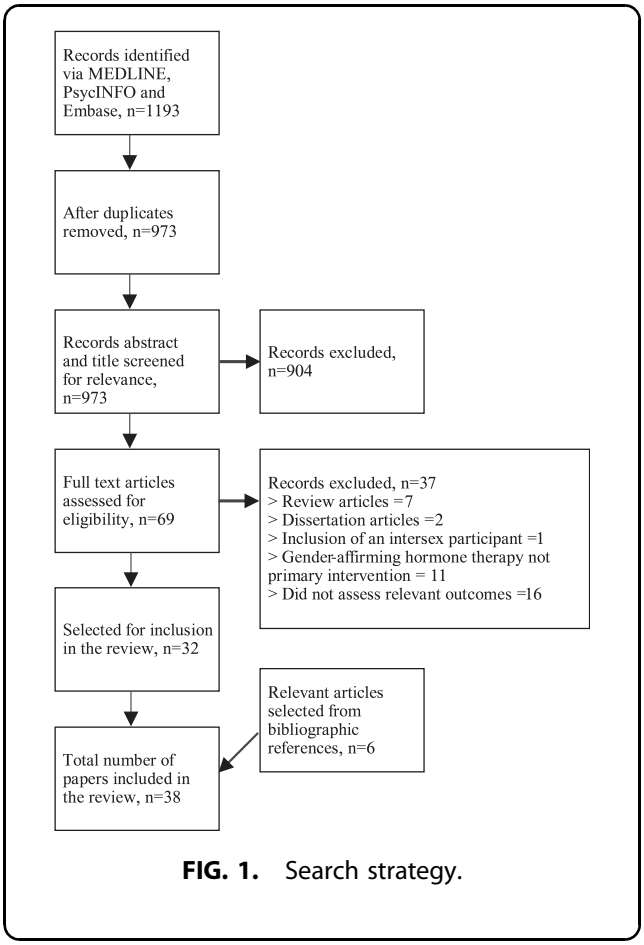

FIG. 1. Search strategy.

identity, compared to transgender people not on hormone therapy. Transgender people using masculinizing GAHT reported higher levels of gender dysphoria related to sociolegal indicators of gender identity, compared to transgender people not on hormone therapy.[9] Fifty-four of the 192 participants not on GAHT at cross-sectional analysis commenced GAHT, and gender dysphoria was measured after 3, 6, 12, and 24 months.[9] Global levels of gender dysphoria decreased at 3 months, then increased across all other time points. When separating subscales, over time, there was lower subjective gender dysphoria, whereas levels of gender dysphoria related to social and sociolegal aspects of gender identity increased.[9]

Another study completed across four European gender identity clinics, measured gender dysphoria at admission to clinic, then again at follow-up, which ranged between 4 and 6 years depending on the participant (Table 1).[10] Using the same questionnaire at both time points, they reported less gender dysphoria in groups that had either commenced GAHT after admission to the clinic, or had received no intervention, but had socially transitioned. No significant differences emerged between these two groups at follow-up.[10]

Only one study was identified examining the influence of GAHT on gender congruence (Table 2).[11] Gender congruence was measured using the Transgender Congruence Scale, a self-reported 15-item instrument assessing levels of an individual's comfort with their gender identity and body-gender congruence. For all transgender people (both those on masculinizing and feminizing hormone therapy), body-gender congruence and body image satisfaction were higher among individuals who had a greater number of gender-affirming treatments (from no treatment to hormones, partial top, partial bottom, and definitive bottom surgery).[11]

The influence of gender-affirming hormones on body uneasiness and body satisfaction

Longitudinal studies reported improvements in body uneasiness[9,12] and body image satisfaction following GAHT (Tables 1 and 3).[10,13] One reported less body uneasiness after 3, 6, 12, and 24 months of GAHT in both transgender people using feminizing and masculinizing hormone therapy.[9] Another reported improvements in body uneasiness in transgender people following 6 months of masculinizing hormone therapy, but found that it was still significantly worse compared to cisgender female control participants before and after GAHT.[12] Utilizing the Body Image Scale (BIS), one study in a sample of seven reported a nonsignificant trend toward higher levels of body satisfaction 3–10 months posthormone therapy.[13] Also using the BIS, higher levels of body satisfaction were reported after 4–6 years of GAHT, compared to scores when first admitted to gender identity clinic. Satisfaction scores at follow-up were also higher in those who had received GAHT compared to individuals who had received no intervention.[10]

When examining cross-sectional evidence, transgender people using feminizing hormone therapy reported less body uneasiness compared to transgender people not using feminizing hormones, with cumulative estradiol dose and androgen blockers predicting body uneasiness scores.[14] The same study reported no difference in body uneasiness between transgender people using masculinizing hormone therapy compared to transgender participants not using masculinizing hormones (Table 2).[14] A later study by the same primary author reported less body uneasiness in transgender

Table 1. Prospective Studies

Author	Year	Country	Defined study population	Age range	Types of GAHT	Follow-up period/duration of GAHT	Outcome measures (relevant)	Main finding(s)
Colizzi et al.[34]	2014	Italy	$N = 107$, $n = 78$ TF, $n = 29$ TM, no prior surgery Newly assessed at gender clinic (formal diagnosis of GID based on DSM-IV)	≥ 18 Years	TF: transdermal estradiol gel (1.82 ± 0.53 mg/day) + cyproterone acetate (100 mg/day). TM: testosterone esters depot (250 mg every 26.24 ± 2.71 days).	12 Months	Anxiety (SAS); depression (SDS); psychopathology (SCL-90-R)	Less anxiety, depression, psychopathology, and functional impairment after GAHT. No significant differences between TF and TM participants.
Costantino et al.[43]	2013	Italy	$N = 50$ TM, no prior surgery Formal diagnosis of GID based on DSM-IV	18–45 Years	Various. Testosterone enanthate, oral testosterone undecanoate, testosterone gel, intramuscular testosterone undecanoate.	12 Months	24 Questions related to mood, well-being and aggressive behavior (6-point-likert scale)	No change in mood and well-being after GAHT.
Defreyne et al.[40]	2018	United Kingdom	$N = 155$, $n = 91$ TF, $n = 64$ TM Assessment at national gender clinic, no criteria reported	Median 27 years IQR 19–45	Not reported.	12 Months	Anxiety and depression (HADS)	Less depression after GAHT in TM and TF, no significant change in anxiety levels.
Heylens et al.[32]	2014	Belgium	$N = 57$, $n = 46$ TF, $n = 11$ TM (Baseline = 56,[a] after GAHT = 47) Formal diagnosis of GID based on DSM-IV	Not reported	Not reported.	3–6 Months	Psychopathology (SCL-90)	Less psychopathology after GAHT. SCL-90 scores similar to mean SCL-90 scores of the general population following GAHT.
Keo-Meier et al.[33]	2015	United States	$n = 48$ TM, $n = 53$ cisgender control males, $n = 62$ cisgender control females Criteria not reported	16–54 Years	Intramuscular depo-testosterone cypionate or ethanate ($n = 46$). Transdermal testosterone ($n = 2$).	3 Months	Psychopathology (MMPI-2)	Less psychopathology in TM after 3 months of testosterone therapy, relative to both female and male cisgender controls.
Lindgren and Pauly[13]	1975	United States	$N = 7$, $n = 4$ TM, $n = 3$ TF Criteria not reported	17–46 Years	Not reported.	3–10 Months	Body image satisfaction (BIS)	No significant change after GAHT, but trended toward improved body satisfaction.
Manieri et al.[20]	2014	Italy	$N = 83$, $n = 56$ TF, $n = 27$ TM Formal diagnosis of GID based on DSM-IV	Mean 33.7 ± 5.4 years	TF: Oral 17-beta-estradiol or transdermal estradiol + cyproterone acetate or spironolactone. TM: transdermal testosterone gel or intramuscular testosterone enanthate.	12 Months	Quality of life (WHOQOL-100)	TF: improved overall quality of life and improved quality of life related to sexual life, body image, and interpersonal relationships after GAHT. TM: improved quality of life related to body image and interpersonal relationships after GAHT.

(*continued*)

Table 1. (Continued)

Author	Year	Country	Defined study population	Age range	Types of GAHT	Follow-up period/duration of GAHT	Outcome measures (relevant)	Main finding(s)
Turan et al.[12]	2018	Turkey	$N=77$, $n=37$ TM, $n=40$ cisgender female controls (matched for age and educational status) Formal diagnosis of GD via DSM-V at medical faculty	Mean 24.6±4.9 years	Intramuscular testosterone esters or intramuscular testosterone undecanoate.	6 Months	Body uneasiness (BUT); psychopathology (SCL-90-R)	Less body uneasiness and psychopathology in TM participants after GAHT. Body uneasiness and psychopathy worse in TM participants compared to cisgender female controls at baseline and 6 months.
van de Grift et al.[10]	2017	Netherlands, Germany, Belgium and Norway	$n=29$ no treatment, $n=36$ GAHT only, $n=136$ GAHT and gender-affirming surgery Formal diagnosis of GID based on DSM-IV	TF: mean 39.2±12.8 years, TM: mean 30.6±11.3 years	TF: oral estradiol valerate 4 mg daily + cyproterone acetate 50 mg daily or transdermal estradiol in those aged >45 years. TM: intramuscular testosterone undecanoate or testosterone gel or intramuscular testosterone esters.	Mean (SD) TF: 4.6 (2.3) years TM: 4.9 (1.6) years	Body image (BIS); GD (UGDS)	Less GD at follow-up. No difference in levels of GD between GAHT vs. no-GAHT group at follow-up. Baseline GD scores in no-GAHT group were significantly lower vs. intervention group. Improved body satisfaction at follow-up. Higher levels of body satisfaction in GAHT vs. no-GAHT group at follow-up.
van Kemenade et al.[41]	1989	Netherlands	$N=14$ TF, no prior surgery Criteria not reported	19–33 Years	Anadron (antiandrogen) without estradiol.	8 Weeks	Anxiety (STAI); Depression (SDS)	No change in the levels of anxiety and depression after GAHT.

[a]One participant did not complete baseline SCL-90.

BIS, Body Image Scale; BUT, Body Uneasiness Test; DSM-IV, The Diagnostic and Statistical Manual of Mental Disorders Fourth Edition; GAHT, Gender-Affirming Hormone Therapy; GD, gender dysphoria; GID, gender identity disorder; HADS, Hospital Anxiety and Depression Scale; IQR, interquartile range; MMPI-2, Minnesota Multiphasic Personality Inventory (Version 2); SAS, Zung Self-Rating Anxiety Scale; SCL-90, Symptom Checklist-90; SCL-90-R, Symptom Checklist-90 Revised; SD, standard deviation; SDS, Zung Self-Rating Depression Scale; STAI, State-Trait Anxiety Inventory; TF, transfeminine; TM, transmasculine; UGDS, Utrecht Gender Dysphoria Scale; WHOQOL-100, The World Health Organization Quality of Life-100.

Table 2. Cross-Sectional Studies

Author	Year	Country	Defined study population	Age range	Types of GAHT	Duration of GAHT	Outcome measures (relevant)	Main finding(s)
Bartolucci et al.[22]	2015	Spain	*N* = 103, no prior surgery *n* = 67 TF (31 GAHT, 36 no-GAHT) *n* = 36 TM (10 GAHT, 26 no-GAHT) Formal diagnosis of GID based on DSM-IV	Mean 30.5 ± 9.47 years	TF: oral estradiol valerate (2–4 mg/day), conjugated estrogen tablets (2.5 mg/day), or transdermal 17 beta estradiol patches (6 mg/day) + cyproterone acetate (25–50 mg/day). TM: intramuscular testosterone undecanoate or transdermal testosterone gel.	Not reported	Sexual quality of life (WHOQOL-100)	Better sexual quality in those on GAHT vs. no-GAHT.
Blanchard et al.[46]	1983	Canada	*N* = 55 TF, *n* = 34 GAHT, *n* = 21 no-GAHT Formal diagnosis at gender identity clinic, no criteria reported	Not reported	Not reported.	Not reported	Psychopathology—depression and tension (MMPI)	No significant difference in levels of depression or tension in TF GAHT vs. no-GAHT.
Bonierbale et al.[37]	2016	France	*N* = 106 TF, *n* = 37 GAHT, *n* = 16 no-GAHT TM, *n* = 15 GAHT, *n* = 38 no-GAHT Formal diagnosis of GID based on DSM-IV	18–58 Years	Not reported.	Minimum 3 months	Psychopathology (MMPI-2)	Less psychopathology in group on GAHT vs. no-GAHT.
Bouman et al.[31]	2016	United Kingdom	*N* = 71 TF (38 GAHT, 33 no-GAHT) *n* = 3 TM (excluded from analysis due to small numbers) Formal diagnosis at gender identity clinic, no criteria reported	> 50 Years, mean 58.9 ± 6.5 years	TF: Oral or patch estradiol. Antiandrogen in 52%. TM: Not reported.	Not reported	Anxiety and depression (HADS); Self-esteem (RSES); interpersonal functioning (IIP-32)	TF on GAHT had less anxiety, less interpersonal problems, improved self-esteem vs. no-GAHT. No difference in levels of depression in GAHT vs. no-GAHT. When controlling for socialization, differences in anxiety, but not in self esteem remained between GAHT vs. no-GAHT.
Bouman et al.[47]	2017	United Kingdom	*N* = 1184 cisgender controls *N* = 899 trans people *n* = 259 GAHT (179 TF, 80 TM) *n* = 640 no-GAHT (393 TF, 247 TM) Self identified as transgender attending transgender health service	15–79 Years	Not reported.	Not reported	Anxiety and depression (HADS)	Overall trans people on GAHT had less anxiety vs no GAHT. TF on GAHT had less anxiety vs. no-GAHT. No difference in anxiety levels in TM GAHT vs. no-GAHT. Nearly threefold increased risk anxiety disorder in no-GAHT group vs. age-matched cisgender controls. Interpersonal problems and low self esteem appeared to predict anxiety symptoms.

(*continued*)

Table 2. (Continued)

Author	Year	Country	Defined study population	Age range	Types of GAHT	Duration of GAHT	Outcome measures (relevant)	Main finding(s)
Colton Meier et al.[21]	2011	United States	$N = 100$ TM $n = 66$ GAHT $n = 34$ no-GAHT Self identified as transgender	18–68 Years	Not reported.	Not reported	Depression, anxiety, and stress (DASS); Quality of life/functional health and well-being (SF-36v2)	TM on GAHT had less anxiety, less depression, less stress and improved health related quality of life.
Fisher et al.[14]	2014	Italy	$N = 125$ $n = 66$ TF (42 GAHT, 24 no-GAHT) $n = 59$ TM (26 GAHT, 33 no-GAHT Formal diagnosis of GID based on DSM-IV	TF: 33.1 ± 10.25 years TM 28.7 ± 6.5 years	TF: 28.6% estradiol valerate, 28.6% transdermal estradiol hemihydrate, 14.3% estradiol gel, 92.9% cyproterone acetate TM: 54.5% testosterone enanthate, 4.5% parenteral testosterone undecanoate, 40.9% transdermal testosterone.	Mean ± SD TF: 467 ± 323 days TM: 1,940 ± 2,595 days	Body uneasiness (BUT); psychopathology (SCL-90-R)	Less body uneasiness in TF on GAHT vs. no-GAHT. No difference in body uneasiness in TM on GAHT vs. no-GAHT. Cumulative estradiol dose predicted less body uneasiness in TF. No difference in SCL-90-R GAHT vs. no-GAHT.
Gomez-Gil et al.[38]	2008	Spain	$N = 163$ $n = 107$ TF (69 GAHT, 38 no-GAHT) $n = 56$ TM (10 GAHT, 46 no-GAHT Formal diagnosis of GID based on DSM-IV	TF Mean 29.9 ± 9 years, 27.6 ± 7.5 years	Not reported.	≥12 Months	Psychopathology (MMPI-2)	TF on GAHT reported less psychological distress. No difference in scores between TM GAHT vs. no-GAHT.
Gomez-Gil et al.[44]	2012	Spain	$N = 187$ $n = 113$ TF (84 GAHT, 29 no-GAHT) $n = 74$ TM (36 GAHT, 38 no-GAHT) Formal diagnosis of GID based on DSM-IV	15–61 Years	TF: either oral route (conjugated estrogens 1.8–2.4 mg/day or estradiol valerate 2–4 mg/day) or transdermal estradiol patches (3 mg twice per week/100 mg/day) generally with cyproterone acetate (25–50 mg/day) TM: either intramuscular injection of testosterone esters depot (1000 mg every 10–14 weeks) or daily transdermal testosterone gel (50 mg daily).	Mean ± SD TF: 11 ± 9.9 years TM: 4.7 ± 5.2 years	Social anxiety (SADS); anxiety and depression (HADS)	Less anxiety and depression in those on GAHT vs. no GAHT. No effect of GAHT duration on anxiety or depression.
Gomez-Gil et al.[23]	2014	Spain	$N = 193$ ($n = 119$ TF, $n = 74$ TM) $n = 120$ GAHT $n = 73$ no-GAHT Formal diagnosis of GID based on DSM-IV or ICD-10	16–67 Years	Not reported.	Not reported	Quality of life (WHOQOL-BREF)	Improved psychological and social quality of life in those on GAHT.
Gooren et al.[28,a]	2013	Thailand	$N = 60$ TF (kathoeys) $n = 44$ GAHT $n = 16$ no-GAHT Self identified as transgender	Mean 30.5 ± 17.5 years	Oral contraceptives predominantly.	Mean ± SD 9.7 ± 6.1 years	Quality of life/functional health and well-being (SF-36)	No differences in functional health and mental well-being/quality of life between TF GAHT vs. no GAHT.

(*continued*)

Table 2. (Continued)

Author	Year	Country	Defined study population	Age range	Types of GAHT	Duration of GAHT	Outcome measures (relevant)	Main finding(s)
Gooren et al.[29,a]	2015	Thailand	$N=120$ $n=60$ TF (kathoeys; 44 GAHT, 16 no-GAHT) $n=60$ TM (toms; 21 GAHT, 39 no-GAHT) Self identified as transgender	TM: Mean 24.8 ± 4.7 years	Not reported.	Mean ± SD TF: 11.7 ± 6.1 years TM: 9.5 ± 4.7 years	Quality of life/functional health and well-being (SF-36)	In TF no differences in functional health and mental well-being/quality of life GAHT vs. no-GAHT. In TM worse bodily pain, vitality, mental health, and general health in those on GAHT vs. no-GAHT.
Gorin-Lazard et al.[24]	2012	France	$N=61$ $n=31$ TF (25 GAHT, 6 no-GAHT) $n=30$ TM (19 GAHT, 11 no-GAHT) Formal diagnosis of GID based on DSM-IV	Mean 34.7 ± 10.3 years	TF: Estrogens + antiandrogens. TM: Testosterone + synthetic progestogens.	≥ 12 Months	Quality of life/functional health and well-being (SF-36)	Improved social, mental, and emotional quality of life in those on GAHT vs. no-GAHT. No difference to age- and sex-matched controls except for physical (worse) and general health (better).
Gorin-Lazard et al.[25]	2013	France	$N=67$ $n=36$ TF (29 GAHT, 7 no-GAHT) $n=31$ TM (20 GAHT, 11 no-GAHT) Formal diagnosis of GID based on DSM-IV	Mean 35.1 ± 10.2 years	TF: Estrogens + antiandrogens. TM: Testosterone + synthetic progestogens.	≥ 12 Months	Self-esteem (SSEI); depression (BDI); quality of life analysis (SQUALA); global assessment of functioning scale (GAF)	Better self-esteem, better quality of life, and less depression in those on GAHT vs. no-GAHT. No difference in global functioning between groups.
Jones et al.[16]	2018	United Kingdom	$N=563$ $n=139$ GAHT ($n=44$ female at birth, $n=95$ male at birth) $n=416$ no-GAHT ($n=166$ female at birth, $n=250$ male at birth) $n=8$ no data Formal diagnosis/assessment at transgender health service, no criteria reported	Mean 29.5 ± 13.7 years	Not reported.	Not reported	Body dissatisfaction (EDI-2); self esteem (RSES); anxiety, and depression (HADS)	Higher levels of self-esteem, less anxiety, less depression, and less body dissatisfaction in those on GAHT vs. no-GAHT.
Jones et al.[15]	2018	United Kingdom	$N=343$ $n=102$ GAHT $n=241$ no-GAHT Formal diagnosis/assessment at transgender health service, no criteria reported	Mean 30.2 ± 11.9 years	Not reported.	Not reported	Body satisfaction (HBDS); anxiety and depression (HADS); self esteem (RSES)	Higher levels of body satisfaction and self-esteem and less anxiety and depression in those on GAHT vs. no-GAHT.
Leavitt et al.[39]	1980	United States	$N=41$ TF $n=22$ GAHT $n=19$ no-GAHT Criteria not reported	18–35 Years	Oral conjugated estrogens (Premarin) and medroxyprogesterone acetate.	≥ 12 Months	Psychopathology (MMPI)	Less psychopathology in TF on GAHT vs. no-GAHT. Longer duration GAHT related to less psychopathology. Some MMPI domains in GAHT treated individuals were in normal limits.

(*continued*)

Table 2. (Continued)

Author	Year	Country	Defined study population	Age range	Types of GAHT	Duration of GAHT	Outcome measures (relevant)	Main finding(s)
Newfield et al.[26]	2006	United States	$N=365$ TM $n=248$ GAHT $n=117$ no-GAHT Self identified as transgender	Mean 32.8±11.2 years	Not reported.	Majority <5 years	Quality of life/functional health and well-being (SF-36v2)	Better functional health and mental well-being/quality in those on GAHT vs. no-GAHT.
Owen-Smith et al.[11]	2018	United States	$N=262$ $n=87$ TM (76 GAHT, 11 no-GAHT) $n=175$ TF (158 GAHT, 17 no-GAHT) Formal diagnosis of GID based on ICD-9	18 to >55 Years	Not reported.	Not reported	Body-gender congruence (TCS); body image satisfaction (RPSPP); anxiety (BAI); depression (CES-D-10)	Higher levels of body congruence and body image satisfaction in those on GAHT vs. no-GAHT. Lower levels of depression and anxiety in those on GAHT vs. no-GAHT.
Pauly and Lindgren[17]	1977	United States	$N=131$ $n=30$ TF (14 GAHT, 16 no-GAHT) $n=27$ TM (13 GAHT, 14 no-GAHT) Criteria not reported	Not reported	Not reported.	5 Months to 10 years	Body image satisfaction (BIS)	Improved body satisfaction in those on GAHT vs. no-GAHT.
Simbar et al.[18]	2018	Iran	$N=60$ $n=30$ GAHT $n=30$ no-GAHT Formal diagnosis of GID, no criteria reported	18–45 Years	Not reported.	≥6 Months	Quality of life (WHOQOL-BREF); Body Image Satisfaction (FBIQ)	No difference in quality of life or body satisfaction between GAHT vs. no-GAHT.
Valashany and Janghorbani[27]	2018	Iran	$N=71$ $n=30$ TF (6 GAHT, 24 no-GAHT) $n=41$ TM (10 GAHT, 31 no-GAHT) Formal diagnosis of GD based on DSM-V	TF: Mean 23.8±5.6 years. TM: Mean 24.2±6.3 years	Not reported.	Mean (SD) TF: 2.7 (9.6) years TM: 4.8 (13.0) years	Quality of life/functional health and well-being (SF-36)	Improvement in some aspects of quality of life when controlling for GAHT duration. Poorer quality of life compared to age- and gender- matched cisgender controls.
van de Grift et al.[19]	2016	Netherlands, Germany, Belgium and Norway	$N=660$ $n=374$ TF ($n=81$ GAHT, $n=293$ no-GAHT) $n=286$ TM ($n=16$ GAHT, $n=270$ no-GAHT) Formal diagnosis of GID based on DSM-IV	TF: mean 34.1±12.6 years. TM: mean 27.0±9.6 years	TF: oral estradiol valerate 4 mg daily + cyproterone acetate 50 mg daily or transdermal estradiol in those aged >45 years. TM: intramuscular testosterone undecanoate or testosterone gel or intramuscular testosterone esters.	Not reported	Body satisfaction (BIS)	No difference in body satisfaction between GAHT vs. no-GAHT.
Witcomb et al.[45]	2018	United Kingdom	$N=913$ $n=261$ GAHT $n=638$ no-GAHT $n=14$ missing data Self identified as transgender	15–79 Years	Not reported.	Not reported	Anxiety and depression (HADS)	Less depression in those on GAHT vs. no-GAHT.
Yang et al.[30]	2016	China	$N=209$ TF $n=37$ no-GAHT $n=172$ no-GAHT Self identified as transgender	18–45 Years	Not reported.	Not reported	Quality of life/functional health and well-being (SF-36)	Lower physical and mental quality of life in those on GAHT vs. no-GAHT.

[a]Same TF group.

BAI, Beck Anxiety Index; BDI, Beck Depression Inventory; CES-D-10, 10-item Center for Epidemiologic Studies Depression Scale; DASS, Depression, Anxiety, and Stress Scale; EDI-2, Eating Disorder Inventory-2; FBIQ, Fisher Body Image Questionnaire; GAF, Global Assessment of Functioning Scale; HBDS, Hamburg Body Drawing Scale; ICD-9, International Classification of Diseases Ninth Revision; ICD-10, International Classification of Diseases Tenth Revision; IIP-32, Inventory for Interpersonal Problems (Short Version); MMPI, Minnesota Multiphasic Personality Inventory; RPSPP, Revised Physical Self-perception Profile; RSES, Rosenberg Self Esteem Scale; SADS, The Social Anxiety and Distress Scale; SF-36, Short Form Health Survey; SF-36v2, Short Form Health Survey Version 2; SQUALA, Subjective Quality of Life Analysis; SSEI, Social Self-Esteem Inventory; TCS, Transgender Congruence Scale; WHOQOL-BREF, World Health Organization Quality of Life Assessment (Abbreviated Version).

Table 3. Dual Design Studies

Author	Year	Country and design	Defined study population	Age range	Types of GAHT	GAHT duration	Outcome measures (relevant)	Main finding(s)
Fisher et al.[9]	2016	Italy Cross-sectional analysis	$N = 359$ $n = 219$ TF (125 GAHT, 94 no-GAHT) $n = 140$ TM (42 GAHT, 98 no-GAHT)	GAHT group: mean 33.9 ± 9.2 years and no GAHT group: mean 29.1 ± 9.3 years	TF: oral estradiol valerate 55%, oral ethinyl estradiol 26.4%, transdermal estradiol hemihydrate 28%, estradiol gel 19.2%, oral finasteride 3.2%, oral dutasteride 4%, cyproterone acetate 78.4%, and spironolactone 1.6%. TM: testosterone enanthate 53%, testosterone undecanoate in 23.3% and transdermal testosterone in 23.3%.	Mean (minimum; maximum) TF: 1331 (31; 13,445) days TM: 323 (33; 1,095) days	Body uneasiness (BUT); psychopathology (SCL-90-R); GD (GIDYQ-AA); depression (BDI II)	In GAHT vs. no-GAHT: Less body uneasiness TF and TM. No difference in levels of psychopathology. Global GD worse TF and TM. Subjective GD better in TF. Social GD worse in TF. Sociolegal GD worse in TM. Less depressive symptoms in TM.
		Longitudinal analysis	$N = 54$ $n = 28$ TF $n = 26$ TM Formal diagnosis of GD based on DSM-V			3, 6, 12 and 24 Months	Body uneasiness (BUT); psychopathology (SCL-90-R); GD (GIDYQ-AA); depression (BDI II)	Reduced body uneasiness. Reduced psychopathology. Global GD improved at 3 months then got worse at 6, 12, 24 months. Subjective GD improved with time. Social and sociolegal GD worsened with time. Less depressive symptoms.
Miles et al.[42]	2006	United Kingdom Cross-sectional analysis	$N = 103$ $n = 74$ TF (47 GAHT, 27 no-GAHT)		Oral conjugated equine estrogens or ethinylestradiol ± cyproterone acetate ± medroxyprogesterone acetate.	Either ≥ 28 or ≥ 3 months	Mood (POMS)	Higher mood scores on composed and confident scales in GAHT vs. no-GAHT groups.
		Longitudinal analysis	$N = 103$ (1) $n = 27$ TF (2) $n = 27$ TF (3) $n = 20$ TF Formal diagnosis of GID based on DSM-IV	(1) Mean 37.1 ± 8.7 years (2) Mean 39.6 ± 9.7 years (3) Mean 40.3 ± 7.5 years		(1) Before and after 3–12 months GAHT (2) ≥ 28 Months GAHT then ≥ 8 weeks withdrawal from GAHT (3) ≥ 3 Months GAHT then re-tested 3–12 months later	Mood (POMS)	(1) No change in mood with GAHT except for higher scores on composed and confident scales. (2) No influence of withdrawal of GAHT on mood. (3) No influence of duration of GAHT on mood.

(*continued*)

Table 3. (Continued)

Author	Year	Country and design	Defined study population	Age range	Types of GAHT	GAHT duration	Outcome measures (relevant)	Main finding(s)
Oda and Kinoshita[35]	2017	Japan Cross-sectional analysis	$N = 155$ TM $n = 53$ GAHT $n = 102$ no-GAHT	15–43 Years	Not reported.	Not reported	Psychopathology (MMPI)	No significant differences in psychopathology between GAHT vs. no-GAHT.
		Longitudinal analysis	$N = 14$ TM Formal diagnosis of GID based on DSM-IV			Mean ± SD 519 ± 365 days	Psychopathology (MMPI)	Improvements in psychopathology with GAHT. Psychotherapy and GAHT combined reduced symptoms of psychotherapy compared to GAHT alone.

BDI II, Beck Depression Inventory 2; GIDYQ-AA, Gender Identity/Gender Dysphoria Questionnaire for Adolescents and Adults; POMS, Profile of Mood States.

people both using masculinizing and feminizing hormones compared to those not on hormone therapy (Table 3).[9] Not all studies have been consistent when looking at cross-sectional data on body satisfaction. Some report higher levels of body satisfaction in those on GAHT,[11,15–17] whereas others report no difference between groups (Table 2).[18,19]

The influence of gender-affirming hormones on QoL

One longitudinal study reported improved QoL following 12 months of GAHT (Table 1).[20] In transgender people commencing feminizing hormone therapy, average QoL scores, as well as QoL related to body image, quality of sexual life, and interpersonal relationships significantly improved after 12 months of GAHT. Similarly, QoL related to body image and interpersonal relationships significantly improved following 12 months of testosterone therapy in people seeking masculinization.[20]

Cross-sectional evidence examining QoL in people using GAHT were conflicting and inconsistent. Some studies reported better QoL in those on GAHT,[21–27] while others reported no difference[18,28] and even worse QoL in people using masculinizing[29] and feminizing[30] GAHT (Table 2). One article assessed sexual QoL only, reporting higher sexual QoL in those on GAHT, compared to those not on hormone therapy (Table 2).[22] One study also reported family support and having an occupation as additional factors associated with improved QoL (Table 2).[23]

The influence of gender-affirming hormones on self-esteem, interpersonal, and global functioning

One longitudinal study assessed the influence of GAHT on interpersonal functioning over time. Both transgender people who used masculinizing and feminizing GAHT reported higher levels of QoL related to interpersonal relationships following GAHT (Table 1).[20] No longitudinal studies examining the influence of GAHT on self-esteem or global functioning were identified.

Cross-sectional studies reported higher levels of self-esteem[15,16,25,31] and less interpersonal problems[31] in participants on GAHT compared to those who were not (Table 2). However, when controlling for interpersonal issues, in particular, socialization, no significant difference between levels of self-esteem between groups was apparent.[31] No differences in the levels of global

functioning were reported between groups who had received GAHT compared to those who had not received hormone therapy.[25]

The influence of gender-affirming hormones on levels of psychopathology

Six longitudinal studies reported less psychopathology following GAHT,[9,12,32–35] all with differing follow-up periods (Tables 1 and 3). Two main questionnaires were utilized, the Minnesota Multiphasic Personality Inventory (MMPI)[33,35] and Symptom Checklist-90 (SCL-90),[9,12,32,34] both are designed to assess a broad range of psychological problems to measure progress of psychological treatments and have been revised and translated over time. The SCL-90 for example measures dimensions, including somatization, obsessive-compulsive, interpersonal sensitivity, hostility, anxiety, depression, paranoid ideation, phobic anxiety, and psychoticism.[36] Psychopathology appeared to be higher in transgender people using masculinizing hormone therapy compared to cisgender female controls matched for age and educational status at baseline and 6 months post-GAHT.[12] Psychotherapy and GAHT combined reduced symptoms of psychopathology compared to GAHT alone[35] and were similar to mean scores in the general population following 3–6 months of GAHT.[32]

Cross-sectional studies also utilized the MMPI[35,37–39] and SCL-90[9,14] to assess psychopathology, with mixed results (Tables 2 and 3). Studies reported less psychopathology in those on GAHT[37,39] or saw no difference between groups.[9,14,35] One study reported less psychopathology in transgender people using feminizing GAHT, but saw no difference between transgender people using masculinizing GAHT compared to transgender people not on hormone therapy.[38] Longer duration of GAHT was related to less psychopathology.[39] In addition, some domains of the MMPI in hormone-treated individuals were reported to be within normal limits.[39]

The influence of gender-affirming hormones on depression, anxiety, and other mood states

Longitudinal studies comparing levels of depression before and after GAHT either reported improvements[9,34,40] or no change (Tables 1 and 3).[41] Anxiety levels were found to improve[34] or in some studies, not change following GAHT.[40,41] One multidesign study examined mood states uniquely in a group of transgender people receiving feminizing GAHT at multiple time points on and off estrogen.[42] Utilizing the Profile of Mood States questionnaire, which measured six mood constructs on a scale (Composed/Anxious; Agreeable/Hostile; Elated/Depressed; Confident/Unsure; Energetic/Tired; and Clearheaded/Confused), the "Composed" scale and "Confident" scale were higher in people on estrogen compared to off estrogen (Table 3).[42] Another longitudinal study found no change in mood and well-being following 12 months of GAHT in a group of transgender people starting masculinizing hormone therapy (Table 1).[43]

Cross-sectional studies comparing levels of depression either reported less depressive symptoms in those on GAHT compared to those not on hormone therapy (Table 2)[11,15,16,21,25,44,45] or saw no difference between groups (Table 2).[31,46] One article reported less depression in transgender people receiving masculinizing GAHT compared to transgender people not on GAHT, but no differences were observed in transgender people receiving feminizing GAHT compared to those not on hormone therapy (Table 3).[9] Anxiety was also lower in those on GAHT compared to participants not on hormone therapy (Table 2).[11,15,16,21,31,44,47] While transgender people on GAHT had lower rates of possible or probable anxiety (53%) compared with transgender people not on GAHT (69%), rates still appeared higher than the 35% reported in the general population.[47] After matching participants to members of the general population based on age and experienced gender, those not on GAHT had almost a threefold increased risk of having an anxiety disorder.[47]

Discussion

This review was designed to examine the influence of GAHT on symptoms of gender dysphoria, including its effects on body satisfaction, QoL, and psychological well-being. The best quality evidence to date are longitudinal (but uncontrolled) studies examining the influence of GAHT over time. Most longitudinal evidence suggests that GAHT improves these outcomes, whereas the cross-sectional data are less consistent. Studies were conducted across different countries and cultures, some with limited access to gender-affirming treatments. Many cross-sectional studies had differing duration and doses of GAHT, with little or no control of confounding variables. This makes it difficult to both compare the research, as well as draw solid conclusions.

Gender dysphoria

Studies examining the influence of GAHT on gender dysphoria/body congruence show mixed results.[9–11] This may reflect the limited nature of existing

measures, as well as highlight the necessity of developing appropriate measures to provide equitable health care to transgender people. While subjective levels of gender dysphoria improved, global-, social-, and sociolegal-related levels of gender dysphoria worsened and this is likely explained by the many cultural and sociolegal difficulties that transgender people face.[9] Factors contributing to gender dysphoria are complex, and it is unrealistic to expect GAHT alone to completely relieve dysphoria and distress. For example, while testosterone therapy may very effectively masculinize physical characteristics such as voice and facial hair, chest size is typically unaffected and so chest dysphoria can worsen due to discordance with other masculinizing physical changes.[1] Alternatively, transgender people who begin feminizing hormone therapy and socially transition may experience increased social distress due to micro- and macroaggressions from others given that many physical changes of their endogenous puberty such as voice are not affected by GAHT.[1] Most societies place value in masculinity, and when it is perceived that someone is giving up this power and taking on feminine characteristics in some form, this can be the target of harassment and violence.

Existing data assessing the impact of GAHT on gender dysphoria were also limited by the comparison of unmatched groups, as well as a lack of control of potential confounding variables, including the effects of both social transition and psychological counseling on levels of gender dysphoria.[10] Studies are also limited by their use of questionnaires. Some have male and female versions, based on sex assigned at birth[48] and their applicability post-transition as well as which questionnaire researchers and clinicians should administer comes into question. The binary nature of the questionnaires does also not allow for assessment of nonbinary and genderqueer identities.[49]

Body uneasiness and body satisfaction

Gender-affirming hormones appear to improve body satisfaction and body uneasiness. Better quality data are longitudinal, all which reported improvements, but in small samples.[9,10,12,13] In addition, only some separated out analysis for feminizing and masculinizing hormone therapy in their sample[9,14] when differences in body dissatisfaction between these groups have been previously reported.[50,51] However, not all studies reported improvements in levels of body satisfaction with GAHT.[18,19] The authors of these suggested that the self-administering nature, dosages, and duration of GAHT might not have been sufficient to achieve desired results. Articles also varied in their use of questionnaires to assess body satisfaction and uneasiness. Some were not developed for transgender populations[52,53] or were noted to be limited in their ability to assess other indicators of body image, such as behaviors, cognition, and feelings.[10]

Quality of life

The literature supports the notion that GAHT improves QoL, however, only one longitudinal study was identified; all others were cross-sectional. Most studies did not control for confounding variables, such as societal factors that may also influence QoL, which is critically important. Studies reporting no difference[18,28] or worse QoL in those on GAHT[29,30] included participants with uncontrolled hormone usage, most outside of medical care. One study conducted in China reporting worse QoL in participants on GAHT stated that at the time of publication, no public hospitals provided professional health care services for transgender people, nor did many provide legal hormone therapy.[30] Results may reflect the health care barriers and discrimination that transgender people face, as well as potential consequences on well-being and QoL.

Self-esteem, interpersonal and global functioning

Gender-affirming hormones appear to improve self-esteem and interpersonal functioning. By influencing physical appearance, GAHT may increase self-perceived gender congruence and lead to improved social skills, self-confidence, and comfort in interacting with others.[25,26] The influence of GAHT on these factors is significant, as interpersonal problems increase the vulnerability of transgender people developing mental health problems.[54] In addition, low self-esteem and poor interpersonal functioning have both been linked to higher rates of anxiety[31,47] and depression[45] in transgender people. One cross-sectional article conducted in France reported no difference in global functioning between transgender individuals on GAHT or not.[25] Those residing in France may more easily access free health care, making it difficult to compare the transgender individuals of the study to those outside of organized care.[25]

Psychopathology, depression, and anxiety

Gender-affirming hormones may have a positive influence on mental health, most reporting less psychopathology, depression, anxiety, and improved mood following GAHT. Some reported levels in hormone

and nontreated individuals to be within normative ranges.[34,38,44] A sample of participants on masculinizing GAHT shifted toward a healthier direction 3 months post-GAHT compared to both matched cisgender male and female controls.[33] This finding is similar to what has been discussed in another review.[55] Studies were completed across different countries and cultures, with different health services and legislation, making cross-cultural validation difficult.[55]

The variability opens up the question as to why transgender people experience psychological distress and why it may improve with hormone therapy. One notion is that the psychological distress that transgender people experience is related to gender incongruence. Undergoing GAHT induces desirable physical characteristics more in keeping with their gender identity, therefore improving psychological well-being.[56] However, other research suggests that the distress and dysfunction transgender people experience is actually more closely linked to the violence and stigmatization they encounter, rather than gender incongruence itself.[57] One study[34] also highlighted the importance of controlling for variables, including life experiences, stigma, and discrimination, as well as exploring the benefit of concurrent psychological counseling on mental health outcomes.

Summary

It appears that GAHT may improve subjective gender- and body-related dysphoria, psychological well-being, and QoL. However, most evidence is of low to moderate quality, predominantly cohort studies and cross-sectional studies. Alleviation of gender dysphoria is the primary goal of GAHT, but we lack a quality measurement tool to assess it.[55] Assessment of secondary outcomes, including mental health and QoL, which arguably may be the most important outcomes of gender-affirming treatments may provide evidence as to the efficacy of GAHT.

There are several limitations to this review. The first being the lack of high-level evidence with most studies lacking control groups of transgender people not using GAHT. While we included articles where the primary intervention was GAHT, it was not always clear whether gender-affirming surgery had occurred during the studies and its impact on articles included in this review is unclear. The importance of subjective experiences of GAHT can also not be ignored; as such, the exclusion of qualitative evidence is another limitation to the review.

Many of the studies also reported varying durations, doses, and types of hormones, or did not report these data. When people are assessed at different stages of their transition, it makes it difficult to draw clear conclusions. Most studies did not separate out results by type of GAHT, and they also did not recognize gender diverse, including nonbinary individuals, which would have enabled assessment of their unique experiences while undergoing GAHT. In addition, most utilized the *DSM* or equivalent criteria as an inclusion requirement for study entry. As such, these individuals can be considered to be under medical supervision, with some receiving concurrent psychological intervention. This restricts study samples to only treatment seeking populations and so limits their applicability to the transgender population as a whole. The inclusion of studies in this review of participants outside of medical care, without a formal diagnosis, and who were self-prescribing hormones also possibly confounds results and potentially underestimates the influence of hormones on those with a diagnosis of gender dysphoria.

Conclusion

GAHT may be linked to improvements in gender dysphoria, body satisfaction, and uneasiness, subsequently improving psychological well-being and QoL in transgender individuals. However, all current research is of low to moderate quality, making it difficult to draw clear conclusions and do not reflect external social factors, which significantly impact on dysphoria, well-being, and QoL. Research that is ethical precludes high-quality studies. Ideally, more robust longitudinal studies examining the impact of GAHT will provide clinical benefit, allowing for realistic expectations, development of necessary support measures, and guide policy in transgender health. The lack of high-quality studies does not represent the absence of benefit, and our call for more research should not preclude the provision of gender-affirming care based upon published expert consensus guidelines.

Authors' Contributions

Conceptualization, T.R.v.L., J.D.Z., and A.S.C.; methodology, T.R.v.L., J.D.Z., and A.S.C.; investigation, T.R.v.L. and A.S.C.; formal analysis, T.R.v.L. and A.S.C.; writing—original draft, T.R.v.L. and A.S.C.; writing—review and editing, T.R.v.L., J.D.Z., and A.S.C.; funding acquisition, A.S.C.; supervision, A.S.C.

Author Disclosure Statement

No competing financial interests exist. No conflict of interest.

Funding Information

A.S.C. is supported by a National Health and Medical Research Council of Australia (NHMRC) Early Career Fellowship (ID 1143333) and receives research support from Viertel Charitable Foundation, Endocrine Society of Australia, Austin Medical Research Foundation and Royal Australasian College of Physicians Foundation.

References

1. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine treatment of gender-gysphoric/gender-incongruent persons: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2017;102:3869–3903.
2. Coleman E, Bockting W, Botzer M, et al. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, version 7. Int J Transgend. 2012;13:165–232.
3. Winter S, Diamond M, Green J, et al. Transgender people: health at the margins of society. Lancet. 2016;388:390–400.
4. Hughto JMW, Reisner SL, Pachankis JE. Transgender stigma and health: a critical review of stigma determinants, mechanisms, and interventions. Soc Sci Med. 2015;147:222–231.
5. Meyer III WJ. World Professional Association for Transgender Health's standards of care requirements of hormone therapy for adults with gender identity disorder. Int J Transgend. 2009;11:127–132.
6. Gooren LJ, Giltay EJ, Bunck MC. Long-term treatment of transsexuals with cross-sex hormones: extensive personal experience. J Clin Endocrinol Metab. 2008;93:19–25.
7. Shires DA, Stroumsa D, Jaffee KD, Woodford MR. Primary care clinicians' willingness to care for transgender patients. Ann Fam Med. 2018;16: 555–558.
8. Moher D, Shamseer L, Clarke M, et al. Preferred Reporting Items for Systematic Review and Meta-Analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4:1.
9. Fisher AD, Castellini G, Ristori J, et al. Cross-sex hormone treatment and psychobiological changes in transsexual persons: two-year follow-up data. J Clin Endocrinol Metab. 2016;101:4260–4269.
10. van de Grift TC, Elaut E, Cerwenka SC, et al. Effects of medical interventions on gender dysphoria and body image: a follow-up study. Psychosom Med. 2017;79:815–823.
11. Owen-Smith AA, Gerth J, Sineath RC, et al. Association between gender confirmation treatments and perceived gender congruence, body image satisfaction, and mental health in a cohort of transgender individuals. J Sex Med. 2018;15:591–600.
12. Turan S, Aksoy Poyraz C, Usta Saglam NG, et al. Alterations in body uneasiness, eating attitudes, and psychopathology before and after cross-sex hormonal treatment in patients with female-to-male gender dysphoria. Arch Sex Behav. 2018;47:2349–2361.
13. Lindgren TW, Pauly IB. A Body Image Scale for evaluating transsexuals. Arch Sex Behav. 1975;4:639–656.
14. Fisher AD, Castellini G, Bandini E, et al. Cross-sex hormonal treatment and body uneasiness in individuals with gender dysphoria. J Sex Med. 2014;11:709–719.
15. Jones BA, Haycraft E, Bouman WP, Arcelus J. The levels and predictors of physical activity engagement within the treatment-seeking transgender population: a matched control study. J Phys Act Health. 2018;15:99–107.
16. Jones BA, Haycraft E, Bouman WP, et al. Risk factors for eating disorder psychopathology within the treatment seeking transgender population: the role of cross-sex hormone treatment. Eur Eat Disord Rev. 2018;26: 120–128.
17. Pauly IB, Lindgren TW. Body image and gender identity. J Homosex. 1977; 2:133–142.
18. Simbar M, Nazarpour S, Mirzababaie M, et al. Quality of life and body image of individuals with gender dysphoria. J Sex Marital Ther. 2018;44: 523–532.
19. van de Grift TC, Cohen-Kettenis PT, Steensma TD, et al. Body satisfaction and physical appearance in gender dysphoria. Arch Sex Behav. 2016;45: 575–585.
20. Manieri C, Castellano E, Crespi C, et al. Medical treatment of subjects with gender identity disorder: the experience in an Italian public health center. Int J Transgend. 2014;15:53–65.
21. Colton Meier SL, Fitzgerald KM, Pardo ST, Babcock J. The effects of hormonal gender affirmation treatment on mental health in female-to-male transsexuals. J Gay Lesbian Ment Health. 2011;15:281–299.
22. Bartolucci C, Gomez-Gil E, Salamero M, et al. Sexual quality of life in gender-dysphoric adults before genital sex reassignment surgery. J Sex Med. 2015;12:180–188.
23. Gomez-Gil E, Zubiaurre-Elorza L, de Antonio IE, et al. Determinants of quality of life in Spanish transsexuals attending a gender unit before genital sex reassignment surgery. Qual Life Res. 2014;23: 669–676.
24. Gorin-Lazard A, Baumstarck K, Boyer L, et al. Is hormonal therapy associated with better quality of life in transsexuals? A cross-sectional study. J Sex Med. 2012;9:531–541.
25. Gorin-Lazard A, Baumstarck K, Boyer L, et al. Hormonal therapy is associated with better self-esteem, mood, and quality of life in transsexuals. J Nerv Ment Dis. 2013;201:996–1000.
26. Newfield E, Hart S, Dibble S, Kohler L. Female-to-male transgender quality of life. Qual Life Res. 2006;15:1447–1457.
27. Valashany BT, Janghorbani M. Quality of life of men and women with gender identity disorder. Health Qual Life Outcomes. 2018; 16:167.
28. Gooren LJ, Sungkaew T, Giltay EJ. Exploration of functional health, mental well-being and cross-sex hormone use in a sample of Thai male-to-female transgendered persons (kathoeys). Asian J Androl. 2013;15: 280–285.
29. Gooren LJ, Sungkaew T, Giltay EJ, Guadamuz TE. Cross-sex hormone use, functional health and mental well-being among transgender men (Toms) and transgender women (Kathoeys) in Thailand. Cult Health Sex. 2015;17: 92–103.
30. Yang X, Zhao L, Wang L, et al. Quality of life of transgender women from China and associated factors: a cross-sectional study. J Sex Med. 2016;13: 977–987.
31. Bouman WP, Claes L, Marshall E, et al. Sociodemographic variables, clinical features, and the role of preassessment cross-sex hormones in older trans people. J Sex Med. 2016;13:711–719.
32. Heylens G, Verroken C, De Cock S, et al. Effects of different steps in gender reassignment therapy on psychopathology: a prospective study of persons with a gender identity disorder. J Sex Med. 2014;11: 119–126.
33. Keo-Meier CL, Herman LI, Reisner SL, et al. Testosterone treatment and MMPI-2 improvement in transgender men: a prospective controlled study. J Consult Clin Psychol. 2015;83:143–156.
34. Colizzi M, Costa R, Todarello O. Transsexual patients' psychiatric comorbidity and positive effect of cross-sex hormonal treatment on mental health: results from a longitudinal study. Psychoneuroendocrinology. 2014;39:65–73.
35. Oda H, Kinoshita T. Efficacy of hormonal and mental treatments with MMPI in FtM individuals: cross-sectional and longitudinal studies. BMC Psychiatry. 2017;17:256.
36. Derogatis LR, Lipman RS, Covi L. SCL-90: an outpatient psychiatric rating scale–preliminary report. Psychopharmacol Bull. 1973;9: 13–28.
37. Bonierbale M, Baumstarck K, Maquigneau A, et al. MMPI-2 profile of French transsexuals: the role of sociodemographic and clinical factors. A cross-sectional design. Sci Rep. 2016;6:24281.
38. Gomez-Gil E, Vidal-Hagemeijer A, Salamero M. MMPI-2 characteristics of transsexuals requesting sex reassignment: comparison of patients in prehormonal and presurgical phases. J Pers Assess. 2008;90:368–374.
39. Leavitt F, Berger JC, Hoeppner J-A, Northrop G. Presurgical adjustment in male transsexuals with and without hormonal treatment. J Nerv Ment Dis. 1980;168:693–697.
40. Defreyne J, T'Sjoen G, Bouman WP, et al. Prospective evaluation of self-reported aggression in transgender persons. J Sex Med. 2018;15:768–776.
41. van Kemenade JF, Cohen-Kettenis PT, Cohen L, Gooren LJ. Effects of the pure antiandrogen RU 23.903 (anandron) on sexuality, aggression, and mood in male-to-female transsexuals. Arch Sex Behav. 1989;18:217–228.

42. Miles C, Green R, Hines M. Estrogen treatment effects on cognition, memory and mood in male-to-female transsexuals. Horm Behav. 2006;50: 708–717.
43. Costantino A, Cerpolini S, Alvisi S, et al. A prospective study on sexual function and mood in female-to-male transsexuals during testosterone administration and after sex reassignment surgery. J Sex Marital Ther. 2013;39:321–335.
44. Gomez-Gil E, Zubiaurre-Elorza L, Esteva I, et al. Hormone-treated transsexuals report less social distress, anxiety and depression. Psychoneuroendocrinology. 2012;37:662–670.
45. Witcomb GL, Bouman WP, Claes L, et al. Levels of depression in transgender people and its predictors: results of a large matched control study with transgender people accessing clinical services. J Affect Disord. 2018; 235:308–315.
46. Blanchard R, Clemmensen LH, Steiner BW. Gender reorientation and psychosocial adjustment in male-to-female transsexuals. Arch Sex Behav. 1983;12:503–509.
47. Bouman WP, Claes L, Brewin N, et al. Transgender and anxiety: a comparative study between transgender people and the general population. Int J Transgend. 2017;18:16–26.
48. Schneider C, Cerwenka S, Nieder TO, et al. Measuring gender dysphoria: a multicenter examination and comparison of the Utrecht Gender Dysphoria Scale and the gender identity/gender dysphoria questionnaire for adolescents and adults. Arch Sex Behav. 2016;45:551–558.
49. McGuire JK, Beek TF, Catalpa JM, Steensma TD. The Genderqueer Identity (GQI) Scale: measurement and validation of four distinct subscales with trans and LGBQ clinical and community samples in two countries. Int J Transgend. 2019;20:289–304.
50. Marone P, Iacoella S, Cecchini M, et al. An experimental study of body image and perception in gender identity disorders. Int J Transgend. 1998;2:97–103.
51. Becker I, Nieder TO, Cerwenka S, et al. Body image in young gender dysphoric adults: a European multi-center study. Arch Sex Behav. 2016; 45:559–574.
52. Fisher S. Body Experience in Fantasy and Behavior. New York: Appleton-Century-Crofts, 1970.
53. Cuzzolaro M, Vetrone G, Marano G, Garfinkel P. The Body Uneasiness Test (BUT): development and validation of a new body image assessment scale. Eat Weight Disord. 2006;11:1–13.
54. Davey A, Bouman W, Arcelus J, Meyer C. Interpersonal functioning among individuals with gender dysphoria. J Clin Psychol. 2015;71:1173–1185.
55. Dhejne C, Van Vlerken R, Heylens G, Arcelus J. Mental health and gender dysphoria: a review of the literature. Int Rev Psychiatry. 2016;28: 44–57.
56. Kuiper B, Cohen-Kettenis P. Sex reassignment surgery: a study of 141 Dutch transsexuals. Arch Sex Behav. 1988;17:439–457.
57. Robles R, Fresán A, Vega-Ramírez H, et al. Removing transgender identity from the classification of mental disorders: a Mexican field study for ICD-11. Lancet Psychiatry. 2016;3:850–859.

Cite this article as: van Leerdam TR, Zajac JD, Cheung AS (2023) The effect of gender-affirming hormones on gender dysphoria, quality of life, and psychological functioning in transgender individuals: a systematic review, *Transgender Health* 8:1, 6–21, DOI: 10.1089/trgh.2020.0094.

Abbreviations Used

BAI = Beck Anxiety Index
BDI = Beck Depression Inventory
BDI II = Beck Depression Inventory 2
BIS = Body Image Scale
BUT = Body Uneasiness Test
CES-D-10 = 10-item Center for Epidemiologic Studies Depression Scale
DASS = Depression, Anxiety, and Stress Scale
DSM = The Diagnostic and Statistical Manual of Mental Disorders
DSM-IV = The Diagnostic and Statistical Manual of Mental Disorders Fourth Edition
DSM-V = The Diagnostic and Statistical Manual of Mental Disorders Fifth Edition
EDI-2 = Eating Disorder Inventory-2
FBIQ = Fisher Body Image Questionnaire
GAF = Global Assessment of Functioning Scale
GAHT = gender-affirming hormone therapy
GD = gender dysphoria
GID = gender identity disorder
GIDYQ-AA = Gender Identity/Gender Dysphoria Questionnaire for Adolescents and Adults
HADS = Hospital Anxiety and Depression Scale
HBDS = Hamburg Body Drawing Scale
ICD-9 = International Classification of Diseases Ninth Revision
ICD-10 = International Classification of Diseases Tenth Revision
IIP-32 = Inventory for Interpersonal Problems (Short Version)
IQR = interquartile range
MMPI = Minnesota Multiphasic Personality Inventory
MMPI-2 = Minnesota Multiphasic Personality Inventory (Version 2)
POMS = Profile of Mood States
QoL = quality of life
RPSPP = Revised Physical Self-perception Profile
RSES = Rosenberg Self Esteem Scale
SADS = The Social Anxiety and Distress Scale
SAS = Zung Self-Rating Anxiety Scale
SCL-90 = Symptom Checklist-90
SCL-90-R = Symptom Checklist-90 Revised
SD = standard deviation
SDS = Zung Self-Rating Depression Scale
SF-36 = Short Form Health Survey
SF-36v2 = Short Form Health Survey Version 2
SQUALA = Subjective Quality of Life Analysis
SSEI = Social Self-Esteem Inventory
STAI = State-Trait Anxiety Inventory
TCS = Transgender Congruence Scale
TF = transfeminine
TM = transmasculine
UGDS = Utrecht Gender Dysphoria Scale
WHOQOL-100 = The World Health Organization Quality of Life-100
WHOQOL-BREF = World Health Organization Quality of Life Assessment (Abbreviated Version)