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ORIGINAL ARTICLE

Hormonal therapy and sex reassignment: a systematic review and meta-analysis of quality of life and psychosocial outcomes

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Summary

Objective To assess the prognosis of individuals with gender identity disorder (GID) receiving hormonal therapy as a part of sex reassignment in terms of quality of life and other self-reported psychosocial outcomes.

Methods We searched electronic databases, bibliography of included studies and expert files. All study designs were included with no language restrictions. Reviewers working independently and in pairs selected studies using predetermined inclusion and exclusion criteria, extracted outcome and quality data. We used a random-effects meta-analysis to pool proportions and estimate the 95% confidence intervals (CIs). We estimated the proportion of between-study heterogeneity not attributable to chance using the I^2 statistic.

Results We identified 28 eligible studies. These studies enrolled 1833 participants with GID (1093 male-to-female, 801 female-to-male) who underwent sex reassignment that included hormonal therapies. All the studies were observational and most lacked controls. Pooling across studies shows that after sex reassignment, 80% of individuals with GID reported significant improvement in gender dysphoria (95% CI = 68–89%; 8 studies; I^2 = 82%); 78% reported significant improvement in psychological symptoms (95% CI = 56–94%; 7 studies; I^2 = 86%); 80% reported significant improvement in quality of life (95% CI = 72–88%; 16 studies; I^2 = 78%); and 72% reported significant improvement in sexual function (95% CI = 60–81%; 15 studies; I^2 = 78%).

Conclusions Very low quality evidence suggests that sex reassignment that includes hormonal interventions in individuals with GID likely improves gender dysphoria, psychological functioning and comorbidities, sexual function and overall quality of life.

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Introduction

Therapy with cross-sex hormones is used as a primary sex reassignment intervention or as an adjunct to sex reassignment surgery in individuals with gender identity disorder (GID). Hormonal therapies clearly exert a rapid and direct effect on gender specific behaviours such as aggressiveness, arousal, verbal fluency and visuospatial abilities.[1] Several studies have reported sex reassignment to be associated with favourable changes in family, psychological and social life, sexual relationships and gender dysphoria, defined as the distress that originates from the difference between one's biological sex and one's basic sense of being a male or a female.[2–4]

Despite these putative benefits, individuals with GID who undergo this transition continue to have high prevalence of psychiatric comorbidities such as depression and anxiety disorders, as well as a suicide rate that is higher than that of the general population.[2,5] Hormonal therapies may also be associated with adverse effects that should be considered in addition to other costs and burdens of treatments. These adverse events have improved with the use of newer transdermal preparations and the routine administration of lower doses,[6,7] but may continue to be of concern to patients and providers.

We sought to systematically review the literature for the best available evidence regarding the benefits and risks of hormonal therapy administered in this context. In this manuscript, we summarize the available evidence about benefits in terms of self-reported outcomes such as the resolution of gender dysphoria and the effects on sexual function, psychiatric comorbidities and quality of life.

Methods

The report of this protocol-driven systematic review adheres to the standards for reporting Meta-analysis Of Observational Studies in Epidemiology (MOOSE).[8]

Eligibility criteria

We considered studies to be eligible for this review if they enrolled male-to-female (MF) or female-to-male (FM) individuals

who received endocrine interventions as a part of sex reassignment.

We included studies regardless of their language or sample size; and anticipating that these studies will likely be nonrandomized (observational) and uncontrolled, we included all study designs except single case reports. We excluded review articles, commentaries and letters that did not contain original data, andstudies of individuals with GID in which there was no mention of endocrine interventions or protocols involving hormone therapy; and studies with follow-up duration of less than 3 months.

Study identification

An expert reference librarian designed and conducted the electronic search strategy with input from study investigators with expertise in conducting systematic reviews. To identify eligible studies, we searched electronic databases (Ovid MEDLINE, Ovid Embase, Ovid PsycInfo, Thomson Scientific Web of Science and Elsevier Scopus) from 1966 to February 2008.

The search strategy employed a combination of controlled vocabulary for the concept of transsexualism (where available: Ovid MEDLINE and Ovid Embase), and text words. The concept of 'transgender' was developed using a combination of database specific vocabulary such as transsexualism or sex reversal, gonadal in concert with textwords: transsexual, transgender, transperson, sexual transition, sexual (or gender) reassignment, gender dysphoria, sexual dysphoria, gender identity, cross-gender, MF or FM, male-to-female and female-to-male. The terms for quality of life included various quality-of-life scales (qol, hrqol, qaly, quality adjusted), depression, regret, well-being, satisfaction, adjustment, self-esteem, body image, suicide, health status, mental status, sexual behaviour, sexual dysfunction. Where available, the controlled vocabulary was enhanced with the textwords. A detailed list of subject headings and text words is available upon request.

In addition, we sought additional references from bibliographies of eligible studies and content experts. Teams of reviewers working independently and in duplicates screened all abstracts and titles and, upon retrieval of candidate studies, reviewed the full text publications and determined study eligibility.

Disagreements were resolved by consensus (the two reviewers discussed the discrepancy and reached a decision) or arbitration (if disagreement was not resolved by the two reviewers, a third reviewer adjudicated the difference). We estimated chance-adjusted agreement amongst reviewers using the kappa statistic.

Data collection

Teams of reviewers were worked independently and in duplicate using standardized forms extracted descriptive, methodological and outcome data from all eligible studies.

Data collected from studies included a description of the population (MF or FM, comorbid psychiatric conditions, mean age and number of participants), description of the exposure (type, dose, route and duration of hormonal treatment), study design and quality components, and data corresponding to the outcomes of interest: (1) resolution of gender dysphoria, (2) status of psychiatric comorbidities, (3) quality of life and (4) satisfaction with sexual function.

Quality assessment

We employed the GRADE approach[9,10] to rate the quality of research evidence, taking into account the elements that can strengthen the quality of observational studies such as strong associations, direction of confounding and dose–response relationships.[10] For each study, we assessed how the population was selected, how the exposure (hormone therapy) documented (self-report *vs*. medical chart documentation), whether outcomes were assessed via self-report or clinical/structured interview, the duration and adequacy of study follow up, and the proportion of participants lost to follow up. We assessed chance-adjusted agreement on study quality using the kappa statistic with disagreements resolved by consensus or arbitration.

Statistical analysis

We planned to perform random effect meta-analysis[11] to pool association measures (odds ratios) from controlled studies and proportions from uncontrolled studies. We planned to explore treatment effects in all transsexuals as well as to explore effect in MF and FM populations separately. To quantify inconsistency in treatment effects across studies, we used the I^2 statistic,[12] which represents the proportion of variability across trials that is not attributable to random error or chance. StatsDirect 2·5·4 (StatsDirect Statistical Software Ltd., UK, 2005) was used for statistical analysis.

Results

Study identification

Figure 1 depicts the study selection process. Twenty-eight studies proved eligible for inclusion in this review. These studies enrolled 1833 participants (1091 MF, 801 FM). In general, MF individuals were older than FM individuals (mean age: 38 and 31, respectively). The majority of the 27 included studies originated from Europe and nine of them were translated from German, French and Turkish. Agreement among reviewers about study selection assessed by Kappa statistic was 0·84. Study characteristics are described in Table 1.

Methodological quality

None of the studies were randomized and only three were controlled.[13–15] However, controls in Smith *et al.*,[13] were individuals who refused treatment or did not quite fit the diagnostic criteria of GID, which weakens the inference from this comparison.

Twenty studies were cross-sectional and eight were longitudinal. The exposure (hormonal therapy) was self-reported in most studies and the details of treatments were in general not reported. In all of the included studies but five,[4,14–17] data were presented

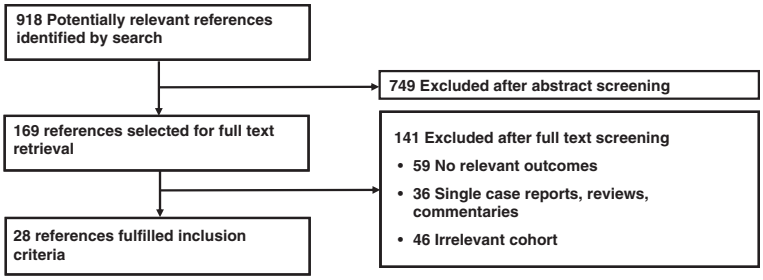

Fig. 1 The process of study selection.

for sex reassignment as a whole (hormonal therapy + sexual reassignment surgery); therefore, it was difficult to separate the impact of hormones from that of surgery. In one study,[18] hormonal therapy was administered with regular psychotherapy interventions making the assessment of hormone effects similarly challenging. The outcomes were ascertained by structured interview or clinical exam in 21 studies and by a questionnaire in seven studies, one of them conducted through an Internet site. Follow-up averaged 6 years, which we considered to be adequate to assess outcomes of interest in all but one study.[17] Agreement among reviewers about study quality assessed by Kappa statistic ranged from 0·64 to 1·0.

Outcomes

Table 2 describes reported outcomes in included trials.

Resolution of gender dysphoria

Pooling across studies shows that after sex reassignment, 80% of individuals with GID reported significant improvement in gender dysphoria (95% CI = 68–89%; 8 studies; I^2 = 82%). Proportion in MF subgroup is 71% (41–93%) and in FM subgroup is 86% (65–98%).

When measured by the Utrecht Gender Dysphoria Scale (UGDS/UGS), FM and MF individuals had minimal gender dysphoria remaining after transition, which was comparable to gender concordant controls without GID[2,19,20] and better than dysphoria in untreated individuals with GID.[13] They reported good satisfaction with the new assigned sex,[4,20–23] physical appearance,[4,13,19,23,24] had no doubts about their new gender role or their ability about maintaining this role in the future.[4] Satisfaction with primary and secondary sex characteristics was significantly higher when pre- and posttransition therapy data were compared.[19,20] Most individuals in these studies did not report regrets about transition therapy.[2,13,20,25] In one study, however, 3/17 individuals regretted sex reassignment and 2/3 sought reversal procedures.[26]

Compared with FM, MF individuals had more remaining gender dysphoria after the transition.[2] Homosexual MF individuals reported more regrets about the transition than those who were nonhomosexual.[19]

Psychiatric comorbidities

Pooling across studies shows that after sex reassignment, 78% of individuals with GID reported significant improvement in psychiatric symptoms (95% CI = 56–94%; 7 studies; I^2 = 86%). This proportion in the MF subgroup is 70% (33–96%) and in the FM subgroup is 84% (73–92%).

Psychiatric comorbidities were fairly prevalent in individuals with GID. A cross-sectional study showed a lifetime prevalence of Axis I diagnoses (mood disorders, anxiety disorders, somatoform disorders, schizophrenia, substance abuse and eating disorders) of 71% and current prevalence of 39%; a third of these participants were on hormonal therapy.[5] The cross-sectional design of the study limits inference about the temporal relationship between the exposure and the outcomes.

Male-to-female and FM individuals had the same psychological functioning level as measured by the Symptom Checklist inventory (SCL-90), which was also similar to the psychological functioning level of the normal population[2] and better than that of untreated individuals with GID.[13] Similar results were demonstrated using the short form of the Minnesota Multiphasic Personality Inventory, which measures Negativism, Somatization, Shyness, Psychopathology and Extroversion.[13,15,19,20] A comparative assessment of MF individuals using hormones *vs.* those who were not, showed that they had less psychopathology. The neurotic and psychotic disturbances they had were also considered to fall within the normal limits. Longer duration of hormone use was associated with better psychological adjustment.[15] Postsex reassignment, 76% of MF and 81% of FM reported improvement of their global psychological condition.[27]

Suicide attempt rates decreased after sex reassignment but stayed higher than the normal population rate.[2,18,24,28] In one study, although most individuals reported improvement in their psychological status (19/23); the remaining individuals worsened and had increased intake of alcohol and anxiolytics.[29]

Individuals with a pre-existing or more severe psychopathology were found to have retained more psychological symptoms and worse outcomes posttransition.[2,19] Similarly, nonhomosexual individuals had worse psychological outcomes.[19] MF individuals experienced negative emotions more intensely than FM both before and after hormone treatment.[17]

Quality of life

Pooling across studies shows that after sex reassignment, 80% of individuals with GID reported significant improvement in quality of life (95% CI = 0·72–0·88; 16 studies; I^2 = 78%). This proportion in the MF subgroup is 84% (68–95%) and in the FM subgroup is 78% (67–87%).

Table 1. Baseline characteristics and study quality

Author, year	Total no./ intervention/ control	Participants	Age (year)	Hormonal therapy	Mean duration of hormone treatment	Length of follow up†	Study design	Exposure ascertainments	Outcome ascertainment	Loss to follow up†
Hoenig, 1971[35]	9/NA/NA	MF 6; FM 3; Post-SRS cohort from Canada	33·3 (25–45)	7 of 9 on hormone therapy; MF: Stilboestrol (4); Hormone Implant (1); FM: Testosterone (2)	NR	3·75 years (1–10).	Cross-sectional	Self-report	Interview, questionnaire	11%
Wyler, 1979[36]	18/NA/NA	12 MF; 6 FM; 16/18 post-SRS; 2 had Klinefelter syndrome	MF 29 (19–49); FM 25 (21–31)	All individuals took HR; Type not specified	At least one year	2 years (2–45 months)	Cross-sectional	NR	Not reported	39%
Leavit, 1980[15]	61/42/19	42 MF on hormones; 19 MF, not on hormones	24·6 (18–35)	Oral and parenteral oestrogens	At least one year	NR	Cross-sectional	NR	Interview, questionnaire	**NR**
Kröhn, 1981[24]	24/NA/NA	18 MF; 6 FM; Post-SRS	MF 22–55; FM 25–38	All FM and All but 1 MF on HR; type not specified	NR	4–5 years	Cross-sectional	MF: NR; FM: authors prescribed and administered HR	Semi-structured interview + psychological tests + physical examination	NR
Sorensen, 1981[29]	23/NA/NA	Danish MF at least 1 year after SRS	25–55	All of them on various oestrogen formulations	NR	6 years	Cross-sectional	Chart-review	Standardized questionnaire	10%
Kuiper, 1988[4]	141/141/200	Treatment group: MF (105; 55 completed treatment and 50 were incomplete, i.e. only on hormones); FM (36; 25 completed treatment and 11 were incomplete, i.e. only on hormones); Control group: (body image): 100 male and 100 female students, Netherlands	MF 32; FM 28·3; All 35	Majority on HR	>2 years	NA	Cross-sectional	Self-report	Semi-structured interview, questionnaire	0
Pfäfflin, 1990[27]	85/NA/NA	42 MF; 43 FM; Post-SRS	MF 39 (25–68); FM 35 (21–65)	Taken by 41 MF and 42 FM. Type not reported. 15 MF and 2 FM began HR by themselves (not prescribed by a physician)	NR	MF 5·1 postgenital surgery; FM 6·7 years postbreast surgery	Single cohort, pre and post	Chart review and self report	Chart review, semi-structured interview by 2 examiners, Physical exam, and questionnaire	NR

Table 1. *Continued*

Author, year	Total no./ intervention/ control	Participants	Age (year)	Hormonal therapy	Mean duration of hormone treatment	Length of follow up†	Study design	Exposure ascertainments	Outcome ascertainment	Loss to follow up†
Kaube, 1991[28]	30/NA/NA	10 MF; 20 FM; All are post-SRS	MF: 40 (29–49); FM: 33 (24–42)	All individuals received hormonal therapy before and after surgery	NR	3·6 years (0·8–11)	Cross-sectional	NR	Semi-structured interview	53%
Yuksel, 1991[18]	21/6/NA	5 MF and 16 FM Pre SRS Turkish individuals	24 (18–40)	6/21 received HR; type not specified	NR	4 years	Single cohort, pre and post	NR	Clinical interview	NR
Tsoi, 1993[22]	81/NA/NA	45 MF and 36 FM transsexuals from Singapore, 2–5 years post-SRS	26	Individuals were on hormones, type is not reported	NR	NA	Cross-sectional	NR	Semi-structured questionnaire	NR
Olsson, 1996[25]	5/NA/NA	Post-SRS Swedish MF	NR	All received HR Type not specified	NR	11·4 years (Range: 6–15)	Cross-sectional	Self report	Interview	0
Cohen-Kettenis, 1997[20]	22/NA/NA	7 MF and 15 FM; >1 year after SRS	17·5 pretest; 22 posttest	12 started HR between 16–18; Type not specified	NR	1–5 years	Single cohort, pre and post	Self report and chart review	Clinical interview	0
Rauchfleisch, 1998[26]	17/NA/NA	13 MF and 4 FM were contactable out of a cohort of 69	MF: 32·8 years (19–50) FM: 33	All had HR, generally one year before SRS; type not reported	Not reported	Post-SRS (MF 14 years and FM 9·5 years)	Cross-sectional	Self report	Semi-structured interview	75%
Rehman, 1999[31]	28/NA/NA	Post-SRS MF	38	All received HR Type not specified.	7 years	NA	Cross-sectional	NR	Questionnaire	0
Schroder, 1999[34]	17/NA/NA	MF, 11-year Post-SRS, 80% Caucasians	46	All had history of HR but 84% were currently on it. Regimens consisted of oestrogens, progesterone, or both	NR	NA	Cross-sectional	Self report	Survey, structured interview, photoplethysmography	NR
Slabbekoorn, 2001[17]	101/NA/NA	MF (54); FM (47); Netherlands	MF 32·9; FM 25·7; All 27	MF: oral cyproterone acetate PO 50 mg twice a day in combination with either ethynyl-estradiol PO, 0·05 mg; Twice a day (32) or 17ß oestradiol-plasters TD, 0·1 mg/day (22). FM: Testosterone esters IM, 250 mg/2 weeks (42); undecanoate testosterone PO, 200 mg/day (5)	14 weeks	14 weeks	Single cohort, pre and post	Self report	Questionnaire, interview	0

Table 1. *Continued*

Author, year	Total no./ intervention/ control	Participants	Age (year)	Hormonal therapy	Mean duration of hormone treatment	Length of follow up†	Study design	Exposure ascertainments	Outcome ascertainment	Loss to follow up†
Smith, 2001[13]	41/20/14	Treatment group: 7 MF and 13 FM who were 1–4 years post-SRS. Controls were male and female applicants for SRS who were denied/ declined treatment due to not fulfilling diagnostic criteria	17 at pretest and 21 at posttest	All individuals in treatment group had hormonal therapy. Type and dosage not reported	NR	1–4 years for treatment group and 1–7 years for controls	Prospective controlled cohort study	Self report	Semi-structured interview	17%
Hepp, 2002[33]	29/NA/NA	30 MF and 17 FM were contactable out of a cohort of 47 identified by billing codes of transsexual who consulted in their clinic between 1990 and 1995	30 (19–51)	29/47 currently on HR, type not reported	67 months (19–114)	NA	Cross-sectional	Self report	Face-to-face interviews (25); phone interview (8); questionnaire (29). Semi-structured interview for all patients (33) including the International diagnosis checklist for personality disorders; psychometric tests only for those post-SRS (25)	30%
De Cuypere, 2005[3]	55/NA/NA	MF: 32; FM: 23; Dutch speaking, underwent SRS between1986–2001 in Belgium	MF 41·5; FM 33·2; All 38	MF: Cyproterone acetate, estradiol, conjugated oestrogens, estradiol + cyproterone acetate, and oestrogen + progesterone. 1 participant on no HR. FM: Progestin, lynestrenol, IM testosterone, and oral testosterone undecanoate. 1 participant on no HR.	Reversible Castration (1 year); pre SRS HR (at least 1 year)	MF: 3·8; FM: 6·2; Both groups: 4·8 years	Single cohort, pre and post	Self report	Structure interview, questionnaire	0
Hepp, 2005[33]	31/NA/NA	20 MF + 11 FM; 7/31 had SRS, attendants of outpatient psychiatric programme for transgender identity disorder in Switzerland	33	10/31 were on hormones, type not specified	2·7 years (2 months–12 years)	NA	Cross-sectional	NR	Structured clinical interview applying standardized diagnostic criteria	NR

Table 1. *Continued*

Author, year	Total no./ intervention/ control	Participants	Age (year)	Hormonal therapy	Mean duration of hormone treatment	Length of follow up†	Study design	Exposure ascertainments	Outcome ascertainment	Loss to follow up†
Smith, 2005[19]	325/ 188/NA	Individuals who completed hormone and SRS at an Amsterdam clinic; MF 117; FM 71	MF 38·6; FM 29·6; All 35·2	NR	Average duration of hormones prior to SRS (all): 20·4 months (range 12–73 months)	NA	Single cohort, pre and post	Self report	Semi-structured interview, questionnaire	58%
De Cuypere, 2006[2]	62/62; 87 Dutch females and 58 Ducth males were controls for gender dysphoria; 86 Norwegian transsexuals were controls for QoL	35 MF and 27 FM, Dutch speaking transsexuals, >1 year post-SRS	MF 41·4 FM 33·3	Individuals were on dual-phase hormonal schedule (Reversible first then irreversible), types not reported	NR	MF: mean 4·1; FM: Mean:7·6	Cross-sectional	Chart review	Clinical examination by physicians and psychologists was obtained in most individuals, only 6 filled a questionnaire	28%
Lawrence, 2006[37]	232/NA/ NA	232 MF	44	Most were on hormones and stopped before SRS, details NR	NR	3 years post-SRS	Cross-sectional	Self report	Mailed survey	57%
Miles, 2006[16]	64/NA /NA	MF desiring SRS from UK: First group (HR+) was tested before are after starting HR (27); Second group (HR) stopped HR as a prerequisite before SRS tested on and then off HR (27); Control group for repeated testing (20), on HR > 3 months	45	Ethinylestradiol, Ethinylestradiol/ Androcur, Premarin, Premarin/ cyproterone acetate, Premarin/Provera	HR+ 3–12 months after starting HR; HR−: 8 weeks after stopping; Control: 3–12 months after starting HR	2–12 months	Cohort study, pre and post	Self report	Questionnaire	0
Newfield, 2006[14]	446, 248, 117	FM, only data from 384 US participants was analysed, data compared between FM who received hormones *vs.* FM who did not and *vs.* national norms	32·6	Testosterone replacement, details not reported	NR	NA	Cross-sectional, with a control group of FM that did not receive testosterone	Internet survey	Internet survey	NR

Table 1. *Continued*

Author, year	Total no./ intervention/ control	Participants	Age (year)	Hormonal therapy	Mean duration of hormone treatment	Length of follow up†	Study design	Exposure ascertainments	Outcome ascertainment	Loss to follow up†
Revol, 2006[21]	63/NA /NA	MF post-SRS	33 (22–56)	All received HR; Initial phase of cyproterone acetate followed by life-long oestrogen therapy	Not reported	NA	Cross-sectional	Chart review; HR prescribed by same team	Questionnaire; physical examination	65%
Zimmermann, 2006[23]	40/NA /NA	24 MF and 16 FM s/p SRS > 6 months were contactable out of a cohort of 90; group has relatively high level of education and a socio-economic status	38 (23–51)	All had HR; type end dose not reported	Not reported	3·1 years (0·5–19 years)	Cross-sectional	Chart review (Prescribed by the same team)	Questionnaire	56%
Kuhn, 2007[30]	25/NA /NA	18 MF and 7 FM from Switzerland, median 12 years after SRS.	MF 48; FM 38	17/18 MF were on estradiol; 3 were on Finasteride and 3 were on cyproterone acetate; All FM on Testosterone (6 parenteral, 1 oral)	NR	Median: 13 years for MF, 12 years for FM; For all individuals: 16 years	Cross-sectional	Self report	Clinical exam and interview; study focus was mainly on genitourinary aspects of QoL	NR

MF: male-to-female transsexuals; FM: female-to-male transsexuals.
†In cross-sectional studies, we meant by length of follow the time between sex reassignment and study; and by loss to follow-up, the number of patients who were contactable out of initial study cohort.

Table 2. Outcomes of interest

Author, year	Resolution of gender dysphoria	Quality of life	Sexual function	Psychiatric comorbidity
Hoenig, 1971[35]	General social adjustment: stable in only 2/9	Employed: 5/8; On National Assistance: 3/8 no; Family attitude: supportive or sympathetic 6/6	7/8 were sexually active	
Wyler, 1979[36]		MF: reported improved communication (4/8), stable relationships (5/8) and better professional integration (7/8); FM: 2/2 had stable relationships with women	4/8 MF reported inadequate vagina for intercourse	MF: 7/8 reported feeling psychologically better after transition; 1 became depressed (he had attempted suicide before SRS); FM: 2/2 reported improvement
Leavitt, 1980[15]				MF treated with oestrogens displayed less psychopathology as demonstrated on MMPI inventory
Kröhn, 1981**[24]	Physical appearance: self-reported (examiner reported); MF at least satisfactory in 16/18 (13/18); FM at least satisfactory in 6/6 (6/6)	Socioeconomic situation: MF at least satisfactory in 14/18 (15/18); FM at least satisfactory in 5/6 (5/6)	MF at least satisfactory in 18/18 (14/18). FM at least satisfactory in 6/6 (6/6); 5/6 FM live in monogamy with heterosexual women and reported orgasm by clitoral stimulation. MF: 14 were sexually active, 6 had stable partner relationships, 1 remained married but had relations with men. Half reported good lubrication of their neovagina during sexual excitation. Histological examination showed metaplasia of original penis skin. Authors think this functional adaptation was due to oestrogen effect and sexual activity	Psychological state: MF at least satisfactory in 17/18 (16/18); FM at least satisfactory in 6/6 MF: occasional depressive mood in 7 (less frequent than before surgery), decrease of suicidal thoughts in 3 individuals, transient suicidal thoughts in only three subjects, no suicide attempts. Values of personality tests moved on the single personality scales at least to the limit of expected statistical range
Sorensen, 1981[29]	More than half of the participants were unhappy with appearance (14/23 hair growth on face, 5/23 baldness) and 11/23 desired additional cosmetic surgery	14/23 unemployed. No change in social status class using the Institute of Social Research classification. Economic conditions: the majority considered their economic situation satisfactory.	9/23 were sexually active within 6 months postoperatively, 8/23 after 6 months, 6/23 had no sexual life postoperatively; 13/23 were sexually satisfied	3/29 attempted suicide, 4 of the noncore group found their psychic condition aggravated. ($P < 0{\cdot}05$) and 19 found it improved or unchanged. 1 admitted to a psychiatric institution. five reported taking anxiolytics in larger doses now than preoperatively and 4/23 had greater use of alcohol
Kuiper, 1988[4]	136 (97·1%) reported no or hardly any doubts about their own gender identity. Satisfaction with own behavior as a man or a woman: 106 (75%) satisfied or very satisfied; Ability to pass as a member of the new gender: FM 33 (95%); MF 84 (80%) describe integration as good or very good; Confidence in ability to maintain new gender role: 118 (83·6%) have confidence	92 (65·2%) happy/very happy; 33 (23·4%) moderately happy and 16 (11·3%) unhappy. Feeling happy correlated with improved psychosocial functioning. No individuals ascribed feelings of dysphoria to intrapsychic problems attending to new gender role		After treatment, 1 FM and 15 MF attempted suicide

Table 2. *Continued*

Author, year	Resolution of gender dysphoria	Quality of life	Sexual function	Psychiatric comorbidity
Pfäfflin, 1990*[27]		76·6% of FM and 47·4% of MF had a stable job. Results of examiners assessment, mean (SD). Social situation: MF (N = 42): Pre-SRS 1·71 (0·92); Post- SRS 3·31 (0·68); Change 1·60 (0·68); FM (N = 43): Pre-SRS 1·91 (0·78); Post- SRS 3·14 (0·98); Change 1·65 (1·09); Professional (employment) situation: MF (N = 40): Pre-SRS 1·90 (1·01); Post- SRS 3·03 (1·19); Change 1·13 (1·34); FM (N = 43): Pre-SRS 2·18 (0·9); Post- SRS 3·35 (0·97); Change 1·26 (1·05)	23 MF and 31 FM had a stable partner at time of follow-up; 5 MF and 4 FM had no sexual relations	33 MF and 35 FM consider their global psychological condition to be good or very good. Psychological situation as evaluated by examiners: MF (N = 42): Pre-SRS 1·26 (0·63); Post-SRS 3·55 (0·67); Change 2·29 (0·83); FM (N = 43): Pre-SRS 1·47 (0·63); Post-SRS 3·51 (0·77); Change 2·07 (0·92)
Kaube, 1991[28]	7/10 MF gave up mammary augmentation because of satisfactory oestrogen-induced mammary augmentation	15/30 reported partnership situation improved; 14/30 reported situation unchanged; 1 (MF) had no partner; 27/30 declared they coped well with life after SRS. 3 declared there was no difference; 26/30 satisfied with results of HR and 21/30 satisfied with global results of SRS	25/30 considered sexuality to be important in their life. 24 of them declared their sexual life to be more satisfactory than before. 1 (who had had penectomy) was unsatisfied	Suicide attempts before SRS: 3 MF (1 attempt per individuals); 8 FM (mean 4 times per individuals). Suicide attempts after SRS: 2 FM (1 for each individuals) and none of the MF. All individuals s denied alcohol and drug abuse and hospitalization for Psychiatric reasons
Yuksel, 1991[18]		Professional and employment situation improved from 11/21 reporting good situation to 16/21; relationships with family markedly improved and they became more accepting and supportive; participants were adherent to treatment and became role models for newer applicants		Suicidal rates improved (no quantification of outcome)
Tsoi, 1993[22]	Satisfaction with sex status MF(37/45); FM (29/36)	Satisfaction with work and finance was MF (43/45) and FM (34/36)	Satisfaction with sexual activity was MF (29/45) and FM (22/36). More MF(41/45) were satisfied with new sex organs compared with FM (14/36)	
Olsson, 1996[25]	0/5 expressed direct regret	Social relationships were to a great extent unchanged after SRS; 3/5 had a tendency to decreased socializing post and felt not totally accepted; 3/5 continued to be successful in their occupations; 3/5 expressed their displeasure with HR and associated it with 1) being a reminder of condition, 2) feeling unwell, 3) poor sexuality	Post-SRS, all were sexually active; 2/5 reported reduced sexual activity	

Table 2. *Continued*

Author, year	Resolution of gender dysphoria	Quality of life	Sexual function	Psychiatric comorbidity
Cohen-Kettenis, 1997[20]	None of the subjects indicated regrets UGDS scores: MF: pre mean = 48·4 (SD = 7·5); post mean 15·8 (4·3); $P < 0·001$. FM: pre 52·9 (5·4); post 14·5 (2·9); $P < 0·001$	89% felt accepted and supported socially	71% expressed satisfaction with sex life; 14% neutral view	Short version of Dutch MMPI: scores were similar to Dutch normative data with statistically significant improvement in extroversion suggesting a tendency to be more active towards social contacts. There were significant increase in dominance and self-esteem and decrease in inadequacy
Rauchfleisch, 1998[26]	Most individuals reported they were doing well. 3 MF regretted SRS and 2 had a reversal procedure after follow-up interview. One of them is schizophrenic.	Social conditions and quality of life of the 13 MF had significantly deteriorated; 9 of them depend on life annuity or on social welfare assistance. They were socially very isolated. Results in FM were slightly better; 2 of them are fully professionally active and lived in constant personal relationships of several years of duration	8 MF not being able to experience sexual pleasure. Only 3 MF describe their libido adequate	10 MF suffered from anxiety, depression or addictions. 1 MF developed schizophrenia post-SRS; 2 FM suffered from depression and addiction and likely had affective lability Authors report discrepancy between satisfaction with SRS and depression
Rehman, 1999[31]		27 of 28 reported life becoming easier and more comfortable	14/28 reported satisfaction with sexual function	2/28 reported suicidal feelings shortly after surgery. The others, including those who expressed suicidal feelings prior to SRS, reported feeling more psychologically stable
Schroder, 1999[34]			16/17 MF reported being engaged in partnered sexual activities. 9/17 reported sexual satisfaction and the mean rating was 5·4 (scale from 0–10, higher is better)	
Slabbekoorn, 2001[17]			Sexual Interest: MF mean score (SD) 4·1(2·8) pre-HR and 4·7 (2·9) HR. 4·9 (2·9) and 6·2(2·8), respectively	AIM and SAQ tools: MF experienced significantly more positive emotions ($P < 0·05$), whereas FM experienced significantly more aggressive ($P < 0·01$) and sexual feelings ($P < 0·05$) than they actually expected as a result of HR. There were no changes over time, but a group difference was found for negative emotions. Overall, MF expected and experienced more feelings of being tired and flat, tense and nervous, gloomy and depressed, having changeable moods than FM

Table 2. *Continued*

Author, year	Resolution of gender dysphoria	Quality of life	Sexual function	Psychiatric comorbidity
Smith, 2001[13]	UGS scale; mean (SD); Treatment: Pretest 51·7 (6·3); posttest 14·8 (3·2); Controls: 46·7 (13·9); 31·1 (14·9); *P* 0·002	The Affect Balance Scale (only the negative components of the scale used); Treatment (mean = 4·4, SD = 3·2); Control: (mean = 6·2, SD = 2·6); (*P* = NS)	7/10 were sexually satisfied; 11/16 achieved orgasm regularly	Dutch versions of short MMPI and the SCL-90. The control group had more psychological dysfunctional profile than treated group. Neither group showed significant differences between pretest and posttest.
Hepp, 2002***[33]	Subscales of the FbeK: mean (SD) in MF/FM/ total/norm values. FBeK-insecurity/ unpleasant sensations 3·4(2·3)/4·4(3·8)/3·7(2·9) /5·3(4·1); FBeK-attractiveness/ self-confidence: 10·2(2·0) /9·3(2·0)/10·0(2·0)/8·9(2·9); FBeK-body-accentuation/ sensitivity: 11·4(3·1)/8·0(1·2)/ 10·2(3)/11·1(3·8). No norms available for the FSI, scores go from 1 (best social integration) to 5 (worst social integration); FSI: 1·9(0·5)/ 1·6(0·4)/1·8(0·5)	No. of individuals who lived in stable relationship increased from 8 (at first referral) to 17 at follow-up. Improvement most noticed in FM group. FM patients kept their job more often than MF and occasionally got promotion/ advancement. MF more often changed job or were demoted. Authors think it is partially due to female hormones which could induce affective lability. FLZ-Global satisfaction with life: 56(34·8)/78·9(25·3)/ 64·3(33)/60·5(37·3); FLZ-Satisfaction with health: 72·9(45·4)/91·6(20·1)/ 79·7(38·6)/74·4(41·5)		HADS-Anxiety: 4·7(4·8)/ 5(3·7)/4·8(4·3)/5·8(3·2); HADS-Depression: 3(3)/2(1·9)/2·6 (2·7)/3·4(2·6)
De Cuypere, 2005[3]		Transsexuals had more stable relationships after SRS + HR (52·7%) compared to before (35·5%); *P* = 0·025; FM had more difficulty in starting a new relationship after transition.	After SRS + HR, 80% all participants expressed their satisfaction with their relational and sexual life; 5/55 (9%) reported not having any sexual activity (3 MF and 2 FM). For those who had sexual activity, 30 (60%) were very satisfied with their sex life, 18% remained neutral, and 22% were dissatisfied.	25% of MF were treated for depression
Hepp, 2005[33]				HADS scale: No Axis I diagnosis current 19 (12MFT, 7FMT), lifetime 9 (4MF, 5FM); Mood disorders: current 4 (4MF, 0FM), lifetime 14 (11MF, 3FM); Schizophrenia and other psychotic disorders: current 0, Lifetime 2 (2FM), substance related disorders: current 3 (3MF), lifetime 14 (10MF, 4FM); Anxiety disorders: current: 8 (4MF, 4FM), lifetime 7 (3MF, 4FM); Somatoform disorders: current 3 (3MF), eating disorders: lifetime 1 (1 FM)

Table 2. *Continued*

Author, year	Resolution of gender dysphoria	Quality of life	Sexual function	Psychiatric comorbidity
Smith, 2005[19]	Low posttest scores represent a virtual absence of gender dysphoria after SRS. UGS [mean (SD)]. Pretest 54·3 (7·1); Posttest 14·8 (3); ($P < 0·001$). Lindgren and Pauly's Body Dissatisfaction Scale: 98 (91·6%) were satisfied with their appearance. Primary sex characteristics: Pretest 18·1 (2·7); Posttest 6·6 (3·2); P < 0·001). Secondary Sex Characteristics: Pretest 34·8 (6·9); Posttest 25·2 (13·7); ($P < 0·001$). Neutral Body Character: Pretest 46·8 (9·6); Posttest 36·5 (8·0); ($P < 0·001$)	Social Life and Social Contacts: -The majority ($n = 90$, 89·1%) felt accepted by most people; 8 (7·9%) by some and 3 (3%) by no one. Altogether, 84 individuals (83·2%) felt supported their new gender role by almost everyone they new. 11 (10·9%) felt supported by some people. Despite the fact that 6 individuals (5·9%) did not feel supported, they were able to rely on some individuals during difficult times. 4 (3·9%) had no one to turn to when times got hard. Still, the vast majority (99, 96·1%) could rely on at least some others during difficult times. In total, 18 (17·3%) sometimes felt they were being laughed at, 2 (1·9%) had experienced being ridiculed by strangers; 84 (80·8%) had never experienced any such adverse reactions. Over 98% ($n = 102$) felt they were completely taken seriously by most people. Two (1·9%) only felt taken seriously by a few close friends. No one reported not being taken seriously by anyone. MF and FM felt equally accepted. However, FM had more support in the new gender role ($P = 0·01$) and were more able to rely on significant others during difficult times ($P = 0·03$). Although MF were more often laughed at or ridiculed ($P < 0·001$), they reported feeling taken equally seriously by (almost) all people ($P = 0·08$). Homosexuals felt more supported (Z = 2·0, $P = 0·04$) and taken more seriously than nonhomosexuals ($P = 0·01$)	The majority (46/50, 88·5%) of those with steady sexual partners were satisfied with their sex life. Three expressed a neutral view and 2 were dissatisfied. the 84 individuals (82·4% of the follow-up sample) who were sexually active, the majority (53, 63·1%), achieved orgasm always or regularly, 16 (19%) sometimes and 15 (17·9%) never. More of the sexually active FM (81·6%) than of the MF (42·1%) achieved orgasm always or regularly ($P = 0·01$). Both sexes reported equal satisfaction with their sex life ($P = 0·5$)	In general, follow-up scores indicated fewer psychological problems. Scores on Negativism and Shyness had improved. Scores on Somatization, Psychopathology, and Extroversion showed a tendency towards improvement P = <0·006). Psychological Functioning (Dutch Short MMPI). *Scores*: Negativism, Pretest 22·6 (7); Posttest 17·1 (7·8); ($P < 0·001$); Shyness: Pretest 14·7 (9·3); Posttest 10·0 (7·3); ($P < 0·001$); Depression: Pretest 29·3 (11·3); Posttest 22·5 (8·4); ($P < 0·001$); Inadequacy: Pretest 15·8 (5·8); Posttest 13·5 (4·5); P < 0·001); Psychoneuroticism: Pretest 143·0 (40·7); Posttest 120·3 (31·4); ($P < 0·001$)
De Cuypere, 2006[2]	UGS scale, mean (SD): 35 MF: 16·6 (6·3); 27 FM: 13·7 (3·9). No significant difference could be shown for the gender dysphoria left after SRS between the MF and a Dutch female control group without gender dysphoria (mean = 15·7; $N = 87$) ($P = 0·415$). Neither did the FM and a Dutch male control group without gender dysphoria (mean = 14·2; $n = 58$, $P = 0·510$)	GAF-scale: MF: 76·2 (14·3); FM: 85·2 (9·9). No significant difference between this population and a comparable group of 86 Norwegian transsexuals (mean = 78·0; $P = 0·265$). The younger the applicants were at the time of their first consultation, the better their daily function was		SCL-90. Scores of MF and FM were similar and comparable to the general population. Self-reported suicide-attempt rate improved from 29·3% before treatment to 5·1% after treatment; $P = 0·004$; general population's rate is 0·15%

Table 2. *Continued*

Author, year	Resolution of gender dysphoria	Quality of life	Sexual function	Psychiatric comorbidity
Lawrence, 2006[37]	No participant reported consistent regrets about SRS, 6% reported occasional regrets. Mean overall happiness with SRS results is 8·7 (0–10 scale); SD 1·7	Participants' mean reported improvement in QoL 7·9 (0–10 scale); SD 2·6	Mean overall happiness with sexual function is 7·8 (0–10 scale); SD 2·4	
Miles, 2006[16]		No change in cognition or memory		POMS tool used. Overall, mood did not differ except for the Composed and Confident scales
Newfield, 2006[14]		FM had diminished mental-health related QoL compared with the general US population. These findings are consistent when compared against specific age and sex norms. Using F-36v2, Testosterone group scored significantly better in domains of vitality, social functioning, role emotional and mental health. Mental summary score 41·22 (11·9) compared to 36·08 (12·6); $P = 0{\cdot}001$. Physical Summary Score 53·29 (9·6) compared to 53·67 (9·2); $P = 0{\cdot}347$		
Revol, 2006[21]	Global satisfaction: $n = 22$, mean = 7·6/10, range: 0–10	Quality of life: $n = 22$, mean = 8,4/10, range (0–10)	Sexual function (existence of intercourse, frequency, quality): (0–10 scale): $n = 19$, mean = 7/10 range (0–10). Genitalia appearance: $n = 22$, mean = 8/10 (4–10); clitoral sensitivity: $n = 21$, mean = 8·4/10(3–10); Vaginal function: $n = 21$, mean = 7·2/10(0–10)	
Zimmermann, 2006****[23]	35 (87·5%) very satisfied or satisfied with their body (no difference between two sexes); 16 FM and 22 MF very satisfied or satisfied with their new gender identity	Quality of life in operated transsexuals was significantly lower ($P < 0{\cdot}001$) than a representative sample of normal population; 26 think their social acceptance is improved, two worsened, 12 unchanged; total values of health items on the FLZ^M questionnaire were not different from normal population	22 (55%) were very satisfied or satisfied with sexual life in their new sex. More satisfaction in FM	

Table 2. *Continued*

Author, year	Resolution of gender dysphoria	Quality of life	Sexual function	Psychiatric comorbidity
Kuhn, 2007[30]		Participants' contentness on visual analogue score (very happy): MF 10/18; FM: 7/7		

SRS, sex reassignment surgery; HR, hormonal treatments; MF, male-to-female transsexual, QoL, quality of life; NR, not reported; NA, not applicable.
UGS/UGDS, The Utrecht Gender Scale: 12-item scale, the individuals rated his/her agreement on a 5-point scale. The higher the score, the more gender dysphoria is present.
MMPI, Minnesota Multiphasic Personality Inventory, 83 items measuring Negativism, Somatization, Shyness, Psychopathology and Extroversion. Higher scores indicate more dysfunction on the first four scales but less on Extroversion.
GAF-scale, The global Assessment of Functioning Scale (DSM-IV): a scale that assesses 10 different aspects of functioning and evaluates the general functioning in daily life. Higher score correlates with better functioning.
SCL-90, The Symptom Checklist is a 90-item inventory inquiring about the presence of various psychological and physical complaints the week prior to the interview, scored on a 5-point scale.
SF-36v2, Short-Form 36-Question Health Survey version 2.
HADS scale, Hospital Anxiety and Depression scale.
POMS, Profile of Mood states.
Expectancy list of mood and sexual interest: 15-item list rated on a 10-point scale, 1 = no change, 10 = very much)
AIM, Affect Intensity Measure; SAQ, Short Anger Situation Questionnaire.
*Questionnaires used are German translation of questionnaires developed at the Minneapolis University Clinic for SRS. Self-assessment questionnaire contains 80 questions with 5-point answers referring to medical treatment, professional situation, family, friends, partnership, sexual experiences, gender role and psychological condition. In the questionnaire used for examiner assessment, scores go from 1 to 4 (higher is better) in each one of three areas: social, professional and psychological states. Assessment concerned 12 preceding months.
**Psychological tests used are: (1) FPI (Freiburger Persönlichkeit Inventar = Freiburger Personality Inventory) and (2) Giessen-Test. Results in numbers refer to number of individuals in every score according to self-evaluation/medical evaluation.
***Hepp, 2002: Scales used are the German version of the Hospital Anxiety and Depression scale (HADS), *Fragebogen zur Lebenszufriedenheit (FLZ)* questionnaire for satisfaction with life; *Fragebogen zur Beurteilung des eigenen Körpers (FBeK)* questionnaire to assess own body; *Fragebogen zur sozialen Integration (FSI)* questionnaire for social integration.
****Zimmerman, 2006: Questionnaire '*Fragen zur Lebenszufriedenheit Modul*' FLZ^{M} = Questions on life satisfaction module.

In most of the included studies, at least two thirds of individuals with GID reported improvement in some aspects of their quality of life such as more stable relationships, better adjustment, satisfaction with sex reassignment, and overall happiness and contentness.[3,4,18–23,30,31] In a study by Rehman *et al.*, 27/28 MF individuals reported life becoming easier and more comfortable posttransition.[31] In another study by Smith *et al.*,[13] quality of life measured by the Affect Balance Scale (only the negative components of the scale used) was better in treated MF and FM compared with those untreated; but the difference did not achieve statistical significance. The treated individuals in this study had better resolution of dysphoria and improved psychosocial and psychological functioning. Van Kemenade *et al.* found that treatment with an antiandrogen for 8 weeks increased feelings of relaxation and energy in MF transsexuals.[32]

Financial, professional status and employment situation were satisfactory postsex reassignment and when compared with before transition, they were perceived as improved.[18,24,25,27,29]

In terms of hormonal therapies effects, Kaube *et al.* reported that 26/30 individuals were satisfied with hormonal therapy compared to 21/30 satisfied with SRS.[28] Another study showed that MF treated with oestrogen had no significant change in cognition or memory when they were taking hormones compared with when they were not.[16] In addition, although FM scores on the Short Form 36-Question health Survey (SF-36v2) were lower than population norm, those who received testosterone replacement had significantly higher quality-of-life scores than those who did not.[14]

Nevertheless, 4/24 studies reported worsening of the quality of life; mainly in MF.[2,25,26,33] Rauchfleisch *et al.* reported all their 13 MF subjects to continue to be in social isolation, have poor quality of life and be dependent on welfare and national assistance; and Olsson *et al.* showed continued poor socializing and lack of improvement in social relationships after transition therapy in 3/5 MF, who also expressed their displeasure with hormonal therapy because it reminded them of their condition and of feeling unwell. MF scored significantly lower than FM on the Global Assessment of Functioning (GAF) Scale[2] and demonstrated worse socialization and career, employment and financial success.[33]

Individuals whose transsexual symptoms manifested at a younger age reportedly had better adjustment to the new gender role;[2,22] and when reassignment procedures were administered before adulthood, favourable postoperative psychological and social functioning were noted.[20] Authors describe a trend for worse overall health in MF individuals which could be due to their older age and higher prevalence of smoking.[3]

Satisfaction with sexual function

Pooling across studies shows that after sex reassignment, 72% of individuals with GID reported significant improvement in sexual

function (95% CI = 60–81%; 15 studies; I^2 = 78%). This proportion in MF subgroup is 63% (45–79%) and in FM subgroup is 80% (68–89%).

The researchers of included studies assessed sexual satisfaction, sexual health and sexual function by using semi-structured interviews, clinical encounters, or designed their own questionnaires to evaluate satisfaction with intercourse, sex life and orgasm. In most studies, more than half of MF or FM reported higher satisfaction of sexual function in terms of existence, frequency or quality.[3,13,19–24,28,29,34] On the contrary, only in one study, Rauchfleisch *et al.* reported poor sexual satisfaction and outcomes.[26]

Discussion

Our findings

We systematically reviewed the literature to determine the benefits of hormonal therapies given to individuals with GID as a part of sex reassignment. We found 28 studies with fairly long follow-up duration that demonstrated improvements in gender dysphoria, psychological functioning and comorbidities, lower suicide rates, higher sexual satisfaction and, overall, improvement in the quality of life. Individuals with early onset transsexual manifestations and those with homosexual tendencies may have better prognosis. Individuals with pre-existing psychopathology tend to have worse prognosis. Limited data suggest that MF transsexuals may have worse outcomes than FM counterparts.

Limitations and strengths

The evidence in this review is of very low quality[9,10] due to the serious methodological limitations of included studies. Studies lacked bias protection measures such as randomization and control groups, and generally depended on self-report to ascertain the exposure (i.e. hormonal therapy was self-reported as opposed to being extracted from medical records). Our reliance on reported outcome measures may also indicate a higher risk of reporting bias within the studies. Statistical heterogeneity of the results was also significant. Furthermore, since hormonal therapies were administered as a part of sex reassignment, inferences regarding hormones solely are very weak and are confounded by the effects of sex reassignment surgery and psychotherapy, which were provided implicitly or explicitly in most studies. Benefits noted in individuals undergoing this transition can certainly be attributable to these two co-administered interventions. We excluded studies that did not mention hormonal therapies to remedy this indirectness of evidence; this exclusion poses another limitation to our review because it may have diminished the total body of literature. Lastly, the heterogeneity of methods, in which the outcome of satisfaction with sexual function was assessed, may further limit inferences about this outcome. This limitation does not apply to other outcomes such as gender dysphoria, which was assessed across studies with standardized scales.

It is also important to recognize the impact of cultural factors and treatment availability on the outcomes of reassignment therapies. Cultures that reject gender atypicality would subject transsexuals to more victimization and social stigma, which may worsen pre- and posttreatment social and psychological functioning levels. Individuals in countries without access to treatment may also have worse outcomes. Therefore, cultural differences should be considered when applying the results of this review, mostly derived from European studies, to other populations.

The strengths of this review stem from the rigorous methodology that included comprehensive search that is not limited by language restrictions, the use of explicit inclusion and exclusion criteria of research evidence, as well as extracting data and making judgements in duplicate in order to reduce random error and bias. To our knowledge, this is the first systematic review to summarize and synthesize evidence about quality of life and related self-reported outcomes in individuals with GID receiving hormonal treatments.

Implications for practice and future research

The potential benefits of hormonal treatment to individuals with GID demonstrated in this review should be balanced against possible adverse events such as thromboembolism and cardiovascular effects of hormones. Considering the very low quality of evidence regarding the balance between the benefits and risks of treatment, the role of patients' values and preferences as well as the availability/affordability of treatments become paramount. Clinicians should convey the existing uncertainty to individuals seeking treatment and elicit their choices as a major factor in the process of decision making. Individuals with disabling and severe gender dysphoria and psychologic impairment may opt for treatment; conversely, individuals who are older or have higher risk for complications due to hormonal therapy may opt against treatment. In addition, an issue of particular importance in this context is obtaining the proper diagnosis. Individuals with uncertain diagnosis display more dysfunctional psychological profile than those in whom diagnosis is confirmed and receive treatment.[13]

Further research is needed to ascertain benefits and harms of hormonal treatments in this context. The design for future studies will likely continue to be observational considering the psychological impact of GID, the strong convictions of study participants that would introduce bias, and the nonreversible aspects of some of the treatments used (although randomized trials are feasible when it comes to comparing alternative hormone regimens for instance). The validation and consistent use of standardized scales would facilitate inference and comparisons between subgroups that may include patients with pre-existing psychiatric illness or different level of social support. Cross-cultural studies are also needed to assess the impact of cultural stigma and victimization on treatment outcomes, which may lead to more individualized treatments.

Conclusion

Very low quality evidence suggests that hormonal therapies given to individuals with GID as a part of sex reassignment are likely to

improve gender dysphoria, psychological functioning and comorbidities, sexual function and overall quality of life. MF transsexuals may have worse outcomes than FM individuals.

Competing interests/financial disclosure

The authors (MHM, MBE, MZG, RJM, AM, PJE, VMM) have nothing to disclose.

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