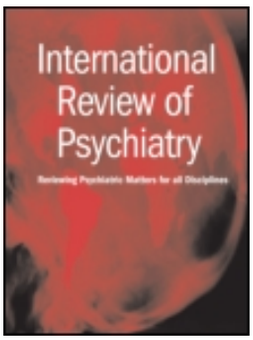

International Review of Psychiatry

ISSN: 0954-0261 (Print) 1369-1627 (Online) Journal homepage: http://www.tandfonline.com/loi/iirp20

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To cite this article: Cecilia Dhejne, Roy Van Vlerken, Gunter Heylens & Jon Arcelus (2016) Mental health and gender dysphoria: A review of the literature, International Review of Psychiatry, 28:1, 44-57, DOI: 10.3109/09540261.2015.1115753

To link to this article: http://dx.doi.org/10.3109/09540261.2015.1115753

Published online: 02 Feb 2016.

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INTERNATIONAL REVIEW OF PSYCHIATRY, 2016
VOL. 28, NO. 1, 44–57
http://dx.doi.org/10.3109/09540261.2015.1115753

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REVIEW ARTICLE

Mental health and gender dysphoria: A review of the literature

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ABSTRACT

Studies investigating the prevalence of psychiatric disorders among trans individuals have identified elevated rates of psychopathology. Research has also provided conflicting psychiatric outcomes following gender-confirming medical interventions. This review identifies 38 cross-sectional and longitudinal studies describing prevalence rates of psychiatric disorders and psychiatric outcomes, pre- and post-gender-confirming medical interventions, for people with gender dysphoria. It indicates that, although the levels of psychopathology and psychiatric disorders in trans people attending services at the time of assessment are higher than in the cis population, they do improve following gender-confirming medical intervention, in many cases reaching normative values. The main Axis I psychiatric disorders were found to be depression and anxiety disorder. Other major psychiatric disorders, such as schizophrenia and bipolar disorder, were rare and were no more prevalent than in the general population. There was conflicting evidence regarding gender differences: some studies found higher psychopathology in trans women, while others found no differences between gender groups. Although many studies were methodologically weak, and included people at different stages of transition within the same cohort of patients, overall this review indicates that trans people attending transgender health-care services appear to have a higher risk of psychiatric morbidity (that improves following treatment), and thus confirms the vulnerability of this population.

ARTICLE HISTORY
Received 2 July 2015
Revised 30 October 2015
Accepted 30 October 2015
Published online 28 January 2016

KEYWORDS
Gender dysphoria; transsexualism; mental health; psychiatric disorders; depression; anxiety

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Introduction

The Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People, version 7 (SOC-7) by the World Professional Association for Transgender Health (WPATH), provides clinical guidance in 'how to assist transsexual, transgender, and gender nonconforming people with safe and effective pathways to achieving lasting personal comfort with their gendered selves, in order to maximize their overall health, psychological well-being, and self-fulfilment. This assistance may include primary care, gynaecological and urological care, reproductive options, voice and communication therapy, mental health services (e.g. assessment, counselling, psychotherapy), and hormonal and surgical treatments' (Coleman et al., 2012). SOC-7 argues that the mental health professional should work within a multi-disciplinary team or in close contact with other gender specialists. The main roles of mental health professionals within gender care have been described as:

1. To facilitate the diagnosis of gender dysphoria
2. To assess for psychiatric co-morbidity
3. To explore the readiness for gender-confirming medical intervention (Coleman et al., 2012).
4. To support the trans person through the health pathway (Lev, 2009).

Although some professionals in the field have described the involvement of a mental health professional in the care of trans people as a responsible form of care (Selvaggi & Giordano, 2014), it could be argued that this is the direct result of transsexualism or gender dysphoria being considered a psychiatric diagnosis. The placement of the diagnoses (either gender dysphoria or transsexualism) within the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) (American Psychiatric Association, 2013), and within the Mental and Behavioural Disorders chapter of the *International Classification of Diseases and Health Related Problems* (World Health Organization, 1992), has been subject to continuing debate. The first appearance of these diagnoses in the aforementioned publications (using different

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terms) may be related to the social and medical attitudes at the time when Harry Benjamin started to describe and treat trans people (Drescher et al., 2012). Whether incongruence with one's gender is a natural variation or a pathology, and how this view may influence discrimination, stigma and access to medical treatment, is well discussed in a paper by Meyer-Bahlburg (2010).

The WHO's proposal for the next edition of the ICD (ICD-11) is to replace the current diagnostic term 'transsexualism' with 'gender incongruence', and to move this diagnosis from chapter 5 to a new chapter entitled 'Conditions related to sexual health' (Drescher et al., 2012). This will support the view of many that a diagnosis describing trans people should not be part of a psychiatric category (Richards et al., 2015). This could help to remove some of the stigma which trans people currently encounter. However, by doing so, it also raises questions concerning the future role, if any, of mental health professionals in transgender care.

One of the roles may be connected to the high prevalence of psychiatric morbidity among trans people described in the literature (Gomez-Gil et al., 2009; Hepp et al., 2005; Heylens et al., 2014a; Mazaheri Meybodi et al., 2014a), which may require assessment and management by a mental health professional. The literature in this area is confusing, as different prevalence rates of psychiatric co-morbidity have been described.

With this in mind, this paper has two aims:

1. To review the available literature that looks at the prevalence of psychiatric disorders and psychopathology among trans people
2. To review the available literature describing the psychiatric outcome following gender-confirming medical interventions (GCMI), either cross-sex hormone treatment (CHT) and/or gender-confirming genital surgery (GCGS)

As the terminology in this field has changed over the years, the term 'trans people' will be used in this review to refer to individuals with gender dysphoria attending transgender health-care services and, in most cases, seeking gender-confirming medical interventions.

Methodology

Eligibility criteria

Studies were selected only if participants were diagnosed by health professionals, and/or had been accepted for gender-confirming interventions, and had empirical data relating to the prevalence of psychiatric morbidity or psychopathology pre- or post-treatment. Articles dealing exclusively with self-harm (non-suicidal self-injury), suicidality, autism, eating disorders or individuals under 18 years old were not included, as they are part of other reviews within this special edition. Only studies in English and with more than 10 participants were selected.

Information sources and search

An electronic literature search was conducted between January 2000 and April 2015 using PubMed. Articles in the *International Journal of Transgenderism* (not in PubMed) were also included, in order to identify more studies. Additionally, reference sections of identified articles were also examined for further relevant publications. The search used the following words in the title and/or abstract.

1. For terms referring to trans people: *transsexualism, transsexual, transgender, gender dysphoria, gender identity disorder, trans**
2. For psychiatric disorders and psychopathology: *mental health, psychopathology, psychiatric, depression, anxiety*

Every term used for trans people was combined using the 'or' and the 'and' operator with every term used for psychiatric disorders and psychopathology.

Study selection

A total of 647 studies were identified. By the screening of titles and abstracts, 47 studies fulfilled the eligibility criteria and were selected for more in-depth analysis. Out of these 47 studies, nine were excluded because they did not provide data regarding psychiatric disorders or psychopathology, but focused primarily on quality of life or sexual health, thus a total of 38 studies were selected for this review. Data extraction was performed using a standardized table with the following categories: title, authors, date of publication, participants, age at assessment, study design, diagnostic criteria used, control group, measurements related to psychiatric disorder and/or psychopathology, prevalence rates of psychiatric disorders, and conclusions of the study. For those papers investigating outcome, information regarding follow-up was also included, as well as the outcome on psychopathology and/or psychiatric disorders. The data is summarized in two tables: Table 1 shows cross-sectional studies describing prevalence rates of psychiatric disorders and/or psychopathology in trans people (27 studies). This table includes trans people at different stages of treatment. Table 2 shows longitudinal studies describing psychiatric outcome of post gender-confirming medical interventions (11 studies).

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Table 1. Cross-sectional studies investigating psychiatric disorders and psychopathology in trans people.

Authors (year) Country	Number of trans participants/ diagnosis/ mean age at assessment	Treatment status: (on CHT or post-GCGS)	Study design	Comparative groups	Outcome measure	Prevalence in trans	Conclusion
Haraldsen & Dahl (2000) Norway	35 FtM 51 MtF DSM-III-R DSM-IV 34.0 years FtM 33.3 years MtF	CHT NR GCGS Mixed pre- and post-surgery	Single centre (Gender clinic) Cross-sectional	CC 1068 Personality disorder (PD) 101	SCID-I SCID-II GAF SCL-90R	Axis 1 disorders (mostly depression and anxiety) 32.5% Axis 2 disorders 19.8% SCL-90R as per CC	Groups: Trans lower scores in SCL-90R than PD Gender: MtF lower SCL-90R compared to FtM
Miach et al. (2000) Australia	82 MtF: 48 GID 34 GIDAANT DSM-III-R 33.5 years	CHT NR GCGS 0%	Single centre (Gender clinic) Cross-sectional	GID vs GIDAANT	MMPI-2	Psycho-pathology: Low in 85% of GID High in 47% of GIDAANT	GID differs significantly in degree of psycho-pathology from GIDAANT
Kersting et al. (2003) Germany	12 FtM 29 MtF DSM-IV 34.7 years	CHT NR GCGS 17%	Single centre (Gender clinic) Cross-sectional	Psychiatric inpatients 115 Normative data	DES SCID-D	Dissociative symptoms: Trans similar to psychiatric inpatients	DES and SCID-D limited validity in trans people
Hepp et al. (2005) Switzerland	11 FtM 20 MtF DSM-IV 33.2 years	CHT 32% GCGS 23%	Single centre (Gender clinic) Cross-sectional	No	SCID-I, -II HADS	Axis I disorder current (mostly anxiety) 38.7% Axis I disorder, lifetime (mostly mood disorder and substance abuse) 71% Axis II disorder 41.9%	Gender, age, treatment status: No differences
Kim et al. (2006) Korea	43 MtF DSM-IV 20.4 years	CHT 88% GCGS 26%	Single centre (Identified as part of the military service examination with gender dysphoria) Cross-sectional	Cis men 47 Matched for age and education	BDI SADS SES	BDI (mean) 21.4 SADS (mean) 13.6 SES (mean) 16.5	Trans significantly higher scores on depression and social anxiety, and lower scores on self-esteem than controls
Gomez-Gil et al. (2008)[a] Spain	56 FtM 107 MtF DSM-IV 27.3 years FtM 29.9 years MtF	CHT NR GCGS 0%	Single centre (Gender clinic) Cross-sectional	Normative data	MMPI-2	MMPI: Within normal range	Gender: MtF not on CHT scored higher than on CHT FtM no difference regarding CHT status Limitation: Pre-/post groups not the same
Gomez-Gil et al. (2009)[a] Spain	159 MtF 71 FtM DSM-IV-TR ICD-10 27.3 years FtM 29.7 years MtF	CHT 49% GCGS 0%	Single centre (Gender clinic) Cross-sectional	No	MINI	Psychiatric disorders Life time: Mood and adjustment disorders 56% (MtF) and 70.4% (FtM) Non-alcohol substance abuse/ dependence 30.2% (MtF) Generalized anxiety disorder 8.8% (MtF) and 5.6% (FtM) Current: Social phobia 8.2% (MtF) and 11.3% (FtM)	Adjustment disorders and substance abuse more frequent in MtF vs FtM

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Table 1. Continued

Authors (year) Country	Number of trans participants/ diagnosis/ mean age at assessment	Treatment status: (on CHT or post-GCGS)	Study design	Comparative groups	Outcome measure	Prevalence in trans	Conclusion
Madeddu et al. (2009) Italy	34 MtF 16 FtM DSM-IV-TR 31.7 years	CHT 36% GCGS 0%	Single centre (Gender clinic) Cross-sectional	No	SCID-II	Axis II disorders 52% Most frequent PD Narcissistic	No Axis II differences between genders
Weyers et al. (2009) Belgium	50 MtF ICD-10 43.06 years	CHT 100% GCGS 100%	Single centre (Gender clinic) Cross-sectional	Normative data	SF-36	Mental health problems: No difference to normative data	Less Psychopathology if in a relationship
Hoshiai et al. (2010) Japan	349 FtM 230 MtF DSM-IV 26.5 years FtM 32.0 years MtF	CHT 32% GCGS 12%	Single centre (Gender clinic) Cross-sectional	No	Clinical interview and clinical records	Axis I disorder 13.6% Adjustment disorder 6.7% Anxiety disorder 3.6% Mood disorder 1.4%	MtF more Axis I disorders compared to FtM
Bandini et al. (2011)[b] Italy	109 MtF DSM-IV-TR 36.0 years	CHT 70.6% GCGS 25.7%	Single centre (Gender clinics) Cross-sectional	Trans with and without childhood maltreatment (CM)	Psychiatric interview SCL-90R	Psychiatric disorder (life time): 66.7% (CM) 37.2% (non-CM) SCL-90R: no difference between groups	CM group higher body dissatisfaction and worse life time mental health
Dhejne et al. (2011) Sweden	191 MtF 133 FtM ICD-8,-9,-10 33.3 years FtM 36.3 years MtF	CHT NR GCGS 100%	Multi centre (National register) Cross-sectional	CC 3240 matched for age, natal and new assigned gender	Death (including suicide) Psychiatric morbidity and abuse	When compared to 1973-2003 controls: Mortality 2.8 HRadj Any psychiatry diagnoses: 2.8 HRadj Suicide attempts: 4.9 HRadj When compared 1989-2003 to controls: Mortality the same. Any psychiatry diagnoses: 2.8 HRadj Suicide attempts: the same	Gender: no difference, natal or assigned gender Female or male control group: No difference
Simon et al. (2011) Hungary	30 MtF 17 FtM DSM-IV 28.0 years FtM 26.0 years MtF	CHT NR GCGS 0%	Single centre (Gender clinic) Cross-sectional	CC= 157	SCL-90R	Psychopathology: SCL-90R: No differences compared to controls	MtF elevated levels of interpersonal sensitivity
Gomez-Gil et al. (2012)[a] Spain	74 FtM 113 MtF ICD-10 DSM-IV-TR 29.7 years	CHT 35.8% GCGS 42.2%	Single centre (Gender clinic) Cross-sectional	Trans with and without treatment Normative data	SADS HAD-A HAD-D	Social anxiety, depression and anxiety: SADS, HADS scores normal range except for HAD-A Differences CHT or not: CHT group lower scores	Gender: No difference CHT: CHT group better when compared to not treated Limitation: Pre-/post groups were not the same
Gorin-Lazard et al. (2012)[c] France	30 FtM 31 MtF DSM-IV-TR 29.9 years FtM 39.4 years MtF	CHT 72.1% GCGS NR	Multi centre (Gender clinic) Cross-sectional	No	BDI	Depression: 25% significant scores in the BDI	Gender: no difference
Auer et al. (2013) Germany	32 FtM 57 MtF ICD-10	CHT 100% GCGS 65%	Single centre (Endocrinology clinic) Cross-sectional	CC 336 age and sex (natal and phenotype) matched	SCL-90R	Psychopathology: SCL-90R worse scores on all scales compared controls	Gender: Depressive symptoms higher in MtF FtM have profile as cis men MtF more similar to cis women

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Table 1. Continued

Authors (year) Country	Number of trans participants/ diagnosis/ mean age at assessment	Treatment status: (on CHT or post-GCGS)	Study design	Comparative groups	Outcome measure	Prevalence in trans	Conclusion
	32.3 years FtM 47.9 years MtF						
Fisher et al. (2013)[b] Italy	92 MtF 48 FtM DSM-IV-TR 32.6 years	CHT 69.8% GCGS 22.1%	Single centre (Gender clinic) Cross-sectional	No	SCID-I-II SCL-90R	Axis I disorders 18.7% Mood and adjustment disorder 10.8% Anxiety disorder 5% Axis II disorders 4.3%	Gender: no difference
Gorin-Lazard et al. (2013)[c] France	31FtM 36 MtF DSM-IV-TR 35.1 years	CHT 73.1% GCGS NR	Multi-centre (Gender clinics) Cross-sectional	Trans with and without CHT	BDI SSEI	Depression and self-esteem: Trans on CHT less depressive symptoms, better self esteem	NA Limitation: Pre-/post groups were not the same
Davey et al. (2014) UK	63 MtF 40 FtM ICD-10 45.7 years	CHT 78.6% GCGS 16.5%	Single centre (Gender clinic) Cross-sectional	CC 103 Controlled by age	SCL-90R	Psychopathology: SCL-90R scores higher in trans	Social support did not significantly predict psychopathology
Duisin et al. (2014) Serbia	21 MtF 9 FtM DSM-IV-TR 30.4 years	CHT NR GCGS 0%	Single centre (Gender clinic) Cross-sectional	CC 30	SCID-II	Axis-II diagnosis 66.6% (most frequent paranoid and avoidant)	Difference: GID group more Axis-II disorders compared to CC group Gender: MtF more psychopathology compared to FtM
Fisher et al. (2014)[b] Italy	59 FtM 66 MtF DSM-IV-TR 28.7 years FtM 33.1 years MtF	CHT 0% GCGS NR	Multi-centre (Gender clinics) Cross-sectional	Trans with and without CHT	SCL-90R BUT GSI	Psychopathology: No difference between both on SCL-90R BUT GSI: MtF with CHT group had less body uneasiness than not treated group	Body uneasiness effectively diminished with CHT Limitation: Pre-/post groups were not the same
Judge et al. (2014) Ireland	159 MtF 59 FtM DSM-IV-TR 32.6 years	CHT 20.2% GCGS 1.6%	Single centre (Gender clinic) Cross-sectional	No	Psychiatric assessment by mental health professional	Depression (lifetime) 34.4% Schizophrenia 3.67% Bipolar disorder 2.29%	High prevalence of psychiatric conditions Limitation: No controls
Heylens et al. (2014a) Belgium Germany Netherlands Norway	182 MtF 123 FtM DSM-IV-TR 22.8-31.2 years FtM 21.6-36.5 years MtF (Depends on country)	CHT 0% GCGS 0%	Multicentre 4 countries Cross-sectional	No	MINI SCID-II	Axis I diagnosis (current) 38% Affective problems 27% Anxiety problems 17% Axis I (current and lifetime) 70% Affective problems 60% Anxiety problems 28% Axis II diagnosis 15%	Gender, age of onset: No differences
Mazaheri Meybodi et al. (2014a) Iran	47 MtF 36 FtM DSM-IV-TR Age: NR	CHT 92.9% GCGS 0%	Single centre (Gender clinic) Cross-sectional	No	SCID-I	Axis-I diagnosis 62.7% Major depressive disorder (33.7%) Specific phobia (20.5%) Adjustment disorder (15.7%)	High prevalence of Axis I diagnosis Limitation: No controls
Mazaheri Meybodi et al. (2014b) Iran	39 MtF 31 FtM DSM-IV-TR Age: NR	CHT 92.9% GCGS 0%	Single centre (Gender clinic) Cross-sectional	No	MCMI-II	Axis II diagnosis 81.4% (57.1% narcissistic)	High prevalence of Axis II diagnosis Limitation: No controls
Claes et al. (2015) UK	103 MtF 52 FtM	CHT 0% GCGS 0%		No	SCL-90R RSE	Psychopathology: MtF reported significantly higher scores	

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Table 1. Continued

Authors (year) Country	Number of trans participants/ diagnosis/ mean age at assessment	Treatment status: (on CHT or post-GCGS)	Study design	Comparative groups	Outcome measure	Prevalence in trans	Conclusion
	ICD-10 34.5 years		Single centre (Gender clinic) Cross-sectional			on paranoid ideation, interpersonal distrust, anxiety, depression and obsessive-compulsive complaints compared with FtM	Gender: MtF significantly lower level of self-esteem compared to FtM
Colizzi et al. (2015) Italy	85 MtF 33 FtM DSM-IV-TR 30.2 years	CHT 0% GCGS 0%	Single centre (Gender clinic) Cross-sectional	No	DDIS DES	Dissociative disorders 29.6%	Gender: No differences

BDI, Beck depression inventory; BUT-GSI, Body Uneasiness Test Global Severity Index (the total score of BUT); CC, Cis controls; CHT, = cross-sex hormonal treatment; DES, Dissociative Experience Scale; DDIS, Dissociative Disorders Interview Schedule; FtM, female-to-male subjects, trans men; GAF, Global Assessment of Functioning Scale; GCGS, gender confirmation genital surgery; GD, Gender dysphoria; GID, gender identity disorder; GIDAANT, gender identity disorder of adolescence and adulthood, non-transsexual type; GSI, Global Severity Index; HADS, Hospital Anxiety and Depression Scale; HAD-A, HAD-Anxiety subscale to HADS; HAD-D, HAD-Depression sub scale to HADS; HRadj, adjusted hazard ratio; MINI, Mini International Neuropsychiatric Interview; MMPI-2, Minnesota Multiphasic Personality Inventory, second version; MCMI-II, Millon Clinical Multiaxial Inventory, second version; MtF, male to female subjects, trans women; NR, not reported; RSE, Rosenberg Self-Esteem scale; SADS, Social Avoidance and Distress Scale; SCID-I and II, Structured Clinical Interview for DSM-IV, Axis I and II disorders; SCID-D, Structured Clinical Interview for DSM-IV-Dissociative Disorders; SCL-90R, Symptom Checklist-90 (revised); SES, Self-Esteem Scale; SF-36, Short Form 36-item Questionnaire; SSEI, Social Self-Esteem Inventory.

[a,b,c]Studies using the same data.

Description of studies

Cross-sectional studies

The 27 studies were all conducted in different transgender health-care services or gender identity clinic services, using data collected as part of the assessment (whether prospectively or retrospectively). The diagnosis was made according to DSM criteria (ranging from DSM-III-R to DSM-5) (American Psychiatric Association, 1987, 1994, 2000, 2013) and, in six studies, according to the ICD-10 (World Health Organization, 1992). Only three studies described psychiatric co-morbidity and/or psychopathology in patients exclusively without any form of treatment for gender dysphoria (Claes et al., 2015; Colizzi et al., 2015; Heylens et al., 2014a). The remainder of the studies included people at different stages of treatment, or the treatment status was unknown or not reported. Only five studies were multi-centred and, with the exception of one (Kim et al., 2006), participants were all recruited through transgender health-care services.

The studies concluded that the prevalence of psychiatric co-morbidity and psychopathology was high. However, only seven studies used a control group, and only four of them matched the cis controls with the trans population studied for factors known to affect psychopathology (such as age). Most studies used normative data to reach a conclusion as to whether the prevalence found was high or not. The most commonly used measurement to assess for psychiatric disorders was the Structured Clinical Interview for DSM (SCID) (First et al., 2002), and for psychopathology, the Symptom Checklist -90 (SCL-90) (Derogatis et al., 2010). For more details, please see Table 1.

Longitudinal studies

The 11 longitudinal studies evaluate changes in psychiatric disorders and/or psychopathology following gender-confirming medical interventions. Three studies assess the patients following cross-sex hormones, six following gender-confirming genital surgery, and two studies following both treatments. Six of the studies also provide cross-sectional data pretreatment compared with normative values. The information regarding follow-up time was recorded in all of the studies and ranged from six months (Udeze et al., 2008) to 13.3 years (Ruppin & Pfäfflin, 2015). Lost to follow-up ranged from 0% (Colizzi et al., 2013, 2014) to 49.3% (Ruppin & Pfäfflin, 2015). For more information about these studies, see Table 2.

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Table 2. Follow up studies investigating outcome of psychiatric disorders and psychopathology post gender treatment in trans people.

Authors (year) Country	Number of trans participants/ diagnosis/ mean age at assessment	Treatment status: (on CHT or post GCGS)	Study design	Comparative groups	Length of follow-up post-treatment	Lost to follow-up	Outcome measure	Results
Slabbekoorn et al. (2001) Netherlands	47 FtM 54 MtF DSM-III-R 25.7 years FtM 32.9 years MtF	CHT 100% GCGS 0%	Single centre (Gender Clinic) Prospective	Pre- vs post-CHT	14 weeks post-CHT	0	AIM SAQ	Differences pre-/post-treatment: MtF: positive emotions increased after CHT FtM less intensity for both negative and positive emotions after CHT
Smith et al. (2001) Netherlands	13 FtM 7 MtF DSM-III-R 16.6 years	CHT 100% GCGS 100%	Single centre (Gender clinic) Prospective	Pre- vs post-GCGS Control: 21 patients who have been denied/ declined GCGS	1–4 years post-GCGS 1–7 years controls	17%	Dutch Short MMPI SCL-90	Differences pre-/post-treatment: Treated group no longer gender dysphoric, psychologically and socially functioning well. Neither group showed significant differences between pre- and post-GCGS on SCL-90
Smith et al. (2005) Netherlands	71 FtM 117MtF DSM-IV 29.6y FtM 38.6y MtF	CHT 100% GCGS 100%	Single centre (Gender clinic) Prospective	Pre- vs post-GCGS Normative	1–4 years post-GCGS	16%	UGDS Dutch Short MMPI SCL-90	Cross-sectional pretreatment: As normative data Differences pre-/post-treatment: Fewer psychological problems post-treatment. Gender dysphoria absence post-treatment Predictors: FtM psychological better outcome than MtF Heterosexual as per natal sex worse outcome
De Cuypere et al. (2006) Belgium	27 FtM 35 MtF Diagnosis: NR 26.9 years FtM 37.8 years MtF (pre-GCGS)	CHT 100% GCGS 100%	Single centre (Gender clinic) Retrospective	Pre- vs post-GCGS Normative	4.1 years MtF 7.6 years FtM	42%	UGDS SCL-90	Cross-sectional pretreatment: SCL-90 as normative data Differences pre-/post-treatment: Fewer psychological problems post-treatment. Gender dysphoria absence post-treatment. Suicide attempt drop from 29.3% to 5.1% Predictors: Younger when applying for GCGS and attractive better outcome.
Udeze et al. (2008) UK	40 MtF DSM-IV 47.3 years	CHT NR GCGS 100%	Single centre (Gender clinic) Prospective	Pre- vs post-GCGS	0.5 years post-GCGS	NR	SCL-90R Psychiatric clinical interview for ICD-10	Cross-sectional pre-treatment: no psychiatric diagnosis Differences pre-/post-treatment: No differences in SCL-90R scores Limitation: scores of SCL-90 low already at pretreatment
	14 FtM 18 MtF	CHT 88% GCGS 100%	Multicentre (2 gender clinics)	Pre- vs post-GCGS	9 years post-GCGS	30%	Psychiatric symptoms	Cross-sectional pretreatment: 30–50% insomnia, depression or

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Table 2. Continued

Authors (year) Country	Number of trans participants/ diagnosis/ mean age at assessment	Treatment status: (on CHT or post GCGS)	Study design	Comparative groups	Length of follow-up post-treatment	Lost to follow-up	Outcome measure	Results
Johansson et al. (2010) Sweden	ICD-10 27.8 years FtM 37.3 years MtF		Prospective				Global outcome patient and clinician	anxiety. 7.1% received ongoing psychiatric treatment. Differences pre-/post-treatment: Global clinician outcome: Improved 62% Unchanged 24%. Global patient outcome: Improved 95% Worse 5%. Gender: no differences Age of onset: no differences
Pimenoff & Pfäfflin (2011) Finland	17 FtM 15 MtF Diagnosis NR 37.5 years FtM 44.4 years MtF	CHT 100% GCGS 100%	Single centre (Gender clinic) Retrospective	Pre- vs post-GCGS	5 years post-GCGS	16.2%	University of Minnesota Questionnaire	Differences pre-/post-treatment: Psychological and social functioning improved significantly Gender: No differences except for vocational functioning which was better for FtM
Colizzi et al. (2013)* Italy	25 FtM 45 MtF DSM-IV-TR 26.7 years FtM 29.2 years MtF	CHT 100% GCGS 0%	Single centre (Gender clinic) Prospective	Pre- vs post-CHT	1 year post-CHT	0	PSS	Differences pre-/post-treatment: Perceived stress lower post-treatment and as per normative data
Colizzi et al. (2014)* Italy	29 FtM 78 MtF DSM-IV-TR 26.7 years FtM 29.2 years MtF	CHT 100% GCGS NR	Single centre (Gender clinic) Prospective	Pre- vs post-CHT Normative	1 year post-CHT	0	SCID-1 SAS SDS SCL-90R	Cross-sectional pre-treatment: SAS above normal range SDS and SCL-90R in normal range except anxiety subscale Differences pre-post treatment: SAS, SDS, SCL-90R scores lower post CHT
Heylens et al. (2014b) Belgium	11FtM 46 MtF DSM-IV-TR NR	CHT 100% GCGS 81%	Single centre (Gender clinic) Prospective	Pre- vs post-CHT (47) vs post-GCGS (42) Normative	3–6 months post-CHT 1–12 months post-GCGS	7.5–26.3%	SCL-90 Psychosocial questionnaire	Cross-sectional pretreatment: SCL-90 worse than normative data Differences pre-/post-treatment: Post treatment SCL-90 as normative data 95% better mood 93% happier 81% less anxious 79% more self confidence 98% better body relation Less drugs and alcohol abuse
Ruppin & Pfäfflin (2015) Germany	36 MtF 35 MtF ICD-10 14.1 years FtM 13.7 years MtF	CHT 100% GCGS 97.1%	Single centre (Gender clinic) Retrospective	Pre- vs post-treatment	13.3 years	49.3%	SCL-90R IIP FPI-R	Differences pre-/post-treatment: SCL-90R significantly better on all subscales post treatment particularly interpersonal sensitivity IIP significant lower values at follow-up

AIM, affect intensity measure; CHT, cross-sex hormonal treatment; FPI-R, Freiburg Personality Inventory; FtM, female to male subjects, trans men; GCGS, gender confirmation genital surgery; IIP, Inventory of Interpersonal Problems; MMPI-2, Minnesota Multiphasic Personality Inventory, second version; MtF, male to female subjects, trans women; NA, not applicable; NR, not reported; PSS, Perceived stress scale; SCID-I, Structured Clinical Interview for DSM-IV, Axis I disorders; SAS, Zung Self-Rating Anxiety Scale; SAQ, Short Anger Situation Questionnaire; SCL-90, Symptom Checklist-90; SCL-90R, Symptom Checklist-90 revised; SDS, Zung Self-Rating Depression Scale; UGDS, Utrecht Gender Dysphoria Scale.
*Studies using the same data.

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Results

Cross-sectional studies

Psychopathology

Studies investigating prevalence rates of psychopathology range from rates that are comparable to the general population (Colizzi et al., 2014; Simon et al., 2011; Smith et al., 2005) to the trans group having worse scores than the cis controls (Auer et al., 2013; Davey et al., 2014; Heylens et al., 2014b). The prevalence and nature of psychopathology in trans women was found to be more comparable to cis women than to cis men, the former showing a two- to threefold higher occurrence of affective problems when compared with cis men (Auer et al., 2013).

Psychiatric disorders, Axis I

The Axis I diagnoses found in all the studies reviewed were mainly affective and anxiety disorders. The occurrence of severe psychiatric conditions, such as schizophrenia or bipolar disorder, was rare. Only one study looking at Axis I disorders compares a trans group with a cis control group matched for age, natal sex and new assigned sex (Dhejne et al., 2011). This study, which uses data from the national register in Sweden, focuses on trans people following gender-confirming medical interventions and found higher rates of psychiatric disorders and suicide in this group. It found, however, that there was an improvement over time, i.e. rates of psychiatric disorders and suicide became more similar to controls over time; for the period 1989–2003, there was no difference in the number of suicide attempts compared to controls.

Psychiatric disorders, Axis II

Only one study (Duisin et al., 2014) used a (non-matched) control group when assessing Axis II psychiatric disorders. This found higher rates of personality disorders in the trans group, primarily paranoid and avoidant personality disorders. The study is limited by the small number of patients studied. The rest of the studies that assessed Axis II disorders did not use control groups. The prevalence rates of Axis II disorders ranged from 4.3% (Fisher et al., 2013) to 81.4% (Mazaheri Meybodi et al., 2014b). The type of personality disorder varied from predominantly cluster B (Hepp et al., 2005; Madeddu et al., 2009; Mazaheri Meybodi et al., 2014b) to predominantly cluster C (Heylens et al., 2014a).

Risk factors for psychopathology and psychiatric disorders

The majority of the studies comparing trans women and trans men found no differences in psychiatric disorders and psychopathology between the two groups. Four studies did find psychiatric disorders and psychopathology to be more prevalent among trans women than trans men (Claes et al., 2015; Duisin et al., 2014; Gomez-Gil et al., 2009; Hoshiai et al., 2010). Conversely, Haraldsen & Dahl (2000) found that trans women scored lower on the SCL-90R test than trans men.

One study (Heylens et al., 2014a) found no differences between the age of onset and psychiatric disorders.

As found in the general psychiatric literature, two studies investigating psychopathology among trans people also found that being in a relationship was a positive factor, associated with a reduction of psychopathology (Gorin-Lazard et al., 2012; Weyers et al., 2009).

Longitudinal studies

An improvement of psychiatric morbidity and psychopathology following GCMI was seen in all of the studies except one (Udeze et al., 2008). This study found no differences between pre- and post-SCL-90R scores, which is probably due to the low levels of psychopathology as measured by the SCL-90R pretreatment. The majority of the studies found post-treatment scores on questionnaires measuring psychopathology and gender dysphoria to be similar to normative data.

Predictors for positive outcome following GCMI

Four longitudinal studies explored post-treatment outcome predictors and found better outcomes for trans men (Smith et al., 2005) and those who were young on assessment (De Cuypere et al., 2006). Two studies did not find gender or age of onset to be predictors of outcome following GCGS (Johansson et al., 2010; Pimenoff & Pfäfflin, 2011). Interestingly, one study compared patients who had been compliant with their treatment plan with those who had not, and found no differences in outcome (Pimenoff & Pfäfflin, 2011).

Discussion

The aim of this review was to explore the literature in the field of mental health/psychiatry and gender dysphoria. Overall, it was found that trans people attending transgender health-care services present with a high prevalence of psychiatric disorders and psychopathology.

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The review indicates that the level of psychopathology appears to be higher in this population than in cis controls, although it cannot reach firm conclusions as to whether the rate of psychiatric disorders is higher in trans people than in controls, due to the lack of well-matched controlled studies exploring psychiatric disorders.

The only study using a robust methodology concludes that trans people present with higher levels of psychiatric disorders post-GCMI than cis controls. However, this study looks at trans people who were treated in some cases more than 20 years ago, when society and interventions may have been very different. Studies investigating the outcome of trans people who transitioned a long time ago will be very different from those looking at individuals who transitioned in the 21st century, and although this study offers longer follow-up data, these will be affected by changes in the levels of transphobia and discrimination over time. Furthermore, surgical results were less good at that time, which is also known to affect transgender health negatively (Bauer et al., 2015; Lawrence & Zucker, 2012).

The studies reviewed in this paper include trans people at different stages of transition within the same cohort, which is confusing, and does not allow for clear conclusions to be drawn as to the levels of psychopathology and psychiatric disorders in non-treated trans people. Only one study (Heylens et al., 2014a) provides clear information regarding the rates of psychiatric disorders pretreatment. It found that, at the time of assessment and before treatment was commenced, 38% of those attending transgender health-care services presented with an Axis I diagnosis, and 15% with an Axis II diagnosis.

As all of the studies use data collected at the time of assessment at a transgender health-care service, the results regarding levels of psychopathology and psychiatric disorders cannot be generalized to trans people not in contact with clinical services. In order to clarify whether there is a difference between these groups it may be interesting to look at studies exploring lifetime psychiatric disorders. Four studies provide this information (Bandini et al., 2011; Gomez-Gil et al., 2009; Hepp et al., 2005; Heylens et al., 2014a). Of particular importance is the study by Heylens et al. (2014a), which showed clear differences between current (38%) and lifetime (70%) levels of psychiatric disorders. This shows that the rate and severity of psychiatric disorders and psychopathology may be underrepresented if data is taken only from trans people at the time they are being assessed at transgender health services; the rate may be considerably higher in those who are not on a pathway towards treatment.

The majority of the psychiatric problems detailed in the studies relate to affective disorders such as depression and anxiety. Major psychiatric problems (e.g. schizophrenia and bipolar disorder) were not found any more frequently in trans people than in the general population. Dissociative disorders were only evaluated in one study (Colizzi et al., 2015).

The results with respect to gender differences in both pre- and post-treatment cross-sectional studies were contradictory. The majority of the studies showed no differences between the genders, but, except for one study (Haraldsen & Dahl, 2000) those studies that did identify differences found that trans women were more prone to develop psychological/psychiatric problems than trans men (Colton-Meier et al., 2013; De Cuypere et al., 1995; Landén et al., 1998; Lothstein, 1984). This finding could indicate that trans women show a psychological and vulnerability profile for the development of affective disorders that resembles that of natal women (Auer et al., 2013). Biologically, this could be explained by recent findings using neuro-imaging that reveal that non-treated trans women have cerebral cortical thickness similar to cis women (Zubiaurre-Elorza et al., 2012). However, the increased levels of psychiatric disorders in trans women could also be explained by the higher risk of stigma and discrimination within this group; this may contribute to the interpersonal problems that one study found made trans women more hypersensitive to rejection (Davey et al., 2015; Simon et al., 2011).

The fact that some studies that included trans people who had been treated with GCMI found higher levels of psychopathology and psychiatric disorders (Dhejne et al., 2011) than cis controls cannot be used as evidence for the efficacy (or otherwise) of GCMI. Studies that compared different cohorts of patients (pre CHT/GCGS versus post CHT/GCGS) are only helpful in this regard when they are well controlled for psychopathology and for known factors affecting psychopathology, between both groups (Gomez-Gil et al., 2012; Gorin-Lazard et al., 2013; Fisher et al., 2014).

The effect that gender-confirming medical interventions have in improving mental health can only be concluded from longitudinal studies. This review found that longitudinal studies investigating the same cohort of trans people pre- and post-interventions showed an overall improvement in psychopathology and psychiatric disorders post-treatment. In fact, the findings from most studies showed that the scores of trans people following GCMI were similar to those of the general population. Although this is likely to be a response to the gender-confirming treatment itself, i.e. the sense of

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the body being more aligned to the person's experienced gender, it cannot be ruled out that it relates instead or as well to the benefits that accrue from being validated and accepted for treatment (Nuttbrock et al., 2011). In order to help clarify this it is important to look at follow-up studies that assess trans people a relatively long time after treatment. Five studies (De Cuypere et al., 2006; Johansson et al., 2010; Pimenoff & Pfäfflin, 2011; Ruppin & Pfäfflin, 2015; Smith et al., 2001) that followed trans people for more than 2 years (maximum 13.3 years) post-treatment showed encouraging results that point towards the benefits of treating trans people with GCMI.

Although it was not the main aim of this review, we also explored risk factors for psychiatric disorders among the trans population. Victimization (social stigma, discrimination, transphobia, sexual abuse, gender abuse), difficulties accessing health care and social services, gender (as explained above) and interpersonal problems were all found to put trans people at risk of developing psychiatric disorders, particularly depression. Trans individuals were also found to receive, or perceived themselves to receive, less social support from their family and friends than non-trans siblings and matched general population (Davey et al., 2014; Factor & Rothblum, 2007; Gooren et al., 2015; Kim et al., 2006; Simon et al., 2011). Social and parental support, completed medical transition, and disclosure of transgender identity were all protective factors (Bandini et al., 2011; Bauer et al., 2015; Bazargan & Galvan, 2012; Bockting et al., 2013; Clements-Nolle et al., 2006; Davey et al., 2015; Gehring & Knudson, 2005; Gooren et al., 2015; Lombardi et al., 2001; Nuttbrock et al., 2011, 2014; Rotondi, 2011).

Quality of the studies

Almost all of the studies reviewed showed selection bias. Since most included only individuals attending transgender health-care services, the results are not generalizable to the overall trans population. Many studies are also limited by the inclusion of trans people at different stages of treatment. Longitudinal studies are also limited by lost-to-follow-up data and short follow-up time; only registry-based studies do not have lost-to-follow-up data, but their cross-sectional design fails to measure improvement of psychopathology within the same individual following GCMI. Furthermore, they are limited by the lack of matching according to known risk factors for psychiatric disorders and psychopathology within the general population (Dhejne et al., 2011).

Implications for future research

Although the studies measuring the prevalence of psychiatric disorders in trans people attending clinical services are robust and reach firm conclusions, future studies could explore the rates among those trans people not attending clinical services. Future studies could also benefit from more detailed and better controlled longitudinal studies. Due to the low prevalence of trans individuals attending clinical services (Arcelus et al., 2015), larger cohort multicentre studies such as the European Network Initiative of Gender Incongruence (ENIGI) project (Kreukels et al., 2012) may strengthen recruitment rates. Studies such as this may be limited by several factors including the variability of the interventions provided and the levels of discrimination and transphobia in different countries.

Although psychiatric morbidity should be studied as a secondary outcome of gender-confirming medical interventions, studies should primarily explore the role of those interventions in reducing gender dysphoria. A robust measure is needed to relate the primary outcome for GCMI to gender dysphoria. The variability of tools to measure gender and body dysphoria does not allow firm conclusions to be drawn, and this suggests the need for a stronger measurement tool.

In summary, this review indicates that, although the levels of psychopathology and psychiatric disorders of trans people attending transgender health-care services are higher than the cis population at the time of assessment, they do improve following gender-confirming medical intervention, in many cases reaching normative values. Information on trans people not in contact with services is lacking. While gender-confirming medical intervention improves mental health, trans people are still a vulnerable group.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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