# Epidemiologic Considerations on Transsexualism

5

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## 5.1 Introduction

To define what key literature and source of knowledge may offer epidemiologic considerations on a human condition such as gender dysphoria and transsexualism, it might be useful to recall that etiologic epidemiology is *the scientific observation of human beings for the purpose of discovering a cause of a disease* and that clinical epidemiology is *the study of determinants and effects of clinical decisions*. In the search for both causes and effects of human conditions, the first step must be a flawless and stable definition of the condition. Once such a definition has been accepted, variants are recognized – eventually determining mutually exclusive categories – then used for a relatively long time and in many geographic populations, then epidemiologic measures can be estimated including measures of frequency, measures of association, and measures of impact [1].

The first difficulty dealing with the epidemiologic evidence accrued related to the *incongruence between a subject's experienced gender* (*gender identity*) *and assigned gender* concentrates with the apparent conundrum of what area of medicine, if any, such a condition intercepts. The difficulty of choosing a definition has been considered in other chapters of this textbook, particularly the chapter by Cohen et al. entitled *Psychological Characteristics and Sexuality of Natal Males with Gender Dysphoria* [2].

The availability of a common, consensus-based definition is essential to classify conditions that may have a common etiologic web, similar signs and symptoms, diagnostic procedures, treatments, and type and burden of care. Lack of such a background for a sufficient time period and across populations, with the obvious conclusion of possible presence of ascertainment bias, does not allow easy comparison of disease frequency estimation, much less of other more sophisticated epidemiologic measures such as associations and impacts. Therefore, such measures, if calculated, must be used with caution and, if presented, are prone to controversy.

## 5.2 Methodological Issues

Table 5.1 describes variations of terms by historical periods, sources of terms, and categories within the defined condition.

As listed in Table 5.1, before 1975, neither the International Classification of Diseases (ICD) by the World Health Organization (WHO) nor the Diagnostic and Statistical Manual of Mental Disorders (DSM) by the American Psychiatric Association (APA) included any terms, names, and codes that referred to the *incongruence between a subject's experienced and assigned gender*. At that time the scientific literature, as

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**Table 5.1** Variations of terms by historical periods, sources of terms, and categories

| Term | Transsexualism, desire to change sex | Gender identity disorder, transsexualism | Gender identity disorder | Gender dysphoria | |
|---|---|---|---|---|---|
| Time period of use | <1975 | 1975–2013 | 1994–2013 | 2013– | |
| Realm in medicine | Psychiatric symptoms, within schizophrenia or borderline personality disorder diagnosis | A psychiatric condition separate from other psychiatric diseases | A psychiatric condition separate from other psychiatric diseases | A psychiatric condition separate from other psychiatric diseases with presence of clinically significant distress associated with the condition | Not a psychiatric condition?<br>Not a disorder at all?<br>Rather a gender variant? |
| Sources of term and classification | Case reports and case series (<1975) | ICD-9 (1975) [3]<br>DSM-III (1980) [4]<br>ICD-10 (1994) [5] | DSM-IV (1994) [6] | DSM-5 (2013) [7]<br>ICD-11 (2017?) | Cohen et al., this book [2]<br>Dreger in *Pacific Standard* [8] |
| Number of variants or level of severity within the condition | Many | 2 (yes vs no) | 2 (yes vs no) | Many | Many |

explored by bibliographic engines developed by the US National Library of Medicine (PubMed and derivatives), depended on the clinical work conducted in the 1950s that led to Harry P. Benjamin's description of the "transsexual phenomenon" in the USA [9]. At the time the literature had already coined terms such as "androgyne," "transvestism," "transgender," and "transsexual" and symptoms such as "desire to cross-dress" and "desire to change sex" had been identified and reported mostly in case reports and case series and scientific studies [10]. In the absence of a recognized classification of these conditions, nevertheless diagnostic psychological tests (i.e., the Bem Sex Role Inventory (BSRI) were developed (1971). The BSRI characterized personality as masculine, feminine, androgynous, or undifferentiated and was based on gender stereotypes, so what it was measuring was how well the person fit into a traditional sex role. At the same time, in terms of classification and etiology, transsexualism was considered mostly just as a symptom of another psychiatric disorder, especially schizophrenia or eventually a borderline personality disorder. As a consequence, there was neither interest nor a recognized definition and unique diagnosis and coding that allowed for the measurement of disease frequency. Therefore, before 1975 its epidemiology remained vague, and there could be numerous variants and levels of severity within the condition.

As far as clinical epidemiology, i.e., the study of determinants and effects of clinical decisions based on the transgender recognition or diagnosis by the subject and or by the medical community, medical journals reported male-to-female (MtF) and female-to-male (FtM) sex reassignment even before WWII but mostly as anecdotes. In 1965, the Hopkins Hospital became the first academic institution in the USA to perform sex reassignment surgeries. Before 1975 psychoanalytic literature held the belief that beneath the desire to change sex may lie a serious psychopathology – even of a psychotic nature – and that transsexual wishes may arise from oedipal conflict, preoedipal fixation, or schizophrenic processes [11]. Only in 1977 initially the Harry Benjamin International Gender Dysphoria Association (HBIGD), later (2007) renamed as the

World Professional Association for Transgender Health (WPATH), join to provide standard of care (SOC) for transgender persons, which currently has produced its 7th edition (SOC7) [12].

In 1975 the ICD-9 of the WHO introduced specific psychiatric terms, conditions, and codes separate from other psychiatric diseases for sexual and gender identity disorders, particularly:

302: Sexual and Gender Identity Disorders, among which are:
302.5: Trans-sexualism
302.6: Gender Identity Disorder in Children
302.85: Gender Identity Disorder in Adolescents or Adults

This classification created the opportunity for any gender identity disorder and for transsexualism in particular to calculate disease frequency, associations with subject's characteristics and measures of impact.

In 1980 the DSM-III of APA confirmed the ICD-9 classification while specifying that the transsexualism diagnosis required:

A. Sense of discomfort and inappropriateness about one's anatomic sex
B. Wish to get rid of one's own genitals and to live as a member of the other sex
C. The disturbance has been continuous (not limited to periods of stress) for at least 2 years
D. Absence of physical intersex or genetic abnormality
E. Not due to another mental disorder, such as schizophrenia

Codes changed in ICD-10:

F64: Gender Identity Disorders
F64.0 Transsexualism
F64.1 Dual-Role Transvestism
F64.2 Gender Identity Disorder of Childhood
F64.8 Other Gender Identity Disorders
F64.9 Gender identity disorder, unspecified)

However, definitions remained relatively stable. Instead DSM-IV accommodated all strong and persistent cross-gender identification accompanied by persistent discomfort with one's assigned sex previously listed separately as Gender Identity Disorder of Childhood, Gender Identity Disorder of Adolescence or Adulthood, and Transsexualism at both sexes and all ages in the unique DSM-IV code 532: Gender Identity Disorder.

As a result, between 1975 and 2013, the estimate of the overall frequency of "gender identity disorder" may have been consistent between classification systems (ICD vs DSM), whereas the frequency of transsexualism could only be measured based on ICD as DSM from 1994 to 2013 collapsed all subcategories within gender identity disorders. In addition, for all epidemiologic research conducted to date in this field, we should not underestimate the chance that exists for ascertainment bias (especially underreporting) for all the individuals who did not match the five DSM-IV diagnostic criteria for transsexualism but still could fit into the "gender identity disorder." It is likely that the estimate of the frequency of such a group depended on historical period, societal pressures, sex assigned at birth, country, and especially attitudes and proficiency on the subject by the local medical communities. Differences in these nonbiological determinants may have caused biased estimates of the frequency of these conditions.

Also the future of epidemiologic estimates will depend, as for the past, primarily on case definition and attitudes toward case ascertainment. The long-lasting tendency to move gender identity questioning initially away from psychiatry and then away from the concept of "medical abnormality," as advocated by some groups of subjects and professionals, may at the end determine the elimination of gender identity disorder, as it happened for definitions of homosexuality, which was no longer listed as a category of disorder in the seventh printing of the DSM-II, in 1974, and again from the DSM-III. In fact, in DSM-5 with the new term "gender dysphoria" and its definition as "A psychiatric condition separate from other psychiatric diseases with presence of clinically significant distress associated with the condition," the clinical existence of a mental disorder in this field is restricted to the "significant distress" that may accompany gender identity issues. From the epidemiologic standpoint and to measure the frequency of this condition, it is then likely that accordingly the number of subjects meeting this definition will be reduced further, from previous, broader definitions which did not require such a "significant distress." ICD-11

(expected to be released in 2017) and SOC7 of WPATH are consistent with this approach. In conclusion, the transsexual, transgender, and gender nonconforming people are likely to be considered more and more for their health needs rather than as carriers of a pathological condition. Consequently, in the future the epidemiologic measurement of the frequency of this health characteristic is likely to identify a human variation that has no specific abnormality meaning per se but is of clinical interest because it might be associated sometimes with pathological conditions or might require clinical intervention to satisfy a need of the subject.

## 5.3 Epidemiologic Associations Between Gender Dysphoria and Mental Health Disorders

Reports of these associations have been relatively common. Heylens et al. investigated psychiatric problems within the European Network for the Investigation of Gender Incongruence (ENIGI) [13]. The network had study bases in Amsterdam (Netherlands), Ghent (Belgium), Hamburg (Germany), and Oslo (Norway). Participants were 305 adults seeking gender reassignment therapy and surgery at the four gender clinics and fulfilling DSM-IV-TR criteria for a diagnosis of gender identity disorder. Data were collected between January 2007 and October 2010. The Utrecht Gender Dysphoria Scale (UGDS) was used to measure the degree of experienced gender dysphoria. The Mini International Neuropsychiatric Interview – Plus version 5.0.0 (MINI-Plus) was used to measure Axis I diagnoses at the time of the interview ("current diagnosis") and disorders that have a longer history ("current and lifetime diagnosis"). The Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II) was used to assess Axis II diagnoses; this is a semi-structured clinical interview. In 38 % of the individuals with gender identity disorder, a current DSM-IV-TR Axis I diagnosis was found, mainly affective disorders and anxiety disorders. Furthermore, almost 70 % had a current and lifetime diagnosis. All four countries showed a similar prevalence, except for affective and anxiety disorders, and no difference was found between individuals with early-onset and late-onset disorders. An Axis II diagnosis was found in 15 % of all individuals with gender identity disorder, which is comparable to the general population. In conclusion, people with gender identity disorder show more affective and anxiety problems than the general population [13].

Some authors found associations between GD and autism spectrum disorders. Therefore, they were cautious about irreversible treatments (sexual reassignment surgery) before autism spectrum disorders were excluded and a genuine issue of transsexualism was confirmed. In particular, John Parkinson [14] reported the incidence of Asperger's syndrome as above average in young people presenting with gender dysphoria. Patients with Asperger's syndrome, however, were prone to obsessive preoccupations and the apparent dysphoria may in some cases prove to be a transient obsession.

A recent epidemiologic survey reported that individuals with pervasive developmental disorders (PDD) often have identity crises, which sometimes include gender dysphoria [15]. It has been proposed that the rate of PDD may be almost 1 % and that many PDD cases might not be diagnosed properly in childhood. PDD are characterized by two essential symptoms: impairment in social interaction and restricted, repetitive, and stereotyped patterns of behavior, interests, and activities. PDD include autistic disorder, Asperger's disorder, and PDD-not otherwise specified (PDD-NOS). These three disorders are part of autism spectrum disorders. Among 204 children and adolescents who visited a GID clinic in the Netherlands, 7.8 % were diagnosed with autism spectrum disorders after a careful diagnostic procedure by a multidisciplinary team. Taken together, these authors considered PDD and GID still closely related to each other.

The Japanese Society of Psychiatry and Neurology published guidelines for the assessment and treatment of GID in 1997 and revised them in 2006. As a result, GID has become well known as a clinical entity in Japan, and there have been an increasing number of Japanese patients complaining of gender dysphoria. At the same time also their guidelines caution clinicians to

consider an underlying diagnosis of PDD when encountering patients with gender dysphoria [15].

An association between personality disorder and gender dysphoria has been reported [16], with prevalence of personality disorder varying between 20 and 70 % in different studies. Personality disorder is defined as an enduring pattern of thinking and feeling about oneself and others that significantly and adversely affect how an individual functions in the various aspects of life (DSM-5). Personality disorder prevalence among GD cases with anxious symptoms might be even higher.

Results of positive effects of treatment were found instead in a large review of the literature conducted by Murad et al. [17]. In terms of psychological health among subjects who were treated for reassignment surgery, the authors concluded on the basis of 28 studies, with 1,833 persons with gender dysphoria (1,093 natal males and 801 natal females) and an average follow-up of 6 years, that 78 % of persons had less psychiatric problems after treatment of their GD than before. For people with GD, gender reassignment thus seemed to have positive influence on their mental health.

## 5.4 Suicide and Non-psychiatric Associations

A Swedish cohort study of 324 persons with transsexualism was followed after sex reassignment (also termed gender confirmation intervention) [18]. The objective of this study was to shed new light on transsexual persons' health after sex reassignment. In particular, the study investigated all-cause mortality, suicide, cardiovascular diseases, and neoplasms. Morbidity included any psychiatric disorder (gender identity disorders excluded), alcohol/drug misuse and dependence, definite/uncertain suicide attempt, and injuries. Finally, court convictions for any criminal offense and any violent offense were investigated. Gender reassignment was as follows: male-to-female (MtF), $N = 191$, and female-to-male (FtM), $N = 133$. For each transsexual (exposed) person, ten non-transsexual (unexposed) comparison subjects were randomly selected. Considerably higher risks for total mortality and selected causes of death were measured. Specifically, compared to unexposed subjects, overall survival of transsexual persons started to diverge from that of matched comparators after about 10 years of follow-up. The increased adjusted hazard ratios (aHR) were 2.9 (95 % CI: 1.9–4.5) for all causes of death, 2.5 (1.2–5.3) for death from cardiovascular diseases, 2.1 (1.0–4.6) for cancer death, and 19.1 (5.8–68.9) for suicide. This mortality pattern is rather consistent among both male-born and female-born subjects. Any psychiatric hospitalization, substance abuse, suicide attempts, any injury, and any crime were also significantly higher among the exposed cohort members. However, in subgroup analyses, suicide attempts were more frequent among MtF (aHR: 10.4 (4.9–22.1)) versus comparators, whereas crime was frequent only within the FtM subgroup (aHR: 4.1 (2.5–6.9)).

Another major long-term epidemiologic follow-up study of mortality was conducted in the Netherlands among 966 male-to-female (MtF) and 365 female-to-male (FtM) transsexuals receiving treatment with cross-sex hormones [19]. An increased mortality in hormone-treated MtF transsexuals (122 observed, 81 expected, SMR = 1.51; 95 % CI: 1.47–1.55) was associated with both hormone- and non-hormone-related causes. Strong associations were found with lung cancer, hematological neoplasms, ischemic heart disease, cerebrovascular accidents, AIDS, and external causes (particularly illicit drug use and suicide and unknown/ill-defined symptoms). No deaths from breast cancer were identified in this cohort. However, in previous publications from this cohort [20], breast cancer was reported in one MtF and one FtM. The former case had a 30-year exposure to estrogens. The latter occurred in a subject with bilateral mastectomy while receiving treatment with testosterone that had lasted 10 years. This occurred in residual mammary tissue and may be caused by testosterone, which is partially aromatized to estradiol. Furthermore, other results from this set of publications related to this cohort included frequent venous thrombosis (6–8 %) among ethinyl estradiol users and deleterious effects on cardiovascular risk in MtF androgen-deprived, estrogen-using transsexuals, while

increased cardiovascular morbidity or mortality was not clearly demonstrated among FtM transsexuals with prolonged use of androgens.

## 5.5 Prevalence of GD

BMJ Best Practice (http://bestpractice.bmj.com/bestpractice/monograph/992/basics/epidemiology.html) reports the prevalence of gender dysphoria as approximately 1.67 per 100,000 born males (i.e., about 1 in every 60,000) and 1 per 100,000 born females [21]. In Northern Europe, the prevalence of transsexualism has been estimated at approximately 1:12,000 cases in males and 1:30,000 cases in females. In the USA, there seems to be no significant association between transsexualism and social class, intelligence, or ancestry. As discussed previously in this chapter, cases reported by gender identity clinics may be increasing, but this may reflect better access to diagnosis and treatment rather than increasing incidence.

In 1998, the prevalence in Scotland of gender dysphoria among patients aged over 15 years was calculated as 8.18 per 100,000, with an approximate sex ratio of 4:1 in favor of male-to-female patients. One-third of gender-dysphoric patients known to practices had registered in the preceding 12 months, suggesting that patients with this condition are increasingly likely to present for medical care. Questionnaires were sent to senior partners in all general practices in Scotland designed to elicit experience of patients with gender dysphoria: a subjective experience of incongruity between genital anatomy and gender identity. Responses were received from 73 % of practices [22].

Prevalence estimates by special interest organizations in the UK such as the Gender Identity Research and Education Society (The Number of Gender Variant People in the UK – Update 2011 http://www.gires.org.uk) [23] show much higher proportions. In terms of absolute numbers, 12,500 may have presented for treatment representing a prevalence of 20 per 100,000 (both born genders combined). The same organization suggests a strong increase also based on change of cultural climate.

According to a recent Japanese study, FtM-type GID patients are present with a point prevalence of at least 90/100,000 and an estimated lifetime prevalence of 0.001–0.002 % [24].

In Serbia, the prevalence of transsexualism according to cases seen at the only clinic performing sex reassignment has been estimated about 1/100,000. The relatively young age of those applying for sex reassignment and the sex ratio of 1:1 distinguish the population in Serbia from others reported in the literature [25].

Most previous studies of the prevalence of transsexualism have used data from individuals seeking sex reassignment surgery. New Zealand is unique in that transsexual people can apply to have an "X" for the sex on their passport if they have a name on their birth certificate that is congruent with the sex opposite to their birth assigned sex and provide a statutory declaration stating they have lived as a member of that sex. From the information provided by the New Zealand Passports Office, the authors ascertained that the prevalence of transsexualism among New Zealand passport holders was at least 16/100,000 (i.e., 1 in every 6,364). The prevalence of male-to-female transsexualism was 27/100,000 (i.e., 1 in every 3,639), and the corresponding figure for female-to-male transsexualism was 4/1,000,000 (i.e., 1 in every 1:22,714). The estimates from New Zealand were higher than most previous estimates of transsexualism prevalence. There was also a larger-than-expected ratio of male-to-female transsexual people to female-to-male transsexual people (6:1), which could in part be due to female-to-male transsexual people being relatively overrepresented among those transsexual people for whom we did not have data on the direction of sex change, or this may be indicative of the demography of transsexualism in Australasia [26].

In Belgium, the overall prevalence is 1:12,900 for male-to-female and 1:33,800 for female-to-male transsexuals. In Wallonia (the French-speaking region of Belgium), the prevalence is significantly lower than in Flanders (the Dutch-speaking region) and in Brussels (the bilingual

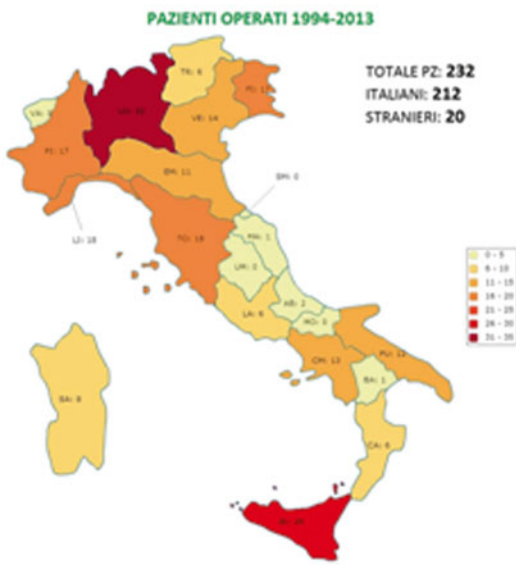


**Fig. 5.1** Region of residence of subjects who underwent sex reassignment in Trieste, Italy

capital region). In the total Belgian population, the male/female sex ratio is 2.43:1, again with a substantial difference between Wallonia on the one hand and Flanders on the other. The authors suggest that transsexualism in Wallonia is socially less acceptable: persons suffering from gender dysphoria in that part of Belgium might encounter more problems accessing gender clinics and receiving treatment [27].

A much higher prevalence was calculated from a population survey in Massachusetts, USA including 28,176 respondents. 131 or 0.5 % responded yes to the question "Some people describe themselves as trans- gender when they experience a different gender identity from their sex at birth. For example, a person born into a male body, but who feels female or lives as a woman. Do you consider yourself to be transgender?" A more detailed definition of the term transgender was read to those who expressed confusion [28].

In terms of the absolute number of treated cases at the largest Italian sex reassignment clinic, Fig. 5.1 shows the geographic distribution by Italian region of residence (Trombetta C, 2014, personal communication).

## 5.6 Methods to Estimate Frequency in Hidden Populations and Conclusive Remarks

The validity of the evolving epidemiology of GD, inexorably dependent on its case definition and on the consistency of application of such a case definition across times and latitudes, is further at risk because it also depends on the cultural and medical acceptance of local communities. If gender-dysphoric persons or gender variants were a hidden population, because of stigma or of other reasons, it is likely that prevalence was underestimated, health services were not provided, and group was non-influential. Subjects requiring medical attention with high probability would travel or even migrate to have their needs satisfied. On the other hand, if only the medical or surgical interventions represented a marker of the condition in time and space, this might reintroduce the abnormality to this population. To provide a correct estimate of the size of such a minority population in order to fulfill common needs associated with any human life, the surfacing of this hidden population should be pursued. It is beyond the scope of this book to present the statistical and demographic methodology necessary to reach such a goal. In brief, an ideal sampling procedure should be established that yields not only a sample independent of its starting point but also an unbiased sample of the underlying population with a known degree of consistency from which confidence intervals can be computed [29]. With some approximation, the goal might be to devise means for drawing samples that produce a good cross section or the coverage of heterogeneity in the target population. Among the many methods that may be adopted, respondent-driven sampling has been employed in subjects who might have been persecuted, who were victims of violence, who have posttraumatic stress disorder, and many others. Such a method is of special interest because it might reduce sampling bias that affects many of the current studies on this field.

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