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_____ April 20th, 2015 _____

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**Systematic Review and Meta-Analysis of Worldwide Prevalence Estimates of
Transgenderism and Gender Non-Conformity**

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BSc

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2009

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An abstract of

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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Abstract

Systematic Review and Meta-Analysis of Worldwide Prevalence Estimates of Transgenderism and Gender Non-Conformity

By Lindsay Collin

BACKGROUND: Evidence-based care of transgender persons requires better data on the prevalence of transgenderism and gender non-conformity in the general population.. We conducted a systematic review and meta-analysis of the current state-of the science on prevalence estimates the effects of various definitions, methodological study characteristics, and differences across countries.

METHODS: PubMed, Embase and Medline were searched to identify relevant studies. We evaluated studies reporting prevalence estimates of transgenderism and grouped them based on the case definition applied to the numerator. Summary estimates were derived using a random-effects model. Overall and stratum-specific meta-prevalence estimates (mPs) and 95% confidence intervals (CIs) were accompanied by tests for heterogeneity, and meta-regressions to assess possible sources of heterogeneity.

RESULTS: A total of 29 studies met the inclusion criteria for the systematic review and a further 24 studies provided necessary data summary analyses produced overall mP estimates for total transgender prevalence, and for male-to-female (MTF) and female-to-male (FTM) prevalence estimates. Overall mP for studies reporting gender confirmation therapy was 13.0 (95% CI, 0.4-24.7) and among transgender-related diagnoses 6.7 (95% CI, 4.5-9.0). Significant heterogeneity was observed across both of these groups ($I^2 >99.9\%$, $p < 0.01$). Among studies reporting gender non-conformity the mP was 453 (95% CI, 381-525) with I^2 of $<1\%$. Similar results were observed for MTF and FTM prevalence estimates in each of the groups.

CONCLUSIONS: The literature on prevalence of transgenderism highlights the importance of adhering to specific case definitions because the results may range several hundred-fold depending on how the numerator was ascertained.

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INTRODUCTION

Definitions

The adjectives 'transgender,' and 'gender non-conforming,' are used to describe a heterogeneous group of individuals who transcend cultural definitions and categories of gender (Bockting 1999). Transgenderism is an umbrella category that includes various states of discontent with one's sex assignment and the desire and/or belief that one belongs to a different gender (Newfield et al. 2006). In understanding the concept of transgenderism, it is necessary to differentiate between the biological sex and gender. An individual's biological sex refers to their chromosomal make up that determines the expression of primary sex characteristics and is assigned at birth based on this identification (Lombardi 2001). In contrast, an individual's gender identity is the intrinsic sense of being male, female or of a different gender (Blair et al. 2014; Bockting 1999; Bockting et al. 2011). An individual's gender role can be considered the public manifestation of their gender identity (Cohen-Kettenis and Gooren 1999). Gender has been described as both a social and psychological state, where the social gender encompasses how individuals present themselves in public and the psychological gender refers to the self-identification. The two states may or may not be in agreement (Lombardi 2001). With these considerations in mind gender identity no longer appears to conform with the binary categories of an individual's anatomical and genetically determined sex, but rather viewed by many as a continuum (Hage and Karim 2000).

Gender dysphoria is the distress that results from a discomfort with one's sex assigned at birth and their personal gender identity (Fisk 1974). The strong feeling of

discomfort with one's natal sex may justify a formal diagnosis, formerly called as "gender identity disorder" (Burgess et al. 2007; Fisk 1974), which is more recently being replaced with the term "gender dysphoria" (Cohen-Kettenis and Pfäfflin 2010). Gender dysphoria (GD) may lead the individual to desire the anatomy and/or social role of a different gender (Carroll 1999). As the manifestations of GD vary among transgender persons, the intensity of dysphoria may influence the decision whether or not to take steps towards physical gender reassignment, perhaps more appropriately known as 'gender confirmation' (Alegria 2011). It has been described previously in the literature that an individual with GD may have one of four possible outcomes: unresolved dysphoria, acceptance of natal gender, part-time cross-gender behavior, or full-time cross-gender living and medical gender confirmation (Carroll 1999).

Typically, the transition begins with a real-life experience, which involves living full-time in the desired gender role (Bockting 2008; Byne et al. 2012). The real-life experience may be accompanied by psychotherapy to explore the individual's comfort in the expression of their gender identity and to treat any coexisting mental health concerns (Bockting 2008). This aspect of transitioning can allow the individual to become accustomed to the new gender role, reduce gender dysphoria and improve social and sexual functioning (Gooren 2011). The real-life experience is often required before further transition options can be explored (Meyer et al. 2001).

If the individuals desire to undergo further gender transition treatment, they may seek hormonal and/or surgical steps to achieve male-to-female (MTF) or female-to-male (FTM) gender confirmation (Coleman et al. 2012). The act of seeking or undergoing change in primary or secondary sex characteristics involves feminizing or masculinizing

medical interventions such as surgery, hormonal therapy, or both. Medical gender confirmation therapy (GCT) typically accompanies a permanent change in their gender role, which is defined as transsexualism (Coleman et al. 2012). Hormonal therapy is a partially reversible procedure that includes the administration of gonadal hormones used to bring about the desired secondary sex characteristics (Byne et al. 2012). The main goal of surgical GCT is alter an individual's primary sex characteristics in order to reflect the self-identified gender. Common secondary surgical procedures may include cosmetic alteration of the face, breast, or body. In addition, some individuals elect to undergo speech and voice therapy, and facial hair removal (Deutsch and Feldman 2013). Both hormonal therapy and gender confirmation surgeries have been found to relieve gender dysphoria and improve psychological well-being (Murad et al. 2010; Newfield et al. 2006; Smith et al. 2005).

Knowledge Gaps

In 2011, the Institute of Medicine (IOM) released a report on the health of lesbian, gay, bisexual and transgender persons. The report emphasized the importance of transgender health research to better understand the needs of this population (Institute of Medicine 2011). The Healthy People 2020 initiative underscored the importance of the commitment of eliminating health disparities affecting the LGBT populations by providing accessible and quality care (Cahill and Makadon 2014). The transgender community has been identified as a population with specific health issues that need to be identified, better understood and addressed.

Despite increased research focus on transgender health some of the very basic issues in this area remain largely unresolved. For example little is known about the prevalence of gender dysphoria or the proportion of the population who should be considered transgender. The reported estimates are greatly affected by differences in methodology, and variable definition of who should be considered transgender (Addis et al. 2009; Coleman et al. 2012; Lombardi 2001).

A number of previous reviews sought to synthesize the available information regarding the demographic characteristics of the transgender population (Meier and Labuski 2013; Zucker and Lawrence 2009). However in view of rapidly expanding literature, a re-evaluation of the data available to-date is warranted. Moreover, most previous reviews of this issue focused on a summary of reported findings, but did not systematically assess the impact of methodology and definitions on prevalence estimates. With these data gaps in mind, the objectives of the present review were to: 1) evaluate the state-of the science on epidemiology of transgenderism; 2) examine the effect of various definitions and methodological characteristics on study results; 3) compare findings reported in different countries and over different periods of time; and 4) examine the differences between estimates reported in the peer-reviewed publications and those that appeared in the so called “gray” literature

METHODS

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al. 2015). Relevant publications were identified via electronic literature databases Medline, EMBASE and PubMed using multiple combinations of search terms “prevalence”, “gender identity disorder”, “gender dysphoria”, “transgender”, and “transsexual.” The electronic search included all papers published thorough January 2015. To identify reports missed by electronic searches we hand-searched the *Archives of Sex Behavior* and the *International Journal of Transgenderism*, as well as reference lists from studies and relevant reviews. We also included gray literature identified through Google Scholar and general internet searches. We define gray literature as any report that was not published in peer-reviewed journals or scientific monographs (Dean et al. 2011).

Study Selection

We aimed to find all publications reporting population prevalence estimates of transgenderism. We did not restrict eligibility based on language, study type, or publication status. Two reviewers LC and MG independently reviewed each citation. Each report was assessed according to the following a priori eligibility criteria: 1) reported results with prevalence estimates in an adult population, 2) reported numerator for prevalence estimate 3) identification of denominator or a description of how prevalence estimate was calculated. Publications that did not report prevalence estimates or numerator that was used to calculate the prevalence were excluded from the analysis. When the study populations overlapped, the more recent prevalence estimate was used in the meta-analysis, but all studies were described in the systematic review.

Outcome Measures

The main outcome measure of interest in this review was population prevalence estimate of transgenderism. Secondary outcomes of interest included specific prevalence estimates for male-to-female (MTF) or female to male (FTM) transgender persons.

Data Abstraction and Management

The two reviewers LC and MG, who were not masked with respect to the author, institution or journal, abstracted the data from eligible publications. Information was tabulated to allow data management and descriptive analyses. Inconsistencies in the data entry were resolved by consensus. The author of one study (Gates 2011) was contacted and replied regarding additional information needed for meta-analysis.

For each publication, the data extracted for summary analysis included the definition of the numerator (e. g., diagnosis of GD or gender identity disorder, use of hormonal therapy, or history of gender confirmation surgery), the type of denominator (e.g. general population of a given area, or a total number of participants in a survey), the overall and gender-specific prevalence estimates, numerators used in calculations, and denominators (if reported). Many of the publications reported the numerators used for calculations (number of transgender persons identified in the population) and prevalence estimates, but did not include the denominator. Using the prevalence and the numerator, the denominator values were then calculated for the purposes of the current review. In order to apply meta-analytic techniques to the reported prevalence estimates, the standard errors for each estimate were calculated using OpenEpi on-line statistical software

(Sullivan et al. 2009). Additional data extracted from each report included author, location, date of study, and MTF-to-FTM ratio.

Data Synthesis

Results from eligible publications reporting transgender population prevalence estimates were stratified according to the case definition used to ascertain the numerator. Categories for case definition included: gender confirmation surgery (GCS), hormonal therapy (HT), gender identity disorder (GID) or gender dysphoria (GD) diagnoses, and incongruent gender identity. Studies that used methods inconsistent with any of the above definitions were examined and discussed separately, but not included in the meta-analysis. In instances where the publications used the same source population, the more recent publication was used in the analysis.

Data extracted from the publications were analyzed to calculate a pooled summary estimate of transgender prevalence weighted by sample size. Heterogeneity was assessed by a Q-value and its derivative I^2 in order to describe the variation across the reported prevalence estimates. A value of $> 50\%$ for the I^2 statistic represents considerable heterogeneity (Deeks et al. 2008). The summary statistics were calculated using random effects models and the results were expressed as meta-prevalence (mP) estimates with the corresponding 95% confidence intervals (CI). In addition, subgroup and meta-regression analyses were performed in order to determine sources of heterogeneity. Variables that were considered as possible sources of heterogeneity included: year the study was conducted, geographic region, and the type of publication (peer-reviewed vs. not peer-reviewed). All statistical analyses were performed using

STATA software package (version 13.0, STATA Corporation, College Station, TX, USA).

RESULTS

Overview of the relevant studies

A total of 1,464 references were screened by title and abstract (**Figure 1**). After exclusion of descriptive studies and studies among adolescents and children, a total of 83 publications underwent full text review. An additional 24 “gray literature” reports were also reviewed. Of the 107 full-text publications reviewed, 78 were excluded because they did not report relevant information. A total of 29 publications were included in the qualitative synthesis described previously. Three publications were excluded from the meta-analysis because they reported results based on overlapping data (Blosnich et al. 2013; Eklund et al. 1988; Gates 2011). Two additional studies reported estimates of transgenderism using administrative changes to name or sex were also excluded from the analysis because these two studies used unique case definitions and were not comparable to the rest of the literature. Therefore, a total of 24 publications were used for meta-analysis and meta-regression.

Qualitative review of the literature

Of the 29 publications that met the criteria for inclusion in the qualitative review 16 were conducted in Europe, seven were based in the United States, and two were from Japan. Iran, Australia, New Zealand, Sweden, and Singapore each contributed a single study. The years of publication ranged from 1968 to 2015. The design features of the studies and their main findings are presented below. We begin by discussing studies that defined transgender persons as those who underwent surgical or hormonal gender confirmation therapy. We then review studies assessing prevalence of transgender-

related diagnoses such as “transgenderism,” “gender dysphoria” (GD) or “gender identity disorder” (GID). We conclude the review with a summary of studies that defined endpoints of interest as gender non-conformity or gender incongruence, and also evaluate occurrence of legal or administrative name or gender changes.

Prevalence of Gender Confirmation Therapy

As shown in Table 1, eight publications have estimated the prevalence of transgenderism by considering only those individuals who sought or received gender confirmation surgery (GCS). Three of these publications were from the US, four from Europe and one from Singapore. The publication dates ranged from 1968 to 2014.

In the United States the earliest estimate of the proportion of transsexuals in the general population was reported in 1968 (Pauly 1968). Based on the data from various specialized centers (most notably the Gender Identity Clinic at the Johns Hopkins Hospital) Pauly identified 2000 MTF and 500 FTM persons who requested GCS since 1953. Using the total US population in 1968, the resulting prevalence was estimated at 1/100,000 for MTF and 0.25/100,000 for FTM. Unlike other similar studies, which calculated prevalence of MTF and FTM among natal men and women, respectively, Pauly divided each numerator by the total population. This produced a roughly two-fold underestimate of the gender-specific results.

More recently Conway attempted to calculate an approximate prevalence of transsexualism through estimation of annual gender confirmation surgeries performed in the United States between 1960 until 2002 (Conway 2002). Although the source of the information is not clear, Conway estimates that there have been 32,000 natal males in the

United States who have undergone GCS. Based on the assumption that there are approximately 80,000,000 males aged 18 to 60 years old the MTF prevalence in the United States is 40/100,000.

In another similar report, Horton estimated the number of gender confirmation surgeries performed annually based on information obtained from clinics and surgeons who are members of the Harry Benjamin International Gender Dysphoria Association (Horton 2008). Based on the responses and unspecified missing data imputation, the author determined that there must have been 1,166 GCS procedures performed during 2001 alone. The author further extrapolates overall prevalence by multiplying the surgeries by years of eligibility, or the average life expectancy of males and females, and determines the prevalence estimates to be 39.5/100,000 MTF and 24/100,000 FTM. The rationale for the missing data imputation and extrapolation to average life expectancy is not particularly clear.

Several recent prevalence estimates for the receipt of or referral for GCS are available from Europe. Two of those reports were published in Spain, one in Belgium and one in Italy. In 2011, Esteva et al. sent out questionnaires to regions of Spain that have established Gender Identity Units (Esteva et al. 2012). In the questionnaires the authors inquired about the number of applicants for GCS, and detailed information regarding the services offered at the clinic. Each clinic that received a questionnaire responded and the authors determined that there were 3,303 individuals who solicited surgical treatment. Using the total Spanish population between ages 15 and 65 years as the denominator, the prevalence estimate was reported as 10/100,000, which according to the authors is comparable to other European studies.

A study in Belgium estimated the proportion of the population that had undergone GCS from 1985 until 2003 through retrospective collection of data on procedures performed by plastic surgeons and gender teams (De Cuypere et al. 2007). Gender teams and plastic surgeons were sent questionnaires regarding procedures performed and 24% of the questionnaires were returned. Among the gender teams and plastic surgeons that agreed to participate, the study identified 412 Belgian-born transsexuals (292 MTF and 120 FTM) corresponding to prevalence estimates of 7.74/100,000 and 2.96/100,000. The reported figures may underestimate the true population prevalence because of incomplete participation of the plastic surgeons; however the authors indicate that in a relatively small country such as Belgium, the number unaccounted patients would be minimal.

Based on information available from Italian clinics performing GCS procedures Caldarera and Pfäfflin identified 424 MTF and 125 FTM surgeries performed between 1992 and 2008 (Caldarera and Pfäfflin 2011). Using data from the National Institute of Statistics to estimate the denominator, the authors calculated prevalence of 0.5/100,000 and 0.4/100,000 for MTF and FTM. The authors acknowledged that their estimates were lower than those reported in other countries and attributed the difference to missing data or cultural factors.

A study in Sweden identified requests for GCS based on data from the National Board of Health and Welfare Statistics (Dhejne et al. 2014). There were 767 applicants (478 MTF and 289 FTM) of which 681 were approved and underwent the procedure (429 MTF and 252 FTM). Using the Swedish population as of December 2010, the prevalence estimates for applications for GCS were 12.9/100,000 MTF and 7.5/100,000 FTM. The authors calculated the prevalence among those who were approved for therapy and

underwent GCS to be 11.6/100,000 MTF and 6.6/100,000 FTM. The authors noted that over the 50 year study period there was an increase in the number of people seeking GCS.

Only one study assessing prevalence of surgical gender confirmation was conducted outside of North America or Europe. Tsoi calculated prevalence of transsexualism by identifying patients in Singapore who had sought GCS and who were subsequently diagnosed as transsexuals by psychiatrists (Tsoi 1988). The author reported that up until 1986, there were 458 (343 MTF and 115 FTM) Singapore-born transsexuals reported by the Department of Obstetrics and Gynecology and by private surgeons. Using the total male and female population of Singapore in 1986, the prevalence was reported as 35.2/100,000 and 12.0/100,000 for MTF and FTM respectively. The author cites cultural acceptance of transgenderism and more established gender confirmation surgical procedures as possible reasons for the higher than previously reported prevalence estimates.

Two studies conducted in the Netherlands at the Free Amsterdam University clinic used the initiation of hormonal therapy (HT) among persons with gender dysphoria as the definition of transgenderism (Table 1). In 1976 the clinic established a gender team and based on data collected through 1986, 538 individuals had begun HT at that facility (Eklund et al. 1988). Of those 399 were MTF and 139 FTM. Using the Dutch Bureau of Statistics data for population estimates, the prevalence was calculated as 5.6/100,000 MTF and 1.9/100,000 FTM.

In a more recent study based at the same clinic, the analysis was extended through the end of 1990 (Bakker et al. 1993). By that time the clinic was providing HT to 713

Netherlands-born transgender patients over the age of 15 years; 507 MTF and 206 FTM. The total population of the Netherlands from 1990 was used to determine the prevalence estimates of 8.4/100,000 MTF and 3.3/100,000 FTM. Bakker et al. state that the prevalence estimates have risen dramatically over the years.

Prevalence of transgender-related diagnoses

Ten studies calculated the prevalence estimate of transgender-related diagnoses using ICD codes for TG, GID, or GD (Table 2). The terminology describing this condition and the diagnostic criteria have evolved over the years since the original definition (Benjamin et al. 1966). Spain, Japan and the United States each contributed two studies and England, Northern Ireland, Ireland, and Iran each contributed one study in this category with publication dates ranging between 1968 and 2014.

Hoenig & Kenna conducted a study aiming to identify all patients diagnosed with GID at the University Department of Psychiatry at the Royal Infirmary, Manchester between 1958 and 1968 (Hoenig and Kenna 1974). The study relied on referral of patients from other clinics. The clinic identified 66 individuals with GID. Using the population of the Manchester Region on June 30, 1970, the prevalence estimates were calculated as 1.9/100,000 total, 2.8/100,000 for MTF, and 0.9/100,000 for FTM.

In a study based in Northern Ireland O’Gorman collected information from the Department of Mental Health, Queen’s University, Belfast (O’Gorman 1982). Twenty-eight individuals diagnosed as transsexual were identified (21 MTF and 7 FTM) over an unspecified fourteen year period. Using an approximation of the population in Northern Ireland the prevalence was estimated at 1.9/100,000.

Esteva et al. estimated the prevalence of GID based on clinic data from the Gender Identity Disorder Unit in Andalucía, Spain (Esteva et al. 2006). The clinic reported that from its opening in 1999 until October 2004, they had seen a total of 391 individuals with GID, 243 MTF and 148 FTM. Using the total population of Andalucía in 2004, the corresponding prevalence estimates were reported as 10.3/100,000 for MTF and 6.5/100,000 for FTM. The authors state that these prevalence estimates are higher than previously reported and outline the importance of early detection and integral treatment in order to improve social adaptation.

In another Spanish study Gomez Gil et al. estimated the prevalence of transsexualism in Catalonia using ICD-10 diagnostic code of F64.0 (transsexualism) at the Hospital Clinic in Barcelona from 1996 through 2004 (Gomez Gil et al. 2006). The authors identified 161 patients (113 MTF and 48 FTM) who were living in Catalonia and based on population data from the regional Institute of Statistics, the prevalence estimates for MTF and FTM were calculated as 4.8/100,000 and 2.1/100,000, respectively. The authors also calculated the Barcelona-specific prevalence of 5.5/100,000 for MTF and 2.5/100,000 for FTM indicating a higher urban prevalence of transgenderism. The authors state that transsexualism has been marginalized in Spain and this may contribute to the lower than previously observed prevalence estimates.

In Japan, the prevalence of GID was determined from the outpatient GID Clinic of Okayama University hospital between April 1997 and October 2005 (Okabe et al. 2008). Using the DSM-IV criteria, 579 patients (230 MTF and 349 FTM) constituted the numerator. Assuming a denominator of 40 million people living in western Japan the prevalence estimate for FTM GD patients was 0.9/100,000.

Another Japanese study sought to assess the prevalence of GID based on data collected at the Gender Identity Disorder Clinic at the Sapporo Medical University Hospital between December 2003 and January 2010 (Baba et al. 2011). Identification of cases was based on diagnoses using ICD-10 and DSM-IV codes. The study identified 343 patients (104 MTF and 238 FTM). Using the population of Hokkaido as the denominator, the MTF and FTM prevalence estimates were 3.97/100,000 and 8.20/100,000 respectively. The authors conclude that FTM may be more prevalent in Japan than in other parts of the world, which is in agreement with the previous report from that country (Okabe et al. 2008).

Ahmadzad-Asl et al. aimed to estimate the prevalence of GID in Iran between 2002 and 2009 through review of records at the Tehran Psychiatric Institute and identification of subjects with a diagnosis of GID according to the DSM-IV criteria (Ahmadzad-Asl et al. 2010). 281 individuals were identified (138 MTF and 143 FTM) yielding prevalence estimates of 0.7/100,000 total, 0.69/100,000 for MTF and 0.74/100,000 for FTM. The authors postulate that the patriarchal socio-cultural characteristics in Iran may explain the roughly equal numbers of MTF and FTM, which contrasts with reports from other countries that have observed a higher MTF: FTM ratio.

Using the DSM-IV/V criteria, Judge and colleagues retrospectively collected information on patients diagnosed with GD at the Department of Endocrinology in St. Columcille's Hospital in Dublin between 2005 and 2014 (Judge et al. 2014). Among 218 patients referred to the clinic, 159 were MTF and 59 were FTM. Based on the 2011 census data the prevalence estimates were reported as 6.8/100,000 total, 9.88/100,000 for MTF and 3.6/100,000 for FTM.

In a recent study conducted in the United States Blosnich et al. used the Veterans Health Administration (VHA) electronic medical records from 2000 through 2011 to examine the prevalence of GID among veterans (Blosnich et al. 2013). The numerator for the study included individuals that received an ICD-9 diagnostic code of either 302.85 (gender identity disorder) or 302.6 (gender identity disorder not otherwise specified). Using the VHA data and electronic record database to define the denominator the authors report prevalence estimates for different years starting in 2002. The 2002 prevalence estimate was 12.52/100,000 and the prevalence reported in 2011 was 22.88/100,000 indicating an almost two-fold increase over the ten-year study period. Although the data did not distinguish MTF from FTM, it is important to note that the VHA population is 95% natal male. The prevalence of GID among veterans appears to be higher than the estimates cited in previous reviews.

In a more recent VA-based publication, Kauth et al. also used the electronic medical records (Kauth et al. 2014). ICD-9 diagnoses used to identify cases included 302.85, 302.6, and 302.5 (transsexualism) and cases were identified between 2006 and 2013. Prevalence in 2013 was reported as 32.9/100,000 (95% CI: 21.6, 44.1). It is important to keep in mind that this result is not directly comparable those reported in the Blosnich et al. study due to expanded criteria for the case definition. In addition the denominator the Kauth et al study included all VHA enrollees. By Blosnich et al. calculated the prevalence among VHA utilizers.

Table 2 also includes three studies (from Sweden, Australia and Scotland) which calculated the prevalence of transgenderism by surveying national clinics specializing in

treatment of transgender patients. All three studies present relatively old data with publication dates between 1968 and 1999.

Walinder attempted to estimate the prevalence of transgenderism in Sweden in 1968 through a survey of psychiatric clinics (Wålinder 1968). Questionnaires were mailed out asking the clinics to report information regarding transvestite and transsexual individuals who may have sought medical attention at the clinic as of December 1965. Seventy-six percent of the psychiatrists approached confirmed providing treatment to transgender persons and 67 individuals were identified in the responses. After including 43 additional individuals known to the author the numerator used for calculations was 110. Using census data from Sweden, the prevalence estimates were calculated as 1.9/100,000 total; 2.7/100,000 for MTF and 1/100,000 for FTM.

Prevalence of GD in Australia between June 1976 and June 1978 was estimated through distribution of questionnaires to subscribers of the Australian and New Zealand Journal of Psychiatry (Ross et al. 1981). According to the authors, all psychiatrists in Australia receive this journal. A total of 904 questionnaires were distributed and 263 were returned (29.1%). Based on the completed questionnaires, 243 transgender individuals (209 MTF and 34 FTM) were identified. Prevalence estimates were calculated using the population of Australia 15 years of age or older as of June 31st 1978, and were determined to be 2.4/100,000 total, 4.2/100,000 for MTF and 0.7/100,000 for FTM.

Wilson et al. surveyed senior partners at all general medical practices in Scotland in 1998 (Wilson et al. 1999). The questionnaire asked for information regarding the number of patients registered to the practice as well as the number of patients with GD.

Just under three-quarters (73%) of the surveys were completed and returned, identifying 273 patients with GD. The denominator for calculation of the prevalence was based on the number of patients over the age of 15 registered to the respondent's practices standardized to match the age distribution of the general population in Scotland. The resulting GD population prevalence estimate was 8.18/100,000.

Prevalence of Gender Nonconformity

Four studies utilized survey-based data to estimate prevalence of incongruent gender identity and gender non-conformity (Table 4). Two of these studies were based in the United States, one in the Netherlands and one in Belgium.

Conron et al. analyzed data collected between 2007 and 2009 from the Massachusetts Behavioral Risk Factor Surveillance Study (MA-BRFSS) (Conron et al. 2012). The survey was administered to 28,662 adults aged 18 to 64 years. Each participant was asked: "*Some people describe themselves as transgender 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?*" There were 131 participants who responded 'yes' to that question, corresponding to a prevalence of 500/100,000 persons. The authors acknowledge that their estimate may have been affected by misclassification bias due to the broad scope of the question. Another limitation of the data is a lack of information on natal sex and current gender identity.

Gates combined reports from the MA-BRFSS as reported by Conron et al., the 2003 California LGBT Tobacco Survey, and the 2009 California Health Interview survey

in order to estimate the number transgender adults in the United States (Conron et al. 2012; Gates 2011). The MA-BRFSS reported that 0.5% of adults in Massachusetts identified as transgender. The 2009 California Health Interview Survey estimates that 3.2% of adults in California are LGBT. Based on the 2003 California LGBT Tobacco Survey 2.4% of LGBT persons self-identify as transgender. Using these considerations Gates further estimated that the prevalence of transgender persons among California adults is 0.1%. Gates then states that the average of the percentages from Massachusetts and California allows estimating the US prevalence of approximately 0.3% or 300 per 100,000 individuals.

Kuyper and Wijsen estimated the prevalence of transgenderism among 15- to 70-year old residents of the Netherlands using data from an internet-based sexual health study conducted in 2012. The study aimed to identify individuals with incongruent gender identities and gender dysphoric feelings. The final sample included 8,064 participants, who were asked questions regarding gender identity and gender dysphoric feelings and the responses were recorded on a Likert Scale. The results were reported as the percentage of natal men or women with ambivalent or incongruent gender identities who also reported both aspects of gender dysphoria, dislike of natal sex characteristics and desire for hormone therapy and/or surgery. Although the exact cases definition is not clear, among natal men the reported prevalence was 600/100,000 and among natal females the corresponding estimate was 200/100,000. About 20% of those invited to participate in the internet-based survey, completed the questionnaire and met the eligibility criteria. The authors acknowledge that the low participation may limit the generalizability of the results to the general Dutch population.

Van Caenegem et al. estimated prevalence of gender nonconformity and gender incongruence based on a population survey of adolescent and adult (age range 14-80 years) residents of the Flanders region, Belgium (Van Caenegem et al. 2015). Survey participants were randomly selected from the Belgian National Register. Forty percent of eligible persons completed the survey. The final denominators for prevalence calculations included 1,799 participants (864 natal males and 905 natal females). Questions pertaining to gender identity and gender expression were assessed via a computer assisted personal interview. Based on a 5-point Likert scale (ranging from 1-totally disagree to 5-totally agree) the participants were asked to score statements “*I feel like a woman*” and “*I feel like a man*”. A person was considered gender ambivalent if the same answer (e.g., a score of 1 or a score of 2) was given to both statements. Gender incongruence was defined as a lower score assigned to the natal sex than to the opposite sex. Using these definitions, the prevalence for gender incongruence was estimated to be 700/100,000 natal men and 600/100,000 natal women. The corresponding estimates for gender ambivalence among natal men and women were 2,200/100,000 and 1,900/100,000, respectively.

Prevalence of legal name or sex changes

Two studies, one from Germany and another from New Zealand, reported population prevalence of transgenderism based on documented administrative sex or name change.

Weitze and Osburg relied on the 1981 German Transsexuals’ Act (TSG), which allowed applicants to change their first name or their legal sex status. The study

examined the decisions rendered during the first ten years since implementation of the law (Weitze and Osburg 1996). Questionnaires were submitted to the courts, and information regarding the number of relevant applications and corresponding court decisions was collected. . During the study period, the courts issued decrees on 683 first name changes and 733 rulings on legal reestablishment of sex. These rulings concerned 1,199 individuals of which 1,047 received the approval. Using the adult population of West Germany before reunification, the prevalence was estimated at 2.1/100,000. The natal male-to-female ratio of applicants was approximately 3:1.

In New Zealand individuals may request a change of their gender code from 'M' or 'F' to 'X'. To examine the frequency of this change, Veale contacted the New Zealand Department of Internal Affairs Passport Office (Veale 2008). A total of 385 such changes were identified in 2008, and given the number of passport holders in New Zealand the prevalence was calculated as 16/100,000. Considering that 49% of passport holders in New Zealand were male and 51% were female the corresponding prevalence estimates were 27/100,000 for MTF and 4.4/100,000 for FTM with a sex ratio of 6:1. This study is limited in that the original sex status on the passport was not always known.

Meta-Analysis

Among the nine studies reporting estimates for individuals who sought or received gender confirmation therapy, the summary analysis revealed a total mP of 12.5/100,000 (95%CI: 0.4, 26.7) with a range between 0.9 and 31.9, 18.0/100,000 (95%CI: 9.1, 27.0, range 1.0-40) for MTF, 7.2/100,000 (95%CI: 3.6, 10.8, range 0.25-24.0) for FTM (Table 4). The studies were further stratified based on whether or not the

publication was peer reviewed. The mP (95 % CI) estimate for the six peer reviewed publications was 9.2/100,000 (4.8, 13.6) for all studies combined, 12.5 (95%CI: 7.0, 17.9) for MTF and 5.1/100,000 (2.6, 7.6) for FTM. The corresponding mP (95% CI) estimates among non-peer reviewed publications were 26.8 (0-57.7), and 21.1 (0-35.4), for MTF and FTM respectively. Significant heterogeneity was present in all of the analyses ($I^2 > 99\%$, $p < 0.01$). Meta regression demonstrated no significant association between year of publication and prevalence in this group (regression coefficient = -0.38 p-value= 0.5).

A meta-analysis of the twelve studies that assessed prevalence of transgender-related diagnoses produced an overall mP estimate of 6.7/100,000 (95%CI: 4.5, 9.0); 5.8/100,000 (95%CI: 3.5, 8.1) for MTF and 2.5/100,000 (95%CI: 1.9, 3.1) for FTM (Table 5). After removing a study of US veterans that appeared to be an outlier the summary estimate for total prevalence was 4.1/100,000 (95%CI: 2.8, 5.5) (Blosnich et al. 2013). Once again there was pronounced heterogeneity of results ($I^2 = 99.2\%$ p-value < 0.01). Meta-regression demonstrated that neither study location (regression coefficient = -5.1 p-value=0.10) nor year of publication (regression coefficient = 0.23 p-value=0.16) were associated with reported results. .

As shown in Table 6, among studies that examined prevalence of gender non-conformity the summary estimates were much higher than in the previous two groups 452.7 (95%CI: 380.6, 524.8) overall, 607.7/100,000 (95%CI: 371.0, 844.4) for MTF, and 220.6 (95%CI: 58.5, 382.7) for FTM. Unlike the other two groups however the results were highly homogenous ($I^2 < 1$).

DISCUSSION AND CONCLUSIONS

Whereas direct comparison of prevalence estimates across studies is difficult due to the geographic, cultural and methodological differences, the key issue that needs to be addressed is the heterogeneity of the definition of transgenderism. In several previous reviews (Meier and Labuski 2013; Zucker and Lawrence 2009), all studies that reported the proportions of transgender individuals in a population were discussed together, and for this reason most found that the results were too inconsistent to draw conclusions. By contrast, we would argue that once the studies are sub-classified according to case definition the results are not as wide ranging as previously thought.

Studies estimating the prevalence of receipt or requests to receive gender hormonal or surgical gender confirmation therapy between 1968 until 2014, have reported relatively similar results. The prevalence estimates in this category of studies ranged between 1 and 10 per 100,000 individuals, with three exceptions. Horton and Conway, both estimated prevalence of receipt of GCS in the US to be around 40 per 100,000 (Conway 2002; Horton 2008). Both reports fall into the category of “gray literature”, which can be defined as any report that was not published in peer-reviewed journals or scientific monographs (Dean et al. 2011). Both reports suggest that the available data underestimate the true prevalence of GCS, however the basis for this conclusion and the methodology used to calculate the prevalence estimates is not clear. Another study that reported a higher prevalence estimate was conducted in Singapore. As this was the only study assessing GCS outside of North America or Western Europe the discrepancy with other reported results may stem from cultural or medical practice-related differences between Southeast Asia and Western countries. (Winter 2009).

Among studies reporting prevalence of transgender-specific diagnoses most (10 of 13) estimates ranged from between 1 and 10 per 100,000 individuals. Three studies reported results outside of this range.

A study from Iran calculated prevalence of less than 1 per 100,000 (Ahmadzad-Asl et al. 2010). It has been reported that treatment for GD in Iran, although legal, is heavily regulated (Javaheri 2010); however more information is needed to draw conclusions about the differences between Iranian and Western data.

Two US-based studies using the Veteran's Health Administration (VHA) electronic medical records reported higher than previously observed prevalence of GID in the 20-30 per 100,000 range (Blosnich et al. 2013; Kauth et al. 2014). The discrepancy between the VHA studies and other reports may have several explanations. It is likely that the availability of high quality electronic data and a more complete ascertainment of both the numerator and the denominator offer a more accurate result. Alternatively, as the Blosnich et al analysis was based on comparatively recent data, the higher prevalence of gender identity disorder reported in that study may reflect the secular trend of ever-increasing proportion of persons who acknowledge their transgender status and seek appropriate care. It is also possible, however, that the prevalence among veterans is truly higher than that in the general population; in keeping with the "flight to hypermasculinity" phenomenon, which may disproportionately affect veterans (Brown 1988).

The meta-analyses of both the treatment- and the diagnosis-based studies identified significant statistical heterogeneity even after stratification by publication type and after removal of outliers. It is important to emphasize, however, that this

heterogeneity is likely explained by vary low variance of study-specific estimates, rather than by the extent of disagreement across studies. The very low variance of the prevalence estimates is attributable to the fact that the denominator in many calculations was the assumed total population of the study area rather than a sample of that population.

The prevalence of self-reported transgender status and gender-non-conformity appears to be orders of magnitude higher than the corresponding treatment- or diagnosis-based estimates. The results of four survey based studies ranged from 200-700 per 100,000 persons (Conron et al. 2012; Gates 2011; Kuyper and Wijzen 2014; Van Caenegem et al. 2015). All four studies used somewhat different methods and all may have been affected by substantial non-response (Schneider et al. 2012). Nevertheless, the relatively consistent findings in this group of studies indicate that gender-nonconformity is far more widespread than what could be expected based on clinical data.

It also notable that unlike the results for the treatment- and diagnosis-based studies the meta-analysis for gender non-conformity revealed little heterogeneity. The variance among the studies reporting gender non-conformity was larger than in the other groups due to the relatively small size of each study.

To summarize, the current literature on prevalence of transgenderism highlights the importance of adhering to specific case definitions because the results may range several hundred-fold depending on how the numerator was ascertained.

With respect to methodological issues a particular shortcoming of the extant literature, and of this meta-analysis, is the lack of good denominator data, which led to an overestimated precision of many study-specific estimates. Prevalence by definition is a

proportion; that is a ratio in which all observations in the numerator arise from a pre-defined denominator (Gordis 2004). It is notable that the majority of studies included in this review first quantified the numerator and then used an approximated population size to arrive at a prevalence estimate. With these limitations in mind future research should employ established formal methods of prevalence calculations, such as those used in recent studies of US veterans (Blosnich et al. 2013; Kauth et al. 2014). As many transgender persons do not receive the diagnosis, future studies should also take advantage of modern informatics tools that go beyond ICD codes and include evaluation of free text available in the electronic medical records. An important prerequisite of an accurate prevalence estimate is outcome validation to decrease misclassification; this may require detailed record abstraction or use of alternative, preferably independent, data sources.

Another notable finding of this review is the need to consider cultural differences of how transgender persons are perceived and treated in a society. A more definitive weight-of-evidence assessment and a better understanding of the geographic, demographic and cultural differences in prevalence of transgenderism and gender non-conformity will be possible when studies conducted in different population groups use the same or similar methodology.

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TABLES AND FIGURES

Figure 1: Flow cart of the literature search and retrieval for publications reporting transgender population prevalence estimates

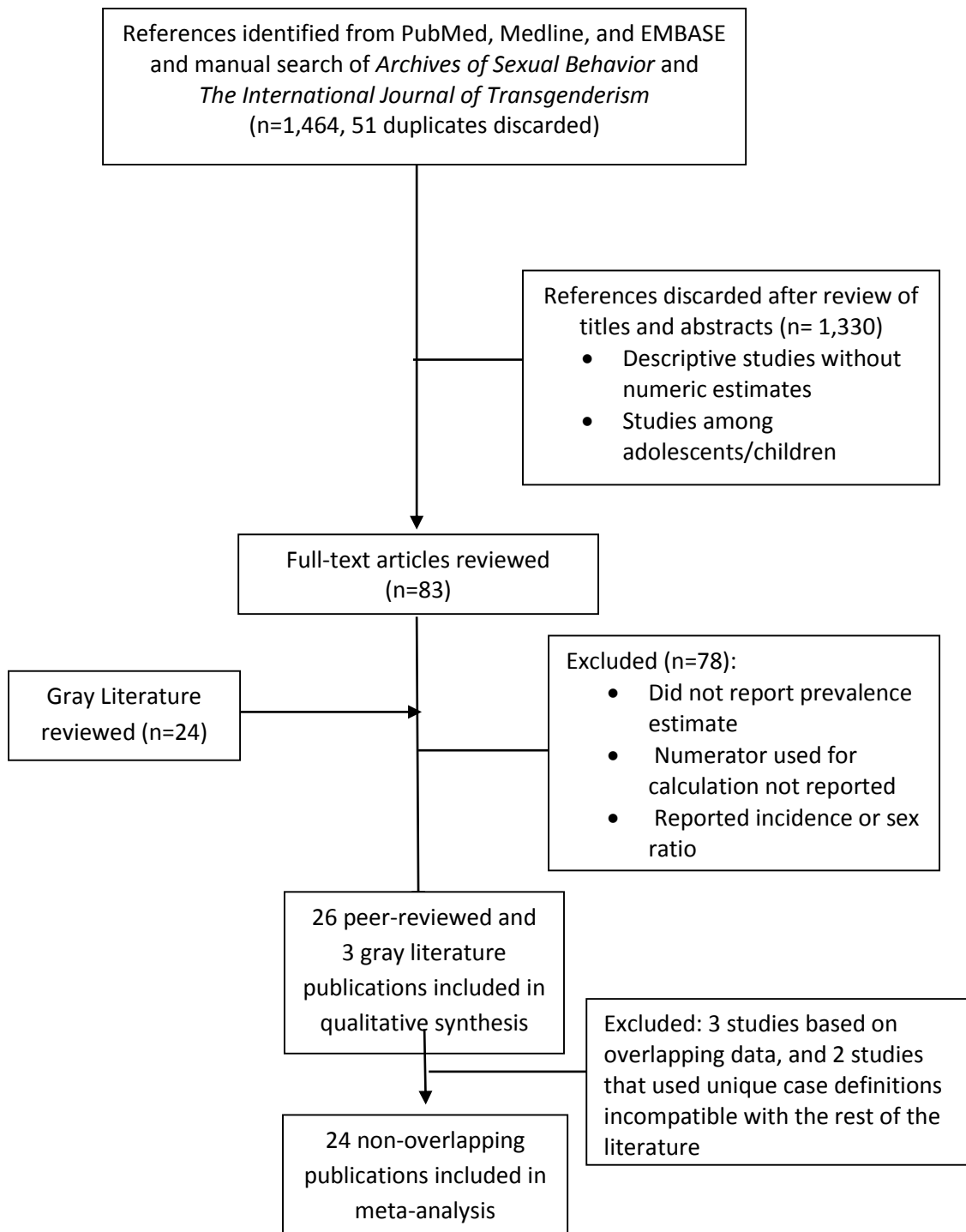


Table 1: Prevalence of receipt or requests to receive gender confirmation therapy

Reference	Location Time period	Case definition	Source of Numerator	Numerator			Source and size of Denominator	Prevalence (per 100,000)			Ratio MTF:FTM
				Total	MTF	FTM		Overall	MTF	FTM	
Caldarera and Pfäfflin, 2011	Italy, 1992-2008	GCS receipt	Surgical Clinics	549	424	125	National Institute of Statistics 2009: Total 59,619,290 (28,949,747 males and 30,669,543 females)	0.9	1.5	0.4	3.39:1
Conway 2002	US, 1960-2002	GCS receipt	Estimate (source not clear)		32,000		Estimate: 80,000,000 males 18-60 years of age		40		
De Cuypere et al. 2007	Belgium, 1985-2003	GCS receipt	Questionnaires sent to “gender teams” and plastic surgeons	412	292	120	January 2003 population: 3,758,969 males and 4,048,095 females		7.7	3.0	2.43:1
Dhejne et al. 2014	Sweden, 1960-2010	Request and (receipt) of GCS	National Board of Health and Welfare Statistics	767 (681)	478 (429)	289 (252)	December 2010 population: 3,704,685 males and 3,791,791 females	10.2 (9.1)	12.9 (11.6)	7.5 (6.6)	1.7:1
Esteva et al. 2012	Spain, 1999-2011	Request for GCS	Questionnaires sent to Gender Identity Units	3303			Spanish population 15-64 years old, 33,030,000*	10.0			1.9:1
Horton 2008	US, 2001	GCS receipt	Survey of clinics and individual members of the Harry Benjamin Society. Results multiplied by average lifespan (rationale not clear)	89,782	54,464	34,400	US Residents 2000: 281,421,906	31.9	39.5	24	
Pauly 1968	US, Dates not specified	Request for GCS	Author’s communication with specialized centers		2000	500	200,000 total US population used for both MTF and FTM calculations**		1.0	0.25	4:1
Tsoi 1988	Singapore, until 1986	Request for GCS	Documented diagnosis of transsexualism as part of pre-GCS evaluation	458	343	115	Population June 1986: 979,300 males and 954,900 females		35.0	12.0	3:1
Bakker, A et al. 1993	Netherlands, 1976-1990	Receipt of HT	Free University of Amsterdam (AZVU) clinic records	713	507	206	Center of Statistics: 6,019,546 males and 6,252,566 females		8.4	3.3	2.5:1

Eklund, PLE et al. 1988	Netherlands, 1976-1986	Receipt of HT	Free University of Amsterdam (AZVU) clinic records	538	399	159	Dutch Census Data: 7,125,000 males and 8,368,421 females*	1980: 2.2	1980: 0.5	3:1
								1983: 3.8	1983: 1.0	
								1986: 5.6	1986: 1.9	

*Denominator calculated from the numerator from the reported prevalence **Prevalence calculated using total population as the denominator

Table 2: Prevalence of transgender-specific diagnoses

Reference	Location	Case definition	Source of Numerator	Numerator			Source and size of Denominator	Prevalence (per 100,000)			Ratio
				Total	MTF	FTM		Overall	MTF	FTM	
Ahmadzad-Asl, et al. 2011	Iran, 2002-2009	GID diagnosis DSM-IV-TR	Tehran Psychiatric Institute	281	138	143	Center of Statistics of Iran, population aged 15-44 39,526,948	0.7	0.69	0.74	0.96:1
Baba et al. 2010	Hokkaido, Japan, Dec 2003-Jan 2010	GID diagnosis ICD-10 and DSM-IV	Sapporo Medical University Hospital	342	104	238	Native Japanese Hokkaido Residents 5,500,000		3.97	8.2	1:2
Blosnich, et al. 2013	VA system, US, 2002-2011	GID diagnosis ICD-9 codes 302.85 (GID) or 302.6 (GID NOS)	Confirmed GID diagnosis in VHA, FY 2000-2011	2002: 569 2011: 1329			Total VHA patients 4,544,353 (2002), 5,795,165 (2011)	2002: 12.5 2011: 22.9			
Esteva et al. 2006	Andalucía, Spain, 1999-2004	GID diagnosis	Regional Gender Identity Disorder Unit		243	148	Regional Population: 2,359,223 males and 2,276,923 females*		10.3	6.5	1.64:1
Gomez-Gil et al. 2006	Catalonia, Spain, 1996-2004	ICD-10 F64.0 (transsexualism)	Psychiatric and Psychology Institute at the Barcelona Hospital, 1996-2004		Catalonia: 113	Catalonia: 48	Catalonia: 2,376,538 males 2,308,611 females Barcelona: 1,996,708 males 1,776,269 females)	Catalonia: 4.8	Catalonia: 2.1		2.6:1
Barcelona: 100								Barcelona: 5.5	Barcelona: 2.5		
Hoening and Kenna, 1974	England and Wales, 1958-1968	GID	Royal Infirmary Manchester at the University Department of Psychiatry,	66	49	17	Manchester population June 30th 1970: 3,498,700 (1,652,000 Males 1,846,700 Females)	1.9	2.9	0.9	3.25:1

Judge et al. 2014	Ireland, 2005-2014	GID, DSM-IV/V	GD Clinic Referrals 2005-2014	218		2011 Census Reports: total 3,205,882*	6.8	9.88	3.6	2.7:1
Kauth et al. 2014	VA system, US, 2006-2013	GID diagnosis ICD-9 codes 302.85, 302.6, 302.5	Confirmed GID diagnosis VHA, FY 2006-2013	2567		VHA Enrollees 7,809,269		32.9		
O'Gorman et al. 1982	Northern Ireland, dates not specified	GID	Clinic based, over 14 years	28	21	7 Northern Ireland Population 1,500,000**	1.9			3:1
Okabe et al. 2008	Japan, April 1997- October 2005	GID, DSM-IV	GID Clinic-Okayama University Hospital	579	349	230 Inhabitants of Western Japan, Estimated at 40,000,000**		0.9		1.5:1
Ross, MW et al. 1981	Australia, 1976-1978	Transsexual	Questionnaires to registered psychiatrists	243	209	34 Australia's population on June 31, 1978 10,616,188*	2.4	4.2	0.7	6.1:1
Walinder, et al. 1968	Sweden, as of 1965	GID	Survey of psychiatrists	110		Not stated 6,272,886*	1.9	2.7	1.0	2.5:1
Wilson, et al. 1999	Scotland, 1998	GD	Questionnaires to general medical practices	273	218	55 Registered patients over 15 years of age 3,336,261 (1622,090 Males 1,714, 171 Females)	8.2	13.4	3.2	4:1

*Denominator calculated from the numerator from the reported prevalence **Prevalence calculated using total population as the denominator

Table 3: Prevalence of self-reported transgender status and gender non-conformity

Author	Location	Case	Source	Numerator			Source and size of Denominator	Prevalence (per 100,000)			Ratio
	Time Period	Definition	Numerator	Total	MTF	FTM		Overall	MTF	FTM	MTF:FTM
Conron, et al. 2011	Massachusetts, US, 2007-2009	Self-identify as transgender	Massachusetts Behavioral Risk Factor Surveillance Survey 2007-2009	131			28,176	500			
Kuyper and Wijsen, 2014	Netherlands, 2013	Incongruent gender identity	Sexual Health Survey		48	16	8,064		600	200	3:1
Gates, 2014	US	Self-identify as transgender	Massachusetts Behavioral Risk Factor Surveillance Survey in 2007-2009, 2003 CA LGBT Tobacco Survey					300			
Van Caenegem, et al. 2015	Flanders, Belgium, 2011-2012	Incongruent gender identity	Sexual Health Survey		7	6	1,799		700	600	1.2:1

Table 4: Meta-Analysis Prevalence Estimates of receipt or requests to receive gender confirmation therapy

All Studies (n=9)	Estimate	95% CI	I-Square	P for Heterogeneity
Total	13.0	(0.4, 24.7)	100%	<0.01
MTF	19.0	(9.1, 27.0)	100%	<0.01
FTM	7.1	(3.6, 10.8)	100%	<0.01
Stratified By Publication Type				
Peer Reviewed Publications				
Total	9.2	(4.9, 13.6)	99.90%	<0.01
MTF	12.5	(7.0, 17.9)	99.60%	<0.01
FTM	5.1	(2.6, 7.6)	99.30%	<0.01
Non-Peer Reviewed Publications				
Total	-	-	-	-
MTF	26.8	(.0, 57.7)	100%	<0.01
FTM	12.1	(0, 35.4)	100%	<0.01

Table 5: Meta-Analysis Prevalence Estimates of Transgender Specific Diagnoses

All				
Studies	Estimate	95% CI	I-Square	P for Heterogeneity
Total	6.7	(4.5, 9.0)	100%	<0.01
MTF	5.8	(3.5, 8.1)	99%	<0.01
FTM	2.5	(1.9, 3.1)	98%	<0.01
Drop VHA Study Data				
Total	4.1	(2.8, 5.5)	99.2%	<0.01

Table 6: Meta-Analysis Prevalence Estimates of Gender Non-Conformity

All Studies	Estimate	95% CI	I-Square	P for Heterogeneity
Total	452.7	(380.7, 524.8)	0%	0.59
MTF	607.7	(371.0, 844.4)	0%	0.86
FTM	220.6	(58.5, 382.7)	1%	0.32