Journal of Autism and Developmental Disorders
https://doi.org/10.1007/s10803-019-04298-1

ORIGINAL PAPER

Prevalence of Autism Spectrum Disorder and Attention-Deficit Hyperactivity Disorder Amongst Individuals with Gender Dysphoria: A Systematic Review

Emily Thrower[1] · Ingrid Bretherton[1] · Ken C. Pang[2,3,4] · Jeffrey D. Zajac[1] · Ada S. Cheung[1]

Abstract
Autism spectrum disorders (ASD) and attention-deficit hyperactivity disorder (ADHD) can compromise health and may be more prevalent amongst individuals with gender dysphoria (GD). Symptoms such as attention or social difficulties can impact assessment of GD, understanding of health information, and engagement in clinical care. To ensure neurodevelopmental conditions are adequately considered in gender health services, we aimed to systematically review the literature examining the prevalence of ASD and ADHD amongst individuals with GD. In this systematic review based on the PRISMA guidelines. MEDLINE and PsycINFO databases were searched for studies examining the prevalence of ASD and/or ADHD in individuals with GD or investigated the rate of GD in cohorts with ASD or ADHD. All English peer-reviewed publications were included. The search strategy identified 179 studies. After applying exclusion criteria, a total of 30 studies were identified, 22 studies which examined the prevalence of ASD or ADHD in people with GD. A further 8 studies examined the reverse; prevalence of GD in people with ASD. The few studies employing diagnostic criteria for ASD suggest a prevalence of 6–26% in transgender populations, higher than the general population, but no different from individuals attending psychiatry clinics. Few studies examine prevalence of ADHD. Low-level evidence exists to suggest a link between ASD and GD. Further population-based and controlled studies using diagnostic criteria for ASD and ADHD are required.

Keywords Transgender persons · Gender dysphoria · Attention-deficit hyperactivity disorder · Autism disorders

Introduction

Transgender healthcare services are in higher global demand than ever before (Cheung et al. 2018; Delahunt et al. 2018). In response, gender health services are swiftly expanding and being redesigned. This development presents a critical opportunity to tailor health care provision to specific health needs and alleviate the significant mental health burden associated with gender dysphoria (GD). Compelling evidence indicates a high prevalence of depression and anxiety amongst individuals with GD (Heylens et al. 2014; Reisner et al. 2015, 2016); furthermore, neurodevelopmental conditions such as autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) may well be more common in transgender individuals (Dawson et al. 2017; Gunter Heylens et al. 2018; Jones et al. 2012; Pasterski et al. 2014).

Both ASD and ADHD can severely compromise health and wellbeing, particularly if left undiagnosed (Ebejer et al. 2012; Simonoff et al. 2008). Symptoms such as attention difficulties, deficits in communication and social skills, obsessional interests, and stereotyped behaviour can significantly impact assessment of GD, understanding of health information, and engagement in clinical care (American Psychiatric Association 2013).

There is a widely held opinion of clinicians that there is an over-representation of neurodevelopmental conditions amongst individuals with GD and when the evidence to

✉ Ada S. Cheung
adac@unimelb.edu.au

1 Department of Medicine (Austin Health), The University of Melbourne, Studley Road, Heidelberg, VIC, Australia

2 Department of Adolescent Medicine, Royal Children's Hospital, Parkville, VIC, Australia

3 Murdoch Children's Research Institute, Parkville, VIC, Australia

4 Department of Paediatrics, The University of Melbourne, Parkville, VIC, Australia

Published online: 15 November 2019

support this belief was questioned in a recent essay, vigorous debate ensued (Strang et al. 2018; Turban and van Schalkwyk 2018b; van der Miesen et al. 2018a). As such, we sought to review the updated evidence to investigate the prevalence of ASD and additionally for ADHD amongst individuals with GD in order to ensure such conditions are adequately considered in the unfolding design of gender health services and to better serve our patients.

Methods

Preferred reporting items for systematic review and meta-analysis (PRISMA) reporting guidelines were used in the development of this systematic review (Liberati et al. 2009).

Eligibility Criteria

All levels of evidence were included in this review, provided that the report was published in a peer-reviewed journal and in the English language. Qualitative studies and case reports were excluded as prevalence data were not able to be obtained.

Information Sources and Search Strategy

The first author consulted an expert reference librarian to design and conduct the electronic database search with input from the last author. Eligible studies were identified by searching the electronic databases Ovid MEDLINE® and Ovid PsycINFO® from inception to 30th September 2019. Controlled vocabulary supplemented with keywords were used to define the population (transgender individuals), and outcome of interest (autism spectrum disorder, Aspergers syndrome or attention deficit hyperactivity disorder).

Relevant papers were elicited by searching article titles and abstracts for transgender terms (*transgender, gender dysphori*, transsexual*, gender identity disorder*) combined with relevant neurodevelopmental terms (*autism spectrum disorder, autism, Aspergers syndrome, adhd, attention deficit hyperactivity disorder*) using the Boolean OR and AND operators. Inclusion criteria were studies assessing incidence of autistic traits, ASD, or ADHD amongst cohorts with GD. We also reviewed the reverse, GD in cohorts of individuals with ASD and/or ADHD. As original prevalence data could not be inferred from papers not in English, review articles, and case reports, these were excluded. A search of reference lists for articles pertaining to the topic elicited five further articles. In total, 30 studies were identified. A flow diagram in Fig. 1 illustrates the search process.

Study Selection

Our full search strategy is outlined in Fig. 1.

Data Collection

Data was collected via an electronic form to capture the data items listed below.

Data Items

Participant Characteristics

Age, presence of GD, transgender, autism spectrum disorder or attention deficit hyperactivity disorder, birth-assigned sex, current gender identifier.

Study Characteristics

Method utilised (diagnostic vs. screening), recruitment method, sample size.

Control or Comparison Population

Age, recruitment method, birth-assigned sex, presence of psychiatric disorder.

Outcomes

Prevalence of ASD or ADHD in individuals with GD.

Statistical Results

Adjusted and unadjusted prevalence or incidence estimates, number of patients, age of patients.

Results

174 studies were identified using MEDLINE, and PsycINFO and 5 additional studies were identified from bibliographic references. 110 studies remained after duplicates were removed. After screening title and abstracts, 53 were removed due to lack of relevance, and 2 for being in a language other than English. When the full-text articles were reviewed for eligibility, studies which could not comment on prevalence were removed, including 9 case studies, 2

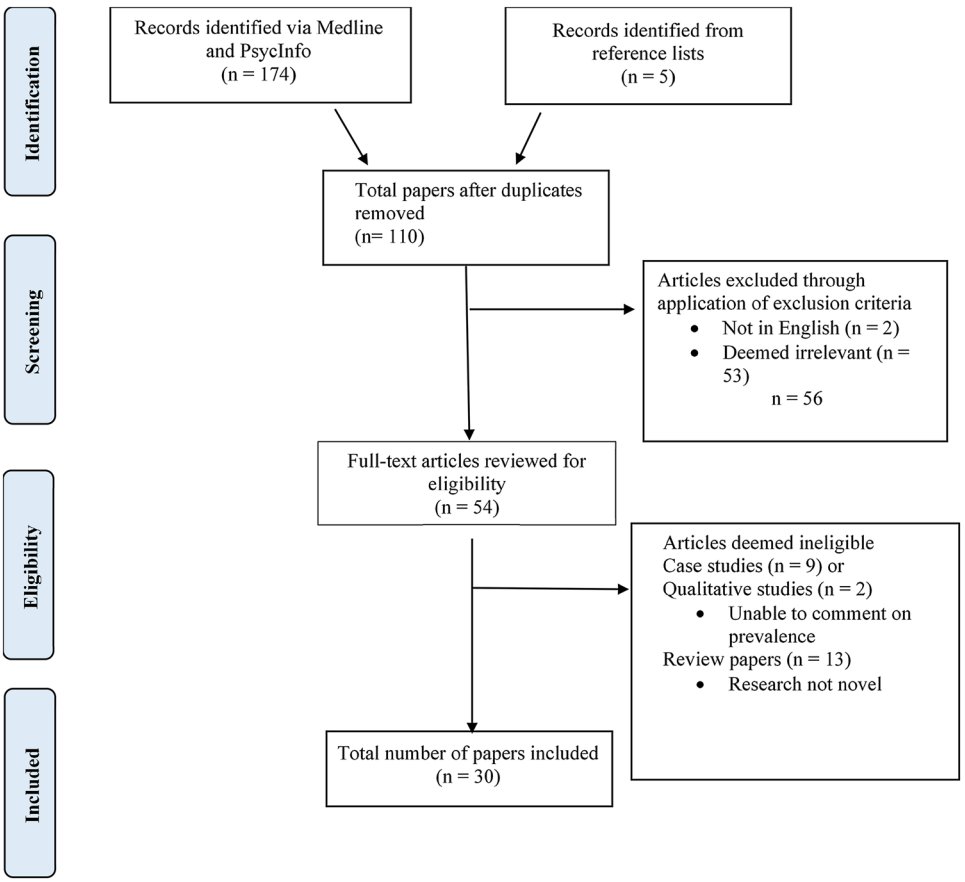

Fig. 1 Search process

qualitative studies, and 13 review papers. A summary of all the 30 identified remaining studies appears in Table 1.

Prevalence of ASD in Individuals with GD

Twenty-one of the identified papers described the prevalence of ASD, or autistic traits, within cohorts of individuals with GD. Table 1 groups studies according to age of study population, as this influences measures used by researchers and allows for ease of comparison. Prevalence ranged widely depending on the measures and cut-offs used. It is important to note that only 10 of the 21 papers included participants assessed using diagnostic measures. In a clinical chart review of 532 adults with GD, 6% had a prior diagnosis of ASD (Gunter Heylens et al. 2018). In children and adolescents referred to gender clinics, a cross-sectional analysis (n = 204) found 7.8% met diagnostic criteria for ASD (de Vries et al. 2010), and 13.3% had been diagnosed with ASD in a clinical chart review (n = 218) of children and adolescents attending a UK gender service (Holt et al. 2016). When measuring parameters such as social shortcomings, far higher rates of positive screening tests for ASD were observed; ranging from 6% to 68% (Table 1).

Prevalence of ADHD in Individuals with GD

Prevalence of ADHD has been assessed in four cross-sectional analyses (Cheung et al. 2018; Dawson et al. 2017; Holt et al. 2016; Kaltiala-Heino et al. 2015). A clinical chart review found that 8.3% of children and adolescents (n = 218) referred to a gender service had a prior diagnosis of ADHD (Holt et al. 2016). Amongst adults, in a convenience sample of 54 transgender adults participating in an online survey, 20.4% self-reported a prior diagnosis of ADHD (Dawson et al. 2017). More recently, a 2019 study reviewing electronic medical records revealed a prevalence rate of ADHD in 4.3% of transgender adults (Cheung et al. 2018).

GD in Individuals with ASD or ADHD

Whilst not the primary focus of the review, a summary of studies addressing the reverse; GD amongst individuals with neurodevelopmental conditions, is summarised in Table 1. Studies utilising screening tools demonstrated conflicting findings. Initial uncontrolled studies suggested that gender variance based on the parent-reported Child Behaviour Checklist comprising a single item 110 "wishes to be opposite sex" found that positive responses occurred up to 7–8 times more frequently in individuals with ASD compared

Table 1 Key papers

Study (first author, year)	Design	Groups	Type of measure	Measures	Relevant findings
Prevalence of autism spectrum disorder in individuals with gender dysphoria					
Adults					
Heylens (2018) (Gunter Heylens et al. 2018)	Cross-sectional analysis and retrospective analysis of clinical chart data	Adults with gender dysphoria or GID Cross-sectional analysis n = 63 Clinical chart data n = 532	Formal diagnosis and screening test	Social Responsiveness Scale—Adult version (SRS-A) Autism Quotient (AQ) Chart analysis for prior diagnosis of ASD	27.1% mild-severe social shortcomings 4.8% scored above cut-off for AQ 6% prior diagnosis of ASD
Pasterski (2014) (Pasterski et al. 2014)	Cross-sectional analysis	Adults with gender dysphoria or GID, n = 91	Screening test	AQ	5.5% above cut-off for AQ
Jones (2012) (Jones et al. 2012)	Cross-sectional analysis	Transgender adults: Trans men n = 61 Trans women n = 198 Typical adults n = 174 Adults with Asperger syndrome n = 125	Screening test	AQ	30% Medium or narrow autism phenotype in sample of trans men
Kristensen (2015) (Kristensen and Broome 2015)	Cross-sectional analysis	Adults with gender dysphoria n = 446	Formal diagnosis and screening test	Past diagnosis of ASC AQ-10	13% had a past diagnosis of ASC 39% of cohort scored ≥ 6/10 on the AQ
Fielding (2018) (Fielding and Bass 2018)	Retrospective case-cohort study	Adults referred to a gender clinic n = 153	Formal diagnosis	Question regarding previous formal diagnosis	7.8% reported past diagnosis of ASD
Mermaat (2018) (Vermaat et al. 2018)	Cross-sectional analysis	Adults referred to clinic for gender dysphoria n = 326 Typically developing adults n = 1316	Screening test	AQ	No difference in AQ between gender dysphoric and typically developing populations
Stagg (2019) (Stagg and Vincent 2019)	Cross-sectional analysis	Trans or non-binary adults n = 109 Cisgender adults n = 68	Formal diagnosis and screening	Past diagnosis of ASC	14% of transgender or nonbinary participants had past diagnosis of ASC, cf. 4% cisgender participants
Nobili (2018) (Nobili et al. 2018)	Cross-sectional analysis	Transgender adults n = 656 Matched cisgender controls n = 656	Screening test	AQ short	45% of participants 'assigned female at birth' in the transgender group scored above the cut-off of ≥ 70, cf. 30% of AFAB in the cisgender group
Children and adolescent cohorts					
de Vries (2010) (de Vries et al. 2010)	Cross-sectional analysis	Children and adolescents referred to a gender clinic n = 204	Formal diagnosis	Diagnostic Interview for Social and Communication Disorders 10th revision (DISCO-10)	7.8% ASD

Table 1 (continued)

Study (first author, year)	Design	Groups	Type of measure	Measures	Relevant findings
Shumer (2016) (Shumer et al. 2016)	Retrospective cross-sectional analysis of clinical chart data	Youth aged 8-20 years old presenting to a gender clinic n = 39	Screening test	Review of charts for past application of Asperger Syndrome Diagnostic Scale (ASDS) a screening tool for ASD.	23.1% possible (n = 1), likely (n = 6) or very likely (n = 2) Asperger Syndrome
Skagerberg (2015) (Skagerberg et al. 2015)	Cross-sectional analysis and retrospective analysis of clinical chart data	Young people with gender dysphoria attending a gender clinic n = 166	Screening test	SRS	54.2% in mild/moderate or severe range for social shortcomings
VanderLaan (2015)—1 (VanderLaan et al. 2015)	Cross-sectional analysis	Children with gender dysphoria, n = 49	Screening test	SRS	44.9% in clinical range for autism
VanderLaan (2015)—2 (VanderLaan et al. 2015)	Cross-sectional analysis	Children referred to a gender clinic n = 534 Gender-clinic referred children's siblings n = 419 Clinic-referred and non-clinic referred children n = 1201	Screening test	Teacher's Report Form items 9 and 66	Item 9 elevated compared to participants' siblings Item 66 elevated compared to non-referred children, not compared to clinic-referred children
Zucker (2017) (Zucker et al. 2017)	Cross-sectional analysis and cross-validation study with VanderLaan (2015a, b)—2	Children referred to a gender clinic n = 386 Children referred to psychiatric clinic n = 965 Non-referred children n = 965	Screening test	Teacher's Report Form items 9 and 66, assessing obsessional interests and compulsions	Item 9 significantly endorsed compared to control and psych-referred samples Item 66 elevated compared to control, but not relative to children referred to psychiatric facilities
Akgul (2018) (Akgul et al. 2018)	Cross-sectional analysis	Children and adolescents with gender dysphoria n = 25 Typically-developing (TD) children and adolescents n = 50	Screening test	Social Responsiveness Scale (SRS) Behaviour Rating Inventory of Executive Function	68% in mild-severe range for social shortcomings in transgender sample Significantly higher BRIEF global scores compared to control group
Van der Miesen (2017) (van der Miesen et al. 2017)	Cross-sectional analysis	Children with gender dysphoria n = 490 Children with ASD n = 196 TD children n = 2507	Screening test	Children's Social Behaviour Questionnaire	Higher rates of autistic traits on all domains for children with gender dysphoria compared to TD children
Nahata et al. (2017) (Nahata et al. 2017)	Retrospective cross-sectional analysis of clinical chart data	Children and adolescents identifying as transgender (n = 79)	Formal diagnosis	Review of clinical chart data for previous diagnosis of ASD	Previous diagnosis of ASD in 5% of the sample
Leef (2019) (Leef et al. 2019)	Cross-sectional analysis	Children referred for gender dysphoria n = 61 Children referred for other clinical concerns n = 40	Formal diagnosis	Medical record review	Of the children referred for gender dysphoria, 21.3% had a former clinical diagnosis of ASD

Table 1 (continued)

Study (first author, year)	Design	Groups	Type of measure	Measures	Relevant findings
Prevalence of ADHD and gender dysphoria					
Holt (2016) (Holt et al. 2016)	Retrospective cross-sectional analysis of clinical chart data	Children and adolescents referred to a gender clinic n = 218	Formal diagnosis	Review of clinical chart data, referral letters and reports for past diagnosis of Autism Spectrum Conditions (ASC) and/or ADHD	ASC present in 13.3% ADHD present in 8.3%
Dawson (2017) (Dawson et al. 2017)	Cross-sectional analysis	Adults identifying as transgender, n = 54 Total sample n = 6727	Formal diagnosis	Question relating to history of diagnosis of ADHD	Past diagnosis of ADHD in 20.4% of participants
Kaltiala-Heino (2015) (Kaltiala-Heino et al. 2015)	Retrospective cross-sectional analysis and qualitative analysis of clinical chart data	Adolescents attending an adolescent gender identity service for sex reassignment therapy n = 47	Formal diagnosis	Review of participant clinical data for past diagnosis of ASD or ADHD	ASD had been diagnosed in 26% of participants ADHD had been diagnosed in 11% of participants
Cheung (2018) (Cheung et al. 2018)	Cross-sectional analysis	Transgender adults n = 540	Formal diagnosis	Review of electronic medical records	4.8% had past diagnosis of ASC 4.3% had past diagnosis of ADHD
Gender dysphoria in cohorts with diagnosed ASD or ADHD					
Strang (2014) (Strang et al. 2014)	Retrospective cross-sectional analysis of clinical chart data	Children referred with: ASD n = 147 ADHD n = 126 Medical neurodevelopmental disorder n = 116 Control sample n = 165 Non-referred children from CBCL sample n = 1605	Screening test	Child Behaviour Checklist (CBCL) item 110: "Wishes to be opposite sex" to assess gender variance	Participants with ASD were 7.59 times more likely to express gender variance than the non-referred group. Participants with ADHD were 6.64 times more likely to express gender variance than the non-referred group.
George (2017) (George and Stokes 2017)	Cross-sectional analysis	Adults with ASD n = 310 TD individuals n = 261	Screening test	Gender-Identity/Gender-Dysphoria Questionnaire	Rates of gender dysphoria significantly higher in individuals with ASD
May (2017) (May et al. 2017)	Cross-sectional analysis	Children and adolescents with ASD n = 176 Children referred to psychiatric clinics n = 1605 Non-referred children n = 1605	Screening test	Child Behaviour Checklist item 110	4.0% of participants with ASD had gender variance, similar to the referred group

Table 1 (continued)

Study (first author, year)	Design	Groups	Type of measure	Measures	Relevant findings
Janssen (2016) (Janssen et al. 2016)	Retrospective cross-sectional analysis of clinical chart data	Children and adolescents with ASD n = 492 Non-referred children and adolescents n = 1605	Screening test	Child Behaviour Checklist item 110	Participants with ASD were 7.76 times more likely to report gender variance
Dewinter et al. (2017)	Cross-sectional analysis	Adolescents and adults with ASD (n = 675) Control (n = 8064)	Screening test	Questions relating to gender identity	<1% of individuals in the ASD group identified as the sex opposite to that assigned to them at birth 22% of women and 8% of men in the ASD group reported gender non-conforming feelings
Van der Miesen (2018) (van der Miesen et al. 2018b)	Cross-sectional analysis	Adolescents (n = 573) and adults (n = 807) with ASD Adolescents (n = 1016) and adults (n = 846) from the general population	Screening test	Youth Self-Report (item 110 – Wish to be of opposite gender) Adult Self-Report (item 110 as above)	6.5% of adolescents with ASD endorsed item 110 cf. 3.1% of controls 11.4% of adults with ASD endorsed item 110, cf. 5.0% of controls
Walsh (2018) (Walsh et al. 2018)	Cross-sectional analysis	Adults and children with autism n = 669	Formal diagnosis and screening test	Gender identity question	15% of participants self-identified as trans or non-binary
Hisle-Gorman (2019) (Hisle-Gorman et al. 2019)	Retrospective case-cohort study	Children with ASD n = 48,762 Children without ASD n = 243,810	Formal diagnosis	ICD-9 criteria for ASD, GD and related conditions	Children with ASD were over four times as likely to be diagnosed with a condition indicating gender dysphoria

to the general population (Janssen et al. 2016; Strang et al. 2014). However, when compared to children and adolescents referred to clinical services for other mental health concerns, there was no difference in positive responses to item 110 (May et al. 2017). The most definitive findings come from a recent large retrospective case-controlled study of 48,762 children with previously diagnosed ASD matched to 243,810 children without ASD. Based on ICD-9 diagnostic criteria, children with ASD were over four times as likely to be diagnosed with GD (Hisle-Gorman et al. 2019).

Discussion

This is the first systematic review assessing the prevalence of ASD and ADHD in transgender individuals and it demonstrates a paucity of data. The few studies employing diagnostic criteria for ASD suggest a prevalence of 6–26% in people with GD but there are no adequately controlled studies. There are a lack of studies examining prevalence of ADHD. Prevalence of autistic traits identified on screening tools are significantly overestimated amongst transgender populations and unreliable. Further population-based and controlled studies using diagnostic criteria for ASD and ADHD are required.

Prevalence of Autism Spectrum Disorder in Individuals with GD

Whilst many clinicians argue that there is a clear increased prevalence of ASD amongst people with GD, to-date, this has not been based on robust evidence, with existing studies utilising screening tools, self-report, retrospective chart review, and importantly, a lack of control groups (Turban and van Schalkwyk 2018a). The international gold standard for diagnosis of ASD, in contrast, specifies application of diagnostic criteria and rigorous examination including parental interview with developmental history, child observation, and thorough physical examination including hearing assessment (Taylor et al. 2016), hence the findings of studies using ASD screening tools must be viewed with caution.

Adult Cohorts

Of the 21 papers reviewed, seven studies utilised a diagnostic measure (clinical chart review for past diagnoses of ASD) and amongst adults with gender dysphoria found ASD prevalence rates of 4.8–13% (Cheung et al. 2018; Fielding and Bass 2018; Gunter Heylens et al. 2018; Holt et al. 2016; Kaltiala-Heino et al. 2015; Kristensen and Broome 2015; Stagg and Vincent 2019).

Many more studies however, utilised a popular screening test for ASD, the Autism Quotient (AQ), a 50-question self-reported measure (Booth et al. 2013; Kristensen and Broome 2015). The AQ was most commonly analysed as a dichotomous scoring system, where a grade of 32 or higher classified an individual as having autistic traits, providing sensitivity and specificity of 76.71% and 74.07%, respectively (Woodbury-Smith et al. 2005). Based on this cut-off, the prevalence of autistic traits in three studies ranged from 2.1 to 5.5% in people with GD (Gunter Heylens et al. 2018; Pasterski et al. 2014; Vermaat et al. 2018). Findings are certainly not consistent with a recent cross-sectional analysis of 109 trans or non-binary adults which found that 28% surpassed the AQ cut-off of > 32 (Stagg and Vincent 2019), yet other cross-sectional analyses have found no significant difference in AQ results in adults referred to a clinic for GD compared with typically developing adults (Nobili et al. 2018; Vermaat et al. 2018). This clearly highlights significant limitations and lack of utility in the use of AQ as a screening tool amongst people with GD.

These disparate prevalence rates confirm that results depend very much upon methodology and test sensitivity and specificity. The absolute reliability of prevalence rates established from such screening tests is far from conclusive however most tend to suggest a likely higher prevalence of ASD amongst individuals with GD. It is also worth noting that most of the earlier published literature associating ASD and GD takes the form of case reports, in which no inference regarding prevalence can be made (Kraemer et al. 2005; Landen and Rasmussen 1997; Lemaire et al. 2014; Tateno et al. 2015; Williams et al. 1996).

Children and Adolescent Cohorts

Data relating to children and adolescents is more abundant than that available for adults. Three studies conducted medical record reviews to examine past diagnosis of ASD in their cohorts, with variable results ranging from 5 to 26% of children and adolescents referred to a gender clinic (Kaltiala-Heino et al. 2015; Leef et al. 2019; Nahata et al. 2017). The most reliable study used clinical assessment and the Diagnostic Interview for Social and Communication Disorders version 10 (DISCO-10) to identify diagnoses of ASD in 204 children and adolescents referred to a gender clinic in the Netherlands (de Vries et al. 2010). Notably, not all children referred to gender clinics are diagnosed with GD and a confirmed diagnosis of GD was made in 63.2%. Of these confirmed cases, 4.7% were diagnosed with concurrent ASD, 26% were diagnosed with 'subthreshold GD not otherwise specified', and 17.0% were diagnosed with ASD alone. The overall incidence of ASD in this sample was 7.8% and is likely a better representation of the true prevalence compared to medical record reviews. No diagnoses of ASD were made in the cisgender children who comprised 10.8% of those referred to the clinic. This study highlights

considerable overlap between symptoms of ASD and symptoms of gender variance, exemplified by the subthreshold group which may display symptoms which could be interpreted as either ASD or gender variance.

Overlap between symptoms of ASD and symptoms of GD may well confound results. The majority of evidence available for review here is based on cross-sectional studies employing screening tools which lack specificity and are not validated for diagnosis of ASD without additional clinical evaluation. A study by Shumer et al. (2016) found that 23.1% of their cohort of children and adolescents referred to a gender clinic had possible, likely or very likely Asperger Syndrome, based on a parent-completed Asperger Syndrome Diagnostic Scale (ASDS), but they also acknowledged that several questions on the ASDS they utilised to assess ASD symptoms may be confounded by symptoms of GD (Shumer et al. 2016).

It is even less clear when indirect symptoms of autism, such as social skills, cognitive function and obsessional interests are used as screening tools (Skagerberg et al. 2015; VanderLaan et al. 2015a, b; Zucker et al. 2017). The Social Responsiveness Scale (SRS), a screening tool originally used to measure communication and social skill deficits in children, suggests that 45% to 68% of young people with GD have autistic symptoms based on criteria including 'has difficulty relating to peers' (Akgul et al. 2018; Skagerberg et al. 2015; VanderLaan et al. 2015). The SRS has not been validated for use in those with GD and, as deficits in social reciprocity and communication occur in depression and GD (i.e. due to fear of stigma or discrimination), it lacks sensitivity (Moul et al. 2015; Pine et al. 2008; Turban 2018). Executive function tasks, such as planning, decision-making, and memory, which can be compromised in people with ASD, are also not assessed with the SRS (Leung et al. 2016). Akgul et al. (2018) examined both social skills and an indirect measure of executive function using the SRS and the Behavior Rating Inventory of Executive Function (BRIEF) questionnaire respectively (Akgul et al. 2018). Whilst lower executive function in children with GD compared to matched controls was found, given the limitations of the tools, inferences are limited and comprehensive clinical assessment would be more useful.

In addition to compromised social skills and executive function, autism associated obsessional interests may potentially result in a misdiagnosis of autism if an individual demonstrates a strong interest in gendered items associated with the opposite sex (Parkinson 2016; Tateno et al. 2008; Williams et al. 1996). Two studies employed two items from the Child Behavior Checklist (CBCL), a well-validated parent-report questionnaire of behaviour problems designed to assess obsessions (for example, Item 9: 'Can't get his/her mind over certain thoughts') and compulsions (for example, Item 66: 'Repeats certain acts over and over') in children referred to gender clinics. The studies observed that while obsessional interests were certainly higher in children referred to gender clinics compared to a control population, notably, increased levels of compulsions were evident in both children referred to gender clinics and children referred for psychiatric services in general (VanderLaan et al. 2015; Zucker et al. 2017). There is likely an over-representation of autistic symptoms in children and adolescents with GD when compared with healthy control populations (van der Miesen et al. 2017) highlighting limited utility of using such tools to assess ASD in people with gender variance. Furthermore, there may have been a selection bias in previous studies assessing individuals attending gender clinics. Not only may individuals who attend clinics not necessarily have GD, individuals who do have impaired social functioning may be unable to communicate their feelings of GD effectively enough to seek treatment. Further studies utilising diagnostic criteria on differentiating low functioning and high functioning autism in the population with GD are needed.

Prevalence of ADHD and GD

Four studies—two in adult cohorts, and two in paediatric cohorts—suggest a higher prevalence of ADHD amongst people with GD (Cheung et al. 2018; Dawson et al. 2017; Holt et al. 2016; Kaltiala-Heino et al. 2015). A retrospective chart review of a UK paediatric gender clinic found a prevalence of ASD in 13.3% and ADHD in 8.3% of their cohort, both at least five times that of UK general population rates, while a similar study in Finland reported prevalence of 26% and 11% for ASD and ADHD respectively (Holt et al. 2016; Kaltiala-Heino et al. 2015; Russell et al. 2014). Co-occurrence of ASD and ADHD was not reported in either study. In the adult literature, a convenience sample from a paid online survey found that of 6727 participants, 54 identified as transgender, with 20.4% of these 54 individuals receiving a previous diagnosis of ADHD (Dawson et al. 2017). Notably, there were multiple limitations: self-reported diagnoses, a bias towards young internet users, and, as birth-assigned sex was not asked, the sample captured is unlikely to be representative of transgender cohorts (Dawson et al. 2017). A recent Australian study in 540 transgender adults reported past diagnosis of ADHD in 4.3% of participants, and was limited by similar issues (Cheung et al. 2018). Potentially, misdiagnoses of ADHD may also be a contributing factor to high rates of ADHD in this sample. Gender non-conforming youth often present with externalising behaviours (Coleman et al. 2012) and symptoms such as attention deficit, impulsivity, and hyperactivity may be explained in part by ASD rather than ADHD, even though distinguishing the two diagnoses is usually achievable (Dickerson Mayes et al. 2012). While there may be some overlap in symptoms of GD, ASD and ADHD, the rates of ADHD in both paediatric and adult

populations was found to be elevated relative to the general population, hence further research is warranted to establish the true rates of these conditions in transgender individuals.

GD in Cohorts with Suspected or Confirmed ASD or ADHD

When examining autistic traits in individuals with GD, a small number studied the reverse—prevalence of GD or gender variance in individuals with ASD (Dewinter et al. 2017; George and Stokes 2017; Hisle-Gorman et al. 2019; Janssen et al. 2016; May et al. 2017; Strang et al. 2014; van der Miesen et al. 2018b; Walsh et al. 2018). Recently, the largest controlled study involving over 48,000 children with ASD, each matched to five controls, found that children with ASD were over four times as likely to be diagnosed with a condition indicating GD as per the ICD-9, illustrating a clear overrepresentation of GD in the ASD population (Hisle-Gorman et al. 2019). This is the most compelling evidence to date that there is a higher prevalence of GD in those with ASD.

Conclusions

Though evidence suggesting that ASD and ADHD are more prevalent in the transgender community exists, it is of low quality. Retrospective clinical chart reviews assessing formal diagnoses of ASD or ADHD represent the best evidence, but no adequately controlled studies utilise diagnostic criteria. Screening tests cannot be reliably used to determine prevalence of ASD or ADHD. With some overlapping symptoms, the potential for misdiagnosis is possible and any diagnostic tests for ASD and ADHD will need to be validated for use in the transgender population. From a practical clinical perspective for individuals who do have concurrent GD and ASD, guidelines have recently been published highlighting a need for potential extended assessment and decision-making periods (Strang et al. 2018). Most importantly, a diagnosis of ASD should not exclude people from gender-related medical supports. People with neurodevelopmental conditions and GD should be supported in the strengths of neurodiversity and gender diversity and reassured that these conditions do not preclude any forms of affirmative clinical care (Turban and van Schalkwyk 2018b). Further rigorously-designed research examining the prevalence of these conditions amongst people with GD is required to correct the dearth of literature on the topic. Until then, individualised treatment and design of health care services for transgender individuals should consider assessment for, and management of, both ASD and ADHD in their protocols for gender-affirming care.

Acknowledgments Ada Cheung is supported by an Australian Government National Health and Medical Research Council Early Career Fellowship (#1143333) and receives research support from the Viertel Charitable Foundation Clinical Investigator Award, Endocrine Society of Australia Postdoctoral Award and the Royal Australasian College of Physicians Vincent Fairfax Family Foundation. Ken Pang is supported by the Royal Children's Hospital Foundation and receives research support from the Royal Australasian College of Physicians.

Author Contributions ET, IB, KCP, JDZ, and ASC made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data; drafted the work or revised it critically for important intellectual content; approved the version to be published; and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Compliance with Ethical Standards

Conflict of interest The authors have nothing to declare.

References

Akgul, G. Y., Ayaz, A. B., Yildirim, B., & Perdahli Fis, N. (2018). Autistic traits and executive functions in children and adolescents with gender dysphoria. *Journal of Sex and Marital Therapy, 44,* 619.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: American Psychiatric Association.

Booth, T., Murray, A. L., McKenzie, K., Kuenssberg, R., O'Donnell, M., & Burnett, H. (2013). Brief report: An evaluation of the AQ-10 as a brief screening instrument for ASD in adults. *Journal of Autism and Developmental Disorders, 43*(12), 2997–3000. https://doi.org/10.1007/s10803-013-1844-5.

Cheung, A. S., Ooi, O., Leemaqz, S., Cundill, P., Silberstein, N., Bretherton, I., et al. (2018). Sociodemographic and clinical characteristics of transgender adults in Australia. *Transgender Health, 3*(1), 229–238.

Coleman, E., Bockting, W., Botzer, M., Cohen-Kettenis, P., DeCuypere, G., Feldman, J., et al. (2012). Standards of care for the health of trans-sexual, transgender, and gender-nonconforming people, version 7. *International Journal of Transgenderism, 13,* 165–232.

Dawson, A. E., Wymbs, B. T., Gidycz, C. A., Pride, M., & Figueroa, W. (2017). Exploring rates of transgender individuals and mental health concerns in an online sample. *International Journal of Transgenderism, 18*(3), 295–304.

de Vries, A. L., Noens, I. L., Cohen-Kettenis, P. T., van Berckelaer-Onnes, I. A., & Doreleijers, T. A. (2010). Autism spectrum disorders in gender dysphoric children and adolescents. *Journal of Autism and Developmental Disorders, 40*(8), 930–936.

Delahunt, J. W., Denison, H. J., Sim, D. A., Bullock, J. J., & Krebs, J. D. (2018). Increasing rates of people identifying as transgender presenting to endocrine services in the Wellington region. *New Zealand Medical Journal, 131*(1468), 33–42.

Dewinter, J., De Graaf, H., & Begeer, S. (2017). Sexual orientation, gender identity, and romantic relationships in adolescents and adults with autism spectrum disorder. *Journal of Autism and Developmental Disorders, 47*(9), 2927–2934. https://doi.org/10.1007/s10803-017-3199-9.

Dickerson Mayes, S., Calhoun, S. L., Mayes, R. D., & Molitoris, S. (2012). Autism and ADHD: Overlapping and discriminating symptoms. *Research in Autism Spectrum Disorders, 6*(1), 277–285.

Ebejer, J. L., Medland, S. E., van der Werf, J., Gondro, C., Henders, A. K., Lynskey, M., et al. (2012). Attention deficit hyperactivity disorder in australian adults: Prevalence, persistence, conduct problems and disadvantage. *PLoS ONE, 7*(10), e47404. https://doi.org/10.1371/journal.pone.0047404.

Fielding, J., & Bass, C. (2018). Individuals seeking gender reassignment: Marked increase in demand for services. *Bjpsych Bulletin, 42*(5), 206–210.

George, R., & Stokes, M. A. (2017). Gender identity and sexual orientation in autism spectrum disorder. *Autism*. https://doi.org/10.1177/1362361317714587.

Heylens, G., Aspeslagh, L., Dierickx, J., Baetens, K., Van Hoorde, B., De Cuypere, G., et al. (2018). The co-occurrence of gender dysphoria and autism spectrum disorder in adults: An analysis of cross-sectional and clinical chart data. *Journal of Autism and Developmental Disorders, 48,* 2217–2223.

Heylens, G., Elaut, E., Kreukels, B. P., Paap, M. C., Cerwenka, S., Richter-Appelt, H., et al. (2014). Psychiatric characteristics in transsexual individuals: Multicentre study in four European countries. *British Journal of Psychiatry, 204*(2), 151–156.

Hisle-Gorman, E., Landis, C. A., Susi, A., Schvey, N. A., Gorman, G. H., Nylund, C. M., et al. (2019). Gender dysphoria in children with autism spectrum disorder. *LGBT Health, 6*(3), 95–100.

Holt, V., Skagerberg, E., & Dunsford, M. (2016). Young people with features of gender dysphoria: Demographics and associated difficulties. *Clinical Child Psychology and Psychiatry, 21*(1), 108–118. https://doi.org/10.1177/1359104514558431.

Janssen, A., Huang, H., & Duncan, C. (2016). Gender variance among youth with autism spectrum disorders: A retrospective chart review. *Transgender Health, 1*(1), 63–68.

Jones, R. M., Wheelwright, S., Farrell, K., Martin, E., Green, R., Di Ceglie, D., et al. (2012). Brief report: Female-to-male transsexual people and autistic traits. *Journal of Autism and Developmental Disorders, 42*(2), 301–306.

Kaltiala-Heino, R., Sumia, M., Työläjärvi, M., & Lindberg, N. (2015). Two years of gender identity service for minors: Overrepresentation of natal girls with severe problems in adolescent development. *Child and Adolescent Psychiatry and Mental Health, 9,* 9. https://doi.org/10.1186/s13034-015-0042-y.

Kraemer, B., Delsignore, A., Gundelfinger, R., Schnyder, U., & Hepp, U. (2005). Comorbidity of Asperger syndrome and gender identity disorder. *European Child and Adolescent Psychiatry, 14*(5), 292–296. https://doi.org/10.1007/s00787-005-0469-4.

Kristensen, Z. E., & Broome, M. R. (2015). Autistic traits in an internet sample of gender variant UK Adults. *International Journal of Transgenderism, 16*(4), 234–245. https://doi.org/10.1080/15532739.2015.1094436.

Landen, M., & Rasmussen, P. (1997). Gender identity disorder in a girl with autism: A case report. *European Child and Adolescent Psychiatry, 6*(3), 170–173.

Leef, J. H., Brian, J., VanderLaan, D. P., Wood, H., Scott, K., Lai, M.-C.,… Zucker, K. J. (2019). Traits of autism spectrum disorder in school-aged children with gender dysphoria: A comparison to clinical controls. *Clinical Practice in Pediatric Psychology*, No Pagination Specified

Lemaire, M., Thomazeau, B., & Bonnet-Brilhault, F. (2014). Gender identity disorder and autism spectrum disorder in a 23-year-old female. *Archives of Sexual Behavior, 43*(2), 395–398. https://doi.org/10.1007/s10508-013-0141-x.

Leung, R. C., Vogan, V. M., Powell, T. L., Anagnostou, E., & Taylor, M. J. (2016). The role of executive functions in social impairment in autism spectrum disorder. *Child Neuropsychology, 22*(3), 336–344. https://doi.org/10.1080/09297049.2015.1005066.

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gøtzsche, P. C., Ioannidis, J. P. A.,… Moher, D. (2009). The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: Explanation and elaboration. *BMJ (Clinical research ed.), 339*, b2700-b2700. https://doi.org/10.1136/bmj.b2700

May, T., Pang, K., & Williams, K. J. (2017). Gender variance in children and adolescents with autism spectrum disorder from the National Database for Autism Research. *International Journal of Transgenderism, 18*(1), 7–15.

Moul, C., Cauchi, A., Hawes, D. J., Brennan, J., & Dadds, M. R. (2015). Differentiating autism spectrum disorder and overlapping psychopathology with a brief version of the social responsiveness scale. *Child Psychiatry and Human Development, 46*(1), 108–117. https://doi.org/10.1007/s10578-014-0456-4.

Nahata, L., Quinn, G. P., Caltabellotta, N. M., & Tishelman, A. C. (2017). Mental health concerns and insurance denials among transgender adolescents. *LGBT Health, 4*(3), 188–193. https://doi.org/10.1089/lgbt.2016.0151.

Nobili, A., Glazebrook, C., Bouman, W. P., Glidden, D., Baron-Cohen, S., Allison, C.,… Arcelus, J. (2018). Autistic traits in treatment-seeking transgender adults. *Journal of Autism and Developmental Disorders, 48*(12), 3984-3994

Parkinson, J. (2016). Gender dysphoria and autism spectrum disorders: A note of caution. *LGBT Health, 3*(2), 175.

Pasterski, V., Gilligan, L., & Curtis, R. (2014). Traits of autism spectrum disorders in adults with gender dysphoria. *Archives of Sexual Behavior, 43*(2), 387–393.

Pine, D. S., Guyer, A. E., Goldwin, M., Towbin, K. A., & Leibenluft, E. (2008). Autism spectrum disorder scale scores in pediatric mood and anxiety disorders. *Journal of the American Academy of Child and Adolescent Psychiatry, 47*(6), 652–661. https://doi.org/10.1097/CHI.0b013e31816bffa5.

Reisner, S. L., Biello, K. B., White Hughto, J. M., Kuhns, L., Mayer, K. H., Garofalo, R., et al. (2016). Psychiatric diagnoses and comorbidities in a diverse, multicity cohort of young transgender women: Baseline findings from project lifeskills. *JAMA Pediatrics, 170*(5), 481–486.

Reisner, S. L., Vetters, R., Leclerc, M., Zaslow, S., Wolfrum, S., Shumer, D., et al. (2015). Mental health of transgender youth in care at an adolescent urban community health center: A matched retrospective cohort study. *Journal of Adolescent Health, 56*(3), 274–279.

Russell, G., Rodgers, L. R., Ukoumunne, O. C., & Ford, T. (2014). Prevalence of parent-reported ASD and ADHD in the UK: Findings from the Millennium Cohort Study. *Journal of Autism and Developmental Disorders, 44*(1), 31–40. https://doi.org/10.1007/s10803-013-1849-0.

Shumer, D. E., Reisner, S. L., Edwards-Leeper, L., & Tishelman, A. (2016). Evaluation of asperger syndrome in youth presenting to a gender dysphoria clinic. *LGBT Health, 3*(5), 387–390.

Simonoff, E., Pickles, A., Charman, T., Chandler, S., Loucas, T., & Baird, G. (2008). Psychiatric disorders in children with autism spectrum disorders: Prevalence, comorbidity, and associated factors in a population-derived sample. *Journal of the American Academy of Child and Adolescent Psychiatry, 47*(8), 921–929.

Skagerberg, E., Di Ceglie, D., & Carmichael, P. (2015). Brief report: Autistic features in children and adolescents with gender dysphoria. *Journal of Autism and Developmental Disorders, 45*(8), 2628–2632.

Stagg, S. D., & Vincent, J. (2019). Autistic traits in individuals self-defining as transgender or nonbinary. *European Psychiatry: The Journal of the Association of European Psychiatrists, 61,* 17–22.

Strang, J. F., Janssen, A., Tishelman, A., Leibowitz, S. F., Kenworthy, L., McGuire, J. K.,… Anthony, L. G. (2018). Revisiting the link: Evidence of the rates of autism in studies of gender diverse individuals. *J Am Acad Child Adolesc Psychiatry, 57*(11), 885-887. https://doi.org/10.1016/j.jaac.2018.04.023

Strang, J. F., Kenworthy, L., Dominska, A., Sokoloff, J., Kenealy, L. E., Berl, M.,… Wallace, G. L. (2014). Increased gender variance in autism spectrum disorders and attention deficit hyperactivity disorder. *Archives of Sexual Behavior, 43*(8), 1525-1533.

Strang, J. F., Meagher, H., Kenworthy, L., de Vries, A. L. C., Menvielle, E., Leibowitz, S.,… Anthony, L. G. (2018). Initial clinical guidelines for co-occurring autism spectrum disorder and gender dysphoria or incongruence in adolescents. *J Clin Child Adolesc Psychol, 47*(1), 105-115. https://doi.org/10.1080/15374416.2016.1228462

Tateno, M., Tateno, Y., & Saito, T. (2008). Comorbid childhood gender identity disorder in a boy with Asperger syndrome. *Psychiatry and Clinical Neurosciences, 62*(2), 238. https://doi.org/10.1111/j.1440-1819.2008.01761.x.

Tateno, M., Teo, A. R., & Tateno, Y. (2015). Eleven-year follow up of boy with Asperger's syndrome and comorbid gender identity disorder of childhood. *Psychiatry and Clinical Neurosciences, 69*(10), 658. https://doi.org/10.1111/pcn.12328.

Taylor, L. J., Eapen, V., Maybery, M. T., Midford, S., Paynter, J., Quarmby, L.,… Whitehouse, A. J. O. (2016). Diagnostic evaluation for autism spectrum disorder: A survey of health professionals in Australia. *BMJ Open, 6*(9), e012517. https://doi.org/10.1136/bmjopen-2016-012517

Turban, J. L. (2018). Potentially reversible social deficits among transgender youth. *Journal of Autism and Developmental Disorders, 48*(12), 4007–4009. https://doi.org/10.1007/s10803-018-3603-0.

Turban, J. L., & van Schalkwyk, G. I. (2018a). Drs. Turban and van Schalkwyk reply. *Journal of the American Academy of Child and Adolescent Psychiatry, 57*(11), 887–889. https://doi.org/10.1016/j.jaac.2018.07.881.

Turban, J. L., & van Schalkwyk, G. I. (2018b). "Gender dysphoria" and autism spectrum disorder: Is the link real? *Journal of the American Academy of Child and Adolescent Psychiatry, 57*(1), 8–9.e2. https://doi.org/10.1016/j.jaac.2017.08.017.

van der Miesen, A. I. R., Cohen-Kettenis, P. T., & de Vries, A. L. C. (2018a). Is there a link between gender dysphoria and autism spectrum disorder? *Journal of the American Academy of Child and Adolescent Psychiatry, 57*(11), 884–885. https://doi.org/10.1016/j.jaac.2018.04.022.

van der Miesen, A. I. R., de Vries, A. L. C., Steensma, T. D., & Hartman, C. A. (2017). Autistic symptoms in children and adolescents with gender dysphoria. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-017-3417-5.

van der Miesen, A. I. R., Hurley, H., Bal, A. M., & de Vries, A. L. C. (2018b). Prevalence of the wish to be of the opposite gender in adolescents and adults with autism spectrum disorder. *Archives of Sexual Behavior, 47*(8), 2307–2317.

VanderLaan, D. P., Leef, J. H., Wood, H., Hughes, S., & Zucker, K. J. (2015a). Autism spectrum disorder risk factors and autistic traits in gender dysphoric children. *Journal of Autism and Developmental Disorders, 45*(6), 1742–1750.

VanderLaan, D. P., Postema, L., Wood, H., Singh, D., Fantus, S., Hyun, J.,… Zucker, K. J. (2015). Do children with gender dysphoria have intense/obsessional interests? *Journal of Sex Research, 52*(2), 213-219.

Vermaat, L. E. W., van der Miesen, A. I. R., de Vries, A. L. C., Steensma, T. D., Popma, A., Cohen-Kettenis, P. T., et al. (2018). Self-reported autism spectrum disorder symptoms among adults referred to a gender identity clinic. *LGBT Health, 5*(4), 226–233.

Walsh, R. J., Krabbendam, L., Dewinter, J., & Begeer, S. (2018). Brief report: Gender identity differences in autistic adults: Associations with perceptual and socio-cognitive profiles. *Journal of Autism and Developmental Disorders, 48*(12), 4070–4078.

Williams, P. G., Allard, A. M., & Sears, L. (1996). Case study: Cross-gender preoccupations with two male children with autism. *Journal of Autism and Developmental Disorders, 26*(6), 635–642.

Woodbury-Smith, M. R., Robinson, J., Wheelwright, S., & Baron-Cohen, S. (2005). Screening adults for Asperger Syndrome using the AQ: A preliminary study of its diagnostic validity in clinical practice. *Journal of Autism and Developmental Disorders, 35*(3), 331–335.

Zucker, K. J., Nabbijohn, A., Santarossa, A., Wood, H., Bradley, S. J., Matthews, J., et al. (2017). Intense/obsessional interests in children with gender dysphoria: A cross-validation study using the Teacher's Report Form. *Child and Adolescent Psychiatry and Mental Health, 11*(1), 51.