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The Development of the Adult Version of the Signposting Questionnaire for Autism (SQ-A (Adult))

And

A Systematic Review of the Factors Associated with Co-Occurring Gender Dysphoria and Autism Spectrum Disorder

Thesis submitted in partial fulfilment of the requirement for the degree of:

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Thesis Summary

The portfolio thesis presented here covers two areas of autism spectrum disorder (ASD) research; the co-occurrence of ASD with gender dysphoria (GD), and the use of brief questionnaires as part of the process for diagnosing ASD in adulthood. The empirical element of this thesis has been largely set from the beginning, only encountering significant delays during the ethics process. The systematic review however passed through three phases; an initial topic that proved too broad, a second that was subsequently published after data synthesis had begun, and the final paper presented here. While interest in the empirical project naturally led to ASD as a research area, identity, and particularly gender identity is a longstanding clinical interest of mine. As a result, the limited current exploration of its co-occurrence with ASD seemed an ideal opportunity to marry both subjects, and examine the literature in this area. I hope it proves to be of interest to readers.

Paper one

It has been established that GD and ASD co-occur more frequently together than we might expect, given how often each occurs in the general population. The symptoms of each condition can impact how we assess and diagnose the other, but there is very limited guidance on working with this co-occurrence. To examine this issue a systematic review, drawing together all the published literature on the subject was conducted. This comprised all published studies which looked at diagnosed cases of both conditions together, to summarise the features of this phenomenon from three major perspectives; the biological, the social and the psychological. Following a search of three major databases (PsycInfo, Medline and

EMBASE) 439 English language studies were identified and screened. After applying the exclusion criteria 15 studies remained, and these were assessed with a quality appraisal tool to examine how well designed the research was. Following this process, all studies were retained and drawn together. Co-occurrence rates were summarised and explanations for the co-occurrence were identified and classified. Thirteen of these studies examined GD referrals for ASD, with co-occurrence ranging from 2.3% to 26%. One examined ASD clients for GD finding a co-occurrence of 0.07%, and another examined separate groups with GD and ASD so co-occurrence rates were not provided. The review suggests that there are various hypotheses for the links between GD and ASD, but most lack evidence. The challenges this raises for assessment and treatment are discussed.

Paper two

Questionnaire data are frequently collected by diagnostic services for ASD, before people take a standardised clinical interview for diagnosis. While questionnaires are often used to help clinical decision-making, their specific potential to support and streamline the assessment process isn't yet fully explored. One barrier is that we do not yet know how measurement of self-completed questionnaires relates to other aspects of diagnostic assessment.

Paper two is presented in three phases. Phase one describes the developing of a self-report questionnaire (the Signposting Questionnaire for Autism (Adult Version) (SQ-A (Adult)) using previously published carer-report items from the Diagnostic Interview for Social Communication Disorders (DISCO) in collaboration with ASD diagnosed people, who consulted to help develop it. An exercise with expert clinicians finalised the questionnaire

wording, based on the feedback autistic consultants had given. In phase two, a pilot study tested the *pre* and *post*-consultation SQ-A (Adult), and another well-established measure, the Autism Spectrum Quotient (AQ-10) with undergraduates (N=80). This was to examine how reliable the scales were, and whether both versions of the SQ-A correlated after we had changed the wording of several questions. Scale reliability was acceptable for both SQ-A versions, but unacceptable for the AQ-10. Correlations were acceptable between the two versions of the SQ-A.

Phase three compared the SQ-A (Adult) and AQ-10 with clinical interview data (the DISCO-Abbreviated Interview) in a sample that had been referred for assessment, to further explore their potential. The research used routinely collected clinical data from adults referred for an ASD assessment (N=66) to examine its *reliability* and *validity*. Questionnaire and clinical interview data was compared to see how well it correlated (*convergent validity*). The SQ-A (Adult) and AQ-10 were also compared for how well they correlated (*concurrent validity*). The *self* and *other* responses for each person attending for assessment were also compared, to see how well these correlated (*cross-informant reliability*). Convergent and concurrent validity was found for a range of comparisons.

These results suggest there may be value in exploring further how brief questionnaires can inform aspects of diagnostic assessment. A full validation study of the SQ-A (Adult) is recommended. This would include non-clinical control groups and those referred for other clinical reason groups (for example those referred for other neurodevelopmental disorders).

Contents

Acknowledgements

Paper 1 has been prepared for submission to the Journal of Autism and Developmental Disorders in accordance with the guidelines for authors (Appendix 1). Therefore, tables and figures are presented at the end of the paper.

A Systematic Review of the Factors Associated with Co-occurring Gender Dysphoria and Autism Spectrum Disorder

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Abstract

Gender dysphoria (GD) and Autism spectrum disorder (ASD) have an established co-occurrence with each other beyond that expected in the general population. The symptoms of each may affect assessment and diagnosis of the other, but there is a paucity of guidance on working with this co-occurrence. To examine this issue a systematic review was conducted of all published studies examining diagnoses of both conditions to identify and classify the biopsychosocial hypotheses posited for this link. In total 456 English language studies were screened. After exclusions 15 studies were selected. Co-occurrence rates are briefly examined, before synthesising the biopsychosocial features in extant literature; the review however finds most lack evidence. The challenges this raises for holistic assessment and treatment are discussed.

Gender dysphoria (GD) is a diagnostic classification from the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5, American Psychological Association (APA; 2013) defining the distress associated with incongruence between ones assigned birth gender, and the one experienced and identified with in everyday life. The diagnosis requires a consistent and strong identification with experienced, rather than birth gender, and a significant level of distress with biological sexual characteristics, and birth assigned gender and social roles. In its previous iteration the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Test Revision* (DSM-IV-TR; APA 2000) GD was referred to as gender identity disorder (GID). A recent systematic review by Arcelus et al. (2016) suggests an overall meta-analytical GD prevalence of 4.6 per 100,000 people (6.8 transwomen and 2.6 transmen).

The *International Classification of Diseases, 10th Edition* (ICD – 10; World Health Organisation, 1993) classifies the wish to live and be accepted as the opposite gender as 'transsexualism'. Healthcare for the transgender community is experiencing a marked increase in demand globally (Zucker 2017; Delahunt et al. 2018; Wiepjes et al. 2018), necessitating the rapid expansion of existing services and the creation of new ones. The health burdens of gender dysphoria are significant, from the extensive costs and lengthy timeframe to facilitate a full gender transition for an individual, to the wider healthcare burden of high psychiatric comorbidity, particularly in respect of depression and anxiety (Heylens et al. 2014). This high disease burden is also a factor in several neurodevelopmental disorders, particularly ASD. An emergent but consistent body of research has suggested that GD and ASD co-occur together more frequently than they do in the general population (Thrower et al. 2019).

ASD is a lifespan neurodevelopmental disorder with a prevalence of approximately 1 in 132 persons (Baxter et al. 2015). The main symptom domains as per DSM-5 (APA 2013) are social-communication difficulties and restricted and repetitive behaviour patterns. Diagnosis entails detailed developmental history taking, behavioural observation, and needs assessments (National Institute for Health and Care Excellence [NICE] 2012). Diagnostic criteria have also changed between DSM versions with the DSM-5 criteria for ASD replacing several separate diagnoses for the DSM-IV-TR (APA 2000) (e.g. pervasive developmental disorder, Asperger's syndrome) with a more stringent dimensional criteria to improve sensitivity and specificity (Wiggins et al. 2019). A recent systematic review of the epidemiology of ASD suggests that although there are a large number of studies from North America, European and other Western countries, there are no reliable data yet reported for 124 of the 187 countries in the world (Erskine et al. 2017). Thus full understanding of how ASD and its features presents across different cultural contexts is not yet fully established. The picture is significantly worse for GD where significant barriers exist to the delivery of joined up transgender healthcare (Safer et al. 2016).

GD is by definition very distressing for an individual, and the input of a clinical psychologist may prove particularly beneficial in supporting the individual through the various psychological stages of transition up to and including post-transition adjustment to living as the opposite gender. Formulation skills are obviously relevant to supporting this process, but could prove particularly vital in teasing out comorbid conditions such as ASD, assessing how ASD and GD might interact, helping to discern whether both diagnoses are valid and correct, and exploring how they may impact the whole process of gender transition and its management.

Understanding more about this phenomenon by identifying and classifying its features might also meaningfully contribute to theory-practice links. These should be the cornerstone to any best practice guidance for clinical work with such comorbid presentations. Given the extensive and long-standing body of research for ASD, a range of hypotheses around the contributing factors and hallmark features of autism are a logical starting point for examining why the conditions may co-occur. For example, 'extreme male brain theory' (Baron-Cohen 2002) might contribute to explaining cross-sex identification; impaired theory of mind (Frith & Happé 1995) might play a role in identity formation. Additionally, traits such as lowered interest in social interaction in ASD may insulate from the fear of stigmatisation, which might inhibit willingness to experiment with gender identity in the neurotypical population. It would also be useful to examine if specific traits are unique to comorbid GD and ASD, or simply more specific to clinically referred populations (known as 'the specificity question'; Garber and Hollon 1991). This could be a highly relevant contribution towards a theoretical framework for working with the co-occurrence, given the known high levels of psychiatric comorbidity associated with each condition.

Previous reviews have addressed the co-occurrence of GD and ASD on multiple occasions with limited conclusive progress noted (e.g. Glidden et al. 2016; van der Miesen et al. 2016). Most recently Thrower et al. (2019) reviewed the prevalence of GD co-occurrence with ASD and ADHD. While earlier reviews offered a valuable summary of the available data on prevalence (Glidden et al. 2016), and wider biopsychosocial features (van der Miesen et al. 2016) the paucity of evidence available at the time resulted in the inclusion of several weaker sources of evidence such as case reports, or studies examining limited traits or indicators of ASD and GD. The most recent review (Thrower et al. 2019) provides the most comprehensive summary of prevalence, but their review was focused only on establishing

prevalence rather than any potential theoretical underpinnings. Several further studies have been published since these reviews. Unaddressed at present is a contemporary critical appraisal of the biopsychosocial features of this co-occurrence. Previous reviews have necessarily focused on a wide variety of evidence of varying quality due to the dearth of studies. This review focuses on the small number of studies (N=15) with the most stringent inclusion criteria; a diagnosis of both ASD and GD, or a specialist assessment for these conducted as part of the study.

This review aims first to briefly appraise co-occurrence rates in the current literature, where both conditions are diagnosed. Secondly, to identify and classify features and any hypotheses underlying these in the included studies. Finally, to review the impact of these and potential implications for diagnosis and treatment. Most of these studies have been published in the last 4 years, since the last wider-scoped narrative reviews and discussions (Glidden et al. 2016; van der Miesen et al. 2016) were published.

Method

Search Strategy

This narrative systematic review adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al. 2009). A search of the Cochrane library, Prospero and Epistemonikos revealed no reviews in progress on the topic. Three databases were searched from inception to 30th March 2020: PsycInfo, Medline and Embase, for all articles published in English excluding animal studies. Citation searches were also completed on all included studies and prior reviews. Search terms were as follows:

ASD related terms *(autis*.mp., autism spectrum disorders, autistic traits),* and for GD *(gender dysphoria, gender identity, gender nonconforming, transsexualism, gender identity, gender reassignment, transgender, gender identity, and (gender varian* or gender expansive or gender divers* or trans*).mp.).*[1]

Both sets of search terms were combined using the "OR" and "AND" operators as appropriate. All full studies reporting on both diagnosed GD and ASD (whether in the same or separate cohorts) were of initial interest. The literature search was also repeated independently by another researcher.

Eligibility Criteria

The inclusion and exclusion criteria for the study are summarised in Table 1.

(Insert Table 1 here)

All studies that examined both diagnosed ASD and diagnosed GD were eligible for inclusion. Case series and case reports were excluded as the wider prevalence of any features observed and potential implications could not be surmised from these. Conference abstracts, poster summaries and letters to editors were not included, as they could not be adequately quality appraised against full studies. A diagnosis was defined as gathered from a medical/ case file review, recruited from a database for previously diagnosed participants or obtained during the

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[1] [mp= mapped terms for title, abstract, heading word, table of contents, key concepts, original title, tests & measures, mesh. All search terms without "*" were exploded for mapping to wider subject terms for maximum inclusivity].

study. Studies including those who had a GD diagnosis and had completed their transition were included. Studies accepting self-reported diagnoses were not included.

Study Selection and Data Extraction

Screening proceeded through four steps; title, abstract, full-text and formal quality appraisal. The full search strategy is outlined in Figure 1. At the full-text screening stage, data were entered into a database to capture the items outlined below.

(Insert Figure 1 here)

Participant Characteristics

Adult/ child/ adolescent, mean age, confirmation of GD and ASD diagnoses and how established, birth gender (how many participants were assigned male at birth (MAB), assigned female at birth (FAB), non-binary (NB) or unassigned).

Study Characteristics

Confirmed diagnoses (and by what method if provided). Any additional measures used. Recruitment methods and sample size.

Controls

Whether a control condition was established, relevant details on sampling and recruitment methods, and whether participants were typically developing or clinically referred.

Outcomes

Confirmed prevalence of ASD and GD. Summaries of any discussion of key features.

Statistical Results

Any statistical analyses of prevalence estimates (e.g. gender or age comparisons or comparisons made with controls) and any inferences made.

Quality Appraisal

The final screening stage used a formal quality assessment tool which can be found in Appendix 2 (AXIS; Downes et al. 2016) to appraise all aspects of study quality. While numerous quality appraisal tools exist for quantitative studies, many of these are generic, to encompass a wide range of potential different study designs. The AXIS is specifically designed for cross-sectional studies (which the majority of studies reviewed are), having established 20 key methodological features in a peer-reviewed study using the Delphi method (Downes et al. 2016). The 15 studies included were all rated for the presence or absence of these key features, with narrative discussion of their strengths and weaknesses. A summary of all studies is included in Appendix 3, and an example of individual quality appraisal is included in Appendix 4. A sample of four of the studies was also appraised by an independent-rater with agreement on all items. Quality appraisal did not result in any studies being excluded, as all were of a sufficient quality for inclusion.

Results

A total of 662 studies were identified from a search of PsycInfo, Medline and Embase. Following removal of duplicates 456 studies remained. All of these were screened by title, by

both the first author and an independent researcher, with inter-rater reliability of 98.82% established (Cohen's Kappa 0.95). The small number of conflicting decisions were resolved with discussion and abstract screening where necessary. This resulted in 78 studies for abstract screening. At this point all review articles, case studies and otherwise irrelevant articles were removed leaving 47 selected for full-text review with 32 of these subsequently excluded. Fifteen studies were quality assessed as eligible, covering a period between 2010 and 2019. A summary of the search process is provided in Figure 1. Due to the breadth and range of clinical contexts and methodological differences a meta-synthesis was not considered appropriate, so a narrative synthesis follows. A summary of all included studies is provided in Table 2.

(Insert Table 2 here)

Demographics Within the Identified Studies

In the adult studies two papers reported on age demographics with mean age ranging from 27 years old (Cheung et al. 2018) to 29.35 years old (Fielding and Bass 2018). In the child studies nine papers reported mean age data, ranging from 7.97 years old (Leef et al. 2019) to 16.9 years old (Kaltiala-Heino, 2019), with an overall mean age of 13.44 years old.

Of the studies reviewed, 12 examined samples attending a gender identity clinic for assessment (Chen et al. 2016; Cheung et al. 2018; de Vries et al. 2010; Fielding and Bass, 2018; Heard et al. 2018; Heylens et al. 2018; Holt et al. 2016; Kaltiala-Heino et al. 2015, 2019; Nahata et al. 2015; Leef et al. 2019; Skagerberg et al. 2015). Of those who analysed age at point of referral for any gendered difference (Fielding and Bass. 2018; Kaltiala-Heino et al. 2015, 2019) only Fielding and Bass (2018) found significant differences, suggesting FAB's present for assessment earlier (p< 0.001). Holt et al. (2016) analysed age of first GD

feelings rather than referral age and found no significant gendered difference (p>.05). One key feature of Fielding and Bass (2018) is that it is one of the few papers to examine an adult sample. It notes that mean age of those assigned FAB was considerably lower at referral (24.3) compared to those assigned MAB (34.4). This incongruous result may suggest some form of gendered differences present after adolescence, or it may be suggestive of differences in the sociocultural landscape around GD identification and assessment for this generation; e.g. current adults assigned MAB may have delayed presenting for assessment due to previously less supportive social environments, stigma or shame.

In cohorts that analysed ASD related age differences (de Vries et al. 2010; and Hisle-Gorman et al. 2019), both found the mean age of those with ASD presenting for GD assessment was significantly higher (de Vries et al. p<.05; Hisle-Gorman et al. p<0.001) suggesting ASD may have a potential role in delayed identification of GD. Holt et al. (2016) found significantly higher ASD diagnoses and queries in a child and adolescent sample (p<.01) with GD. In terms of gender-related differences Hisle-Gorman et al. (2019) found that in their ASD sample, being FAB made a GD diagnosis significantly less likely (p=0.03).

Prevalence of Diagnosed ASD in a GD sample

In the majority of the studies (13/15) prevalence rates were established in a cohort of GD referrals. A total of 9,765 referrals were examined for ASD prevalence in these studies with prevalence ranging from 2.3% (Heard et al. 2018) to 26% (Kaltiala-Heino et al. 2015) Several of the studies had very small sample sizes, and the smaller sample sizes tended to align with higher prevalence rates. The largest study (Dragon et al. 2017) of N=7,454 transgender Medicare beneficiaries reported ASD prevalence of 3%. Given the fact this study

included all records for a healthcare system, examining verified diagnoses from medical records, it could be argued this is currently the most reliable estimate of prevalence. It is important to note however that the study sample is from a means-tested American healthcare system for those with disabilities, so diagnosis rates of both disorders can still be affected by eligibility criteria that may deny treatment. In all studies, the co-occurrence was over three times the rate at which ASD occurs in the general population of 0.76% (Baxter et al. 2015).

Prevalence of Diagnosed GD in an ASD sample

Only one study of diagnosed GD in an ASD diagnosed cohort was found (Hisle-Gorman et al. 2019). While the sample size was large, this was a medical records review, the retrospective nature of which limits opportunities for rigorous interrogation of individual features of co-occurrences. This study found GD co-occurrence to be 0.07% in the ASD sample, which while noticeably lower than the ASD in GD cohorts above, was still far greater than the rate of GD found in the TD population surveyed (0.01%). An unadjusted conditional logistic regression analysis suggested children were 4.38 times more likely to be diagnosed with GD if they had ASD, than if they were TD. The limited examination of GD in ASD diagnosed cohorts was first touched upon by de Vries et al (2010) who felt that co-occurring ASD was being underreported in their cohort of GD referrals, as ASD was not the primary concern of caregivers.

Associated Factors Identified

A number of associated factors have been put forward to potentially account for the co-occurrence of GD and ASD in the extant literature. Below, the key factors presented in the literature are considered.

Shared Genetic or Epigenetic Underpinnings

A shared genetic or epigenetic underpinning and neurodevelopmental links between GD and ASD is hypothesised by Cheung et al. (2018), who cite similar observations already made between ADHD and ASD (Leitner, 2014). van der Miesen et al. (2018) however raise the additional possibility that the developmental pathway of co-occurring GD and ASD may differ for boys and girls. In a novel study using the Children's Social Behavior Questionnaire (CSBQ; Achenbach & Edelbrock 1983), they found gender at birth associated with different interaction effects on different subdomains of ASD, with those assigned MAB scoring substantially higher on the stereotyped subscale (and with a negligible effect size on the orientation subscale).

Prenatal Hormone Exposure

Several prior studies have supported the idea of the 'extreme male brain' (EMB) as an explanation for the predominance of males in ASD diagnoses (Baron-Cohen, 2002). The theory suggests men are strongly driven by systematising principles, whereas women have stronger tendencies towards empathising (Baron-Cohen 2009). In ASD the male pattern described above is thought to operate in the extreme, with an enhanced ability to systematise (Kaltiala-Heino, 2015; van der Miesen, 2018).

Sex Assigned at Birth

While all studies measuring co-occurrence found rates above that expected in the population, only two (Kaltiala-Heino et al. 2015; 2019) found a higher rate in those assigned FAB, who might be expected to experience ASD at a greater rate than those assigned MAB if biological underpinnings like EMB were proven. This leaves the matching elevation in co-occurrence rates for those assigned MAB across many studies unexplained. These studies are

a notable outlier, and their authors were unable to offer a hypothesis for the incongruence with conflicting observations in other Western countries. While the results of quality assessment do not suggest any key limitations for these studies the sample sizes are quite small, and the sample from the 2015 paper appears to be included in the 2019 study sample, which still remains small at N=99. The disparity between those assigned MAB and FAB in referral rates is also *so* stark (MAB=6, FAB=41, 2015; MAB=15, FAB=84, 2019) that it is reasonable to question whether there are any as yet unidentified barriers to those assigned MAB presenting for assessment in Finland, given the scale of the disparity with other western liberal democracies. The co-occurrence rate of 26% (2015) and 23.5% (2019) for ASD in a GD sample are also the highest of all those reviewed which further marks these studies out as unusual. Gender variance (GV), a wider umbrella term which encompasses all variants and strengths of the various strands of trans identity, does appear to be more common in those assigned FAB but not when GD and ASD is comorbid (Holt, 2016; Hisle-Gorman, 2019).

GD prevalence is traditionally higher in those assigned MAB (Heylens et al. 2014; Bouman et al. 2016). In one of the most methodologically rigorous studies Hisle-Gorman et al. (2019) compared a typically developing (TD) population with an ASD diagnosed one using unadjusted conditional logistic regression, finding ASD made a GD diagnosis four times more likely, with those assigned MAB five times as likely, and those assigned FAB three times. All results were statistically significant and run counter to expectations if EMB were an adequate hypothesis. Nahata et al. (2017) also suggest those assigned MAB are more likely to be diagnosed with ASD in a GD sample, but their results were not significant. Heylens et al. (2018) found a higher level of those assigned MAB amongst the ASD diagnosed in their sample, but no difference in those meeting threshold for a broader autism phenotype in additional testing using the Autism Quotient (AQ; Baron-Cohen et al. 2001).

They note the findings are not in accordance with EMB and cite further research by Kung et al. (2016) questioning the validity of EMB in an ASD sample.

It is possible that co-occurrence may have different underlying mechanisms for males and females. One hypothesis for the co-occurrence of GD and ASD in females comes from studies where girls prenatally exposed to high testosterone levels subsequently developed traits of ASD and gender identity issues (Dessens et al. 2005; Knickmeyer et al. 2006). The only study to examine this did not support this assertion, as it didn't find girls with ASD were any more at risk of developing GD than boys (de Vries et al. 2010).

Individual Relationship with Cultural and Social Norms

Poor understanding of social relationships, and social communications deficits, are hallmark features of ASD (APA, 2013). Feeling different from peers is a common experience in both ASD and GD (Kaltiala-Heino, 2015), and prior case reports suggest those with ASD may attribute feelings of difference to GD, prior to exploring an ASD diagnosis (de Vries, 2010). Cultural difficulties can also play a role in seeking GD diagnosis; for example traditional families and social stigma are acknowledged as a barrier in the Hisle-Gorman et al. (2019), and Fielding and Bass (2018) studies.

Interpersonal traits

Leef et al. (2019) compared GD groups against those referred for other clinical concerns for ASD traits using the Social Responsiveness Scale (SRS; Constantino et al. 2003) and Social Communication Questionnaire (SCQ; Rutter et al. 2003). For GD candidates, only

the SCQ reached significance (ϕ =.026), however when parent report feedback was examined both measures reached statistical significance at the total scale level (SRS; Cohen's d= .73; SCQ; Cohen's d= 1.13). Further analysis suggests the 'social cognition' and 'autistic mannerism' subscales were the source of significant differences between ASD and non-ASD individuals. As a result of these observations, Leef et al. (2019) suggest that GD does not predispose a child to develop ASD, but it is possible some of the characteristic of ASD (such as intense interests or obsessions) may predispose a child to GD. They conclude that longitudinal research is essential to explore this potential explanation further.

There are heightened ASD traits reported in GD samples across several prior studies, including a number which did not review diagnosed samples (see Thrower et al. 2019 for a review). This might suggest that ASD features being observed stem from gender dysphoria itself, rather than indicating genuine ASD. The shortcomings of trait inventories and screening tools are discussed by Thrower et al. (2019), who suggest these findings be treated with appropriate caution. Particularly considering the social deficits common in ASD, several of the studies reviewed suggest these features may stem from unsupportive social environments e.g. social isolation, anxiety, minority stress and bullying, which tend to accompany GD, but can mirror ASD features (Holt et al. 2016; Kaltiala-Heino et al. 2015; Leef et al. 2019; Skagerberg et al. 2016; van der Miesen et al. 2018). Nahata et al. (2017) suggest bullying is also of equal concern and prevalence across MAB and FAB populations with GD. Additionally, the poor understanding of social relationships characteristic of ASD led Landen and Rasmussen (1997) to suggest GD might develop through aversive social interactions, which de Vries (2010) references when reporting on a case where bullying created feelings of aversion to the person's assigned gender. Several of the studies touch upon this link, with ASD and GD traits suggested as potentially indicative of non-supportive

social environments, especially in regards to bullying (Kaltiala-Heino et al. 2015; Leef et al. 2019; Skagerberg et al, 2015, and van der Miesen, et al. 2016).

Comorbid Mental Health Difficulties

Comorbidity of psychiatric disorders (particularly depression, anxiety, self-harm and suicidality) and how this may interact with clinical presentations are considered in seven studies (Cheung et al. 2018; Fielding and Bass., 2018, Heard et al. 2018; Holt et al. 2016; Kaltiala-Heino et al. 2015, 2019 (the 2019 paper however includes the 2015 sample); Nahata et al. 2017). Of these studies only Cheung et al. (2018) and Fielding and Bass (2018) examined adult cohorts. Cheung reported the largest sample (N=540) but this study reported individual conditions not overall psychiatric comorbidity, with depression most common (55.7%). Fielding and Bass reported 59.2% current or past incidence (N=153) suggesting adult co-morbidity is fairly congruent from the limited data available.

In child and adolescent samples the contrast is wider with Holt et al. (2016) at 42% co-morbidity (mean age 14), followed by Heard et al. (2018) at 46.8% (mean age 14), Kaltiala-Heino et al. (2019) at 75% (mean age MAB=16.91, FAB=16.86) and Nahata et al. (2017) at 92.4% (mean age 15). The Nahata et al. study should be treated with some caution as it has a small sample (N=79) and is based on an insurance based healthcare system (the USA) where comorbid diagnoses are more common in part because of the associated increase in access to services they provide. One rationale for the variance in rates may be the age range among the sample. Both Holt et al. (2016) and Heard et al. (2018) had wide age ranges including children, whereas the Kaltiala-Heino et al. (2015; 2019) and Nahata et al. (2017)

studies were restricted to adolescent cohorts. The mean age also suggests there may be an

increase in psychiatric comorbidity the further into adolescence someone presents.

Two other hypotheses may explain the difference in rates between adult and child and

adolescent cohorts. One, generational differences in life experiences between children and

adolescents growing up at present and prior generations presenting with the same conditions

as adults, and two, specific stressors which may result in mental health difficulties such as

bullying and social isolation which are suggested to associate with may disproportionately

associate with presenting as gender dysphoric in childhood or adolescence. Holt et al. (2016)

lends some weight to this suggesting in breaking down comorbidities by condition and

showing that there are noticeable increase across most co-morbid diagnoses in their sample

when comparing the child and adolescent subpopulations, suggesting difficulties particularly

spike as children transition to adolescence.

Developmental Rigidity

As children age, they become increasingly less stereotyped in their beliefs about gender

(Ruble et al. 2007). One suggestion in the studies reviewed is that ASD may prevent children

from reaching flexibility in gender development with GD being a consequence (de Vries et

al. 2010). Hisle-Gorman et al. (2019) suggest impaired ability to think and communicate

about gender in ASD might explain the heightened co-occurrence of GD they found in an

ASD sample, while Holt et al. (2016) suggest the opposite may also be possible; where

people with comorbid ASD and GD could hold more rigid views of what is to be male or

female e.g. black-and-white styles of thinking, and as a result their gender identity may be

less fluid and more fixed than average. While both suggestions are speculative those from

Hisle-Gorman et al's paper do suggest a potentially fruitful avenue for further research, given the very large sample size (N=48,672) and slightly superior quality across narrative synthesis. A further complication is the dearth of studies examining how coexisting intellectual disability (ID) may complicate the formation of gender identity. Only one study examines this issue after reporting 9.4% of co-occurring ASD and GD cases also had a comorbid ID (Hisle-Gorman et al. 2019). This study suggests the nuances of gender identity formation need careful consideration for this population; as a result, they advocate particular caution be taken with any non-reversible biological interventions for GD (Parkes et al. 2009)

Sexuality and Sexual Orientation

The development of sexuality, sexual orientation and sexual experience can be altered in a variety of ways in both GD and ASD. de Vries (2010) suggests while those with GD normally express sexual attraction to their birth sex, in their sample, a diagnosis of comorbid ASD associated with the opposite. They suggest this has clinical relevance, as those with GD attracted to the opposite of their birth sex appear to have worse post-operative outcomes in some studies (Smith et al. 2005). They also caution that they observed some assigned MAB with feminine interests (soft tissues, glitter and longer hair) in their sample which might align with specific sensory input preferences that are also common in ASD; thus the two can easily be conflated. Romantic and sexual experiences were also found to be significantly impaired in GD samples, and yet further impaired if ASD was also comorbid, with all differences reported as significant at p<.05 (Kaltiala-Heino, 2019).

Results in this section should be treated with appropriate caution for several reasons. Firstly, only two of the studies engaged with this issue. Neither of these contained an adult

sample, and one (Kaltiala-Heino, 2019) has already been discussed as reflecting outlier results around birth-assigned sex which were incongruent with other publications. As de Vries et al. (2010) and Hisle-Gorman et al. (2019) note, ASD also appears to be implicated in later presentation for GD assessment. In light of limited coverage in the papers reviewed (and none within adult cohorts) it is fair to conclude that sexuality and sexual orientation, and how this relates to GD and ASD co-occurrence is an under-researched, and poorly understood topic.

Discussion

This systematic review has identified and classified relevant biopsychosocial features of studies where GD and ASD were both diagnosed. Several of these studies were being included as part of a systematic review for the first time. The review was in no small part driven by the lack of any evidence-based framework, to guide clinical work with this co-occurrence across the life course. It was also hoped that the studies might further our understanding of how underpinning theory could be informed by studies of co-occurring ASD and GD. While this review suggests a range of biopsychosocial factors may be characteristic of the co-occurrence of GD and ASD, there is very little compelling evidence that any one factor underlies this presentation. Indeed, one study examining 'the specificity question' suggests multiple causal factors are likely to underlie this co-occurrence (Leef et al. 2019). This suggests that despite the limited evidence, any factor outlined in this review may yet be found to be part of a wider causal network.

Most studies reviewed were of small sample sizes without the use of a control group. This is problematic as there may not be a sufficient sample size to answer the research

questions with confidence, or demonstrate significance of the results. Even if the main aims of the study are met, a small sample often precludes the possibility of more fine-grained analysis of data, such as examining gendered differences, which require splitting the samples for comparisons. How much of an issue this may have been is unclear, as virtually none of the papers engaged with a discussion of power, or justification of their sample size. Frequently, studies examined the GD and ASD co-occurrence as just one of several study goals rather than a primary focus, which, while not problematic in itself, often led to limited critical engagement with hypotheses for the co-occurrence in each paper's discussion. Even with a more selective focus on diagnosed samples, analyses were still hampered by differences in diagnostic pathways, classification systems used, and standards of diagnostic reporting. Several of the studies comment on these difficulties, and some (e.g. Leef et al. 2019) suggest a multiplicity of factors underlie GD and ASD co-occurrence, and more nuanced models are required to examine the presentation. The studies reviewed do however suggest several issues worthy of consideration, particularly the clinical implications they raise, and considerable challenges for future research in light of these. Further research establishing the trait profiles of those with co-occurring diagnoses, and ideally comparing them with control samples, would be a valuable and logical contribution to the evidence base for this area.

One of the obvious implications raised by the studies included in this review is the marked increase in demand for GD related services. Mostly, these are delivered by highly specialist gender identity services, many of which are in their infancy. These comprise a range of disciplines including psychiatry, clinical psychology, endocrinology and speech and language therapy. Five of the studies offered commentary on multi-year tracking of referral rates to these services, with every clinical site experiencing a marked increase in referrals.

The highest of these found a ten-fold increase in referrals for the five-years ending 2016 (Cheung 2018). There are various explanations for this, including addressing previously unmet need, but Fielding and Bass (2018) suggest there may well be a sociocultural contribution being made, by the wider awareness, visibility and acceptance of trans identity, and the needs that may accompany it. This has clinical implications for the accurate and correct diagnosis of GD; increased referral rates, if they are genuinely allied to an underlying condition are positive, albeit challenging, as this would suggest fewer people are trying to manage significant distress without seeking help. This however generates clinical need, which is currently unmet due to a shortage of skilled staff available to undertake these assessments, implying additional staff training is warranted. ASD diagnostic services are also in high demand. Even in countries with well-established diagnostic services such as the UK, wait times for children can average as much as three-and-a-half years (Crane et al. 2016). In Wales there are stark geographical disparities with some health boards assessing within six months, and others taking up to two years for children, and 7-12 months for adults (Holtom et al. 2019). These variable service levels and disparities suggest inter-agency cooperation between specialist diagnostic services would be a highly meaningful contribution towards holistically addressing the needs of people with co-occurring GD and ASD. The potentially synergistic benefits this cooperation could offer in terms of early intervention, focused on prevention of further distress, is just one clinical opportunity that could be exploited with more joined up working.

Another complicating factor is the diagnostically driven contexts of both conditions. Heylens et al. (2018) engage in a discussion around the difference between diagnostic classification systems, particularly the disparity between DSM-IV-TR and DSM-5 criteria and ICD-9 (Slee, 1978) and ICD-10 criteria for diagnosing ASD, and how this may impact on

diagnostic classification. They also suggest that frequently, studies on ASD are still based on DSM-IV criteria rather than DSM-5, drawing attention to research suggesting this hampers reasonable prevalence comparisons (Lehmann and Leavey, 2017). Hisle-Gorman et al. (2019) expand on this by suggesting ICD-9 codings frequently used in these studies do not provide a comprehensive understanding of ASD severity or the pattern of symptoms, while GD codings are likely to underestimate the number of GD cases, as ICD-9 criteria did not include non-binary and diverse identifications. In clinical practice, ensuring the latest diagnostic classifications are used by specialist services remains a clinical imperative. This is also true of instruments for diagnosing both conditions. Lack of standardised assessment protocols for GD hamper research activity which might inform best practice for its assessment, and offer insight on its relationship with ASD. The same is true of ASD assessment where numerous clinical interviews might be used to arrive at the same diagnosis. The interactions and overlaps between GD measures and ASD measures is largely unaddressed and highly clinically relevant. Until these inconsistencies are addressed, studies will likely continue to offer divergent estimates of prevalence and other related features of interest, which clinicians may be able to harness to design therapeutic interventions if they were better understood.

Hisle-Gorman et al. (2019) suggests that difficulty in diagnosing ASD in females might underlie gender differences in ASD and GD co-occurrence, rather than biologically oriented hypotheses such as EMB (Baron-Cohen, 2002). This is supported by Heylens et al. (2018) who raise the related concern that diagnostic tools fail to take gender norms into account, and are not validated for comorbid groups like those with GD. de Vries et al. (2010) reflect that GD feelings in childhood typically cease by adolescence in both TD and ASD populations, which is a key consideration in care planning, and a caution against the use of the more simplistic measures, such as single questions about 'wish to be the opposite gender',

that many previous studies with non-diagnosed populations have used in children. A further concern is raised by Kaltiala-Heino et al. (2015), in that presentation for GD assessment tends to be later for those with comorbid ASD. They note high-functioning autism also tends to be diagnosed later in adolescence, as opposed to early childhood. With co-occurring GD and ASD they found this associated with more significant psychopathology, and broader identity confusion, than those without ASD. Why this is remains unclear, but the role of social communication and social interaction in identity formation is not to be underestimated, and there is certainly scope for future research to examine whether ASD may impair the ability of those with GD to be able to recognise and seek help for this. It is unlikely that GD predisposes someone to ASD, but some evidence suggests it is more likely ASD could predispose someone to GD (Leef et al. 2019; Vanderlaan et al. 2015). Without longitudinal data it will prove difficult to discern the temporal relationship between ASD and GD, but Leef et al. (2019) suggest applying the principle of multi-finality (Cichetti & Rogosch, 2009) to profile features that might differentiate children with ASD who develop GD, from those who do not.

Comorbidity of psychiatric disorders and their potential to interact with clinical presentations is a further relevant consideration. Leef et al. (2019) touch upon this when considering the 'specificity question' (Garber and Hollon 1991), which suggests the elimination of one potential causal factor does not preclude its potential role in a wider causal network yet to be defined. Their specific concern was whether elevated ASD diagnosis was specific to children with GD, or characteristic of clinical populations generally. Their results indicated non-specificity, suggesting a more nuanced model of GD and ASD co-occurrence is required, than the simple univariate causalities previously hypothesised. Kaltiala-Heino et al. (2015) also found social isolation and level of comorbidities significantly contributed to

membership of a confused GD subgroup they hypothesised to exist, suggesting GD severity appears to be influenced by other psychiatric difficulties and psychosocial difficulties. A related factor is healthcare inequality, with Chen et al. (2016) finding that 40% of their sample had been denied hormone-blocking treatments under healthcare insurance, despite a demonstrable link with worsening GD symptoms in the absence of these.

These issues are of course very clinically relevant. Knowing both conditions tend to be picked up later than is usual when they co-occur together raises the possibility that individuals are suffering distress with their symptoms for longer before making the necessary links to obtain support. This has implications for how easy it may be to work with such individuals when they present for support, and these papers establish comorbid psychiatric difficulties are very prevalent alongside the co-occurrence. For this reason it is of paramount importance to adequately profile features of the co-occurrence, to recognise it and offer support for it at the earliest juncture, hopefully avoiding the poorer health outcomes and comorbid psychopathology observed in many individuals experiencing GD and ASD concurrently.

Kaltiala-Heino et al. (2015) share further concerns about the generally poor quality of ASD assessment reporting in prior studies, where there are frequently no second clinicians available to verify diagnoses. This chimes with Hisle-Gorman et al's. (2019) suggestion that, particularly with comorbid ASD and GD, caution should be exercised, when prescribing any non-reversible treatments before comprehensively assessing both conditions, as their shared features (particularly social traits) can be easy to conflate. One potentially useful contribution which services might employ to bridge the gaps identified in care pathways, is utilising the

skills of clinicians with expertise in transdiagnostic approaches (Craske, 2012), who would be well placed to holistically assess the needs of each individual, and their presenting circumstances. This raises a further clinically relevant issue; more skilled clinicians are needed in this area clearly, as is greater service provision more generally. While a range of professional competencies are needed to provide the MDT care required, either extensive recruitment from shortage occupations such as clinical psychology is needed, or significant upskilling from related allied health professional disciplines, or a mix of both. Heard et al. (2018) reflect further on the delay between questioning gender and receiving treatment. They draw links between this and quality of care received and the 'coming out' process (particularly highlighting delayed treatment or denial of service due to stigma, and lack of clinician expertise). As a response, they produce guidance on the way healthcare settings can be more trans-affirmative, in the qualitative analyses of their paper. This is also echoed by Dragon et al. (2017), who suggest systemic discrimination against trans people, and the distrust resulting, further hamper the ability of clinicians to adequately meet the needs of the trans population. They further caution that healthcare inequalities disproportionately impact black and minority ethnic (BME) populations, meaning trans people from these communities are likely even further marginalised.

Nahata et al. (2017) raise a further salient issue; the significant costs of GD treatments in insurance-based healthcare systems, and how these may hamper referral rates and care received. In systems impacted by these issues, much more work is needed on ensuring equality of access and advocacy. This is particularly important given the vulnerabilities both diagnostic groups already experience in isolation, without the additional complications of comorbidity. As a result, meaningful clinical guidelines might be a useful contribution to improving clinical outcomes. Leef et al. (2019) highlight this as another gap; although there

are now initial clinical guidelines for adolescents with GD and ASD (Strang et al. 2018), there are still no formal or informal guidelines at present for children with the co-occurrence, nor are there any for adults. In this respect, it would seem prudent to recommend that a holistic and formulation driven approach, helmed by clinicians with a clear understanding of both conditions, would provide the best opportunity to design appropriate care for this cohort of individuals.

Finally, there are also two features suggested in prior literature as explanations for the co-occurrence but not the studies reviewed. One is the suggestion that GD and ASD might link through the manifestation of OCD features in ASD, and be mistaken for GD if gender is the person's fixation (van der Miesen et al. 2016); however none of the reviewed studies mentioned or offered evidence to support this hypothesis. Another suggestion is that theory of mind (TOM) might influence the development of gender identity, as children with ASD may experience a different sense of self, and as a result a different sense of gender identity compared to others (Pasterski et al. 2014). None of the included studies discussed this hypothesis or offered any evidence to support it, thus the potential contribution TOM might make to co-occurring GD and ASD remains unexplored in this context at present.

Several worthwhile findings have been identified by this review. This is the first paper to catalogue the major biopsychosocial features associated with ASD and GD co-occurrence in gold standard literature from the evidence base. This has highlighted a number of important features. Firstly, it has confirmed the limited current evidence base for any one factor underpinning the co-occurrence, and the potential for research design to investigate the

possibility that a multiplicity of factors are underlying. It also highlights the recent trend for research in the area has been repetition of studies with similar designs, and similar weaknesses, concluding with the same recommendations for future research. This is valuable as it helps refocus priorities for future research by grounding them in current limitations. It has also highlighted the current lack of clinical guidance for working with pre-adolescents or adults with the co-occurrence. This bolsters the essential nature of MDT work and bespoke approaches to care in this area, and particularly with these populations at present. Clinical psychologists are ideally placed to contribute to this work, given that many are already experts in the assessment and diagnosis of ASD, as well as highly experienced in transdiagnostic approaches.

The most obvious shortcoming of the literature synthesised here is its limited range and scope. Many of the studies reported were designed to address multiple purposes, such as a range of co-occurrences or different features of interest. The studies with the largest sample sizes examined entire healthcare systems, without participant input, and reported pure prevalence, while several studies made little attempt to critically engage with their findings, or generate new hypotheses or research ideas specifically about GD and ASD co-occurrence. Of the included studies, the oldest (de Vries et al. 2010) still offers the most complete design and critical engagement with a range of features of ASD and GD co-occurrence. While referred to in most of the other papers, its design has been neither replicated, nor built upon, by any other study with a larger sample size or superior design since. The recommendations of prior studies to engage with a formal diagnosis of both conditions, rather than merely screening or traits measures, has been acted upon. However, there remains a dearth of quality studies examining deeper questions than simple prevalence, to critically engage with and test features of this co-occurrence, and what may underlie it. The current cohort of studies almost universally fail to engage with a discussion of sample size or power, and small sample sizes

clearly appeared to hinder comparison of demographics such as gendered differences, which are key to examination of some hypotheses such as EMB theory (Baron-Cohen, 2002)

In wider critique, all studies meeting the inclusion criteria were conducted in Western countries, with well-established healthcare systems (primarily in Europe, North America and Australasia), where broadly, social liberalism and minimum standards of healthcare apply. Only two studies engaged with the contribution cultural norms may make to treatment seeking for mental health difficulties (Hisle-Gorman et al. 2019; and Fielding and Bass 2018). Fielding and Bass (2018) suggest increased cultural acceptability may be contributing to the increased referral rates being observed. Conversely, Hisle-Gorman et al. (2019) examined medical records of US service personnel children suggesting a tendency towards military family conservatism (particularly around GD) may have artificially suppressed reporting rates. This is of heightened relevance to countries where these conditions are poorly understood, have significant social stigma attached, or might even associate with a risk to personal safety. These difficulties could also be exacerbated in localities with poorly financed healthcare systems, lacking comprehensive assessment or treatment for GD or ASD. Yet more worrying is the related finding that even in the Westernised countries represented here, the rates of general comorbid psychiatric difficulty for people with GD are exceptionally high.

While a review of the best available evidence on the co-occurrence of GD and ASD is valuable and timely, there remain some key limitations. Firstly, although the need for rigorous diagnostic studies of ASD and GD co-occurrence (particularly with control groupings) is frequently cited (Glidden et al. 2016; van der Miesen et al. 2016; Cheung et al.

2018; Thrower et al. 2019), this inevitably excludes from discussion those with sub-clinical traits or symptoms, who are nonetheless impaired in function on a day-to-day basis (van der Miesen, 2016). Frequently, it also means trait measures are not used as part of the design, thus more nuanced understanding of features of both disorders, and how they may interact, is lost. While the AXIS tool does not 'score' each study, most of the studies synthesised could be fairly described as of low to moderate quality given the low sample sizes. Methodologically, standardised approaches to GD assessment and diagnosis are still in their infancy, and ASD diagnoses were often historic and offered little clarity on their origin. Due to this, limited inferences can be drawn from the studies synthesised. For all these reasons, the complicated aetiology and makeup of co-occurring ASD and GD means diagnostic and trait and symptom-based research, or ideally a marriage of both, will continue to be relevant to furthering our understanding of the presentation.

This review also has its own methodological limitations. Firstly, although initial study screening was subjected to full inter-rater reliability checking, time constraints meant that only a sample of quality appraisals were repeated by an independent researcher. The limited range and scope of high-quality studies meant all were included to offer breadth of coverage. This meant biopsychosocial features were often only discussed by a single paper. This is also relevant to demographic factors, where only four studies examined adults, and several omitted gendered comparisons, both of which may be essential to understanding the co-occurrence. Finally, it should also be acknowledged that any researcher will bring their own inherent preconceptions and biases to the process of screening and synthesis, and despite controlling for this with co-raters, the selection of key themes and observations do not preclude different interpretations other researchers might place on the same body of work. A meta-analysis may be a useful contribution as the evidence base advances. This would be one

way to overcome the limited sample sizes often inherent to working with rarer diagnoses, such as GD.

Conclusions

This review was undertaken to consider the features of co-occurring GD and ASD. Most of the included studies were cross-sectional in nature. The findings indicate a range of features which may impact on the prevalence of this co-occurrence, but the evidence for each is limited and weak, hampered by small sample sizes, different diagnostic approaches, and more broadly focused designs. It is however, the first contemporary critical analysis of the co-occurrence of these conditions, in diagnosed samples. A range of clinical implications and challenges have been identified. Standardised approaches to diagnosis, and clinical guidelines for working with the co-occurrence, for all groups, across the lifespan would be valuable. Marrying trait and diagnosis-based research should also be a priority, to improve the quality of research evidence, and move understanding of the underlying profile of this co-occurrence forward.

Tables and Figures

Table 1. Inclusion and exclusion criteria.

Inclusion	Exclusion
An empirical study; in English peer reviewed, reporting on co-occurring diagnosed GD and ASD or independent samples with diagnosis of both	Book chapters, Reviews, Letters to editor, Conference abstracts, Poster summaries, Animal Studies
All age groups	Studies accepting self-reported or unverified diagnoses
Quantitative research (and mixed-methods as long as quantitative data was presented)	Qualitative studies

Table 2 Selected Studies

Study (first author, year)	Country	Design	Participants	Origin of Diagnosis	Measures Used	Key Observations
Adults						
Cheung (2018) (Cheung et al. 2018)	Australia	Retrospective cross-sectional analysis	Transgender adult referrals to primary care and specialist clinics N=540 (MAB=196 FAB=238 NB=99 Unassigned=7)	GD assessed by clinical site ASD diagnosis confirmed via medical records review	Review of electronic records	4.8% also had ASD
Dragon (2017) (Dragon et al. 2017)	USA	Cross-sectional analysis of clinical chart data	Adult Medicare recipients: Disabled trans Medicare beneficiaries (TMBs - N=5321), disabled cisgender Medicare beneficiaries (CMBs; N=6,548,168), aged TMBs (N=2133), and aged CMBs (N=32,588,061)	GD and ASD diagnoses confirmed via review of medical records for appropriate (International Classification of Diseases, Ninth Revision (ICD-9) codes	Review of electronic records	ASD prevalence among: All transgender beneficiaries - 3% All cisgender beneficiaries - 0.3% Entitled on disability grounds - (Transgender 4% Cisgender 1.3%) Entitled on age grounds - (Transgender 0.4% Cisgender 0%) Gendered comparisons not possible due to Medicare system limitations
Fielding (2018) Fielding & Bass (2018)	UK	Retrospective case-cohort study	Adults referred to a gender clinic N=153 (MAB=97 FAB=56)	GD diagnosed by clinical site (N=7 felt to not have GD) ASD diagnosis confirmed via medical records	Review of electronic records	7.8% of those referred had ASD
Heylens (2018) (Heylens et al. 2018)	Belgium	Cross-sectional analysis and retrospective clinical chart data analysis	Adults with GD/ GID Cross-sectional analysis N=63 Clinical chart data analysis N=532 (MAB=351 FAB=181)	GD diagnosis from clinical site ASD diagnosis confirmed in clinical chart data review	GD - clinical interview/ Utrecht Gender Dysphoria Scale (UGDS) Social Responsiveness Scale-Adult (SRS-A) Autism Quotient (AQ)	Cross-sectional sample: 27.1% of sample had mild-severe social shortcomings 4.8% of sample scored above cut-off on AQ Clinical chart data: 6% of sample had an ASD diagnosis

Study (first author, year)	Country	Design	Participants	Origin of Diagnosis	Measures Used	Key Observations
Children and Adolescents						
Chen (2016) Chen et al. (2016)	USA	Cross-sectional analysis	Child and adolescent referrals to a gender clinic N=38 (MAB=16 FAB =22)	GD assessed for by clinical site. ASD confirmed via medical records	Review of electronic records	13.1% in sample had ASD also No gender breakdown and limited sample size
De Vries (2010) (de Vries et al. 2010)	Netherlands	Cross-sectional analysis	Child and adolescent referrals to a gender clinic N=204 (MAB=115 FAB=89)	GD and ASD assessed for by clinical site	GD assessed via standardised clinical interview ASD assessed using Diagnostic Interview for Social and Communication Disorders (DISCO)	7.8% of those referred had ASD (key features of each case are discussed) 4.7% with GD also had ASD 17% with GID-NOS also had ASD Boys with ASD were overrepresented in both child (6 of 7 children) and adolescent (6 of 9 adolescents) cohorts Refutes prenatal androgen theories Substantial variability of GID symptoms in those with ASD Possible sensory input preferences typical of ASD applied to several gender dysphoric boys Homosexual attraction sig. more common in comorbid GID and ASD Gender variant feelings in ASD can be particularly distressing because of ASD-specific rigidity
Heard (2018) (Heard et al. 2018)	Canada	Retrospective cross-sectional clinical chart data analysis and qualitative questionnaire analysis	Child and adolescent referrals to a gender program (N=174) (MAB=52 FAB=122) A subset from within this cohort (N=25) also completed an online survey	GD assessed for by clinical site. ASD confirmed via medical records	A 77-item survey based on previously validated healthcare surveys were given to N=25 of the overall cohort	2.3% also had an ASD diagnosis (and 1.1% with subclinical traits) 38% had comorbid psychiatric diagnoses (depression/ anxiety most common) quality-of-life questions in the survey cohort reflected poor well-being indicators for majority suggestions are made for improving trends inclusivity and healthcare

Study (first author, year)	Country	Design	Participants	Origin of Diagnosis	Measures Used	Key Observations
Hisle-Gorman (2019) (Hisle-Gorman et al. 2019)	USA	Retrospective case-cohort study	Children with ASD N=48,762 Children without ASD (control) N=243,810 Total sample was 80% MAB and 20% FAB to match reported male predominance of ASD	GD and ASD both confirmed via electronic medical records	Confirmation of ICD—9 criteria being met for ASD, GD and related conditions	ASD diagnosed children four times higher incidence of GD and related conditions 9.4% of children with ASD and GD had a coexisting intellectual disability Possible biological link between ASD and GD is suggested likely due to difficult in diagnosing ASD in females More conservative families may be more reluctant to seek GD diagnosis
Holt (2014) (Holt et al. 2014)	UK	Retrospective cross-sectional clinical chart data analysis	Child and adolescent referrals to a gender clinic N=218 (MAB=81 FAB=137)	GD assessed for by clinical site/ Autism Spectrum Condition (ASC) via clinical files	Review of clinical files for ASC diagnosis	13.3% of overall sample had ASC ASC was more common in natal males (18.5%) than natal females (10.2%)
Kaltiala-Heino (2015) (Kaltiala-Heino et al. 2015)	Finland	Retrospective cross-sectional analysis and qualitative clinical chart data analysis	Adolescents attending gender identity service for sex reassignment N=47 (MAB=6 FAB=41)	GD diagnosed by clinical site ASD confirmed via medical records or diagnosis by clinical site (N=3)	GD diagnosed by clinical interview Review of electronic records	26% of participants had ASD 75% of participant had co-occurring psychiatric treatment ongoing Discussion of social isolation as a possible exacerbating factor for GD and a reason for its link with ASD Discussion of potential androgen exposure link between ASD and GD Potential difficulties around adjustment to sex reassignment for those with ASD due to their rigidity discussed.

Study (first author, year)	Country	Design	Participants	Origin of Diagnosis	Measures Used	Key Observations
Kaltiala-Heino (2019) (Kaltiala-Heino et al. 2015)	Finland	Cross-sectional analysis	99 adolescents attending gender identity service (MAB=15 FAB=84) Compared against population samples of 90,953 male and 91,746 female	GD confirmed by clinical site ASD confirmed via clinical files	GD diagnosed by clinical interview Review of electronic records School Health Promotion Study (SHPS) compared for the GD referred against its population sample	Comorbid GD and ASD significantly delays sexual development 23.5% with comorbid ASD had kissed someone (non-ASD 69.5%) OR=0.11. Of 11.8% with comorbid ASD had intimate sexual experiences (non-ASD 45.1%) OR=0.1. sexual experiences were less common among those with early pubertal timing GD started at 12 or later for the majority in both groups (MAB 80%/ FAB 94%)
Leef (2019) (Leef et al. 2019)	Canada	Cross-sectional analysis	GD referred children N=61 (MAB=45 FAB=16) Other clinical concerns (CC) referrals N=40 (boys=28 girls=12)	GD confirmed by clinical site ASD confirmed via clinical file	SRS for ASD traits Child Behaviour Checklist (CBCL) Symptom Checklist-90-Revised (SCL-90-R) Social Communication Questionnaire (SCQ)	21.3% of GD referred children had ASD (0% in the CC group) SRS scores were not significantly different across all severity ranges between GD and CC groups SCQ scores in clinical range were significantly different (21.7% (GD) vs 3.3% (CC) scores were above cut-off)
Nahata (2017) (Nahata et al. 2017)	USA	Retrospective analysis of cross-sectional chart data	Children and adolescents referred to a gender clinic N=79 (Trans males N=51, trans females N=28)	ASD confirmed by clinical chart data all GD referrals were diagnosed with ICD 9/10 criteria	Review of electronic records	6.3% of whole sample had an ASD diagnosis (5.9% of trans males 7.1% of trans females) Comorbidity of GD with a range of other mental health conditions (92.4%) 58.2% were bullied

Study (first author, year)	Country	Design	Participants	Origin of Diagnosis	Measures Used	Key Observations
Skagerberg (2015) (Skagerberg et al. 2015)	UK	Cross-sectional analysis and retrospective clinical chart data analysis	Young people with GD attending a gender identity clinic N=166 (MAB=62 FAB=104)	GD assessed for by clinical site ASD confirmed by clinical chart data	GD diagnosed by clinical interview Review of electronic records SRS	54.2% were in mild/ moderate or severe range for social shortcomings 12% (20) overall had a diagnosis of ASD Discussion of possible association between autistic features and GD in presentations and outcomes Mean raw score was in the mild-to-moderate range (indicative of milder high functioning autism) for both GD cohorts, while TD (typically developing) sample was in normal range
van der Miesen (2017) (van der Miesen et al. 2017)	Netherlands	Cross-sectional analysis	Children with GD N=490 (MAB=248 FAB=242) Children with ASD N=196 (boys=100 girls=96) TD children N=2507 (boys=1,248 girls=1259)	GD diagnosed by clinical site Review of medical records to confirm ASD	Children's Social Behaviour Questionnaire (CSBQ) DSM-IV diagnostic criteria met for ASD	Autistic traits were higher in all domains for GD children and adolescents compared to TD Suggestion that co-occurring pathways for ASD and GD are different within males and females Possible sensory input preferences typical of ASD applied to their relationship with GD Discussion of social isolation as a possible exacerbating factor for GD and a reason for its link with ASD

CBCL (Achenbach & Edelbrock 1983); DISCO (Wing et al. 2002); SCL-90-R (Derogatis & Fitzpatrick 2004); SCQ (Rutter et al. 2003); SRS (Constantino et al. 2003)

Figure Captions

Figure 1. Search Process – PRISMA Flow Diagram

Figure 1 top
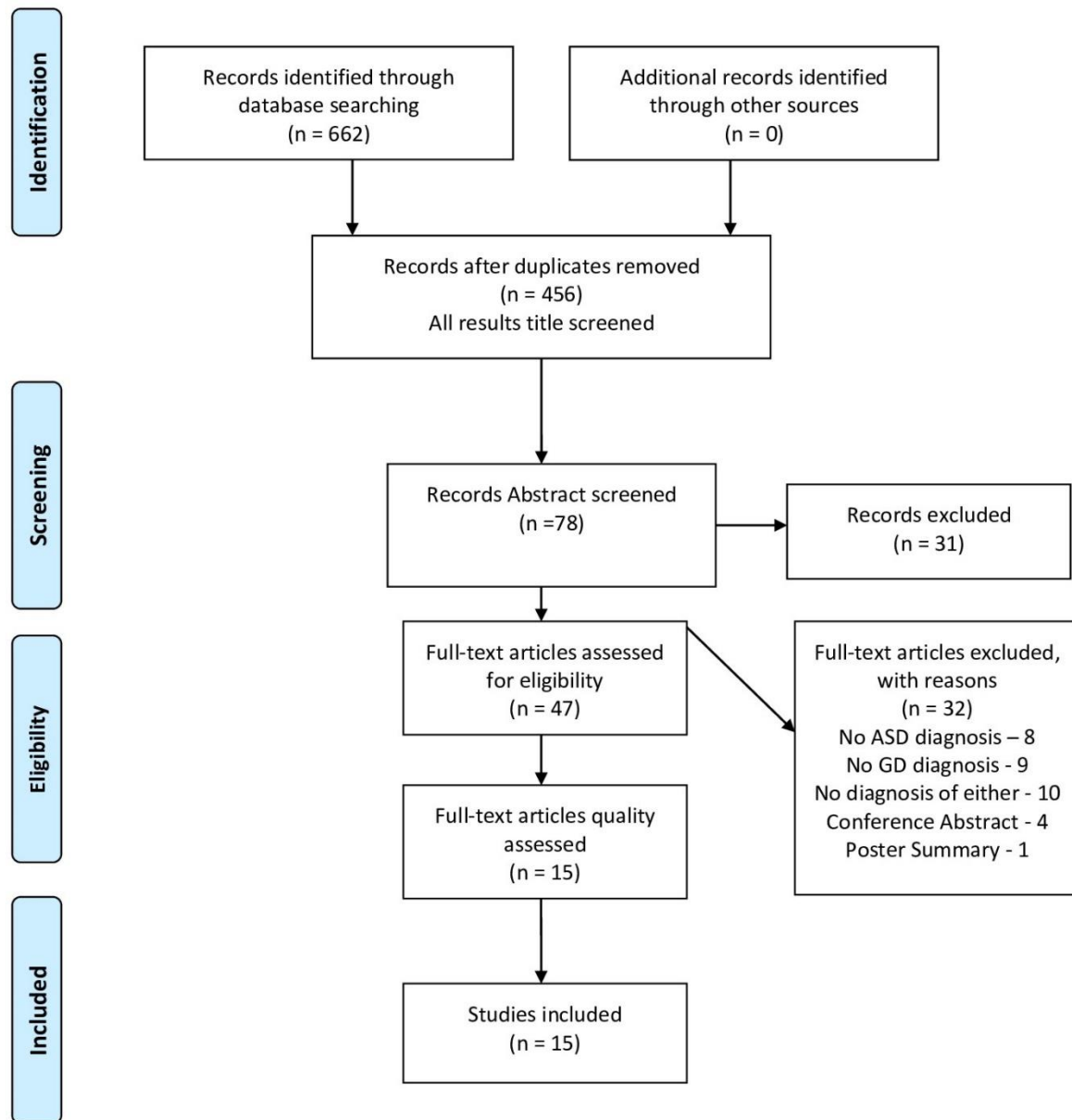
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Paper 2 has been prepared for submission to the Journal of Autism and Developmental Disorders in accordance with the guidelines for authors (Appendix 1). Therefore, tables and figures are presented at the end of the paper.

The Development of the Adult Version of the Signposting Questionnaire for Autism (SQ-A (Adult))

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Abstract

Questionnaire data are frequently collected by diagnostic services for Autism Spectrum Disorder (ASD) to supplement clinical decision-making. However, the *validity* and *reliability* of many ASD questionnaires used in clinical settings needs to be established. In phase one, the Signposting Questionnaire for Autism (Adult) was developed with advice from autistic adults. In phase two its initial psychometric properties were examined in a typically developing population (N=80). In phase three the SQ-A(Adult) was administered in a clinically-referred population (N=66) and comparisons were made between those seeking diagnosis, their loved-ones and assessing clinicians. Results demonstrated *convergent* and *concurrent validity* and c*ross-informant reliability* across several comparisons. Findings are discussed in the context of their potential contribution to further clinical practice, and a full validation study was proposed.

Keywords

Autism spectrum disorder, DSM-5, Adult, Diagnosis, Questionnaires

Autism spectrum disorder (ASD) is a lifespan neurodevelopmental disorder impacting

approximately 1 in 100 adults (Brugha et al. 2011). Its main symptom domains defined by

DSM-5 (American Psychiatric Association, 2013) are social and communication difficulties

and restricted and repetitive behaviour patterns. Diagnosis requires a detailed developmental

history in an interview format, supplemented with behavioural observation and assessment of

needs (National Institute for Health and Care Excellence [NICE], 2012). To achieve this,

standardised developmental interviews such as the Autism Diagnostic Interview (ADI-R;

Lord et al. 1994) or the Diagnostic Interview for Social and Communication Disorders

(DISCO: Leekam et al. 2002; Wing et al. 2002) are widely used. These interviews can require

anywhere from 1.5 to 3 hours of an expert clinician's time to complete, and as such, efforts to

streamline the diagnostic process are needed.

In recent years briefer standardised interviews have been developed, aimed towards

reducing time taken during the referral and diagnostic process, while maintaining accuracy

and standardisation. A shortened version of the DISCO interview (the DISCO-Abbreviated)

containing essential items for diagnosis was tested in an adult and child sample (Carrington et

al. 2014, 2019) and adopted for use by NHS Wales in 2013. Several brief questionnaires have

also been developed from the DISCO; the Signposting Questionnaire for Autism (SQ-A;

Jones et al. in review) for children, and multiple versions of the Repetitive Behaviours

Questionnaire (RBQ) for different clinical populations (Barrett et al. 2015, 2018; Honey et al,

2012; Leekam et al. 2007). These are often used as additional sources of information that

may contribute to clinical decision-making. However, the role questionnaires may play in

informing and supporting the assessment and diagnostic process remains under-explored.

The SQ-A (Jones et al. in review) was originally designed for completion by parents/carers of children; including the 14 most discriminating DSM-5 items from the DISCO interview (Carrington et al. 2015). A validation study of the SQ-A (Jones et al. in review) recently established good internal *consistency*, *criterion* and *convergent validity* in a well-established (UK) and more fledgling (Latvian) diagnostic context, representing the first time a brief questionnaire had been designed specifically to utilise items derived from a DSM-5 diagnostic instrument. Historically however, researchers have failed to fully characterise the psychometric properties of these brief questionnaires (Bolte et al. 2011; Skuse et al. 2009), suggesting an opportunity to examine and potentially address this unmet need with such a measure for adults.

The overarching aim of the study was the development of the SQ-A (Adult); a questionnaire derived from the SQ-A that could help to signpost adults with potential ASD to appropriate services. This was undertaken in three phases; the design of the questionnaire in phase one, initial testing of the SQ-A (Adult) in phase two, and an exploratory analysis in clinically referred adults during phase three. Phase one involved consulting with members of the autistic community to ascertain the acceptability and accessibility of the questionnaire. A panel of expert clinicians then discussed a series of suggested revisions from the autistic consultants to arrive at final item wordings. Phase two, involved testing the SQ-A (Adult) in a non-clinically referred sample of undergraduates, to establish *scale reliability* and examine consistency in reporting of items between its *pre* and *post* consultation versions.

The focus of phase three was an exploration of the SQ-A (Adult)'s psychometric properties in a clinically referred sample. Along with the *self*-report, an *other*-report version

of the *post*-consultation questionnaire was developed, so that data from *other*-respondents could also be captured. The SQ-A (Adult) was examined with several tests of *reliability* and *validity* to address three primary aims. First, *convergent validity* was tested by comparing total scores for the same subset of DISCO items obtained from three different sources (*self* and *other* SQ-A (Adult) questionnaires and the DISCO-Abbreviated clinical interview). Strong correlations would suggest the items perform similarly across a range of contexts. Second, *concurrent validity* was examined by comparing the SQ-A (Adult) to the Autism Spectrum Quotient (AQ-10; Allison et al. 2012). The AQ-10 has been designed for use as a 'red flag' measure to guide referrals. How well the SQ-A (Adult) correlates to a well-established, previously validated measure, evaluating different but related constructs, might suggest the potential for further testing in a referral context. Third *cross-informant reliability* was tested, by examining correlations between *self* and *other* versions of the questionnaires for each case. If significant correlations were established, it would suggest either *self* or *other* questionnaires have potential to be clinically useful in isolation e.g. if a person cannot complete their *self*-questionnaire, or there is no '*other*' informant available.

Phase One – Questionnaire Development

Method

Phase one was conducted in accordance with established and recognised procedures for measure development (see Boateng et al. 2018 for a review) to ensure early exploratory analyses could be built upon by further testing if their clinical potential were established. Among the main considerations were ensuring no existing validated measures addressed the desired outcomes, considering the layout, sequencing, positive/ negative balance and length

of questions, visual layout and design, and approach to sampling (Boynton and Greenhalgh 2004). This phase sought to develop the SQ-A (Adult) questionnaire through a process where autistic adults and expert clinicians contributed to the makeup of the final questionnaire. The SQ-A (Adult) was based on the 14 items of the original parent report SQ- A (Jones et al. in review) along with five additional experimental items highly endorsed (over 30%) by adults with ASD previously (Carrington et al. 2019). One additional item highly endorsed among adults regarding non-verbal responses was not included, as it is a conditional question in the DISCO-Abbreviated (only asked to those who do not communicate verbally). As the item is not routinely included and would not be asked to any adult self-reporting during the DISCO-Abbreviated interview it could not be cross-matched with questionnaire data and was thus excluded.

Participants

Four adults with an ASD diagnosis and six expert clinicians were consulted to refine the questionnaire and make sure it was acceptable and accessible while maintaining its construct validity. The ASD diagnosed adults (two males (aged 49 and 62), two females (aged 22 and 34)) were recruited from a university research register. One contributed face to face, one by telephone, and two via email response. Having received the consultation information (Appendix 6) electronically, the autistic consultants gave informed consent (Appendix 7). A debrief (Appendix 8) was received following the consultation. All autistic consultants received a one-off payment for their contributions.

Materials

The consultation phase aimed to refine the 14 items, together with the five previously highly endorsed items (Carrington et al. 2019) into a *self*-report format. The initial items all

consultants viewed, had only the essential re-wordings necessary to render them appropriate for *self*-report (e.g. 'finds it difficult' became 'I find it difficult').

Procedure

For consultants participating in person, the items were presented one at a time, on paper, followed by the questions, and answers were clarified and transcribed by a researcher. Those participating by telephone were read the items followed by the questions one at a time, and their answers were clarified and summarised by a researcher. Those participating by email received a document with all the items and the questions, in one document they were asked to complete independently. With the autistic consultants, the questionnaire items were presented in the same order for each consultant. This followed the Jones et al. (in review) study order for the first 14 items, followed by the five items from Carrington et al.'s (2019) study. Consultants looked at each item one by one, confirming whether each item made sense, whether it might cause offence, and for any revisions they suggested. The most common request for adjustment reflected concern that the item might be perceived as insensitive.

The feedback from each consultant on each item was then collated and presented in a report to the participating clinicians, showing the items used, each consultants responses (whether positive negative or neutral), and any suggestions for rewording that were made if they weren't satisfied with the item. The feedback passed through a chain of six expert clinicians in total, one by one, allowing them to reflect on the suggestions made. Having read the report and any prior clinician suggestions they offered their own suggestions for potential revisions, balancing sensitivity to feedback received against maintaining *construct validity*, as originally intended by the author (Wing, et al. 2002), before passing this on to the next

clinician to build on the discussion. Final decisions on all suggested revisions were made by the most senior clinician, after all feedback was received.

Results

All items reaching consensus following revisions were included in the final set of 18. Consultant feedback led to 13 items being reworded to varying degrees. One of the five new items regarding unusual responses to visitors, which was highly endorsed among adults in the Carrington et al (2019) study, was adjudged potentially offensive by all autistic consultants. No acceptable balance could be found between honouring consultant feedback for potential rewording and maintaining construct validity, thus the item was deleted entirely.

Phase Two - Testing in an undergraduate population

Method

Participants

In the absence of any *pre*-existing comparable data from which to calculate power, an opportunistic sample was recruited from an undergraduate psychology population (N=90), who participated in return for undergraduate research credits (Appendix 9 and 10). The sample included all who were able to take part within the time available for the data collection phase of the project. Ten participants were later excluded; one who did not complete all three questionnaires, and nine who did not show evidence of appropriate engagement with the study (all questionnaires completed < 3 minutes), leaving N=80 cases included in analysis. Their age range was 18-22 years with a mean age of 19.30 years

(SD=1.036). Ten participants (12.5%) were male, 70 (87.5%) were female. None had an ASD diagnosis. Ethical approval for the study was granted by the Cardiff University School of Psychology Research Ethics Committee.

Materials

SQ-A (Adult)

The SQ-A (Adult) derives from the DISCO (Leekam et al. 2002; Wing et al. 2002), a 320-item diagnostic interview with good *inter-rater reliability* and *criterion validity* (Leekam et al. 2002; Maljaars et al. 2012; Nygren et al. 2009) and good agreement with the Autism Diagnostic Interview-Revised (ADI-R; Lord et al. 1994) and Autism Diagnostic Observation Schedule (ADOS; Lord et al. 2000). A statistically reduced set of 54 'essential' items was established by Carrington et al. (2014). This was reduced to a 14-item 'signposting set' of the most highly discriminating items from the DISCO DSM-5 algorithm, which showed high internal consistency (alpha=.92), sensitivity (.89) and specificity (.89) in a child sample (Carrington et al. 2015). The 14-item signposting set was subsequently converted into a questionnaire format (the Signposting Questionnaire for Autism (SQ-A); Jones et al. in review). The SQ-A (Adult) combines the original 14 SQ-A items and four additional experimental items highly endorsed (over 30%) by adults with ASD in a research sample (Carrington et al. 2019). Both *pre* (Appendix 11) and *post* (Appendix 12) consultation versions of the SQ-A (Adult) were designed; the *post* reflecting revisions agreed during the consultation exercise. The SQ-A (Adult) has a readability consensus (aggregated from several readability measures) of grade level 5, indicating suitability for a reading age of 8-9 years old.

To complete the SQ-A (Adult), respondents tick a box asking whether they *definitely agree, slightly agree, slightly disagree*, or *definitely disagree* with statements such as, "I find it difficult to offer comfort if others are upset." The approach to scoring was identical to that used in Jones et al. (in review) for the SQ-A. Reversals were applied to six questions (1, 4, 5, 9, 10, 15) (e.g. "lack of awareness of other's feelings" became "aware of other's feelings"). Each question was scored and re-coded into a binary score, where each of the 4 options met (1) or did not meet (0) criteria for an autistic feature. Eight items (1, 3,4, 8-10, 13, 15) used dichotomised scoring (definitely/ slightly agree =1, definitely/ slightly disagree = 0). The other 10 items (2, 5-7, 11,12, 14, 16-18) scored 1 only for the extreme response (definitely agree). This was because the binary coding was based on established syntax applied to DSM-IV (Leekam et al. 2002) and DSM-5 (Kent et al. 2013) algorithms, and previous studies with signposting interview items (Carrington et al. 2015, Carrington et al. 2014). A total (range 0-18) was calculated as well as a separate total for the original 14 SQ-A items from Jones et al. (in review) (range 0-14).

AQ-10

The AQ-10 (Allison et al. 2012; see Appendix 13) is a 10-item *self*-report questionnaire shortened from a longer measure, the 50-item Autism Spectrum Quotient (AQ; Baron-Cohen et al. 2001). The questionnaire asks whether respondents *definitely agree, slightly agree, slightly disagree*, or *definitely disagree* with statements such as "I often notice(s) small sounds when others do not." The items relate to social skills, attention switching, attention to detail, communication, and imagination. The AQ-10 has very good sensitivity and specificity in discriminating individuals with ASD from those without ASD with reported sensitivity of

0.88, specificity of 0.91, and positive predictive value of 0.85 in an adult sample (Allison et al. 2012; Booth et al. 2013). The AQ-10 has a readability consensus (aggregated from multiple readability measures) of grade level 5, indicating suitability for a reading-age of 8-9-year olds upwards.

Procedure

Testing was administered online through the survey program Qualtrics (Qualtrics, 2020). Each participant completed three questionnaires in an electronically automated, counterbalanced order, such that each participant took the 19-item *pre*-consultation SQ-A (Adult) or the 18-item *post*-consultation SQ-A (Adult) first, followed by the AQ-10 and the remaining questionnaire third.

Statistical analyses

All quantitative data from this phase were analysed in SPSS 25 (IBM Corp., 2017). Descriptive analyses of demographic data and data screening were completed. The number of participants meeting clinical criteria for each item on the SQ-A (Adult) *pre* or *post* consultation versions were examined for any trends and differences. Total scores for the SQ-A (Adult) (*pre* and *post*-consultation versions) and the AQ-10 were analysed for *reliability* and *validity* with Spearman's correlations due to some of the scale totals being skewed. The scale was analysed for scale *reliability* with Cronbach's alpha. A Cronbach's alpha value of >.70 suggests acceptable internal consistency (Streiner, 2003).

Screening of Questionnaire Data

Distribution of total scores was significantly skewed (Shapiro-Wilk) for all measures. There were three high scoring outliers (±3 SDs from mean); one each on the *pre*-consultation SQ-A (Adult) (total score = 5), *post*-consultation SQ-A (Adult) (total score = 6), and AQ-10 (total score = 8). These were retained as a single high-scoring outlier in a sample of this size would not be unusual, nor would a single case have any meaningful impact on the statistical analysis.

Questionnaire Analysis

Descriptive statistics

Less than 15% of participants met the clinical criteria for any item on the SQ-A (Adult) *pre* or *post* consultation versions, except questions 3 (21.3%/ 25%), 9 (21.3%/ 23.8%), and 15 (16.3% - *pre*-consultation version only). A full table of frequencies is included in Online Resource 1. The mean scores and other descriptive statistics for the questionnaires are presented in Table 1.

Scale reliability

Cronbach's alpha was calculated for both the original 14-item and full 18-item versions of the scale in both *pre* and *post* format, and all demonstrated acceptable levels of internal

consistency. The 18-item versions had slightly higher levels of internal consistency for both questionnaire versions. The AQ-10 did not reach an acceptable level (α =.56) (see Table 1).

(Insert Table 1 here)

Inter-item correlation

When comparing each item on the pre and post SQ-A (Adult), significant differences in the mean scores were found for eight items (2, 4, 5, 6, 8, 13, 14, 18 – see online resource). The *post*-consultation answers for items 2, 4, 5, 6, 8, 13 and 14 associated with higher numbers meeting clinical criteria in each case. Item 18 did not show any difference in numbers meeting clinical criteria.

Convergent Validity

Analyses of the *pre* and *post*-consultation SQ-A (Adult) were completed to examine correlations item by item for both 14 and 18-item subsets to compare their performance. All item pairings were significantly correlated at $p<.035$ or less, with the exception of question 5 ($p=.091$). Multiple paired t-tests examined for differences in mean total scores between each *pre* and *post* item, with significant p-values reported for several items (2, 4, 5, 6, 8, 13, 14, 18). A table highlighting significant t-test results is included in Online Resource 1. A paired-sample t-test suggested the overall performance of the scale was not significantly different between *pre* and *post* versions ($t=-1.37$, $p=.175$) and the overall scales showed strong correlation in both the 14-item ($r=-.591$ $p.<.001$) and 18-item ($r=.659$ $p.<.001$) subsets. While correlations were strong for both, the superior r-value of the 18-item subset resulted in its adoption as the default format for analyses going forward.

Concurrent Validity

The *pre* SQ-A (Adult) total scale demonstrated a weak but significant correlation with the AQ-10 total scale (r=.296, p=.008). The *post* SQ-A (Adult) similarly showed a weak but significant correlation with the AQ-10 total scale (r=.282, p=.011).

Phase three: Testing of the SQ-A (Adult) in a Clinical Setting

Method

In phase three, routinely collected clinical data from the Gwent Integrated Autism Service (IAS) were utilised. The 18-item SQ-A (Adult) *self* and *other* versions (Appendix 14 and 15), and comparable items on the DISCO-Abbreviated interview were compared to examine *convergent validity*. The AQ-10 was used in both a *self* and *other* format (Appendix 16 and 17) to examine *concurrent validity*. In the most recent (2018) reported figures for the clinical site, 164 individuals received an ASD assessment and 158 went on to receive an ASD diagnosis. Information from the DISCO-Abbreviated contributed directly to the diagnostic decision-making, while information from questionnaires and other checklists were consulted at the clinical decision-making stage if required.

Participants

The participants were attending the clinical site for assessment for a possible diagnosis of ASD. Over the research period 76 attended for assessment. Of these, 10 were excluded from

the study (five did not include at least one set of questionnaires, 2 had their diagnostic appointment with a measure other than the DISCO or could not complete it, and three were missing either >10% data on all questionnaires or both of the SQ-A (Adult) measures). N=66 returned enough data for some form of analyses. Participants were 60.6% male (N=40), 36.4% female (N=24) and 3% Trans/ non-binary (N=2). Mean age was 31.21 years (SD = 11.06). Most participants were accompanied by a relative or someone that knew them well (78.8%). N=58 returned a full set of data, with eight participants returning partial data. However, all had a DISCO algorithm sheet (see Materials), four returned at least one *self-*questionnaire, and four at least one *other-*questionnaire. Each of these were included in relevant analyses for the measures returned. All data analysed were routinely collected in the clinical setting. Ethical approval for access to the data was granted by the Healthcare Research Authority and Health Board Research and Development Department.

Power analysis

Initial power analysis with GPower (Faul et al. 2009) indicated that a sample size of 38 would be required for a correlation with a large effect size (.5). Sample size was corroborated by a study comparing the SQ-A with the AQ-10 in children (parent version) (Jones et al. in review). This study found a correlation coefficient of $r^s=.76$ in a sample of 102. In a second independent sample comparing the same questionnaires, a smaller sample of 35 was used and the correlation was still large $r^s= .50$ (Jones et al. in review study 2). Within the same study, *cross-informant* correlations were conducted for the Signposting Questionnaire for Autism (SQ-A) with high correlations again found ($r_s=.61$, $p<.001$) in a sample of 39. The sample size of 66 was therefore deemed sufficient.

Materials

DISCO-Abbreviated Clinical Interview

The DISCO-Abbreviated Interview (Carrington et al. 2014) is a 68-item, semi-structured, clinician-led interview conducted with the individual (and ideally a parent or relative). It takes approximately 1 ½ hours to complete. Clinicians complete an algorithm sheet by assigning a code for each item based on the responses they receive. The DISCO-Abbreviated Interview has its own tailored diagnostic algorithms, which map to international diagnostic criteria (with excellent published psychometric properties that perform as effectively as the full algorithms in discriminating ASD (Carrington et al. 2014)). This study drew upon the 18-item subset of numerically coded DSM-5 data collected during the clinical interview to compare with parallel items in the SQ-A (Adult).

SQ-A (Adult) and AQ-10

The SQ-A (Adult) and AQ-10 *Self*-report versions were both used in identical wording to the undergraduate testing in phase two. All 18 items in the SQ-A (Adult) *post*-consultation version were used in phase three. The *other* versions of the SQ-A (Adult) and AQ-10 were created by making only essential revisions in wording to change them from *self* to *other* report e.g. 'I often notice…' became 'often notices…'. Permissions were obtained from the Autism Research Centre, Cambridge, UK, to make the revisions required to the AQ-10 for this purpose.

Procedure

As part of standard practice by the IAS clinical team, both the adult referred to the service and a person who knows them well complete the questionnaires at home and bring them to their first appointment. Questionnaires were presented in pen and paper format in a counterbalanced order for both *self* and *other* versions (half of the questionnaire bundles had the AQ-10 first and the other half the SQ-A (Adult)). When the adult attended their first appointment, together with their relative/friend, the DISCO-Abbreviated was completed by a clinician.

Questionnaire responses were not consulted by the clinical team before beginning the interview. Following assessment, the clinical team used information from all sources (including questionnaires if required) to provide a consensus diagnosis for the individual. Each participant's data was anonymised with a numerical identifier by the clinical team before transfer to the research team. Once received, a new random identifier was assigned before entering each participant's data, and destroying the original records. All data were transferred to the research team securely. All data were entered manually, and double-checked for accuracy by another member of the research team.

Statistical analyses

All data were analysed in SPSS 25 (IBM Corp., 2017) and the same analyses and procedures as phase two were employed. Bivariate correlation analyses were conducted based on total scale scores. Distributions of scale items were in several cases skewed and therefore Spearman's correlations were needed. Total scores for the 18-item SQ-A (Adult) and AQ-10 *(self and other)* were analysed for *scale reliability* with Cronbach's alpha. The *concurrent validity* of the SQ-A (Adult) in comparison to the AQ-10 was established by looking at group differences, and correlations between measures. *Cross-informant reliability* was examined via *self* and *other* correlations for the questionnaire measures with Spearman's, and *convergent validity* was examined between both groups and the clinician-generated DISCO-Abbreviated algorithm (18 item) total scores. Bonferroni correction was applied where relevant to appropriately reduce the p-value threshold.

Results

Screening of questionnaire data

Little's Missing Completely at Random tests were completed on the original non-recoded items for both versions of each questionnaire. Results were non-significant for all tests, suggesting there was no pattern to missing data. Three cases were excluded from all analyses due to missing data >10% across all measures. Missing data was mostly low, with 58 participants (87.9%) having responses for all items. In any situation where >10% data was missing for a measure (more than one response missing) the measure was excluded from relevant analyses for that case, but the remainder of their data still included. For individual missing datapoints, the participants mean item score was multiplied by the total number of items and rounded up or down to the nearest integer (to revise the total score) with 0.5 as the cut-off point. There were no missing data for the DISCO interview algorithm sheets.

Data was recoded to apply questionnaire item reversals and the binary scoring algorithm (see phase two for details). There was one low scoring outlier ($\pm$3 SD's from mean); on the AQ-10-*self* (score 2). This was retained in the analyses on the basis that although a specialist assessment service, prior service data suggests a small percentage of those referred do not receive an ASD diagnosis, thus a single low-scoring outlier for a sample of this size would not be unusual, nor would a single case have any meaningful impact on the strength of correlations found in this instance.

Questionnaire Analysis

Descriptive Statistics

Descriptive statistics for all measures are presented in Table 2. Each of the SQ-A (Adult) items was attributed a score of 1 (=autistic feature) for at least 40% of the participants, apart from items 5 (18%) and 7 (17%) and 11 (37.1%) for the *self*-version, and 5 (25%), 7 (13%) and 12 (36%) for the *other*-version. Figure 1 presents a frequency analysis graph for the 18 items in the SQ-A (Adult), formatted and mapped to the DSM-5 (American Psychiatric Association, 2013) category descriptors for each item. A full table showing the percentage meeting criteria for each of the 18-items across *self, other* and *clinician*-rating is presented in Online Resource 2. While the percentage meeting clinical criteria for each item were broadly similar across *self* and *other* populations (with the exception of items 13 and 18), clinician ratings noticeably differed across most items. Depending on the item, clinicians were noticeably more (1,4, 5, 10, 12-15, 18) or less (2, 3, 6, 8) likely to endorse a clinical feature.

Each of the AQ-10 items was attributed a score of 1 for at least 50% of respondents on both the *self* and *other* samples.

(Insert Table 2 here)

Reliability and validity of the SQ-A Adult

Convergent Validity

Correlational analyses (Spearman's) of the 18-item *self* and *other* SQ-A (Adult) found the overall scales showed moderate and significant correlation for the *self* (r=.419, p>.001) and strong and significant correlation for the *other* (r=.554, p>.001) with the DISCO DSM-5 Algorithm (18 item subset).

Concurrent Validity

The *self* SQ-A (Adult) total scale showed moderate correlation with the *self* AQ-10 total scale (r=.325, p>.011). The *other* SQ-A (Adult) total scale showed weak correlation with the *other* AQ-10 total scale, and its significance did not survive Bonferroni correction (r=.272, p>.034).

Cross-informant reliability

The *self* and *other* SQ-A (Adult) total scales showed moderate correlation with each other (.499, p>.001).

Discussion

The overall aim of this study was to develop the SQ-A (Adult) and examine its psychometric properties in both a general population and clinical sample; the three phases reported herein were designed to achieve this aim. Phase one developed a new questionnaire, the SQ-A (Adult), with advice from autistic adults, while phase two demonstrated its scale *reliability* and *validity* in a non-clinically referred sample. In phase three, *convergent* and *concurrent* *validity* were established across a range of comparisons in a clinically referred sample. Significant correlations were found between the 18-item SQ-A (Adult) in both *self* and *other*-formats, with the analogous 18 items derived from the DISCO-Abbreviated interview. These represent a promising start to the process of examining how the SQ-A (Adult) may potentially contribute to the assessment and diagnostic pathway in future.

Streamlining of clinical diagnostic pathways remains a clinical imperative, and research has already made progress in abbreviating standardised diagnostic interviews, i.e. DISCO-Abbreviated (Carrington et al. 2014), for routine clinical use, however a signposting measure for adults, derived from the DISCO (Leekam et al. 2002; Wing et al. 2002) and designed for *self*-report has until now been unavailable. As a result, the development of the SQ-A (Adult) and initial testing of its psychometric properties was the goal of this study.

Phase one aimed to develop a questionnaire (the SQ-A (Adult), which directly derived from a DSM-5 compatible diagnostic interview (DISCO), while phase two and three sought to establish its *scale reliability* and *consistency* between versions in an undergraduate and then clinically referred population. The SQ-A (Adult) was based on the SQ-A (Jones et al. in review), which was originally developed for parent report of children's autistic behaviours.

To our knowledge several aspects of the study are unique. As far as we are aware this is the first questionnaire to assess autistic traits developed in consultation with the autistic community. The SQ-A (Adult) was conceived and designed through a consultation process with autistic adults; giving those with lived experience of ASD an opportunity to contribute to shaping a measure, for potential use in clinical practice. This feedback was important in understanding how people respond cognitively and emotionally to the content of items originally intended for caregiver report. Feedback led to revision of most items for the final questionnaire.

In phase two, the *pre-* and *post-*consultation SQ-A (Adult) questionnaires were tested in an undergraduate population. Significant differences in the mean scores meant several *post-*consultation items saw more participants meeting clinical criteria (in other words presenting as 'more autistic' by scoring for the trait on the *post* consultation SQ-A (Adult) but not on the *pre*). Item 18 is of interest, as despite its identical positioning and wording the difference was nonetheless significant, however there was no difference in the number meeting clinical criteria. The contributions from autistic consultants in phase one broadly showed one trend; that several items might be perceived as insensitive in a *self-*report format if unchanged. This invaluable feedback resulted in softening wording for several items; the logical consequence being that more members of a typically developed (TD) population might also endorse them, as appears to be illustrated in the findings above. Importantly, the overall performance of the questionnaire was not significantly different between *pre* and *post* versions.

Phase two also examined the performance of the original 14 items compared to an extended version that brought in four items known to be discriminating in an adult sample. The findings showed consistently low endorsement of autistic features across the sample, with the 18-item version performing marginally better than the 14-item. All 18-items of the SQ-A (Adult) were then used in further exploratory testing in a clinical population. Acceptable *scale reliability* was established, while strong correlations at the scale level were the most notable finding.

The third phase represents the first time that one of the DISCO-associated questionnaires has been transformed into a *self*-report rather than *carer*-report format. *Self*-report is an established format of other ASD questionnaires such as the AQ (Baron-Cohen et al. 2001), but to our knowledge, this is the first *self*-report questionnaire to specifically map onto a DSM-5 compatible diagnostic algorithm. This phase examined the potential utility of the SQ-A (Adult) in a referral context by collecting data from those seeking an autism diagnosis, along with their relatives, when attending an IAS for assessment. There were several aims to this exploration. Firstly, investigating *convergent validity* by comparing scores on the SQ-A (Adult), which are based on DISCO DSM-5 algorithm coding, with the clinician-derived algorithm subtotals of the same items administered in the DISCO-Abbreviated interview. Despite items being adapted from a semi-structured interview (DISCO), requiring expert clinical administration, often with further questioning and clarification, the items still correlated significantly between the two measures. These correlations are promising, suggesting the underlying constructs have survived conversion into *self*-report wording, and significant revision for a number of items during the consultation process. A key aim of the study was examining whether the SQ-A (Adult) might prove a valid and reliable tool, so that its potential to contribute to streamlining the diagnostic

pathway as a *pre*-assessment measure could be explored further. This is a significant first step towards the exploration of that potential.

The second aim of phase three was to explore the *concurrent validity* of the SQ-A (Adult), by comparing it with the AQ-10 (Allison et al. 2012), another brief signposting measure. Although both measures catalogue autistic traits, they explore different constructs. As such, establishing *concurrent validity* (although only moderate) between the SQ-A *self* and the AQ-10 *self,* bolsters the SQ-A (Adult)'s potential to make a meaningful contribution to the diagnostic pathway in future. Further work is however needed to improve *concurrent validity* for the *other* comparisons where correlation was low, and significance did not survive Bonferroni correction.

Finally, *cross-informant validity* was established by comparing DISCO algorithm scores (18-item subset total scores) at the scale level, for correlations between *self* and *other* informants for each case. *Other* informants have consistently been an important element of ASD diagnostic practice. NICE (2011) guidelines caution that ideally someone with lifetime knowledge of the person should take part in the assessment process. This can be a useful adjunct to clinical judgement when feedback or perspectives differ, but is often absent when adults present for diagnosis. Indeed, in our clinical sample almost a quarter (22.2%) were unaccompanied at their appointment. The inclusion of *self* and *other* informants in this study addresses an identified gap in the literature for adults (Mandy et al. 2018), opening another potential avenue to receiving feedback from *other* respondents who cannot attend appointments at a diagnostic service. The correlations established between the SQ-A (Adult) and the DISCO algorithm were moderate (r=>.3) for the *self*-comparisons and strong (r=>.5)

for the *other* comparisons. This is a particularly useful finding, as it has previously been

suggested that insight into one's own difficulties can be a problem in ASD (Mazzone et al.

2012). This suggests there may be equal value in the use of this measure in *other*-informant

format, and indeed that either may have clinical utility in isolation.

While historic narratives have suggested insight may be lacking in those with ASD

(Mazzone et al. 2012), the mean total scores for *self* and *other* SQ-A (Adult) samples actually

proved remarkably similar. This same trend was observed when the AQ-10 *self* and *other*

questionnaires were compared. These findings seem to chime with more recent research

suggesting while personality traits and views may undoubtedly be different, insight levels *are*

comparable between ASD and TD samples (Schriber et al. 2014). As an adjunct to this

however, when viewed item by item clinicians appeared noticeably more or less willing to

endorse a clinical feature, than those reporting by questionnaire. This raises another

interesting priority for future testing of the SQ-A (Adult); examining what might underlie this

mismatch between the views of clinicians and those presenting for assessment with their

loved ones. This is particularly relevant for further investigation as recent research (Ashwood

et al. 2016) examining the AQ (Baron-Cohen et al. 2001) and AQ-10 (Allison et al. 2012) has

suggested that its specificity for an ASD diagnosis is low despite previous findings

suggesting otherwise. Ashwood et al. (2016) caution that low specificity (0.29) and a

negative predictive value of 0.36 meant 64% of those scoring below cut-off actually went on

to receive diagnosis, and that generalised anxiety disorder features which mimic ASD

appeared to lead to false positives. This is one cautionary example which further strengthens

the case for a more in-depth validation study to fully characterise the SQ-A (Adult)'s

psychometric properties.

The findings above provide initial evidence of the potential utility of the SQ-A (Adult) to support the diagnostic pathway for ASD in future. However, there are several further research priorities. Firstly, in their recent study on the original parent-report SQ-A for children, Jones et al (in review) demonstrated the SQ-A reliably discriminates ASD from non-ASD in samples. This was accomplished across two countries with divergent levels of autism provision, suggesting the SQ-A has some measure of cross-cultural *validity*. The study further established sensitivity and specificity for the SQ-A when an ASD group were compared with a control group and a group referred for *other* clinical concerns. Limited sample sizes for the *self* and *other* respondent groups in this study meant further analyses such as those from Jones et al. (in review) above are not yet possible. A full validation study using a cross-cultural sample of ASD and non-ASD participants, alongside those referred for other clinical concerns, would be a logical next step to build upon the work outlined in this study.

While the SQ-A (Adult) contained the same items as the SQ-A, with the aim of providing a useful complement to the existing parent-report version for children, two key adaptations were made. Firstly, the addition of five (eventually reduced to four) additional items that previous research had identified were highly endorsed in an adult sample (Carrington et al. 2019); and secondly, the redrafting of each item for *self*-report, via a consensus building process directly influenced by feedback from autistic adults. Involving those with autism in all aspects of research design and practice is an area of very active debate. In a mixed-methods study on the subject, Pellicano et al. (2011) found significant divergence in views on how meaningfully people with autism are involved in research. The

autistic people sampled felt significantly less meaningfully engaged than researchers estimated. Callard et al. (2012) suggest a key issue is that those with autism are frequently only involved at the point of implementation or intervention, or only as participants in research, rather than actual stakeholders in it, and thus research does not necessarily reflect the priorities of the autism community. A key concept in this debate is the idea of backwards translation, proposed by Zerhouni (2003); that is the use of practice-based evidence to inform research design and practice, rather than evidence-based practice guiding research priorities. This idea has gained particular traction in the ASD community, with numerous studies reflecting the value and ethical imperative of reshaping research practices around increased relevance and resonance to the lives of those being studied (Chalmers, 2004; Lloyd and White, 2011; Partridge and Scadding, 2004; van der Laan and Boenink, 2015).

Limitations

There were several limitations to the study. For phase one, the consultation with autistic consultants was initially envisaged as a group setting of approximately six people, anticipating a move towards an agreed consensus for each questionnaire item. However, responses to invitations were low, meaning only four people could be recruited within the available timeframe. Consultants were also reluctant to meet in person, which ultimately meant none of those contributing discussed their thoughts together in open forum. How much this might have altered feedback received is debatable, as there was generally good consensus on the accessibility and agreeability of items. Where opinions did diverge however, these views were freely expressed and equally considered by the clinicians in the consensus building phase, which might not have occurred in a group setting, so isolated contribution had its advantages also. A related issue is the finding in prior research (e.g. Pellicano et al. 2011)

that those with autism tend to feel that autism researchers are only interested in higher-functioning candidates, and as a result the full range of autism experiences are frequently absent from research. Pellicano et al. (2014) also found researchers acknowledge the same bias towards high-functioning individuals, particularly noting that their feedback can tend to crowd-out the views of those with higher-support needs in any sort of group or forum-based research.

One key area of interest where comparisons were not possible was gender differences. Many adults with ASD may have learned to camouflage certain areas of difficulty, for example by learning social interaction skills by rehearsal and practice, and suppressing repetitive behaviours (Hull et al. 2017). Successful adoption of camouflaging techniques can delay individuals seeking assessment and treatment, leading to underestimation of their difficulties and impairments (Carrington et al. 2019). Several studies (e.g. Hull et al. 2020, Lai et al. 2017, Mandy 2018) suggest social camouflaging may be disproportionately higher in females with ASD, potentially further impacting their referral and diagnosis rates. Potential biases in the interpretation of autistic features in females earlier in life (Carrington et al. 2019), and inadequate characterisation of repetitive behaviours for females in later life (Halladay et al. 2015; Mandy et al. 2012) are further examples of how different the female profile of autism might be. For these reasons, it would be useful to examine how well the SQ-A (Adult) performs for females compared to males.

In the undergraduate testing phase, all recruitment took place in a psychology department, meaning a heavy female skew in the sample, and a very narrow age range. In phase three, the clinical site was a specialist IAS, and the vast majority of those attending for

an assessment do go on to receive a diagnosis. As a result of this, a full validation study allowing comparison with those referred for other clinical concerns, as well as non-referred participants is a logical next step, which was not feasible within the study's remit and timescales. As a final point, the limited sample size available due to the throughput of the clinical site meant that some potentially interesting analyses which might have examined features such as gender differences, could not be completed.

Conclusions

The current study has offered an account of the development and exploratory analysis of the SQ-A (Adult) and its properties in relation to the AQ-10 and a related subset of DISCO-Abbreviated items in a clinical sample. The study has established promising examples of *convergent* and *concurrent validity* and *cross-informant reliability*, which suggest potential utility for the SQ-A (Adult) as part of a clinical diagnostic pathway. A more complete examination of the SQ-A (Adult)'s properties in a full validation study with a larger sample would allow for the exploration of multivariate analyses such as regression, to explore which items might prove most predictive of a subsequent diagnosis.

Ethical Approval

The study was granted ethical approval by Cardiff University School of Psychology Ethics Committee for phase one and two, and the Healthcare Research Authority/ Healthcare Research Wales and Health Board Research and Development departments for phase three (Appendix 18-21). As phase three used routinely collected clinical data, the study was confirmed as exempt from informed consent requirements. All data were processed securely

and anonymously in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki.

Tables and Figures

Table 1. Undergraduate Questionnaire Analyses.

	Pre SQ-A (14)	*Pre* SQ-A (18)	*Post* SQ-A (14)	*Post* SQ-A (18)	AQ-10
Mean (SD)	.95 (1.15)	1.18 (1.31)	1.13 (1.47)	1.36 (1.66)	1.89 (1.65)
Range	0-5	0-5	0-6	0-6	0-8
Median	1	1	1	1	1.5
Cronbach's α	.74	.77	.84	.85	.56

Note: SQ-A (*Pre*/ *Post*) = Signposting Questionnaire for Autism (Adult) *pre* or *post* consultation version; AQ-10 = Autism Spectrum Quotient-10

Table 2. Descriptive statistics for all measures

	SQ-A (*Self*) (*N=62*)	**SQ-A** (*Other*) (*N=62*)	**AQ-10** (*Self*) (*N=62*)	**AQ-10** (*Other*) (*N=62*)	**DISCO** (*N=66*)
Mean	10.31	10.29	7.87	7.40	10.91
Standard Dev.	3.51	3.29	1.91	1.65	3.47
Range	3-17	1-17	2-10	4-10	1-17
Median	11	10.5	8	7.50	11.50
Cronbach's α	.74	.69	.63	.36	N/A

SQ-A = Signposting Questionnaire for Autism (Adult) *self* and *other* (18 items); AQ-10 = Autism Spectrum Quotient-10 *self* and *other*; DISCO = Diagnostic Interview for Social and Communication Disorders Algorithm (18 item version)

Figure Captions

Figure 1. Endorsement Frequency of Each Item on the SQ-A (Adult) for *Self* and *Other*

Versions

(Figure was created using Microsoft Excel)

Figure 1 top
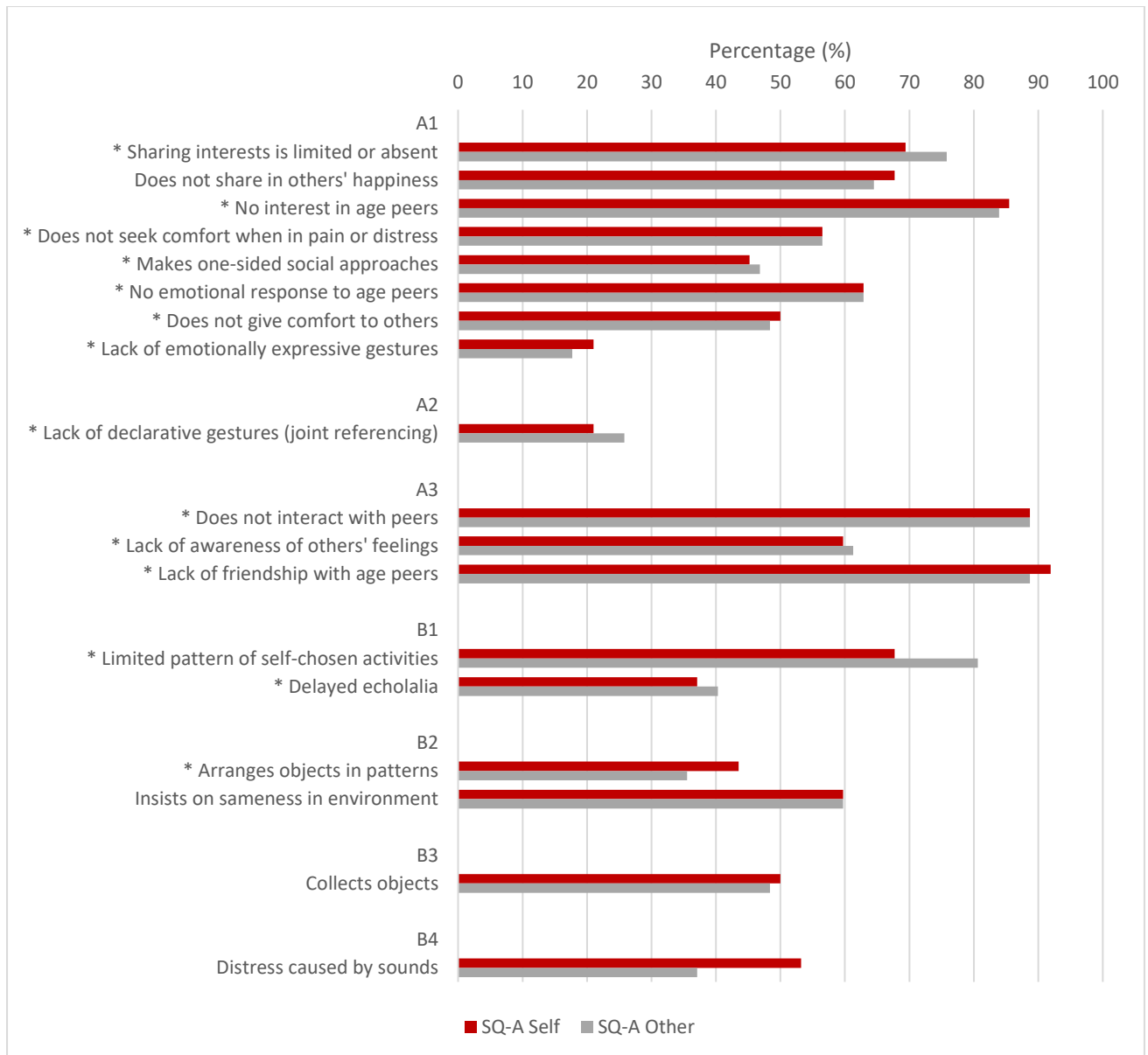
Note: The 18 items are organised and mapped to their Diagnostic and Statistical Manual (DSM-5) categories and descriptors/ N=62 for both *self* and *other* Questionnaires/ * designates one of the original 14-item subset from the SQ-A (Jones et al. in review).

Online Resources

Online Resource 1. Results summary – undergraduate testing

	Paired T-Tests			% Meeting Clinical Criteria	
Content of DISCO Item†	**Mean Pre**	**Mean Post**	**Significant Differences**	**Pre**	**Post**
1. Does not seek comfort when in pain or distress *	3.26	3.28	-	13.8	13.8
2. Does not offer comfort to others	3.66	3.35	t= 4.31; p =. 000	0	1.3
3. No interest in age peers	3.19	3.23	-	21.3	25
4. Sharing interests limited or absent *	3.50	3.25	t=2.55; p=.013	6.3	11.3
5. Lack of emotionally expressive gestures *	3.14	3.39	t= 2.96; p=.004	0	2.5
6. No emotional response to age peers	3.71	3.49	t= 2.76; p =.007	0	0
7. Lack of joint reference pointing ‡	3.11	3.28	-	6.3	2.5
8. Lack of friendship with age peers	3.56	3.34	t=3.38; p=.001	12.5	15
9. Does not interact with peers *	2.99	3.01	-	21.3	23.8
10. Lack of awareness of others' feelings * ‡	3.74	3.71	-	1.3	3.8
11. Delayed echolalia ‡	3.45	3.34	-	3.8	5
12. Arranges objects in patterns	3.24	3.20	-	3.8	3.8
13. Limited pattern of self-chosen activities	3.04	2.84	t= 2.32; p=.023	1.3	3.8
14. Makes one-sided approaches	3.40	3.13	t= 3.75; p=.000	0	1.3
15. Does not share in others' happiness	3.25	3.18	-	16.3	13.8
16. Insists on sameness in environment	3.11	3.11	-	2.5	3.5
17. Collects objects *	3.50	3.64	-	1.3	3.7
18. Distress caused by sounds	3.23	3.43	t=-3.33; p=.001	2.5	2.5

Notes: DISCO = Diagnostic Interview for Social and Communication Disorders; †Items listed are item headers reproduced from Carrington et al., (2015). These were adapted for use in the SQ-A (Adult), which is not reproduced fully here for intellectual property reasons. * = reversed item; ‡ = Identical wording in pre and post versions.

Online Resource 2. Percentage meeting clinical criteria for each SQ-A (Adult) item in *self, other* and *clinician-rated* samples. Note that column 1 (content of DISCO item) are content descriptors, not the full SQ-A questions (with reversals) for clarity of presentation.

Content of DISCO item†	SQ-A Self (N=62)	SQ-A Other (*N*=62)	DISCO (*N*=66)
1. Does not seek comfort when in pain or distress	56.5	56.5	68.2
2. Does not offer comfort to others	50	48.4	36.4
3. No interest in age peers	85.5	83.9	59.1
4. Sharing interests limited or absent	69.4	75.8	90.9
5. Lack of emotionally expressive gestures	21	17.7	45.4
6. No emotional response to age peers	62.9	62.9	10.6
7. Lack of joint reference pointing	21	25.8	24.2
8. Lack of friendship with age peers	91.9	88.7	40.9
9. Does not interact with peers	88.7	88.7	74.2
10. Lack of awareness of others' feelings	59.7	61.3	86.4
11. Delayed echolalia	37.1	40.3	48.5
12. Arranges objects in patterns	43.5	35.5	66.7
13. Limited pattern of self-chosen activities	67.7	80.6	84.8
14. Makes one-sided approaches	45.2	46.8	75.8
15. Does not share in others' happiness	67.7	64.5	90.9
16. Insists on sameness in environment	59.7	59.7	63.6
17. Collects objects	50	48.4	65.2
18. Distress caused by sounds	53.2	37.1	63.6

DISCO = Diagnostic Interview for Social and Communication Disorders; †Items listed are item headers reproduced from Carrington et al., (2015). These were adapted for use in the SQ-A (Adult), which is not reproduced fully here. Missing data were dealt with through scale mean estimation as outlined in main paper.

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Appendix 1: Journal of Autism and Developmental Disorders – Relevant Submission Guidelines

These submission guidelines are abbreviated to the relevant considerations for the submission, and were compiled from the JADD submission guidelines, and accompanying APA Endnote style guide.

N.B. The guidelines are contradictory at points so for the purposes of clarity:

- The initial suggestion to submit in 12-point times New Roman below (rather than a range of fonts in 10-point given later) is followed

- The Springer APA style guide for Endnote recommended for use is more recently updated and follows a simplified version of APA. The main changes are the use of "et al" from the third author onwards, and the omission of commas following author names and 'et al.'

Both were retrieved from: https://www.springer.com/journal/10803/submission-guidelines

Instructions for Authors

Editorial procedure

Double-Blind Peer Review

MANUSCRIPT FORMAT

All JADD manuscripts should be submitted to Editorial Manager in 12-point Times New Roman with standard 1-inch borders around the margins.

APA Style

Text must be double-spaced; APA Publication Manual standards must be followed.

Types of papers

Articles, Commentaries Brief Reports, Letters to the Editor

- The preferred article length is 20-23 double-spaced manuscript pages long (not including title page, abstract, tables, figures, addendums, etc.) Manuscripts of 40 double-spaced pages (references, tables and figures counted as pages) have been published. The reviewers or the editor for your review will advise you if a longer submission must be shortened.

Review your manuscript for these elements

1. Order of manuscript pages

- Title Page with all Author Contact Information & Abstract with keywords and the corresponding author e-mail information.

- Blinded Manuscript without contact information and blinded Abstract, and References

- Appendix

- Figure Caption Sheet

- Figures

- Tables

- Author Note

Manuscript Submission

Permissions

Authors wishing to include figures, tables, or text passages that have already been published elsewhere are required to obtain permission from the copyright owner(s) for both the print and online format and to include evidence that such permission has been granted when submitting their papers. Any material received without such evidence will be assumed to originate from the authors

Title page

The title page should include:

- The name(s) of the author(s)
- A concise and informative title
- The affiliation(s) and address(es) of the author(s)
- The e-mail address, telephone and fax numbers of the corresponding author

Abstract

Please provide an abstract of 120 words or less. The abstract should not contain any undefined abbreviations or unspecified references.

Keywords

Please provide 4 to 6 keywords which can be used for indexing purposes.

Text Formatting

Manuscripts should be submitted in Word.

- Use a normal, plain font (e.g., 10-point Times Roman) for text.
- Use italics for emphasis.
- Use the automatic page numbering function to number the pages.
- Do not use field functions.
- Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.
- Use the equation editor or MathType for equations.
- Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Headings

Please use no more than three levels of displayed headings.

Abbreviations

Abbreviations should be defined at first mention and used consistently thereafter.

Body

- The body of the manuscript should begin on a separate page. The manuscript page header (if used) and page number should appear in the upper right corner. Type the title of the paper centered at the top of the page, add a hard return, and then begin the text using the format noted above. The body should contain:
- Introduction (The introduction has no label.)
- Methods (Center the heading. Use un-centered subheadings such as: Participants, Materials, Procedure.)
- Results (Center the heading.)
- Discussion (Center the heading.)

Headings

Please use no more than three levels of displayed headings.

- Level 1: Centered

- Level 2: Centered Italicized

- Level 3: Flush left, Italicized

Author Note

The first paragraph contains a separate phrase for each author's name and the affiliations of the authors at the time of the study (include region and country).

The second paragraph identifies any changes in the author affiliation subsequent to the time of the study and includes region and country (wording: "authors name is now at affiliation".)

The third paragraph is Acknowledgments. It identifies grants or other financial support and the source, if appropriate. It is also the place to acknowledge colleagues who assisted in the study and to mention any special circumstances such as the presentation of a version of the paper at a meeting, or its preparation from a doctoral dissertation, or the fact that it is based on an earlier study.

The fourth paragraph states, "Correspondence concerning this article should be addressed to…" and includes the full address, telephone number and email address of the corresponding author

References

Citation

Cite references in the text by name and year in parentheses. Some examples:

- Negotiation research spans many disciplines (Thompson 1990).
- This result was later contradicted by Becker and Seligman (1996).
- This effect has been widely studied (Abbott 1991; Barakat et al. 1995; Kelso and Smith 1998; Medvec et al. 1999).

Reference list

The list of references should only include works that are cited in the text and that have been published or accepted for publication. Personal communications and unpublished works should only be mentioned in the text. Do not use footnotes or endnotes as a substitute for a reference list.

Reference list entries should be alphabetized by the last names of the first author of each work.

Journal names and book titles should be *italicized*.

For authors using EndNote, Springer provides an output style that supports the formatting of in-text citations and reference list.

Additional Clarifying Note from Springer Endnote plugin:

This style is based on the *Publication Manual of the APA*. However, as the APA style is a very complex style, Springer's SocPsych style does not include all of its features; for example, the citation of Internet publications has been simplified. If you are citing a reference type that is not included here, please style it according to the basic styles for journals, books, and book sections.

In-text citations with name and year:
One author: Miller (1998) or (Miller 1998) - Two authors: Miller and Smith (2001) or (Miller and Smith 2001) - More than two authors: Miller et al. (1999) or (Miller et al. 1999)

Reference list in alphabetical order.
The list of references should only include works that are cited in the text and that have been published or accepted for publication. Personal communications and unpublished works should only be mentioned in the text.

Tables

- All tables are to be numbered using Arabic numerals.
- Tables should always be cited in text in consecutive numerical order.
- For each table, please supply a table caption (title) explaining the components of the table.
- Identify any previously published material by giving the original source in the form of a reference at the end of the table caption.
- Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

Each table should be inserted on a separate page at the back of the manuscript in the order noted above. A call-out for the correct placement of each table should be included in brackets within the text immediately after the phrase in which it is first mentioned. Copyright permission footnotes for tables are typed as a table note.

Electronic Figure Submission

- Supply all figures electronically.
- Indicate what graphics program was used to create the artwork.
- For vector graphics, the preferred format is EPS; for halftones, please use TIFF format. MSOffice files are also acceptable.
- Vector graphics containing fonts must have the fonts embedded in the files.
- Name your figure files with "Fig" and the figure number, e.g., Fig1.eps.

Figure caption sheet

The figure caption sheet contains a list of only the captions for all figures used. Center the label "Figure Captions" in uppercase and lowercase letters at the top of the page. Begin each caption entry flush left, and type the word "Figure", followed by the appropriate number and a period, all in italics. In the text of the caption (not italicized), capitalize only the first word and any proper nouns. If the caption is more than one line, double-space between the lines, and type the second and subsequent lines flush left. Table notes: Copyright permission footnotes for figures are typed as part of the figure caption.

- Each figure should appear on a separate page. The page where the figure is found should have the figure number and the word "top"[ie, Figure 1 top] typed above the figure. Figures or illustrations (photographs, drawings, diagrams, and charts) are to be numbered in one consecutive series of arabic numerals. Figures may be embedded in the text of a Word or Wordperfect document. Electronic artwork submitted on disk may be in the TIFF, EPS or Powerpoint format (best is 1200 dpi for line and 300 dpi for half-tones and gray-scale art). Color art should be in the CYMK color space. Assistance will be provided by the system administrator if you do not have electronic files for figures; originals of artwork may be sent to the system administrator to be

uploaded. *** After first mention in the body of the manuscript, a call-out for the correct placement of each figure should be included in brackets on a separate line within the text.

Electronic Supplementary Material

Text and Presentations

- Submit your material in PDF format; .doc or .ppt files are not suitable for long-term viability.
- A collection of figures may also be combined in a PDF file.

Numbering

- If supplying any supplementary material, the text must make specific mention of the material as a citation, similar to that of figures and tables.
- Refer to the supplementary files as "Online Resource", e.g., "... as shown in the animation (Online Resource 3)", "... additional data are given in Online Resource 4".
- Name the files consecutively, e.g. "ESM_3.mpg", "ESM_4.pdf".

Captions

- For each supplementary material, please supply a concise caption describing the content of the file.

Disclosures and declarations

All authors are requested to include information regarding sources of funding, financial or non-financial interests, study-specific approval by the appropriate ethics committee for research involving humans and/or animals, informed consent if the research involved human participants, and a statement on welfare of animals if the research involved animals (as appropriate).

The decision whether such information should be included is not only dependent on the scope of the journal, but also the scope of the article. Work submitted for publication may have implications for public health or general welfare and in those cases it is the responsibility of all authors to include the appropriate disclosures and declarations.

Compliance with Ethical Standards

To ensure objectivity and transparency in research and to ensure that accepted principles of ethical and professional conduct have been followed, authors should include information regarding sources of funding, potential conflicts of interest (financial or non-financial), informed consent if the research involved human participants, and a statement on welfare of animals if the research involved animals.

Authors should include the following statements (if applicable) in a separate section entitled "Compliance with Ethical Standards" when submitting a paper:

- Disclosure of potential conflicts of interest

- Research involving Human Participants and/or Animals
- Informed consent

Please note that standards could vary slightly per journal dependent on their peer review policies (i.e. single or double blind peer review) as well as per journal subject discipline. Before submitting your article check the instructions following this section carefully.

The corresponding author should be prepared to collect documentation of compliance with ethical standards and send if requested during peer review or after publication.

The Editors reserve the right to reject manuscripts that do not comply with the above-mentioned guidelines. The author will be held responsible for false statements or failure to fulfill the above-mentioned guidelines

Disclosure of potential conflicts of interest

Authors must disclose all relationships or interests that could influence or bias the work. The corresponding author will include a summary statement **on the title page that is separate from their manuscript,** that reflects what is recorded in the potential conflict of interest disclosure form(s).

See below examples of disclosures:

Funding: This study was funded by X (grant number X).
Conflict of Interest: Author A has received research grants from Company A. Author B has received a speaker honorarium from Company X and owns stock in Company Y. Author C is a member of committee Z.

If no conflict exists, the authors should state:
Conflict of Interest: The authors declare that they have no conflict of interest.

Research involving human participants, their data or biological material

Ethics approval

When reporting a study that involved human participants, their data or biological material, authors should include a statement that confirms that the study was approved (or granted exemption) by the appropriate institutional and/or national research ethics committee (including the name of the ethics committee) and certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. If doubt exists whether the research was conducted in accordance with the 1964 Helsinki Declaration or comparable standards, the authors must explain the reasons for their approach, and demonstrate that an independent ethics committee or institutional review board explicitly approved the doubtful aspects of the study. If a study was granted exemption from requiring ethics approval, this should also be detailed in the manuscript (including the reasons for the exemption).

Appendix 2: The Appraisal tool for Cross-Sectional Studies (AXIS) Manual

N.B. The References on page 105 are for the AXIS tool itself (examples of which are in Appendix 3 and 4

Appraisal tool for Cross-Sectional Studies (AXIS)

Critical appraisal (CA) is used to systematically assess research papers and to judge the reliability of the study being presented in the paper. CA also helps in assessing the worth and relevance of the study [1]. There are many key areas to CA including assessing suitability of the study to answer the hypothesised question and the possibility of introducing bias into the study. Identifying these key areas in CA requires good reporting of the study, if the study is poorly reported the appraisal of suitability and bias becomes difficult.

The following appraisal tool was developed for use in appraising observational cross-sectional studies. It is designed to address issues that are often apparent in cross-sectional studies and to aid the reader when assessing the quality of the study that they are appraising. The questions on the following pages are presented in the order that they should generally appear in a paper. The aim of the tool is to aid systematic interpretation of a cross-sectional study and to inform decisions about the quality of the study being appraised.

The appraisal tool comes with an explanatory help text which gives some background knowledge and explanation as to what the questions are asking. The explanations are designed to inform why the questions are important. Clicking on a question will automatically take you to the relevant section in the help text. The appraisal tool has areas to record a "yes", "no" or "don't know" answer for each question and there is room for short comments as well.

Introduction

The introduction serves to establish the context of the work that is about to be presented in the text of the paper. Relevant primary literature should be discussed and referenced throughout the introduction. The history and current understanding of the problem being researched should be presented. This should be concluded giving a rational as to why the current study is being presented and what the aims and/or hypothesis under investigated are [2,3].

Aims

The aim(s) of the study tells us if the study addresses an appropriate and clearly focused question. If the aim is not clearly stated or not stated at all, it will be difficult and in some cases impossible to assess the extent to which the study objectives were achieved. Ideally, an aim should be stated both at the beginning of the abstract and at the end of the introduction [3]. If the answer to question 1 is no, then it will make it difficult to assess some of the other questions in the critical appraisal process.

Methods

The methods section is used to present the experimental study design of the paper. The methods should be described clearly in easy to understand language and clearly identify measures, exposures and outcomes being used in the study [4]. More specific issues are addressed below.

Study Design

Question 2 is used to assess the appropriateness of using a cross-sectional study to achieve the aim(s) of the study. Cross-sectional studies are observational studies that provide a description of a population at a given time, and are useful in assessing prevalence and for testing for associations and differences between groups [5]. Examples of cross-sectional designs include point-in-time surveys, analysis of records and audits of practice [6]. The reader should try and decipher if a cross-sectional study design is appropriate for the questions being asked by the researcher.

Question 3 asks if sample size justification was reported, but it should also be clear what methods were used to determine the sample size. In some cases clustering of observations within groups can occur (e.g. patients within hospitals or livestock within herds) and this should be taken into account if sample size has been determined. It should be clear whether the inferences drawn actually relate to the attributes for which the sample size was calculated [7]. If sample size justification isn't given or restrictions make it difficult to reach the desired sample size then this should be declared in the text.

Target (Reference) Population

The target or reference population is the overall population that the research is directed towards. When doing a cross-sectional study, a target population is the overall population you are undertaking the study to make conclusions about or the population at risk of acquiring the condition being investigated [8–10] e.g. the total female population in the UK, or all dogs in the USA with cardiovascular disease. (See Figure 1) Question 4 asks if this is clearly defined in the study. It is important that this is understood both by the researcher and the reader; if it is not clearly defined then inferences made by the researcher may be inappropriate.

Sampling Frame

As a reader you need to determine if the sample frame being used is representative of the target population. The study population should be taken from the target population; units from this study population have information that is accessible and available which allows them to be placed in the study. The sampling frame is the list or source of the study population that the researcher has used when trying to recruit participants into the study (Figure 1). Ideally it should be exactly the same composition or structure as the target population. In practice it is generally much smaller, but should still be representative of the target population. Generally, for convenience, the sampling frame is a list of units that are within the target population e.g. list of
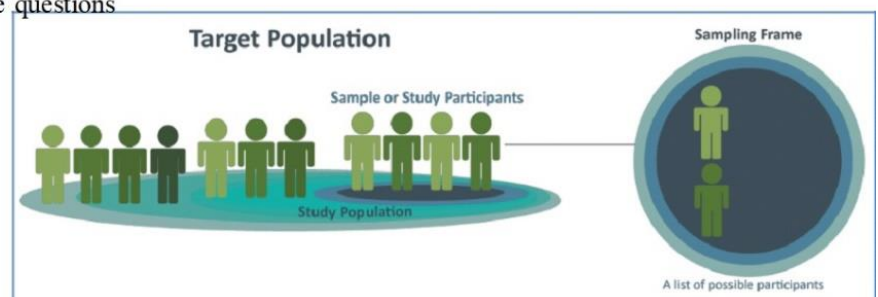
Convenience sampling can be carried out in some situations and are used because the participants are easy to recruit. Convenience samples generally lead to non-representative or biased samples and therefore cannot be used to make assumptions about the characteristics of the target population [11]. Convenience samples are often used for pilot or analytical studies where the need for a representative sample is not required [12], however the authors should make this clear in the text.

Census

A census is where the target population and the study participants are the same at the time the census is taken. In theory questions 5, 6 and 7 don't apply to census studies. However even if a study is described as a census it should be very clearly stated where the study participants have been recruited from, and the reader should make the decision if the study truly is a census. A census may include all the population from the sample frame, but not all the target population; in this scenario questions 5 to 7 need to be addressed.

Sample Selection

Question 6 is used to establish how the researchers got from the sample frame to the participants in the study. It examines the potential for selection bias and how the researcher developed methods to deal with this. The sample selection process is important in determining to what extent the results of the study are generalizable to the target population. For question 6 we are looking in depth at how the sample (study participants) was selected from the sampling frame. It is important to know if there were any inclusion or exclusion criteria used, as inappropriate criteria can dramatically shift how representative the sample is of the target population [8,10,13].

Selection bias can occur if every unit in the sample frame doesn't have an equal chance of been included in the final study [11,14]. Randomisation is used to ensure that each participant in the sampling frame has an equal chance of being included in the sample. If methods of randomisation are not used, not described or are not truly random, this may lead to a non-representative sample being selected and hence affect the results of the study [10,11].

There are many other situational issues to take into account when determining if the population in the sample is likely to represent the target population. Often these issues are outside the control of the researcher, but sometimes are overlooked. One such issue is the healthy worker effect which is a well-known phenomenon in human cross-sectional studies [13]. An example of this is, a researcher trying to do a cross-sectional study to determine health factors in a factory population and decides to sample from workers at work on a particular day. Unfortunately there is a tendency to over select healthy workers as ill workers may tend to be at home on the day of selection. This will in turn

lead to inferences been made about the health of the worker population but is only relevant to healthy workers and not ill workers. A veterinary example of this is a researcher trying to do a cross-sectional study to determine health factors in the general dog population and decides to sample from a local park. Unfortunately there is a tendency to over select healthy animals as sick animals will tend to be left at home and not taken for a walk. This will in turn lead to inference been made about the health of the dog population but is only relevant to healthy dogs and not sick dogs.

Self-selection is another example of selection bias that can be introduced and should be assessed [13]. For example, when using a postal questionnaire to examine eating habits and weight control, people who are overweight might read the survey and be less inclined to complete and return the survey than those with normal weight leading to over representation of people with normal weight. Similarly, if using a postal questionnaire to examine mastitis levels on cattle farms, farmers that have a high somatic cell counts (SCC) might be less inclined to complete the survey than those with normal or low SCC leading to over representation of farms with good SCC (see Non-responders below).

Non-responders

Non-response in cross-sectional studies is a difficult area to address. A non-responder is someone who does not respond either because they refuse to, cannot be contacted, or because their details cannot be documented. As a rule, if participants don't respond it is often difficult and sometimes impossible to gain any information about them. However other baseline statistics may exist that can be used as a comparator to assess how representative the sample is [14] e.g. age, sex, socio-economic classification. Methods used, if any, should be well described so that the results from the analyses can be interpreted. This is important as non-responders may be from a specific group, which can lead to a shift in the baseline data away from that group. This shift can lead to results that don't represent the target population. In some situations the sampling frame doesn't have a finite list or a fully defined baseline population. This also makes it difficult, and in some cases impossible, to quantify non-response and it may be inappropriate to do so in these situations. If the researchers are using non-defined populations this should also be declared clearly in the materials and methods section [15,16].

Measurement Validity & Reliability

Measurement validity is a gauge of how accurately the study measurements used assess the concepts that the researcher is attempting to explore. Measurement reliability is a gauge of the accuracy of the measurements taken or the procedures used during the study. Question 8 is used to address the concepts of measurement validity, and is specifically aimed to address the appropriateness of the measurements being used.

The importance of measurement validity is that it gives weight to applying the statistical inferences from the study to members of the target population. If inappropriate measures are used in the study it could lead to misclassification bias and it will be difficult to determine to what extent the study results are relevant to the target population [12,17].

Question 9 is an attempt to gauge the measurement reliability of the study measures. Measurements must be able to be reproduced and produce identical results if measured repeatedly, so that the measurements would be exactly the same if performed by another researcher. With this in mind, the measurements must be of international or globally accepted standards (e.g. IU standards) where possible and appropriate. If they are being used for the first time they must be trialled, or in the case of questionnaires, they should be piloted before being used.

Statistics

While interpretation of statistics can be quite difficult, a basic understanding of statistics can help you to assess the quality of the paper. Often many different methods can be used correctly to test the same data, but as there is such a wide range available, knowing what tests are most appropriate in particular situations can be hard to decipher. There is an expectation that the researcher has this understanding or has at least sought statistical assistance to ensure that the correct methods are used. Therefore for question 10 the emphasis for the reader is that the statistical methods, software packages used and the statistical significance levels are clearly stated even if the paper is just presenting descriptive statistics. The statistical significance level is usually described as a p-value. In most cases the p-value, at which the null hypothesis is rejected, is set at 0.05. The higher the p-value is set the greater the possibility of introducing a type I error. Confidence intervals should also be declared with p-values or instead of p-values as an indication of the precision of the estimates. It is usual to present a confidence interval of 95% which means that the researchers were 95 per cent confident that the true population value of the outcome lies between these intervals. This can be used to compare groups where an overlap would suggest no difference and a gap between confidence intervals would suggest a difference (Figure 2).

Overall Methods

Question 11 asks if the methods are sufficiently described to enable them to be repeated. If there are sections or even small pieces of information missing it could make a great difference for the reader when interpreting the results and the discussion as they may be unsure if the correct methods are being used.

Results

The results section of a paper is solely for the purpose of declaring the results of the data analysis and no opinion should be stated in this section. This gives the reader the opportunity to examine the results unhindered by the opinion of the researcher. It is important for the reader to form their own ideas or opinions about the results before progressing to the discussion stages.

Basic Data

Question 12 asks for a description of the basic data. Basic descriptive analysis aims to summarise the data, giving detailed information about the sample and the measurements taken in the study. The basic data gives an overview of the process of recruitment and if the sampling methods used to recruit individuals were successful in selecting a representative sample of the target population. If the sampling methods are unsuccessful in selecting a representative sample of the target population, those participants included in the study can often be different to the target population; this leads to inaccurate estimates of prevalence, incidence or risk factors for disease. Descriptive data of the measurements taken in the study give an overview of any differences between the groups, and may give insight into some of the reasons for statistical inferences that are made later in the paper.
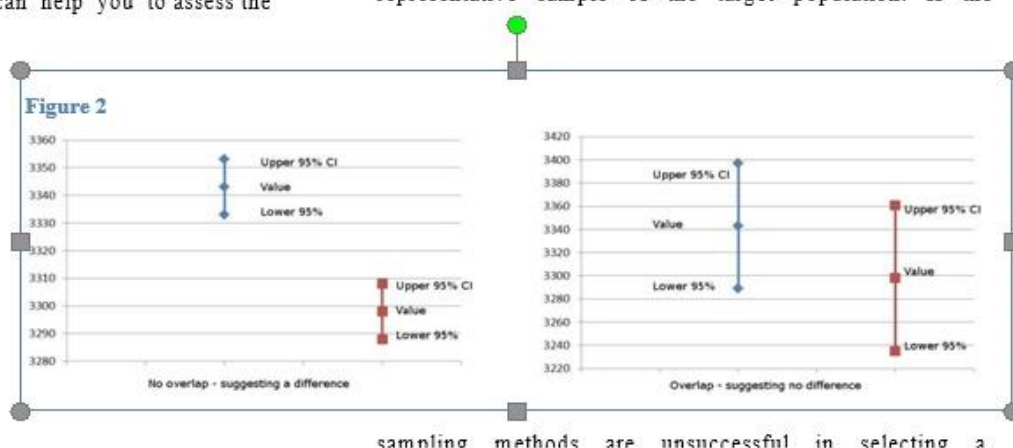
Response Rate

As stated previously it can often be difficult to deal with non-responders. Question 13 requires that there is some attempt made to quantify the level of non-response by the researchers and asks the reader to interpret if the response rate is likely to lead to non-response bias. Question 14 is examining if any information on non-responders was available and if so were they comparable to those that did respond as this could help in answering question 13. Non- response bias occurs if the non-responders are substantially different to the rest of the population in the sample [15].

Figure 2

Question 15 is an exploration of the basic data and asks that the reader spends some time exploring the numbers given in the results; in the text, figures and tables. Information about the level of missing data should also be declared in the results. It is important to check that the numbers add up in the tables and the text. If the study has recruited 100 participants, the tables and the text should include data about 100 participants. If not, the missing data should be clearly declared and the reason for its non-appearance explained.

Comprehensive Description of Results

It is important to check that all the methods described previously lead to data in the results section (question 16). Sometimes the results from all analyses are not described. If this is noted it will be unclear whether the researcher found non-significant results or just didn't describe what was found. If there are results missing that you would expect to find, there is a concern that these missing results may not have been what the researcher wanted to see and hence the authors have omitted them. It is also important that the significance level declared in the methods is adhered to. As the reader, it is important to watch out for phrases such as "tended towards significance" in the text, and if these are used to pay close attention to the results.

Discussion

The discussion of a paper should summarise key results of the study objectives. It should give an overall interpretation of the results of the study keeping in mind the limitations and the external validity of the document. The discussion section should also address both significant and non-significant findings of the study and make comparisons with other research, citing their sources [2,4].

Justified Discussions and Conclusions

In question 17 there is an expectation that the researcher gives an overall summary of the main findings of the study and discusses these in detail. It is important that the reader considers the study as a whole when reading the researcher's conclusion. If the researcher's conclusion is different or is more definitive than the study suggests it should be, it can be an indication that the researcher has misunderstood their own study or has other motives or interests for coming to that conclusion.

It is up to the reader to explore the discussion fully in order to answer question 17. The following points should be taken into account:

Aim

In the discussion section the researcher should discuss all results that pertain to the overall aim of the study, even if they are not significant. If some results are overlooked in the discussion it could suggest that the researcher either doesn't believe the results, or doesn't want to draw attention to

controversial discoveries from the study and may therefore be giving a biased overview of the research conducted.

Selection Bias

There is an expectation that the researcher discusses selection biases and takes these into account when interpreting the results of the study. This also gives a clear view of whether the researcher has an overall understanding of the study design. (See notes on selection bias in the methods section).

Non-response

Was there an interpretation of the results that included non-response? This is particularly important if the response rate was low, as non-responders may be a specific group, and lead to a shift in the baseline data (See notes on non-response in the methods section).

Confounding

Confounding is a major threat to the validity of practical inferences made from statistical analyses about cause and effect. Confounding occurs when the outcome of interest is associated with two different independent variables and one of those variables is closely associated with the outcome only because it is closely associated with the other variable (confounder). This can sometimes be accounted for using statistical methods however sometimes these associations are missed because the confounder isn't measured or isn't considered to be a confounder in the analyses. What then happens is an erroneous conclusion is made; that the variable might have a causal relationship with the outcome. The researcher should consider confounding both in the analyses and in the interpretation of the results [18]. An example would be where in a study on cancer a researcher concludes that increased alcohol intake causes lung cancer; however there was confounding in the sample that the researcher didn't discover. People in the study that were inclined to drink more alcohol were also inclined to smoke more (the confounder) and smoking was the cause of lung cancer not increased alcohol intake. Similarly, a study was undertaken to examine surgical deaths in cats. The researcher concluded that cats that had gaseous anaesthesia were more likely to die during surgery than those that had just injectable anaesthesia. There was confounding in the sample: cats that underwent surgery using gaseous anaesthesia were more likely to be ill or undergoing major surgical procedures (the confounders) and this was the cause for cats being more likely to die during surgery and not the use of gaseous anaesthetics.

Non-significant Results

Discussing non-significant results is as important as discussing significant results and should also be included in the discussion, especially if they have a direct association with the aim being investigated. Non-significant results can be influenced by factors associated with study design and

sample size. If there are biases introduced during the study design this can lead to non-significant results that in reality may be significant (this can work the other way around as well). If there are only small differences between groups, non-significant results may be apparent because the sample size is too small (see sample size justification). Again it is important that the researcher has a clear understanding of this and conveys that in the discussion.

Limitations

In question 18 we explore whether limitations are discussed. Unfortunately all forms of research have some limitations. The question here is whether the researcher has an understanding of the limitations involved in their study design. If this issue is not explored, this is cause for concern that the limitations don't stop at the design and that the researcher has a poor understanding of the study as a whole.

Other

Conflicts of Interest

It is very important that conflicts of interest or bodies involved in funding the study are declared in the text (question 19). This can give an impression as to background reasons for carrying out the study. Where studies are funded by a specific agency the researcher may unconsciously interpret in favour of the agencies' ideals; if the researcher has worked in a specific area their own ideas and beliefs may affect the interpretation of the results. It is up to the reader to identify these and come to the conclusion as to whether these conflicts of interest are relevant or not. This can be declared in different areas of the text and should be stated.

Ethical Approval

Question 20 deals with ethical approval and participant consent. It is important that these are sought before carrying out research on any animal or person.

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Appendix 3: Summary of Quality Assessment for All Studies Using AXIS

		Don't know/ Comment
Introduction		
1	Were the aims/objectives of the study clear?	Yes - aims and objectives were clearly laid out and there was a clear question(s) being answered in all cases.
Methods		
2	Was the study design appropriate for the stated aim(s)?	Yes - in each case the study design made sense to answer the question(s) posed
3	Was the sample size justified?	Mixed - most studies lacked any specific discussion of sample size or justification, and most had no discussion of power. In several cases[1] the sample size was representative of all referrals from the period of measurement/ all records from a healthcare system. For these, all sample questions were answered N/A
4	Was the target/reference population clearly defined? (Is it clear who the research was about?)	Yes – the target population is clearly defined in all studies
5	Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?	There was no sample frame for most studies as they were based on all referrals to a service (see footnote 1). As a result, apart from the inherent issue of excluding coverage of those who don't seek diagnosis, it was felt fair to consider these samples as representative. The remaining studies all appeared to have drawn their sample frame from an appropriate population base.
6	Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?	All studies from footnote 1 appeared to be representative of the target populations (with the same caveat as Q5 in mind).
7	Were measures undertaken to address and categorise non-responders?	For all footnote 1 studies this question was answered N/A. Skagerberg et al. (2016) was a follow-up study with a high non-response rate and no narrative exploration of how this might have been addressed. A high non-response rate to questionnaires is however common. Heylens et al. (2018) appeared to be all referrals from a period but did not confirm this or identify or address the issue of any non-responders.
8	Were the risk factor and outcome variables measured appropriate to the aims of the study?	Confirmation of a DSM-IV/5 or ICD-9/10 ASD and GD diagnosis verified via checking medical records, or given during the course of the study was reported for all studies. Most studies compared simple prevalence rather than using any measures as part of the study but

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[1] Studies addressing all referrals for a period, or using all data from a particular healthcare system were: Chen et al. (2015), Cheung et al. (2018), DeVries et al. (2010), Dragon et al. (2017), Fielding & Bass (2018), Heard et al. (2017), Hisle-Gorman et al. (2019), Kaltiala-Heino et al. (2015, 2019), Nahata et al. (2015). Leef et al. (2019) used two participant pools, one of which was all medical records for a healthcare system.

		those using additional measures such as screening tools all did so appropriately.
9	Were the risk factor and outcome variables measured correctly using instruments/measurements that had been trialled, piloted or published previously?	Method of diagnosis is frequently not reported in medical records and healthcare systems, so most studies could not report on this. Of those that did complete the assessment process as part of the study reporting appeared to be appropriate and using standardised instruments. There are no standardised assessments pathways for GD worldwide, but most common reporting appears to be of multidisciplinary clinical assessment and confirmation of meeting ICD or DSM diagnostic criteria. In sites assessing for GD the assessment process was explained in each case, although the clarity of these explanations varies.
10	Is it clear what was used to determined statistical significance and/or precision estimates? (e.g. p-values, confidence intervals)	Yes - Appropriate analyses were used for all statistics reported.
11	Were the methods (including statistical methods) sufficiently described to enable them to be repeated?	Yes – There was enough description of methods to understand them and how achieved. Skagerberg et al's (2016) results were only very briefly discussed as the format was a brief report.
Results		
12	Were the basic data adequately described?	Yes – in most cases the basic data appear to be adequately described for all studies, with any limitations explained. Heylens et al. (2018), Leef et al. (2019) and Skagerberg et al. (2016) however do not explain how dropouts were addressed, and the first two do not confirm whether the sample represents all referrals for a period.
13	Does the response rate raise concerns about non-response bias?	As most studies were addressing all referrals or all records this doesn't tend to be an issue but the two studies above from Q.12 raise concerns for the reasons stated as we can't be sure how non-response bias might have affected results.
14	If appropriate, was information about non-responders described?	As Q.13 the same two studies are an issue as the non-responders are not adequately described.
15	Were the results internally consistent?	Mixed - all results appear in order for the papers but there is no specific discussion of missing data and how this was treated for most papers, so we are unsure if there was any of how it was treated. This might not be much of a concern for most papers as they are based on clinicians diagnoses and observations which would tend to be complete, but is an issue for others such as questionnaire based studies which would naturally tend to have missing data. Both Kaltiala-Heino et al. (2015, 2019) studies included discussion of missing data, but Skagerberg et al. (2016) which did include questionnaire data does not discuss missing data at all.
16	Were the results presented for all the analyses described in the methods?	Yes – all studies reported the analyses described in their methods.
Discussion		

17	Were the authors' discussions and conclusions justified by the results?	The evidence for hypotheses in all cases is acknowledged to be limited during critical engagement in the relevant papers. All conclusions are given tentatively in line with the very limited evidence base for current hypotheses, and most papers make similar recommendations for future research priorities. In several cases there is limited critical engagement in the discussion with factors of relevance to the review, but only Chen et al. (2015) offered no relevant critical discussion, so only the prevalence results are reported for this study in the narrative synthesis.
18	Were the limitations of the study discussed?	Mixed – most studies engaged with study limitations. Chen et al. (2015) offered no real discussion of limitations, while Leef et al. (2019) does offer a section on limitation, but this is very brief and fails to address one obvious limitation (the low sample size and lack of discussion of power)
Other		
19	Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?	Mixed – most studies offered a declaration regarding any conflicts of interests and funding sources. Leef et al. (2019) did not include a declaration.
20	Was ethical approval or consent of participants attained?	Yes- ethical approval was reported for all cases or confirmed as not required because of study design or data source. Holt et al., (2016) appeared to be an analysis of routinely collected clinical data but this is not confirmed nor is ethics discussed. Skagerberg et al., (2015) is confirmed as an analysis of routinely collected clinical data but ethics and consent are not discussed.

Appendix 4 – Example of a Completed Quality Appraisal using AXIS

De vries et al. 2010 (Amsterdam)

	Paper: ASD in GD children and adolescents	Yes	No	Don't know/ Comment
Introduction				
1	Were the aims/objectives of the study clear?	✓		Yes – section on aims and objectives was clearly laid out and there was a clear question(s) being answered
Methods				
2	Was the study design appropriate for the stated aim(s)?	✓		Yes - a cross-sectional approach made sense to answer the question(s)
3	Was the sample size justified?		✓	No – no specific discussion of sample size/ justification or discussion of power. Sample does appear to represent all referrals from the period but this isn't definitely confirmed. N=204 (all clinical)
4	Was the target/reference population clearly defined? (Is it clear who the research was about?)	✓		Yes – the target population is clearly defined.
5	Was the sample frame taken from an appropriate population base so that it closely represented the target/reference population under investigation?	✓		Technically there is no sample frame as the study appears to be based on all referrals to a service so apart from the inherent issue (e.g. no coverage of those who don't seek diagnosis) the sample is very representative, and it does state this is the only specialist centre for these referrals in Netherlands so should be very representative of those seeking diagnosis.
6	Was the selection process likely to select subjects/participants that were representative of the target/reference population under investigation?			N/A - No selection process applied.
7	Were measures undertaken to address and categorise non-responders?			N/A – No non-responders as no recruitment, but some exclusions are described and justified.
8	Were the risk factor and outcome variables measured appropriate to the aims of the study?	✓		Yes- there is a good description of the all methods and diagnostic procedures.
9	Were the risk factor and outcome variables measured correctly using instruments/measurements that had been trialled, piloted or published previously?	✓		Yes – confirmation of ASD diagnosis made through appropriate diagnostic methods. GD doesn't have standard diagnostic approaches worldwide but this was established with solid MDT assessment procedures which were described.
10	Is it clear what was used to determined statistical significance and/or precision estimates? (e.g. p-values, confidence intervals)	✓		Yes appropriate analyses were used and P values reported for IQ differences, different categories of GD and associated ASD incidence.

11	Were the methods (including statistical methods) sufficiently described to enable them to be repeated?	✓		Yes – There was enough description of methods to understand them and how achieved. No discussion of sample size or power though.
Results				
12	Were the basic data adequately described?		✓	No - Description of the sample was adequate to understand who they were and to be reasonably confident they were representative of target population, but no discussion of sample size justification, power. Author does confirm and explain dropouts though.
13	Does the response rate raise concerns about non-response bias?		✓	No – dropouts were low and explained.
14	If appropriate, was information about non-responders described?			N/A
15	Were the results internally consistent?			Unsure – All results appear in order but there is no specific discussion of missing data so unsure if there was any of how it was treated.
16	Were the results presented for all the analyses described in the methods?	✓		Yes
Discussion				
17	Were the authors' discussions and conclusions justified by the results?	✓		Yes - The discussion and conclusions were a reasoned summary of the results and their implications.
18	Were the limitations of the study discussed?	✓		Yes – A section on limitations was included and is comprehensive and thoughtful
Other				
19	Were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?		✓	Conflicts section was included and no issues
20	Was ethical approval or consent of participants attained?	✓		Yes – ethics was discussed and informed consent confirmed

Appendix 5: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	10
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	10
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	13-14
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	14
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	15
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	14
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	14-15
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	15-16
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	16-17
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	16-17
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	N/A
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	14

| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis. | 18 |

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	17/ Appendix 3
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	17, 18, 44
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	16-17
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	17/ Appendix 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	38-42
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Appendix 3
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	27-35
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	27-35
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	35
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	36

The Adult Autism Signs Questionnaire

Participant Information

Thank you for your interest in taking part in this study on the signs of autism. This sheet gives you information about why we are doing this study and what it involves for you. Please email the researchers if anything is not clear. Our contact details are on the last page.

What is the research about?

People waiting for a diagnosis of autism spectrum disorder (ASD) often wait a long time to be seen, and shortening these waiting times is really important. We have created a short questionnaire that focuses on the key signs of autism. This questionnaire could be used during the diagnostic process to help refer people with possible autism to the right services. Our questionnaire is currently developed for using with children, but we would like to have an adult self-report version. To make sure the questionnaire is useful we need to share it with autistic adults, so they can give us feedback about the questions and how we should ask them.

Who is carrying out this research?

This research is being carried out by members of the Wales Autism Research Centre (WARC) at Cardiff University. The main researcher is Mr Gareth Davies, who is supervised by Prof. Sue Leekam and Dr Catherine Jones. This study is being carried out as part of Gareth Davies' Doctorate in Clinical Psychology.

Why have I been invited to take part?

You have been invited to take part as you are an autistic adult and a member of WARC's Research Recruitment Register. You need to have a clinical diagnosis of ASD to take part and be 18 years or older. Participants need to be able to read

the questionnaire and be able to provide feedback in either written or spoken form.

What are the aims of the research?

We want members of the autistic community to be involved in the decisions about the questionnaire. For example: Are the questions are clear? Are they suitable? Is there anything important we have left out? We will use your feedback to make changes to our questionnaire.

Do I have to take part?

No, it's totally your choice. Read this document, and if you have any questions please email Gareth Davies (his email is on the last page). Talk to other people as well if it helps you decide. Once you have agreed to take part you can change your mind at any time and without having to give us a reason.

What will I have to do?

You would be one of 4 to 6 autistic adults we interview, but we will talk to each of you separately. The meeting will be with Gareth Davies and he will take written notes of the discussion.

During the meeting you will be asked to comment on a list of 19 questions that we might use in the questionnaire. The questions will be similar to ones that are often used in assessments for ASD. You will not be asked to answer any of these questions yourself. An example of a question is below:

"Do you prefer to avoid your peers?"

We will ask for your opinion about each question. Some of the questions we might ask you are:

- Does the question make sense to you?
- Have we used the right wording?
- Would anything help the question make more sense?
- Do you find the question offensive, insensitive or upsetting?

It is important to remember that there is no right or wrong answer; we are interested in your opinions as a member of the autistic community.

If you do not want to give your opinion on a particular question, then you do not have to. You will not have to give a reason for not giving an opinion.

Do I need to do any preparation?

We will send you the list of possible questions that we might use the questionnaire in advance so that you can read them in your own time. However, you do not need to read them before the meeting if you do not want. During the meeting, we will provide the list of questions to you again. You do not have to make any notes or prepare any feedback.

Where will the study take place?

The study will take place on the 3rd Floor of the School of Psychology, Cardiff University, Tower Building, Park Place, Cardiff, CF10 3AT. Gareth Davies will meet you in the reception (ground floor) at your arranged time.

What if I want to give feedback but do not want to come to a meeting?

If you would like to give your feedback but do not want to come to a meeting then you can give feedback over email, by letter, or by talking to Gareth Davies on the telephone or on Skype. If you would prefer to participate in this way, then please let Gareth know (his email is below). You will still be paid £30 if you participate in this way.

You might be concerned about taking part because of particular worries about the environment or format of the meeting. Please feel free to discuss these concerns, or any others, with Gareth.

How long will the meeting take?

The meeting will take about an hour. You will be offered a hot drink and biscuits. Water will be available on the table throughout. You will be able to take a break at any time, and you can end the meeting at any time if you don't want to continue.

Will there be any payment for taking part in the research?

You will be paid £30 at the end of the study for taking part. You will fill in a form and we will pay this directly into your bank account. We are not able to pay travel expenses.

Who will see my data?

All the data we collect during the consultation (i.e. your feedback on the questions) will be made anonymous as we will not record your name when we write down your feedback. We keep the thoughts you have shared but do not record that *you* shared them.

Gareth will combine your feedback with other participants and this combined feedback will be reviewed by the research team to inform the questionnaire development. Please note that once we have combined your feedback with the other participants you will be unable to withdraw your data (i.e. it will be impossible to identify your feedback as it will be anonymous).

Any findings from the research may be written up as a research article and published, presented at conferences, and included in Gareth Davies' doctoral submissions. You will not be identifiable in any of these publications.

Are there any reasons why I should not take part?

Thinking about the questions and discussing your feedback may bring up memories of being diagnosed, or other experiences you have had. It is possible that you might find this upsetting or challenging. You will be sent the questionnaire in advance so that you can look through all the questions and decide if you want to participate. You can withdraw any time if you want to.

How will I benefit from the research?

You will be paid £30 for taking part and this will be paid directly to your bank. There are no other direct benefits to taking part, but your input could help us learn things that benefit other autistic people in the future.

What will happen at the end of the project?

We will use your feedback to finalise our questionnaire. We will then be able to test it in an autistic population to see how well it can discriminate between autistic adults and those without ASD.

Who has reviewed this research?

This study has been reviewed and approved by the Cardiff University School of Psychology Research Ethics Committee.

If you have any questions: You can contact us by email or post. Our contact details are:

Mr Gareth Davies
School of Psychology
Cardiff University
57 Park Place
Cardiff
CF10 3AT
Email: DaviesG70@cardiff.ac.uk

Prof. Susan Leekam
School of Psychology
Cardiff University
Tower Building, Park Place
Cardiff
CF10 3AT
Email: LeekamSR@cardiff.ac.uk

Dr Catherine Jones
School of Psychology
Cardiff University
Tower Building
Park Place
Cardiff
CF10 3AT
Email: JonesCR10@cardiff.ac.uk

Who do I contact if I have a complaint?

Secretary of the Ethics Committee
School of Psychology
Cardiff University
Tower Building
Park Place
Cardiff
CF10 3AT
Tel: 029 2087 0360
Email: psychethics@cardiff.ac.uk

Appendix 7: Autistic Consultant Consent Form

The Adult Autism Signs Questionnaire

If you have any questions, please ask Gareth Davies before you decide whether to take part. You can't take part until you have read the following statements, agreed with them, and signed this form.

Please tick each statement if you agree with them, and then submit the form at the bottom of the page:

I confirm that I have read and understood the participant information sheet. ☐

I confirm that I am 18 years old or older, and have a confirmed ASD diagnosis. ☐

I have had the opportunity to consider the information, ask the researcher questions and I am satisfied with the answers to any questions I asked. ☐

I understand participation is voluntary and I will receive £30 for my time. I am free to withdraw at any time without giving any reason and without any penalty. ☐

I understand that I will be shown a series of potential questions and asked for my thoughts about them. I understand I don't have to give thoughts on any particular question if I don't want to. ☐

I know I can ask the researcher questions at any time. ☐

I understand that the feedback I provide on the questions will be held anonymously, so that it is impossible to trace this information back to me individually. I understand that this information may be retained indefinitely, and it can't be removed from the study once it has been anonymised. ☐

I understand that the researcher will need to share information with their project supervisor if I suggest I am at risk of harming myself or someone else. ☐

I also understand that at the end of the study I will be provided with additional information and feedback about the purpose of the study. ☐

The data controller is Cardiff University and the Data Protection Officer is Matt Cooper CooperM1@cardiff.ac.uk. The lawful basis for the processing of the data you provide is consent.

I, _____(NAME) consent to participate in the study conducted by Gareth Davies, School of Psychology, Cardiff University with the supervision of Prof. Sue Leekam and Dr Catherine Jones

Signed:

Date:

The Adult Autism Signs Questionnaire

Thank you for taking part in our study!

What were the aims of the study?

Complicated assessments are normally needed to help diagnose people with autism. There aren't enough people trained in using these assessments, so waiting lists for assessment can be very long. The DISCO-Abbreviated (a shorter version of one of these assessments) is already showing promising results in reliably diagnosing autism even though it is much shorter. The next step is to design a signposting tool so that non-specialists can refer to the right services as soon as possible.

'The Signposting Questionnaire (a 14-item questionnaire) is being developed and has already been tried out in a version for parents of children. For adults the questionnaire needs to be changed so it is suitable for them.

In this study you gave advice on the development of a questionnaire for adults. We asked for your feedback, to tell us if questions were clearly worded and understandable, and if any of them were upsetting or insensitive to you.

What will be the outcomes of the study?

Your feedback will help us finalise our adult signposting questionnaire. This questionnaire can be completed by adults awaiting diagnostic assessment for ASD to support the diagnostic service. We hope this will have a direct and positive impact on best practice for referrals.

What happens next?

Your anonymous feedback will be used to revise our questionnaire. The new version of the questionnaire will eventually be tested in a group of adults attending an autism diagnostic clinic. Your anonymity means that your name or other identifying details will not be traced to your answers. You will not be able to withdraw your data once the consultation is finished as your comments

are anonymous. Any findings from the project may be published as a journal article, presented at conferences and included in Gareth Davies' Doctoral submissions. We will write about the project findings on the Wales Autism Research Centre website (https://sites.cardiff.ac.uk/warc/). You can also email Gareth Davies at any time if you have any questions about the study.

Who can I contact if I have a complaint?
You can contact one of Gareth Davies' supervisors, Prof. Sue Leekam and Dr Catherine Jones, or the School of Psychology Ethics Committee.

Mr Gareth Davies
School of Psychology
Cardiff University
57 Park Place
Cardiff
CF10 3AT
Email: DaviesG70@cardiff.ac.uk

Prof. Sue Leekam
School of Psychology
Cardiff University
Tower Building, Park Place
Cardiff
CF10 3AT
Tel: 029 208 75372
Email: LeekamSR@cardiff.ac.uk

Dr Catherine Jones
School of Psychology
Cardiff University
Tower Building, Park Place
Cardiff
CF10 3AT

Email: JonesCR10@cardiff.ac.uk

Secretary of the Ethics Committee
School of Psychology
Cardiff University
Tower Building
Park Place
Cardiff
CF10 3AT
Tel: 029 2087 0360
Email: psychethics@cardiff.ac.uk

Appendix 9: Undergraduate Participant Information and Consent (Online Form)

The Adult Autism Signs Questionnaire

Thank you for your interest in taking part in this study on autism signs. This information sheet will provide detailed information about why we are doing this study and what it will involve for you. Please email the researchers to ask about anything that is not clear. Our contact details are at the bottom of the information sheet.

What is the research about?
There are many assessments used in the referral and diagnosis of autism spectrum disorder (ASD). This study aims to compare a new questionnaire for detecting key signs that are seen in autistic individuals, with an existing measure. Although these questionnaires alert us to the signs of autism, anyone in the general population can display any of these individual signs too, so there is no right or wrong score. We want to pilot this with the general population firstly, to make sure the questions make sense to those answering them, and to gain an idea of what the general population tend to score. It is important to note that the questionnaires are not diagnostic, and your responses are collected anonymously, so we cannot provide feedback on them.

What will I have to do?
This study requires you to **answer three short questionnaires (including two very similar versions of our new questionnaire and one existing questionnaire)** containing a number of questions that are used in common assessments for autism spectrum disorders. We would like you to answer these questions honestly. You do not have to answer any question if you do not want.

Will there be any payment for taking part in the research
No financial compensation can be offered for taking part in the project. Cardiff University students who have signed up for the study through the EMS system will receive 2 course credits.

Who will see my data?
All information is held anonymously, which means it cannot be traced back to you. This also means that you cannot withdraw your responses after you have submitted your answers. However, you can withdraw at any time during your participation by closing the browser window. If you are taking part in this study for an EMS credit, you will still receive this credit if you withdraw before completing the study.

Thank you for reading this information. If you have any questions you can contact us:
Mr Gareth Davies
School of Psychology
DaviesG70@cardiff.ac.uk

Dr Catherine Jones

School of Psychology
JonesCR10@cardiff.ac.uk

Further enquiries or any complaints can be made to:
Secretary of the Ethics Committee
School of Psychology
Cardiff University
Tower Building
Park Place
Cardiff
CF10 3AT
Tel: 029 2087 0360
psychethics@cardiff.ac.uk

☐ **I consent to participate in the study conducted by Gareth Davies, School of Psychology, Cardiff University with the supervision of Prof. Sue Leekam and Dr Catherine Jones.**

Appendix 10: Undergraduate Debrief Sheet

The Adult Autism Signs Questionnaire

Thank you for taking part in our study!

What were the aims of the study?

Complicated assessments are normally needed to help diagnose people with autism. There aren't enough people trained in using these assessments so waiting lists for assessment can be very long. The DISCO-Abbreviated (a shorter version of one of these assessments) is already showing promising results in reliably diagnosing autism even though it is much shorter. The next step is to design a signposting tool so that non-specialists can refer to the right services as soon as possible.

'The SIGNS' (a 14-item questionnaire) is already being piloted with children, This tool will be for adults though, so it needs to contain the most significant signs for them, which may be different to children. To design this tool we used prior research to devise a shortlist of possible autism signs and present these to some people with an autism diagnosis, so that we knew all our questions were clearly worded and understandable, and that none of them were upsetting or insensitive to anyone. You have just completed two versions of this questionnaire, one from before our consultation, and one from afterwards. The third questionnaire (the AQ-10) is a similar tool we have asked people to complete for comparison.

From this research, we hope to design a practical brief signposting tool that will be valid for use in adults presenting for autism diagnosis, so that clinicians can make appropriate referrals to the correct services as soon as possible. We hope this will have a direct and positive impact on best practice for referrals and the length of waiting lists.

The questionnaires used in this study are not diagnostic tools and no individual feedback on participant responses are available. However, if you are concerned about any of the questions or issues raised, please refer to http://www.autism.org.uk/
for more information, or consult your GP who will be able to provide support. If you are a Cardiff University student, you may also wish to contact student support (https://www.cardiff.ac.uk/study/student-life/student-support).

If you would like more information regarding the study or have any questions, please contact myself, Prof. Sue Leekam or Dr. Catherine Jones. If you have any further queries or would like to make a complaint, please contact the School of Psychology Ethics Committee. All contact details are listed below.

Mr Gareth Davies School of Psychology Cardiff University 57 Park Place Cardiff	Dr Catherine Jones School of Psychology Cardiff University

CF10 3AT Email: DaviesG70@cardiff.ac.uk Prof. Sue Leekam School of Psychology Cardiff University Tower Building, Park Place Cardiff CF10 3AT Tel: 029 208 75372 Email: LeekamSR@cardiff.ac.uk	Tower Building, Park Place Cardiff CF10 3AT Email: JonesCR10@cardiff.ac.uk Secretary of the Ethics Committee School of Psychology Cardiff University Tower Building Park Place Cardiff CF10 3AT Tel: 029 2087 0360 Email: psychethics@cardiff.ac.uk

Appendix 11 – Signposting Questionnaire for Autism (Pre-Consultation Version)

*** REDACTED – All versions of the SQ-A (Adult) have been redacted for copyright purposes by the author ***

*** REDACTED – All versions of the SQ-A (Adult) have been redacted for copyright purposes by the author ***

Appendix 13 – AQ-10

*** REDACTED – All versions of the AQ-10 have been redacted for copyright purposes by the author ***

*** REDACTED – All versions of the SQ-A (Adult) have been redacted for copyright purposes by the author ***

Appendix 15 – The Signposting Questionnaire for Autism (Adult) Other Edition

*** REDACTED – All versions of the SQ-A (Adult) have been redacted for copyright purposes by the author ***

Appendix 16 – The AQ-10 (Self Edition)

*** REDACTED – All versions of the AQ-10 have been redacted for copyright purposes by the author ***

Appendix 17 – The AQ-10 (Other Edition)

*** REDACTED – All versions of the AQ-10 have been redacted for copyright purposes by the author ***

Appendix 18: University Ethics Approval

From: psychethics <psychethics@cardiff.ac.uk>
Sent: 14 November 2018 12:52
To: Gareth Davies <DaviesG70@cardiff.ac.uk>
Cc: Dougal Hare <HareD@cardiff.ac.uk>; Catherine Jones <JonesCR10@cardiff.ac.uk>
Subject: Ethics Feedback - EC.18.09.18.5340A

Dear Gareth

The Ethics Committee has considered the amendment your PG project proposal: Developing the Signposting Questionnaire for Adults: A questionnaire based on items from the Diagnostic Interview for Social and Communication Disorders (DISCO) (EC.18.09.18.5340A).

The project has been approved.

Please note that if any changes are made to the above project then you must notify the Ethics Committee.

Best wishes,

Adam Hammond

School of Psychology Research Ethics Committee

Cardiff University	Prifysgol Caerdydd
Tower Building	Adeilad y Tŵr
70 Park Place	70 Plas y Parc
Cardiff	Caerdydd
CF10 3AT	CF10 3AT
Tel: +44(0)29 208 70360	Ffôn: +44(0)29 208 70360
Email: psychethics@cardiff.ac.uk	E-bost: psychethics@caerdydd.ac.uk
http://psych.cf.ac.uk/aboutus/ethics.html	

Appendix 19: NHS REC/ HRA/ HCRW Approval Letter

Ymchwil Iechyd
a Gofal **Cymru**
**Health and Care
Research Wales**

**NHS
Health Research
Authority**

Dr Dougal Hare
South Wales Doctorate in Clinical Psychology
School of Psychology, Tower Building
Park Place, Cardiff
CF10 3AT

Email: hra.approval@nhs.net
HCRW.approvals@wales.nhs.uk

27 August 2019

Dear Dr Hare

**HRA and Health and Care
Research Wales (HCRW)
Approval Letter**

Study title:	**Brief Questionnaires to Inform the Diagnostic Assessment Process for ASD**
IRAS project ID:	**XXXX**
REC reference:	
Sponsor	**Cardiff University**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:
- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is XXXX Please quote this on all correspondence.

Yours sincerely,

Thomas Fairman
HRA Approvals Manager

Email: hra.approval@nhs.net

Copy to: *Mr Chris Shaw, (Sponsor Contact)*

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	Version	Date
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Sponsors Insurance Certificate]	1	01 August 2019
IRAS Application Form [IRAS_Form_12082019]	12 August 2019	
Letter from sponsor [Sponsorship Letter]	1	18 July 2019
Organisation Information Document		
Other [Researchers clarification email]	23 August 2019	
Research protocol or project proposal [Protocol]	3	02 August 2019
Schedule of Events or SoECAT	1.0	27 August 2019
Summary CV for Chief Investigator (CI) [Chief Investigator CV]	1.0	23 July 2019
Summary CV for student [Principal Investigator CV]	1.0	23 July 2019
Summary CV for supervisor (student research) [Chief Investigator CV]	1.0	23 July 2019

Appendix 20: University Sponsorship Letter

CARDIFF UNIVERSITY
PRIFYSGOL CAERDYDD

Research and
Innovation Services

Gwasanaethau Ymchwil
ac Arloesi

Cardiff University
McKenzie House, 7th Floor
30-36 Newport Road, Cardiff
CF24 0DE, Wales, UK
Tel +44(0)29 2087 5834
www.cardiff.ac.uk

Prifysgol Caerdydd
Tŷ McKenzie, 7fed Llawr
30-36 Heol Casnewydd, Caerdydd
CF24 0DE, Cymru, DU
Ffôn +44(0)29 2087 5834
www.caerdydd.ac.uk

18th July 2019

Dr Dougal Hare
South Wales Doctoral Programme in Clinical Psychology
School of Psychology
Cardiff University
Tower Building
Park Place
Cardiff
CF10 3AT

Dear Dr Hare,

The use of Brief Questionnaires to Inform the Diagnostic Assessment Process for Autism Spectrum Disorder (ASD)

I understand that you are acting as Chief Investigator and Academic Supervisor for the above DClinPsy project to be conducted by Gareth Davies.

I confirm that Cardiff University agrees in principle to act as Sponsor for the above project, as required by the UK Policy Framework for Health and Social Care Research.

Scientific Review
I can also confirm that Scientific Review has been obtained from: the DClinPsy supervisory review team.

Insurance
The necessary insurance provisions will be in place prior to the project commencement. Cardiff University is insured with UMAL. Copies of the insurance certificate are attached to this letter.

Approvals
On completion of your IRAS form (required for NHS REC and HRA/HCRW/NHS R&D permission), you will be required to obtain signature from the Research Governance team for the 'Declaration by the Sponsor Representative'. Please note that you are also required to provide the Organisation Information Document and Schedule of Events to the Research Governance team for review prior to submission to HRA/HCRW.

Please then submit the project to the following bodies for approval:

- an NHS Research Ethics Committee;
- Health & Care Research Wales (HCRW)- to arrange HRA/HCRW Approval for Welsh NHS sites.

The University is considered to have accepted Sponsorship when Research and Innovation Services has received evidence of the above approvals. **Responsibility for providing the Local Information Pack to NHS organisations is delegated from the Sponsor to the Chief Investigator (or their appropriate delegate). Once an NHS organisation has confirmed capacity and capability, responsibility lies with the Chief Investigator (or their appropriate delegate) to follow an appropriate 'green light' procedure to open the study at that Site.**

Roles and Responsibilities
As Chief Investigator you have signed a Declaration with the Sponsor to confirm that you will adhere to the standard responsibilities as set out by the UK Policy Framework for Health and Social Care Research. In

accordance with the University's Research Integrity & Governance Code of Practice, the Chief Investigator is also responsible for ensuring that each research team member is qualified and experienced to fulfil their delegated roles including ensuring adequate supervision, support and training.

If your study is adopted onto Health & Care Research Wales Clinical Research Portfolio you are required to upload recruitment data onto the portfolio database.

Contracts

- The HRA/HCRW Organisation Information Document will act as the agreement between the sponsor and participating NHS organisations.

May I take this opportunity to remind you that, as Chief Investigator, you are required to:
- register clinical trials in a publicly accessible database before recruitment of the first participant and ensure that the information is kept up to date
- ensure you are familiar with your responsibilities under the UK Policy Framework for Health and Social Care Research;
- undertake the study in accordance with Cardiff University's Research Integrity & Governance Code of Practice (available on the Cardiff University Staff and Student Intranet) and the principles of Good Clinical Practice;
- ensure the research complies with the General Data Protection Regulation 2016/679;
- where the study involves human tissue, ensure the research complies with the Human Tissue Act and the Cardiff University Code of Practice for Research involving Human Tissue (available on the Cardiff University Staff and Student Intranet);
- inform Research and Innovation Services of any amendments to the protocol or study design, (including changes to start /end dates) and submit amendments to the relevant approval bodies;
- respond to correspondence from the REC, HRA/HCRW and NHS organisation R&D offices within the required timeframes;
- co-operate with any audit, monitoring visit or inspection of the project files or any requests from Research and Innovation Services for further information.

You should quote the following unique reference number in any correspondence relating to Sponsorship for the above project:

XXXX

This reference number should be quoted on all documentation associated with this project.

Yours sincerely

Mr Chris Shaw
Research Governance Coordinator
Direct line: +44 (0) 29208 79277
Email: resgov@cardiff.ac.uk

Cc   Mr Gareth Davies (student); Dr Catherine Jones.

Appendix 21: Health Board Research and Development Approval

From: resgov <resgov@cardiff.ac.uk>
Sent: 08 October 2019 11:48
To: HB R&D Department
Cc: Gareth Davies <DaviesG70@cardiff.ac.uk>
Subject: Confirmation of Capacity and Capability

Please accept this email as confirmation of Sponsor green light.

Kind regards

Helen (on behalf of Chris Shaw).

Research Governance Team	**Tîm Llywodraethu Ymchwil**
Research and Innovation Services	Gwasanaethau Ymchwil ac Arloesi
Cardiff University	Prifysgol Caerdydd
7th Floor, McKenzie House	7fed Llawr, Tŷ McKenzie
30-36 Newport Road	30-36 Heol Casnewydd
Cardiff	Caerdydd
CF24 0DE	CF24 0DE
Tel: +44(0)29 2087 9277	Ffôn: +44(0)29 2087 9277
	E-bost: resgov@cardiff.ac.uk
Email: resgov@cardiff.ac.uk	Mae Prifysgol Caerdydd yn elusen gofrestredig rhif 1136855
Cardiff University is a registered charity no. 1136855	
Chris Shaw - Research Governance Coordinator	**Chris Shaw - Cydlynydd Llywodraethu Ymchwil**
Helen Falconer – Research Governance Officer	**Helen Falconer – Swyddog Llywodraethu Ymchwil**
Emma Gore - Research Integrity and Governance Officer	**Emma Gore- Swyddog Llywodraethu a Gonestrwydd Ymchwi**
Kim Mears- Research Governance Administrative Officer	**Kim Mears- Swyddog Gweinyddol Llywodraethu Ymchwil**

Other HB Representatives Copied in

Hi Gareth,

I know it is a little confusing, with the new guidelines.

Because we have not been asked to 'approve' your study as no C&C is required, we can only offer a 'no objection/acknowledgement' to you starting the study in the health board.

As Sponsor rep, Chris Shaw was the nominated person to email.

You are free to being your study, once Chris/one of the sponsors have issued a 'green light' to begin (please copy us into the email).

Best wishes,

HB R&D Department

Thank you for sending details of your study to [HB] We acknowledge receipt of this study, following our review on 25ᵗʰ September 2019.

The HRA Approval letter states we have not been requested to formally confirm Capacity and Capability.

Important changes: A **UK Local Information Pack** *will be introduced on the 5June 2019. Researchers working with NHS / HSC organisations across the UK will benefit from a consistent package to support study set-up and delivery. More information is given in the* [Local Information Pack section of IRAS Help](#).

Kind regards

HB Representatives Details

We constantly strive to improve our services and value your feedback. We'd really like to hear from you and your responses will, of course, remain confidential and you won't be identified in any results. Please click on this link to leave your feedback: www.healthandcareresearch.gov.wales/your-views/

Rydyn ni bob amser yn ymdrechu i wella ein gwasanaethau ac rydyn ni'n gwerthfawrogi'ch adborth. Fe fydden ni'n wirioneddol hoffi clywed oddi wrthych chi ac fe fydd eich ymatebion, wrth gwrs, bob amser yn gyfrinachol ac ni fyddwn ni'n eich enwi mewn unrhyw ganlyniadau. Cliciwch ar y ddolen hon i roi'ch adborth: www.ymchwiliechydagofal.llyw.cymru/your-views-cy

Appendix 22: Quality Assessment Summary of Each Feature for All Included Studies

AXIS Item and Description	Chen 2016	Cheung et al. 2018	De Vries et al. 2010	Dragon (2017)	Fielding and Bass (2018)	Heard (2018)	Heylens et al. 2018	Hisle-Gorman et al. 2019	Holt et al. 2016	Kaltiala-Heino et al.	Kaltiala-Heino (2019)	Leef et al. 2019	Nahata (2017)	Skagerberg et al. 2016	Van Der Miesen et al. 2018
1. Were the aims/objectives of the study clear?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
2. Was the study design appropriate for the stated aim(s)?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
3. Was the sample size justified?	X	X	X	✓	X	X	X	✓	X	X	X	X	X	X	X
4. Was the target/reference population clearly defined?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
5. Was the sample frame taken from an appropriate population base	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
6. Was selection representative of target/reference population under investigation?	N	N	N	N	N	N	N	N	N	N	N	✓	N	U	✓
7. Were measures undertaken to address and categorise non-responders?	N	N	N	N	N	N	X	N	N	✓	✓	X	N	U	U
8. Were risk factor and outcome variables measured appropriate for study?	N	N	✓	N	✓	✓	✓	N	N	✓	✓	✓	✓	✓	✓
9. Did risk factor and outcome variables measured with instruments / measurements trialled, piloted or published previously?	N	N	✓	N	✓	✓	✓	N	✓	✓	✓	✓	✓	✓	U
10. Is it clear what was used to determined statistical significance	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	N	✓	✓
11. Were the methods sufficiently described to be repeated?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
12. Were the basic data adequately described?	X	X	✓	✓	X	X	X	✓	X	✓	✓	X	X	X	X
13. Does the response rate raise concerns about non-response bias?	N	N	X	N	N	N	U	N	N	N	X	U	N	✓	N
14. If appropriate, was information about non-responders described?	N	N	X	N	N	N	U	N	N	✓	✓	X	N	X	N
15. Were the results internally consistent?	U	U	U	✓	✓	✓	U	✓	U	✓	✓	U	✓	✓	✓
16. Were the results for all the analyses described in methods?	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
17. Were discussions and conclusions justified by the results?	N	✓	✓	N	N	N	✓	✓	✓	✓	✓	✓	N	✓	✓
18. Were the limitations of the study discussed?	X	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
19. Any funding or conflicts that might affect interpretation of results?	X	X	X	X	X	U	X	X	X	X	X	U	X	U	X
20. Was ethical approval or consent of participants attained?	✓	N	✓	✓	✓	✓	✓	✓	U	✓	✓	✓	✓	U	✓

Key: ✓ = Item was present; X = item was not present; N = not applicable; U = Unclear – there is not enough information to adequately judge the item. In each case see narrative synthesis in Appendix 3 for discussion of how each item was judged.