Published in final edited form as:

J Child Fam Stud. 2018 June ; 27(6): 1705–1720. doi:10.1007/s10826-018-1026-3.

Broader autism phenotype in parents of children with autism: a systematic review of percentage estimates

Eric Rubenstein^{1,2} and Devika Chawla¹

¹University of North Carolina Gillings School of Global Public Health, Department of Epidemiology, Chapel Hill, NC

²University of Wisconsin-Madison, Waisman Center, Madison, WI

Abstract

The broader autism phenotype (BAP) is a collection of sub-diagnostic autistic traits more common in families of individuals with autism spectrum disorder (ASD) than in the general population. BAP is a latent construct that can be defined using different domains, measured using multiple instruments, and reported using different techniques. Therefore, estimates of BAP may vary greatly across studies. Our objective was to systematically review studies that reported occurrence of BAP in parents of children with ASD in order to quantify and describe heterogeneity in estimates. We systematically searched PubMed and Scopus using PRISMA guidelines for studies quantifying percentage of parents of children with ASD who had BAP. We identified 41 studies that measured BAP in parents of children with ASD. These studies used eight different instruments, four different forms of data collection, and had a wide range of sample sizes (N=4 to N=3299). Percentage with BAP ranged from 2.6% to 80%. BAP was more prevalent in fathers than mothers. Parental BAP may be an important tool for parsing heterogeneity in ASD etiology and for developing parent-mediated ASD interventions. However, the variety in measurement instruments and variability in study samples limits our ability to synthesize estimates. To improve measurement of BAP and increase consistency across studies, universal methods should be accepted and adopted across studies. A more consistent approach to BAP measurement may enable efficient etiologic research that can be meta-analyzed and may allow for a larger evidence base that can be used to account for BAP when developing parent-mediated interventions.

Introduction

Since autism spectrum disorder (ASD) was formally identified by Kanner (1943), it has consistently been observed that parents of children diagnosed with ASD often exhibit social tendencies that are similar to ASD, but do not impair functioning or otherwise reach the

Corresponding Author: E. Rubenstein, 1500 Highland Ave, Rm 529A, Madison WI 53705, Erubenstein2@wisc.edu.
Devika Chawla, 135 Dauer Dr, Chapel Hill NC 27599, Chawlad@live.unc.edu

Eric Rubenstein and Devika Chawla declare no conflicts of interests to declare

Neither author has conflicts of interests to report

Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors. E.R. conceived of the study idea and design. E.R. and D.C. conducted the literature search and review. E.R. organized and drafted the manuscript. E.R. and D.C. reviewed and edited the manuscript.

same level of clinical significance as ASD (Bolton et al., 1994; Landa, Folstein, & Isaacs, 1991; Piven et al., 1994; Piven et al., 1997a; Wolff, Narayan, & Moyes, 1988). The constellation of sub-diagnostic threshold ASD traits in families of children with ASD is referred to as the broader autism phenotype (BAP) (Bolton et al., 1994). Traits of BAP include pragmatic difficulties, broadly-defined communication difficulties, poor social skills, rigidity, broadly-defined stereotyped behaviors, impaired emotional recognition, and aloofness (Gerdtz & Bernier, 2011; Sucksmith, Roth, & Hoekstra, 2011). BAP in adults is associated with anxiety, depression, and obsessive-compulsive disorder and is marked by cognitive traits like weak central coherence, diminished executive functioning, and neurological processing (Gerdtz & Bernier, 2011; Sucksmith et al., 2011). Studying BAP in parents of children with ASD is important since a significant portion of ASD etiology can be attributed to heredity and genetics (Gaugler et al., 2014). Having a parent with BAP and a child with ASD strongly suggests a genetic mechanism (Robinson et al., 2011) and subgrouping by familial predisposition to ASD in research studies can minimize genotypic and possibly phenotypic heterogeneity (Gerdtz & Bernier, 2011; Sucksmith et al., 2011).

Data on BAP in adults are collected with a variety of different instruments. We highlight seven of the most common in Table 1. These instruments are completed through different processes. A self-reported measure has the individual whose BAP traits are being assessed complete a questionnaire on his or her own traits. An informant report has an individual's close friend, spouse, or relative report on their BAP traits, and a clinician observation has a trained professional evaluation of an individual's BAP traits. Each of these methods has strengths and weaknesses; self-report questionnaires can be completed quickly, do not need the participant to find someone to report on them, and do not require a trained professional. Conversely, self-report may be influenced by BAP traits (Sasson, Faso, Parlier, Daniels, & Piven, 2014). Informant reports are bolstered by the amount of time and varying situations where the informant has interacted with the individual, but these measures may also be influenced by an informant's BAP traits (Rubenstein et al., 2017; Sasson et al., 2014). Clinicians may be better at assessing traits in relation to peers and are able to remove some of the variance due to differences among those acquaintances that report. However, clinician observation in large studies may be costly and time consuming. For some instruments, multiple methods of BAP measurement are possible (referred to here as multi-modal). A multi-modal approach may improve accuracy through multiple observations and opinions, but takes more time and resources. Individual instruments have different strengths and weaknesses. The Broader Autism Phenotype Questionnaire (BAPQ) and Broader Phenotype Autism Symptom Scale (BPASS) were specifically designed to measure BAP and were created using samples of people with BAP (Dawson et al., 2007; Hurley, Losh, Parlier, Reznick, & Piven, 2007). The Family History Interview (FHI)-Impression Of Interviewee (IOI) and BPASS include clinician observations (Parr, De Jonge, et al., 2015). The Social Responsiveness Scale-Adult (SRS-A) and Autism Quotient (AQ) have both been shown to effectively measure BAP in non-clinical populations (Constantino & Todd, 2003; Ruzich et al., 2015).

The objective of this systematic review was to synthesize reports of percentage of parents of children with ASD who have BAP. We aimed to place results in the context of different instruments, reporting styles, and other aspects of study design. We then discussed the

importance of parental BAP as a tool that can be used to understand ASD etiology and the implication of measurement heterogeneity. Our review differs from past reviews due to our focus on BAP in parents of children with ASD and our aim to highlight sources of heterogeneity in these estimates.

Method

Systematic review process

We conducted a systematic review of articles that measured BAP in parents of children with ASD, with a primary focus on studies that presented percentages of parents with BAP. We conducted our search in August of 2016 and updated our search in March of 2017 using the same search protocol. There were no date restrictions, but BAP had to be measured as a collection of ASD-like traits, which were first described in 1994 (Bolton et al., 1994). Two independent reviewers were involved in all study selection steps.

Search criteria

We searched PubMed and Scopus titles and abstracts for a combination of text words and mesh terms/index words. Our term list included 'broader', 'broad', or 'quantitative', and 'autism' or 'autistic', and 'phenotype' or 'trait', and 'mother' or 'father' or 'parent' or 'relative' and those words in their plural forms. Further description of searches is provided in Supplement 1. A complete selection schematic is presented in Figure 1. Briefly, our preliminary search excluded reviews, case reports, commentaries, editorials, and letters. We additionally analyzed references cited by past review articles (Constantino, 2011; Cruz, Camargos-Junior, & Rocha, 2013; Gerdtz & Bernier, 2011; Sucksmith et al., 2011). In total, 486 papers were reviewed by title and abstract. After abstract and title review, we excluded 380 papers due to lack of applicability to our topic, for instance studies that measured BAP in siblings but not parents. These same exclusions led to full text review of 106 articles. After review, 65 articles were excluded, primarily because they only measured one trait of BAP or did not present or dichotomize BAP results. Forty-one studies met all criteria and are summarized in this systematic review.

Potential bias

Due to the nature of this research, we believe that there is minimal potential for bias in our review process. Much of the literature identified has the objective of defining the psychometric properties of BAP instruments and these studies present percentages of parents with BAP as part of their descriptive analyses. Therefore, these studies are at a lesser risk for publication bias as compared to studies that assess risk factors or interventions because these studies are descriptive in nature. Limited details on sample selection in studies prevent us from systematic assessment of sampling bias. However, we do list the country of origin and whether the sample was derived from a clinic (i.e. through convenience sampling at a medical provider or referral from a clinic that serves children with developmental disabilities) or through community-wide recruiting (i.e. through research registries, community organizations). We conducted a meta-regression to determine whether a meta-analysis should be conducted. We found significant heterogeneity in study level variables

(instrument, study year, which parent BAP was measured in, informant type, whether controls were used) with $P < 0.001$; therefore, we did not meta-analyze results.

Results

Percentage of parents of children with ASD who have BAP

We identified 41 studies that provided percent of parents of children with ASD who have BAP. All studies used crude percentages of parents with BAP, as no study estimated percent of parents with BAP by means of statistical modeling. The earliest identified study used data collected in 1994 (Fombonne, Bolton, Prior, Jordan, & Rutter, 1997). Percentage of parents of children with ASD who had BAP ranged from 3.0% (Klin, Pauls, Schultz, & Volkmar, 2005) to 52.0% (de Jonge et al., 2015) in mothers, 2.6% (Seidman, Yirmiya, Milshtein, Ebstein, & Levi, 2012) to 80.0% (de Jonge et al., 2015) in fathers, and 5.3% (Szatmari et al., 2000) to 56.0% (Dawson et al., 2007) when pooling both mothers and fathers.

Sample description

The majority of identified studies (78%) were sampled from the community (Table 2). Slightly less than half (48%) were conducted in the US. The most common instrument used was the FHI ($N=20$) followed by the AQ and BAPQ ($Ns=10$). Self-report was the most common type of data collection ($N=25$). Twenty-seven studies reported percentages for all parents who completed the assessment (i.e. not stratified by parent type). Twenty-four reported percentage in fathers of children with ASD and 25 reported percentage in mothers of children with ASD.

Based on a study's specific objective, some assessed different subgroups of parents (Table 3). Subgroups included parents of multiple children with ASD (multiplex), parents with one child with ASD (simplex) (de Jonge et al., 2015; Gerdtz, Bernier, Dawson, & Estes, 2013; Szatmari et al., 2000), parents of a child with high functioning autism or Asperger's syndrome (Ghaziuddin, 2005), Hispanic parents (Page et al., 2016), parents of children with and without developmental regression (Lainhart et al., 2002), and by parent SSRI antidepressant use (Levin-Decanini et al., 2013).

Sample size

Among studies identified, sample sizes ranged from 4 (Levin-Decanini et al., 2013) to 3299 (Davidson et al., 2014) (Table 3, Figure 2). Based on Figure 2, there is some indication that percentage of parents with BAP is greater when sample size was smaller. This may be a result of sample type, as the community-based samples may be larger and encompass children who may not attend clinics that serve children with ASD as compared to smaller clinical samples. However, due to our inability to meta-analyze, we cannot make any formal conclusions.

Parent type

Qualitatively, a higher percentage of fathers had BAP compared to mothers (Table 3, Figure 2), which is consistent with the male: female sex ratio in ASD and may signify a male predisposition for autistic traits (Baron-Cohen et al., 2011). However, father BAP was not

consistently higher in all studies that measured both mother and father BAP (Sasson et al., 2014; Sasson, Lam, Childress, et al., 2013; Seidman et al., 2012; Shi et al., 2015; Whitehouse, Barry, & Bishop, 2007).

Instrument

The FHI resulted in the highest BAP estimates but had a large range (Figure 2). This range may be due to the three different types of reporters (FHI-Self report [FHI-S], FHI-Interview [FHI-I], IOI), change in the instrument over time, and differences in sample demographics. The AQ, BAPQ, and SRS-A had similar ranges to one another, with most studies finding a percentage between 5% and 40%. Some studies defined BAP by meeting 1 or 2 domains. Not surprisingly, when the criteria were stricter (> 2 domains) percentages were lower (Dawson et al., 2007; Szatmari et al., 2000). Qualitatively, percentage of parents with BAP did not vary greatly by informant type. Other instruments like the Communication Checklist-Adult and Pragmatic Rating Scale were not used enough to make inferences.

Results from reviewed studies

Seventeen studies provided the percentage with BAP for parents of controls (either parents of typical developing children, parents of children with Down Syndrome, or non-biological relatives of children with ASD), universally finding BAP to be more common in parents of children with ASD (Table 3). Multiplex families were more likely to have parents with BAP than simplex families (Gerdtz et al., 2013; Losh, Childress, Lam, & Piven, 2008; Szatmari et al., 2000). Fourteen studies assessed the relationship between parent BAP and child ASD phenotype. Positive associations were found between child scores on ASD screeners and parent scores on BAP measures (Hasegawa et al., 2015; Maxwell, Parish-Morris, Hsin, Bush, & Schultz, 2013; Sasson, Lam, Parlier, Daniels, & Piven, 2013; Schwichtenberg, Young, Sigman, Hutman, & Ozonoff, 2010). Additional significant associations were found between child intense preoccupation and father rigidity domain (Smith et al., 2009), and parent and child repetitive and restrictive behavior and interest score (Uljarevic, Evans, Alvares, & Whitehouse, 2016). Levin-Decanini et al. (2013) stratified their results by whether the parent had taken SSRIs and found that there was a relationship between parent BAP and child RRBI among parents not taking SSRIs. Studies found that the father having BAP had larger effect sizes in association with child phenotype compared to mothers with BAP (Maxwell et al., 2013; Schwichtenberg et al., 2010; Smith et al., 2009). Two studies found no associations between maternal BAP and child phenotype (Losh et al., 2009; Schwichtenberg et al., 2010), whereas Hasegawa et al. (2015) found associations between maternal BAP and four of five child SRS domains but no associations between father BAP and child phenotype. Two studies had null results. Bishop et al. (Bishop, Maybery, Maley, et al.) found no association between BAP and child IQ and no difference between children having 'autism' or 'pervasive developmental disorder' by parental BAP status. Taylor et al. (2013) found no association between parental BAP and child ADOS severity.

Discussion

This systematic review addressed percent of parents meeting BAP criteria among parents of children with ASD while focusing on the heterogeneity in methods. Although the concept of

elevated autistic traits in parents of children with ASD has been postulated since the definition of ASD itself (Kanner, 1943), only 41 studies met our review criteria. The bulk of studies that were identified through our systematic search that did not meet our selection criteria compared all parents of children with ASD to control parents, without specifically measuring BAP. Based on the results of our review, estimates of BAP in parents of children with ASD range from 2.6% to 80.0%, illustrating the large variance in this literature. BAP is more common in parents of children with ASD than in controls and more common in fathers than mothers. Sources of heterogeneity in BAP estimates include sample size, population studied, instruments used, and results.

Heterogeneity

BAP is a personality construct that encompasses a wide array of traits, and can be measured using multiple instruments using multiple reporting methods (Gerdtz & Bernier, 2011; Sucksmith et al., 2011). Unsurprisingly, we found that percentage of parents with BAP varied greatly between studies. Our review highlights potential sources of heterogeneity: eligible studies used eight different measures, four different forms of data collection, and great range in sample sizes. The instruments used in the literature were originally created for different purposes and calibrated using different populations. Who serves as the reporter can influence scoring of BAP (Constantino & Gruber, 2012; Sasson et al., 2014), and informant reports often differ when assessing another person's autistic traits (De Los Reyes, 2013; Randazzo, Landsverk, & Ganger, 2003; Sasson et al., 2014). Ultimately, BAP is a latent construct of a sub-clinical condition and thus is intrinsically difficult to measure. Therefore, estimating amounts of these traits is deeply tied to how the construct is defined and measured. This leads to heterogeneity in estimates and inability to meta-analyze and deduce how many parents have BAP.

Heterogeneity in this literature is further amplified by dichotomizing BAP. Dichotomizing a latent variable is largely arbitrary and may lead to increased misclassification (Rothman, Greenland S., & Lash T.L., 2008). Some past studies addressed BAP in parents as a continuous score to reflect the continuous distribution of BAP in a population; this approach is valuable when comparing ASD parent groups and control groups by BAP score (Bishop, Maybery, Maley, et al., 2004; De la Marche et al., 2015; Ingersoll, Meyer, & Becker, 2011; Schwichtenberg et al., 2010). However, there is utility in dichotomizing BAP. Looking at differences in mean scores between ASD cases and controls assumes a certain distribution of BAP scores among parents and does not account for whether the BAP presentation is meaningfully different. Importantly, dichotomizing BAP allows for researchers to create subgroups in a sample of individuals with ASD and their families.

Additionally, BAP measures have variable cut-points to define BAP, both determined by instrument documentation and individual studies. The choice of cut-point can greatly alter ASD research by affecting sample size and power if BAP cut-offs are too specific. If BAP cut-offs are not specific enough, there may be unnecessary statistical noise that can obscure results. Since BAP is a latent trait, careful consideration should be given when using dichotomous cut-points in order to minimize misclassification.

Without congruent measures of BAP, heterogeneity in estimates of parental BAP can lead to an inability to synthesize results across studies and may lead to misclassification bias. Theoretically, if a group of parents meet BAP criteria using the SRS-A but not the AQ, then the results of a study would depend on the instrument used and who the reporter was. Without standardized methodology, researchers need to carefully weigh which instrument, reporting style, and parent to assess when exploring relationships between a facet of ASD and BAP. Further, validation studies are needed to better clarify concordance, sensitivities, and specificities across instruments and reporting styles.

Utility of using dichotomous parental BAP

Using familial BAP to subgroup families for ASD research may improve our ability to detect meaningful associations. BAP-defined subgroups are more homogenous and have been proposed as a way to improve ASD research by minimizing phenotypic and genotypic diversity (Cholemkery, Medda, Lempp, & Freitag, 2016; Lai, Lombardo, Chakrabarti, & Baron-Cohen, 2013; Liu, Paterson, Szatmari, & Autism Genome Project, 2008). By creating subgroups by BAP score, we can study families with children with ASD by likely genetic predisposition. Past studies use multiplex families to represent this likely genetic predisposition to ASD (Bernier, Gerdts, Munson, Dawson, & Estes, 2012; Schwichtenberg et al., 2010; Szatmari et al., 2000) but this method is rife for bias due to reproductive stoppage, where a family stops having children due to the increased need of a child with disability (Wood et al., 2015). Parental BAP may be a better tool to define ASD subgroups by likely genetic predisposition when full genome data is not available. Additionally, there is emerging evidence that parental BAP may have implications for intervention (Parr, Gray, Wigham, McConachie, & Le Couteur, 2015) and a child's ASD diagnostic process (Rubenstein et al., 2017). BAP can be a strong tool that can be used to efficiently research ASD, but measurement accuracy and reliability are crucial.

Parental BAP can be a good source of ASD endophenotypes (Adolphs, Spezio, Parlier, & Piven, 2008; Constantino, 2011; Klusek, Losh, & Martin, 2014; Losh et al., 2009; Losh et al., 2008; Losh & Piven, 2007; Rubenstein et al. 2018; Virkud, Todd, Abbacchi, Zhang, & Constantino, 2009). An endophenotype is a measurable, more homogenous subset of a psychiatric disorder's clinical phenotype that must be associated with the disorder in the population, be heritable, state independent (apparent in an individual whether they have the disorder or not), co-segregate in families, and be found in higher rates in unaffected relatives of children with ASD than in the general population (Gottesman & Gould, 2003; Gould & Gottesman, 2006). Parental BAP as a latent construct can be considered as an endophenotype: BAP traits are associated with ASD (Hasegawa et al., 2015; Maxwell et al., 2013; Sasson, Lam, Parlier, et al., 2013; Schwichtenberg et al., 2010), are seen to be heritable (Constantino & Todd, 2003) and are more prevalent in parents of children with ASD as compared to control parents (Bishop, Maybery, Wong, et al., 2004; de Jonge et al., 2015; Lyall et al., 2014; Sasson, Lam, Parlier, et al., 2013; Szatmari et al., 2000). Traits that comprise the BAP construct can also be considered to be endophenotypes. Past work has examined facial affect (Adolphs et al., 2008; Bolte & Poustka, 2003), empathy (Sucksmith, Allison, Baron-Cohen, Chakrabarti, & Hoekstra, 2013), parent IQ (Liu et al., 2008), and executive functioning (Wong, Maybery, Bishop, Maley, & Hallmayer, 2006) as

endophenotypes. With the potential heterogeneity when using BAP, it is important to be consistent in measurement approach, as different choices when classifying and measuring BAP may lead to different results. Based on this literature review, we recommend that studies work to replicate past results using consistent approaches in measuring BAP, while also continuing to develop efficient BAP measurement tools that can be universally used.

Limitations

This review had several limitations. Some information, like who conducted interviews or who served as informant, was not available in most papers and could not be synthesized. The heterogeneity described in regard to instrument and reporter method prevented us from conducting meta-analyses on percentage of parents with BAP. Additionally, we did not translate non-English papers, which may slightly bias our results, since our results mainly consisted of English speaking populations. Further, studies were slanted toward high-income nations, limiting our ability to generalize these findings to populations in low and middle-income countries. We did not assess unpublished work or doctoral theses, which may limit the comprehensive nature of our search. There may also be a broader publication bias, where null results were not published, although we do not believe this to be a large source of bias due to the nature of papers reviewed. Not all papers clearly provided what cut-offs were used when defining BAP, preventing us from better exploring the effect of more or less strict cut points on percentages. There may be some selection bias into these studies as there may be an over-representation of married couples in studies that collected data on mothers and fathers and potential selection bias if certain groups (more educated, whiter) were more likely to participate in research studies.

Future research

BAP is prevalent in parents of children with ASD, and using BAP as an endophenotype may help us understand child ASD etiology. The current literature provides varying reports of percentage of parents with children with ASD who have BAP, which is greatly affected by heterogeneity in measurement approaches. Sources of this heterogeneity included the instrument used, sample size, and whether the instrument was self-report, informant-report, or clinician-report. Thoughtful consideration should be given when designing and interpreting results of parental BAP studies, as sample type, instrument, and parent type may all affect estimates. More work is needed to examine and improve consistency between studies, which would allow for improved synthesis across studies, improving our ability to evaluate the effects of parental BAP.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This study was funded by Autism Speaks grant 10052

References

- Adolphs R, Spezio ML, Parlier M, Piven J. Distinct face-processing strategies in parents of autistic children. *Current Biology*. 2008; 18(14):1090–1093. DOI: 10.1016/j.cub.2008.06.073 [PubMed: 18635351]
- Baron-Cohen S, Lombardo MV, Auyeung B, Ashwin E, Chakrabarti B, Knickmeyer R. Why are autism spectrum conditions more prevalent in males? *PLoS Biology*. 2011; 9(6):e1001081.doi: 10.1371/journal.pbio.1001081 [PubMed: 21695109]
- Baron-Cohen S, Wheelwright S, Skinner R, Martin J, Clubley E. The Autism-Spectrum Quotient (AQ): Evidence from Asperger Syndrome/High-Functioning Autism, Males and Females, Scientists and Mathematicians. *Journal of Autism and Developmental Disorders*. 2001; 31(1):5–17. <https://doi.org/10.1023/a:1005653411471>. [PubMed: 11439754]
- Bernier R, Gerds J, Munson J, Dawson G, Estes A. Evidence for broader autism phenotype characteristics in parents from multiple-incidence autism families. *Autism Research*. 2012; 5(1):13–20. DOI: 10.1002/aur.226 [PubMed: 21905246]
- Berthoz S, Lalanne C, Crane L, Hill EL. Investigating emotional impairments in adults with autism spectrum disorders and the broader autism phenotype. *Psychiatry Research*. 2013; 208(3):257–264. <https://doi.org/10.1016/j.psychres.2013.05.014>. [PubMed: 23747233]
- Bishop DVM, Maybery M, Maley A, Wong D, Hill W, Hallmayer J. Using self-report to identify the broad phenotype in parents of children with autistic spectrum disorders: a study using the Autism-Spectrum Quotient. *Journal of Child Psychology and Psychiatry*. 2004; 45(8):1431–1436. DOI: 10.1111/j.1469-7610.2004.00325.x [PubMed: 15482503]
- Bishop DVM, Maybery M, Wong D, Maley A, Hill W, Hallmayer J. Are phonological processing deficits part of the broad autism phenotype? *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*. 2004; 128B(1):54–60. DOI: 10.1002/ajmg.b.30039 [PubMed: 15211632]
- Bolte S, Poustka F. The recognition of facial affect in autistic and schizophrenic subjects and their first-degree relatives. *Psychological Medicine*. 2003; 33(5):907–915. [PubMed: 12877405]
- Bolton P, Macdonald H, Pickles A, Rios P, Goode S, Crowson M, ... Rutter M. A case-control family history study of autism. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 1994; 35(5):877–900.
- Bora E, Aydin A, Sarac T, Kadak MT, Kose S. Heterogeneity of subclinical autistic traits among parents of children with autism spectrum disorder: Identifying the broader autism phenotype with a data-driven method. *Autism Res*. 2017; 10(2):321–326. <https://doi.org/10.1002/aur.1661>. [PubMed: 27383033]
- Cholemker H, Medda J, Lempp T, Freitag CM. Classifying Autism Spectrum Disorders by ADI-R: Subtypes or Severity Gradient? *Journal of Autism and Developmental Disorders*. 2016; 46(7): 2327–2339. DOI: 10.1007/s10803-016-2760-2 [PubMed: 26956715]
- Constantino, JN. *Social Responsiveness Scale*. Los Angeles, CA: Western Psychological Services; 2002.
- Constantino JN. The quantitative nature of autistic social impairment. *Pediatric Research*. 2011; 69(5 Pt 2):55R–62R. DOI: 10.1203/PDR.0b013e318212ec6e
- Constantino JN, Abbacchi AM, Lavesser PD, Reed H, Givens L, Chiang L, et al. Developmental course of autistic social impairment in males. *Development and Psychopathology*. 2009; 21(1): 127–138. <https://doi.org/10.1017/S095457940900008X>. [PubMed: 19144226]
- Constantino, JN., Gruber, CP. *Social Responsiveness Scale. 2*. Los Angeles, CA: Western Psychological Services; 2012.
- Constantino JN, Todd RD. Autistic traits in the general population: a twin study. *Archives of General Psychiatry*. 2003; 60(5):524–530. DOI: 10.1001/archpsyc.60.5.524 [PubMed: 12742874]
- Constantino JN, Todd RD. Intergenerational transmission of subthreshold autistic traits in the general population. *Biological Psychiatry*. 2005; 57(6):655–660. <https://doi.org/10.1016/j.biopsych.2004.12.014>. [PubMed: 15780853]

- Coon H, Villalobos ME, Robison RJ, Camp NJ, Cannon DS, Allen-Brady K, et al. Genome-wide linkage using the Social Responsiveness Scale in Utah autism pedigrees. *Molecular Autism*. 2010; 1(1):8. <https://doi.org/10.1186/2040-2392-1-8>. [PubMed: 20678250]
- Cruz LP, Camargos-Junior W, Rocha FL. The broad autism phenotype in parents of individuals with autism: a systematic review of the literature. *Trends in Psychiatry and Psychotherapy*. 2013; 35(4): 252–263. DOI: 10.1590/2237-6089-2013-0019 [PubMed: 27000471]
- Davidson J, Goin-Kochel RP, Green-Snyder LA, Hundley RJ, Warren Z, Peters SU. Expression of the broad autism phenotype in simplex autism families from the Simons Simplex Collection. *Journal of Autism and Developmental Disorders*. 2014; 44(10):2392–2399. DOI: 10.1007/s10803-012-1492-1 [PubMed: 22382605]
- Dawson G, Estes A, Munson J, Schellenberg G, Bernier R, Abbott R. Quantitative assessment of autism symptom-related traits in probands and parents: Broader Phenotype Autism Symptom Scale. *Journal of Autism and Developmental Disorders*. 2007; 37(3):523–536. DOI: 10.1007/s10803-006-0182-2 [PubMed: 16868845]
- de Jonge M, Parr J, Rutter M, Wallace S, Kemner C, Bailey A, ... Pickles A. New interview and observation measures of the broader autism phenotype: group differentiation. *Journal of Autism and Developmental Disorders*. 2015; 45(4):893–901. DOI: 10.1007/s10803-014-2230-7 [PubMed: 25245786]
- De la Marche W, Noens I, Kuppens S, Spilt JL, Boets B, Steyaert J. Measuring quantitative autism traits in families: informant effect or intergenerational transmission? *European Child and Adolescent Psychiatry*. 2015; 24(4):385–395. DOI: 10.1007/s00787-014-0586-z [PubMed: 25086652]
- De Los Reyes A. Strategic objectives for improving understanding of informant discrepancies in developmental psychopathology research. *Development and Psychopathology*. 2013; 25(3):669–682. DOI: 10.1017/S0954579413000096 [PubMed: 23880384]
- Duvekot J, van der Ende J, Constantino JN, Verhulst FC, Greaves-Lord K. Symptoms of autism spectrum disorder and anxiety: shared familial transmission and cross-assortative mating. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 2016; 57(6):759–769. <https://doi.org/10.1111/jcpp.12508>.
- Fombonne E, Bolton P, Prior J, Jordan H, Rutter M. A family study of autism: cognitive patterns and levels in parents and siblings. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 1997; 38(6):667–683.
- Gaugler T, Klei L, Sanders SJ, Bodea CA, Goldberg AP, Lee AB, ... Buxbaum JD. Most genetic risk for autism resides with common variation. *Nature Genetics*. 2014; 46(8):881–885. DOI: 10.1038/ng.3039 [PubMed: 25038753]
- Gerdts J, Bernier R. The broader autism phenotype and its implications on the etiology and treatment of autism spectrum disorders. *Autism Research and Treatment*. 2011; 2011:545901.doi: 10.1155/2011/545901 [PubMed: 22937250]
- Gerdts J, Bernier R, Dawson G, Estes A. The broader autism phenotype in simplex and multiplex families. *Journal of Autism and Developmental Disorders*. 2013; 43(7):1597–1605. DOI: 10.1007/s10803-012-1706-6 [PubMed: 23117424]
- Ghaziuddin M. A family history study of Asperger syndrome. *Journal of Autism and Developmental Disorders*. 2005; 35(2):177–182. DOI: 10.1007/s10803-004-1996-4 [PubMed: 15909404]
- Gottesman II, Gould TD. The endophenotype concept in psychiatry: etymology and strategic intentions. *American Journal of Psychiatry*. 2003; 160(4):636–645. DOI: 10.1176/appi.ajp.160.4.636 [PubMed: 12668349]
- Gould TD, Gottesman II. Psychiatric endophenotypes and the development of valid animal models. *Genes, Brain, and Behavior*. 2006; 5(2):113–119. DOI: 10.1111/j.1601-183X.2005.00186.x
- Hasegawa C, Kikuchi M, Yoshimura Y, Hiraishi H, Munosue T, Nakatani H, ... Minabe Y. Broader autism phenotype in mothers predicts social responsiveness in young children with autism spectrum disorders. *Psychiatry and Clinical Neurosciences*. 2015; 69(3):136–144. DOI: 10.1111/pcn.12210 [PubMed: 24902617]

- Hurley RS, Losh M, Parlier M, Reznick JS, Piven J. The broad autism phenotype questionnaire. *Journal of Autism and Developmental Disorders*. 2007; 37(9):1679–1690. DOI: 10.1007/s10803-006-0299-3 [PubMed: 17146701]
- Ingersoll B, Hambrick DZ. The relationship between the broader autism phenotype, child severity, and stress and depression in parents of children with autism spectrum disorders. *Research in Autism Spectrum Disorders*. 2011; 5(1):337–344. <https://doi.org/10.1016/j.rasd.2010.04.017>.
- Ingersoll B, Hopwood CJ, Wainer A, Brent Donnellan M. A comparison of three self-report measures of the broader autism phenotype in a non-clinical sample. *Journal of Autism and Developmental Disorders*. 2011a; 41(12):1646–1657. <https://doi.org/10.1007/s10803-011-1192-2>. [PubMed: 21331821]
- Ingersoll B, Meyer K, Becker MW. Increased rates of depressed mood in mothers of children with ASD associated with the presence of the broader autism phenotype. *Autism Research*. 2011; 4(2): 143–148. DOI: 10.1002/aur.170 [PubMed: 21480539]
- Kanner L. Autistic Disturbances of Affective Contact. *Nervous Child*. 1943; 2(3):217–250.
- Klin A, Pauls D, Schultz R, Volkmar F. Three diagnostic approaches to Asperger syndrome: implications for research. *Journal of Autism and Developmental Disorders*. 2005; 35(2):221–234. DOI: 10.1007/s10803-004-2001-y [PubMed: 15909408]
- Klusek J, Losh M, Martin GE. Sex differences and within-family associations in the broad autism phenotype. *Autism*. 2014; 18(2):106–116. DOI: 10.1177/1362361312464529 [PubMed: 23188882]
- Lai MC, Lombardo MV, Chakrabarti B, Baron-Cohen S. Subgrouping the autism “spectrum”: reflections on DSM-5. *PLoS Biology*. 2013; 11(4):e1001544.doi: 10.1371/journal.pbio.1001544 [PubMed: 23630456]
- Lainhart JE, Ozonoff S, Coon H, Krasny L, Dinh E, Nice J, McMahon W. Autism, regression, and the broader autism phenotype. *American Journal of Medical Genetics*. 2002; 113(3):231–237. DOI: 10.1002/ajmg.10615 [PubMed: 12439889]
- Landa R, Folstein SE, Isaacs C. Spontaneous narrative-discourse performance of parents of autistic individuals. *Journal of Speech and Hearing Research*. 1991; 34(6):1339–1345. [PubMed: 1787716]
- Levin-Decanini T, Maltman N, Francis SM, Guter S, Anderson GM, Cook EH, Jacob S. Parental broader autism subphenotypes in ASD affected families: relationship to gender, child’s symptoms, SSRI treatment, and platelet serotonin. *Autism Res*. 2013; 6(6):621–630. DOI: 10.1002/aur.1322 [PubMed: 23956104]
- Liu XQ, Paterson AD, Szatmari P. Autism Genome Project Consortium. Genome-wide linkage analyses of quantitative and categorical autism subphenotypes. *Biological Psychiatry*. 2008; 64(7): 561–570. DOI: 10.1016/j.biopsych.2008.05.023 [PubMed: 18632090]
- Losh M, Adolphs R, Poe MD, Couture S, Penn D, Baranek GT, Piven J. Neuropsychological profile of autism and the broad autism phenotype. *Archives of General Psychiatry*. 2009; 66(5):518–526. DOI: 10.1001/archgenpsychiatry.2009.34 [PubMed: 19414711]
- Losh M, Childress D, Lam K, Piven J. Defining key features of the broad autism phenotype: a comparison across parents of multiple- and single-incidence autism families. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*. 2008; 147B(4):424–433. DOI: 10.1002/ajmg.b.30612
- Losh M, Piven J. Social-cognition and the broad autism phenotype: identifying genetically meaningful phenotypes. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 2007; 48(1):105–112. DOI: 10.1111/j.1469-7610.2006.01594.x
- Lyall K, Constantino JN, Weisskopf MG, Roberts AL, Ascherio A, Santangelo SL. Parental social responsiveness and risk of autism spectrum disorder in offspring. *JAMA Psychiatry*. 2014; 71(8): 936–942. DOI: 10.1001/jamapsychiatry.2014.476 [PubMed: 25100167]
- Maxwell CR, Parish-Morris J, Hsin O, Bush JC, Schultz RT. The broad autism phenotype predicts child functioning in autism spectrum disorders. *Journal of Neurodevelopmental Disorders*. 2013; 5(1):25.doi: 10.1186/1866-1955-5-25 [PubMed: 24053506]

- Mohammadi MR, Zarafshan H, Ghasempour S. Broader autism phenotype in Iranian parents of children with autism spectrum disorders vs. normal children. *Iranian Journal of Psychiatry*. 2012; 7(4):157–163. [PubMed: 23408558]
- Page J, Constantino JN, Zambrana K, Martin E, Tunc I, Zhang Y, ... Messinger D. Quantitative autistic trait measurements index background genetic risk for ASD in Hispanic families. *Molecular Autism*. 2016; 7(1):39.doi: 10.1186/s13229-016-0100-1 [PubMed: 27606047]
- Parr JR, De Jonge MV, Wallace S, Pickles A, Rutter ML, Le Couteur AS, ... Bailey AJ. New Interview and Observation Measures of the Broader Autism Phenotype: Description of Strategy and Reliability Findings for the Interview Measures. *Autism Research*. 2015; 8(5):522–533. DOI: 10.1002/aur.1466 [PubMed: 25959701]
- Parr JR, Gray L, Wigham S, McConachie H, Le Couteur A. Measuring the relationship between the parental Broader Autism Phenotype, parent-child interaction, and children's progress following parent mediated intervention. *Research in Autism Spectrum Disorders*. 2015; 20:24–30. DOI: 10.1016/j.rasd.2015.07.006
- Pickles A, Parr JR, Rutter ML, De Jonge MV, Wallace S, Le Couteur AS, et al. New interview and observation measures of the broader autism phenotype: impressions of interviewee measure. *Journal of Autism and Developmental Disorders*. 2013; 43(9):2082–2089. <https://doi.org/10.1007/s10803-013-1810-2>. [PubMed: 23547019]
- Pickles A, Starr E, Kazak S, Bolton P, Papanikolaou K, Bailey A, et al. Variable expression of the autism broader phenotype: findings from extended pedigrees. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 2000; 41(4):491–502.
- Piven J, Palmer P, Jacobi D, Childress D, Arndt S. Broader autism phenotype: evidence from a family history study of multiple-incidence autism families. *American Journal of Psychiatry*. 1997a; 154(2):185–190. <https://doi.org/10.1176/ajp.154.2.185>. [PubMed: 9016266]
- Piven J, Palmer P, Landa R, Santangelo S, Jacobi D, Childress D. Personality and language characteristics in parents from multiple-incidence autism families. *American Journal of Medical Genetics*. 1997b; 74(4):398–411. [PubMed: 9259376]
- Piven J, Wzorek M, Landa R, Lainhart J, Bolton P, Chase GA, Folstein S. Personality characteristics of the parents of autistic individuals. *Psychological Medicine*. 1994; 24(3):783–795. [PubMed: 7991760]
- Randazzo KV, Landsverk J, Ganger W. Three informants' reports of child behavior: parents, teachers, and foster parents. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2003; 42(11):1343–1350. DOI: 10.1097/01.chi.0000085753.71002.da [PubMed: 14566172]
- Robinson EB, Koenen KC, McCormick MC, Munir K, Hallett V, Happe F, ... Ronald A. Evidence that autistic traits show the same etiology in the general population and at the quantitative extremes (5%, 2.5%, and 1%). *Archives of General Psychiatry*. 2011; 68(11):1113–1121. DOI: 10.1001/archgenpsychiatry.2011.119 [PubMed: 22065527]
- Rothman, KJ., Greenland, S., Lash, TL. *Modern Epidemiology*. 3. Philadelphia, PA: Lippincott, Williams & Wilkins; 2008.
- Rubenstein E, Edmondson Pretzel R, Windham GC, Schieve LA, Wiggins LD, DiGuseppi C, ... Daniels J. The Broader Autism Phenotype in Mothers is Associated with Increased Discordance Between Maternal-Reported and Clinician-Observed Instruments that Measure Child Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*. 2017; 47(10):3253–3266. DOI: 10.1007/s10803-017-3248-4 [PubMed: 28748335]
- Rubenstein, E., Wiggins, LD., Schieve, LA., Bradley, C., DiGuseppi, C., Moody, E., et al. Associations between parental broader autism phenotype and child autism spectrum disorder phenotype in the Study to Explore Early Development. *Autism*. 2018. <https://doi.org/10.1177/1362361317753563>
- Ruser TF, Arin D, Dowd M, Putnam S, Winklosky B, Rosen-Sheidley B, et al. Communicative competence in parents of children with autism and parents of children with specific language impairment. *Journal of Autism and Developmental Disorders*. 2007; 37(7):1323–1336. <https://doi.org/10.1007/s10803-006-0274-z>. [PubMed: 17180460]
- Ruta L, Mazzone D, Mazzone L, Wheelwright S, Baron-Cohen S. The Autism-Spectrum Quotient–Italian version: a cross-cultural confirmation of the broader autism phenotype. *Journal of Autism*

- and Developmental Disorders. 2012; 42(4):625–633. <https://doi.org/10.1007/s10803-011-1290-1>. [PubMed: 21626054]
- Ruzich E, Allison C, Smith P, Watson P, Auyeung B, Ring H, Baron-Cohen S. Measuring autistic traits in the general population: a systematic review of the Autism-Spectrum Quotient (AQ) in a nonclinical population sample of 6,900 typical adult males and females. *Molecular Autism*. 2015; 6:2.doi: 10.1186/2040-2392-6-2 [PubMed: 25874074]
- Sasson NJ, Faso DJ, Parlier M, Daniels JL, Piven J. When father doesn't know best: selective disagreement between self-report and informant report of the broad autism phenotype in parents of a child with autism. *Autism Research*. 2014; 7(6):731–739. DOI: 10.1002/aur.1425 [PubMed: 25339495]
- Sasson NJ, Lam KS, Childress D, Parlier M, Daniels JL, Piven J. The broad autism phenotype questionnaire: prevalence and diagnostic classification. *Autism Research*. 2013; 6(2):134–143. DOI: 10.1002/aur.1272 [PubMed: 23427091]
- Sasson NJ, Lam KS, Parlier M, Daniels JL, Piven J. Autism and the broad autism phenotype: familial patterns and intergenerational transmission. *Journal of Neurodevelopmental Disorders*. 2013; 5(1):11.doi: 10.1186/1866-1955-5-11 [PubMed: 23639131]
- Schwichtenberg AJ, Young GS, Sigman M, Hutman T, Ozonoff S. Can family affectedness inform infant sibling outcomes of autism spectrum disorders? *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 2010; 51(9):1021–1030. DOI: 10.1111/j.1469-7610.2010.02267.x
- Seidman I, Yirmiya N, Milshtein S, Ebstein RP, Levi S. The Broad Autism Phenotype Questionnaire: mothers versus fathers of children with an autism spectrum disorder. *Journal of Autism and Developmental Disorders*. 2012; 42(5):837–846. DOI: 10.1007/s10803-011-1315-9 [PubMed: 21706249]
- Shi LJ, Ou JJ, Gong JB, Wang SH, Zhou YY, Zhu FR, ... Luo XR. Broad autism phenotype features of Chinese parents with autistic children and their associations with severity of social impairment in probands. *BMC Psychiatry*. 2015; 15:168.doi: 10.1186/s12888-015-0568-9 [PubMed: 26202327]
- Smith CJ, Lang CM, Kryzak L, Reichenberg A, Hollander E, Silverman JM. Familial associations of intense preoccupations, an empirical factor of the restricted, repetitive behaviors and interests domain of autism. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 2009; 50(8):982–990. DOI: 10.1111/j.1469-7610.2009.02060.x
- Starr E, Berument SK, Pickles A, Tomlins M, Bailey A, Papanikolaou K, Rutter M. A family genetic study of autism associated with profound mental retardation. *Journal of Autism and Developmental Disorders*. 2001; 31(1):89–96. [PubMed: 11439758]
- Sucksmith E, Allison C, Baron-Cohen S, Chakrabarti B, Hoekstra RA. Empathy and emotion recognition in people with autism, first-degree relatives, and controls. *Neuropsychologia*. 2013; 51(1):98–105. DOI: 10.1016/j.neuropsychologia.2012.11.013 [PubMed: 23174401]
- Sucksmith E, Roth I, Hoekstra RA. Autistic traits below the clinical threshold: re-examining the broader autism phenotype in the 21st century. *Neuropsychology Review*. 2011; 21(4):360–389. DOI: 10.1007/s11065-011-9183-9 [PubMed: 21989834]
- Szatmari P, MacLean JE, Jones MB, Bryson SE, Zwaigenbaum L, Bartolucci G, ... Tuff L. The familial aggregation of the lesser variant in biological and nonbiological relatives of PDD probands: a family history study. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 2000; 41(5):579–586.
- Taylor LJ, Maybery MT, Wray J, Ravine D, Hunt A, Whitehouse AJ. Brief report: do the nature of communication impairments in autism spectrum disorders relate to the broader autism phenotype in parents? *Journal of Autism and Developmental Disorders*. 2013; 43(12):2984–2989. DOI: 10.1007/s10803-013-1838-3 [PubMed: 23619954]
- Uljarevic M, Evans DW, Alvares GA, Whitehouse AJ. Short report: relationship between restricted and repetitive behaviours in children with autism spectrum disorder and their parents. *Mol Autism*. 2016; 7:29.doi: 10.1186/s13229-016-0091-y [PubMed: 27303619]
- Virkud YV, Todd RD, Abbacchi AM, Zhang Y, Constantino JN. Familial aggregation of quantitative autistic traits in multiplex versus simplex autism. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*. 2009; 150B(3):328–334. DOI: 10.1002/ajmg.b.30810

- Wheelwright S, Auyeung B, Allison C, Baron-Cohen S. Defining the broader, medium and narrow autism phenotype among parents using the Autism Spectrum Quotient (AQ). *Mol Autism*. 2010; 1(1):10. <https://doi.org/10.1186/2040-2392-1-10>. [PubMed: 20678260]
- Whitehouse AJ, Barry JG, Bishop DV. The broader language phenotype of autism: a comparison with specific language impairment. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 2007; 48(8):822–830. DOI: 10.1111/j.1469-7610.2007.01765.x
- Whitehouse AJ, Coon H, Miller J, Salisbury B, Bishop DV. Narrowing the broader autism phenotype: a study using the Communication Checklist-Adult Version (CC-A). *Autism*. 2010; 14(6):559–574. <https://doi.org/10.1177/1362361310382107>. [PubMed: 20923891]
- Wolff S, Narayan S, Moyes B. Personality characteristics of parents of autistic children: a controlled study. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 1988; 29(2):143–153.
- Wong D, Maybery M, Bishop DV, Maley A, Hallmayer J. Profiles of executive function in parents and siblings of individuals with autism spectrum disorders. *Genes, Brain, and Behavior*. 2006; 5(8): 561–576. DOI: 10.1111/j.1601-183X.2005.00199.x
- Wood CL, Warnell F, Johnson M, Hames A, Pearce MS, McConachie H, Parr JR. Evidence for ASD recurrence rates and reproductive stoppage from large UK ASD research family databases. *Autism Research*. 2015; 8(1):73–81. DOI: 10.1002/aur.1414 [PubMed: 25273900]
- Yucel GH, Belger A, Bizzell J, Parlier M, Adolphs R, Piven J. Abnormal Neural Activation to Faces in the Parents of Children with Autism. *Cerebral Cortex*. 2015; 25(12):4653–4666. <https://doi.org/10.1093/cercor/bhu147>. [PubMed: 25056573]

Figure 1.

Review schema

^aSearch criteria excluded reviews, case reports, commentaries, editorials, and letters, article not in English, and studies conducted on animals.

^bOther resources included author identified papers and references from other review articles.

Figure 2.

Scatter plot of percentage of parents of children with autism spectrum disorder with the broader autism phenotype, by instrument, sample size, and parent type

AQ Autism Quotient, BAPQ Broader Autism Phenotype Questionnaire, BPASS Broader Phenotype Autism Screening Scale, FHI, Family History Interview (includes Informant, self-report, and impression of interviewer), MPAS-R Modified Personality Assessment-Revised, SRS-A Social Responsiveness Scale Adult

Graph does not include Communication Checklist-Adult and Pragmatic Rating Scale due to too few studies

Table 1

Descriptions of instruments that measure the broader autism phenotype in adults

Measure	Author, year	Description	Cut off	Psychometric properties
Autism Spectrum Quotient (AQ)	(Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001)	-50 question self-administered instrument -Five domains include attention switching, social skill, attention to detail, communication, and imagination -Intended for individuals with normal/high IQ (Baron-Cohen, et al., 2001)	-1 to 2 standard deviations above mean (Wheelwright, Auyeung, Allison, & Baron-Cohen, 2010)	-Test retest correlation=0.7 -Internal consistency in domains range from 0.63 to 0.77 (Baron-Cohen, et al., 2001) -Cronbach's alpha internal consistency coefficient of 0.72 (Ingersoll, Hopwood, Wainer, & Brent Donnellan, 2011a) -Cronbach's alpha internal consistency coefficient of 0.95 (Constantino & Todd, 2005), 0.95 (Ingersoll, et al., 2011a)
Social Responsiveness Scale- Adult (SRS-A)	(Constantino & Todd, 2005)	-65-item likert scale questionnaire -A friend, spouse, or relative completes on the parent. -The questionnaire takes 15–20 minutes to complete -To measure five distinct domains to define ASD and ASD-like traits; domains are social awareness, social cognition, social communication, social motivation, and autistic mannerisms -Not associated with IQ level, age (Constantino, 2002; Constantino, et al., 2009)	- A score greater than or equal to an adjusted T score of 60 (Constantino, 2002) -Participants in the top 20% of scores in a population based sample (Lyall, et al., 2014)	-Cronbach's alpha internal consistency coefficient of 0.95 (Constantino & Todd, 2005), 0.95 (Ingersoll, et al., 2011a)
Broader Autism Phenotype Questionnaire (BAPQ)	(Hurley, et al., 2007)	-Items derived from previous direct assessments of autistic traits (Modified Personality Assessment Schedule Revised, ASR, PRS) -Creates scales corresponding to three primary components: aloofness, rigid personality, pragmatic language problems -Informant and self-report versions -36 total items across three scales, scoring ranges from 1–6 (6 having more ASD traits)(Hurley, et al., 2007)	-Sex specific BAP cutoffs defined by ROC curves that maximize sensitivity and specificity Males: 3.55 self 3.65 informant Females: 3.17 self 3.46 informant (Sasson, et al., 2013a) -Scores above 2 indicate BAP (Dawson, et al., 2007)	-Sensitivity and specificity > 0.7 -Cronbach's alpha =0.96 -Subscales significantly correlated with one another (Hurley, et al., 2007)
Broader Phenotype Autism Symptom Scale (BPASS)	(Dawson, et al., 2007)	-Parent interview by trained professional plus direct observation -Four domains: social motivation, social expressiveness, communication, and flexibility -4 or 5 point scales ranging from highly atypical to above average -IQ not consistently associated with BPASS score(Dawson, et al., 2007)	-Scores above 2 indicate BAP (Dawson, et al., 2007)	-Inter-rater reliability ranged from 0.71 to 0.95 depending on domain -Cronbach's alpha ranged from 0.6 to 0.91 across domains
Family History Interview	(Bolton, et al., 1994), (Piven, Palmer, Jacobi, Childress, & Arndt, 1997a), (de Jonge, et al., 2015; Parr, et al., 2015a; Pickles, et al., 2013)	-Three measures: informant interview (FHI-I), self-report (FHI-S), and impression of interviewee (IOI) -Items focused on qualitatively similar social/communicative deficits and other behaviors reported in the ASD and developmental disability -77 Items, 30 to 60 minutes in length -Rating from 0-not reaching scoring threshold to 2-associated impairment -Factor analysis suggests two factor solution: social communication and rigidity, reading and spelling impairments (Parr, et al., 2015a)	-Clinical significance determined by summing results with scoring algorithm, if score 1 then evidence of BAP	-Kappa >0.6 -Cronbach alpha for informant report=0.87, self report=0.78 --0.72 correlation between FHI-I and FHI-S, 0.57 between FHI-S and IOI, 0.45 between FHI-I and IOI (de Jonge, et al., 2015)
Modified Personality Assessment Schedule	(Piven, et al., 1997a; Piven, et al., 1994)	-Trained professional conducted semi- structured interview of ASD traits -Interview and informant report	-Characteristics rated 2=present, 1=unknown, 0=absent (Losh, et al., 2009a)	-71% sensitivity, 90% specificity (Piven, et al., 1997b)

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Measure	Author, year	Description	Cut off	Psychometric properties
		-Focuses on six traits (aloof, anxious, hypersensitive, overly conscientious, rigid, and untactful)(Losh, et al., 2008)	-Algorithm of sum of traits = BAP (Piven, et al., 1997b)	- Reliability: aloof 0.860, untactful 0.749, rigid 0.823, and overly conscientious: 0.830 (Klusek, et al., 2014).

Table 2

Summary statistics for papers identified in the systematic review

	Studies N=41	
	N	%
Parent *		
Mother alone	25	61.0
Father alone	24	58.5
Both	27	65.9
Report type *		
Clinician	2	4.9
Informant	21	51.2
Interview	10	24.4
Multi-modal	22	53.7
Self	25	61.0
Instrument *		
AQ	10	24.4
BAPQ	10	24.4
BPASS	2	4.9
CC-A	1	2.4
FHI	20	48.8
MPAS-R	4	9.8
PRS	4	9.8
SRS-A	5	12.2
Country		
Australia	5	12.2
United States	20	48.8
United Kingdom	4	9.8
Other	9	22.0
Sample type		
Community	32	78.0
Clinic	8	19.5
Internet	1	2.4
Sample size		
Mean, SD	359.6	590.8

Categories are not mutually exclusive

Multi-modal indicates more than one data collection method

AQ Autism Quotient, BAPQ Broader Autism Phenotype Questionnaire, BPASS Broader Phenotype Autism Screening Scale, FHI Family History Interview, FHI-S Family History Interview Self, IOI Impression of Interviewer, FHI-I Family History Interview-Informant, MPAS-R Modified Personality Assessment-Revised, SRS-A Social Responsiveness Scale Adult, CC-A Communication Checklist-Adult

Studies that present percentages of parents of children with autism spectrum disorder who have the broader autism phenotype

Table 3

Author	Instrument (BAP Domain) ^a	Sample type ^b (Country)	Report type	Parent	N	Child ASD status/domain	% of parents with BAP
Fombonne et al. (1997)	FHI	Clinic (UK)	Interview	F/M	160	ASD	10.0
Szatmari et al. (2000)	FHI (1 domain)	Community (Canada)	Interview	F	681	ASD	28.3
	FHI (2 domain)					ASD	9.5
	FHI (1 domain)					ASD	16.7
	FHI (2 domain)					ASD	4.0
	FHI (1 domain)					ASD	22.5
	FHI (2 domain)					ASD	10.4
	FHI (1 domain)					ASD SX	19.0
	FHI (2 domain)					ASD SX	5.3
	FHI (1 domain)					ASD MX	26.4
	FHI (2 domain)					ASD MX	8.3
Pickles et al. (2000)	FHI (1 domain)	Clinic (UK)	Informant	F/M	337	Non bio relative	6.8
	FHI (2 domain)					Non bio relative	2.4
	FHI					ASD	12.1
	FHI					DS	9.8
	FHI					ASD	15.0
Starr et al. (2001)	MPAS-R, PRS	Clinic (UK)	Interview	F/M	86	ASD	27.8
						ASD w regression	32.9
Lainhart et al. (2002)	AQ	Community (USA)	Clinician	F/M	18	ASD w no regression	36.9
						ASD	13.5
						TD	15.4
						ASD	3.5
						TD	21.3
Bishop et al. (2004a)	AQ	Community (AUS)	Self	F	52	ASD	3.4
Bishop et al. (2004b)	AQ	Community (AUS)	Self	F/M	114	ASD	21.0
						ASD	3.0
Klin et al. (2005)*	FHI	Community (USA)	Interview	F	-	ASD	12.0
						ASD	29.0
Ghaziuddin et al. (2005)	FHI	Community (USA)	Interview	F/M	220	ASD	58
						Asperger's	29.0

Author	Instrument (BAP Domain) ^a	Sample type ^b (Country)	Report type	Parent	N	Child ASD status/domain	% of parents with BAP
Dawson et al. (2007)	BPASS (Expressiveness) (Communication) (Expressiveness) (Communication) FHI (1 BAP domain) (/ 2 domain)	Community (USA/Canada)	Multi-modal	F/M	39	HFA	20.5
				F	172	ASD	16.0
				F	172	ASD	13.5
				M	151	ASD	6.0
				M	151	ASD	5.0
			Interview	F/M	299	ASD	50.3
					299	ASD	11.4
Hurley et al. (2007)	BAPQ	Community (USA)	Multi-modal	F	35	ASD	40.0
				M	43	ASD	9.3
				F/M	86	ASD	31.4
			Self	F/M	86	ASD	25.0
			Informant	F/M	86	ASD	25.0
Losh et al. (2007)	MPAS-R, PRS, (2 domain)	Community (USA)	Multi-modal	F/M	48	ASD	50.0
Ruser et al. (2007)	PRS	Community (USA)	Clinician	F/M	47	ASD	15.0
Whitehouse et al. (2007)	AQ	Community (AUS)	Self	F	10	ASD	10.0
				M	20	ASD	25.0
Losh et al. (2008)	MPAS-R, PRS (2 domain)	Community (USA)	Multi-modal	F/M	78	SX ASD	33.0
				F/M	48	MX ASD	56.0
				F/M	60	DS control	10.0
Losh et al. (2009b)	MPAS-R (Social)	Community (USA)	Multi-modal	F/M	83	ASD	26.5
Whitehouse et al. (2010)	CC-A	Community (AUS)	Informant	F/M	238	ASD	25.6
				F/M	187	TD	16.0
Wheelwright et al. (2010)	AQ	Community (UK)	Self	F	571	ASD	33.0
				F	349	TD	22.0
				M	1429	ASD	23.0
				M	658	TD	9.0
Coon et al. ^b (2010)	SRS-A	Community (USA)	Informant	F/M	518	ASD	12.1
Ingersoll et al. (2011)	AQ	On-line survey (USA)	Self	F/M	149	ASD	10.0
Ruta et al. (2012)	AQ	Clinic (Italy)	Self	F	115	ASD	43.5

Author	Instrument (BAP Domain) ^a	Sample type ^b (Country)	Report type	Parent	N	Child ASD status/domain	% of parents with BAP
Seidman et al. (2012)	BAPQ	Community (Israel)	Multi-modal	F	150	TD	20
				M	130	ASD	26.2
				M	150	TD	11.3
				F	38	ASD	2.6
				F	38	ASD	10.5
				F	38	ASD	7.9
Mohammadi et al. (2012)	AQ	Clinic (Iran)	Informant	M	38	ASD	13.1
				M	38	ASD	21.0
				M	38	ASD	15.8
				F	96	ASD	50.0
				F	96	TD	11.0
				M	96	ASD	37.0
Levin-Decanini et al. (2013)	BAPQ	Community (USA)	Self	M	96	TD	11.8
				F	115	ASD w no SSRI use	17.4
				F	4	ASD w SSRI use	20.0
Taylor et al. (2013)	AQ	Community (AUS)	Self	M	136	ASD w no SSRI use	11.8
				M	19	ASD w SSRI use	36.8
				F	82	ASD	26.8
Berthoz et al. (2013)	AQ	Community (France)	Self	M	82	ASD	25.6
				F/M	87	ASD	13.8
Maxwell et al. (2013)	BAPQ	Community (USA)	Multi-modal	F/M	47	TD	8.2
				F	245	ASD	21.0
				F	129	TD	7.0
Sasson et al. (2013a)	BAPQ	Community (USA)	Multi-modal	M	245	ASD	10.0
				M	129	TD	1.0
				F/M	490	ASD	26.0
				F/M	258	TD	8.0
				F	359	ASD	19.0
				F	490	TD	8.9
				M	352	ASD	23.2
				M	491	TD	8.1

Author	Instrument (BAP Domain) ^a	Sample type ^b (Country)	Report type	Parent	N	Child ASD status/domain	% of parents with BAP
Sasson et al. (2013b)	BAPQ	Community (USA)	Multi-modal	F/M	711	ASD	36.0
Gerdts et al. (2013)	BPASS (social domain)	Community (USA)	Multi-modal	F/M	981	TD	14.1
				F	71	MX ASD	66.0
				F	40	SX ASD	33.0
				M	84	MX ASD	44.0
				M	41	SX ASD	32.0
Sasson et al. (2014)	BAPQ	Community (USA)	Informant	F	222	ASD	17.6
			Self	F	222	ASD	9.5
			Informant	M	222	ASD	19.8
			Self	M	222	ASD	20.3
Davidson et al. (2014)	BAPQ	Community (USA)	Multi-modal	F	1582	ASD	14.5
				M	1596	ASD	8.5
				F/M	3178	ASD	11.5
	SRS-A		Informant	F	1647	ASD	7.3
				M	1652	ASD	5.3
				F/M	3299	ASD	6.3
Lyall et al. (2014)	SRS-A	Community (USA)	Informant	F/M	2365	ASD	27.5
				F/M	482	TD	14.7
				F	1372	ASD	32.6
				F	242	TD	18.1
				M	993	ASD	22.5
				M	240	TD	20.0
Shi et al. (2015)	BAPQ	Community (China)	Multi-modal	F	299	ASD	13.0
			Self	F	299	ASD	9.0
			Informant	F	299	ASD	11.0
			Multi-modal	F	299	TD	2.9
			Self	F	299	TD	3.6
			Informant	F	299	TD	4.7
			Multi-modal	M	274	ASD	30.8
			Self	M	274	ASD	29.1
			Informant	M	274	ASD	21.4

Author	Instrument (BAP Domain) ^a	Sample type ^b (Country)	Report type	Parent	N	Child ASD status/domain	% of parents with BAP
de Jonge et al. (2015)	FHI-I FHI-S IOI FHI-I FHI-S IOI FHI-I FHI-S IOI	Community (NL)	Multi-modal	M	274	TD	20.8
			Self	M	274	TD	17.5
			Informant	M	274	TD	10.2
			Informant	F	26	MX ASD	80.0
			Interview	F	26	MX ASD	73.0
			Multi-modal	F	26	MX ASD	55.0
			Informant	F	29	DS	7.0
			Self	F	29	DS	28.0
			Multi-modal	F	29	DS	28.0
			Informant	M	27	MX ASD	48.0
Duvekot et al. (2016)	SRS-A	Clinic (NL)	Self	M	27	MX ASD	52.0
			Multi-modal	M	27	MX ASD	52.0
			Informant	M	30	DS	6.0
			Self	M	30	DS	3.0
			Multi-modal	M	30	DS	3.0
			Self	F	224	ASD	37.4
			Informant	F	224	ASD	38.4
			Self	M	182	ASD	33.7
			Informant	M	182	ASD	29.0
			Multi-modal	F	20	ASD	40.0
Yucef et al. (2015)	BAPQ	Clinic (USA)	Multi-modal	M	20	ASD	35.0
				F/M	40	ASD	37.5
			Interview	M	18	ASD	35.7
			Informant	F/M	140	ASD	15.0
				F/M	125	TD	4.0
			Self	F	314	ASD	25.2
				F	69	TD	8.1
				M	359	ASD	17.8
				M	77	TD	5.8
				F/M	673	ASD	21.5
Parr et al. (2015b)	FHI-S	Community (UK)					
Page et al. (2016)	SRS-A	Community (USA)					
Bora et al. (2017)	AQ	Community (Turkey)					

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Some studies used specific instrument domains or number of domains to measure BAP

Clinic sampling is study recruitment through convenience sampling or referral from service providers of children with developmental disabilities, community sampling is recruitment through other population based resources (e.g. online surveys, mailers, registries)

Includes pedigrees

DS Down Syndrome

MX Multiplex, SX Simplex, TD typically developing, F Father, M Mother, F/M Either parent AQ Autism Quotient, BAPQ Broader Autism Phenotype Questionnaire, BPASS Broader Phenotype Autism Screening Scale, FHI Family History Interview, FHI-S Family History Interview Self, IOI Impression of Interviewer, FHI-I Family History Interview-Informant, MPAS-R Modified Personality Assessment-Revised, SRS-A Social Responsiveness Scale Adult, CC-A Communication Checklist-Adult Clinic samples are convenience samples hospitals and other medical centers

Community samples include recruiting through ASD registries, schools, community organizations

Multi-modal indicates more than one data