Improving autism detection: The role of practitioner reported influences and a combined parent-clinician informant screening instrument

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Keywords
Autism spectrum disorder; autistic disorder; asperger syndrome, pervasive developmental disorder – not otherwise specified; ASD; ASD assessment; ASD diagnosis; ASD screening; Autistic Behavioural Indicators Instrument (ABII); Autistic Behavioural Indicators Instrument – Combined (ABII-C); Autistic Behavioural Indicators Instrument – Parent Questionnaire (ABII - PQ); clinician-observation; diagnostic challenges; diagnostic gap; parent-report; parent questionnaire.
Abstract

The accuracy of screening instruments in detecting children displaying symptomatic profiles of autism spectrum disorder (ASD) needs improvement (Zwaigenbaum et al., 2015b). The purpose of ASD screening is to initiate earlier evidence-based intervention. Currently, in Australia, access to government supported intervention is available only to those children who have a confirmed ASD diagnosis. Thus, an additional purpose of screening is to optimise the timing of referral for diagnostic evaluation. Although diagnostic evaluation can achieve a reliable ASD diagnosis between two to three years of age, diagnosis occurs in most children after the age of four years (Centres for Disease Control and Prevention [CDC], 2014). This lapse of time between when children with ASD can be identified and when they are being diagnosed suggests there is a diagnostic gap (Bent, Barbaro & Dissanyake, 2015; Shattuck et al., 2009). A diagnostic gap may impede the implied benefits of ASD screening. Therefore, attempts to improve the accuracy of ASD screening instruments require parallel attempts to concurrently identify the factors that may impact the length of a diagnostic gap.

This program of research had two aims: First, to examine the assessment and diagnostic practices and challenges that may influence the timing of ASD diagnosis in Australia; and second, to adapt a single informant ASD screening instrument into a combined parent-clinician informant screening instrument. Combining parent and clinician ratings to inform ASD evaluations has been recommended (Volkmar et al., 2014). Yet, ASD screening instruments rely on single informant data which could increase misclassification risk. It has already been shown that parents and clinicians rate symptoms across core ASD domains differently (Lemler, 2012). Discrepancies between informant sources could lead to different screening outcomes for the same
child. A combined parent-clinician screening instrument could reduce this risk and improve ASD detection.

Study 1 was a national survey of Australian practitioners involved in the diagnostic evaluation of young children for ASD (psychologists, $n = 54$; paediatricians, $n = 42$; psychiatrists, $n = 8$). This study aimed to investigate practitioner perceptions of ASD assessment and diagnosis to identify the factors that may influence the timing of ASD diagnosis and contribute to a diagnostic gap. Less than five percent of all practitioners ($n = 104$) reported recommending an ASD diagnosis in children under two years of age, with nearly two thirds of practitioners most likely making a diagnostic recommendation in children after the age of three years. Over 60% of practitioners reported a combination of factors that are likely having an additive contribution on the diagnostic gap including: an inability to see children early enough because of initial assessment waiting lists (75%), perceived diagnostic difficulty in younger children (79%), implementation of a watch and wait approach to diagnosis (92%), and perceived limitations of diagnostic aids, including assessment measures (63%) and the diagnostic criteria (69%). Results suggest a number of factors may influence the timing of ASD diagnosis for Australian children and could contribute to a diagnostic gap.

Study 2 sought to further investigate the psychometric properties of a single informant clinician-administered ASD screening instrument, the Autistic Behavioural Indicators Instrument (ABII; Ward & Gilmore, 2010). The ABII was administered to children with a best-estimate clinical Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR) autism spectrum disorder (ASD) diagnosis, aged between two and six years ($n = 51$, $M_{\text{child age}} = 3.6$ years, $SD = 1.01$). There was significant moderate agreement for the
classification of ASD between the ABII and the diagnostic criteria for ASD, as outlined in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5), and significant fair agreement between the ABII and the established Autism Diagnostic Observation Schedule (ADOS) and Childhood Autism Rating Scale – Second Edition, Standard Version (CARS2-ST). True positive diagnostic classifications were similar across the ABII ($n = 47, 92.2\%$) and ADOS ($n = 45, 88.2\%$), and significantly higher than the CARS2-ST ($n = 30, 58.8\%$). The ABII total scale score was strongly positively correlated with both the ADOS and CARS2-ST total scores. Results suggest the ABII’s test characteristics are comparable to those of established measures and the intercorrelations between selected measures support its convergent validity.

Study 3 describes the adaptation of the clinician-administered ABII as a parent-report screening instrument, the Autistic Behavioural Indicators Instrument – Parent Questionnaire (ABII-PQ). The ABII-PQ was trialled in a sample of parents of children, aged between 12 months and six years, with a best-estimate clinical DSM-IV-TR ASD diagnosis ($n = 65, M_{\text{child age}} = 4.03, SD = 1.13$) or typical development (TD, $n = 37, M_{\text{child age}} = 2.09, SD = 1.13$). Internal consistency was high, $\alpha = .92$. Receiver operator curves (ROC) analysis identified the optimal ABII-PQ cut-off score which yielded high sensitivity (.97) and specificity (.95). ABII-PQ scores discriminated children with ASD from children with TD. Correct classification rates were high for the ASD (92\%) and TD (95\%) samples. Classification accuracy was high for children across the autism spectrum (autistic disorder: $n = 35, 100\%$; asperger’s syndrome, $n = 14, 93\%$; pervasive developmental disorder – not otherwise specified: $n = 14, 93\%$). The ABII-PQ shows promise as a parent questionnaire version of the ABII.
Study 4 combined scores from the clinician-administered ABII and its parent-report equivalent, the ABII-PQ, to examine whether a combination score improved ASD classification. ASD classification accuracy was evaluated for the two screening instruments and three combination scores, in a sample of children with a best-estimate clinical DSM-IV-TR ASD diagnosis, aged between two and six years ($n = 51$, $M_{\text{child age}} = 3.6$ years, $SD = 1.01$). Results showed the ABII and ABII-PQ were significantly associated, $r = .62$, $p = .01$, and did not differ significantly on final correct ASD classification, with both instruments classifying 92.2% of children. However, final agreement on ASD classification between instruments was poor, $\kappa = .19$, $p = .184$. One method of combining scores from the ABII and ABII-PQ significantly increased classification, correctly classifying 100% of children with ASD. Results show single informant screening instruments could produce a different screening outcome, potentially increasing misclassification risk. Combining parent and clinician rated instruments could significantly improve ASD classification.

Study 5 conducted a preliminary evaluation of the combined parent-clinician informant ASD screening instrument, the Autistic Behavioural Indicators Instrument – Combined (ABII-C). The ABII-C was trialled in a sample of siblings of children with a best-estimate clinical DSM-IV-TR ASD diagnosis, aged between 20 and 46 months ($n = 28$, $M_{\text{child age}} = 27$ months, $SD = .56$). All children were screened using the ABII-C, along with established instruments including: Early Screening of Autistic Traits Questionnaire (ESAT), Modified Checklist for Autism in Toddlers (M-CHAT), Brief Infant Toddler Social Emotional Assessment (BITSEA), CARS2-ST, and ADOS. Children were diagnostically evaluated for a best-estimate clinical DSM-5 ASD diagnosis by practitioners who were blind to screening outcomes. Children were re-screened across all instruments 12 months after initial screening.
Parents were followed-up 24 months after initial screening to confirm stability of screening outcomes and diagnosis. ABII-C internal consistency, $\alpha=91$, and test retest reliability, $r=95$, were excellent. The ABII-C was strongly correlated with each of the ASD specific instruments at both initial and 12 month screenings. At initial screening, the ABII-C was the only screening instrument that correctly predicted 100% of children who went on to receive an ASD diagnosis or to be regarded to have neurotypical development. The outcomes from this study warrant further investigation of the potential added value a combined parent-clinician screening instrument may have on improving the detection of early symptomatic profiles of ASD.

Overall, this research program sought to contribute toward addressing a broader goal of improving the timing of ASD identification and diagnosis. The advancement of an ASD screening instrument and the identification of the factors that could decrease the length of a diagnostic gap form initial attempts toward reaching this goal. Outcomes from this program of research suggest improvements to the ASD diagnostic process and show the potential added value of a combined parent-clinician informant ASD screening instrument. Integration of a combined parent-clinician informant ASD screening instrument, in combination with improved diagnostic process, could form initial steps to reducing the length of a diagnostic gap.
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<th>Description</th>
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<tbody>
<tr>
<td>AABASD</td>
<td>Australian Advisory Board on Autism Spectrum Disorders</td>
</tr>
<tr>
<td>AACAP</td>
<td>American Academy of Child and Adolescent Psychiatry</td>
</tr>
<tr>
<td>AAP</td>
<td>American Academy of Pediatrics</td>
</tr>
<tr>
<td>ABII</td>
<td>Autistic Behavioural Indicators Instrument</td>
</tr>
<tr>
<td>ABII-C</td>
<td>Autistic Behavioural Indicators Instrument – Combined</td>
</tr>
<tr>
<td>ABII-PQ</td>
<td>Autistic Behavioural Indicators Instrument – Parent Questionnaire</td>
</tr>
<tr>
<td>ABS</td>
<td>Australian Bureau of Statistics</td>
</tr>
<tr>
<td>AD</td>
<td>Autistic Disorder</td>
</tr>
<tr>
<td>ADOS</td>
<td>Autism Diagnostic Observation Schedule</td>
</tr>
<tr>
<td>APA</td>
<td>American Psychiatric Association</td>
</tr>
<tr>
<td>AS</td>
<td>Asperger Syndrome</td>
</tr>
<tr>
<td>ASD</td>
<td>Autism Spectrum Disorder</td>
</tr>
<tr>
<td>BITSEA</td>
<td>Brief Infant Toddler Social Emotional Assessment</td>
</tr>
<tr>
<td>BS</td>
<td>Behavioural Subscale</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control</td>
</tr>
<tr>
<td>CTM</td>
<td>Comprehensive Treatment Model</td>
</tr>
<tr>
<td>DSM-IV-TR</td>
<td>Diagnostic Statistical Manual of Mental Disorders, Fourth Edition, Test Revision</td>
</tr>
<tr>
<td>DSM-5</td>
<td>Diagnostic Statistical Manual of Mental Disorders, Fifth Edition</td>
</tr>
<tr>
<td>ESAT</td>
<td>Early Screening of Autistic Traits Questionnaire</td>
</tr>
<tr>
<td>GP</td>
<td>General Practitioner</td>
</tr>
<tr>
<td>HR</td>
<td>High-risk</td>
</tr>
<tr>
<td>M-CHAT</td>
<td>Modified Checklist for Autism in Toddlers</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
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<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>OT</td>
<td>Occupational Therapist</td>
</tr>
<tr>
<td>PDD-NOS</td>
<td>Pervasive Developmental Disorder – Not Otherwise Specified</td>
</tr>
<tr>
<td>SAS</td>
<td>Social Attention Subscale</td>
</tr>
<tr>
<td>SLI</td>
<td>Speech and Language Impairment</td>
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<tr>
<td>SS</td>
<td>Sensory Subscale</td>
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<tr>
<td>TD</td>
<td>Typical Development</td>
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<td>WHO</td>
<td>World Health Organization</td>
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Statement of Original Authorship

The work contained in this thesis has not been previously submitted to meet requirements for an award at this or any other higher education institution. To the best of my knowledge and belief, the thesis contains no material previously published or written by another person except where due reference is made.

Signature:

Date:    5.09.2016
Preface

The Human Research Ethics Committee of Queensland University of Technology (QUT-HREC # 0900001353) approved this research. This project was granted an occupational workplace health and safety clearance. The format of this thesis follows guidelines prescribed by the American Psychological Association (6th edition). Statistical analyses were conducted using the Statistical Package for Social Sciences, version 23.0. Changes resulting from the publishing process may have been made to the studies presented in this thesis since they were submitted for publication. Note that the tables are presented in the text of the paper as opposed to at the end, and a single thesis reference list is provided as opposed to a reference list at the end of each paper, as for submission.
Acknowledgements

I would like to thank all of the children, families and clinicians who participated in this research project. Your participation has placed us a step closer toward improving the timing of ASD identification. My sincere thanks to all the medical, allied health, early educators, early learning and intervention centers and autism organisations who helped to inform parents of the research project. To Professor Karen Sullivan and Professor Linda Gilmore, I express my gratitude of all of your support over the years. Your encouragement, wisdom and guidance is admirable and I am forever thankful.

To my wonderful husband, family and friends, thank you for all of your love and emotional support.

I would like to dedicate this thesis to children with ASD and their families. I would also like to dedicate this thesis to the clinicians who may grapple with the challenges associated with early identification of children with ASD and in supporting these children to access timely intervention. It is hoped the findings herein contribute toward improving the lives of children with ASD and their families.
"For healthcare providers, we have a message that's pretty direct about autism. And
the message is: The 4-year-old with autism was once a 3-year-old with autism, which
was once a 2-year-old with autism."

Dr. Jose Cordero (2013).

Founding Director of the National Center on Birth Defects and Developmental
Disabilities, part of the Centers for Disease Control and Prevention (CDC).
Chapter 1: Introduction

1.1  Context and Research Problem

It is generally believed that evidence-based intervention for children with autism spectrum disorder (ASD) should begin as early as possible (Reichow, Barton, Boyd & Hume, 2012). From two years of age, evidence-based ASD specific interventions become available (Boyd, Odom, Humphreys & Sam, 2010; Wong et al., 2014, 2015) and have been recognised as established methods to improve the developmental outcomes of children with ASD (National Autism Centre, 2015; Prior, Roberts, Rodger, Williams & Sutherland, 2011). However, it is likely that a large proportion of children with ASD do not access evidence-based ASD specific intervention until well after their second birthday. Currently in Australia, access to government supported early intervention is available only to those children who have a confirmed ASD diagnosis (Department of Social Services [DSS], 2015). ASD diagnostic confirmation is also important to ensure ASD specific evidence-based intervention is implemented (Kalkbrenner et al., 2011). The average age of diagnosis in Australia, as elsewhere, does not occur until after the age of four years (Australian Bureau of Statistics [ABS], 2012; Bent et al., 2015; CDC, 2014). Diagnosis at this age would mean access to evidence-based intervention for many children with ASD is delayed. Delayed access to intervention has been associated with significant negative implications for children with ASD, their families and society (National Research Council, 2001).

Most children with ASD are thought to be able to be correctly diagnosed following comprehensive diagnostic evaluation by two to three years of age (CDC,
2014). Yet, the average age of initial diagnostic evaluation does not occur until 44 months of age, potentially delaying the time at which a diagnosis could have been achieved (CDC, 2014). This period of time between when ASD can be identified and when actual diagnosis occurs was first referred to as a diagnostic “gap” by Shattuck and colleagues (2009, p.475), and this phrase has since been adopted by others (Bent et al., 2015). Though there are likely a number of broader factors contributing to this gap between when children can be identified and when final ASD diagnosis is reached (Shattuck et al., 2009), the timing of child referral for diagnostic evaluation is potentially implicated. Optimising the timing of referral for diagnostic evaluations may be an important first step toward supporting children with ASD to reach evidence-based intervention sooner.

In the absence of a single definitive test for ASD, early behavioural detection methods, such as ASD specific screening instruments, provide a method to identify children displaying symptomatic profiles of ASD. The purpose of screening is to support earlier access to comprehensive diagnostic evaluation and if necessary, evidence-based intervention (Rogers et al., 2014). Although the benefits of early detection through screening had previously been thought to be limited due to the absence of valid intervention programs, efficacy research has shown that intervention can be effective from two years of age (Boyd et al., 2010; Wong, 2014, 2015). Additionally, emerging evidence shows the potential to intervene in infants as young as six months of age who are displaying symptomatic profiles of ASD (Baranek et al., 2015; Koegel, Singh, Koegel, Hollingsworth & Bradshaw, 2014; Rogers et al., 2014), or who are classified as a high-risk sibling (Green et al., 2013; Steiner, Gengoux, Klin & Chawarska, 2013). These advancements in very early intervention make improvements to early detection methods increasingly important. While
intervention under the age of two years requires validation to establish long term outcomes, development of accurate methods of detecting children who may benefit from very early intervention are required to ensure these detection methods are available at the time very early intervention programs become available.

Given that final diagnostic confirmation serves as a gatekeeper for many children with ASD accessing evidence-based intervention, a second purpose of screening is to initiate earlier referral of children displaying symptomatic ASD profiles for diagnostic evaluation (Carbone, Farley & Davis, 2010). Since 2006, screening children for ASD has been recommended (American Academy of Pediatrics [AAP], 2006). Earlier this year, the recommendation to screen all children for ASD at routine 18 and 24-month health check-ups was reconfirmed (American American Academy of Pediatrics News [AAP News], 2016). The use of standardised ASD specific screening instruments at 18 months and at 24 months of age form part of screening recommendations (AAP, 2006; CDC, 2014). ASD screening instruments can provide practitioners with a standardised inexpensive and quick method to quantify ASD symptoms (Zwaigenbaum et al., 2015b). Research has shown that, from 24 months of age, existing instruments can assist in earlier detection and promote earlier ASD diagnosis (Zwaigenbaum et al., 2015c). However, under the age of 24 months, existing screening instruments are susceptible to a high rate of misclassification (Al-Qabandi, Gorter & Rosenbaum, 2011; Barbaro & Dissanyake, 2012).

Misclassification of children on screening instruments can result in considerable burden for the child, family, health-care system and society (Lavelle et al., 2014). Failure to identify children with ASD can be as detrimental as incorrectly classifying a child without ASD (Bölte et al., 2013; Lavelle et al., 2014; Lipkin &
Misclassification can produce under- or over-inclusive referrals for diagnostic evaluation. Under-inclusive referrals prolong the diagnostic gap for children with ASD by delaying their detection while over-inclusive referrals cause undue parental stress and may trigger an unnecessarily costly and time consuming diagnostic evaluation of children who did not require it (Dixon, Granpeesheh, Tarbox & Smith, 2011). Ongoing refinement and development of ASD specific screening tools for use in children under the age of 24 months is therefore required (Al-Qabandi et al., 2011; Barbaro & Dissanyake, 2012).

Best practice guidelines for the evaluation of ASD recommend combining parent-report with clinician-observation of ASD symptomatic traits (AAP, 2006; Volkmar et al., 2014). Diagnostic accuracy and stability improves when evaluation methods combine information from both standardised parent-interview and clinician-administered measures (Volkmar et al., 2014). Yet, existing ASD screening instruments rely on single informant data to guide ASD risk ascertainment. It has already been shown that single informant ASD instruments can inaccurately measure the full range of symptoms across ASD domains (Lemler, 2012). It is also already known that parents provide differential information on symptomatic profiles compared to trained practitioners, and without the combination of both informant sources, the measurement of symptoms across ASD domains is likely inaccurate and incomplete (Lemler, 2012). Therefore, single informant ASD screening instruments may increase misclassification risk.

Although the notion of combining information from parent-report with clinician-ratings is likely an informal practice in screening children with ASD, existing tools do not provide clinicians with a single tool that combines the two information sources. Previous examinations have also not considered how to best
combine scores from ASD instruments to identify an optimal method of combination. A screening instrument that provides a standardised method to quantify ASD risk, using a combination score from a parent-clinician ASD screening instrument, may increase classification accuracy and the stability of screening outcomes. In turn, this may help to support the earlier referral of children for diagnostic evaluation at the time at which a reliable diagnosis could be achieved.

While further advancement of ASD screening instruments should help to support children to reach diagnostic evaluation sooner, evidence elsewhere suggests that the timing of ASD diagnosis is influenced by a broader range of factors that extend beyond the timing of initial diagnostic evaluation (Kennedy, 2013; Shattuck et al., 2009). To ensure the follow on benefits of undergoing an early diagnostic evaluation ensue, it is necessary to identify the potential factors that could influence the timing of ASD diagnosis once children reach the practitioner. This research program sought to investigate practitioner reported assessment and diagnostic practices and challenges that may influence the timing of ASD diagnosis in Australia. In addition to this, this research program attempted to further develop an early behavioural detection method, adapting a single informant ASD specific screening instrument into a combined parent-clinician informant ASD screening instrument.

1.2 Importance of and Need for the Research Program

ASD is no longer considered a rare disorder (Kuehn, 2007) and is regarded as one of the most common developmental disabilities (Newschaffer et al., 2007). Since the first epidemiological study in 1966, where the estimated prevalence was approximately 4.5/10 000 (Lotter, 1966), today ASD is estimated to impact at least one percent of the world’s population (Elsabbagh et al., 2012; Nygren et al., 2012;
Williams et al., 2014a). Recent years have seen a marked increase in the reported prevalence of diagnosed cases of ASD (Hansen, Schendel & Parner, 2015) and the ASD incidence rate has been forecast to continue to rise (Rogers, 2011). Australia alone has seen a 79% increase in the number of children diagnosed with ASD since 2009 (ABS, 2012). Similar increasing trends have been reported internationally (Centres for Disease Control and Prevention [CDC], 2012). This increased prevalence is thought to reflect more children being identified, largely due to improved practitioner and community awareness, diagnostic practices, and the expansion of diagnostic criteria to include milder symptom presentations, rather than a true increase in the number of children being affected (Hansen et al., 2015; King & Bearman, 2009; Liu, King & Bearman, 2010). This rise in ASD prevalence has been associated with increased burden on health-care systems (Lavelle et al., 2014) and it is regarded as a significant public health concern (Centres for Disease Control and Prevention [CDC], 2009).

The need to improve the timing of identification and diagnosis of children with ASD is now recognised as a significant issue internationally (Andersson, Miniscalco & Gillberg, 2013; Bölte et al., 2013). The best-known predictor of functional outcomes for children with ASD is an earlier age at evidence-based intervention onset (Perry, Blacklock & Dunn Geier, 2013; Smith, Klorman & Mruzek, 2015). While evidence elsewhere suggests that many children with ASD access pre-diagnostic intervention already (Monterio et al., 2016), this is potentially less likely for children who require access to government supported intervention. Access to evidence-based ASD specific interventions would be more likely post-diagnosis (Kalkbrenner et al., 2011). Early intervention not only has the potential to improve child outcomes but also to yield fiscal savings (Synergies Economic Consulting,
Thus, identification of factors that support timely ASD diagnosis to facilitate earlier access to intervention has been regarded to be of great public health importance (Kalkbrenner et al., 2011).

The current age of diagnosis occurs well beyond the time at which an accurate and reliable diagnosis is possible (Bent et al., 2015). In Australia, the most frequently reported diagnostic age is 71 months (Bent et al., 2015). Thus, many Australian children may be at risk of experiencing a substantial diagnostic gap. Examinations outside of Australia have found children with ASD can face a diagnostic gap that can extend to up to five years or longer (Kennedy, 2013; Shattuck et al., 2009). Reducing the average length of a diagnostic gap is important. Lengthier diagnostic gaps are associated with greater potential for a negative impact on the individual, family, and society, and can also increase the burden on education and public health systems (Baxter et al., 2015). Lengthier diagnostic gaps increase delays in accessing services that may help to reduce the devastating sequelae of ASD (Lovaas, 1987). Studies that identify the factors that impact on the length of a diagnostic gap are needed to discover whether and how it might be reduced. This program of research attempted to address this need.

Although improving the timing of referral for diagnostic evaluation may form an initial step in supporting timely ASD diagnosis, this referral is often reliant upon child health-care practitioners, such as general practitioners (Carbone et al., 2010). Reliance on the accurate detection of symptomatic ASD profiles by the less trained general practitioner (Ozonoff et al., 2009), particularly during brief encounters (Gabrielsen et al., 2015), can be difficult and therefore has the potential to delay referral. Although by the time of a child’s second birthday, behavioural markers of ASD are evident in most children (Barbaro & Dissanyake, 2009; Jones, Gliga,
Bedford, Charman & Johnson, 2014; Yirmiya & Charman, 2010), and although up to 80% of parents have reported their developmental concerns to their general practitioner (Kozlowski, Matson, Horovitz, Worley & Neal, 2011), these clues can go under the radar or be overlooked.

In the current Australian health-care system, limited time and resources can impede comprehensive and in depth child evaluations (State-Wide Autism Project [SWAP], 2012; Western Australia Autism Diagnosticians forum Inc. [WADDF], 2012). During brief clinical evaluations, the range of behavioural features that may present can be limited (Gabrielsen et al., 2015). Additionally, the general practitioner may not always be adept in eliciting information from parents to inform the presence of early symptomatic ASD profiles (Guerrero, Rodriguez & Flores, 2011; Zuckerman, Lindly & Sinche, 2015), and may fail to escalate parental concerns, instead providing a passive or reassuring response (Daniels & Mandell, 2014; Guerrero et al., 2011; Zuckerman et al., 2015). Thus, general practitioners may be in need of brief ASD screening instruments to help guide their detection of children who require referral for diagnostic evaluation. Evidence elsewhere suggests the potential for ASD screening during the routine 18 and 24-month child health check-ups to provide a convenient and feasible opportunity to support the general practitioner to identify children in need of diagnostic evaluation (CDC, 2014; Gura, Champagne & Blood-Siegfried, 2011). Despite many available ASD specific screening instruments, misclassification has been high and improvements are needed (Al-Qabandi et al., 2011; Barbaro & Dissanayake, 2012; Zwaigenbaum et al., 2015b). This program of research attempted to address this need.

While improving the accuracy of ASD specific screening instruments in detecting children displaying symptomatic profiles of ASD could improve the timing
of referral for diagnostic evaluation, evidence suggests timely referral may not result in timely diagnostic confirmation. It is therefore important that attempts to improve ASD screening instruments are met with attempts to identify the potential barriers that impede timely ASD diagnosis. Without this dual approach, the benefits of early detection and referral could be limited. This program of research attempts this dual approach.

1.3 Demarcation of Scope

The diagnostic pathway for a child with ASD involves two stages, screening and comprehensive diagnostic evaluation (Centers for Disease Control and Prevention [CDC], 2015). Thus, this research program was driven by two aims. First, the research program examined practitioner reported assessment and diagnostic practices and challenges that may influence the timing of ASD diagnosis in Australia. Second, this research program sought to adapt a single informant ASD screening instrument into a combined parent-clinician informant ASD screening instrument. The hope was that by improving the accuracy of a screening instrument and illuminating the problems that practitioners perceive with ASD diagnostic evaluations, that changes could be suggested to improve screening practices and diagnostic processes.

This program of research was not intended to include all of the practitioners involved in ASD evaluations. While a range of other practitioners, including speech pathologists and occupational therapists, are also involved in the multidisciplinary evaluation of children with ASD, their assessments more commonly involve comprehensive language assessments and developmental, motor and sensory assessments, respectively (Allied Health Professionals Australia [AHPA], 2015). These practitioners make an important contribution to ASD evaluations. However,
sampling these professionals was outside the scope and aims of this research program. Additionally, this thesis was not intended to investigate all of the potential factors that may influence the timing of ASD diagnosis. Sociodemographic factors, child and parent characteristics, and access to diagnostic services can also impact on the timing of ASD diagnosis (Bent et al., 2015). Examination of how these factors may differentially impact on assessment and diagnostic practices was outside the scope of this thesis. The aim of this research program was to explore practitioner reported perceptions and factors that may contribute to a diagnostic gap. Consequently, the research did not seek to confirm the presence or length of a diagnostic gap or to establish diagnostic trends per se.

The second aim of the research program was to adapt a single informant ASD screening instrument into a combined parent-clinician informant screening instrument. The search for a biomedical test, including identification of potential genetic, neurological or other biochemical markers for ASD, is moving forward apace (Halepoto, Bashir & Al-Ayadhi, 2012). However, the inclusion of such tests was outside the scope of this research program. In addition to this, while a range of perinatal and neonatal factors may be implicated in increasing ASD risk, and thus may help to inform early screening measures (Gardener, Spiegelman & Buka, 2011), this program of research was intended to contribute toward the advancement of early behavioural markers of ASD, and therefore did not include examination of potential perinatal and neonatal risk markers. ASD screening research would benefit greatly from mapping the trajectory of ASD symptom emergence and ASD risk by screening children from birth. Such a study was outside the scope of the current research program. In addition, although cognitive, speech and language and adaptive impairment, along with degree of comorbidity, can differentially influence ASD
symptom emergence and severity (Zwaigenbaum et al., 2015c), the inclusion of such evaluation was outside the scope of this research thesis.

The focus of the thesis was on updating our understanding of ASD diagnostic evaluations in Australia and on exploring potential improvement to a current ASD screening instrument. Thus, this program of research was not intended to examine diagnostic accuracy. In order to draw conclusions regarding the psychometric properties of a screening instrument, information on diagnostic confirmation is necessary. Conducting diagnostic evaluations was outside the scope of this thesis. As such, all ASD diagnostic evaluations had been conducted by practitioners independent of the research program. These practitioners were all registered practitioners in clinical practice and as such, children who had a diagnosis of ASD in the program of research had all received a verified ASD diagnosis and were all formally identified as having ASD. A verified diagnosis is one that would be accepted by Australian health authorities for the purpose of providing access to subsidised services. In Australia, as elsewhere, best-estimate clinical diagnosis remains the gold standard for ASD diagnosis (Volkmar, Chawarska & Klin, 2005). Best-estimate clinical diagnosis is defined as a diagnostic procedure that integrates information from multiple sources, including the diagnostic criteria and information from standardised diagnostic instruments, to guide clinical judgement and final diagnostic recommendations (Le Couteur, 2011).

It is beyond the scope of this thesis to provide a comprehensive summary of all of the research examining early ASD symptom emergence, or to provide a detailed review of all of the existing ASD screening instruments. Many comprehensive reviews of studies mapping the trajectory of early ASD symptom emergence (Elsabbagh & Johnson, 2010; Jones et al., 2014; Rogers, 2009; Yirmiya
& Charman, 2010) and of the existing ASD screening instruments (Charak & Stella, 2001-2002; Garcia-Primo et al., 2014; Hampton & Strand, 2015; Norris & Lecavalier, 2010; Zwaigenbaum et al., 2015b), are already available.

1.4 Significance of the Research

This program of research is significant because it seeks to improve the timing of identification of children with ASD. This thesis attempts to do this by informing our understanding of what assessment and diagnostic practices and challenges may be impeding timely diagnosis in Australia and by contributing to the advancement of an ASD screening instrument developed for use in children from 12 months of age. Figure 1.1 depicts the average timeline from ASD symptom emergence to diagnostic confirmation for most children with ASD and positions the aims of the program of research within this timeline. This research is important as it seeks to provide further information to guide improvements from the screening process through to the final diagnosis.
Aim 1: Examine assessment and diagnostic practices and challenges that influence timing of ASD diagnosis in Australia.

Aim 2: Adapt single informant ASD screening instrument into combined parent-clinician ASD screening instrument.

**Figure 1.1.** The average timeline from symptom emergence to diagnostic confirmation for children with ASD and the positioning of the aims of research program within this timeline. ASD = autism spectrum disorder; AD = autistic disorder; AS = asperger’s syndrome; PDD-NOS = pervasive developmental disorder – not otherwise specified.
The first aim of this research was to update our knowledge of practitioner reported assessment and diagnostic practices and challenges to identify potential factors that may contribute to a diagnostic gap. This aim of the research program is important as it is the first attempt to survey Australian practitioners since the release of universal recommended best practice assessment guidelines in 2006 (AAP, 2006), and to survey psychologists, who form an integral part of ASD evaluations in Australia (AHPA, 2015). The outcomes from this research may help to inform potential improvements to the assessment and diagnostic process for Australian children, and by doing this, help to reduce the average length of a diagnostic gap.

The second aim of this research was to adapt a single informant ASD screening instrument into a combined parent-clinician informant ASD screening instrument and conduct a preliminary evaluation of it. This aim of the research program is important as it attempts to further advance an early behavioural detection method for ASD. This research program examined whether single informant screening instruments have the potential to reach different screening outcomes for the same child as a function of informant source, and explored different methods of combining scores from a parent and clinician rated ASD instrument to see if classification accuracy improves.

1.5 Overview of Thesis Structure

This doctoral thesis was prepared for submission in accordance with Queensland University of Technology guidelines for PhD thesis by published papers. The thesis is comprised of 9 chapters. Chapter 1 describes the importance of improving the timing of ASD identification, and outlines the need for concurrent attempts to improve ASD screening instruments with identification of the factors that can influence the timing of final diagnostic confirmation. Chapter 2 provides an
overview of the literature to set the context of the thesis. Chapter 3 introduces the research program and outlines the contribution of each paper to the overall thesis aims. Chapters 4 through 8 present the papers that have been accepted or submitted for publication or that have been prepared for submission. Chapter 9 provides a general discussion of the results from the research program, discusses theoretical and clinical implications of the findings, and outlines the strengths, limitations, and directions for future research.

1.6 Chapter Summary

This chapter presented the importance of early intervention for children with ASD. Evidence-based ASD specific interventions for children with ASD are available from two years of age. Yet the majority of Australian children with ASD would access intervention beyond this age (Bent et al., 2015). Screening children using standardised ASD screening instruments has the potential to guide the early referral of children for diagnostic evaluation. However, the rates of misclassification associated with existing instruments, and the potential for broader factors that extend beyond early referral to impact on the timing of ASD diagnosis, warrants further examination and improvement. Understanding the developmental emergence of behavioural markers within core ASD domains, the optimal method to quantify and measure symptoms across the full spectrum of ASD, and the potential factors that impact the timing of ASD identification and diagnosis, are all necessary components to the broader goal of supporting children with ASD to access evidence-based intervention sooner. The next chapter of this thesis provides an overview of the literature that relates to the early identification of children with ASD and highlights the potential gaps that have been addressed and examined in the research program.
Chapter 2: Literature Review

Chapter 1 introduced the potential benefits of improving the accuracy of ASD screening instruments and identifying the potential factors that influence diagnostic evaluations. The purpose of this chapter is to describe the factors that can impact on the timing of ASD diagnosis and contribute to the length of a diagnostic gap, provide a select review of the early behavioural markers of ASD and existing screening instruments, and describe the suspected characteristics of screening instruments that could optimise classification accuracy.

2.1 Conceptualisation and Aetiology of ASD

ASD is behaviourally defined and characterised by impairments in social communication and the presence of repetitive and stereotyped behaviours and sensory symptomology (American Psychiatric Association [APA], 2013). ASD is understood to be a complex and heterogeneous disorder with varying clinical phenotypes that can range in severity (Fernell, Eriksson & Gillberg, 2013). Children with ASD are diverse in their clinical presentations (Irwin, MacSween & Kerns, 2011). How ASD has been conceptualised and operationalised has changed since its initial description (Kanner, 1943). Understanding the aetiology and the behavioural markers of ASD, and description of the core deficits, is important to highlight the critical role of clinicians in identifying a disorder that is still reliant on the clinical detection of a range of symptoms with varying degrees of manifestation and severity. Defining the signs and symptoms of ASD provides important information to contextualise the difficult endeavours faced by clinicians in the identification and diagnosis of ASD and to help understand why, after over seven decades since the
initial description of key features of ASD, practitioners are still grappling with diagnostic challenges.

The aetiology of ASD is considered idiopathic (i.e., of unknown cause) and heterogeneous (Caronna, Milunsky & Tager-Flusberg, 2008). Genetic variants are thought to account for biological vulnerabilities (Carter & Scherer, 2013). Interacting genetic and environmental factors (Chaste & Leboyer, 2012) are thought to contribute to neurodevelopmental alterations that either cause or increase vulnerability to ASD (Persico & Bourgeron, 2006). It is thought that environmental factors may trigger ASD symptoms in genetically predisposed individuals, rather than having any direct cause (Raising Children Network, 2013). ASD has a significant heritability factor that is estimated to be as high as 90% (Spence, 2004). Siblings of children with ASD have a recurrence rate that can be as high as 18.7% (Ozonoff et al., 2011). The recurrence rate in identical twins can be as high as up to 75%, and can range up to 34% in fraternal twins (Frazier et al., 2014). Greater impairment across core ASD domains is associated with increased recurrence risk in siblings (Bolton et al., 1994). Compared to the general population, siblings of children with ASD have nearly a 20-fold greater risk of ASD and greater risk of displaying features of a broader autism phenotype (Chawarska et al., 2014). Up to 30% of siblings of children with ASD will have other developmental disabilities (Constantino, Zhang, Frazier, Abbacchi & Law, 2010; Iverson & Wozniak, 2007). The risk of having a second child with communication or cognitive deficits is several times higher than for the general community (Le Couteur et al., 1996). The expression of ASD traits within the general population also displays a degree of heritability (Constantino & Todd, 2003).
2.2 Diagnostic Evaluation of ASD

There remains no medical test for ASD. Thus, diagnostic evaluations rely on clinical detection of operationalised symptom criteria (Cangialose & Allen, 2014; Fernell et al., 2013) and clinician integration of information from multiple informant sources (Huerta & Lord, 2012). No single score from any test or observation of a single behaviour is sufficient to make a diagnosis of ASD. For this reason, best-estimate clinical diagnosis remains the gold standard for ASD diagnosis (Volkmar et al., 2005, 2014). In Australia, the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5; APA, 2013) is used to operationalise ASD symptom criteria. Prior to release of the DSM-5 (APA, 2013), the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR; American Psychiatric Association [APA], 2000) was used. Diagnostic clarity often requires repeat evaluations and can be guided by the use of standardised instruments (Huerta & Lord, 2012). While not diagnostic, two standardised instruments have been recommended as gold standard instruments to support ASD diagnostic evaluations, the Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, Dilavore & Risi, 1999), a clinician rated measure, and the Autism Diagnostic Interview-Revised (ADI-R; Rutter, Le Couteur & Lord, 2003), a semi-structured clinician interview based on parent-report.

2.2.1 Best-estimate clinical diagnosis.

Best-estimate clinical diagnosis is regarded as the gold standard method for ASD diagnosis in both clinical practice and research (Volkmar et al., 2005, 2014). This procedure of diagnosis integrates information from multiple sources, including the diagnostic criteria and information from standardised diagnostic instruments, to guide clinical judgement and final diagnostic recommendations (Le Couteur, 2011).
Synthesising information from these information sources to guide best-estimate clinical diagnosis improves diagnostic accuracy and stability (Volkmar et al., 2014).

2.2.2 Diagnostic criteria for ASD.

A set of operationalised symptom criteria for ASD have been described since 1980 and have since been revised in five publications of the Diagnostic and Statistical Manual of Mental Disorders. Since the original publication, major shifts in ASD conceptualisation and diagnosis have ensued. A detailed review of the historical revisions to the operationalised symptom criteria is outside the scope of this thesis, however these revisions have been documented elsewhere (for a review see: Gillberg, 2011; Irwin et al., 2011). Recently, a major revision to the set of operationalised symptom criteria moved away from a distinct categorical diagnostic system (Andersson et al., 2013), as previously used in the DSM-IV-TR (APA, 2000), to a dimensional approach to classification with a variant range of symptom severity (Fernell et al., 2013), currently outlined in the DSM-5 (APA, 2013).

The current diagnostic classification system used in the DSM-5 (APA, 2013) employs a single broader diagnostic category of ASD, replacing the previous subdivisions outlined in the DSM-IV-TR (APA, 2000), which included: autistic disorder (AD); asperger’s syndrome (AS); and pervasive developmental disorder, not otherwise specified (PDD-NOS). To meet threshold for an ASD diagnosis under the new symptom criteria in the DSM-5 (APA, 2013) requires impairment and persistent deficits in two domains, namely social communication and restricted, repetitive patterns of behaviour, interests or activities. A severity level, ranging from ‘level 1: requiring support’ to ‘level 3: requiring substantial support’ is used to reflect symptom severity. This diagnostic change moves away from the original conceptualised triad of impairments, which defined ASD on the basis of a cluster of
core deficits in three domains, namely social interaction, language and communication, and repetitive and restricted behaviour and interests. Social and communication deficits have been merged into a single social communication domain. The restricted, repetitive patterns of behaviour, interests or activities domain has been expanded to include sensory symptomology. Another key change to the diagnostic criteria in the DSM-5 (APA, 2013) is the addition of specifiers to describe the presence or absence of accompanying intellectual and language impairment, which can influence the way ASD symptomology manifest (Hus & Lord, 2013). The revised diagnostic classification system now permits the provision of a comorbid diagnosis, potentially acknowledging the significant comorbidity of ASD (Coury, 2010; Osterling, Dawson & Munson, 2002).

The rationale for changing how ASD is operationalised in the DSM-5 (APA, 2013) is thought to include improvement to diagnostic precision and potential for earlier diagnosis (APA, 2013). While the effect of these changes is not yet known, there has been concern that these changes could have a false impact on prevalence rates (Koegel, Koegel, Ashbaugh & Bradshaw, 2014). That is, it was thought that children who were already diagnosed under the previous DSM-IV-TR (APA, 2000) criteria could lose their ASD diagnosis, or that children who could have received a DSM-IV-TR (APA, 2000) diagnosis would not reach diagnostic threshold under the new DSM-5 (APA, 2013) criteria (Taheri & Perry, 2012). However, evaluation of the DSM-5 (APA, 2013) criteria in children with a DSM-IV-TR (APA, 2000) diagnosis showed most children would retain their diagnosis under the new criteria (Huerta, Bishop, Duncan, Hus & Lord, 2012). The broadening of symptomatic criteria in the DSM-5 (APA, 2013) to include sensory symptoms, which are
considered a core characteristic of ASD (Maestro et al., 2005), could improve the sensitivity of the new criteria.

2.2.3 Gold standard instruments to guide ASD diagnostic evaluations.

Clinician use of gold standard instruments in their ASD diagnostic evaluations is recommended (AAP, 2006; Australian Advisory Board on Autism Spectrum Disorders [AABASD], 2011; Volkmar et al., 2014). Gold standard instruments can support the clinician in reaching a valid and reliable best-estimate clinical diagnosis. These instruments provide a standardised method to quantify symptomatic features of ASD and support the clinician to integrate information from parental description and clinician ratings of behavioural markers for ASD. There is general agreement that the clinician rated ADOS (Lord et al., 1999) and parent-report interview, the ADI-R (Rutter et al., 2003), are gold standard instruments to support ASD diagnostic evaluations (Gray, Tonge & Sweeney, 2008; Huerta & Lord, 2012).

The Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1999). The ADOS is a gold standard standardised semi-structured play-based observational instrument for use in children over the age of two years. The ADOS was developed to measure ASD symptoms as operationalised under the previous diagnostic criteria, and therefore requires new validation with the DSM-5 (APA, 2013) diagnostic criteria. The ADOS was first introduced as a method of standardising direct observations of social behaviour, communication, and play in children suspected of having ASD (Lord, Rutter, DiLavore & Risi, 2008). The ADOS consists of a series of structured and semi-structured presses for interaction, and the coding of specific target behaviours and general ratings of the quality of behaviours. The ADOS consists of four modules, one of which is selected for administration based upon the child’s expressive language ability. The ADOS scoring algorithm provides
diagnostic cut-offs for DSM-IV-TR (APA, 2000) AD or ASD, which included DSM-IV-TR (APA, 2000) AS or PDDD-NOS. Higher scores are indicative of greater level of impairment. The ADOS requires specialist training and administration time takes approximately one hour.

In children over the age of three years, the ADOS can distinguish children with ASD from children with neurotypical development (i.e., children who are regarded to display neurologically typical brain development and to not be on the autism spectrum) (Logsdon-Breakstone, 2013), and children with other developmental delays and disabilities (e.g., children with a global developmental delay or intellectual impairment (Chawarska, Klin, Paul & Volkmar 2007; de Bildt et al., 2004; Gotham, Risi, Pickles & Lord, 2007; Gray et al., 2008). However, in children under the age of three years, the ADOS can be over-inclusive, incorrectly classifying children who do not have ASD (Risi et al., 2006; Ventola et al., 2006).

Until recently, the ADOS was the only available gold standard clinician-observation instrument and therefore its clinical utility in younger populations was low (Risi et al., 2006; Ventola et al., 2006). However, in 2012, the ADOS-2 (Lord et al., 2012), was released, which included revised algorithms for use in children over the age of three years and a toddler module for use in children aged between 12 and 30 months of age with a nonverbal mental age requirement of 12 months (Huerta & Lord, 2012; Luyster et al., 2009). The ADOS-2 has demonstrated good reliability and validity (Guthrie, Swineford, Nottke & Wetherby, 2013; Luyster et al., 2009; Oosterling et al., 2010a) and improved instrument sensitivity and specificity (Luyster et al., 2009; Overton, Fielding & Garcia, 2008). Although the long-term stability of an ASD classification using the ADOS-2 (Lord et al., 2012), is yet to be fully established, initial psychometrics are promising. The use of the ADOS-2 (Lord et al.,
2012) may help to support practitioners in their diagnostic evaluations of children under the age of three years.

**The Autism Diagnostic Interview-Revised (ADI-R; Rutter et al., 2003).** The ADI-R is a gold standard semi-structured clinician administered parent-report interview for use in children over the age of two years. The ADI-R was also developed to measure ASD symptoms as operationalised under the previous diagnostic criteria and therefore also requires validation with the DSM-5 (APA, 2013) diagnostic criteria. The ADI-R evaluates communication, social development, play, and restricted, repetitive, and stereotyped behaviours in children suspected of having ASD. The ADI-R requires specialist training, and administration time can take between one and a half and two and a half hours.

The ADI-R has been established as a useful instrument to support diagnostic evaluations in children over the age of three years (Huerta & Lord, 2012). However, in children under the age of three years, the ADI-R can be less accurate and can miss correctly classifying children with ASD (Charman & Baird, 2002; Cox et al., 1999; Lord, 1995; Saemundsen, Magnusson, Smari & Sigurdardottir, 2003; Stone et al., 1999; Ventola et al., 2007), and can incorrectly classify children with an intellectual impairment, severe global developmental delay, and language delay (Lord et al., 1993). Until recently, the ADI-R was the only available gold standard instrument based on parent-report, and therefore its clinical utility in younger populations was low (Gray et al., 2008; Rutter et al., 2003). However, in 2013, a set of revised scoring algorithms for use in children from 12 months of age was released (Kim, Thurm, Shumway & Lord, 2013). While the revised toddler algorithms have demonstrated improved diagnostic validity (Kim & Lord 2012; Kim et al., 2013), they can be under-inclusive, incorrectly classifying children with ASD in the little-to-no concern
range (de Bildt et al., 2015). The long-term stability of an ASD classification using the revised ADI-R scoring algorithms is yet to be fully established, however initial psychometrics are promising. The use of the revised ADI-R scoring algorithms may help to support practitioners in their diagnostic evaluations of children under the age of three years (Kim et al., 2013).

2.2.4 Best practice guidelines to guide ASD diagnostic evaluations.

Clinical evaluations for ASD can be a difficult endeavour even for trained practitioners. Given the heterogeneity of ASD, and myriad constellation of expression of traits and behavioural characteristics, it can be difficult to encompass the full range of ASD symptomology in a single diagnostic test or set of diagnostic criteria. The practitioner is therefore required to accurately capture and quantify an extensive range of indicators that can emerge at varying stages of development and to differing degrees of impairment. In an attempt to support practitioners in their evaluation of children with ASD, considerable efforts have been made to identify optimal diagnostic processes that lead to improved diagnostic stability (Volkmar et al., 2014). Best practice guidelines have been developed to guide assessment procedures for children with ASD to optimise diagnostic efficiency and accuracy. These best practice guidelines have been informed by research and expert clinical consensus, and when implemented, can improve the stability of early ASD diagnosis (Pascal, 2010; Volkmar et al., 2014).

In brief, universal gold standard best practice guidelines for ASD diagnostic evaluation prescribe a best-estimate clinical diagnosis that is reached through a multi-method assessment process that involves the combined use of clinical judgment with diagnostic criteria and standardised parent-report and clinician rated observational instruments that demonstrate moderate to good sensitivity and
specificity (AABASD, 2011; AAP, 2006; Volkmar et al., 2014). Recommended gold standard assessment measures include the clinician rated ADOS (Lord et al., 1999) and parent rated ADI-R (Rutter et al., 2003). The most reliable and valid best-estimate clinical diagnosis of ASD is attained when clinicians follow best practice guidelines and combine information from parent-report of symptomatic features across developmental history and contexts with their own clinical observations of current behaviours (Lord et al., 2006; Risi et al., 2006; Sikora, 2008). Combining these two informant sources in a formal and standardised manner, through the use of parent-report instruments like the ADI-R (Rutter et al., 2003), and clinician-administered instruments like the ADOS (Lord et al., 1999), further enhances diagnostic reliability and validity (Corsello et al., 2007; Kim & Lord, 2012).

Australian best practice guidelines for the identification, assessment and diagnosis of ASD (AABASD, 2011), share similarities with international guidelines, including those outlined in the United States of America (Volkmar et al., 2014), New Zealand (Ministries of Health and Education, 2008), and United Kingdom (National Initiative for Autism: Screening and Assessment [NIASA], 2003). In common with international best practice guidelines, Australian guidelines recommend continuing ASD specific training to enhance practitioner surveillance and detection skills and knowledge, minimal waiting times from referral to diagnosis, multidisciplinary comprehensive assessment, and intervention for both the child and family following diagnosis (AABASD, 2011; Pascal, 2010). Australian guidelines for comprehensive multidisciplinary assessment outline the integration of diagnostic and functional assessment by a team of medical practitioners involving either a paediatrician or psychiatrist, and allied health practitioners involving a psychologist, speech pathologist and occupational therapist (AABASD, 2011; AHPA, 2015). Assessment
should be conducted over a number of sessions and should include: a thorough developmental and family history; behavioural observations; medical assessment, cognitive assessment; language assessment; an evaluation of adaptive skills; and the combined use of clinical judgment with diagnostic criteria and standardised parent-report and clinician rated observational measures that demonstrate moderate to good sensitivity and specificity (AABASD, 2007; Bishop & Norbury, 2002; Filipek et al., 2000; Volkmar et al., 2014).

In the United States of America, updated practice parameters have recently been released and now also recommend: the use of ASD specific measures that identify the core ASD symptoms; screening for ASD to identify those in need of further evaluation; genetic testing; physical examination; audiological assessment; assessment of other co-morbid conditions, adaptive skills, unusual abilities, such as calendar calculations or artistic talents and sleep abnormalities; and evaluation by occupational therapists and physical therapists for further assessment and intervention (Volkmar et al., 2014).

### 2.3 Pathway of ASD Diagnosis in Australia

The current prescribed pathway of ASD diagnosis in Australia most commonly involves referral from a general practitioner to a paediatrician or psychiatrist, either in the public or private sector (AHPA, 2015). In the public sector, assessment and diagnosis is completed at no fee; however, waiting periods can range up to two years or longer (SWAP, 2012; WADDF, 2012). Waiting periods in the private sector are significantly shorter, ranging from six weeks to eight months; however, assessment in the private sector can be costly for families with fees that can range up to $2 750 for an ASD assessment (SWAP, 2012; Taylor et al., 2016; WADDF, 2012). In the private sector, limited subsidised assessment services are
available. The Medicare benefits scheme is Australia’s universal health scheme designed to offer health services at a reduced cost (Australian Government Department of Health, 2013). In most instances, the Medicare benefit does not subsidise the full cost of an ASD diagnostic evaluation and families will incur an out of pocket expense.

In both the public or private sector, the paediatrician or psychiatrist makes an assessment of the child. If the presentation of ASD is clear-cut, the paediatrician or psychiatrist can ascribe a best-estimate ASD diagnosis, integrating information from their clinical judgement, the symptom criteria outlined in the DSM-5 (APA, 2013), parent report and clinical observation, without further assessment. In less clear-cut presentations, on suspicion of ASD, the paediatrician or psychiatrist can refer the child for comprehensive multidisciplinary assessment. In the public sector, multidisciplinary assessment would be free. In the private sector, a maximum of four multidisciplinary assessment sessions, which can be allocated between a psychologist, speech and language pathologist, and occupational therapist), can be subsidised through the Medicare benefits scheme. Again, in most instances, the Medicare benefit paid to cover the cost of a multidisciplinary assessment session does not cover the practitioner’s full fee and the service would incur an out of pocket expense for the family (Australian Government Department of Health, 2013). For example, the total maximum Medicare benefit paid for a single psychological assessment session for ASD is $84.80 (Australian Government Department of Health, 2013). The current recommended schedule fee for a single 50-minute psychological assessment session is $238.00, which would not adequately provide sufficient time to complete a comprehensive ASD assessment or include an assessment report outlining diagnostic recommendations (Australian Psychological
Society [APS], 2016). A recent survey of health practitioners \((n = 99)\) in Australia found the number of ASD assessment sessions required to inform an ASD diagnostic recommendation ranged from one to 6.5 sessions, with the total length of assessment time ranging from 30 to 600 minutes (Taylor et al., 2016). On completion of multidisciplinary assessment, the child returns to the medical practitioner, who synthesises the information from all of the assessment sources to guide a best-estimate clinical ASD diagnosis (AHPA, 2015). Figure 2.1 presents the most common pathway for autism spectrum disorder diagnosis in Australia.

*Figure 2.1. The most common pathway for autism spectrum disorder diagnosis in Australia. OT = occupational therapist.*

### 2.4 The Importance of Early Diagnosis

It has been established that early ASD diagnosis can have a significant positive impact (Zwaigenbaum et al., 2015a). Optimising the timing of diagnosis can initiate a sequence of additive benefits that extend well beyond the diagnosed individual. For this reason, there is general agreement that ASD diagnosis should occur as early as possible, with the view that early intervention during a developmental period where neuroplasticity is highest is of great importance in promoting positive prognostic outcomes (Dawson, 2008; Dawson et al., 2010;
Infant development during the first two years of life is characterised by rapid growth and change. Thus, by the time the average child with ASD is diagnosed and reaches intervention, the gap in abilities between a child with ASD and a child with neurotypical development can be wide (Bradshaw, Steiner, Gengoux & Koegel, 2015). Early intervention can help to reduce this gap. Early intervention can also prevent the development or exacerbation of future symptomology (Dawson et al., 2012). However, there may be a critical window for early intervention during the first three years of life due to the dynamic and plastic nature or early brain development in children with ASD (Dawson et al., 2012; Webb, Jones, Kelly & Dawson, 2014). In the field of ASD intervention it is generally agreed that the earlier the onset the greater the potential for better outcomes.

Efficacy research has provided building evidence that early ASD specific interventions can be effective for some children from two years of age (Boyd et al., 2010; Odom, Boyd, Hall & Hume, 2014; Wong et al., 2014, 2015). Two forms of evidence-based intervention have been delineated in the literature, comprehensive treatment models (CTM) and focused interventions (Wong et al., 2015). CTM involve interventions designed to improve broad learning or the developmental impact of ASD core deficits (Wong et al., 2015). CTM are developed around a conceptual framework and are characterised by operationalised procedures, intensity (i.e., involve a substantial number of intervention hours per week), longevity (i.e., are implemented across one or more years), and the breadth of potential outcomes (i.e., improved communication, behaviour and social competence) (Odom et al., 2014; Wong et al., 2015). While up to 30 CTM have been identified in the literature (Odom, Collet-Klingenberg, Rogers & Hatton, 2010), three CTM, the Lovass model
or its variation the Early Intensive Behavioural Intervention (Reichow & Barton, 2014), the Early Start Denver Model (Dawson et al., 2010), and LEAP (Strain & Bovey, 2011), have shown positive outcomes in randomised control studies. Randomised control studies are thought to be the benchmark for evaluating the efficacy of early intervention (Reichow et al., 2012). There are a number of randomised control studies in progress to evaluate other CTM that have shown positive outcomes and longitudinal follow-up studies to establish long term outcomes (Wong et al., 2015). Focused interventions are designed to target a single skill or goal, continue until the goal is achieved, and are therefore usually shorter in duration compared to CTM (Odom et al., 2010). Focused interventions are employed in CTM, for example, Discrete Trial Teaching and peer-mediated instruction and intervention (Wong et al., 2015). Up to 27 focused interventions have met criteria for being evidence-based, for a review see Odom et al. (2010) and Wong et al. (2015).

Randomised control studies have demonstrated that CTM and focused interventions prior to three years of age can improve short-term outcomes for some children with ASD including a reduction in core ASD deficits and symptom severity, and an improvement in cognitive and adaptive behaviours (Dawson et al., 2010; 2012; Kasari, Gulsurd, Wong, Kwon & Locke, 2010). In addition to randomised control studies, controlled clinical trials provide evidence that the timing of intervention may be important, with younger child age at commencement of intervention predictive of greater positive outcomes (Perry et al., 2013; Smith & Iadarola, 2015; Smith et al., 2015). Children who receive appropriately targeted intervention by two to three years of age achieve more positive gains in verbal and non-verbal communication, intelligence test scores, social skills, adaptive functioning, and peer interaction, as well as reductions in symptom severity and
maladaptive behaviours, compared to children who receive the same intervention after the age of three (Goin & Myers, 2004; Kasari, Gulsrud, Freeman, Paparella & Hellemann, 2012; Landa, Holman & Garrett-Mayer, 2007; Rogers, 1998; Sheinkopf & Siegel, 2004). Early intervention also has the potential to ameliorate some of the associated negative secondary consequences of the primary social attention and communication impairments, and can prevent the future exacerbation of deviances from the typical course of development (Charman & Baird, 2002; Mundy & Neal, 2000). Although there is limited research that has tracked the long-term outcomes of early intervention, greater rates of independent living, secured employment and friendships and relationships, have been associated with younger age at starting intervention (Howlin, 1997).

Practitioner expertise in the delivery of evidence-based ASD specific intervention (Wong et al., 2015), parental compliance (Moon, 2010), level of parental stress (Irvin, Patten & Boyd, 2014; Shine & Perry, 2010), and individual child characteristics, including the degree of symptom severity (Fein et al., 2013), and cognitive ability (Perry et al., 2008), can all influence the effectiveness of ASD intervention. The potential of these factors to effect the fidelity of intervention and child outcomes will be important to account for in the delivery of intervention in clinical practice to ensure clinical intervention efficacy mirrors research intervention efficacy. Also, while a number of interventions display accumulating evidence to demonstrate the potential to improve short term child outcomes, and the absence of rigorous evaluation does not necessarily preclude their potential effectiveness (Wong et al., 2015), parents will likely require support to be guided toward evidence-based interventions (Singer & Ravi, 2015). Between 50 to 75% of parents of children with ASD report accessing some form of intervention for ASD that is not evidence-based
(Hanson et al., 2007; Wong & Smith, 2006). With a number of evidence-based interventions shown to improve, in the very least, short-term child outcomes, directing parents away from potentially ineffective methods will be an important role of practitioners to supporting children with ASD and their parents (Singer & Ravi, 2015).

Early detection methods have previously been thought to be impeded by the absence of available and effective very early intervention. While the purpose of early detection is to prevent or mitigate ASD symptoms by initiating access to early intervention, intervention under the age of two years had not previously been developed or evaluated. Recent years have seen exciting advancements in the potential for very early intervention in infants as young as six months of age (Rogers et al., 2014). While these very early intervention studies are preliminary, intervention in children displaying symptomatic profiles of ASD (Baranek et al., 2015; Koegel et al., 2014b; Rogers et al., 2014), and in high-risk infant siblings (Green et al., 2013; Steiner et al., 2013), have shown the potential to reduce symptomatic ASD profiles and improve short-term developmental outcomes. These results are promising and suggest the future advancement of early detection methods to identify children under the age of two years could be met with available evidence-based treatment options.

Early intervention may also yield positive fiscal outcomes. ASD is currently estimated to cost Australia $8 billion per year (Synergies Economic Consulting, 2014). A recent report released by Synergies Economic Consulting (2014), shows a potential overall reduction in this cost if Australia invested in early intervention. The report proposed that an expenditure of $118 million a year on early intervention, which would target approximately 1,200 pre-school children with ASD, would result in a total net economic benefit of an estimated $1.22 billion a year. Early
intervention has been argued to be more cost efficient than a watch and wait approach to ASD diagnosis (Koegel et al., 2014a). Late diagnosis can have significant lifelong implications for the child with ASD and their families. Most parents experience considerable stress related to parenting a child with atypical development and the uncertainty and time associated with waiting for a diagnosis can increase anxiety (Charman & Gotham, 2013). The absence of a diagnosis or the provision of an incorrect diagnosis can increase family stress and conflict, restricts receipt of specialised support and correct assistance, and can limit parental understanding, management and positive parent-child interactions, which can exacerbate the child’s difficulties (Charman & Gotham, 2013; Koegel et al., 2014a).

Early identification and diagnosis of ASD can provide the opportunity for families to learn of the associated genetic risks of ASD to subsequent children (Committee on Children with Disabilities, 2001). Informing parents of recurrence risk may be important to enhance early surveillance methods to detect emergent traits and support earlier diagnosis in siblings who have ASD.

The magnitude of gains associated with early intervention can vary and the short term positive prognostic outcomes may not be universal to all children with ASD (Williams et al., 2014b). The optimal timing to begin and the intensity and duration of intervention, and the long term gains of intervention are yet to be fully established (Williams et al., 2014b). However, early intervention can be important to improving the lives of children with ASD and their families (Bölte et al., 2013) and forms part of the Australian best practice guidelines, which recommend intervention begin as soon as characteristics of ASD are noted and continue for as long as required (Prior & Roberts, 2012, p. 5). The potential benefits of early intervention, particularly when intervention has been implemented before the age of three years,
highlights the critical need to detect children with ASD as early as possible, and ideally, before their third birthday. However, for many Australian children with ASD, diagnosis occurs past this point. ASD diagnostic numbers peak after the age of five years (ABS, 2012). Thus, there is a high potential that children with ASD reach intervention past the ideal age. Given the seemingly maximised benefit of intervention before three years of age, further investigation is warranted to identify possible factors that may contribute to diagnosis past this optimal age.

2.5 ASD Intervention in Australia

Although some Australian parent may be able to afford to access pre-diagnostic intervention for their child or children, currently, a verified ASD diagnosis is required to access government supported intervention. The Helping Children with Autism Program (HCWAP) (DSS, 2015) is a government funded ASD intervention package that is only accessible by those children who have received a verified ASD diagnosis before their sixth birthday. The HWCAP is capped at $12 000 and ceases at the child’s seventh birthday (DSS, 2015). Ongoing intervention once the HCWAP funding is exhausted or once the child turns seven, will in most instances incur an out of pocket expense for families. Through the Medicare benefits scheme, children with a verified ASD diagnosis can access up to a maximum of 20 subsidised intervention sessions, that can be allocated between a psychologist, speech and language pathologist and occupational therapist (Australian Government Department of Health, 2013). These sessions must be utilised before the time of the child’s 15th birthday. These intervention services will likely attract an out of pocket expense as the benefit paid does not typically cover the full practitioner fee for the intervention service. After a child has exhausted these funding options, unless they have a diagnosed comorbid chronic medical condition or disease, or a mental health
disorder, there is currently no other ASD specific funded intervention services available privately.

The HCWAP is scheduled to be replaced with the National Disability Insurance Scheme (NDIS) (DSS, 2015) across the next two to three years. Currently, this scheme is still in its trial phase and is not accessible for the majority of Australians. For children under the age of six years, the NDIS is proposed to provide government supported early intervention for children who either have a verified diagnosis of ASD or who have been identified as having a developmental delay. After the age of six years, a verified ASD diagnosis will be required to access intervention under the NDIS (DSS, 2015). The NDIS will therefore include parameters for pre-diagnostic intervention under the age of six years by allowing the provision of intervention for children identified as having a developmental delay but who have not yet been verified with an ASD diagnosis. While this proposed government scheme will deemphasise formal diagnostic verification as a prerequisite for access to government funded intervention, identification of the presence of developmental delay will be required. Developmental delay is identified when a child displays significant delay in the acquisition of milestones or skills within the domains of gross motor, fine motor, speech and language, cognitive, personal/social, or activities of daily living (Poon, LaRosa & Shashidhar, 2010). As with ASD, children displaying more severe presentations of developmental delay, particularly physical and cognitive delays, will be identified earlier on in development (Mann, Crawford, Wilson & McDermott, 2008). Physical and cognitive delays are not universal to children with ASD, and therefore children with ASD could be at risk of later identification of developmental delay and therefore later access to the NDIS. Ongoing attempts to improve the timing of ASD identification will remain important
so that children displaying early ASD profiles can access services under the NDIS early on in their development and to ensure children receive evidence-based ASD specific interventions (Wong et al., 2014, 2015).

2.6 The Impact of Symptom Variation on Diagnosis

ASD is characterised by significant heterogeneity in: aetiology; neurobiology; symptom onset and trajectory; degree of symptom severity; cognitive, language and adaptive impairment; degree of overlapping non-specific symptomology; and comorbidity with other development disorders (Zwaigenbaum et al., 2015c). This symptom variation can influence the timing of diagnosis. It is well established that the timing of identification and diagnosis for children across the full ASD continuum varies as a function of symptom severity (CDC, 2014; Chawarska et al., 2014; (Rosenberg, Landa, Law, Stuart & Law, 2011). Marked differences in symptom severity can range from a non-verbal child with cognitive impairment and severe social and behavioural symptoms, to a verbally fluent child with average to above average intelligence (Huerta & Lord, 2012). The spectrum of impairments associated with ASD results in significant variability in diagnostic age (CDC, 2014). Diagnostic trends show a strong association between symptom severity and diagnostic age. Children with more severe deficits are diagnosed much earlier compared to children with less severe ASD presentations (Mandell, Novak & Zubritsky, 2005; Rosenberg et al., 2011; Shattuck et al., 2009).

Signs of ASD can vary significantly in children. Some children can display clear symptom profiles from a very early age, while other children can present with less evident signs until after a period of neurotypical development followed by regression of skills (Chawarska et al., 2014). In other children, symptoms may progressively accumulate over time after an initial asymptomatic or prodromal
period, followed by an increase in symptoms later on in development (Estes et al., 2015). Some children with ASD can display a slow accumulation of symptoms up to the age of 18 months, while other children can display minimal prognostic signs until a rapid increase in symptoms begins after 36 months (Chawarska et al., 2014). Symptom expression can also change due to cognitive and language functioning (Bishop, Richler & Lord, 2006; Sigman & McGovern, 2005), co-occurring medical and psychiatric conditions, learning disabilities, and deficits in adaptive function (Coury, 2010; Fillipek et al., 1999; Osterling et al., 2002). Diagnosis earlier in life has also been associated with intellectual impairment, severe language deficits, increased presence of repetitive and stereotyped motor mannerisms, being male, and developmental regression (Chawarska et al., 2014; Mandell et al., 2005; Rosenberg, et al., 2011; Shattuck et al., 2009).

2.7 Stability of Diagnosis Under the Age of Three

The stability of an ASD diagnosis under the age of three years, that is, the rate of diagnostic confirmation at reassessment at a later age (Zwaigenbaum et al., 2015b), has been the subject of significant discussion and investigation. While debate remains regarding the earliest age an accurate ASD diagnosis can reliably be achieved, it is without question that diagnostic stability improves with age and symptom severity and that diagnosis from two years of age can be accurate and stable for the majority of children with ASD (Charman et al., 2005; Landa & Garrett-Mayer, 2006; Lord et al., 2006). Symptoms of ASD become evident and unfold within the first two to three years of life and varying developmental pathways to ASD can result in varying ages at timing of diagnosis (Chawarska et al., 2014; Gotham, Pickles & Lord, 2012). While some children may not meet full diagnostic criteria until later on in development, clear diagnostic profiles are evident in most
children by two to three years of age and could be diagnosed following comprehensive diagnostic evaluation (CDC, 2014; Coo et al., 2012).

Studies investigating the accuracy and stability of an ASD diagnosis have found between 75% to 100% of children diagnosed under two years of age (Chawarska et al., 2007; Guthrie et al., 2013; Kleinman et al., 2008; van Daalen et al., 2009), or between two to three years of age (Charman et al., 2005; Cox et al., 1999; Kleinman et al., 2008), have maintained their ASD diagnosis into later childhood. Diagnosis by the age of two to three years is regarded as feasible, reliable, valid and stable (CDC, 2014). Although more severe presentations of ASD display stronger rates of stability across time, between 80 to 100% of children diagnosed under three years of age, across the full continuum of mild to severe variants of ASD, are found to maintain their diagnosis (Woofenden, Sarkozy, Ridley & Williams, 2012; Zwaigenbaum et al., 2015a).

2.8 The Diagnostic Gap

The period of time between when ASD can be identified (in most children by two to three years of age) and when actual diagnosis occurs (in most children after four years of age) is referred to as a diagnostic gap (Shattuck et al., 2009, p.475). Again, although for some children it is possible that diagnosis by the age of three years may not be achievable, as full symptomatic profiles required for diagnosis may not have emerged completely, for a large proportion of children with ASD, the timing of final diagnosis is occurring well after emergence of complete symptomatic profiles (CDC, 2014; Shattuck et al., 2009). Studies investigating the timing between parental expression of initial concerns and final ASD diagnosis, suggest the presence of a diagnostic gap for a large proportion of children with ASD. Many children with ASD are being diagnosed at least two years after parents first suspect and raise
concerns of atypical development and signs of ASD (Gray & Tonge, 2001; Sivberg, 2003; Wiggins, Baio & Rice, 2006).

In a recent examination of 15,000 Australian children diagnosed with ASD under the age of seven, less than three percent were diagnosed by age two, the average age of diagnosis was approximately four years, and the most frequently reported diagnostic age was closer to six years (Bent et al., 2015). Similar diagnostic trends have been observed internationally. In the United States of America (USA), less than one fifth of children who received an ASD diagnosis were diagnosed before their third birthday with the median age of diagnosis reported to be older than four years (CDC, 2014). A study investigating the timing of identification among 2,568 children with ASD across 13 different sites in the USA, found a median age of diagnosis of 5.7 years, with a suggested diagnostic gap that could range from 2.7-3.7 years (Shattuck et al., 2009). A survey of 2000 families in the United Kingdom (Kennedy, 2013) also found that over half the families reported waiting up to five years or longer for an ASD diagnosis. Only 38% of children from the surveyed families received a diagnosis before their fifth birthday, despite more than three quarters of parents reporting suspicions of ASD symptoms well before this age. In a study of 6,214 parents of children with ASD, although the average age of initial parental concern was 19.6 months, the average age of diagnosis was not reported until 57.7 months (Rosenberg et al., 2011).

The diagnostic gap is likely due to a combination of factors that have an additive contribution to delaying final diagnostic verification. Although the timing of ASD identification can be influenced by the timing of full symptom presentation to meet diagnostic criteria, it is generally accepted that comprehensive diagnostic evaluation can yield correct diagnoses in most children with ASD from two to three
years of age (CDC, 2014). In presentations when diagnostic ascertainment can be reached by age two to three years, accurate and timely referral of these children for comprehensive diagnostic evaluation is of great importance to initiate the diagnostic process. These children are regarded as already displaying a constellation of behavioural markers of ASD at this early age (Estes et al., 2015; Ozonoff et al., 2010; Zwaigenbaum et al., 2005) and with timely referral, could be evaluated and commence intervention. For those children with a subtle symptomatic profile, again, accurate detection and timely referral can initiate earlier evaluation or developmental surveillance under the care of a trained practitioner, and identification of suitable pathways for intervention. With the median age of timing of initial diagnostic evaluation for children with ASD not until 44 months of age (CDC, 2014), it is likely that the timing of referral of children for comprehensive diagnostic evaluation by their general practitioner is implicated in contributing to the average length of diagnostic gap.

2.8.1 The impact of general practitioner response to parental concerns.

The general practitioner plays a critical role in the timely detection of children in need of further ASD diagnostic evaluation. They frequently act as first responders to parental concerns, first observers of ASD behavioural markers (Carbone et al., 2010) and serve as gatekeepers for the referral of children for comprehensive diagnostic evaluation (AABASD, 2012). In most instances, they are in a unique position to conduct developmental surveillance of children during a developmental period where ASD symptoms emerge and accumulate, which can inform the early detection of the presence of an ASD trajectory and initiate earlier referral for comprehensive diagnostic evaluation (CDC, 2014). Yet, with the timing of first evaluation for ASD often delayed until well after a child’s third birthday, general
practitioners may not be responding to early parent-report or detecting early behavioural manifestations of ASD.

It is well documented that at least 50% of parents of children with ASD present to the general practitioner with concerns that are specific to ASD related domains within the first year of life (Chawarska et al., 2007; Nadel & Poss, 2007; Ozonoff et al., 2008; Shattuck et al., 2009). This increases to up to 80% by the time of the second birthday (Baghdadli, Picot, Pascal, Pry & Aussilloux, 2003; De Giacomo & Fombonne, 1998; Kozlowski et al., 2011), and up to 93% by the third birthday (Matson, Wilkins & Gonzalez, 2008). Parental report of concerns at 12 months of age can be highly predictive of an eventual ASD diagnosis (Hess & Landa, 2012; Ozonoff et al., 2009; Sacrey et al., 2015; Wetherby et al., 2009), particularly in high-risk siblings where parental concern can predict up to 95% of children who receive a later ASD diagnosis (Rogers et al., 1992). Parental detection of atypical behaviours in their children who go on to receive an ASD diagnosis can occur significantly earlier than parents of children with an intellectual impairment and other developmental delays and disabilities (De Giacomo & Fombonne, 1998; Kozlowski et al., 2011). Parents of children with ASD can be adept in the early detection and report of behavioural manifestations across the full ASD continuum. Parental detection of ASD symptoms can be accurate in both children with more and less severe presentations of ASD (Chawarska et al., 2007; De Giacomo & Fombonne, 1998).

Although the majority of parents of children with ASD first note and report concerns within the first two years of life, how the general practitioner responds or elicits this information can impact on the average length of diagnostic gap (Guerrero et al., 2011; Zuckerman et al., 2015). Previous investigations of routine health check-
ups have found that not all general practitioners immediately provide a proactive response to parental concerns or instigate immediate referral for comprehensive diagnostic evaluation (Daniels & Mandell, 2014; Guerrero et al., 2011; Zuckerman et al., 2015) or take parent concerns seriously (Howlin & More, 1997). Rather, some may instead reassure parents regarding their child’s development or provide passive responses, such as adopting a watch and wait approach, monitoring the child and delaying referral for diagnostic evaluation until ASD symptoms become more clear (Rutter, 2006). This watch and wait approach may be suitable in instances when there are insufficient signs to flag ASD and therefore monitoring the child for ASD would be preferable to prevent potentially unnecessary parental stress and referral for diagnostic evaluations that may not be needed. However, this watch and wait approach can occur even in the presence of overt ASD specific symptoms and therefore can delay referral to trained practitioners who may have been able to accurately identify ASD symptoms to provide a timely diagnosis (Daniels & Mandell, 2014; Guerrero et al., 2011; Zuckerman et al., 2015). Parents of children with ASD have been found to be less likely to receive an active response from the general practitioner compared to parents of children with other developmental disabilities, restricting the opportunity for parental concerns to be confirmed and early referral for comprehensive diagnostic evaluation (Zuckerman et al., 2015).

In an investigation of practitioner responses to parental concerns of children with ASD, less than half of the children had been administered a developmental assessment, referral for comprehensive diagnostic evaluation was made only just over half of the time, and nearly one third of children did not receive a proactive response (Zuckerman et al., 2015). The frequency of reassuring responses was high. Almost half of parents had been told their child would “grow out of it”, just over
40% were told it was “too early to tell if anything was wrong” and just over 30% were told that there was “nothing wrong with their child / the child’s behaviour was normal” (Zuckerman et al., 2015). Final ASD diagnosis occurred on average three years after parents’ initial expression of concerns (Zuckerman et al., 2015). These results suggest that a portion of the diagnostic gap may be attributed to general practitioners failing to actively respond to initial parental concerns and to initiate referral for comprehensive diagnostic evaluation at first report of ASD symptom presentation.

Although some parents of children with ASD can be skilled in the detection of developmental deviance and proactive in sharing concerns with their general practitioner, other parents may not recognise or report signs of atypicality as early on. Parents who have heightened worry due to already having a child with ASD can be more sensitised to developmental deviance and therefore tend to report concerns earlier in development (Galscoe, 1999; Ozonoff et al., 2009; Zwaigenbaum et al., 2005). A study investigating the timing of parental report of concerns regarding their children with ASD found, while parents of children who already have a child diagnosed with ASD can report concerns regarding their child as early as ten months of age, first time parents can report concerns later, at around 16 months of age, as can parents who already have children with neurotypical development, who report concerns on average at 14 months of age (Herlihy, Knoch, Vibert & Fein, 2015). Sociodemographic factors can also impact on the timing of age at first parental report. Parents from developing countries, and from backgrounds with low income and low education tend to report concerns later on in their child’s life (Reich, 2005). However, the accuracy of reported concerns does not differ between parents on the basis of education, socioeconomic status or parent experience as a function of having
other children (Rogers et al., 1992). Parental under-report and/or denial of symptoms and developmental deviance can also impact on the timing of parental report (De Giacomo & Fombonne, 1998).

Timely general practitioner response to parental concerns combined with general practitioner elicitation of specific developmental history from parents, is likely necessary to reduce the average length of a diagnostic gap. Proactive response to parental concerns during routine health check-ups will likely yield critical information to initiate identification of developmental deviance, leading to earlier referral for diagnostic evaluation and diagnosis (Morelli et al., 2014). However, parents may not always detect the full range of ASD symptoms in their child and may have difficulty in recognition of subtle deficits and impairments associated with ASD (Le Couteur, Haden, Hammal & McConachie, 2008; Lemler, 2012). Parents are not trained experts in child development, or in the earliest manifestations of ASD, which can lead to under reporting of symptoms (De Giacomo & Fombonne, 1998; Le Couteur et al., 2008). In these instances, practitioner detection might be required to identify children displaying behavioural markers of ASD to initiate further investigation and potential referral for comprehensive diagnostic evaluation. However, a number of practitioner difficulties in detection of ASD traits may also contribute to the average length of a diagnostic gap.

### 2.8.2 The impact of general practitioner detection of ASD symptoms.

Although comprehensive diagnostic evaluation can be proficient in the clinical detection of children with ASD, detection by untrained observers (Ozonoff et al., 2008) and detection during brief clinical observations can be difficult (Gabrielsen et al., 2015). Even trained raters can fail to detect children with ASD during a brief clinical observation (Gabrielsen et al., 2015). A recent study conducted by
Gabrielsen and colleagues (2015) found trained raters missed detecting just over one third of children already diagnosed with ASD ($n = 42$) during a ten-minute clinical observation. During these brief clinical observations, children with ASD displayed infrequent atypical behaviours or signs of ASD, instead predominately displaying a range of neurotypical behaviours for 89% of the time. Although, compared to children with a language deficit and neurotypical development, the children with ASD did display significantly higher rates of atypical behaviour and significantly lower rates of neurotypical behaviours, the overall ratio of neurotypical to atypical behaviours in the children with ASD misguided practitioner detection. The infrequent expression of behavioural markers of ASD during a ten-minute time sample made detection of children with ASD very difficult, especially in younger children who were significantly less likely to be detected by trained raters. Reduced symptom expression during brief behavioural samples likely means that general practitioners are observing inaccurate samples of current behaviours during their brief consultations (Halfon, Stevens, Larson & Olson, 2011).

The general practitioner may only observe snap shots of current behaviours, which may impede knowledge of full symptom presentation because ASD symptom manifestation can vary significantly across contexts (Hepburn & Moody, 2011; Klin, Saulnier, Tsatsanis & Volkmar, 2005). Children with ASD can exhibit varying degrees of neurotypical and atypical behaviour as a function of differing situations, environments and people (Hepburn & Moody, 2011). General practitioners observe children during structured environments and interactions, which can inhibit the expression of ASD traits and therefore restrict the general practitioner’s capacity to detect symptoms (Klin et al., 2005; Lemler, 2012, Wetherby et al., 2009). General practitioners also share a different relationship with the child compared to the parent,
which could impede or exacerbate the expression of certain behaviours and symptoms during clinical consultations (Le Couteur et al., 2008; Lemler, 2012).

Although general practitioners are highly trained medical professionals, significant discrepancies in their knowledge of ASD compared to a trained practitioner in the specialised field of ASD can contribute to the average length of a diagnostic gap. General practitioners without specialised ASD training can be uncertain of the early signs of milder presentations of ASD and can also find it difficult to distinguish symptoms of ASD from other developmental disorders and disabilities with overlapping symptom profiles (Coo et al., 2012; Shattuck et al., 2009). General practitioner uncertainty and difficulty in detecting children displaying ASD symptoms can also lead to implementation of a watch and wait approach (Dosreis, Weiner, Johnson & Newschaffer, 2006; Lord, 1995; Rutter, 2006).

Given that it is difficult to detect ASD symptom expression during brief clinical observations, and with the expression of neurotypical behaviours often more frequently displayed in children with ASD than atypical behaviours (Gabrielsen et al., 2015), general practitioners are likely to be misguided in their risk ascertainment of ASD, thereby misleading their referral impressions for children in need of comprehensive diagnostic evaluation for ASD. The precision of detection of early behavioural manifestations of ASD by general practitioners, particularly during their brief encounters, is likely hindered due to time constraints and level of expertise in the quantification of symptoms to ascertain accurate diagnostic profiles. Therefore, children with ASD are likely to be under-identified and their timely and accurate referral for comprehensive diagnostic evaluation therefore delayed, further contributing to the average length of a diagnostic gap.
2.8.3 The impact of waiting times.

Once a child has been screened and then referred for comprehensive diagnostic evaluation for ASD, the likelihood of lengthy waiting periods further contributes to the average length of a diagnostic gap. In Australia, waiting periods for ASD diagnostic evaluation can range from six weeks to eight months in the private sector and between 14 months to two years in the public sector (SWAP, 2012; WADDF, 2012). For many Australian families, diagnostic evaluations through the public system would be the only available option due to the high fees and limited Medicare rebates available in the private sector. Clear disparities in the length of diagnostic gap due to waiting periods implicate sociodemographic factors as likely contributing to the diagnostic gap. Level of family income has been associated with the timing of diagnosis, with children from lower income families more likely to be diagnosed much later in life (Mandell et al., 2005). Although some investigations have found race and ethnicity may also impact on the length of diagnostic gap, with Caucasian children found to enter the diagnostic process earlier (Mandell et al., 2005), other examinations have found comparable lengths of a diagnostic gap (Wiggins et al., 2006).

By the time children with ASD undergo their initial diagnostic evaluation, they have already most likely experienced a diagnostic gap. The magnitude of this gap likely varies as a function of: timing of initial parental expression of concerns and practitioner provision of active rather than passive response to these concerns; practitioner precision in detecting ASD behavioural markers and screening of children for ASD during routine health-care visits to initiate timely referral for diagnostic evaluation; and the length of waiting periods. At this stage of the
diagnostic pathway variations in clinician evaluation procedures may further contribute to the average length of a diagnostic gap.

2.8.4 The impact of variations in diagnostic evaluations.

Although best practice guidelines have been developed to guide assessment procedures for children with ASD to optimise diagnostic efficiency and accuracy, they are not mandated, prescriptive or intended to define the sole standard of evaluation (Volkmar et al., 2014). This can lead to significant variations in assessment protocols and diagnostic pathways of children with ASD. While children with clear-cut presentations of ASD can correctly be identified by the age of two years on the basis of clinical judgment alone (McConachie, Le Couteur & Honey, 2005; Shattuck et al., 2009), children with subtle presentations of ASD can be more difficult to detect and the use of standardised instruments can help to guide practitioners in their evaluation of determining whether established clinical thresholds for diagnosis are met (Lord et al., 2012; Shattuck et al., 2009). Although clinical judgement in clear-cut cases may expedite the evaluation process and support the ultimate goal of practitioners to deliver a timely cost effective ASD diagnosis, in less clear-cut presentations, the use of clinical judgement in the absence of standardised instruments can contribute to the average length of a diagnostic gap due to practitioner uncertainty (Shattuck et al., 2009).

Practitioner uncertainty can also lead to implementation of a watch and wait approach, where practitioners delay the provision of a diagnosis until they can be more certain of its accuracy. In some ASD presentations, a watch and wait approach to diagnosis may be appropriate. For a portion of children with ASD, full symptom manifestation to reach diagnostic ascertainment may not occur until later on in development (Estes et al., 2015; Guthrie et al., 2013). Therefore, an ASD diagnosis
may not have been achievable or appropriate as some children may not present with the full range of symptoms required to reach diagnostic thresholds. However, diagnostic clarity may be improved with the use of standardised tools, which could help toward reaching a reliable diagnosis earlier (Lord et al., 2012).

Reliance on clinical judgement without the use of standardised measures can result in significant variations in final diagnostic outcomes. In an investigation of children diagnosed with ASD \((n = 2102)\), between the ages of four and 18 years, when clinical judgement was used in isolation to provide an ASD diagnosis, practitioners varied in the type of ASD diagnosis (e.g., DSM-IV-TR AD, AS or PDD-NOS) they recommended (Lord et al., 2012). Comparatively, consistent diagnostic recommendations were reached when the ADOS (Lord et al., 1999) and ADI-R (Rutter et al., 2003) were used. This result suggests that a child’s ASD diagnosis, in regard to the degree of symptom severity that is prescribed in the new diagnostic criteria, could also vary between practitioners if clinical judgement is used in isolation. If this is the case, it is probable that diagnostic variation is present between children with ASD when there are variations from best practice guidelines.

Previous investigations examining the use of standardised instruments in clinical practice suggest variations in the implementation of best practice guidelines likely characterise the assessment process for many children with ASD (Randall et al., 2016; Skellern, McDowell & Schluter, 2005; Wiggins et al., 2006). In an examination of children diagnosed with ASD in the United States \((n = 115)\), 70% of the children had been diagnosed without the use of an ASD gold standard instrument or an alternative instrument (Wiggins et al., 2006). In the 30% of cases where a standardised instrument was reportedly used, the ADOS (Lord et al., 1999) was administered in only seven percent of assessment cases while the ADI-R (Rutter et
al., 2003) was reported as never used. When practitioners did report use of an alternative instrument, the Childhood Autism Rating Scale (CARS; Schopler, Reichler & Renner, 1988), which is a behavioural rating scale based on clinician observations of unstructured activities in children from two years of age, was used in 68% of assessments. The CARS (Schopler et al., 1988) is a brief, easy to use instrument that requires minimal training and is less expensive than the ADI-R (Rutter et al., 2003) or ADOS (Lord et al., 1999). While this may explain its use in clinical practice where time constraints could impede comprehensive evaluation procedures (Wiggins et al., 2006), the CARS (Schopler et al., 1988) may not adequately inform the early differential diagnosis of ASD. The CARS (Schopler et al., 1988) can be over inclusive of children with other developmental delays and disabilities which may misguide practitioners in their evaluation procedures and contribute to the diagnostic gap (Lord, 1995; Perry et al., 2005).

The assessment and diagnostic evaluation of children with ASD has previously been characterised by variation and a reliance on informal and unstructured ASD assessments (Randall et al., 2016; Skellern et al., 2005). In an examination of Queensland paediatricians and child psychiatrists (n = 105) involved in the evaluation of children for ASD, reported use of gold standard assessment instruments, such as the ADOS (Lord et al., 1999) and ADI-R (Rutter et al., 2003), was low, with only 19% of practitioners reporting using these instruments during their assessment process (Skellern et al., 2005). Again, the most frequently reported instrument used in diagnostic evaluations for children with ASD was the CARS (Schopler et al., 1988). A recent survey of Australian paediatricians involved in the diagnosis of ASD (n = 124) also found variation in reported ASD diagnostic process and infrequent use of standardised instruments, with most paediatricians reporting
rarely or never using a standardised observational (70%) or parent-report (51%) instrument (Randall et al., 2016). Again, the CARS (Schopler et al., 1988) was the most frequently reported instrument used to guide diagnostic evaluations. Variation in diagnostic evaluations has also been found between between private and public sectors (SWAP, 2012). Within the private sector, perhaps due to the significant costs involved for families in undertaking gold standard assessment measures, their use has been reported to be less likely (SWAP, 2012). Although within public settings, where government funded assessments are provided and therefore more likely, waiting periods can span up to 14 months, adding considerable time to the average length of a diagnostic gap for families who cannot afford private assessments (SWAP, 2012).

In some cases, deviation from best practice guidelines may have also been attributed to the lack of available resources for use in children under two years of age. Until recently, the ADOS (Lord et al., 1999) and ADI-R (Rutter et al., 2003) were both designed for use in children over the age of two years and had been associated with high misclassification errors in children under three years of age (Allen, Silove, Williams & Hutchins, 2007; Chawarska et al., 2007; Gray et al., 2008; Risi et al., 2006; Scambler, Hepburn & Rogers, 2006; Ventola et al., 2007; Zwaigenbaum & Stone, 2006). However, given that: the the majority of children undergo their initial diagnostic age evaluation for ASD around 44 months of age (CDC, 2014); at the time of the survey the average age of initial assessment for ASD was likely later; the timing of ASD identification has improved significantly over the past decade (CDC, 2014); and both the ADOS (Lord et al., 1999) and the ADI-R (Rutter et al., 2003) display strong psychometric properties in children from three years of age, a lack of available resources for use in children under the age of two
years may not have had a strong influence on practitioners reasons for variation from
best practice guidelines. With the release of both the ADOS-2 (Lord et al., 2012) and
the revised ADI-R algorithms (Kim et al., 2013), practitioners will now have a
standardised parent-report and clinician-observation instrument for use in children
from 12 months of age. While the availability of these instruments may help to guide
diagnostic evaluation in younger children, it is likely that their availability may not
have a significant overall impact on reducing the average length of a diagnostic gap
unless other improvements are also made.

2.8.5 The impact of discrepancies between parent and practitioner ratings
of ASD symptoms.

Significant variations between parent-report and clinician quantification of
ASD symptoms have the potential to increase the average length of a diagnostic gap
(De Giacomo & Fombonne, 1998; Lemler, 2012). Environmental discrepancies and
differences in knowledge and expertise between parents and clinicians likely explain
how informants can both miss detection of ASD behavioural indicators but also
provide potentially more accurate descriptions on the presence of other symptoms
within specific ASD domains (Lemler, 2012). Parents have been found to be less
likely to detect and/or under-report symptoms, particularly in the social and
communication domains, and can be more likely to detect or over-report symptoms
in the behavioural domain (Lemler, 2012; Wetherby et al., 2009). Clinicians can be
less likely to detect behavioural symptoms but more likely to detect symptoms within
the social communication domain (Filipek et al., 1999; Le Couteur et al., 2008;
Lemler, 2012; Pilowsky, Yirmiya, Shulman & Dover, 1998; Wiggins & Robins,
2008). Reliance on a single informant could therefore increase the risk of inaccurate
or impartial symptom measurement and increase misclassification.
Parent-report and practitioner rating of ASD behavioural markers on standardised instruments can result in different ASD categorisations in the same child. Poor diagnostic agreement between the parent rated ADI-R (Rutter et al., 2003) and clinician rated ADOS (Lord et al., 1999) has been documented and suggests parents and clinicians, to some degree, provide different ratings across different dimensions of ASD (Le Couteur et al., 2008; Lemler, 2012; Pilowsky et al., 1998; Risi et al., 2006; Ventola et al., 2006; Wiggins & Robins, 2008). When the ADOS (Lord et al., 1999) and ADI-R (Rutter et al., 2003) are used as a single instrument to quantify ASD symptoms, both can over or underscore symptomology and produce misclassification errors (Le Couteur et al., 2008; Lemler, 2012; Pilowsky et al., 1998; Risi et al., 2006; Ventola et al., 2006; Wiggins & Robins, 2008). Similar discrepancies have been found between other parent-report instruments and direct clinician-observation measures (Saemundsen et al., 2003; Stone, Hoffman, Lewis & Ousley, 1994; Wiggins & Robins, 2008). Although a proportion of discrepant ratings between instruments may be attributed to the unique psychometric properties of the instrument, how ASD is operationalised and measured, and the cut-off score that is used (García-Primo et al., 2014), it is likely that a large proportion of variance is explained by respondent and environmental characteristics (Lemler, 2012). In order to accurately capture the full continuum of ASD symptomology and to gain knowledge of symptom expression across time, combining parent-report with clinical observation may be critical to inform diagnostic recommendations.

Aggregating data from parent-report and clinician-observation has a complimentary effect on contributing to diagnostic formulation and confirmation (Le Couteur et al., 2008), with combined use generally recommended and considered
gold standard (Zander, Sturm & Bölte, 2015). The combined use of parent-report and clinician-observation provide additive contributions that can improve diagnostic validity. When information from the ADI-R (Rutter et al., 2003) and ADOS (Lord et al., 1999) has been considered together, diagnostic accuracy can improve and misclassification errors are reduced. A number of studies investigating the combined use of the ADOS (Lord et al., 1999) and ADI-R (Rutter et al., 2003) report well-balanced sensitivities (i.e., a measurement of the correct classification of children with ASD) and specificities (i.e., a measurement of the correct classification of children without ASD) ranging from 77% to 80% and higher, compared to separate instrument use, which resulted in a significant loss of specificity (Kim & Lord, 2012; Risi et al., 2006; Zander et al., 2015).

Discrepant rating of child symptoms is not unique to ASD or between parent and clinician informant sources. Discordance between informant ratings has also been well documented in the child psychopathology literature. Significant differences in the ratings of child symptoms of conduct disorder, attention deficit and hyperactivity disorder, emotional disorders, social functioning, personality, and self-esteem, can occur as a function of informant source differences (Brown et al., 2006; De Los Reyes, Alfano & Beidel, 2011; De Pauw et al., 2009). Low inter-rater agreement has been found between parents and teachers (Brown et al., 2006), mothers and fathers (Gupta, Lausten & Pozzoli, 2012), and even between trained clinicians (Andersson et al., 2013). While it is generally accepted that informant source discrepancies do not signify errors or incorrect or correct observations (Achenbach, 2006; Brown et al., 2006) a number of potential biases have been documented as influencing informant ratings. These can include memory and evaluative biases, halo-effects, and social desirability (De Pauw et al., 2009).
Combining multi-informant ratings in the assessment of children is generally regarded as being more sensitive than using a single informant method and can improve the accuracy of symptom measurement and classification for a wide range of child assessment measures and conditions (Goodman, Renfrew & Mullick, 2000).

2.9 Improving General Practitioner Referrals to Reduce the length of Diagnostic Gap

It is likely that, while ASD diagnosis remains reliant on behavioural markers, diagnostic challenges and gaps may ensue for a number of children depending on symptom manifestation. However, for the majority of children with ASD, referral for diagnostic evaluation before their third birthday, could, in most instances, result in a stable ASD diagnosis, and for some children, referral before their second birthday could yield a similar outcome (CDC, 2014). A potential key component to reducing the average length of a diagnostic gap may therefore be initiating the timely and accurate referral of children for ASD diagnostic evaluation. The accuracy of referrals is of great importance. The over-referral of children with non-specific ASD symptoms could: increase waiting times for children who do require further evaluation of ASD and place further stress on already constrained systems; initiate unnecessary timely and expensive ASD specific assessments; delay assessments for other developmental delays and disabilities; and potentially increase undue parental distress (Bölte et al., 2013; Horlin, Falkmer, Parsons, Albrecht & Falkmer, 2014; Lipkin & Hyman, 2011; Shattuck & Grosse, 2007). The under-referral of children with ASD could delay diagnosis and restrict access to resources and interventions services that may help to improve developmental outcomes (Reichow et al., 2012).

As mentioned earlier, general practitioners can play a critical role in the identification and referral of children in need of diagnostic evaluation for ASD
(Carbone et al., 2010). However, their precision in eliciting ASD specific information from parents (Zuckerman et al., 2015), and in quantifying symptoms of ASD to ascertain risk (Gabrielsen et al., 2015), can impact on referral accuracy. General practitioners are likely in need of training to detect red flags of a symptomatic ASD profile and ASD specific instruments to guide their accurate detection and referral of children for ASD diagnostic evaluation (Charak & Stella, 2001-2002).

2.10 ASD Markers in Children Under 12 Months of Age

Outcomes from neurobiological studies implicate possible underlying pathological neurobiological factors in the timing of ASD symptom emergence (Courchesne, Carper & Akshoomoff, 2003; Lenroot & Yeung, 2013). Neurobiological studies have identified initial signs of early biological differences in children who go on to be diagnosed with ASD, with early abnormal brain growth, characterised by accelerated overgrowth in brain volume and associated larger head circumference, potential early signs (Courchesne et al., 2003; Nordahl et al., 2011).

In a longitudinal study of children from birth to five years of age (Courchesne et al., 2003), compared to neurotypical children, children who received a diagnosis of ASD displayed a trajectory of brain growth across the first few years of life, with significantly smaller head circumference from birth to the first year birthday, followed by brain volume overgrowth by 14 months of age. However, approximately 40% of the sample did not display this pattern of growth, which suggests variation in biological features of ASD could be present. These results have been replicated in a series of other studies (Dawson et al., 2007; Hazlett et al., 2005).

It appears that this pattern of accelerated brain overgrowth during the first year of life may be associated with an increased number of neurons and possible defects
in pruning (a process of synapse elimination which begins at birth and is complete in early adulthood), and apoptosis (a form of cell death as a normal part of development) (Courchesne et al., 2007; Courchesne et al., 2011). Although little is known on how ASD symptom onset maps onto abnormal brain growth, variations in growth between children with ASD infer distinct neural and biological phenotypes (Nordahl et al., 2011). Accelerated brain growth during the first two years of life in children with ASD may mirror the onset of behavioural symptoms with variations in brain growth amongst children with ASD possibly accounting for variations in symptom onset and severity (Houenou & Chaste, 2015). Although outcomes from neurobiological studies are promising, they do not yet support routine neuroimaging as a method of detection due to significant heterogeneity in findings. Therefore, identification of the early behavioural markers of ASD is required.

Although ASD has historically been thought to be present from birth (Kanner, 1943), the behavioural manifestations of ASD do not appear to be present from birth. Research is yet to identify definitive behavioural and diagnostic markers for ASD within the first 12 months of life (Estes et al., 2015; Zwaigenbaum et al., 2015c). At least within the first six months of life signs of ASD appear minimal if not absent, suggestive of a possible prodromal period (Estes et al., 2015; Ozonoff et al., 2010; Zwaigenbaum et al., 2005). Although symptomatic profiles begin to emerge after six months of age, it is not until 12 months of age that markers become more evident (Barbaro & Dissanyake, 2009; Jones et al., 2014; Yirmiya & Charman, 2010). The distinguishing social communication deficits and repetitive and stereotyped behavioural features of ASD required to fulfil diagnostic criteria appear to become more marked after a child’s first birthday (Brian et al., 2008; Elison et al., 2014;
Filliter et al., 2015; Gammer et al., 2015; Ozonoff et al., 2008; Sullivan et al., 2007; Wolff et al., 2014).

The past decade has seen an exponential growth in studies of the earliest detectable signs of ASD and early risk markers for ASD. Converging behavioural findings from prospective studies of high risk infants and siblings of children with ASD, retrospective videotape analysis and parental report, and developmental surveillance and screening studies, suggest a prodromal period in the first six months of life, followed by emergence of symptoms that continue to accumulate across the next two to three years (Estes et al., 2015; Ozonoff et al., 2010; Zwaigenbaum et al., 2005). Between six months to 12 months of age, a number of potential precursors and emergent signs of ASD become apparent including: reduced motor control (Flanagan, Landa, Bhat & Bauman, 2012); difficulties disengaging visual attention, referred to as “sticky attention” (Elison et al., 2013; Sacrey, Bryson & Zwaigenbaum, 2013); deficits in social attention and social orienting skills, characterised by preferences for non social stimuli and reduced reference to the eyes and face (Chawarska, Macari & Shic, 2013; Klin, 2013; Maestro et al., 2001, 2005; Merin et al., 2007; Ozonoff et al., 2008, 2010); reduced social smiling (Zwaigenbaum et al., 2005); atypical sensory motor development (Estes et al., 2015) and sensory behaviours, characterised by intense visual preoccupation with objects; and temperament dysregulation, characterised by increased emotional distress (Bryson et al., 2007; Zwaigenbaum et al., 2005). In a seminal paper from Zwaigenbaum and colleagues (2005) children who later went on to receive an ASD diagnosis displayed a number of emerging features from six months of age. These early features included: atypicalities in eye contact; visual tracking; disengagement of visual attention; orienting to name; social smiling; social interest; decreased
expression of positive affect by 12 months; imitation; and prolonged latency to
disengage visual attention, “sticky attention”; sensory-oriented behaviours; object
fixation; reactivity; extreme emotional distress reactions which had been preceded by
passivity in the first six months; delayed expressive and receptive language.

2.11 ASD Markers in Children Between 12-24 Months of Age

By 12 months of age, symptoms of ASD are thought to have emerged in most
children and to have become more evident (Barbaro & Dissanyake, 2009; Jones et
al., 2014; Ozonoff et al., 2010; Yirmiya & Charman, 2010). By the first birthday, a
number of the emergent signs first observed in infants at six to twelve months of age,
become more apparent and begin to distinguish children with ASD from other groups
of children (Ozonoff et al., 2010). At this age, and up to the second birthday, a
constellation of key behavioural markers begins to distinguish children who go on to
receive a diagnosis of ASD from children who do not, including: impaired social
attention and communication skills; increased repetitive behaviour with objects;
temperament dysregulation; and increased sensory atypicalities (Barbaro &
Dissanyake, 2012; Bryson et al., 2007; Chawarska et al., 2013; Elison et al., 2013;
Jones et al., 2014; Zwaigenbaum et al., 2005). At 12 months of age impairments in:
pointing; eye contact; response to name; imitation; and gestures, have been found to
be key distinguishing features of ASD (Barbaro & Dissanyake, 2012). By 18-24
months of age: reduced showing; pretend play; response to and initiation of joint
attention; and impaired gaze emerge as key behavioural markers (Barbaro &
Dissanyake, 2010, 2012; Landa et al., 2007; Sullivan et al., 2007).

High-risk infant sibling studies have also provided clues on ASD symptom
emergence. A prospective investigation of nine siblings of children with ASD found
that although earlier symptom onset was associated with increased level of symptom
severities, all children displayed emergent signs of ASD from 12 months of age regardless of level of symptom severity and degree of cognitive impairment (Bryson et al., 2007). From 12 months of age, siblings of children with ASD displayed a combination of impairments in social attention and communication, characterised by a lack of interest/pleasure in, and/or self-initiated contact with others, and behavioural and sensory symptoms, characterised by increased visual fixation, sensory atypicalities, repetitive behaviours, and temperament dysregulation, characterised by marked irritability, intolerance for intrusion, proneness to emotional distress, difficulties in emotional regulation and negative affect (Bryson et al., 2007).

The synthesised outcomes from prospective longitudinal studies implicate a developmental trajectory of behavioural markers of ASD, which is seemingly characterised by an initial prodromal period in the first six months, followed by a period of decline in skills and growth of symptoms. By 18 months of age, overt symptoms within key ASD domains become even more apparent, including indicators within the social communication (Bedford et al., 2012; Cornew, Dobbins, Akshoomoff, McCleery & Carver, 2012), behavioural (Christensen et al., 2010), and sensory domains (Maestro et al., 2005).

Although for some children with ASD, symptomatic profiles will be clearly evident early on, for others, subtle features will emerge and require careful monitoring and detection. ASD is thought to have multiple behavioural phenotypes (Nordahl et al., 2011), with the timing and progression of ASD symptom onset variable and seemingly influenced by ASD symptom severity. Children with more severe presentations of ASD appear to be more likely on the trajectory of ASD earlier on, and those children with less severe presentations, display later symptom onset (Estes et al., 2015). This variation in clinical presentation of ASD likely means
the timing of detection will also vary, with some children with ASD more likely to be detected earlier on while others more likely to be detected in later childhood.

2.12 Screening for Symptomatic ASD Profiles

Diagnosing ASD involves two steps: developmental screening and comprehensive diagnostic evaluation (CDC, 2015). Developmental screening initiates identification of early signs of ASD, which is critical to initiate comprehensive diagnostic evaluation and timely diagnosis (American Academy of Pediatrics News [AAP News], 2015). While screening children for ASD has been a controversial issue, and further research is required to address the limitations associated with existing instruments and to establish long term outcomes of early detection through screening programs (Al-Qabandi et al., 2011; Campos-Outcalt, 2011), screening children for detection of symptomatic ASD profiles is recommended (AAP, 2006; AAP News, 2016). Recursive screening processes, that involve repeat evaluations across development, can increase the opportunity to identify behavioural markers of ASD as early as possible (Oosterling et al., 2010b).

In the absence of a definitive test to confirm ASD, screening children may continue to carry a level of risk. However, screening can provide the opportunity to identify developmental deviance and to inform parents regarding their child’s development. Informing and educating parents regarding their child’s unique profile of strengths and weakness, possible symptoms of ASD, and the intervention options available, allows parents to be informed decision makers in their child’s development. As informed decision makers, parents may then decide whether to pursue a diagnostic evaluation for ASD or intervention. Some parents may be concerned of potential adverse effects associated with a diagnostic label (Filipek at al., 1999; Gray, 1993; Kinnear, Link, Ballan & Fischbach, 2016), and some parents
may perceive intervention as an attempt to change and normalise their child (O’Dell & Brownlow, 2015). However, most parents have expressed a desire to be informed of potential symptomatic profiles of ASD as early as possible (Marcus & Stone, 1993) and most parents report relief after the provision of a diagnosis (Midence & O’Neill, 1999). In order for parents to remain informed stakeholders in their child’s development it is important that they are informed as early as possible of the potential for ASD. Supporting parents to understand the potential benefits of early detection of ASD, and establishing a collaborative partnership between parents and practitioners will be important to support the mutual goal of working towards the best interest of the child and optimising child outcomes (Graf, 2015; Moon, 2010).

In order to expedite identification and diagnosis of ASD, the American Academy of Pediatrics (AAP, 2006) has recommended a series of steps including: routine developmental surveillance of all children at every primary health-care visit from infancy; use of developmental screening tools at nine, 18, 24 and 30 months; use of ASD specific screening tools at 18 months and 24 months; immediate screening with an ASD specific screening instrument if a child fails routine developmental surveillance or screening; and increased monitoring of siblings of children with ASD and high risk infants based on preterm birth or low birth weight or other reasons.

Routine developmental surveillance has been described as a flexible and continuous process of clinician observation of child behaviours during the provision of health-care, eliciting and responding to parental concerns, obtaining developmental history and attempting to identify children at risk of developmental delay without the use of screening instruments (AAP, 2006; Dworkin, 1993). While routine developmental surveillance is a method with considerable merit, as it
provides a continuous process of monitoring a child’s development and symptom expression across time, that without some form of a standardised screening instrument to guide the quantification of ASD specific makers, this approach to detection could miss too many children with ASD. This is because practitioners can find it difficult to detect children displaying symptomatic ASD profiles during routine brief clinical observations (Gabrielsen et al., 2015). Previous research has found that this is the case for both children with ASD and developmental delay, with the use of a developmental surveillance method in isolation associated with increased risk of false negatives (Glascoe, 2005).

Screening is described as the use of a brief standardised instrument that has reported high sensitivity and specificity for the population’s risk status (AAP, 2006). Recursive screening, or regular and repeated screening can improve the early detection of children with ASD (Lipkin & Hyman, 2011). ASD specific screening instruments can elicit information from parents regarding the presence of symptomatic traits across development and behavioural markers for practitioner observation. ASD specific screening instruments provide practitioners with a standardised inexpensive and quick method to quantify ASD symptoms, establish level of risk, inform referral, and guide initiation of timely and costly diagnostic evaluations (Zwaigenbaum et al., 2015b). Until such a time that a definitive test can detect ASD, screening instruments that can reliably and validly identify early ASD behavioural markers provide a method to improve detection (Lipkin & Hyman, 2011).

Although a number of ASD screening instruments have been developed and can help to inform decisions regarding referral and initiation of more comprehensive diagnostic evaluation in children from 24 months of age and up, their use in children
under 24 months of age remains questionable (Al-Qabandi et al., 2011; Barbaro & Dissanyake, 2012; Zwaigenbaum et al., 2015). Improving the accuracy and stability of screening instruments, particularly for use in children under 24 months of age is an important first step in reducing the average length of a diagnostic gap.

2.13 Evaluation of Screening Instruments in Children under 24 Months

Screening instruments are evaluated on a number of psychometric properties. Instrument sensitivity and specificity are believed to be the most important (Dixon et al., 2011; García-Primo et al., 2014). Screening instruments should demonstrate high instrument sensitivity, a measurement of the correct classification of children with ASD, the *true positive* rate, and high specificity, a measurement of the correct classification of children without ASD, the *true negative* rate (Dixon et al., 2011). Well-balanced sensitivity and specificity values above .70 are recommended to reduce misclassification of children with ASD, referred to as *false negative* rate, and without ASD, referred to as the *false positive* rate (Dumont-Mathieu & Fein, 2005). A trade off between instrument sensitivity and specificity is common (García-Primo et al., 2014). Screening instruments with high specificity often have low sensitivity, increasing the false-negative rate, while instruments with high sensitivity often have low specificity, increasing the false-positive rate (García-Primo et al., 2014). To minimise the risk of children with ASD failing to be detected, instrument sensitivity is suggested to be the measure of greatest concern when evaluating a screening instrument (Coonrod & Stone, 2005). However, instrument specificity is important to minimise the risk of falsely identifying children without ASD, which as noted previously can carry a number of consequences due to over inclusiveness (Charman & Gotham, 2013; Dixon et al., 2011). The context of the evaluation, specifically the
base rate of the condition being screened for, can also influence the priority placed on sensitivity versus specificity (Streiner, 2003).

Screening instruments are also evaluated on the degree to which they can prospectively measure the actual presence of ASD symptoms in children who screen positive or negative, a measurement of the positive predictive value (PPV), and the absence of ASD in children who screen positive or negative, a measurement of the negative predictive value (NPV) (Dixon et al., 2011). Negative and positive predictive values are expressed as a percentage, with values recommended to be close to 100% to demonstrate good instrument utility (Parikh, Mathai, Parikh, Chandra Sekhar & Thomas, 2008). In addition to evaluating a screening instrument based on its psychometric properties, screening instruments are also evaluated on their time and cost efficiency, ease of administration and scoring, and levels of instrument restriction, ascertained by the level of training required and practitioner expertise to administer and score the instrument (Dixon et al., 2011). In order to have high clinical utility, a screening instrument not only needs to accurately and rapidly quantify behavioural markers of ASD, but also needs to have a wide breadth of potential use by being inexpensive and easy to use with limited training and across multiple levels of practitioner profession.

Screening instruments have been developed to either screen all children regardless of risk, described as a level 1 screening instrument, or to screen children who have already been identified as at risk, either due to the expression of signs, developmental deviance, family history, or a positive screen on a level 1 instrument, described as a level 2 screening instrument (Zwaigenbaum et al., 2015b). Both level 1 and level 2 screening instruments predominately employ either parent-report, or clinician ratings that are based on either clinician questionnaire or administration of a
set of structured tasks. Rarely do screening instruments combine parent-report with clinician ratings into a single instrument. Parent-rated instruments are generally completed by parents without the clinician and can provide a time and cost efficient method of sourcing information regarding the child’s presentation of ASD symptoms across development and multiple contexts (Mackrides & Ryherd, 2011). Clinician rated instruments are directly administered by a clinician, where the clinician either rates the child’s behaviour during structured or unstructured clinical observations, or administers a series of tasks that are designed to trigger the behavioural markers for ASD. Compared to parent-rated instruments, clinician-rated instruments can provide more in-depth information in the context of expert knowledge, however they are also associated with increased cost and time to administer (Mackrides & Ryherd, 2011).

A comprehensive documentation of all of the existing screening instruments, and a review of the extensive body of literature critically evaluating and assessing their psychometric properties, is outside the scope of this thesis. In the past decade there has been prolific instrument development and evaluation (Dixon et al., 2011) and many comprehensive reviews of these measures have been published (AAP, 2006; Charak & Stella, 2001-2002; Hampton & Strand, 2015; Norris & Lecavalier, 2010; Zwaigenbaum et al., 2015b). A brief and non-exhaustive overview of existing instruments, specifically developed for use in children under the age of 24 months, will be provided in this section to describe instrument characteristics and psychometric properties. Table 2.1, which is presented after a review of the selected instruments, presents the instrument characteristics of the selected ASD screening instruments for children under the age of 24 months.
2.13.1 Combined parent-clinician screening instruments.

*Checklist for Autism in Toddlers (CHAT; Baron-Cohen, Allen & Gillberg, 1992).* The CHAT was the very first ASD specific screening instrument. The CHAT was a free to use level 1 screening instrument and was the only screening instrument that used a multi-method assessment approach to detect symptomatic profiles of ASD, combining parent-report (nine questions) and clinician-observation (five items where the practitioner describes observations of behaviours observed during direct interaction with the child) (Dixon et al., 2011). The CHAT was intended for use by trained health-care professionals to detect ASD features in children from 18 months of age. Administration time was approximately five to ten minutes. The CHAT contained five critical items measuring: pretend play; protodeclarative pointing; joint attention; social interest and social play. Failure on these items was indicative of a positive screen for high risk of ASD. Children who failed items measuring only protodeclarative pointing were considered medium risk. All other children were deemed low risk. If a child failed the CHAT, a second screen within one month was recommended. A positive screen at follow-up was to be used to initiate referral for diagnostic evaluation.

Despite its initial promise (Baron-Cohen et al., 1992), high misclassification limited its utility. Over 80% of children who had gone on to receive a diagnosis of ASD by the age of seven years had failed to be detected on the CHAT at their initial 18-month screen (Baird et al., 2000; Scambler, Rogers & Wehner, 2001). The CHAT has also been shown to be less sensitive to milder presentations of ASD, with children with DSM-IV-TR (APA, 2000) diagnoses of AS and PDD-NOS routinely failing to reach threshold for a positive screen (Baird et al., 2000). The CHAT has also been regarded to have a higher than acceptable false positive rate (Baird et al., 2000).
The CHAT has subsequently been revised into the Modified Checklist for Autism in Toddlers (M-CHAT; Robins, Fein & Barton, 1999). Other revisions have also been attempted including the Modified Checklist for Autism in Toddlers – revised with Follow-up (M-CHAT-R/F; Robins et al., 2014), and Quantitative Checklist for Autism in toddlers (Q-CHAT; Allison et al., 2008). There are now no screening tools that combine parent-report and clinician-administered items into one screening tool. The CHAT is not listed as an adequate screening tool for use within clinical practice (CDC, 2015).

### 2.13.2 Parent-report screening instruments

**Modified Checklist for Autism in Toddlers (M-CHAT; Robins et al., 1999).**

The M-CHAT is a free to use level 1 screening instrument. The M-CHAT is the revised version of the CHAT, with the most significant revision the removal of the clinician-observation section. It was argued by the authors of the M-CHAT that removal of the clinician rated component would reduce administration time and therefore increase the potential for improved clinical uptake and utility, and that parent-report can be more reliable in detection of ASD symptoms than clinician-observation during brief clinical evaluations (Robins et al., 1999). While these arguments have some merit, they do not adequately consider: 1) the cost-to-benefit ratio associated with an additional five to 10-minute screening time to potentially improve detection and result in earlier identification; 2) the limitations inherent to parent-report in ASD symptom detection; and 3) the potential added value of combining parent and clinician ratings in improving the reliability and stability of an early ASD screen.

The M-CHAT therefore relies on a single method of assessment to detect ASD, namely parent-report. The other significant revisions were made to improve
instrument sensitivity and involved the inclusion of additional items in an attempt to measure ASD symptom across both mild to severe variants of ASD and decreasing the cut-off score (Dixon et al., 2011). The M-CHAT contains 23 yes/no items that measure deficits in: sensory and motor function; social interaction; language and communication; and joint attention. A positive screen is reached when a child fails two or more of six critical items. The M-CHAT is intended as a level 1 screen, however, it has shown potential as a level 2 screening instrument (Kleinman et al., 2008; Robins, 2008; Robins, Fein, Barton & Green, 2001). The M-CHAT can be accurate in the prospective identification of children with ASD from 24 to 30 months of age, with a high PPV (Chlebowskí, Robins, Barton & Fein, 2013). However, instrument specificity can be low in children under 24 months (Pandey et al., 2008), and over 24 months (Eaves, Wingert, Ho & Mickelson, 2006; Snow & Lecavalier, 2008). The M-CHAT is the only parent-report instrument listed as an adequate screening tool for use within clinical practice (CDC, 2015).

**Modified Checklist for Autism in Toddlers–Revised with Follow-Up (M-CHAT-R/F; Robins et al., 2014).** The M-CHAT-R/F is intended as a level 1 screening instrument and is a revision of the M-CHAT. The M-CHAT-R/F also relies on a single method assessment to detect ASD. The revision involved: 1) removal of three items that had performed poorly; 2) a simplification of item wording; 3) reduction of screen age to 16-30 months; and 4) development of three risk ranges for scoring (Zwaigenbaum et al., 2015b). The M-CHAT-R/F remains a free to use instrument and is intended as a two-stage screener that takes approximately 10-15 minutes to administer. Stage 1 involves parents responding to 20 yes/no questions that are scored to assess risk status, ranging from low (positive screen on < 3 items), medium (screening on 3-7 items) and high (8 or more items are endorsed). Children
who screen medium risk are then involved in stage 2 of the screening process, which involves administration of the failed items. If the score remains above 2 the child is referred for diagnostic evaluation. Children who screen high risk during the first stage can bypass the second stage and be referred immediately for diagnostic evaluation. Compared to the M-CHAT, the M-CHAT-R/F has shown improved sensitivity and positive predictive value, detecting more children with ASD and reducing the number of children requiring follow-up (Robins et al., 2014), however, the M-CHAT is still listed as parent-rated screening tool for use within clinical practice (CDC, 2015).

Quantitative Checklist for Autism in toddlers (Q-CHAT; Allison et al., 2008). The Q-CHAT is designed as a level 1 screening instrument and is the most recent revision of the CHAT. The Q-CHAT relies on a single method of assessment to detect ASD, namely parent-report. The Q-CHAT is a free to use instrument and includes 25 items that measure: pretend play; joint attention; language development; repetitive behaviours; and social communication. ASD symptoms are measured across a 5-point scale rather than a dichotomous scoring system that rates the behavioural marker as either present or absent. While the Q-CHAT has shown good instrument sensitivity and specificity in children aged 18-24 months (Allison et al., 2008; Magiati et al., 2015), further psychometric examination is required and the Q-CHAT has not yet been validated in clinical settings. An abbreviated version of the Q-CHAT, which includes ten items, has also produced high and well-balanced sensitivity and specificity (Allison, Auyeung & Baron-Cohen, 2012). The Q-CHAT is not listed as an adequate screening tool for use within clinical practice (CDC, 2015).
Early Screening for Autistic Traits (ESAT; Dietz, Swinkles, van Daalen, Van Eneland & Buitlaar, 2006; Swinkles et al., 2006). The ESAT is intended as a level 1 parent-report screening instrument and also relies on a single method assessment to inform risk status of ASD. The ESAT is available free of charge direct from the authors. The ESAT has two formats, an initial four-item pre-screener and a follow up 14 item full screener. The four-item pre-screener measures symptoms across: play; emotional expression; and response to stimuli, and takes three minutes to complete. A positive screen is indicated by failure on one or more of the items and initiates subsequent screening using the full 14 item version. The full ESAT takes approximately 10-15 minutes to administer and measures: pretend play; joint attention; interest in others; eye contact; verbal and nonverbal communication, stereotypies; preoccupation; reaction to sensory stimuli; emotional reaction; and social interaction. The ESAT has yielded excellent sensitivity but poor specificity in children aged 14-15 months (Dietz et al., 2006; Swinkles et al., 2006). The ESAT has also shown some promise in identifying children with ASD as young as eight to 24 months of age, but again specificity has been poor (Oosterling et al., 2009). In a study of infants aged from birth to 36 months, the ESAT contributed to the earlier diagnosis of children with ASD, leading the authors to make the suggestion that the ESAT may be a good instrument to guide more comprehensive diagnostic evaluation for ASD (Oosterling et al., 2009). The ESAT is not listed as an adequate screening tool for use within clinical practice (CDC, 2015).

2.13.3 Clinician rated screening instruments

Screening Tool for Autism in Two-Year-Olds (STAT; Stone, Coonrod & Ousley, 2000). The STAT is a 12-item interactive level 2 screening instrument that relies on the single method of clinician ratings to identify risk for ASD in children
aged 24-36 months. The STAT measures symptoms across four social communicative domains including: play; motor imitation; requesting; and directing attention. Administration time takes approximately 20 minutes. The STAT is only authorised to be administered by practitioners who have undergone the specific training on administration, scoring and interpretation, and is available at a cost. Items are rated as pass, fail or refused. In children aged 24-36 months, the STAT has shown well-balanced and high sensitivity and specificity, however, specificity is low at 24 - 42-month follow-up assessment (Stone et al., 2000; Stone, Coonrod, Turner & Pozdol, 2004). The STAT has also shown some promise in younger children, aged 14-23 months of age, however the instrument has not yet been clinically validated for use in this age range (Stone, McMahon & Henderson, 2008). While the STAT has shown potential, and is listed as an adequate screening tool (CDC, 2015), the predominance of studies evaluating its use have come from non clinical settings with small sample sizes and therefore further research is required (Dixon et al., 2011).

**Autism Detection in Early Childhood (ADEC; Young, 2007).** The ADEC is a level 2 clinician-administered instrument developed for use in children aged 12 months to 3 years. Administration time takes approximately 10-15 minutes, requires practitioner review of a detailed administration manual and training DVD and the instrument is available at a cost. The ADEC measures 16 discrete behaviours that include core deficits of ASD including: social communication skills; play skills; sensory-motor skills; and regulation. Each item is scored as either 0, 1 or 2 with higher score indicating more atypical performance. A cut off-score of 10 or below is indicative of a low risk screen, 11-13 as moderate, scores of 14 to 19 as high risk and scores above 19 as very high risk. The ADEC was originally developed to only detect more severe presentations of ASD, as operationalised by DSM-IV-TR (APA,
2000) AD. Although the ADEC has demonstrated excellent sensitivity and good specificity and high positive and negative predictive values in children with DSM-IV-TR (APA, 2000) AD and children with neurotypical development and developmental disorders (Nah, Young, Brewer & Berlingeri, 2014; Young, 2007), psychometric properties had not been available for the full range of ASD presentations. However, recently, use of the risk score categories has provided preliminary evidence of possible detection in children across the full spectrum (Dix, Fallows & Murphy, 2015). While the ADEC shows promise, it is currently not listed as an adequate screening instrument (CDC, 2015).

*Autism Observation Scale for Infants (AOSI; Bryson, Zwaigenbaum, McDermott, Rombough & Brian, 2008).* The AOSI is a semi structured play based experimenter-administered instrument developed for use in infants from six to 18 months. The AOSI is still under research and is not commercially available. The AOSI takes approximately 20 minutes to administer and measures: visual tracking; disengagement of attention; orientation to name; reciprocal social smiling; response to facial expression; social anticipation; and imitation. Initial outcomes from a prospective investigation in a high-risk infant sibling cohort of children aged six months of age, found AOSI scores at 12 months of age were predictive of an ASD diagnosis at 36 months of age, but were not predictive at six months of age (Bryson et al., 2008). The AOSI shows considerable promise as a very early screener, particularly in high-risk infant siblings. High-risk infant siblings under the age of 12 months can be distinguished from low-risk controls on a number of AOSI items (Gammer et al., 2015; Georgiades et al., 2013). Although further research is required to validate its use as a screening instrument, the AOSI is contributing to our knowledge of the very early emergence of ASD symptoms.
The Autistic Behavioural Indicators Instrument (ABII; Ward & Gilmore, 2010). The ABII is a semi-structured play-based clinician-administered screening instrument developed for use in infants from 12 months of age. The ABII is still under research and is not commercially available. The ABII is intended as a level 1 screening instrument. Administration and scoring time takes approximately five to ten minutes. The ABII is designed for use by a range of health practitioners, including psychologists, speech pathologists, occupational therapists, nurses, and general practitioners, and requires review of administration and scoring procedures prior to use. The ABII is an 18-item non-verbal screening instrument that includes a fixed sequence of standardised and structured tasks that elicit specific target behaviours across social attention, sensory and behavioural domains. The ABII assesses the presence of behavioural markers with an early emergence within key ASD domains. For a review of instrument development see Ward and Gilmore (2010). The social attention subscale (SAS) comprises tasks that measure social orienting (e.g., preferential gaze to social or non-social stimuli), and joint attention behaviours (e.g., preferences for shared engagement with a caregiver or solitary play), and displays of affect across social and non-social stimuli. The sensory subscale (SS) comprises tasks that measure visual, tactile, and oral sensory seeking behaviours (e.g., duration of time engaged in sensory exploration), and the presence of hypo- or hyper-responsiveness. The behavioural subscale (BS) comprises naturalistic observations of children when demands or denials are placed on the child (e.g., frequency and duration of behavioural protests). Higher subscale and total ABII scores represent a greater presence of autistic behavioural indicators. In an initial examination of the utility of the ABII in classifying children, aged between two to six years, with a DSM-IV-TR (APA, 2000) AD diagnosis ($n = 20$), a speech and
language impairment \((n = 20)\), and neurotypical development \((n = 20)\), a cut-off score of 11 correctly classified all of the children (Ward & Gilmore, 2010).
### Table 2.1

*Selected Measures and Instrument Characteristics of ASD Screening Instruments for Children Under the Age of 24 Months*

<table>
<thead>
<tr>
<th>Tool</th>
<th>Age (months)</th>
<th>Time (minutes)</th>
<th>Cost</th>
<th>Training</th>
<th>Reference</th>
<th>Population (n, M&lt;sub&gt;age&lt;/sub&gt;, range)</th>
<th>Se</th>
<th>Sp</th>
<th>NPV</th>
<th>PPV</th>
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</thead>
<tbody>
<tr>
<td><strong>Combined parent-clinician Informant Screening Instrument</strong></td>
<td></td>
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<tr>
<td>CHAT</td>
<td>18-24</td>
<td>5-10</td>
<td>Free</td>
<td>Minimal</td>
<td>Baron-Cohen et al., 1992</td>
<td>n=50 low risk M=18.3</td>
<td>.38</td>
<td>.98</td>
<td>-</td>
<td>-</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>n=41 high risk M=19.3</td>
<td>17–21 months</td>
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<td></td>
</tr>
<tr>
<td><strong>Parent-informant Screening Instruments</strong></td>
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<tr>
<td>M-CHAT</td>
<td>16-30</td>
<td>5-10</td>
<td>Free</td>
<td>Minimal</td>
<td>Kleinman et al., 2008</td>
<td>n=3 309 low risk M=20.53</td>
<td>-</td>
<td>-</td>
<td>.11</td>
<td>.60</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>n=484 high risk M=24.25</td>
<td>16–30 months</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>n=1 112 low risk M=26</td>
<td>18-30 months</td>
<td>.87</td>
<td>.99</td>
<td>-</td>
<td>.80</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>n=123 high risk M=26</td>
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<tr>
<td>M-CHAT-R/F</td>
<td>16-30</td>
<td>10-15</td>
<td>Free</td>
<td>Minimal</td>
<td>Robins et al., 2014</td>
<td>n=16 115 low risk M=20.95</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>.48</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>16-30 months</td>
<td></td>
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</tr>
<tr>
<td>Q-CHAT</td>
<td>18-24</td>
<td>5-10</td>
<td>Not commercially available</td>
<td>Minimal</td>
<td>Allison et al., 2011</td>
<td>n=754 low risk M=36</td>
<td>.91</td>
<td>.89</td>
<td>-</td>
<td>.58</td>
</tr>
<tr>
<td>Instrument</td>
<td>Ages</td>
<td>Duration</td>
<td>Type</td>
<td>Author(s)</td>
<td>Sample Size</td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>NPV</td>
<td>PPV</td>
<td>CHAT</td>
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<tr>
<td>ESAT</td>
<td>14-24</td>
<td>10-15</td>
<td>Not commercially available</td>
<td>Minimal</td>
<td>Dietz et al., 2006; Swinkles et al., 2006</td>
<td>n=31 724 low risk</td>
<td>M=14.9</td>
<td>14-15 months</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>STAT</td>
<td>24-36</td>
<td>20</td>
<td>Cost</td>
<td>Intensive</td>
<td>Stone et al., 2008</td>
<td>n=71 high risk</td>
<td>M=16.4</td>
<td>12-23 months</td>
<td>.95</td>
<td>.73</td>
</tr>
<tr>
<td>ADEC</td>
<td>12-36</td>
<td>10-15</td>
<td>Cost</td>
<td>Intensive</td>
<td>Dix et al., 2015</td>
<td>n=53 high risk</td>
<td>M=32.2</td>
<td>12-36 months</td>
<td>.87</td>
<td>.62</td>
</tr>
<tr>
<td>AOSI</td>
<td>6-18</td>
<td>20</td>
<td>Not commercially available</td>
<td>Minimal</td>
<td>Bryson et al., 2008</td>
<td>n=32 high risk</td>
<td>M=6.7</td>
<td>n= 34 high risk</td>
<td>.84</td>
<td>.98</td>
</tr>
<tr>
<td>ABII</td>
<td>12-36</td>
<td>5-10</td>
<td>Not commercially available</td>
<td>Minimal</td>
<td>Ward &amp; Gilmore, 2010</td>
<td>n=20 AD</td>
<td>M=3.9</td>
<td>n= 20 low risk</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Note: Se = sensitivity; Sp = specificity; NPV = negative predictive value; PPV = positive predictive value; CHAT = Checklist for Autism in Toddlers; M-CHAT = Modified Checklist for Autism in Toddlers; M-CHAT-R/F = Modified Checklist for Autism in Toddler- Revised with Follow-Up; Q-CHAT = Quantitative Checklist for Autism in Toddlers; ESAT = Early Screening for Autistic Traits; STAT = Screening Tool for Autism on Two-year olds; ADEC = Autism Detection in Early Childhood; AOSI = Autism Observation Scale for Infants; ABII = Autistic Behavioural Indicators Instrument.
2.14 Accuracy of Screening Instruments in Children Under the 24 Months

While some screening instruments have demonstrated good clinical utility in children over the age of 24 months (Zwaigenbaum et al., 2015b), in children under this age they can be over inclusive, lacking specificity and over identifying children who do not have ASD, or under inclusive, lacking sensitivity and failing to detect children with ASD (Al-Qabandi et al., 2011). Two reviews of the existing screening instruments for use in children under the age of 24 months have shown that current tools lack the accuracy required to mitigate the risks associated with screening children for ASD due to high misclassification (Al-Qabandi et al., 2011; Barbaro & Dissanyake, 2010).

Although existing screening instruments are associated with higher misclassification in children under the age of 24 months, their use at 18 months of age can still be informative (Zwaigenbaum et al., 2015b), thus the recommendation to screen children using an ASD specific tool at 18 months (AAP, 2006; AAP News, 2016). Although developmental screening instruments can help to flag children at risk of ASD (Zwaigenbaum et al., 2015b), they are not designed to specifically identify children with ASD and therefore may guide referrals for further diagnostic evaluation that are over or under inclusive. Lack of available valid and reliable screening instruments for use in children under the age of 24 months, holding off on the use of ASD specific screening instruments until the age of 18 months, and then using screening instruments at this time when risk of misclassification can be high, together, may increase the average length of a diagnostic gap. Children with ASD could therefore be at risk of remaining undetected in their first 18 months of life. Given the associated risks of later detection, further exploration of the characteristics
of ASD specific screening instruments that may improve classification and prospective identification of children with ASD are necessary.

2.15 Potential Characteristics to Improve Screening Instruments

Although the rate of ASD symptom emergence in the first 2 years of life can be characterised by a slow and varying onset (Zwaigenbaum et al., 2015a), converging evidence from studies mapping the behavioural trajectory of ASD symptoms across the first two years of life show a number of key behavioural markers are observable (Estes et al., 2015; Ozonoff et al., 2010; Zwaigenbaum et al., 2005). These results suggest existing screening instruments may not adequately operationalise and measure the earliest emerging and distinct behavioural markers of ASD. Difficulties in the correct classification of children displaying symptomatic ASD profiles on existing screening instruments may be an artefact of measurement limitations rather than the absence of quantifiable behavioural markers to correctly ascertain risk. The significant advances in our knowledge and understanding of how to best detect children displaying symptoms of ASD, particularly over the past decade, informs directions for new instrument development. Identification of children with ASD based on the earliest emerging and distinct features of ASD, through combined parent-report and clinician-observation, has empirical foundations to support potential improvements to the early detection of children with ASD. How the early detection of children with ASD could be improved will now be discussed.

2.15.1 Primary rather than secondary indicators.

Improving the timing of detection of children across the full continuum of severe to mild variants of ASD requires identification of the key behavioural markers with an early onset. The inclusion of symptomology that is not identifiable until later in the course of development would delay detection and contribute toward the
average length of diagnostic gap. Some of the hallmark features of ASD that are relied upon for ASD detection include secondary indicators, that is, symptoms that do not emerge until later childhood (Clifford et al., 2007). Reliance on ASD using secondary indicators would delay detection because these symptoms would not be evident in young children due to their age and developmental stage (Nadel & Poss, 2007; Watson et al., 2007). For example, the inclusion of impairments in peer interactions and pretend play would delay detection until after two years of age because these are both skills that are not present in neurotypical children until around this age (Osterling et al., 2002). Screening instruments that seek to detect ASD based on impaired speech and language would delay their use until later in development, as delayed speech and language is generally not evident until 18 months of age (De Giacomo & Fombonne, 1998; Downey et al., 2002). The inclusion of restricted and repetitive behaviours as risk markers for ASD in screening instruments would also delay ASD detection as these markers are not typically observed in children until between two and four years of age, with more than half of children with ASD under the age of four not displaying these behaviours (Charman et al., 2005; Howlin & Asgharian, 1999; Militerni, Bravaccio, Falco, Fico & Palermo, 2002).

Examination of the key variables that improve early detection, predictive validity, and diagnostic stability indicate the importance of detection of combined primary unique indicators, that is, the earliest manifestations of ASD symptomology that provide maximum discrimination from other diagnostic populations, across combined ASD domains (Baranek, 1999; Bryson et al., 2007; Clifford & Dissanayake, 2008; Stone et al., 2000). The early developmental profiles of children with ASD display a number of key indicators that are unique to the autism phenotype and that typically emerge within the first year of life. Impairments and elevated
symptomology across the domains of social attention behaviours (Trillingsgaard, Sorensen, Nemec & Jorgensen, 2005; Ventola et al., 2007; Werner, Dawson, Osterling & Dinno, 2000), sensory perceptual behaviours (Baranek, 1999; Maestro et al., 2005), and behavioural symptomology (Dominick, Davis, Lainhart, Tager-Flusberg & Folstein, 2007; Whitaker, Joy, Edwards & Harley, 2001) have been found to be unique indicators for ASD and to discriminate children with ASD from other groups of children.

Some markers of ASD become either more or less apparent across time, while some identifiable markers during toddlerhood differ to markers in later childhood (Charman & Stone, 2006; Chawarska et al., 2014; Lord et al., 2006). For example, although failing to respond to name and joint attention are markers of ASD in toddlers, by preschool age, most children with ASD can pass these tasks (Chawarska et al., 2007; Sullivan et al., 2007). Impaired eye contact can also be more identifiable in the early years of development than at later stages (Ozonoff et al., 2010), whilst repetitive and stereotyped behaviours can be more overt in children from four to five years of age with minimal signs often reported in children at two years of age (Andersson et al., 2013). Some symptoms of ASD require presentation at specific developmental times to be unique markers of ASD and not non-specific symptoms that may also be present in other children with developmental delays and children with neurotypical development. For example, under the age of four years, stereotyped language was not only present in children with ASD, but also present in children with neurotypical development, non ASD disorders and children without complex language (Kim & Lord, 2011).

2.15.2 Combined indicators.

Detecting ASD based on the combination of symptomology across multiple
domains, in particular combined impairments in social attention and sensory perceptual behaviours, could improve diagnostic stability, predictive validity, correct classification and discrimination from other groups of children (Baranek, 1999; Bryson et al., 2007; Stone et al., 2000). A previous prospective investigation of children at high risk of ASD from six months of age (Bryson et al., 2007) found that all of the children displayed a combination of impairments in social-communicative development, characterised by a lack of interest in others and a reduced frequency of seeking contact with others, and atypical sensory behaviours, specifically visual fixation, and motor mannerisms. Other examinations provide further evidence for the importance of ASD detection on the basis of a combination of symptomology. Stone and colleagues (2000) found that a combination of impairments in play, imitation, and directing attention, correctly classified 100% of children with ASD, while Baranek (1999) found a combination of impairments in social attention behaviours and sensory perceptual behaviours to correctly predict 93.75% of children with ASD and distinguish them from children with developmental delays and disorders (Baranek, 1999).

**Social attention indicators.** Impairments in social attention behaviours, such as social orienting and joint attention, are amongst some of the early markers of ASD (Clifford & Dissanyake, 2008). Children with ASD display a reduced interest in social stimuli particularly toward the features of the human face. From as early as two to six months of age, eye-tracking technology detects reduced orientation to the eye region of the face in children who go on to receive a diagnosis of ASD (Jones & Klin, 2013). By six months of age, children with ASD prefer to orientate their gaze toward non-social stimuli, and at this age, this preference discriminates children with ASD from those with neurotypical development (Maestro et al., 2001). By 20 months
of age this preference distinguishes children with ASD from children with intellectual impairment (Baranek, 1999; Osterling et al., 2002), and children with developmental delay (Swettenham et al., 1998). Recent studies of toddlers with ASD using eye-tracking technology found that from 14 months of age, children with ASD displayed a preference for visual examination of geometric images compared to photographs of children (Pierce et al., 2011). Increased displays of positive affect toward non-social stimuli in children with ASD from as early as six months of age are also early markers of ASD and discriminate children with ASD from children with neurotypical development (Maestro et al., 2001; Ozonoff, Williams & Landa, 2005; Zwaigenbaum et al., 2005).

Joint attention behaviours, that is, the sharing of attention and interest with others through pointing, showing and co-ordinating looks between objects and people (Zwaigenbaum et al., 2015c) also discriminate children with ASD from children with neurotypical development and other developmental disorders and disabilities from an early age. Impairments in responding joint attention behaviours, such as failure to track the attention of others by following their eye gaze, head turn or point, and initiating joint attention behaviours, such as failure to share or direct attention by alternating gaze between an object and an adult to share attention, and failure to direct the attention of others by showing or pointing, are early indicators of ASD and can discriminate children with ASD from children with neurotypical development (Carpenter, Pennington & Rogers, 2002; Clifford & Dissanayake, 2008; Dawson et al., 2004; Swettenham et al., 1998; Werner et al., 2000; Wimpory, Hobson, Williams & Nash, 2000), children with intellectual impairment (Osterling et al., 2002), children with developmental disorders and disabilities (Baranek, 1999; Carpenter et al., 2002; Clifford et al., 2007; Clifford & Dissanayake, 2008; Dawson et
al., 2004), children with language delays (Lord, 1995; McArthur & Adamson, 1996), and children with Down Syndrome (Lewy & Dawson, 1992). At 14 months of age, reduced responding joint attention behaviours (Landa et al., 2007; Sullivan et al., 2007; Yoder, Stone, Walden & Malesa, 2009) and reduced initiating joint attention behaviours (Goldberg et al., 2005; Stone et al., 2007) can both be prospective indicators of ASD. In high risk siblings of children with ASD, reduced initiating joint attention behaviours distinguished those children who received a diagnosis of ASD at 18 months of age from those who did not (Cornew et al., 2012).

**Sensory indicators.** Atypical patterns of sensory symptomology have an early emergence in children with ASD (Ben-Sasson et al., 2009) and are often a first sign that parents detect in their child with ASD (Baker et al., 2008). Between nine to 12 months of age, compared to children with developmental disabilities and neurotypical development, children with ASD display a dominance in early sensorimotor exploration, spending extended periods of time engaged in repetitive sensory exploration of objects, characterised by elevated rates of mouthing objects (Baranek, 1999) and intense visual inspection of objects (Bryson et al., 2007; Carcani-Rathwell, Rabe-Hasketh & Santosh, 2006; Chawarska et al., 2007; Jones, Quigney & Huws, 2003; Militerni et al., 2002; Moore & Goodson, 2003; Zwaigenbaum et al., 2005). Excessive mouthing and prolonged visual inspection may be prospective markers of ASD.

Elevated sensory behaviours are considered to be a core characteristic of young children with ASD. These sensory markers have been found to discriminate children with ASD from children with neurotypical development (Baranek, 1999; Baranek et al., 2006; Ben-Sasson et al., 2009; Zwaigenbaum et al., 2005), intellectual impairment (Baranek, 1999; Lord, 1995), language delays (Lord, 1995), and children
with developmental disorders of mixed aetiology (Baranek, 1999; Baranek et al., 2006; Ben-Sasson et al., 2009; Lord, 1995).

**Behavioural indicators.** While the presence of early behavioural indicators of ASD is less established and requires further investigation (Zwaigenbaum et al., 2015c) research studies conducted to date indicate that children with ASD may display an early profile of distinct behavioural symptomology. From six to 12 months of age, children with ASD can be distinguished from children without ASD on the presence of a profile of temperament dysregulation, characterised by: extreme stress reactions; marked irritability; intolerance for intrusion; proneness to emotional distress; and difficulties in emotional regulation (Bryson et al., 2007; Zwaigenbaum et al., 2005). By 24 months of age, temperament dysregulation continues to be a marker of ASD, distinguishing siblings of children with ASD who do go on to be diagnosed with ASD from both siblings of children with ASD who do not have ASD and children with no family history of ASD (Garon, Bryson & Zwaigenbaum, 2009). Increased symptoms of temperament dysregulation distinguish children with ASD from children with speech and language impairment (Dominick et al., 2007). At 12 months of age, children with ASD can also be distinguished based on an increased presence of repetitive and atypical use of objects, characterised by repetitive spinning, rotating or lining up of toys (Ozonoff et al., 2008; Zwaigenbaum et al., 2005) and prolonged visual inspection and fixation of objects (Bryson et al., 2007; Zwaigenbaum et al., 2005).

### 2.15.3 Unique rather than non-specific indicators.

Identifying ASD based on non-specific symptomology, that is, symptoms that are not unique to ASD but are also evident in children with other developmental delays and disabilities, can impede the early differential diagnosis of ASD, result in
over-inclusive referrals for specialist ASD evaluations, and may also contribute to lengthening the diagnostic gap. Case studies, analyses of home videos, retrospective parental reports and prospective studies have provided some insight into the clinical features that are not unique to ASD in the first two years of life. For example, impairments in speech and language and communication, are used as a red flag for immediate ASD evaluation (Filipek, 1999). However, impairments in speech and language and communication are universal to children with ASD, developmental delays, speech and language impairment and intellectual impairment (Bodfish, Symons, Pareker & Lewis, 2000; Nadel & Poss, 2007; Noterdaeme, Mildenberger, Sitter & Amorosa, 2002; Rice, Warren & Betz, 2005; Ventola et al., 2007). Restricted and repetitive behaviours are non-specific indicators of ASD in very young children, with the presence of these behaviours failing to discriminate children with ASD from children with neurotypical development, and language disorders, intellectual impairment, and developmental delays in very young children (Baranek, 1999; Carcani-Rathwell et al., 2006; Cox et al., 1999; Loh et al., 2007; Lord, 1995; Militerni et al., 2002; Osterling & Dawson, 1994; Osterling et al., 2002; Richler, Bishop, Kleinke & Lord, 2007; Wetherby et al., 2004).

One diagnostic population that is particularly difficult to discriminate from children with ASD using existing diagnostic criteria and measures include children with a speech and language delay and communication disorders (Camarata, 2014; Lord, Shulman & DiLavore, 2004). Children with a speech and language impairment share considerable overlap in ASD symptomology (Conti-Ramden, Simkin & Botting, 2006; Whitehouse, Barry & Bishop, 2007) and can appear as if they have ASD (Stone, Lemanek, Fishel, Fernandez & Altmeier, 1990). At least in some children with speech and language impairment, features of ASD, such as social
communication impairments, difficulties in peer relationships, and behavioural problems, are present and can increase over time in a similar developmental trajectory displayed from by children with ASD (Bishop & Norbury, 2002; Michelotti et al., 2002; Whitehouse et al., 2007). Under the previous DSM-IV-TR (APA, 2000) diagnostic criteria, between 25 to 100% of children and adolescents with speech and language impairment meet diagnostic criteria for an ASD (Conti-Ramden et al., 2006; Michelotti et al., 2002; Noterdaeme et al., 2002).

Research has also revealed that children with ASD and speech and language impairment cannot be discriminated based on preverbal skills, such as early vocalisations and receptive language (Mitchell et al., 2006). Therefore, impairments in communication, both before and after the onset of spoken words, along with a range of social communication and behavioural symptomology, would fail to discriminate children with speech and language impairment from children with ASD. This overlap in symptomology between children with ASD and speech and language impairment can complicate and delay diagnosis as it can be difficult to ascertain whether the social communication impairments and behavioural symptomology displayed by these groups of children are primary social and behavioural deficits which are more characteristic of ASD or secondary behaviours that are a result of difficulties in communication and therefore more characteristic of a speech and language disorder.

2.15.4 The presence rather than absence of indicators.

Detecting children with ASD on the presence rather than absence of ASD specific traits, could improve classification accuracy and reliability of early diagnosis. When diagnosis is dependent on the absence of skills and behaviours, misclassification increases (Robins et al., 2001). With many of the characteristic
symptoms of ASD required for diagnosis not emerging until later childhood, the absence of these symptoms during infancy and toddlerhood does not preclude ASD. Additionally, children with neurotypical development, those with anxious temperaments and those characterised as “late bloomers”, may not demonstrate a specific skill or behaviour during a single observation, however, this does not indicate ASD. For example, the absence of communication and social interaction, criteria considered to be symptomatic of ASD, may be confused with shyness in a neurotypical child (Robins et al., 2001). Additionally, the late bloomer, the child who does not develop their skills until later than normally expected but who does eventually develop these skills without intervention, may be misclassified with ASD when the absence of behaviour is the sole criteria for diagnosis (Wetherby et al., 2004). The presence of identified unique autistic traits could improve the reliability of early diagnosis and could identify more precise indicators that distinguish children with ASD from other diagnostic populations.

2.15.5 Combined parent and clinician ratings.

With universal best practice guidelines for the assessment of ASD prescribing a multi-method process, which incorporates both parent-report and clinician-observational methods (Volkmar et al., 2014), screening for ASD could benefit from adopting a similar approach. Parent-report provides a measurement of the expression of traits across time and within naturalistic environments. Direct clinician-observation measures symptoms in the context of expert knowledge of child development and ASD symptom presentation (Huerta & Lord, 2012). Combined together, parent-report and clinician-observation provide both independent and complimentary additive contributions to the evaluation of children with ASD (Huerta & Lord, 2012). Reliance on a single informant can be over or under inclusive of ASD.
symptoms and increase the risk of different recommendations about ASD diagnosis for the same child (Le Couteur et al., 2008; Lemler, 2012; Wiggins & Robins, 2008).

Combining information from parent-report and clinician-observation can provide considerably different and therefore essential diagnostic information (Zander et al., 2015). Best practice evaluation guidelines endorse a collaborative partnership between the parent and the clinician, recommending the combined use of a standardised parent-report and clinician-observation instrument to guide diagnostic decision making (AAP, 2006). Although practitioners are likely informally combining information from both parent-report and clinician administered instruments in their ASD evaluation procedures already, recommendations on how to best combine scores from ASD instruments have not been provided. Previous research has not yet considered optimal scoring algorithms, and therefore there has been a lack of consensus on how to best combine data from multiple informants. The use of a formal scoring method has the advantage that it is easily replicated and its accuracy can be quantified. A number of possible methods of integration could be considered. An initial approach would be to consider parent-report and clinician-observation as equally important and to weight scores from both informant sources accordingly. Alternatively, one informant could be considered as a primary source and therefore scores from this instrument weighted differently with scores from the other playing a secondary or supplementary role. Given that parents and clinicians provide distinctive contributions to ASD detection, each with their own unique advantages and disadvantages, a combined scoring approach that synthesises information and treats scores from both sources as equally important to contributing to overall classification, may be considered the preferable approach.
2.15.6 Methods of combining multi-informant scores

Previous attempts at combining scores from ASD specific instruments predominately employ a mutual categorical agreement method, with diagnostic assignment attained when threshold cut-off is reached on both instruments (Lemler, 2012; Zander et al., 2015). Thus, each instrument must be in agreement with each other on ASD classification in order for a positive screen. However, previous research has already documented that this approach to combining scores could potentially be flawed. Research has consistently shown discrepant symptom report between parent and clinician rated instruments, which can lead to disagreement between instruments and in diagnostic assignment (Le Couteur et al., 2008; Lemler, 2012; Wiggins & Robins, 2008). Each informant source can be under-inclusive of the full range of symptoms required to meet diagnostic threshold, therefore, a mutual categorical scoring model may be associated with high misclassification. For example, under a mutual categorical-agreement method, if a child failed to reach diagnostic threshold on a clinician rated instrument but attained threshold on the parent-report measure, the child would fail to reach cut-off and therefore potentially be classified as non ASD. However, this classification may be inaccurate for reasons ranging from reduced time sampling and expression of symptoms during structured clinical interactions (Gabrielsen et al., 2015) to reliance on a clinician administrated instrument that measures current ASD symptom expression at the risk of excluding the measurement of potential progressive symptom emergence that can be garnered through parent-report (Chawarska et al., 2014).

A review of the literature outside of ASD assessment identified a number of aggregation strategies that have previously been examined in the integration of multi-informant ratings in child assessment. The first method of integration incorporates
the above mentioned mutual categorical agreement method, and has been referred to as either a *both/and rule* (Wright, Waschbusch & Frankland, 2007) or an *and algorithm* (De Pauw et al., 2009). Under this scoring model, all raters must report the symptom as being present before the child is considered as a positive classification or case. An alternative method incorporates a binary scoring model, assigning a diagnosis if threshold attainment is met according to either instrument. This method of integration has been referred to as an *either/or rule* (Wright et al., 2007) or an *or algorithm* (De Pauw et al., 2009). If this binary model was applied in ASD assessment, if a child failed to reach diagnostic threshold on a clinician rated instrument but attained threshold on the parent-report measure, the child would reach cut-off and therefore potentially be classified as ASD. However, although this model may help to account for the possibility that clinician and parent-report instruments can be in disagreement with each other (Lemler, 2012), it does not synthesise information from the two informant sources to guide diagnostic formulation, rather, it continues to rely on single instrument usage to classify ASD risk. Both the mutual categorical agreement and binary methods can be at risk of a loss of rater-specific information (De Pauw et al., 2009).

The binary and mutual-categorical agreement methods of combining scores have also previously been examined when combining parent and teacher ratings and child self report on the Strengths and Difficulties Questionnaire (SDQ; Goodman, 1997) to guide prediction probabilities for conduct disorder, emotional disorder, hyperactivity disorder and psychiatric disorder (Goodman et al., 2000). In this examination, the binary method of combining scores increased the false positive rate for emotional disorders. To reduce the potential for false positive classifications, the authors altered the SDQ scoring algorithm to require agreement between the parent
and teacher ratings, a mutual-categorical agreement method, in order for a probable positive classification on the SDQ. The authors retained the binary scoring model to predict a possible classification. The outcomes from this examination suggest that while both the the mutual-categorical agreement and binary methods of combining multi-informant scores can be useful in guiding probability ratings for the presence of a disorder, they may not form an optimal method of combining scores.

An averaging strategy, whereby scores are added together and an average score used to guide classification, has been a common method of integration of scores, however, because this strategy does require some level of agreement between raters, discrepant results can still occur (De Pauw et al., 2009). The use of a common score, identified through statistical principal component analysis, has also been investigated (De Pauw et al., 2009). While this statistical scoring algorithm can help to account for a large amount of variance between scores, the incremental improvement to a combined rather than single informant score can be reduced when a common rater score is used (De Pauw et al., 2009). While this outcome may show the potential for informant source differences or biases to inflate symptom scores, the potential loss of sensitivity could make this scoring algorithm a sub-optimal strategy in combining scores due to the increased risk of false negative classifications.

A final approach to combining scores, which has not previously been explored in the ASD context, would be to consider an additive scoring model, which employs a similar system to how most individual instruments are scored and interpreted. Under this model, scores from both instruments are weighted equally and added together to provide an overall total score, with diagnostic assignment attained when scores reach above a pre-determined cut-off. An advantage of this scoring model is that it employs a continuous scale to measure and quantify ASD symptoms,
which may help to guide ascertainment of risk assessment, and also provides the option of identifying optimal cut-off scores that yield well-balanced sensitivity and specificity and high positive and negative predictive values.

2.15.7 Combined parent-clinician ratings of the additive presence of unique primary combined behavioural ASD indicators.

Although general consensus holds that ASD should be identified as early as possible (Fernell et al., 2013), children with ASD appear to experience a diagnostic gap (Shattuck et al., 2009). While screening children for ASD is recommended (AAP, 2006; AAP News, 2015), and may form one approach to contribute to reducing the length of diagnostic gap, existing screening instruments may carry inherent risks in children under 24 months age, due to misclassification (Al-Qabandi et al., 2011; Barbaro & Dissanyake, 2010). With a lengthier diagnostic gap associated with poorer prognostic outcomes (Dawson et al., 2010; Kasari et al., 2012), continued efforts to refine and enhance screening instruments are required.

While research to date has essentially informed the required methods to optimise the early identification of ASD, the combination of these methods is yet to be merged into a single screening instrument. Improving the stability and accuracy of positive and negative screens may be hinged upon the quantification of full rather than partial symptomatic profiles of ASD and the presence of unique primary combined behavioural ASD indicators.

2.15.8 Developmental surveillance in combination with recursive screening.

Variation in the timing of ASD symptom emergence in children with ASD necessitates ongoing developmental surveillance in combination with recursive screening, to improve classification accuracy (Lipkin & Hyman, 2011). Routine and
repeat monitoring and recursive screening of children for signs of ASD can be more sensitive than a discrete or a one-off screening (Barbaro & Dissanyake, 2010). Developmental surveillance methods in combination with screening children for recurring at risk ASD behaviours, using a set of red flag items, has shown promise in the prospective identification of children with ASD. In a study conducted by Barbaro and Dissanyake (2010), nurses ($n = 241$) were trained to use a set of behavioural items to monitor and screen infants ($n = 20000$) for red flags of ASD during their routine health check-ups at eight, 12, 18 and 24 months. Of the children who were identified as at risk for ASD, 81% were diagnosed by two years of age (Barbaro & Dissanyake, 2010). A revised program, the Social Attention and Communication Study-Revised (SACS-R), is currently being implemented in New South Wales, Queensland and Western Australia and aims to support the diagnosis of at least 50% of children with ASD by the age of two years and at least 70% by the age of three years.

Recursive screening using an ASD specific screening instrument at 18 and 24 month routine health-care check-ups has been found to significantly improve the timing of ASD diagnosis (Robins et al., 2014). In a study of 16 071 infants from a low risk paediatric sample, children who were screened using the M-CHAT-R/F (Robins et al., 2014), which uses a 2 stage screening process to identify children at risk for ASD, found that 47.5% of children who screened high risk for ASD using the recursive screening process received an ASD diagnosis two years younger than the national mean age of diagnosis (Robins et al., 2014). Outcomes from this study show the potential for recursive screening using ASD specific screening instruments to significantly improve the timing of ASD identification.
2.15.9 Barriers to screening.

Despite the recommended use of both general developmental and ASD specific screening instruments (AAP, 2006; AAP News, 2016), their uptake in clinical practice has been low (Roux et al., 2012). Only 23 percent of practitioners (n = 646) report routinely using developmental screening tools (Sand et al., 2005), while as few as eight percent (n = 441) (Dosreis et al., 2006) and up to only 28% (n = 51) (Gillis, 2009) report using ASD specific screening tools. A number of barriers have been documented that impede the integration of screening instruments in routine clinical practice. These barriers include time constraints, poor familiarity with screening instruments, lack of consensus on a single recommended tool, and the costs involved in screening (Dobrez et al., 2001; Dosreis et al., 2006; Gillis, 2009; Rydz, Shevell, Majnemer & Oskoui, 2005).

While solutions to reduce the multiple barriers to screening are likely complex (Gillis, 2009), standard routine screening procedures can be implemented successfully into clinical practice at a low cost (CDC, 2014; Pierce et al., 2011). The use of valid, brief and inexpensive screening instruments, during routine child healthcare check-ups, that do not require additional practitioner training to administer or score, provide a convenient and feasible opportunity to recursively screen children. Implementation of screening practices outside of medical settings could also form an alternative method to overcome some of the barriers that impede screening during routine health-care check-ups (Gillis, 2009). While this approach requires further evaluation to establish utility and efficacy, involving early child educators in screening procedures has shown preliminary promise in supporting ASD detection (Dereu et al., 2012) and may provide a convenient and feasible opportunity for screening children. Although the long term cost-benefit of integrating routine
screening into clinical practice is yet to be fully established, early results show promise.

2.16 Chapter Summary

Chapter 2 has highlighted the need for advancement of early detection methods to improve the early identification of children with symptomatic ASD profiles. The potential to intervene in symptomatic and high-risk infants from as early as six months of age necessitates parallel development of very early detection methods to ensure we have accurate methods to identify the children who need to access these interventions when they become available and validated. This chapter has also described the importance of identifying the factors that may impede timely diagnosis. Currently, in Australia, an ASD diagnosis is required for many children to access government funded intervention. Therefore, attempts to improve early detection methods need to be met with concurrent attempts to identify the required improvements to the ASD diagnostic process. The next chapter of this thesis will describe the overall focus of the research program.
Chapter 3: Research Design

The literature review presented in Chapter 2 highlighted the importance of improving the timing of identification of children with ASD and the difficulties associated with early identification and diagnosis. Many changes are required to address the broader goal of improving the timing of ASD identification and diagnosis. Understanding the potential factors that influence the timing of ASD diagnosis and improving the accuracy of ASD screening instruments may form initial improvements. The purpose of this chapter is to describe the current program of research. The Human Research Ethics Committee of Queensland University of Technology (QUT-HREC # 0900001353) approved this research (refer Appendix D for a copy of the original approval certificate).

3.1 Research Aims and Research Questions

The overall aims of the research program were to examine the assessment and diagnostic practices and challenges that impact on the timing of ASD diagnosis and to adapt a single informant ASD screening instrument into a combined parent-clinician informant screening instrument. This program of research was driven by two research questions. First, ‘What practitioner factors impact ASD diagnostic evaluations?’ Second, ‘Does a combined parent-clinician informant screening instrument improve ASD detection?’ The research aims and research questions of the thesis and individual studies are outlined in table 3.1.
Table 3.1

**Research Aims and Questions of the Thesis and Individual Studies**

<table>
<thead>
<tr>
<th>Research Aim 1: Examine assessment and diagnostic practices and challenges that influence the timing of ASD diagnosis in Australia.</th>
<th>Research Aim 2: Adapt a single informant ASD screening instrument into a combined parent-clinician informant ASD screening instrument.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Research Question 1:</strong> What practitioner factors impact ASD diagnostic evaluations.</td>
<td><strong>Research Question 2:</strong> Does a combined parent-clinician informant screening instrument improve ASD detection?</td>
</tr>
<tr>
<td><strong>Study 1</strong> Practitioner perceptions of the assessment and diagnosis of autism in Australia.</td>
<td><strong>Study 2</strong> Agreement between a brief autism observational instrument and established ASD measures.</td>
</tr>
<tr>
<td><strong>Study 3</strong> Adapting the Autistic Behavioural Indicators Instrument (ABII) as a parent questionnaire (ABII-PQ).</td>
<td><strong>Study 4</strong> Combining parent and clinician ratings of behavioural indicators of ASD improves diagnostic classification.</td>
</tr>
<tr>
<td><strong>Study 5</strong> Using a combined parent-clinician informant screening instrument to predict ASD diagnosis.</td>
<td></td>
</tr>
<tr>
<td><strong>Study 1 Aim:</strong> Examine practitioner reported assessment and diagnostic practices and challenges that may contribute to a diagnostic gap.</td>
<td><strong>Study 2 Aim:</strong> Evaluate the psychometric properties of the clinician-administered ABII, which forms the parent rated component of the combined parent-clinician informant screening instrument, the ABII-C.</td>
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<tr>
<td><strong>Study 3 Aim:</strong> Adapt the clinician-administered ABII as a parent questionnaire (ABII-PQ) to form the parent-rated component of combined parent-clinician informant screening instrument, the ABII-C.</td>
<td><strong>Study 4 Aim:</strong> Explore discrepancies between the parent and clinician informant instruments on ASD classification and different methods of combining scores to improve classification accuracy.</td>
</tr>
<tr>
<td><strong>Study 5 Aim:</strong> Conduct a preliminary evaluation of the ABII-C to examine its predictive accuracy.</td>
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<tr>
<td>Study 1 research questions:</td>
<td>Study 2 research questions:</td>
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<tr>
<td>• Do practitioners report assessment and diagnostic challenges in young children?</td>
<td>• What is the sensitivity of the ABII in classifying children across mild to severe variants of ASD?</td>
</tr>
<tr>
<td>• Do practitioners report waiting periods for diagnostic evaluations?</td>
<td>• Does the ABII correlate with existing clinician-administered ASD instruments?</td>
</tr>
<tr>
<td>• Do practitioners report implementation of best practice guidelines for ASD evaluation?</td>
<td>• Does the ABII agree with DSM-5 diagnostic criteria on ASD classification?</td>
</tr>
<tr>
<td>• Are ASD evaluations still characterised by variation and reliance on informal and unstructured ASD assessments, as reported by Skellern and colleagues (2005) in a survey of Queensland medical practitioners?</td>
<td>• Does the ABII-PQ and the ABII measure symptoms within core ASD domains differently?</td>
</tr>
</tbody>
</table>

3.1.1 Target population and setting.

Chapter 2 described the process of ASD diagnosis in Australia. In Australia, paediatricians, psychiatrists and psychologists are most commonly involved in the diagnostic evaluation of children with ASD and in the administration of gold standard ASD assessment instruments, including the ADOS and ADI-R (AABASD, 2011; AHPA, 2015). For this reason, this group of practitioners were sampled for study 1. This cohort of practitioners was thought to most likely represent Australian practitioners involved in ASD evaluations.

The literature review highlighted the influence of ASD symptom severity on the timing of ASD identification and diagnosis. In order to improve the timing of detection across the full spectrum of ASD, screening instruments require high instrument sensitivity in children with mild through to severe variants of ASD. In addition to this, one important stage of instrument validation involves establishing whether or not the instrument measures what it attempts to measure (Dixon et al., 2011). For these reasons, children who already had an ASD diagnosis, across the full ASD spectrum, were recruited for studies 2 through 4. The initial target age range was set at 18 to 36 months and expanded to 48 months following low participant numbers. However, given the average timing of ASD diagnosis in Australia, participant numbers remained low, and the final age range was expanded to include children up to the age of six years to increase sample sizes.

Chapter 2 also described ASD as having a strong heritability factor. The prevalence rate of ASD in siblings is as high as 18.7% compared to a general population incidence of one percent (Ozonoff et al., 2011). The high recurrence rate of ASD in siblings, from a research perspective, make this cohort of children a viable sample in prospectively identifying children with ASD, with the baby/sibling design.
the major approach currently used in studies examining the prospective identification of ASD (Pierce et al., 2011). With this in mind, siblings of children diagnosed with ASD were specifically selected for study 5. While it is acknowledged that sampling siblings does have an intrinsic sampling bias (Pierce et al., 2011), this method of design increased the risk rate of having a cohort of children who would be diagnosed with ASD. It was projected that, given the recurrence rate of ASD in high-risk siblings, a cohort of 60 children would yield approximately 11 children who would go on to receive a diagnosis of ASD, and a cohort of 49 children who would either display features of a broader autism phenotype or neurotypical development to allow for comparative analysis (Chawarska et al., 2014).

As indicated in Chapter 2, in Australia, children can access both private and public services to undergo evaluation for ASD. For this reason, participants for studies 1 through 5 were recruited from these types of settings. The majority of children with a verified ASD diagnosis in Australia under six years of age would be engaged in some form of multidisciplinary intervention and/or early educational program (DSS, 2015). Parents of children diagnosed with ASD have likely been connected with ASD associations and online support groups as part of the services offered through the HCWAP (DSS, 2015). Thus, these locations were targeted to recruit children for studies 2 through 5. Although this cohort predominately represents treatment seeking participants, it is probable that the majority of children in the target population for the research program would be characterised as treatment seeking. In Australia, any child who is under the age of seven years, and who received their formal ASD diagnosis prior to their sixth birthday, can access a pre-determined allocation of government supported multidisciplinary intervention under the Helping Children with Autism Package (DSS, 2015). Therefore, the recruited
sample is potentially representative of children diagnosed with ASD in the target age range, and the sites of recruitment representative of where parents and siblings of children diagnosed with ASD are engaged.

3.2 Structure of Research Program

Figure 3.1 depicts the structure of the research program and the participant samples used in each of the studies.
Aim 1: Examine assessment and diagnostic practices and challenges that influence timing of ASD diagnosis in Australia.

Study 1 (n=104)
Practitioner perceptions of the assessment and diagnosis of Autism in Australia

Study Aim
Examine assessment and diagnostic practices and challenges that contribute to a diagnostic gap

Psychologists n=54
Paediatricians n=42
Psychiatrists n=8

ASD n=51

Study 2 (n=51)
Agreement between a brief Autism observational instrument and established ASD measures

Study Aim
Further establish psychometric properties for the ABII

ASD n=51

Study 3 (n=102)
Adapting the ABII as a parent questionnaire (ABII-PQ)

Study Aim
Adapt the ABII as parent questionnaire

ASD n=51

Study 4 (n=51)
Combining parent and clinician ratings of behavioural indicators of ASD improved diagnostic classification

Study Aim
Examine whether a combined ABII and ABII-PQ score improves ASD classification

ASD n=51

Study 5 (n=28)
Using a combined parent clinician informant screening instrument to predict ASD diagnosis

Study Aim
Conduct a preliminary evaluation of the ABII-C

HR Siblings n=28

Figure 3.1. Structure of the research program and the participant samples used in each of the studies. * The ABII was developed under the supervision of Prof Gilmore in the partial fulfilment of the requirements of my Master degree in Educational and Developmental Psychology. ABII = Autistic Behavioural Indicators Instrument; ABII-PQ = Autistic Behavioural Indicators Instrument – Parent Questionnaire; ABII-C = Autistic Behavioural Indicators Instrument - Combined; ASD = autism spectrum disorder; AD = autistic disorder; AS = asperger’s syndrome; HR = high-risk; PDD-NOS = pervasive developmental disorder – not otherwise specified; SLI = speech and language impairment; TD = typical development.
Four unique samples of participants were recruited for the research program. Study 1 was a national survey of Australian practitioners involved in ASD evaluations and sampled psychologists, paediatricians and psychiatrists. Studies 2 and 4 involved a single sample of children with a verified best-estimate clinical DSM-IV-TR (APA, 2000) or DSM-5 (APA, 2013) ASD diagnosis. Study 3 used a sample of parents of children with a DSM-IV-TR (APA, 2000) ASD diagnosis or who were regarded neurotypical development. Study 5 sampled a cohort of siblings of children diagnosed with a DSM-IV-TR (APA, 2000) ASD diagnosis. Participant information and consent forms for each of the studies and a copy of a research flyer used for participant recruitment can be found in Appendix E through H.

3.3 Account of Research Progress Linking the Research Papers

An outline of each of the individual studies and their contribution to the research aims was presented in figure 3.1 and is reiterated briefly below to show the link to the published papers that are presented in the following chapters. The specific hypothesis and rationale for each study are outlined in the Introduction of each paper and therefore are not repeated here.

3.3.1 Study 1.


Study 1 was designed to update our understanding of ASD assessment and diagnostic practices and challenges that may influence the timing of ASD diagnosis in Australia. Recruited participants included practitioners who are routinely involved in evaluation of young children for ASD. Paediatricians, psychiatrists, and psychologists completed an anonymous self-administered survey, which measured
practitioner report and perceptions of ASD assessment and diagnostic challenges. The survey was a modified version of a survey used in a previous investigation of Queensland paediatrician’s and psychiatrists (Skellern et al., 2005). This paper addressed the aims of the research program by examining the practitioner reported factors that likely interact to impact the timing of diagnosis of ASD and contribute to the potential for a diagnostic gap.

3.3.2 Study 2.


Study 2 was designed to further establish psychometric properties of the clinician-administered component of the combined parent-clinician informant screening instrument, ABII-C. Although the clinician-administered ABII had previously been developed and initial psychometric properties reported in a sample of children with a DSM-IV-TR (APA, 2000) AD diagnoses ($n = 20$), neurotypical development ($n = 20$) and speech and language impairment ($n = 20$) (Ward & Gilmore, 2010), instrument sensitivity in children across the full autism spectrum, as operationalised in the DSM-IV-TR (APA, 2000) or DSM-5 (APA, 2013), had not been examined. In addition to this, the ABII (Ward & Gilmore, 2010) had not previously been evaluated against established clinician-administered instruments, including the ADOS (Lord et al., 1999) and the CARS2-ST (Schopler, Van Bourgondien, Wellman & Love, 2010), or the newly released DSM-5 (APA, 2013) diagnostic criteria. This paper addressed the aims of the research program by evaluating the reliability and validity of the clinician-administered component of the combined parent-clinician informant screening instrument, ABII-C.
3.3.3 Study 3.


The purpose of Study 3 was to adapt the clinician-administrated ABII as a parent questionnaire, the ABII-PQ. The ABII-PQ forms the parent-rated component of the combined parent-clinician informant screening instrument, ABII-C. This paper describes the modification of ABII items as parent questions and presents initial psychometric properties of the parent-report ABII-PQ in a sample of children across the full range of ASD diagnostic subcategories, as operationalised in the DSM-IV-TR (APA, 2000), and children with neurotypical development. This paper addressed the aims of the research program by evaluating the reliability and validity of the parent-report component of the combined parent-clinician informant screening instrument, ABII-C.

3.3.4 Study 4.


The first aim of study 4 was to examine whether single instrument usage of the parent-report ABII-PQ and the clinician-administered ABII could lead to different screening outcomes for the same child with an ASD diagnosis. The second aim of Study 4 was to explore different methods of integrating scores from the two screening instruments to examine whether a combination score improved ASD
classification accuracy. The measures used in this study were the same as study 2. This paper addressed the aim of the research program by examining the potential for single informant screening instruments to reach different screening outcomes for the same child and exploring different methods of combining scores from the ABII and ABII-PQ to optimise ASD classification accuracy.

3.3.5 Study 5.


Study 5 was a preliminary evaluation of the combined parent-clinician informant screening instrument, the ABII-C. This paper described a screening study of siblings of children with ASD and compared the ABII-C with a battery of existing instruments including the: M-CHAT (Robins et al., 1999); BITSEA (Briggs-Gowan & Carter, 2006); ESAT (Dietz et al., 2006; Swinkles et al., 2006); ADOS (Lord et al., 1999); and CARS2-ST (Schopler et al., 2010). Children were diagnostically evaluated by independent practitioners who were blind to child screening outcomes. Children were re-screened across all instruments 12 months after their initial screening. Parents of children were followed-up 24 months after initial screening to confirm stability of screening outcomes and diagnosis. This paper addressed the aim of the research program by providing initial psychometric information on the combined parent-clinician informant screening instrument, the ABII-C.

3.4 Discussion of Methodological Considerations

3.4.1 Survey.

The first study of this research program used a survey to elicit practitioner perceptions of ASD assessment and diagnostic challenges in their evaluations of
children for ASD. The survey also sought to ascertain the age at which practitioners reported routinely making ASD diagnostic recommendations to establish the potential for a diagnostic gap in Australia. This study used a similar methodology and a modified version of a practitioner survey employed in a previous examination of Queensland paediatricians and psychiatrists involved in the diagnostic evaluation of children for ASD (Skellern et al., 2005). However, unlike the Skellern and colleagues (2005) examination, the current study surveyed psychologists as well as paediatricians and psychiatrists and sought to survey practitioners across Australia as opposed to Queensland only.

The survey used in the current study, which is described in the first paper of this research program and is included in Appendix A, was modified to include items to: 1) gather information on practitioner characteristics, including practice location and setting, length of experience, number of referrals per month, whether additional ASD specific training had been completed; 2) ascertain the characteristics of the children seen for diagnostic evaluation, including predominate child age at ASD diagnostic recommendation; 3) elicit information regarding factors that may impact on the timing of diagnosis including, waiting periods, diagnostic uncertainty and difficulty in younger children, adoption of the watch and wait approach, perceived limitations of the utility of gold standard measures and diagnostic criteria in younger children; 4) describe assessment methods, protocols and duration to determine whether ASD evaluations vary across practitioners; and 5) estimate the frequency of implementation of best practice guidelines that had been updated since the prior survey.
3.4.2 Instruments.

Administration guidelines and scoring procedures of the ABII, ABII-PQ and ABII-C, are described in their respective papers. The ABII and ABII-PQ are included in Appendix B and Appendix C, respectively. A range of established instruments were selected for inclusion in the research program. These instruments included the ADOS (Lord et al., 1999), CARS2-ST (Schopler et al., 2010), M-CHAT (Robins et al., 1999), ESAT (Dietz et al., 2006; Swinkles et al., 2006), and the BITSEA (Briggs-Gowan & Carter, 2006), all of which have been described in the chapter 2 and in the relevant papers.

A number of criteria guided the selection of the instruments for inclusion in the research program. The ADOS (Lord et al., 1999) and the CARS2-ST (Schopler et al., 2010), were specifically chosen for comparative analysis in studies 2 and 5, as both are standardised instruments that require clinician evaluation of ASD symptoms, similar to the ABII (Ward & Gilmore, 2010). Inclusion of the ADOS (Lord et al., 1999) and CARS2-ST (Schopler et al., 2010), provide the opportunity to validate the ABII (Ward & Gilmore, 2010) against existing instruments, an important stage of instrument evaluation (Dixon et al., 2011). In addition to this, the ADOS (Lord et al., 1999) has been recommended as a gold standard observational instrument (Reaven, Hepburn & Ross, 2008), while the previous version of the CARS2-ST (Schopler et al., 2010), the CARS (Schopler, 1988), has been reported to be the most frequently used instrument by clinicians in their evaluations of children for ASD (Wiggins et al., 2006).

Both the ADOS (Lord et al., 1999) and the CARS2-ST (Schopler et al., 2010) are more comprehensive instruments compared to the ABII (Ward & Gilmore, 2010). The ABII is intended as a screening instrument and not to replace these more
thorough measures. However, comparing a brief and inexpensive screening instrument, against these more time consuming and costly instruments may be of benefit. The use of screening instruments as a preliminary measure to ascertain ASD risk could guide decisions regarding initiation of more comprehensive expensive diagnostic evaluations.

The selection criteria that guided inclusion of the ASD specific screening instruments for study 5 were based on instrument characteristics that are thought to increase clinical utility (Dixon et al., 2011). Screening instruments were selected if they were: 1) time-efficient; 2) inexpensive; 3) suitable for administration without requiring formalised training and experience with ASD; and 4) easy to administer and score. Specific selection criteria guided inclusion of each individual screening instrument.

The M-CHAT (Robins et al., 1999) is a single informant ASD specific screening instrument that was specifically chosen for inclusion in study 5 for a number of reasons. First, the M-CHAT (Robins et al., 1999) was developed to replace the only other combined parent-clinician screening instrument, the CHAT (Baron-Cohen et al., 1992). The M-CHAT (Robins et al., 1999) has undergone rigorous testing, is one of the most widely used ASD screening instruments (Robins et al., 2014), and is listed as the parent-rated screening tool for use in clinical practice (CDC, 2015). The M-CHAT (Robins et al., 1999) is therefore considered a robust screening instrument to compare the ABII-C against.

The other ASD specific parent-report screening instrument selected for inclusion in the research program was the ESAT (Dietz et al., 2006; Swinkles et al., 2006). Although the ESAT (Dietz et al., 2006; Swinkles et al., 2006) is less well established than the M-CHAT (Robins et al., 1999), it has shown promise in a
younger population compared to the M-CHAT (Robins et al., 1999). Preliminary evidence suggests the ESAT (Dietz et al., 2006; Swinkles et al., 2006) could be used as a pre-screening instrument from birth through to 36 months (Oosterling et al., 2009a; Oosterling et al., 2009b; Swinkles et al., 2006). Given the intended age range of ABI-C is from 12 months of age, inclusion of a screening instrument in the research program that can also be used from this age provided an option for comparative analysis.

The BITSEA (Briggs-Gowan & Carter, 2006), was the final instrument selected for inclusion in study 5. While the BITSEA (Briggs-Gowan & Carter, 2006), is not an ASD specific screening instrument, and although it does not fulfil all of the instrument characteristics that are thought to increase clinical utility (Dixon et al., 2011), it provides a measure to explore any differences between ASD specific and general screening instruments in the prospective identification of children with ASD. Current recommendations for screening outline the use of non ASD specific screening instruments under the age of 18 months, with ASD specific screening instruments not recommended for use until 18 months of age (AAP, 2006; AAP News, 2016). General screening instruments that include items that measure non-specific ASD symptoms may increase misclassification risk (Coury, 2010).

3.4.3 Diagnostic criteria.

In the progression of this research program a revised set of diagnostic criteria was released. At the commencement of the research program, ASD diagnostic criteria was operationalised in the DSM-IV-TR (APA, 2000). In 2013, the new diagnostic criteria were released in the DSM-5 (APA, 2013). The DSM-IV-TR (APA, 2000) and DSM-5 (APA, 2013) symptom criteria were reviewed in Chapter 2.
3.4.4 Outcome measures.

Independent practitioners involved in the diagnostic evaluation of children with ASD provided verified best-estimate clinical diagnosis for all child participants in studies 2 through 5. These practitioners were not involved in the research program and were therefore blind to any screening or assessment outcomes. With the exception of study 3, diagnostic confirmation letters were required for inclusion in the research program. A diagnostic confirmation letter outlines the DSM-IV-TR (APA, 2000) or DSM-5 (APA, 2013) ASD diagnosis and is required for verification purposes within Australia and to access government supported intervention.

3.4.5 Participant recruitment and screening.

A convenience sampling strategy was used in each of the studies in the research program. Common to all studies, participants were invited to participate if they fulfilled the inclusion criteria and did not meet any of the exclusion criteria. The inclusion and exclusion criteria specific to each study design are described in their respective papers.

Participant recruitment for psychometric evaluation. It is understood that, in order to psychometrically evaluate a screening instrument and validate its utility, information on instrument sensitivity and specificity is required (Dixon et al., 2011). Instrument sensitivity and specificity are important psychometric properties to report as they are generally dependent on each other, i.e., as instrument sensitivity increases, instrument specificity usually decreases (Dixon et al., 2011).

The ABII had previously undergone initial psychometric evaluation in a sample of children with and without a DSM-IV-TR (APA, 2000) AD diagnosis and produced well balanced sensitivity and specificity (Ward & Gilmore, 2010). However, psychometric information for the parent-report equivalent of the ABII, the
ABII-PQ, and the combined version of the two instruments, the ABII-C, have not been established. In order to calculate reliability, validity, sensitivity and specificity, the for the ABII-PQ and ABII-C, study 3 sampled children with and without a diagnosis of ASD and study 5 sampled children siblings who had a heightened ASD risk. While attempts were made in study 5 to employ a research program that could report instrument sensitivity and specificity for the combined parent-clinician informant screening instrument (ABII-C), final sample characteristics did impede this form of psychometric evaluation. Paper 5 of the research program describes the final sample characteristics and implications for the psychometric evaluation of the ABII-C.

**Item Response checks.** The research program employed a mix of online and paper research methods. To reduce missing data, item response checks were employed when the option was available. Studies 1 and 3 employed both online and paper research methods for completion of the practitioner survey and parent-report ABII-PQ. In the online versions, a force response validation check was applied. Participants were required to provide a response to each question before progressing to the next item or exiting the survey if they did not chose to respond. When participants responded using the anonymous paper versions of the survey and the parent-report ABII-PQ, item response checks were not possible.

Parent respondents in studies 4 and 5 completed identifiable parent-report instruments. Any parent-report instrument that was incomplete was followed up with the respondent to invite a response to any unanswered items. Standardised administration and scoring procedures were adhered to in studies 2, 4 and 5, requiring the completion of each item on the instrument before proceeding to the next.
Data cleaning and assumption checking approaches. The data in each individual study was examined for missing data and breaches of relevant assumptions. The implementation of item response checks, examiner follow up of any incomplete parent-report instruments in studies 4 and 5, and examiner adherence to administration guidelines of the instruments, minimised missing data. Missing values analyses revealed no missing data in any of the studies.

Assumptions of normality were examined to determine suitability for parametric analyses using Kolmogorov-Smirnov test and Levene’s test of homogeneity of variance. When violations of assumptions were observed, equivalent nonparametric tests were used. The data were analysed using IBM SPSS statistics Version 23.0. Statistical significance was evaluated using an alpha level of $p = .05$. No adjustments to critical $p$ value were set as the effect size was calculated to provide a measure of magnitude of the difference.

3.5 Chapter Summary

This chapter provided an overview of the research questions that guided the research program. Two overarching research questions were identified. First, ‘What practitioner factors impact ASD diagnostic evaluations?’ Second, ‘Does a combined parent-clinician informant screening instrument improve ASD detection?’ This chapter also defined the specific research aims and presented the original contribution of the five studies to address the research questions. The chapter concluded by presenting the methodological considerations that guided participant recruitment and data sampling and analysis. Chapters 4 though 8 of the thesis will present the studies in the form of individual papers that are accepted or submitted for publication, or that have been prepared for submission.
Chapter 4: Practitioner Perceptions of the Assessment and Diagnosis of Autism in Australia
Statement of Contribution of Co-Authors for Thesis by Published Paper

The following is the format for the required declaration provided at the start of any thesis chapter which includes a co-authored publication.

The authors listed below have certified* that:

1. they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
2. they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
3. there are no other authors of the publication according to these criteria;
4. potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit, and
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Karen A Sullivan*  Aided experimental design, data analysis and interpretation, and critical revision of manuscript.

Linda Gilmore*  Aided experimental design, data analysis and interpretation, and critical revision of manuscript.

Principal Supervisor Confirmation

I have sighted email or other correspondence from all Co-authors confirming their certifying authorship.

Name Signature Date
Abstract

Objective: Autism spectrum disorder (ASD) can potentially be diagnosed by three years of age. Yet, 2012 Australian diagnostic data showed most children are diagnosed after this age. This study examined whether an ASD diagnostic gap exists and explored practitioners’ perceptions of the assessment and diagnostic process.

Method: Using a modified version of an existing questionnaire, we undertook a national survey of Australian practitioners who assess infants and children with possible ASD (psychologists, \( n = 54 \); paediatricians, \( n = 42 \); psychiatrists, \( n = 8 \)).

Results: Approximately 63% of practitioners reported most likely recommending an ASD diagnosis in a child three years or older. Over 60% of practitioners identified the following factors as influencing their practice in relation to ASD diagnosis in children under three years of age: preference for a “watch and wait approach” (92%); the perceived difficulty of the diagnosis (79%); inability to see children early enough because of initial assessment waiting list (75%), and; the perceived limitations of diagnostic aids, including assessment measures (63%) and the diagnostic criteria (69%). Variations in assessment and diagnostic practices were reported by the three professional groups.

Conclusion: A number of factors may influence the timing of ASD diagnosis for children in Australia and could contribute to a diagnostic gap. The practitioner-reported challenges suggest potential improvements to the ASD diagnosis process.

Key Words: ASD; autism assessment; autism diagnosis; diagnostic challenges; diagnostic gap
Practitioner perceptions of the assessment and diagnosis of autism in Australia.

**Introduction**

Autism spectrum disorder (ASD) is a heterogeneous and complex disorder encompassing a broad range of severity of included symptomology (Williams et al., 2014a). Despite research implicating biological, neurological and/or genetic causal factors, ASD is both defined and diagnosed on the basis of behavioural symptomology (Pierce et al., 2011). With no single definitive test or known cause, the accurate clinical detection of behavioural features highlights the critical role of practitioners in the diagnosis of ASD.

Since the first epidemiological survey in the 1960s, the reported prevalence of ASD has increased from 4/10 000 to 1/100 (Elsabbagh et al., 2012; Williams et al., 2014a). Australia alone has seen a 79% increase in the number of children diagnosed with ASD since 2009 (Australian Bureau of Statistics [ABS], 2012). This increase is most likely a reflection of more children with ASD being detected rather than a true increase in the number of children affected (Hansen, Schendel & Parner, 2015; King & Bearman, 2009; Liu, King & Bearman, 2010). Improved practitioner and community awareness and changes to diagnostic practice and process, including expansion of the diagnostic criteria to include milder presentations, have all been suggested as factors that are relevant to the epidemiology of ASD (Hansen et al., 2015; King & Bearman, 2009; Liu et al., 2010). Given that the number of children who will be diagnosed with ASD is forecast to rise by three percent per annum (Rogers, 2011), it is increasingly likely that practitioners who work with young children will encounter children on the autism spectrum.
There is some evidence that early intensive behavioural intervention provides improved developmental outcomes for some children with autism, including gains in adaptive behaviour, language and IQ (for review, Reichow, Barton, Boyd & Hume, 2012). Although the magnitude of gains can vary, and optimal timing, intensity and duration of intervention are yet to be established (Williams et al., 2014b), guidelines for good practice intervention in Australia outline that intervention should begin as soon as characteristics of ASD are noted and continue for as long as required (Prior & Roberts, 2012). There is some evidence to suggest that the timing of intervention may be important, with a number of studies showing that children who received appropriately targeted intervention under the age of three years displayed greater developmental gains and reduced core symptom severity compared to children who received the same intervention after the age of three (Goin & Myers, 2004; Landa, Holman & Garrett-Mayer, 2007; Sheinkopf & Siegel, 2004). Early intervention can also provide a national economic benefit. ASD is currently estimated to cost Australia $8 billion per year, and if Australia invested in early intervention this cost could potentially be reduced by $1.22 billion per year (Synergies Economic Consulting, 2013).

Retrospective and prospective studies investigating ASD symptom onset suggest initial symptom emergence occurs in most cases within the first 12 months (for review, Barbaro & Dissanyake, 2009; Jones, Gliga, Bedford, Charman & Johnson, 2014; Yirmiya & Charman, 2010), with possible variations in symptom presentation within core domains that accumulate across the first two to three years of life (Guthrie, Swineford, Nottke & Wetherby, 2013; Rogers, 2009). Although the detection and diagnosis of ASD is complex, largely due to differing symptom trajectories and degrees of impairment (Coo et al., 2012; Shattuck et al., 2009),
diagnosis between two to three years can be reliable, valid and stable (Centers for Disease Control and Prevention [CDC], 2014). Between 75% -100% of children diagnosed under two years of age, or between two to three years of age, have maintained an ASD diagnosis into later childhood (for review, children under two years of age: Chawarska et al., 2007; Cox et al., 1999; Guthrie et al., 2013; children between two and three years of age: Charman et al., 2005; Kleinman et al., 2008; Lord et al., 2006).

In Australia, the average age of diagnosis is approximately four years, with a diagnostic trend indicating a peak in diagnostic numbers in children after the age of five (ABS, 2012; Bent, Barbaro & Dissanyake, 2015). This diagnostic trend indicates that a large proportion of children with ASD are being diagnosed later in development, potentially well after initial symptom presentation. Shattuck and colleagues (2009) have identified a large gap (p. 475) between when ASD can be identified and when children are being identified. The authors examined the timing between when practitioners can generally diagnose ASD, between the ages of 2-3 years, and when actual diagnosis was reported to occur, finding a gap that ranged from 2.7-3.7 years. This diagnostic gap may be due to a combination of factors that have an additive contribution to delaying final diagnostic verification, including a number of parental and practitioner factors, individual child characteristics, ASD symptom presentation and degree of severity, availability of diagnostic tools for use in children under the age of three, and a number of system constraints.

A range of factors is thought to contribute to an ASD diagnostic gap. These include: parental difficulty in recognition of subtle deficits and impairments associated with ASD (Le Couteur, Haden, Hammad & McConachie, 2008; Lemler, 2012); parental under-report and/or denial of symptoms and developmental deviance...
practitioner failure to elicit specific information from parents to guide diagnostic formulation or to investigate concerns, providing instead reassuring or passive responses (Zuckerman, Lindly & Sinche, 2015); practitioner difficulty detecting early signs of milder presentations (Coo et al., 2012; Shattuck et al., 2009); client characteristics (e.g., higher IQ, higher age, being female), and the absence of overlapping co-morbid conditions and developmental regression (Chawarska et al., 2014; Shattuck, et al., 2009); limitations in current available screening and diagnostic tools that yield high misclassification errors, particularly in children under the age of three years (Al-Qabandi, Gorter & Rosenbaum, 2011; Barbaro & Dissanyake, 2010); variations between parent-report and clinician quantification of ASD symptoms (De Giacomo & Fombonne, 1998; Lemler, 2012); practitioner uncertainty and implementation of a developmental surveillance approach known as the “watch and wait” strategy, which delays diagnosis until later on in development where diagnostic certainty increases (Rutter, 2006); and system constraints, including lengthy wait lists and disparities in the provision of services in public and private health sectors. In Australia, waiting periods can range from 6 weeks to eight months in the private sector compared to waiting times of between fourteen months to two years in the public sector (State-Wide Autism Project [SWAP], 2012; Western Australia Autism Diagnosticians forum Inc., 2012).

The timely and accurate diagnosis of ASD can be difficult. In order to detect ASD as early as possible, characteristics need to be noted very early on and diagnostic tools need to reliably measure symptoms to help guide early diagnostic recommendations. However, symptom presentation can vary, and for some children, traits may not be noted and full diagnostic criteria may not be attained until much
later on in development (Coo et al., 2012; Shattuck et al., 2009). In addition to this, diagnostic assessment in children under the age of three can be difficult, as most diagnostic tools, such as the Autism Diagnostic Observation Schedule (ADOS: Lord, Rutter, DiLavore & Risi, 1999), and Autism Diagnostic Interview - Revised (ADI-R: Rutter, Le Couteur & Lord, 2003) have not been designed for use in children this age, contributing to diagnostic uncertainty (Dosreis, Weiner, Johnson & Newschaffer, 2006; Williams et al., 2014b). Although toddler versions of these tools have recently become available, such as the ADOS-2 (Lord et al., 2012) and the revised ADI-R algorithms (Kim, Thurm, Shumway & Lord, 2013), the long-term stability of a diagnosis using these tools is yet to be established. Given that the manifestations of ASD can vary, and practitioners have up until very recently been limited in available diagnostic tools for children under the age of three which could contribute to diagnostic uncertainty in this age group, the provision of best practice guidelines have been developed to support practitioners in the early assessment of children who may have ASD (Volkmar et al., 2014).

Australian best practice guidelines recommend continuing ASD specific training to enhance practitioner surveillance and detection skills and knowledge, minimise waiting times from referral to diagnosis, use of a comprehensive multidisciplinary assessment to support diagnoses where necessary, and intervention for both the child and family following diagnosis (Australian Advisory Board on Autism Spectrum Disorders [AABASD], 2011). The current prescribed standard pathway of ASD assessment in Australia involves referral from a general practitioner (GP) to a paediatrician or psychiatrist, either in the public or private sector (Allied Health Professionals Australia [AHPA], 2015). The medical specialist makes an assessment of the child. If the presentation of ASD is clear-cut, the medical specialist
may ascribe a diagnosis without further assessment in order to provide a time and cost efficient diagnostic process. In less clear-cut presentations, on suspicion of ASD, the paediatrician or psychiatrist can refer the child for comprehensive multidisciplinary assessment. Guidelines for comprehensive multidisciplinary assessment outline the integration of diagnostic and functional assessment by a team of medical practitioners involving either a paediatrician or psychiatrist, and allied health practitioners involving a psychologist, speech pathologist and occupational therapist (AABASD, 2011; AHPA, 2015). On completion of these sessions, the child returns to the medical specialist who after taking into account the reports provided by the allied health practitioners, will determine if the child meets criteria for a formal diagnosis (AHPA, 2015). Within Australia there are documented variations between public and private practice settings in the provision of multidisciplinary assessment. Within public settings, where government funded assessments are provided, multidisciplinary assessment may be more likely, however, waiting periods can span up to 14 months (SWAP, 2012). In the private sector, multidisciplinary assessment may be less likely due to the significant costs involved for families in undertaking assessment from multiple practitioners (SWAP, 2012).

Almost 10 years ago, Skellern, McDowell and Schluter (2005) investigated diagnostic practices among Queensland paediatricians and psychiatrists, highlighting the process of ASD diagnosis was characterised by considerable variation and a reliance on informal and unstructured assessments of children. Few practitioners (19%) reported the use of “gold standard” assessment instruments, such as the ADOS or Autism Diagnostic Interview, during their assessment process. The authors cited time constraints, extended waiting periods, and a lack of resources (including the expense involved in training, administering and scoring formal tests, and the absence
of Medicare reimbursements codes to support the use of such tests in private settings), as factors that may contribute to variation from best practice guidelines.

The aims of this study were to update our understanding of ASD assessment and diagnostic practices in Australia, to elicit practitioner perceptions of assessment and diagnostic challenges, to ascertain the client age at ASD diagnosis that practitioners report as most common, and to ascertain if a diagnostic gap, as described by Shattuck et al. (2009), is present in Australia. The current study used methodology similar to Skellern et al. (2005), except that it also included psychologists, whose role in the assessment of ASD is now outlined in Australian best practice guidelines (AABASD, 2011), and it also targeted practitioners across Australia as opposed to Queensland only.

**Method**

**Participants**

A total of 104 paediatricians, psychologists, and psychiatrists across Australia were surveyed. Professionals who routinely see infants and children for the assessment of ASD were eligible to participate. A number of recruitment methods were employed. Phase 1 of recruitment involved an advertisement in professional association newsletters alerting practitioners to the survey and a link to an online version of it. Phase 2 involved distribution of surveys to practitioners who were identified from: (a) listings on professional registration boards; (b) ASD specialist provider lists; (c) online directories; (d) registered providers under the Helping Children with Autism Package; and (e) affiliation with ASD specialised organisations and clinics. During phase 2, 217 practitioners were identified. These practitioners were either mailed or emailed a survey packet (61 paediatricians, 23 psychiatrists and 133 psychologists). The survey packet contained individually
addressed cover letters and a link to complete the survey online. Phase 3 involved distributions of surveys at ASD professional development events, conferences and seminars.

The final sample consisted of 42 paediatricians (40%), 54 psychologists (52%) and 8 psychiatrists (7%). Thirty-nine percent \( (n = 41) \) of the sample was from Queensland, 25% \( (n = 26) \) from New South Wales, 21% \( (n = 22) \) from Victoria, 11% \( (n = 12) \) from Western Australia, and 3% from South Australia \( (n = 3) \). Practitioners from Tasmania, Northern Territory and the Australian Capital Territory did not respond to the survey. No information was available from non-respondents to determine why they did not participate.

**Measure**

The survey (see Appendix) was based on Skellern et al.’s (2005) measure. It was modified to include items to: (a) gather information on the characteristics of the sampled practitioners, including practice location and setting, length of experience, number of referrals per month, additional ASD specific training; (b) ascertain the characteristics of the children seen for assessment, including their age at ASD diagnosis; (c) characterise the assessment process, including wait list time, assessment method, protocol and duration; (d) estimate adherence to best practice guidelines and the reason for any deviations, and; (e) assess practitioners’ perceptions of the utility of “gold standard” diagnostic aids, including the ADOS, ADI-R, and the diagnostic criteria outlined in the Diagnostic Statistical Manual of Mental Disorders, fourth edition, test revision (DSM-IV-TR; American Psychiatric Association [APA], 2000), and their diagnostic confidence in assessing ASD in children under age two.

The survey consisted of closed-ended response categories using either
categorical tick-boxes or Likert scales (that asked respondents to provide frequency estimates from “often” to “not at all” or to rate their level of agreement from “strongly disagree” to “strongly agree”). The measure was pilot tested with three Queensland practitioners (one practitioner from each professional group), and resulted in the addition of an option for further comment. The final anonymous survey was self-administered and could be completed either via hardcopy or online.

Statistical Analysis

To examine practitioner-reported diagnostic practices and perceived diagnostic challenges, Chi Square and Fisher’s exact test for categorical data, and Kruskall-Wallis test for continuous variables were conducted. When overall comparisons were found to be statistically significant, follow-up tests were conducted to evaluate pairwise differences to establish how the groups differed from each other.

Results

The characteristics of the practitioner sample are presented in Table 1. There were significantly fewer psychiatrists than other professionals in the sample, $\chi^2(2) = 32.85, p < .001$. There were no significant differences between the professional groups based on practice setting, $\chi^2(2) = 4.65, p = .098$ (most of them [66%] practised within a large city). There were clear distinctions between the three professional groups on a number of characteristics including number of years in practice $\chi^2(2) = 9.73, p = .008$, practice type (private versus public, versus combined, $p = .001$), whether or not they had undertaken ASD specific training, $p < .001$), and their referral numbers, $\chi^2(2) = 18.93, p < .001$. Follow-up pairwise comparisons found that psychologists differed significantly from both paediatricians and psychiatrists on a number of characteristics. As a group, psychologists reported fewer years in
practice compared to psychiatrists, $U = 98.00, z = -2.54, p = .011, r = .32$, and paediatricians, $U = 816.00, z = -2.40, p = .016, r = .25$. Psychologists were more likely to be in private practice (53.7%) compared to paediatricians (19%) and psychiatrists (37.5%), $p < .001$, and more likely to have undergone additional ASD specific training, $p < .001$. Paediatricians were more likely to report higher ASD referral numbers, compared to psychiatrists, $U = 53.00, z = -3.12, p < .001, r = .44$, and psychologists, $U = 649.00, z = -3.69, p < .001, r = .38$. 
Chapter 4: Practitioner Perceptions of the Assessment and Diagnosis of Autism in Australia

Practitioner-reported Diagnostic Practices and Perceived Diagnostic Challenges

A number of factors that could contribute toward a diagnostic gap were identified (refer Table 2). Overall, 73% of the sample reported having children on a wait list for an initial appointment, with, 55% \( (n = 57) \) reporting wait times in excess of one month. Paediatricians (95.2%) and psychiatrists (100%) were significantly
more likely than psychologists (50%) to have children on a wait list $p < .001$, and to have longer waiting times, $\chi^2(2) = 28.97, p < .001$. The predominant age practitioners reported making or recommending a diagnosis was above three years (62.5%) with fewer than 5% of practitioners reporting that they routinely made or recommended a diagnosis in children less than two years. Paediatricians were more likely to report making or recommending a diagnosis in younger children compared to psychiatrists, $U = 94.50, z = -2.11, p = .035, r = .30$; and psychologists, $U = 741.50, z = -3.31, p < .001, r = .34$. Practitioners reported that it takes them longer to assess young children with ASD compared to other developmental delays or difficulties (100% of psychiatrists, 83.3% of psychologists and 78.6% of paediatricians agreed with this statement). There was a statistically significant difference in the length of time taken to complete an ASD assessment, $\chi^2(2) = 21.95, p < .001$, with psychologists taking significantly longer to complete assessments compared to both paediatricians, $U = 553.00, z = -4.50, p < .001, r = .46$ or psychiatrists, $U = 122.00, z = -2.07, p = .019, r = .26$.

Implementation of the “watch and wait” approach to diagnosis (Rutter, 2006) was common amongst practitioners, with 92.3% of the sample reporting using this approach at some time in their clinical practice. Psychologists reported adopting this approach less frequently than both paediatricians, $U = 689.50, z = -3.49, p < .001, r = .36$, or psychiatrists, $U = 74.50, z = -3.20, p < .001, r = .41$. Most of the participants sampled (79%) reported that they found it difficult to make or recommend a diagnosis of ASD in a child under the age of two years. However, there were significant differences between the groups of practitioners on this topic; psychologists reported weaker levels of agreement with the statement that ASD diagnosis is difficult compared to both psychiatrists, $U = 99.00, z = -2.54, p = .011, r = .26$. 

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Chapter 4: Practitioner Perceptions of the Assessment and Diagnosis of Autism in Australia
Overall, 62.5% of the sample reported low levels of agreement with statements about the usefulness of ASD specific measures, such as the ADOS (Lord et al. 1999) and ADI-R (Rutter et al. 2003), for children under the age of three years. The three groups were found to differ in the level of agreement on this point, $\chi^2(2) = 6.81, p = .033$, with psychiatrists reporting weakest agreement compared to both paediatricians, $U = 85.00, z = -2.23, p = .026, r = .32$ and psychologists, $U = 90.00, z = -2.68, p = .007, r = .34$. Clinicians (69.3%) generally agreed that the DSM-IV-TR diagnostic criteria (APA, 2000) were not always applicable to children under the age of three years (no group difference). Diagnostic confidence was reported by clinicians to improve after the age of three years, with 85.7% of paediatricians, 77.6% of psychologists and 100% of psychiatrists reporting higher levels of confidence in recommending a diagnosis past this age.
Table 2

Reported Diagnostic Trends and Clinician Perceptions that May Contribute to the Diagnostic Gap

<table>
<thead>
<tr>
<th></th>
<th>Total (n=104)</th>
<th>Paediatricians (n=42)</th>
<th>Psychologists (n=54)</th>
<th>Psychiatrists (n=8)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Wait period</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wait list (Y/N)</td>
<td>75 (72.9)</td>
<td>40 (95.2)</td>
<td>27 (50)</td>
<td>8 (100)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Wait Time &gt;1 Month</td>
<td>57 (54.8)</td>
<td>33 (78.6)</td>
<td>17 (31.5)</td>
<td>7 (87.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Average assessment time</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Hour</td>
<td>13 (12.5)</td>
<td>11 (26.2)</td>
<td>2 (3.7)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>&lt; 4 Hours</td>
<td>46 (44.2)</td>
<td>22 (52.4)</td>
<td>18 (33.3)</td>
<td>6 (75)</td>
<td></td>
</tr>
<tr>
<td>&lt; 6 Hours</td>
<td>24 (23.1)</td>
<td>6 (14.3)</td>
<td>16 (29.6)</td>
<td>2 (25)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&lt; 10 Hours</td>
<td>12 (11.5)</td>
<td>2 (4.8)</td>
<td>10 (18.5)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>&gt; 10 Hours</td>
<td>9 (8.7)</td>
<td>11 (2.4)</td>
<td>8 (14.8)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td><strong>Predominant Diagnostic Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;24 Month</td>
<td>5 (4.8)</td>
<td>4 (9.5)</td>
<td>1 (1.9)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>&lt;36 Months</td>
<td>34 (32.7)</td>
<td>20 (47.6)</td>
<td>13 (24.1)</td>
<td>1 (12.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&gt;36 Months</td>
<td>65 (62.5)</td>
<td>18 (42.9)</td>
<td>40 (74.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7 (87.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Watch and wait approach to diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>8 (7.7)</td>
<td>2 (4.8)</td>
<td>6 (11.1)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Occasionally</td>
<td>40 (38.5)</td>
<td>11 (26.2)</td>
<td>28 (51.9)</td>
<td>1 (12.5)</td>
<td></td>
</tr>
<tr>
<td>Sometimes</td>
<td>37 (35.6)</td>
<td>17 (40.5)</td>
<td>17 (31.5)</td>
<td>3 (37.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Often</td>
<td>19 (18.3)</td>
<td>12 (28.6)</td>
<td>3 (5.6)</td>
<td>4 (50)</td>
<td></td>
</tr>
<tr>
<td><strong>Diagnostic difficulty &lt; 2 years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>82 (78.8)</td>
<td>35 (85.6)</td>
<td>46 (70.3)</td>
<td>8 (100)</td>
<td>.011</td>
</tr>
<tr>
<td><strong>Perceived utility of Gold Standard measures and diagnostic criteria &lt; 3 years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASD tools</td>
<td>37.5 (39)</td>
<td>42.9 (18)</td>
<td>38.9 (21)</td>
<td>0 (0)</td>
<td>.033</td>
</tr>
<tr>
<td>DSM Criteria</td>
<td>30.7 (32)</td>
<td>35.8 (15)</td>
<td>31.5 (17)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td><strong>Diagnostic confidence &gt; 3 years</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.345</td>
</tr>
</tbody>
</table>

*P value derived using either Fisher’s exact test or Mann-Whitney U Test*
Practitioner-reported Implementation of Diagnostic Aids

Table 3 describes the frequency with which practitioners reported the use of diagnostic aids. As a group, psychologists reported being more likely to implement standardised interviews and standardised observations to assist the diagnostic process than both paediatricians and psychiatrists \((p < .001)\), and they were more likely than paediatricians to report using day care/teacher reports \((p = .020)\), and more likely than psychiatrists to report using cognitive assessments \((p < .001)\). Both psychologists and psychiatrists were more likely to report using the DSM-IV-TR (APA, 2000) diagnostic criteria compared to paediatricians \((p < .001)\).

Table 3

Reported Usage of ASD Diagnostic Aids by the Three Professional Groups, Paediatricians, Psychologists and Psychiatrists

<table>
<thead>
<tr>
<th></th>
<th>Paediatricians ((n=42))</th>
<th>Psychologists ((n=54))</th>
<th>Psychiatrists ((n=8))</th>
<th>(P)-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standardised Interview (e.g. ADI-R)</td>
<td>3 (7.1)</td>
<td>28 (51.9)</td>
<td>0 (0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Standardised Observation (e.g. ADOS)</td>
<td>16 (38.1)</td>
<td>40 (74.1)</td>
<td>0 (0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>DSM-IV-TR</td>
<td>30 (71.4)</td>
<td>49 (90.7)</td>
<td>8 (100)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Multidisciplinary Reports</td>
<td>34(81)</td>
<td>33 (61.1)</td>
<td>5 (62.5)</td>
<td></td>
</tr>
<tr>
<td>Day care/Teacher reports (e.g. Occupational Therapy, Speech Pathology)</td>
<td>29 (69)</td>
<td>48 (88.9)</td>
<td>5 (62.5)</td>
<td>&lt;.020</td>
</tr>
<tr>
<td>Clinical Judgement</td>
<td>37 (88.1)</td>
<td>46 (85.2)</td>
<td>8 (100)</td>
<td></td>
</tr>
<tr>
<td>Cognitive Assessment</td>
<td>22 (52.4)</td>
<td>39 (72.2)</td>
<td>0 (0)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*\(P\)-value derived using Fisher’s exact test. ADI-R = Autism Diagnostic Interview. ADOS = Autism Diagnostic Observation Schedule.
Discussion

This research examined the assessment and diagnostic practices reported by Australian practitioners who routinely see children for ASD. Results suggest that the standardised assessment of children with ASD has improved over the past 10 years and is more in line with best practice recommendations because informal assessment practices were not commonly described. A previous study in Queensland (Skellern et al., 2005) involving paediatricians and psychiatrists only, found the assessment and diagnostic process of children with ASD was characterised by considerable variability and reliance on informal and unstructured assessment practises. In this survey, a very low proportion of medical practitioners reported using “gold standard” instruments themselves, such as the ADOS (Lord et al., 1999) and ADI-R (Rutter et al., 2003); however, these tools were being used by the professionals to which they referred. The results suggest that the best practice guidelines could be being met by a partnership between medical and allied health professionals.

Consistent with Australian and international diagnostic trends (ABS, 2012; Shattuck et al., 2009), practitioners in this study reported predominately making or recommending a diagnosis of ASD in children older than three years. Less than five percent of practitioners reported making a recommendation for a diagnosis in children under the age of two years. According to Shattuck and colleagues (2009), this reported timing of diagnostic recommendation past the age of three years would represent a diagnostic gap. With evidence suggesting ASD symptomology is present in most children under three years of age, and in some cases as early as nine to 12 months (Jones et al., 2014), and that a reliable and stable diagnosis of ASD can potentially be prescribed in children between two to three years of age (CDC, 2014), it could be inferred that there is an ASD diagnostic gap.
Examination of the diagnostic practices and perceived diagnostic challenges reported by practitioners in this survey may provide some insight into possible factors that may contribute to a diagnostic gap and why diagnoses are often recommended in children over the age of three years. An initial potential factor, which may delay the process from the outset, was the high proportion of practitioners’ reporting having children on waiting lists for initial practitioner review, with over three quarters of medical practitioners reporting waiting periods that extended beyond one month. Given that the standard pathway of assessment and diagnosis for ASD begins and ends with medical professionals (AABASD, 2011; AHPA, 2015), lengthy waiting periods may have a large impact on the diagnostic gap. Recommending a diagnosis under the age of two years was reported by practitioners to be difficult. Practitioners reported diagnostic uncertainty in this age group, with a high proportion reporting use of the “watch and wait” strategy when diagnostic presentations were unclear. Practitioners also reported perceived limitations of “gold standard” instruments and diagnostic criteria in children under two years of age. It could be that further education and training may improve diagnostic confidence.

Several study limitations need to be acknowledged. Although there is substantial evidence that a diagnostic gap exists elsewhere, results from this study cannot confirm the presence of a diagnostic gap in Australia. Rather, its presence is inferred by practitioners’ report of a predominant diagnostic age above three years. Related, this study does not address diagnostic accuracy, only practitioner perceptions of the process and associated challenges. Although an effort was made to survey practitioners across Australia in both rural and urban settings, and from various professions, not all Australian states or territories were represented, only
11% of respondents were from non-urban settings, and only eight psychiatrists participated; thus limiting the generalisability of the results. The expansion of the number of categorical options provided to record the length of waiting periods would have yielded more specific information regarding actual waiting periods reported by practitioners. Finally, inter-professional comparisons should be interpreted cautiously because of the different points in the diagnostic process to which these groups contribute, which apart from being an issue in itself, may mask differences in the clientele serviced by these groups.

Future research could assess usage of new or revised tools to facilitate ASD diagnosis, such as the ADOS-2 (Lord et al., 2012), the revised ADI-R algorithms for children aged 12 to 47 months of age (Kim et al., 2013) and Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5: APA, 2013). It should also include other professional groups who may be involved in the multidisciplinary assessment of ASD such as speech pathologists and occupational therapists. Further, the exploration of collaboration between professionals for the purpose of ASD assessment, including through a multidisciplinary process as recommended in the guidelines (AABASD, 2011) would be of interest. Finally, updated guidelines in the USA have recommended new practice parameters that involve the following additions to the ASD assessment process: the use of ASD specific measures that identify the core symptoms, screening for ASD to identify those in need of further evaluation, genetic testing, physical examination, hearing tests, and assessment of other co-morbid conditions; adaptive skills; unusual abilities, such as calendar calculations or artistic talents; sleep abnormalities; and evaluation by occupational therapists and physical therapists for further assessment and intervention (Volkmar et al., 2014). Future research could examine the use or potential use of such data for
Overall, this study suggests that ASD diagnostic practices have improved since Skellern et al. (2005) examined this issue. Whilst the comparison to that study must be made cautiously, it appears that formal and standardised approaches to assessment, as are prescribed in best practice guidelines, are being employed, and whilst practice variation remains, the use of recommended methods is occurring. Despite this change, it still seems that an ASD diagnostic gap as described by Shattuck et al. (2009) can be inferred from these data. Given that, in Australia, formal diagnostic verification is required to gain access to government funded and Medicare rebateable early intervention services, attempts to reduce this potential gap to improve timely and accurate detection of ASD in Australian are important. The diagnostic challenges that practitioners reported suggest that reducing wait lists and improving confidence in diagnosis in children under three years of age could help improve the diagnostic process.
Chapter 5: Agreement Between a Brief Autism Observational Instrument and Established Measures
Statement of Contribution of Co-Authors for Thesis by Published Paper

The following is the format for the required declaration provided at the start of any thesis chapter which includes a co-authored publication.

The authors listed below have certified* that:

1. they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
2. they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
3. there are no other authors of the publication according to these criteria;
4. potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit, and
5. they agree to the use of the publication in the student’s thesis and its publication on the QUT ePrints database consistent with any limitations set by publisher requirements.

In the case of this chapter:

<table>
<thead>
<tr>
<th>Contributor</th>
<th>Statement of contribution*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samantha L Ward</td>
<td>Conception and design of the research project, data collection and analysis, and preparation of manuscript</td>
</tr>
<tr>
<td></td>
<td>Date: 22.04.2016</td>
</tr>
<tr>
<td>Karen A Sullivan*</td>
<td>Aided experimental design, data analysis and interpretation, and critical revision of manuscript.</td>
</tr>
<tr>
<td>Linda Gilmore*</td>
<td>Aided experimental design, data analysis and interpretation, and critical revision of manuscript.</td>
</tr>
</tbody>
</table>

Principal Supervisor Confirmation

I have sighted email or other correspondence from all Co-authors confirming their certifying authorship.

Name __________________________ Signature __________________________ Date __________________________

142 Chapter 5: Agreement Between a Brief Autism Observational Instrument and Established Measures
Abstract

Objective: Limited time and resources necessitate the availability of accurate, inexpensive and rapid diagnostic aids for autism spectrum disorder (ASD). The Autistic Behavioural Indicators Instrument (ABII) was developed for this purpose, but its psychometric properties have not yet been fully established.

Method: The clinician-administered ABII, the Autism Diagnostic Observation Schedule (ADOS), the Childhood Autism Rating Scale – Second Edition, Standard Version (CARS2-ST), and Diagnostic and Statistical Manual of Mental Disorders (DSM-5) diagnostic criteria were individually administered to children with an independent paediatrician DSM-IV-TR or DSM-5 autism spectrum diagnosis, aged 2-6 years ($n = 51, M_{\text{child age}} = 3.6$ years). The agreement between each of the measures on autism diagnostic classification was calculated and compared, and the intercorrelations between the instruments examined.

Results: There was significant moderate agreement for the classification of autism between the ABII and the DSM-5, and significant fair agreement between the ABII and ADOS and ABII and CARS2-ST. True positive diagnostic classifications were similar across the ABII ($n = 47, 92.2\%$) and ADOS ($n = 45, 88.2\%$), and significantly higher than the CARS2-ST ($n = 30, 58.8\%$). The ABII total scale score was strongly positively correlated with both the ADOS and CARS2-ST total scores.

Conclusion: The ABII’s test characteristics were comparable to those of established measures and the intercorrelations between selected measures support its convergent validity. The ABII could be added to the clinician’s toolbox as a screening test.
Introduction

Although the detection and diagnosis of autism spectrum disorder (ASD) is complex, it is generally agreed that the defining core features of ASD emerge within the first two to three years of life for most children and can be detected by trained professionals following comprehensive diagnostic assessment at two years of age (Centers for Disease Control and Prevention [CDC], 2014; Guthrie, Swineford, Nottke & Wetherby, 2013). Yet, a large proportion of children are not seen for specialist diagnostic evaluation for ASD until after the age of three (Shattuck et al., 2009; Ward, Sullivan & Gilmore, in press). Optimising the timely and accurate referral of children with ASD for specialist evaluation is therefore critical to facilitate diagnosis. General practitioners play a pivotal role in the identification of children in need of referral for specialist ASD evaluation (Carbone, Farley & Davis, 2010). They are often the initial respondents to parental concerns (Filipek et al., 1999) and can therefore initiate early referral of children for specialist ASD assessment. However, during brief health-care visits it is difficult to elicit ASD specific information from parents (Zuckerman, Lindly & Sinche, 2015) or quantify the symptoms to assess risk (Gabrielsen et al., 2015). This can reduce the accuracy of referrals for specialist review, which itself could have several negative flow on effects, including delayed diagnosis (Reichow, Barton, Boyd & Hume, 2012). Allied health clinicians, such as psychologists, also play a pivotal role in the multidisciplinary assessment of children with ASD (Ward et al., in press). They are often involved in completing
comprehensive diagnostic assessment, which can be an expensive and timely process (Charman & Gotham, 2013). Brief and inexpensive methods of quantifying ASD risk could help to inform psychologists in their decisions regarding initiation of in-depth evaluation.

The use of ASD specific screening instruments in primary health and allied health-care settings can contribute to optimising timely and accurate referral of children with ASD (Charak & Stella, 2001-2002). However, existing instruments have yielded high misclassification errors and produced lower than desirable sensitivity and specificity values, limiting their utility in clinical settings (Al-Qabandi, Gorter & Rosenbaum, 2011; Barbaro & Dissanyake, 2010). The accurate differential detection of children with ASD from children with other developmental disorders and delays is important to guide referrals, to reduce costly diagnostic assessment, and to reduce undue parental distress associated with false positive screens on instruments (Bölte et al, 2013; Lipkin & Hyman, 2011). One of the most common non-specific “red flags” of ASD is speech and language delay (Johnson & Myers, 2007). Children with speech and language delay are over classified as having ASD on a number of existing screening instruments (Whitehouse, Barry & Bishop, 2007). The inclusion of non-specific symptomology, such as speech and language delay, to ascertain ASD risk, complicates and delays the detection of ASD. It can produce over inclusive referrals of children and bases detection on the absence of a skill that is not evident until later on in the child’s development (Downey et al., 2002).

The detection of ASD based on primary unique ASD indicators, that is, those indicators that have an early emergence and that are specific to ASD (Clifford, Young & Williamson, 2007) improves referral accuracy (Bölte et al., 2013). Formal
diagnostic evaluations for ASD are associated with high demands in terms of cost and time for already constrained systems, and possible increased stress for families (Horlin, Falkmer, Parsons, Albrecht & Falkmer, 2014; Shattuck & Grosse, 2007). With early detection of children deemed to be of increasing importance to facilitate earlier diagnosis (Bölte et al, 2013), there is scope for continued development of screening tools to improve the accuracy of referrals. To this end, a number of parent questionnaires have been developed to help to identify children in need of further ASD diagnostic evaluation. While parent interview serves as an important informant source in the symptomatic description and quantification of ASD behaviours (Sacrey et al., 2015), direct behavioural observation is also important, particularly when guided by standardised instruments specifically designed to elicit key ASD behaviours (American Academy of Pediatrics [AAP], 2006; Charak & Stella, 2001-2002; Hampton & Strand, 2015; Norris & Lecavalier, 2010).

A recently developed semi-structured brief observational instrument, the Autistic Behavioural Indicators Instrument (ABII: Ward & Gilmore, 2010), has shown preliminary utility in classifying children aged two to six years with and without Autistic Disorder (AD). In an initial examination of instrument classification efficiency, the ABII correctly classified all children with AD ($n=20$) and produced no misclassification errors of children with typical development ($n=20$) or speech and language impairment ($n=20$). The ABII is a unique instrument in that it is currently the only brief non-verbal observational instrument designed to quantify ASD risk based on the increased presence, rather than absence, of unique indicators of ASD. Conceptually, this feature may help to reduce misclassification errors (Wetherby et al., 2004). In addition, the ABII has previously shown very good discrimination of children with speech and language impairment. It does not require children to have...
developed the use of language or to understand spoken language and is designed to elicit key unique indicators of ASD for rapid quantification to ascertain ASD risk. The ABII was designed to optimise referral accuracy and is not intended to replace “gold standard” diagnostic evaluation procedures that involve comprehensive assessment methods.

The current study sought to further establish the psychometric properties of the ABII by exploring 1) the classification accuracy of children across the full range of diagnostic subcategories as operationalised in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR: APA, 2000), including Autistic Disorder (AD), Asperger’s Syndrome (AS), and Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS); 2) the classification accuracy of children across the full range of current diagnostic subcategories as operationalised in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5: APA, 2013), including Autistic Spectrum Disorder (ASD), severity level 1, severity level 2 and severity level 3; and 3) examining agreement on DSM-IV-TR and DSM-5 autism diagnostic classification between the ABII and existing autism instruments. These measures included the Autism Diagnostic Observation Schedule (ADOS: Lord, Rutter, DiLavore & Risi, 1999), a “gold standard” semi-structured observation instrument, and the Childhood Autism Rating Scale – Second Edition, Standard Version (CARS2-ST: Schopler, Van Bourgondien, Wellman & Love, 2010), a clinician-observation instrument of unstructured activities. The ADOS and the CARS2-ST were specifically chosen for comparative analysis as both are standardised instruments requiring clinician evaluation. Similar to the ABII, the ADOS and CARS2-ST provide a method of quantifying direct clinician observations of ASD behaviours, thus enabling the comparison of the ABII with similar clinician-
observation tools.

Method

Participants

Participants included children with an independent paediatrician verified diagnosis of autism using the criteria outlined in the DSM-IV-TR and DMS-5, aged between 2 and 6 years (n = 51, $M_{child\ age}$ = 3.6 years). A set of revised criteria and a change to the diagnostic subcategory were released in the DSM-5. Children who were diagnosed prior to the release of the revised criteria (n = 24, 47.1%) had been independently diagnosed using the DSM-IV-TR diagnostic criteria (Autistic Disorder [AD], n=13 (21%); Asperger’s Syndrome [AS], n = 7, 13.7%; Pervasive Developmental Disorder – Not otherwise specified [PDD=NOS], n = 4, 7.8%). Children who were independently diagnosed after the release of the DSM-5 (n = 27, 52.9%) had been diagnosed using the revised diagnostic criteria (autism spectrum disorder, severity level 1, n = 11 (21.6%); severity level 2, n = 7 (13.7%); severity level 3, n = 9 (17.6%). There was no significant difference in the distribution of children based on level of symptom severity, as outlined in the DSM-IV-TR and DSM-5 diagnostic subcategories, with both more severe (DSM-IV-TR diagnosis of AD: n=13, 21% or DSM-5 diagnosis of ASD, severity level 3, n = 9, 17.6%), and less severe (DSM-IV-TR diagnosis of AS, n = 7, 13.7%, PDD=NOS, n = 4, or a DSM-5 diagnosis of ASD, severity level 1, n = 11, 21.6% or severity level 2, n = 7, 13.7%) presentations represented in the sample, $\chi^2(1) = .961$, $p = .327$. Children with more severe presentations were significantly younger than those children with less severe presentations, $t(49) = -5.35$, $p < .000$, CI [-1.68, -.76]. $\eta^2 = .37$. The final cohort was predominately male (male, n = 40, female, n = 11), $\chi^2(1) = 16.49$, $p < .001$, however there was no significant difference in gender distribution between
more severe presentations (male = 14, female = 6) and less severe presentations (male = 24, female = 5), *fisher exact, p = .50, φc = .12.*

**Measures**

The Autistic Behavioural Indicators Instrument (ABII; Ward & Gilmore, 2010). The ABII is intended to be administered by registered general practitioners and allied health clinicians as a level 1 screening instrument to identify children in need of specialist diagnostic evaluation for ASD (National Initiative for Autism: Screening and Assessment [NIASA], 2003). The ABII assesses the presence of behavioural markers with an early emergence within key ASD domains. The ABII is an 18 item non-verbal screening instrument that includes a fixed sequence of standardised and structured tasks that elicit specific target behaviours across social attention, sensory and behavioural domains (see Ward and Gilmore, 2010 for a review of instrument development). The social attention subscale (SAS) comprises tasks that measure social orienting (e.g., preferential gaze to social or non social stimuli), and joint attention behaviours (e.g., preferences for shared engagement with a caregiver or solitary play), and displays of affect across social and non-social stimuli. The sensory subscale (SS) comprises tasks that measure visual, tactile, and oral sensory seeking behaviours (e.g., duration of time engaged in sensory exploration), and the presence of hypo- or hyper—responsiveness. The behavioural subscale (BS) comprises naturalistic observations of children when demands or denials are placed on the child (e.g. frequency and duration of behavioural protests). On all of the ABII items, a score of 0 represents typical behavioural responses and a score of 1 represents the presence of autistic behavioural indicators. Scores are added within each domain to calculate a subscale score and the aggregate of subscales is calculated to provide a total ABII scale score. Higher subscale and total ABII scores
represent a greater presence of autistic behavioural indicators. A total ABII score of 11 or above is indicative of a “positive” screen. In an initial examination of the utility of the ABII in classifying children aged 2 to 6 years with a DSM-IV-TR diagnosis of Autistic Disorder, a speech and language impairment, and neurotypical development (Ward & Gilmore, 2010), a cut-off score of 11 produced maximum sensitivity and specificity. Administration of the structured tasks on the ABII generally takes five to ten minutes, depending on the level of engagement and ability of the child.

**The Autism Diagnostic Observation Schedule (ADOS; Lord et al., 1999).**

The ADOS is a standardised semi-structured play based observational tool considered a “gold standard” instrument to guide diagnosis of ASD in children 2+ years of age. The instrument has a series of structured and semi-structured presses for interaction, accompanied by coding of specific target behaviours and general ratings of the quality of behaviours. The ADOS consists of four modules, one of which is selected for administration based upon the child’s expressive language ability. Modules 1 to 3 were used in the current study (Module 1: \(n = 13\); Module 2: \(n = 13\); Module 3: \(n = 36\)). The ADOS algorithm provides diagnostic cut-offs for autistic disorder, ASD, and non-ASD. Higher scores on the ADOS are indicative of greater impairment in core areas of deficit. The ADOS requires specialist training and takes approximately 40-60 minutes to administer. The measure has demonstrated strong psychometric properties (Lord et al., 2008). A revised version of the ADOS was released in 2012 (ADOS-2; Lord et al. 2012), but was not available when the data were collected for the current study.

**The Childhood Autism Rating Scale – Second Edition, Standard Version (CARS2 –ST; Schopler et al., 2010).** The CARS2-ST is a behavioural rating scale used to identify the presence and severity of symptoms of ASD in children 2+ years
of age and to distinguish them from children with other developmental disorders. Items on the CARS2-ST are drawn from five prominent systems for diagnosing ASD. The CARS2-ST is completed after direct observation of the child during unstructured activities. Ratings are based on a 4-point response scale that measures the intensity, abnormality and duration of behaviours. Based on combined ratings from the 15 items, the child’s score can be classified as indicative of mild, moderate, or severe autism, or no autism. Higher CARS2-ST scores indicate more severe forms of ASD. The CARS2-ST takes approximately 5 to 10 minutes to administer and can be used by a range of professionals (e.g. physicians, special educators and psychologists). The CARS2-ST has demonstrated sound psychometric properties (Schopler et al., 2010).

**The Diagnostic and Statistical Manual of Mental Disorders, fifth edition, (DSM-5) diagnostic criteria for ASD.** The Diagnostic and Statistical Manual of Mental Disorders, fifth edition, (DSM-5; APA, 2013), provides the diagnostic criteria used by clinicians to diagnose ASD. Revised criteria for ASD were released in the fifth edition. A single broader diagnostic category of autism spectrum disorder has replaced previously sub-categorised labels of AS, AD, and PDD-NOS, as outlined in the previous edition (DSM-IV-TR; APA, 2000). To meet diagnostic classification for ASD requires impairment and persistent deficits across criteria in two domains, namely social communication and restricted, repetitive patterns of behaviour, interests or activities. A specifier of severity can be applied ranging from ‘level 1: requiring support’ to ‘level 3: requiring substantial support’.

**Procedure**

Parents were made aware of the study through a research flyer distributed at medical appointments, allied health intervention sessions, special education schools,
and autism organisations. All parents provided informed consent and ethical approval was obtained from the Human Research Ethics Committee of Queensland University of Technology prior to conducting the study. All children commenced testing sessions by engaging in an initial unstructured play session of approximately five minutes duration. During this time the child was permitted to play freely with toys either alone, with the primary caregiver, or with the examiner. The administration order of the ABII and the ADOS was randomly assigned and counterbalanced. After these tests were administered the examiner completed the CARS2-ST and the DSM-5 diagnostic criteria for ASD. All measures were completed in the same test session for each participant and administered by a registered psychologist trained in the administration and scoring of each instrument. Total testing time varied from 45 minutes to 90 minutes depending on the child’s level of engagement and ability.

**Results**

**Correlations and Group Differences for the Total Instrument Scores**

The ABII total scale score was strongly correlated with both the ADOS ($r = 0.56, p < .01$) and CARS2-ST ($r = 0.71, p < .01$). To investigate any differences in instrument total scores based on ASD symptom severity, the sample was divided into two groups. Group 1 comprised children with more severe presentations (DSM-IV-TR diagnosis of AD and DSM-5 diagnosis of ASD level 3). Group 2 included children with less severe presentations (DSM-IV-TR diagnosis of AS and PDD-NOS and DSM-5 diagnosis of ASD level 1 and level 2). There were significant differences between the two groups in total instrument score with a large effect. Group 1 had significantly higher total scale scores on each of the instruments (see table 1 for means, standard deviations and $t$-test statistics).
Table 1

Means, Standard Deviations and t-test Statistics Based on DSM-IV-TR or DSM-5 Symptom Severity

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th></th>
<th>Group 2</th>
<th></th>
<th>df</th>
<th>t</th>
<th>CI [LL, UL]**</th>
<th>η²</th>
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<tbody>
<tr>
<td>ABII</td>
<td>18.08</td>
<td>2.69</td>
<td>14.19</td>
<td>3.92</td>
<td>49</td>
<td>4.11*</td>
<td>1.99, 5.79</td>
<td>.26</td>
</tr>
<tr>
<td>CARS2-ST</td>
<td>40.70</td>
<td>7.67</td>
<td>27.06</td>
<td>3.86</td>
<td>49</td>
<td>7.98*</td>
<td>10.17, 17.11</td>
<td>.56</td>
</tr>
<tr>
<td>ADOS</td>
<td>24.40</td>
<td>4.87</td>
<td>15.85</td>
<td>4.38</td>
<td>49</td>
<td>6.60</td>
<td>5.95, 11.16</td>
<td>.47</td>
</tr>
</tbody>
</table>

Note: Group 1, n = 25 (autistic disorder, n = 13, and autism spectrum disorder severity level 3 n = 9). Group 2, n = 26 (asperger’s syndrome, n = 7, pervasive developmental disorder – not otherwise specified, n = 4, autism spectrum disorder, severity level 1, n =11, and severity level 2, n = 7).

* p < .001
** 95% Confidence Interval (CI) Lower Limit and Upper Limit [LL,UL]

Given that child age can influence diagnosis and symptom emergence, the pooled data were split into two age groups and the effect of age on these variables was examined. Group 1 was younger than 4 years of age (n = 29, M_{child age} = 2.85 years, SD = .40) and group 2 were 4 years or older n =22, M_{child age} = 4.61 years, SD = .59). There was no significant age group difference in the proportion of children who were correctly classified on either the ABII, fisher exact, p =.303, φ_c =.19, or ADOS, fisher exact, p =.073, φ_c =.28. Older children were significantly more likely to be classified on the CARS2-ST, fisher exact, p <.001, φ_c =.64.

Classification Efficiency of the ABII, ADOS and CARS2-ST

There were no significant differences in the proportion of children diagnosed with more or less severe presentations who screened positive on the ABII, Fisher exact, p =.110, φ_c =.29. However, children with less severe presentations were significantly more likely to screen a false positive on the ADOS, Fisher exact, p =.023, φ_c =.36 and the CARS2-ST, Fisher exact, p <.001, φ_c =.741. Table 2 presents the true positive (TP) and false negative rates (FN) and z statistics for the
classification rates of the ABII, ADOS and CARS2-ST by the whole sample and by DSM-IV-TR and DSM-5 diagnostic subcategory.

For the classification of all children with a DSM-IV-TR and DSM-5 diagnosis, the ABII (TP: n = 47, 92.2%) demonstrated similar diagnostic classification efficiency with no significant differences when compared to the ADOS (TP: n = 45, 88.2%). Compared to the CARS2-ST (TP: n = 30, 58.8%), the ABII correctly classified significantly more children as having ASD, z = 3.92, p < .05. Correct classification rates were similar across the ABII and ADOS for children diagnosed with AD, AS, PDD-NOS, and ASD severity level 3. The ABII correctly classified more children with ASD level 1 compared to the ADOS, z = 3.20, p < .05, however, classified fewer children with ASD severity level 2 compared to the ADOS z = -2.80, p < .05. Compared to the CARS2-ST, the ABII correctly classified more children with all DSM-IV-TR and DSM-5 diagnoses, with the exception of children with a DSM-5 ASD diagnosis severity level 3, where there were no significant differences. For the cohort, there was a significant moderate agreement on ASD classification between the ABII and DSM-5 diagnostic criteria, κ = 0.50, p = .001, and significant though fair agreement between the ABII and ADOS, κ = 0.34, p = .013, and ABII and CARS2-ST, κ = 0.22, p = .013.
Table 2

*True positive (TP) and False Negative (FN) ASD Classification of Children and z Statistic*

<table>
<thead>
<tr>
<th></th>
<th>TP</th>
<th>FP</th>
<th>z</th>
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<tbody>
<tr>
<td></td>
<td>ABII</td>
<td>ADOS</td>
<td>ABII</td>
</tr>
<tr>
<td>All ASD</td>
<td>47 (92.2)</td>
<td>45 (88.2)</td>
<td>4 (7.8)</td>
</tr>
<tr>
<td>AD</td>
<td>13 (100)</td>
<td>13 (100)</td>
<td>-</td>
</tr>
<tr>
<td>AS</td>
<td>5 (71.4)</td>
<td>4 (57.1)</td>
<td>2 (28.6)</td>
</tr>
<tr>
<td>PDD-NOS</td>
<td>3 (75)</td>
<td>3 (75)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>ASD 1</td>
<td>11 (100)</td>
<td>9 (81.8)</td>
<td>-</td>
</tr>
<tr>
<td>ASD 2</td>
<td>6 (85.7)</td>
<td>7 (100)</td>
<td>1 (14.3)</td>
</tr>
<tr>
<td>ASD 3</td>
<td>9 (100)</td>
<td>9 (100)</td>
<td>-</td>
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<tr>
<th></th>
<th>TP</th>
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<tbody>
<tr>
<td></td>
<td>ABII</td>
<td>CARS2-ST</td>
<td>ABII</td>
</tr>
<tr>
<td>All ASD</td>
<td>47 (92.2)</td>
<td>30 (58.8)</td>
<td>4 (7.8)</td>
</tr>
<tr>
<td>AD</td>
<td>13 (100)</td>
<td>12 (92.3)</td>
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<tr>
<td>AS</td>
<td>5 (71.4)</td>
<td>2 (28.6)</td>
<td>2 (28.6)</td>
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<tr>
<td>PDD-NOS</td>
<td>3 (75)</td>
<td>2 (50)</td>
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</tr>
<tr>
<td>ASD 1</td>
<td>11 (100)</td>
<td>2 (18.2)</td>
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</tr>
<tr>
<td>ASD 2</td>
<td>6 (85.7)</td>
<td>3 (42.9)</td>
<td>1 (14.3)</td>
</tr>
<tr>
<td>ASD 3</td>
<td>9 (100)</td>
<td>9 (100)</td>
<td>-</td>
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</table>

*Note: All ASD, n= 51 (DSM-IV-TR diagnosis of Autistic Disorder (AD), n=13, Asperger’s Syndrome (AS), n=7, Pervasive Developmental Disorder – Not otherwise specified (PDD-NOS), n=4, DSM-5 diagnosis of autism spectrum disorder (ASD) severity level 1 (ASD 1), n = 11, severity level 2 (ASD 2), n = 7, severity level 3 (ASD) 3, n = 9.*

*p < .05*

**Discussion**

Current rates of referral for specialist diagnostic evaluation are occurring later than desirable, delaying formal ASD diagnosis for many children (CDC, 2014). ASD specific screening instruments could improve ASD detection during primary healthcare visits, guiding physician referral for specialist assessment. ASD screening instruments can also contribute to informing decisions from allied health clinicians.
whether to proceed with costly diagnostic instruments. Given that diagnostic
evaluation procedures are time consuming and expensive the accuracy of diagnostic
evaluation referrals and decisions to initiate comprehensive assessment is important.
To increase clinical utility, instruments need to strike a balance between detection
accuracy, and time and cost efficiency. The ABII was designed to address this
requirement, providing an inexpensive screening instrument to elicit ASD behaviours
for rapid quantification. The ABII is not designed to make a diagnosis or to replace
specialist clinician diagnostic consultation. Rather, the ABII is designed to inform
the accuracy of referrals to facilitate earlier detection of children in need of further
specialist diagnostic evaluation. This study provides further information on the
psychometric properties of the ABII (Ward & Gilmore, 2010) by examining its
classification efficiency of children diagnosed with DSM-IV-TR or DSM-5
diagnostic criteria for autism, establishing its correlation with existing instruments
(ADOS and CARS2-ST) and comparing its agreement with diagnostic criteria
(DSM-5), ADOS and the CARS2-ST in the classification of children with autism.

The ABII yielded acceptable correct classification efficiency, agreeing with
an independent paediatrician diagnosis of ASD in close to ninety percent of cases.
The ABII total scale score was strongly correlated with both the ADOS and the
CARS2-ST, demonstrating good interrelationship between the ABII and these
previously established and validated measures on the classification of children with
ASD. The ABII was in moderate agreement for the classification of ASD with the
DSM-5 and and in fair agreement with the ADOS and CARS-2-ST. Classification
efficiency on the ABII was similar to the ADOS and higher compared to the CARS2-
ST. In addition, the accurate detection of children across the autism spectrum was
high on the ABII, with both more and less severe presentations of ASD, as
determined by DSM-IV-TR and DSM-5 ASD diagnostic subcategory, screening positive on the ABII. In comparison, children with less severe presentations of autism were more likely to be misclassified on both the ADOS and the CARS2-ST. Although the ABII is an empirically derived instrument designed to measure the presence of specific behavioural markers of ASD with an early emergence, results from this examination suggest these specific indicators may be present up to the age of six years. Both younger and older children were correctly classified on the ABII, with no significant differences in classification accuracy based on age. This result warrants further investigation. ASD symptoms unfold over time (Estes et al., 2015), which may influence symptom manifestation and detection, potentially resulting in differences in symptom presentation between younger and older children. Theoretically, this evolving presentation of behavioural markers of ASD may result in the requirement for age specific screening instruments. A screening instrument that is highly sensitive at one age may not be as sensitive at another age, depending on when specific symptoms emerge. In this examination, the ABII correctly detected a very high proportion of children across all DSM-IV-TR and DSM-5 diagnoses of autism between the ages of 2 years to 6 years, suggesting that it may be a highly sensitive measure for detecting ASD indicators that is not influenced by symptom severity and age.

The difficulty that practitioners report in detecting ASD during brief clinical observations (Gabrielsen et al., 2015), in combination with practical time and resource constraints during standard primary child health-care visits, may increase the risk of either misidentification of children in need of further referral for ASD, or over identification of children with non specific developmental concerns and delays, producing inaccurate referrals. Further research is required to investigate how well
the ABII can distinguish children with ASD from children with other developmental concerns and disabilities.

With direct clinician-observation an important informant source in the measurement of ASD symptoms, and with structured behavioural observational instruments providing a potential source to improve detection of ASD behaviours (Charak & Stella, 2001-2002), continuing efforts are required to develop reliable and valid instruments. Few direct behavioural observation instruments to aid in the detection of children in need of further diagnostic evaluation are currently available for use. The ABII may help to address this resource gap, along with providing an instrument that possesses unique features compared to existing instruments. The ABII is the only brief non-verbal observational instrument designed to quantify ASD “risk” based on the increased presence rather than absence of unique indicators of ASD. These features may reduce misclassification errors.

**Limitations and Future Directions**

Although the present study aimed to further establish psychometric properties of the ABII in correctly classifying children across the full range of diagnostic subcategories of autism as operationalised under both DSM-IV-TR and DSM-5 diagnostic criteria, inclusion of children without an ASD diagnosis would have enabled additional exploration of specificity values, along with possible alteration to ASD severity cut-off scores to establish level of ASD severity, in line with the diagnostic criteria and ADOS and CARS2-ST severity cut-off scores. Therefore, results from this investigation should be regarded as exploratory. A future prospective longitudinal investigation would be of benefit to establish sensitivity, specificity, positive predictive validity and negative predictive validity, and to
compare the agreement between the ABII and the newly released revised ADOS-2 (Lord et al., 2012).

A further study limitation is that the examiner was not blind to child diagnosis. This may have influenced the observation and rating of ASD indicators. Although children were not assessed for IQ and speech and language skills in this study, unlike the CARS2-ST and ADOS, there was not a significant difference in the classification rates of children diagnosed with more or less severe presentations of autism, as outlined in the DSM-IV-TR and DSM-5 diagnostic subcategories and severity levels. This result may provide preliminary evidence that the ABII is measuring behavioural markers within key ASD domains that are present in children across the full spectrum of autism. While there was no significant difference in classification accuracy of the ABII between older and younger children, future research could further explore and control for any potential effect of age on classification. Finally, although screening children for ASD is of potential benefit to inform the accuracy of referrals, any screening instrument can carry inherent risk due to misclassification errors. ASD is an heterogeneous disorder with symptoms that can unfold across the early years of a child’s life, therefore screening should not be seen as a discrete process; rather, developmental surveillance methods need to be employed with possible screening at multiple stages, a practice that would necessitate inexpensive and rapid instruments with strong psychometric properties. Until such time that an instrument fulfils these requirements, screening for ASD needs to remain a cautionary practice.

Conclusions

This examination sought to expand upon previously reported psychometric properties of the ABII. Results indicate the ABII performs similarly to the ADOS
and is superior to the CARS2-ST in the classification of children across the autism spectrum, and it is strongly correlated with both measures. In this study, the ABII was in fair agreement with each of the measures and moderate agreement with the DSM-5 diagnostic criteria for ASD. Although not intended to replace comprehensive assessments or measures, the ABII could be a useful addition to clinicians’ batteries by providing a rapid method of quantifying ASD indicators to inform referral accuracy of children in need of further diagnostic evaluation of ASD.

Acknowledgements

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Conflicts of Interest

None

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.”
Chapter 6: Adapting the Autistic Behavioural Indicators Instrument (ABII) as a Parent Questionnaire (ABII-PQ)
Statement of Contribution of Co-Authors for Thesis by Published Paper

The following is the format for the required declaration provided at the start of any thesis chapter which includes a co-authored publication.

The authors listed below have certified* that:

1. they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
2. they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
3. there are no other authors of the publication according to these criteria;
4. potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit, and
5. they agree to the use of the publication in the student’s thesis and its publication on the QUT ePrints database consistent with any limitations set by publisher requirements.

In the case of this chapter:


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<th>Statement of contribution*</th>
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<td>Samantha L Ward</td>
<td>Conception and design of the research project, data collection and analysis, and preparation of manuscript</td>
</tr>
<tr>
<td>Signature</td>
<td></td>
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<td>Date: 22.04.2016</td>
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<tr>
<td>Karen A Sullivan*</td>
<td>Aided experimental design, data analysis and interpretation, and critical revision of manuscript.</td>
</tr>
<tr>
<td>Linda Gilmore*</td>
<td>Aided experimental design, data analysis and interpretation, and critical revision of manuscript.</td>
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Principal Supervisor Confirmation

I have sighted email or other correspondence from all Co-authors confirming their certifying authorship.

Name          Signature          Date
Abstract

Background: Both parent-report and clinician-administered ASD screening instruments are important to accurately inform ASD risk ascertainment. The aim of this study was to adapt a clinician-administered ASD screening instrument, the Autistic Behavioural Indicators Instrument (ABII), as a parent questionnaire equivalent (ABII-PQ).

Method: The modification of ABII items into parent questions is described. The ABII-PQ was trialled in a sample of parents of children, aged between 12 months and six years, with an autism spectrum disorder (ASD, n = 65, M_{child age} = 4.03 years) or typical development (TD, n = 37, M_{child age} = 2.09 years).

Results: Internal consistency was high, α = .92. Receiver operator curves analysis identified the optimal ABII-PQ cut-off score which yielded high sensitivity (.97) and specificity (.95). Classification accuracy was high for children across the autism spectrum (Autistic Disorder: n =35, 100%; Asperger’s Syndrome, n =14, 93%; Pervasive Developmental Disorder – Not Otherwise Specified: n =14, 93%).

Conclusion: The ABII-PQ shows promise as a parent questionnaire version of the ABII.

Key Words: Autism spectrum disorder, ASD, autism screening, parent questionnaire, ABII, ABII-PQ
Adapting the Autistic Behavioural Indicators Instrument (ABII) as a Parent Questionnaire (ABII-PQ)

Introduction

While comprehensive expert evaluation is thought to reliably identify children with autism spectrum disorder (ASD), accurate detection by less trained practitioners can be challenging (Ozonoff et al., 2009), particularly during brief encounters (Gabrielsen et al., 2015). Yet, referral of children in need of expert ASD evaluation is typically dependent upon detection by primary health-care providers who may have less training and who routinely observe only snapshots of the child during brief clinical observations (Centers for Disease Control and Prevention [CDC], 2014). The apparent difficulty that some practitioners have in detecting ASD symptomatic profiles may potentially delay diagnosis. Although expert evaluation can yield a stable ASD diagnosis between two and three years of age, children are generally not referred to experts until well after their third birthday (CDC, 2014). Thus, primary health-care providers need brief instruments to help guide their detection of children who require expert referral.

The Autistic Behavioural Indicators Instrument (ABII; Ward & Gilmore, 2010) is an 18 item semi-structured clinician-administered ASD screening instrument designed as a brief tool that is suitable for use by practitioners with minimal training in ASD. The ABII is a level 1 screening instrument (Zwaigenbaum et al., 2015) for use in children from 12 months of age. The ABII is the only non-verbal observational instrument to rapidly quantify ASD risk based on the increased presence, rather than absence, of unique primary indicators of ASD. These instrument characteristics may reduce misclassification as identification of ASD is not based on non-specific
symptoms or symptoms that have a later emergence. The ABII has shown promise in
correctly classifying children across the autism spectrum and its test characteristics
are comparable to those of established measures including the Autism Diagnostic
Observation Schedule (ADOS; Lord, Rutter, DiLavore & Risi, 1999), and the
Schopler, Van Bourgondien, Wellman & Love, 2010; Ward, Sullivan & Gilmore, in
press).

The current study aimed to adapt the clinician-administered ABII as a parent
questionnaire equivalent, the Autistic Behavioural Indicators – Parent Questionnaire
(ABII-PQ), and report initial psychometric properties. Parents are an important
source to inform ASD detection. They have increased opportunities to observe ASD
symptoms and to monitor symptom emergence across time. Parental detection of
ASD-related concerns at 12 months of age can accurately predict ASD diagnosis
(Sacrey et al., 2015). With diagnostic evaluations for ASD supported by the
combined use of parent-report and clinician administered tools (Volkmar et al., 2014;
Zander, Sturm & Bölte, 2015), it is likely that screening evaluations could also
benefit from this combined approach.

Method

Design

This study is an observational cross-sectional study in which scores on the
ABII-PQ are compared for a group of parents of children with ASD or TD.

Participants

A total of 102 parents of children with ASD \( n = 65, 63.7\% \) or typical
development (TD) \( n = 37, 24.2\% \) completed an anonymous version of the ABII-
PQ. Parents were eligible to participate if they had a child between the ages of 12
months and six years with either: (i) an ASD diagnosis; or (ii) typical development
(TD) and the absence of any diagnosed developmental delay, disability, medical condition, or mental health condition. Children were not evaluated by the researchers for ASD confirmation, but their parents reported that their child’s diagnosis had been verified (it had been provided by a paediatrician or psychiatrist and was recognised by the Australian government, including for the purposes of providing access to services). Children with TD were significantly younger ($M = 2.89$ years, $SD = 1.13$, range = 1-6) than children with ASD ($M = 4.37$ years, $SD = 1.13$, range = 2-6), $U = 443.00, z = -5.41, p < .001, r = .54$. Both the ASD (Boys: $n = 56$, 86.2%: Girls: $n = 9$, 13.8%) and TD groups (Boys: $n = 24$, 64.9%: Girls: $n = 13$, 35.1%), were predominately male, $\chi^2(1) = 32.98, p < .001$.

**Materials**

The ABII-PQ is a parent-report measure of both current and past observations of possible ASD indicators across social attention, sensory and behavioural domains. A pilot version of the ABII-PQ items was conducted with 10 parents, five of whom had a child with a Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR; American Psychiatric Association [APA], 2000) autism spectrum diagnosis (Autistic Disorder [AD], $n = 2$; Asperger syndrome [AS], $n = 2$; Pervasive Developmental Disorder – Not otherwise Specified [PDD-NOS], $n = 1$), and five of whom had a child without ASD. This pilot resulted in the modification of items to include both current and retrospective questions (items were changed from “do you find...” to “Do/did you find..”). No other modifications were required.

All items on the ABII-PQ were derived directly from the ABII. In instances where a behavioural indicator of ASD (e.g., social orienting) was measured using more than one item or method on the ABII (e.g., duration of gaze to social and non-
social stimuli), the item was adapted into a single question on the ABII-PQ. As with the ABII, on the ABII-PQ, items in the social attention subscale were designed to measure social orienting, joint attention, displays of affect, and preferences for social or non-social stimuli (e.g., Do/Did you find that your child preferred to look away from human faces?). The sensory subscale assesses parental report of the presence of either hypo- or hyper-sensitivity to sensory stimuli (e.g., Do/Did you find your child preferred to touch, mouth or look at toys rather than play with them in a typical fashion?). Behavioural subscale items elicit parental report of difficulties in emotional regulation (e.g., Do/Did you find your child difficult to soothe?). Table 1 shows the ABII-PQ items. All items are presented as Yes/No questions. The ABII-PQ is scored as for the ABII. That is, after reverse scoring selected items, each item is scored zero for a neurotypical response or one if the response indicates the presence of a primary unique autistic behavioural indicator. Scores are added within each domain to calculate a subscale score and the aggregate of subscales calculated to provide a total ABII-PQ scale score. Higher scores on each of the subscales and the total ABII-PQ scale score indicate a greater presence of autistic behavioural indicators.

**Procedure**

Ethical approval was obtained from the Human Research Ethics Committee of Queensland University of Technology (QUT-HREC # 0900001353) prior to conducting the study. Under this approval, consent was inferred from the return of a completed questionnaire.

Two versions of the ABII-PQ were created (paper and electronic). These two versions were identical apart from their format. The electronic version was
constructed using Key Survey (WorldAPP, 2014). Both versions commenced with demographic questions, followed by the ABII-PQ items.

Paper versions of the ABII-PQ and research flyers providing the url to the online version were distributed in primary health-care settings including medical, allied health and early education centres. Online research flyers were posted on autism forums and websites. The ABII-PQ paper version was either returned by parents in a self addressed sealed envelope or to reception personnel for collection ($n = 49$). Electronic responses were entered by parents directly online and were received by the researchers upon submission ($n = 52$). The ABII-PQ was then scored by a single rater as per standard instructions.

**Results**

**Reliability**

Internal consistency was below acceptable threshold across all of the ABII-PQ individual items, $\alpha = <.70$. This result was expected as the ABII-PQ items are not designed to assess a unitary dimension of ASD. Rather, individual items are designed to measure an autistic behavioural indicator within one of three core ASD domains, namely social attention, sensory, or behavioural. Internal consistency for the ABII-PQ subscales and total ABII-PQ scale was examined. As expected, internal consistency was high for the social attention subscale (SAS), $\alpha = .88$ and behavioural subscale (BS), $\alpha = .91$. Internal consistency was below acceptable threshold for the sensory subscale (SS), $\alpha = .65$. Removal of item 10, “Do / Did you find your child did not react or respond to noise?”, improved internal consistency of the SS to, $\alpha = .73$. Item 10 was subsequently removed from the ABII-PQ and all analyses report on the revised 11 item scale. Internal consistency was high for the total ABII-PQ scale (ABII-PQ), $\alpha = .92$. 

168 Chapter 6: Adapting the Autistic Behavioural Indicators Instrument (ABII) as a Parent Questionnaire (ABII-PQ)
**Item Analysis**

Chi-square analysis showed all of the ABII-PQ items significantly discriminated children with ASD from children with TD. Table 1 displays the comparison of children with ASD and TD who scored positive on the ABII-PQ items.

**Sensitivity and Specificity**

The Receiver Operator Curve (ROC) analysis was used to identify optimal cut-off scores for a positive screen on the subscales and total scale. For the subscales, a cut-off score of three was identified on the SAS and cut-off scores of one were identified for both the SS and BS. A cut-off score of five was identified for the total ABII-PQ scale. Acceptable sensitivity (Se) and specificity (Sp) values were reached across all subscales (SAS: Se = .93, Sp = .92, AUC = .969, p < .001 95% CI [.933 – 1.0]; SS: Se = .88, Sp = .81, AUC = .910, p < .001 [.849-.978]; BS: Se = .86, Sp = .74, AUC = .85, p < .001 [.759-.932]), and for the total scale (ABII-PQ: Se = .97, Sp = .95, AUC = .98, p < .001 [.944-1.0]).
Table 1

Comparison of Children with ASD and TD Who Scored Positive on the ABII-PQ Items

<table>
<thead>
<tr>
<th>ABII-PQ Item</th>
<th>ASD n (%)</th>
<th>TD n (%)</th>
<th>$\chi^2$</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Do/Did you find it difficult to gain your child’s attention?</td>
<td>56 (86.2)</td>
<td>7 (18.9)</td>
<td>45.13</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2) Do/Did you find it difficult to direct your child’s attention toward an object?</td>
<td>53 (81.5)</td>
<td>1 (2.7)</td>
<td>58.82</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>3) Do/Did you find that your child preferred to look away from human faces?</td>
<td>49 (75.4)</td>
<td>2 (5.4)</td>
<td>46.19</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>4) Do/Did you find your child preferred to play with objects rather than play with you or other individuals?</td>
<td>40 (61.5)</td>
<td>3 (8.1)</td>
<td>27.60</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>5) Do/Did you find that your child smiled when looking at human faces?</td>
<td>56 (86.2)</td>
<td>6 (16.2)</td>
<td>48.38</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6) Do/Did you find your child made few attempts to show you things?</td>
<td>45 (69.2)</td>
<td>7 (18.9)</td>
<td>23.88</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>7) Do/Did you find your child smiled more at objects and toys compared to people?</td>
<td>42 (64.6)</td>
<td>1 (2.7)</td>
<td>37.06</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>8) Do/Did you find your child was sensitive to: Noise, Touch, Smells, and/or Tastes?</td>
<td>60 (92.3)</td>
<td>10 (27)</td>
<td>46.67</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>9) Do/Did you find your child preferred to touch, mouth or look at toys rather than play with them in a typical fashion?</td>
<td>52 (80)</td>
<td>4 (10.8)</td>
<td>45.59</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>10) Do/Did you find your child did not react or respond to noise*</td>
<td>15 (23.1)</td>
<td>-</td>
<td>10.01</td>
<td>.002</td>
</tr>
<tr>
<td>11) Do/Did you find your child difficult to soothe?</td>
<td>57 (87.1)</td>
<td>10 (27)</td>
<td>38.50</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>12) Do/Did you find your child had difficulties in emotional regulation?</td>
<td>58 (89.2)</td>
<td>9 (24.3)</td>
<td>44.70</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

* Item removed from final ABII-PQ to improve internal consistency of the sensory subscale.
**Discriminant Function Analysis**

A discriminant function analysis (DFA) was performed using the 11 ABII-PQ items to determine the ability of the ABII-PQ to classify children as either ASD or TD and to identify the most discriminative ABII-PQ items. The DFA correctly classified 96.9% of children with ASD and 97.3% of children with TD. Table 2 shows the autistic behavioural indicator that is measured on each of the ABII-PQ items and the standardised canonical discriminant function coefficients for each item, with ABII-PQ items rearranged in order of highest weights. Based on these weights, six optimal items were identified: 2) “responding to joint attention”, 12) “temperament dysregulation”, 5) “social smiling”, 4) “shared engagement”, 9) “sensory exploration”, and 8) “hypersensitivity”.

These six best ABII-PQ items were examined to determine whether a critical item cut-off score improved instrument sensitivity and specificity compared to the cut-off score identified using a ROC analysis. At a cut-off score of ≥2 critical items, $Se = 1.0$ and $Sp = .81$. Increasing the cut-off score to ≥3 critical items reduced $Se = .98$ but increased $Sp = .92$. However, the ROC identified cut-off score produced optimal well balanced $Se = .97$ and $Sp = .95$, and was subsequently used for all analyses.
Table 2

The Autistic Behavioural Indicator Measured on Each of the ABII-PQ Items and the Standardised Canonical Discriminant Function Coefficients

<table>
<thead>
<tr>
<th>ABII-PQ Item</th>
<th>Subscale</th>
<th>Function 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>2) Responding to joint attention*</td>
<td>Social Attention</td>
<td>.457</td>
</tr>
<tr>
<td>12) Temperament dysregulation*</td>
<td>Behavioural</td>
<td>.299</td>
</tr>
<tr>
<td>5) Social smiling*</td>
<td>Social Attention</td>
<td>.279</td>
</tr>
<tr>
<td>4) Shared engagement*</td>
<td>Social Attention</td>
<td>.240</td>
</tr>
<tr>
<td>9) Sensory exploration*</td>
<td>Sensory</td>
<td>.227</td>
</tr>
<tr>
<td>8) Hypersensitivity*</td>
<td>Sensory</td>
<td>.211</td>
</tr>
<tr>
<td>3) Social orienting</td>
<td>Social Attention</td>
<td>.160</td>
</tr>
<tr>
<td>11) Difficulty soothing</td>
<td>Behavioural</td>
<td>.128</td>
</tr>
<tr>
<td>1) Shared attention</td>
<td>Social Attention</td>
<td>.124</td>
</tr>
<tr>
<td>6) Initiating joint attention</td>
<td>Social Attention</td>
<td>-.105</td>
</tr>
<tr>
<td>7) Non-social smiling</td>
<td>Social Attention</td>
<td>-.004</td>
</tr>
</tbody>
</table>

* Discriminant function analysis identified six critical items

Classification of Children on the ABII-PQ

When compared to the data on the developmental status of the children whose parents participated in this study, of the 65 screen-positive cases, 63 (96.9%) were diagnosed with ASD and two (3.1%) were TD. Table 3 presents the overall classification outcomes and means and standard deviations for the ABII-PQ total scale and subscale scores. All differences between children with ASD and TD were in the expected direction. The ABII-PQ discriminated children with ASD from children with TD across all subscales (SAS: $\chi^2(1) = 63.90$, $p < .001$, $\varphi_c = .79$; SS: $\chi^2(1) = 53.45$, $p < .001$, $\varphi_c = .72$; BS: $\chi^2(1) = 37.93$, $p < .001$, $\varphi_c = .61$), and total scale (ABII-PQ: $\chi^2(1) = 85.43$, $p < .001$, $\varphi_c = .92$. Children with ASD scored significantly higher for the presence of ABII-PQ indicators across all subscales (SAS: $U = 75.50$, $z = -7.94$, $p < .001$, $r = .79$; SS: $U = 208.50$, $z = -7.62$, $p < .001$, $r = .75$; BS: $U = 371.50$, $z = -7.62$, $p < .001$, $r = .75$).
z = -6.74, \( p < .001, r = .67 \) and total scale score (ABII-PQ: \( U = 49.50, z = -8.08, p < .001, r = .80 \)).

Table 3

*The Classification Outcomes, Means and Standard Deviations for the ABII-PQ Total Scale and Subscales*

<table>
<thead>
<tr>
<th>Classified ASD</th>
<th>Mean (SD)</th>
<th>Classified ASD</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>ASD</td>
<td>TD</td>
</tr>
<tr>
<td><strong>Total Scale</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABII-PQ</td>
<td>63 (96.9)</td>
<td>2 (5.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.74 (2.03)</td>
<td>2 (1.72)</td>
</tr>
<tr>
<td><strong>Subscales</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social attention</td>
<td>55 (84.6)</td>
<td>1 (2.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.25 (1.72)</td>
<td>.73 (1.21)</td>
</tr>
<tr>
<td>Sensory</td>
<td>51 (78.5)</td>
<td>3 (8.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.75 (.50)</td>
<td>.38 (.64)</td>
</tr>
<tr>
<td>Behavioural</td>
<td>59 (90.8)</td>
<td>12 (32.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.77 (.61)</td>
<td>.51 (.80)</td>
</tr>
</tbody>
</table>

* Significant differences derived using either Mann-Whitney U or Chi-Square analyses

The Association Between Age, Gender, ASD Symptom Severity and ABII-PQ Classification.

A logistic regression was performed to assess whether ABII-PQ classification, after controlling for age, gender and diagnostic status (ASD or TD), significantly predicted the children who would be classified as ASD. The full model was significant, \( \chi^2 (3, n = 102) = 101.66, p < .001, OR 52.61, 95\% CI [46.82 – 59.23] \). The Hosmer and Lesmeshow test indicated a good fit, \( \chi^2 = 8.79, p = .36 \). The model as a whole explained between 63.1\% (Cox and Snell R Square) and 86.4\% (Nagelkerke R square) of the variance in ABII-PQ classification and correctly classified 96.1\% of children. The strongest predictor of ABII-PQ classification was
diagnostic status, \( p < .001 \). Age and gender, did not significantly predict ABII-PQ classification \((p’s \leq .319)\). Degree of symptom severity, ascertained by DSM-IV-TR diagnostic subcategory, was examined to explore any potential differences in the way children with ASD were classified on the ABII-PQ. There were no significant differences in the way children with AD \((n = 35, 100\%)\), AS \((n = 14, 93.3\%)\) or PDD-NOS \((n = 14, 93.3\%)\) were classified on the ABII-PQ.

**Discussion**

The purpose of the current study was to adapt the clinician-administered ABII (Ward & Gilmore, 2010), as a parent questionnaire equivalent, the ABII-PQ, and report initial psychometric properties. The ABII-PQ is intended to screen children for the presence of behavioural indicators of ASD to identify children who may need developmental surveillance or comprehensive diagnostic evaluation. Results from this initial investigation of the ABII-PQ are promising. Children with ASD screened positive on more ABII-PQ items compared to children with TD. All ABII-PQ items significantly discriminated children with ASD from children with TD. Statistically derived cut-off scores were examined and each produced sensitivity and specificity values that are above the recommended .70 value (Dumont-Mathieu & Fein, 2005). While the false positive rate was low using either the ROC \( \geq 5 \) derived score, two children, or DFA \( \geq 3 \) critical item score, three children, any degree of misclassification warrants caution and highlights the importance of follow-up evaluations. Classification rates for children across the full ASD continuum of symptom severity (AD, AS and PDD-NOS) was also high, and age, gender and degree of symptom severity did not significantly influence ABII-PQ classification.

We acknowledge that, because children in this study were already diagnosed with ASD, their parents may have over-reported the presence of ASD indicators, as
they may be more aware of ASD symptoms compared to parents of undiagnosed children. This study is limited by the absence of diagnostic confirmation of children because parents self-identified as a parent of a child with an ASD diagnosis or typical development. However, given that best-estimate clinical diagnosis, guided by the use of standardised instruments and diagnostic criteria, is the gold standard for ASD diagnosis (Volkmar et al., 2014), it could be assumed children reached diagnostic confirmation through this method of evaluation.

Future research is required to establish psychometric properties of the ABII-PQ in a younger population, in children with an ASD diagnosis under the new diagnostic criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5; APA, 2013) and to compare its utility against existing parent-report screening instruments. Future research could consider including items to tap behaviours that are not characteristic of ASD (or not considered to be diagnostic indicators of ASD) as parents of both typically developing children and those with ASD would be expected to respond similarly to such items. Future research could investigate the factor structure of the ABII-PQ 11 items to explore whether a set of items within an identified domain improves detection. Other methods of item analysis should also be employed since the chi-square method that we used is relatively weak. A longitudinal screening study that determines the utility of the ABII-PQ as a screening instrument in both clinical and unselected samples is warranted. A larger sample would allow further comparison between the use of the ≥5 cut-off and ≥3 critical item cut-off scores to identify an optimal scoring algorithm. Development of a derivative early educator scale could be of use in supporting the integration of information from multi-informants into ASD screening. Finally, given that combining data from parent-report and clinician-
observation can have a complementary effect to contributing to ASD detection (Volkmar et al., 2014; Zander et al., 2015) future research could investigate any added value to ASD detection through the combined use of the the ABII and ABII-PQ.

The ABII-PQ is only intended for parental access under the provision of a health-care practitioner. It could be attractive for use as a screener for ASD because it is a time efficient way of eliciting structured parent-report of ASD symptoms, including social attention indicators for ASD, which have proven particularly difficult to assess (Lemler, 2012). In this study, approximately eighty-five percent of parents of children with ASD correctly classified their children within this domain. Given that social attention symptomology is amongst some of the early indicators of ASD (Barbaro & Dissanyake, 2012), an instrument that can elicit accurate parental-report on the presence of these symptoms may contribute to improved screening outcomes. The ABII-PQ also fits within DSM-5 core ASD criterion, with items measuring symptoms across social communication, sensory and behavioural domains.

**Conclusion**

Parent-report screening instruments that accurately quantify ASD symptoms across key ASD domains and severity levels, may complement other data to improve the accuracy of referrals for expert evaluations. The ABII-PQ shows preliminary promise as a parent-report screening instrument in children across the full autism spectrum.
Chapter 7: Combining Parent and Clinician Ratings of Behavioural Indicators of Autism Spectrum Disorder Improves Classification
Statement of Contribution of Co-Authors for Thesis by Published Paper

The following is the format for the required declaration provided at the start of any thesis chapter which includes a co-authored publication.

The authors listed below have certified* that:

1. they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
2. they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
3. there are no other authors of the publication according to these criteria;
4. potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit, and
5. they agree to the use of the publication in the student’s thesis and its publication on the QUT ePrints database consistent with any limitations set by publisher requirements.

In the case of this chapter:


<table>
<thead>
<tr>
<th>Contributor</th>
<th>Statement of contribution*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samantha L Ward</td>
<td>Conception and design of the research project, data collection and analysis, and preparation of manuscript</td>
</tr>
<tr>
<td>Signature</td>
<td></td>
</tr>
<tr>
<td>Date: 3.06.2016</td>
<td></td>
</tr>
<tr>
<td>Karen A Sullivan*</td>
<td>Aided experimental design, data analysis and interpretation, and critical revision of manuscript.</td>
</tr>
<tr>
<td>Linda Gilmore*</td>
<td>Aided experimental design, data analysis and interpretation, and critical revision of manuscript.</td>
</tr>
</tbody>
</table>

Principal Supervisor Confirmation

I have sighted email or other correspondence from all Co-authors confirming their certifying authorship.

Name ___________________________ Signature ___________________________ Date ___________________________
Abstract

Reliance on a single informant method in the evaluation of autism spectrum disorder (ASD) can increase misclassification. Yet, current ASD screening instruments predominately rely on a single informant approach. This study combined scores from two ASD screening instruments, the clinician administered Autistic Behavioural Indicators Instrument (ABII) and its parent questionnaire equivalent (ABII-PQ), to examine whether a combination score improved ASD classification in a sample of children with ASD ($n = 51$, $M_{\text{child age}} = 3.6$ years, $SD = 1.01$, range = 2-6 years). Results showed the ABII and ABII-PQ were significantly associated, $r = .62$, $p = .01$, and did not differ significantly on final correct ASD classification. However, final agreement on ASD classification between instruments was poor, $\kappa = .19$, $p = .184$. One method of combining scores from the ABII and ABII-PQ significantly improved classification, correctly classifying 100% of children with ASD. Results show combining scores from parent and clinician rated screening instruments could improve ASD classification.

Key Words: Autism spectrum disorder; autism screening; parent-report; clinician-observation; ABII; ABII-PQ
Combining parent and clinician ratings of behavioural indicators of autism spectrum disorder improves diagnostic classification.

**Introduction**

Improving the timing of referral of children with autism spectrum disorder (ASD) for diagnostic evaluation is a first step toward addressing a broader universal problem of improving the timing of ASD diagnosis (World Health Organization [WHO], 2013). Early ASD diagnosis is important to support children and their families to access ASD specific evidence-based early intervention (Kalkbrenner et al., 2011). Early onset of evidence-based early intervention can improve developmental outcomes for some children with ASD (Perry, Blacklock & Dunn Geier, 2013; Smith, Klorman & Mruzek, 2015; Wong et al., 2014, 2015). Although a stable ASD diagnosis can be made for most children with ASD between two and three years of age, the majority of children do not undergo their initial diagnostic evaluation until around 44 months of age and do not receive a final ASD diagnosis until after their fourth birthday (Centres for Disease Control [CDC], 2014). While some children may already access pre-diagnostic intervention (Monterio et al., 2016), without formal ASD identification, this intervention may not be evidence-based ASD specific intervention (Kalkbrenner et al., 2011) and in Australia, a final diagnosis is required to access government supported intervention (Department of Social Services [DSS], 2015). A diagnosis later in development can have the potential to reduce the opportunity to intervene during a time where neuroplasticity is highest (Landa, Holman, O’Neil & Stuart, 2011; Reichow, Barton, Boyd & Hume, 2012). Improving timing of ASD specific evidence-based intervention onset may be important to improving the lives of children with ASD and their families (Bölte et al., 2013).
Screening children for symptomatic ASD profiles can help to improve the timing of ASD identification (American Academy of Pediatrics [AAP], 2006; American Academy of Pediatrics News [AAP News], 2015). However, screening can carry inherent risk due to misclassification (Al-Qabandi, Gorter & Rosenbaum, 2011). Misclassification can increase burden on the child, family, health-care system and society (Bölte et al., 2013; Lavelle et al., 2014). Misclassification can produce under- or over-inclusive referrals for diagnostic evaluation. Under-inclusive referrals can prolong final diagnostic confirmation for children with ASD, while over-inclusive referrals cause undue parental stress and initiate potentially unnecessary costly and time consuming diagnostic evaluations (Dixon, Granpeesheh, Tarbox & Smith, 2011).

A characteristic of existing screening instruments that could increase misclassification, is their reliance on single informant data. Existing screening instruments use either stand-alone parent-report or clinician ratings. It is already known that parents and clinicians rate symptoms within core ASD domains differently. Clinicians can be more reliable in the detection of symptomology within the social communication domain, while parents can be more reliable in the identification of symptomology within the behavioural domain (Le Couteur, Haden, Hammal & McConachie, 2008; Lemler, 2012; Wiggins & Robins, 2008). Informant source differences could therefore have the potential to influence final ASD identification. It has already been shown that single informant ASD instruments, including the parent-report Autism Diagnostic Interview – Revised (ADI-R; Rutter, Le Couteur & Lord, 2003), and the clinician administered Autism Diagnostic Observation Scheduled (ADOS; Lord, Rutter, DiLavore & Risi, 1999), can disagree on final ASD classification (Kim & Lord, 2012; Le Couteur et al., 2008; Ventola et
al., 2006). Their combined use has been recommended (Volkmar et al., 2014; Zander, Sturm & Bölte, 2015), and may reduce the potential for discrepant symptom measurement between informant sources to influence final ASD classification outcomes.

Another characteristic of screening procedures that could contribute to misclassification is the environment in which the screening occurs. Screening children for symptomatic profiles of ASD is recommended during well-child care visits (AAP, 2006; American Academy of Pediatrics News [AAP News], 2016). These well-child care visits are generally short in duration (Halfon, Stevens, Larson & Olson, 2011). It has been shown that during brief visitations, the range of ASD behavioural features that are present for observation (Gabrielsen et al., 2015), and the elicitation of information from parents regarding ASD symptoms (Zuckerman, Lindly & Sinche, 2015) can be restricted. With brief well-child care visits likely already at risk of capturing partial samplings of ASD symptoms, in conjunction with the potential for single informant measures to inaccurately capture the full range of ASD symptoms, formal ASD screening instruments are needed to provide a rapid method of quantifying information from both parent and clinician ratings.

With the exception of the Checklist for Autism in Toddlers (CHAT; Baron-Cohen, Allen & Gillberg, 1992), which did combine parent and clinician ratings to screen children from 18 months of age, screening instruments do not combine information from these two informant sources. While the CHAT (Baron-Cohen et al., 1992) had high instrument specificity and sensitivity in identifying children with a Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR; American Psychiatric Association [APA], 2000) diagnosis of autistic disorder (AD), instrument sensitivity in identifying children with less severe
symptom presentations, including children with asperger’s syndrome (AS) and pervasive developmental disorder – not otherwise specified (PDD-NOS) was poor (Baird et al., 2000; Scambler, Hepburn & Rogers, 2006).

In order to improve instrument sensitivity and uptake in clinical settings, the CHAT (Baron-Cohen et al., 1992) was modified into the Modified Checklist for Autism in Toddlers (M-CHAT; Robins, Fein & Barton, 1999). The M-CHAT (Robins et al., 1999) is now a single informant parent-report screening instrument. The clinician rated component was removed on the argument that clinician observation during brief clinical encounters can be less reliable in ASD symptom detection compared to parent-report and ASD screening instruments need to be brief to increase clinical utility. While inaccurate clinician symptom detection could occur (Gabrielsen et al., 2015), reliable measurement of symptoms across ASD domains has been shown to require combined parent and clinician ratings (Lemler, 2012). Also, the benefits associated with reducing the portion of misclassification risk that is associated to potential measurement limitations, may outweigh the costs associated with an additional five to 10-minute screening time. Removal of the clinician observation section in the revised M-CHAT (Robins et al., 1999) may have come at the expense of instrument specificity (Eaves, Wingert, Ho & Mickelson, 2006; Pandey et al., 2008; Snow & Lecavalier, 2008). The M-CHAT (Robins et al., 1999) can also be less sensitive in classifying children across the full autism spectrum (Kleinman et al., 2008).

Combining parent and clinician ratings into a single screening instrument may be important to yield well-balanced sensitivity and specificity. While practitioners are likely informally combining information from both sources in their screening procedures already, previous investigations have not considered how to
best combine scores from ASD screening instruments. The use of a formal method has the advantage that it is easily replicated and its accuracy can be quantified. For example, parent and clinician ratings could be considered as equally important, and scores from both informant sources would be weighted accordingly. Alternatively, one informant could be considered as a primary source, and scores from this source could be weighted differentially (i.e., higher than the scores from a secondary or supplementary source). Given that parents and clinicians contribute distinctive information, a combined scoring approach could help to synthesise information in a systematic way to improve ASD identification. A number of possible methods of integration could be considered.

Different methods of combining data from multi-informant ratings in child assessment have been evaluated and could provide a model for a combined ASD screening score. The first method of integration incorporates a mutual categorical agreement method, referred to as either a both/and rule (Wright, Waschbusch & Frankland, 2007) or an and algorithm (De Pauw et al., 2009). Under this scoring model, all raters must be in agreement and report the symptoms as being present before the child is considered as a positive classification or case. Studies examining the combined use of ASD diagnostic tools, the ADI-R (Rutter et al., 2003) and the ADOS (Lord et al., 1999), have employed a mutual categorical-agreement method (Lemler, 2012; Zander et al., 2015). A second method incorporates a binary scoring model, assigning a positive classification if a single rater reports the symptom as present and threshold attainment is met according to either instrument. This method of integration has been referred to as an either/or rule (Wright et al., 2007) or an or algorithm (De Pauw et al., 2009). This latter approach may demonstrate improved sensitivity compared to a mutual categorical-agreement method, which may be
limited by the limitations inherent with each informant source. For example, under a mutual categorical-agreement method, if a parent rated instrument failed to detect a child who did have ASD, but the clinician rated instrument did correctly classify the child as having ASD, a false negative classification would be attained. An averaging strategy, whereby scores are added together and an average score used to guide classification, has been a common method of integration of scores; however, because this strategy does require some level of agreement between raters, discrepant results can still occur (De Pauw et al., 2009). The use of a common score, identified through statistical principal component analysis, has also been investigated (De Pauw et al., 2009). However, the incremental improvement to a combined rather than single informant score can be reduced when a common rater score is used (De Pauw et al., 2009). A final approach to combining scores, which has not previously been explored in relation to ASD instruments, would be to consider an additive scoring model. Under this model, scores from both instruments are weighted equally and added together to provide an overall total score, with ASD assignment attained when scores reach above a pre-determined cut-off. This scoring model employs similar scoring procedures to most ASD screening and assessment instruments.

The current study sought to examine different methods of combining data from the clinician rated ASD screening instrument, the Autistic Behavioural Indicators Instrument (ABII; Ward & Gilmore, 2010), and its parent-report equivalent, the Autistic Behavioural Indicators Instrument – Parent Questionnaire (ABII-PQ). These screening instruments were selected on the basis that their instrument characteristics may have the potential to improve the differential detection of children displaying mild to severe ASD symptomatic profiles (Ward & Gilmore, 2010; Ward et al., in press a). The ABII has shown high instrument
sensitivity and specificity, to be strongly correlated with the ADOS (Lord et al., 1999) and Childhood Autism Rating Scale – Second Edition, Standard Version (CARS2-ST; Schopler, Van Bourgondien, Wellman & Love, 2010), and to demonstrate fair agreement on ASD classification with the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5; American Psychiatric Association [APA, 2013], ADOS, and CARS2-ST (Ward, Sullivan & Gilmore, in press a).

It was hypothesised that: 1) while the ABII and ABII-PQ total scale scores would be strongly correlated, and both instruments would provide independent contributions to ASD classification, agreement on final ASD classification between the instruments would be poor; 2) the instruments would significantly differ in their measurement of symptoms within the social attention, sensory and behavioural subscales, with the ABII expected to classify more children in the social attention subscale and the ABII-PQ expected to classify more children in the sensory and behavioural subscales; 3) a combination score from the two instruments using a binary or additive scoring method would significantly improve ASD classification; and 4) a mutual categorical-agreement scoring method would significantly reduce ASD classification accuracy.

Method

Participants

The participant characteristics are presented in Table 1. The sample comprised 51 parents and their children ($M_{\text{child age}} = 3.6$ years, $SD = 1.01$, Range 2 – 6 years), who had a verified best-estimate clinical autism spectrum diagnosis from practitioners involved in the diagnostic evaluation of children for ASD. These practitioners were not involved in the research program. Final diagnostic
confirmation had been reached by practitioners using a best-estimate clinical diagnosis procedure. These practitioners were registered in clinical practice and therefore child ASD diagnosis had been verified and these children formally identified as having an ASD diagnosis. Diagnostic confirmation letters were required for inclusion in the study.
Table 1

Demographic Characteristics of the Sample by DSM-IV-TR or DSM-5 Diagnostic Subcategory

<table>
<thead>
<tr>
<th></th>
<th>Total n=51</th>
<th>DSM-IV-TR AD n=13 (21%)</th>
<th>DSM-IV-TR AS n=7 (13.7%)</th>
<th>DSM-IV-TR PDD-NOS n=4 (7.8%)</th>
<th>DSM-5 Severity 1 n=11 (21.6%)</th>
<th>DSM-5 Severity 2 n=7 (13.7%)</th>
<th>DSM-5 Severity 3 n=9 (17.6%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chronological Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M (SD)</td>
<td>3.60 (1.01)</td>
<td>2.893 (.79)</td>
<td>3.91 (1.21)</td>
<td>3.53 (.58)</td>
<td>4.44 (.79)</td>
<td>4.21 (.69)</td>
<td>2.93 (.58)</td>
</tr>
<tr>
<td>Range</td>
<td>2.03-6</td>
<td>2.03-4.03</td>
<td>3.02-6</td>
<td>3.01-4.05</td>
<td>3.09-5.11</td>
<td>3.09-5.08</td>
<td>2.08-4.03</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>40 (78.4%)</td>
<td>8 (20%)</td>
<td>7 (17.5%)</td>
<td>3 (7.5%)</td>
<td>9 (22.5%)</td>
<td>5 (12.5%)</td>
<td>8 (20%)</td>
</tr>
<tr>
<td>Female</td>
<td>11 (21.6%)</td>
<td>5 (45.5%)</td>
<td>0 (0%)</td>
<td>1 (9.1%)</td>
<td>2 (18.2%)</td>
<td>2 (18.2%)</td>
<td>1 (9.1%)</td>
</tr>
</tbody>
</table>

Note: DSM-IV-TR AD = autistic disorder; DSM-IV-TR AS = asperger’s syndrome; DSM-IV-TR PDD-NOS = pervasive developmental disorder – not otherwise specified.
Depending on the age and timing of best-estimate clinical diagnosis, children had been diagnosed using either DSM-IV-TR (APA, 2000; \( n = 24, 47.1\% \)) or DSM-5 diagnostic criteria (APA, 2013; \( n = 27, 52.9\% \)). There was no significant difference in the distribution of children based on level of symptom severity, ascertained using DSM-IV-TR (APA, 2000) or DSM-5 (APA, 2013) diagnostic subcategories. Both more severe (categorised by DSM-IV-TR (APA, 2000) AD or DSM-5 (APA, 2013) ASD, severity level 3) and less severe (categorised by DSM-IV-TR (APA, 2000) AS or PDD=NOS, or DSM-5 (APA, 2013) ASD, severity level 1, or severity level 2) presentations were represented in the sample, \( \chi^2(1) = .961, p = .327 \).

**Measures**

**The Autistic Behavioural Indicators Instrument (ABII; Ward & Gilmore, 2010).** The ABII is an 18 item play based semi-structured clinician-administered screening instrument. The ABII measures the additive presence of combined unique primary ASD indicators. The ABII includes a fixed sequence of standardised and structured tasks designed to elicit specific target behaviours across social, sensory and behavioural domains. The social attention subscale (SAS) comprises a set of tasks designed to measure social orienting (e.g., preferential gaze to social or non-social stimuli), joint attention behaviours (e.g., preferences for shared engagement with a caregiver or solitary play), and displays of affect across social and non-social stimuli. The sensory subscale (SS) comprises a set of tasks designed to measure visual, tactile, and oral sensory seeking behaviours (e.g., duration of time engaged in sensory exploration), and the presence of hypo- or hyper-responsiveness. The behavioural subscale (BS) comprises naturalistic observations of temperament dysregulation (e.g., frequency and duration of behavioural protests during demands or denials). On all of the ABII items, a score of
0 represents neurotypical behavioural responses and a score of 1 represents the presence of autistic behavioural indicators. Scores are added within each domain to calculate a subscale score and the aggregate of subscales calculated to provide a total ABII scale score. Higher subscale and total ABII scores represent a greater presence of autistic behavioural indicators. A total ABII score of $\geq 11$ is indicative of a positive screen.

The Autistic Behavioural Indicators Instrument –Parent Questionnaire (ABII-PQ). The ABII-PQ is an 11 item parent-report version of the ABII. Items are adapted from the ABII and modified into parent questions (e.g., ABII Item 7: preference for shared engagement with primary caregiver versus solitary play, was modified to ABII-PQ item 6: Do/Did you find your child preferred to play with objects rather than play with you or other individuals?). In instances where the ABII measures a behavioural indicator of ASD (e.g., social orienting) across more than one item or method on the ABII (e.g., duration of gaze to social and non-social stimuli), the item was adapted into a single question on the ABII-PQ. The ABII-PQ scoring procedures are the same as for the ABII. The ABII-PQ was trialled in a sample of parents of children, aged between 12 months and six years, diagnosed with ASD ($n = 65$) or children regarded to have neurotypical development ($n = 37$). At a total scale ABII-PQ score of $\geq 5$, sensitivity ($Se$) was .97 and specificity ($Sp$) was .95. Well balanced $Se$ and $Sp$ values were reached at cut-off scores across the subscales (SAS: $\geq 3$; SS: $\geq 1$; $\geq 1$). The area under the curve (AUC) was .98, $p = <.001$, 95% CI: .94-1.0.

The mutual categorical-agreement, binary and additive scoring models.

Three different methods of combining scores were examined. Scoring model one employed a mutual categorical-agreement system. Under this scoring model,
threshold cut-off must be attained on each instrument for a positive screen. Scoring model two involved the use of a binary scoring system. This scoring system used attainment cut-off on either instrument to reach threshold. Scoring model three employed an additive scoring system. Under this model, total scale scores from both the ABII and ABII-PQ are added to produce a total combined scale score. A pilot study of 12 children with a DSM-IV-TR (APA, 2000) autism spectrum diagnosis (AD: \( n=3 \); AS: \( n=6 \); PDD-NOS: \( n=3 \)) and eight children regarded to have neurotypical development, aged 2-6 years, was conducted to identify a total combined ABII and ABII-PQ score. Receive Operator Curves (ROC) analysis identified an optimal cut-off score of \( \geq 10 \) (\( Se = 1.0 \) and \( Sp = 1.0 \)).

**Procedure**

Eligible children and their parents were invited to participate through distribution of a research flyer at both private and public medical and allied health assessment, diagnostic and intervention clinics, early education centers, and through autism specific organisation mailing lists, websites and parent forums. The ABII and ABII-PQ were administered in a single test session. Administration of the instruments was randomly assigned and counterbalanced. Approximately half of the parents (\( n = 25 \)) completed the ABII-PQ first, while the remaining parents and children (\( n = 26 \)) completed the ABII first.

**Statistical Analysis**

The statistical analysis program IBM SPSS statistics Version 23.0 was used for all data handling and analysis. Chi Square analysis was used to compare the demographic characteristics of children. Pearson’s correlation coefficient and Cohen’s Kappa were performed to examine the association and agreement between the instruments.
A logistic regression analysis examined the impact of child demographic characteristics on likelihood of ASD classification. ASD classification accuracy was compared for the two screening instruments and three combination scores using a \( z \) statistic to provide a direct and parsimonious way of testing the difference between true positive (TP) and false negative (FN) classification percentages. For all analyses, a significance level was set at .05.

**Ethics**

This study was approved by the Human Research Ethics Committee of Queensland University of Technology, and the parents of children provided informed consent.

**Results**

**Correlations Between the ABII and ABII-PQ Total Scale and Subscale Scores**

Although there was a significant and strong positive correlation between the ABII and ABII-PQ total scale scores, \( r = 0.67, p < .01 \), and at the subscales, between the SAS scores, \( r = 0.52, p < .01 \), the SS, \( r = .23, p = .113 \), and BS, \( r = -.16, p = .255 \), scores were not correlated.

**The Effect of ASD symptom Severity and Age on ABII and ABII-PQ Classification**

A logistic regression was performed to assess the impact of ASD symptom severity and age on the likelihood of ABII and ABII-PQ classification. Neither model was significant, ABII, \( \chi^2(3, n = 51) = 5.92, p = .115 \), ABII-PQ, \( \chi^2(3, n = 51) = 5.92, p = .115 \). Degree of ASD symptom severity, ascertained by diagnostic subcategory, \( p = .962, p = .670 \), or age, \( p = .716, p = .303 \), did not significantly predict ABII or ABII-PQ classification.

On the ABII, true positive (TP) rates were higher for children with AD (TP = 25, 100%) compared to children with AS (TP = 15, 83.3%), \( z = 2.12, p < .05 \).
Children with PDD-NOS (TP = 7, 87.5%), did not differ from children with AD, z = 1.80, p > .05, or children with AS, z = .33, p > .05. On the ABII-PQ, true positive (TP) rates were similar for children with AD (TP = 25, 100%) and children with AS (TP = 16, 88.9%), z = 1.70, p > .05. Children with PDD-NOS (TP = 6, 75%), were less likely to be correctly classified compared to children with AD, z = -2.58, p < .05. Children with PDD-NOS and AS did not differ on how they were classified on the ABII-PQ, z = .91, p > .05. Children with AD, AS or PDD-NOS were just as likely to be correctly classified on the ABII as they were on the ABII-PQ.

**Classification and agreement between the ABII and ABII-PQ on ASD classification**

Table 2 presents the true positive (TP), false negative (FN) and agreement between instruments. To examine any significant differences between the percentage correct classification the z statistic was used. While the ABII (TP = 47/51, 92.2%) and ABII-PQ (TP = 47/51, 92.2%) did not differ significantly in final ASD classification, z = -1.39, p > .05, their disagreement on the classification of six children resulted in overall poor agreement between instruments, κ = .19, p = .184.
Table 2

Classification Rates and Agreement (Kappa) on ASD Classification Between the Autism Behavioural Indicators Instrument (ABII) and ABII Parent Questionnaire (ABII-PQ) Total Scale and Subscale Scores

<table>
<thead>
<tr>
<th>Instrument</th>
<th>True Positive</th>
<th>False Negative</th>
<th>Agreement</th>
<th>$\kappa$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Scale</td>
<td>ABII</td>
<td>47 (92.2)</td>
<td>4 (7.8)</td>
<td>45 (88.2)</td>
<td>.19</td>
</tr>
<tr>
<td></td>
<td>ABII-PQ</td>
<td>47 (92.2)</td>
<td>4 (7.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subscale</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social attention</td>
<td>ABII</td>
<td>47 (92.2)</td>
<td>4 (7.8)</td>
<td>48 (94.2)</td>
<td>.38</td>
</tr>
<tr>
<td></td>
<td>ABII-PQ</td>
<td>47 (92.2)</td>
<td>4 (7.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensory*</td>
<td>ABII</td>
<td>24 (47.1)</td>
<td>24 (52.9)</td>
<td>26 (50.9)</td>
<td>.04</td>
</tr>
<tr>
<td></td>
<td>ABII-PQ</td>
<td>50 (98)</td>
<td>1 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Behavioural*</td>
<td>ABII</td>
<td>28 (54.9)</td>
<td>23 (45.1)</td>
<td>23 (45.1)</td>
<td>.05</td>
</tr>
<tr>
<td></td>
<td>ABII-PQ</td>
<td>50 (98)</td>
<td>1 (2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$n = 51$. *Significant difference between instruments on ASD classification derived using $z$ statistic, $p < .05$.

At the subscale level, on the SAS, the ABII (TP = 47/51, 92.2%) and ABII-PQ (TP = 47/51, 92.2%) correctly classified similar rates of children, $z = -1.39$, $p > .05$; however, their disagreement on the classification of three children resulted in overall fair instrument agreement, $\kappa = .38$, $p = .001$. Significant differences were found between the ABII and ABII-PQ in the classification of children on the SS’s and BS’s, resulting in poor agreement between the instruments. On the SS, the ABII (TP = 24/51, 47.1%) significantly classified fewer children compared to the ABII-PQ (TP = 50/51, 98%), $z = -5.77$, $p < .05$, $\kappa = .04$, $p = .341$. On the BS, again, the ABII (TP = 28/51, 54.9%) significantly classified fewer children compared to the ABII-PQ (TP = 50/51, 98%), $z = -5.13$, $p < .05$, $\kappa = .05$, $p = .265$.

Classification Efficiency of the Scoring Models Compared to the Individual Instruments

Table 3 displays the TP and FN classifications for comparisons between the instruments with the scoring models. Combing scores using the additive scoring...
model significantly improved classification compared to single instrument usage, correctly classifying 100% of children with ASD, \( z = 2.06, p < .05 \). While the binary scoring model increased classification to 98%, this was not a significant improvement, \( z = 1.39, p > .05 \). This result was due to one child being misclassified on both the ABII and ABII-PQ. Finally, although under the mutual scoring model, classification was reduced 86.3%, this was not significant, \( z = -.97, p > .05 \).

Table 3

<table>
<thead>
<tr>
<th>Scoring Model</th>
<th>True Positive</th>
<th>False Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Instrument Scores</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABII</td>
<td>47 (92.2)</td>
<td>4 (7.8)</td>
</tr>
<tr>
<td>ABII-PQ</td>
<td>47 (92.2)</td>
<td>4 (7.8)</td>
</tr>
<tr>
<td>Combined Scores†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Additive*</td>
<td>51 (100)</td>
<td>0</td>
</tr>
<tr>
<td>Binary</td>
<td>50 (98)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Mutual</td>
<td>44 (86.3)</td>
<td>7 (13.7)</td>
</tr>
</tbody>
</table>

\( n = 51. \) † Three combined scores were used: Additive score = ≥10; Binary score = positive screen on either the ABII or ABII-PQ; Mutual score = positive screen on both the ABII and ABII-PQ. *Significant difference between instruments and scoring model on ASD classification derived using \( z \) statistic, \( p < .05 \).

Discussion

This study explored different methods of combining scores from the clinician-administered ABII and its parent-report equivalent the ABII-PQ, to examine whether a combined score improved ASD classification. Results support the combining of parent and clinician ratings to improve the screening classification of ASD. While each single informant instrument provided independent contributions to correctly classifying children with ASD, disagreement between the parent and clinician rated instruments on final ASD classification demonstrates the potential for
Combining single informant screening instruments to reach different screening outcomes for the same child. Combining scores under an additive scoring model significantly improved ASD classification, correctly classifying 100% of children with ASD. Although not significant, classification accuracy was reduced to approximately 86% under the mutual categorical-agreement scoring method. These outcomes may inform future attempts on how to best synthesise information from ASD parent-report and clinician rated screening instruments to improve ASD classification.

Discrepancies between the parent and clinician rated instruments, in the measurement of symptoms within behavioural and sensory ASD domains, followed predicted patterns. More children were misclassified on the behavioural and sensory subscales on the clinician rated instrument (ABII) compared to the parent rated instrument (ABII-PQ). These discrepancies could be influenced by informant source differences. It has already been shown that children with ASD display reduced expression of symptoms in brief clinical settings (Gabrielsen et al., 2015). Although the ABII has been specifically designed to elicit ASD indicators, its behavioural and sensory subscales both include items that rate the observed presence of these symptoms during the short time of instrument administration.

There were no significant discrepancies in the ratings of symptoms within the social attention subscale between the ABII and ABII-PQ. This result was not predicted as it was expected that the parent rated ABII-PQ would be less accurate in the classification of children with ASD on this subscale. Previous examinations have shown parents under-report symptoms within the social communication domain (Le Couteur et al., 2008; Lemler 2010; Wiggins & Robins, 2008). However, the parent rated ABII-PQ correctly classified over 90% of children on the social attention subscale. Although this result may show that the ABII-PQ accurately elicits
information from parents on the presence of these symptoms, it may also show the potential for parents who are already informed of their child’s ASD diagnosis to be more aware or vigilant to detecting these ASD symptoms.

Results suggest that, although combining scores from a parent and clinician rated screening instrument under an additive scoring model significantly improved classification accuracy, an additive scoring model that weights scores differentially may improve classification accuracy further. Results show the potential for discrepant ratings on the presence of ASD symptoms between parent and clinician rated ASD screening instruments. While results both parent and clinician informant instruments are important in providing information on the presence of ASD indicators, outcomes from this study, in combination with previous research (Le Couteur et al., 2008; Lemler, 2012; Wiggins & Robins, 2008), suggest improvements to classification accuracy may occur if scores within behavioural and sensory domains are scored higher on the parent rated instrument, and scores within the social attention domain are scored higher on the clinician rated instrument.

This study has a number of limitations. The study cohort was comprised of children already diagnosed with a DSM-IV-TR (APA, 2000) or DSM-5 (APA, 2013) autism spectrum diagnosis. Although the aim of this research was to determine whether a combination score would improve ASD classification, inclusion of both clinical and unselected samples would enable further investigation of possible cut-off scores for the combination scoring systems. Sampling children already diagnosed on the autism spectrum may also increase the potential for selection bias in the report of ASD symptoms. Parents in this study may have been influenced by prior knowledge of autism and its behavioural indicators and therefore more adept at reporting these indicators, compared to parents without such knowledge. The clinician informant in
this study was not blind to child diagnosis, and it is possible that this influenced the observation and rating of autism indicators. Although age and ASD symptom severity did not influence the likelihood of classification on either the ABII or ABII-PQ, it was a limitation that there was no control for intelligence, as well as speech, language, and adaptive functioning.

Future research could further investigate possible alterations to the cut-off score on the additive model to further explore if a reduction to the cut-off score, the use of critical items, or a weighted model improves overall classification. Future research could explore the option of a severity sub-classification “risk” cut-off score, in line with current DSM-5 (APA, 2013) diagnostic criteria severity levels. Further examination of the additive scoring model may be required to investigate the positive and negative predictive values in cases where extreme disparities are present between the two instruments on the overall presence of ASD indicators. For example, cases where one instrument fails to detect the presence of any ASD indicators while the other instrument detects all ASD indicators as being present. Finally, a screening study is required to establish whether a combination score from parent and clinician rated instruments does significantly reduce ASD misclassification risk.

Summary

Outcomes from this study may inform screening practices; an important contribution to the field as ASD screening is becoming more important and is increasingly recommended (AAP, 2016). Results provide initial evidence that single informant screening instruments may increase misclassification, and supports combining information from parent and clinician rated ASD screening instruments using an additive scoring model to improve ASD classification. Results suggest further improvement to ASD classification under a weighed additive scoring model.
Study outcomes may apply more broadly to informing procedures of how to best combine scores from parent and clinician rated ASD instruments that are used to guide diagnostic evaluations.
Chapter 8: Using a Combined parent-clinician Informant Screening Instrument to Predict Autism Spectrum Disorder
Statement of Contribution of Co-Authors for Thesis by Published Paper

The following is the format for the required declaration provided at the start of any thesis chapter which includes a co-authored publication.

The authors listed below have certified* that:

1. they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
2. they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
3. there are no other authors of the publication according to these criteria;
4. potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit, and
5. they agree to the use of the publication in the student’s thesis and its publication on the QUT ePrints database consistent with any limitations set by publisher requirements.

In the case of this chapter:


<table>
<thead>
<tr>
<th>Contributor</th>
<th>Statement of contribution*</th>
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<tbody>
<tr>
<td>Samantha L Ward</td>
<td>Conception and design of the research project, data collection and analysis, and preparation of manuscript</td>
</tr>
<tr>
<td>Karen A Sullivan*</td>
<td>Aided experimental design, data analysis and interpretation, and critical revision of manuscript.</td>
</tr>
<tr>
<td>Linda Gilmore*</td>
<td>Aided experimental design, data analysis and interpretation, and critical revision of manuscript.</td>
</tr>
</tbody>
</table>

Principal Supervisor Confirmation

I have sighted email or other correspondence from all Co-authors confirming their certifying authorship.

Name: __________________________ Signature: __________________________ Date: __________________________
Abstract

This study conducted a preliminary evaluation of a combined parent-clinician informant screening instrument, the Autistic Behavioural Indicators instrument–Combined (ABII-C). The ABII-C, along with established instruments including: Early Screening of Autistic Traits Questionnaire (ESAT), Modified Checklist for Autism in Toddlers (M-CHAT), Brief Infant Toddler Social Emotional Assessment (BITSEA), Childhood Autism Rating Scale–Second Edition, Standard Version (CARS2-ST), and Autism Diagnostic Observation Schedule (ADOS), were administered in a high-risk sibling cohort ($n = 28$, $M_{\text{child age}} = 27$ months, $SD = .56$, range = 20-46 months). Children were evaluated for a best-estimate clinical autism spectrum disorder diagnosis by practitioners who were blind to screening outcomes. Children were re-screened across all instruments after 12 months, and parents followed-up after 24 months to determine the stability of screening outcomes and diagnosis. The ABII-C internal consistency, $\alpha = .91$, and test retest reliability, $r = .95$, were excellent. The ABII-C was strongly correlated with each of the ASD specific instruments. At initial screening, the ABII-C was the only screening instrument to correctly predict 100% of children who went on to receive a best-estimate ASD diagnosis or be regarded to show neurotypical development. This study provides initial psychometric information on the ABII-C. Outcomes warrant further investigation of the potential added value a combined parent-clinician informant screening instrument may have on improving ASD screening.

Key Words: Autism spectrum disorder; ASD; ASD screening, parent questionnaire, clinician observation
Introduction

The early detection of children displaying symptomatic profiles of autism spectrum disorder (ASD) is important (Bölte et al., 2013). Early detection can initiate evidence-based intervention to help prevent or mitigate ASD symptoms (Rogers et al., 2014). While the implied benefits of early detection of children with ASD were thought to have previously been impeded by the absence of very early intervention, emerging evidence suggests there is potential to positively intervene in symptomatic (Baranek et al., 2015; Koegel, Singh, Koegel, Hollingsworth & Bradshaw, 2014; Rogers et al., 2014), and high-risk infants (Green et al., 2013: Steiner, Gengoux, Klin & Chawarska, 2013), from as young as six months of age. Between two to three years of age, efficacy research has shown evidence for the effectiveness of intervention (Boyd, Odom, Humphreys & Sam, 2010; Reichow, Barton, Boyd & Hume, 2012; Wong et al., 2014, 2015). It is generally accepted that the earlier intervention can begin, the greater the predictive positive outcomes (Perry, Blacklock & Dunn Geier, 2013; Smith, Klorman & Mruzek, 2015). The potential of very early intervention necessitates parallel development of very early detection methods to ensure their concurrent availability (Rogers et al., 2014).

Although for some children with ASD, symptom onset may occur later in development (Estes et al., 2015), for most children, symptomatic profiles begin to emerge from six months of age (Estes et al., 2015) and continue to accumulate across the next 12 months (Barbaro & Dissanyake, 2012; Chawarska, Macari & Shic, 2013; Elison et al., 2013; Jones, Gliga, Bedford, Charman & Johnson, 2014; Sacrey, Bryson & Zwaigenbaum, 2013). However, accurately capturing information regarding the presence of these symptoms for measurement to guide reliable early
ASD detection has proven difficult (Al-Qabandi, Gorter & Rosenbaum, 2011; Barbaro & Dissanyake, 2012; Zwaigenbaum et al., 2015). These difficulties may be an artefact of measurement limitations rather than the lack of identifiable ASD markers. In the absence of biomedical tests to identify ASD, ASD specific screening instruments provide a form of behavioural detection methods to identify children displaying symptomatic ASD profiles (Lipkin & Hyman, 2011). Despite the availability of a number of ASD specific screening instruments, high rates of misclassification, particularly in children under 24 months of age, limits clinical utility (Al-Qabandi et al., 2011; Barbaro & Dissanyake, 2012; Zwaigenbaum et al., 2015).

One potential measurement limitation associated with all current ASD specific screening instruments, is their reliance on single informant data to guide detection of symptoms within core ASD domains. With the exception of one previously combined parent-clinician instrument, The Checklist for Autism in Toddlers (CHAT; Baron-Cohen, Allen & Gillberg, 1992), which has since been modified into a single informant parent-report screening instrument, the Modified Checklist for Autism in Toddlers (M-CHAT; Robins, Fein & Barton, 1999), current screening instruments use either stand-alone parent or clinician ratings to guide detection of symptomatic ASD profiles. Reliance on single informant instruments to guide ASD detection could increase misclassification. The single use of a clinician-rated instrument can increase misclassification due to the potential for impartial symptom measurement within the behavioural domain, while the single use of a parent rated instrument could increase the risk of misclassification due to the potential for impartial symptom measurement within the social communication domain (Le Couteur, Haden, Hammal & McConachie, 2008; Lemler, 2012; Wiggins...
Combining information from both informant sources in screening instruments may be required to improve the accuracy of symptom measurement across core ASD domains (Volkmar et al., 2014; Zander, Sturm & Bölte, 2015).

The Autistic Behavioural Indicators Instrument - Combined (ABII-C), is comprised of the clinician-administered ASD screening instrument, the Autistic Behavioural Indicators Instrument (ABII; Ward & Gilmore, 2010), and its parent-report equivalent, the Autistic Behavioural Indicators Instrument- Parent questionnaire (ABII-PQ). The ABII measures symptoms of ASD across core ASD domains and quantifies ASD risk based on the combined additive presence of across social attention, sensory and behavioural indicators. The ABII has demonstrated high instrument sensitivity and specificity and good reliability and validity (Ward & Gilmore, 2010; Ward et al., in press a).

The current study combined the single informant ABII and ABII-PQ into a combined parent-clinician informant ASD screening instrument. This study conducted a preliminary evaluation of the ABII-C in a high-risk sibling cohort to establish initial psychometric properties.

**Method**

**Participants**

Informed consent and ethical approval was obtained from the Human Research Ethics Committee of Queensland University of Technology. Twenty-eight siblings of children with a Diagnostic Statistical Manual of Mental Disorders, fourth edition, test revision (DSM-IV-TR; American Psychiatric Association [APA], 2000) autism spectrum diagnosis, aged between 20 and 46 months at initial screen ($M_{\text{child age}} = 27$ months, $SD = .56$), took part in the study. Siblings of children with ASD were specifically selected to increase the ASD risk rate in the cohort. Compared to the
general population, who have an estimated ASD prevalence of approximately 1.2%, ASD prevalence in siblings is significantly higher, between 2-18% (Centers for Disease Control [CDC], 2014). The sample was predominately male (male, \( n = 25 \), female, \( n = 3 \)), \( \chi^2(1) = 17.29, p < .001 \). Exclusionary criteria included known genetic and developmental disorders, hearing and vision impairment, and premature birth.

Between initial screening and 12-month follow-up, all children were diagnostically evaluated by practitioners for a best-estimate clinical ASD diagnosis. These practitioners were not involved in the study and therefore blind to screening outcomes. These practitioners were registered practitioners in clinical practice and therefore all child ASD diagnoses had been formally verified. Practitioners included paediatricians (\( n = 4 \)) with over 20 years experience in the diagnostic evaluation of children for ASD. At 12-month follow-up (\( M_{\text{child age}} = 39 \) months, \( SD = .56 \)), 24 out of 28 children (85.7%) had received a best-estimate clinical Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5; American Psychiatric Association [APA], 2013) ASD diagnosis. The number of children who received an ASD diagnosis was much higher than expected and based on recurrence rates we would have expected \( \approx \) four to six children to have received an ASD diagnosis. Of these 24 children, eight (28.6%) had received a diagnosis of ASD, severity level 1, four (14.3%) received a diagnosis of ASD, severity level 2, and 12 (42.9%) had been diagnosed with ASD, severity level 3. Both more severe (categorised by DSM-5 ASD severity level 1) and less severe (categorised by DSM-5 ASD severity level 1 or 2) ASD symptom presentations were proportionally represented in the cohort, \( \chi^2(2) = 4.00, p = .148 \). Four children (14.3%) had not been diagnosed with ASD. Of these four children, two were regarded by the practitioners to display neurotypical development. The remaining two children had both received a diagnosis of speech
and language delay. At 24-month follow-up ($M_{\text{child age}} = 51$ months, $SD = .56$), 100% diagnostic stability was reported for all twenty-four children diagnosed with ASD. Of the four children who had not received a best-estimate clinical ASD diagnosis, diagnostic status had not changed since 12-month follow-up.

**Instruments**

**The Autistic Behavioural Indicators Instrument – Combined (ABII-C).**

The ABII-C is the combined version of the clinician-administered ABII (Ward & Gilmore, 2010), and its parent questionnaire adaptation, the ABII-PQ. The ABII is a semi-structured 18-item non-verbal clinician administered instrument designed to assess the presence of ASD symptomatology. The ABII includes a fixed sequence of standardised and structured tasks designed to elicit specific target behavioural indicators of ASD across social, sensory and behavioural domains. On all of the ABII items, a score of 0 represents neurotypical behavioural responses and a score of 1 represents the presence of autistic behavioural indicators. Scores are added within each domain to calculate a subscale score and the aggregate of subscales calculated to provide a total scale score. Higher subscale and total scores represent a greater presence of autistic behavioural indicators. Total subscale scores are combined to reach a total scale score and a cut-off score is used to assign a positive screen for ASD. On the ABII, a total cut-off score of $\geq 11$ has been used to indicate a positive screen for ASD. High instrument sensitivity ($Se$) and specificity ($Sp$) has been reached at this cut-off score in samples of children aged between two and six years (Ward & Gilmore, 2010; Ward et al., in press a).

The ABII was adapted as an 11-item parent questionnaire (ABII-PQ) to measure parent-report of both current and past possible indicators of ASD also across social attention, sensory and behavioural domains. All items on the ABII-PQ are
derived from the ABII (e.g., ABII Item 7: preference for shared engagement with primary caregiver versus solitary play, was modified to ABII-PQ item 6: Do/Did you find your child preferred to play with objects rather than play with you or other individuals?). All items are presented as Yes/No questions and scored the same as for the ABII. The ABII-PQ was trialled in a sample of parents of children, aged between 12 months and six years (n = 102), with either a DSM-IV-TR (APA, 2000) autism spectrum diagnosis (AD: n = 35; Asperger Syndrome [AS]: n = 15; Pervasive Developmental Disorder – Not Otherwise Specified [PDD-NOS]: n = 15), or regarded to have neurotypical development (n = 35). Receiver operator curve (ROC) analysis identified an optimal cut-off score of 5 which yielded maximum sensitivity (Se = .97) and specificity (Sp = .95). The area under the curve (AUC) was .98, p = <.001, 95% CI: .94-1.0.

The ABII-C was piloted in a sample of 12 children with a DSM-IV-TR (APA, 2000) autism spectrum diagnosis (AD: n =3; AS: n = 6; PDD-NOS: n = 3), and eight children regarded to have neurotypical development, aged between two and six years. ROC identified an optimal ABII-C total scale cut-off score of ≥8, Se = 1.0 and Sp = of 1.0, AUC = 1.0, p = <.001, 95% CI: 1.0 -1.0.

The Early Screening of Autistic Traits Questionnaire (ESAT; Dietz, Swinkles, van Daalen, van Eneland & Buitlaar, 2006; Swinkles et al., 2006). The ESAT is a 14-item yes/no parent completed checklist to screen children with ASD aged between 14-36 months. The ESAT includes items across the domains of pretend play, joint attention, interest in others, verbal and non-verbal communication, stereotypes, pre-occupations, reaction to sensory stimuli, emotional reaction and social interaction. Children who score a response of “no” on three or more items screen positive.
The Modified Checklist for Autism in Toddlers (M-CHAT; Robins et al., 1999). The M-CHAT is a 23 yes/no item parent-report screening instrument designed to screen toddlers between 16-30 months of age, to assess risk for autism spectrum disorders (ASD). Six items on the M-CHAT are considered critical items: protodeclarative pointing, response to name, interest in peers, bringing things to show parents, following a point, and imitation. A positive screen for ASD on the M-CHAT is indicated if a child fails the screening of two of six critical items, or any three of the 23 items. A revised version of the M-CHAT, the Modified Checklist for Autism in Toddlers revised with follow-up (M-CHAT-R/F; Robins et al., 2014), has since been released but was not available at time of data collection for this study.

The Brief Infant Toddler Social Emotional Assessment (BITSEA; Briggs-Gowan & Carter, 2006). The BITSEA is a 42 item screening tool to evaluate children aged 12-35 months at risk of, or who are currently demonstrating social, emotional and behavioural problems and delays in competence, including ASD. Items on the BITSEA measure externalising problems, internalising problems, dysregulation, maladaptive behaviours, and atypical behaviours. Parents rate each item on a 3-point scale (0 = not true/rarely, 1 = somewhat true/sometimes, 2 = very true/always). Total problem and competence cut-off scores are provided with a percentile rank. A percentile rank of 25 or higher is deemed “possible problem”, with a percentile rank of 15 or lower “possible deficit/delay range”. Although the BITSEA describes a set of 17 key items (9 items from the Problem scale and 8 items from the competence scale) that are regarded to be associated with ASD (Briggs-Gowan & Carter, 2006), previous research has established that ASD screening accuracy is highest when the competence score is used rather than the 17 ASD items (Kruizinga et al., 2014). In addition to this, no single cut off score using the 17 ASD items has
yielded acceptable sensitivity and specificity (Gardner et al., 2013). Therefore, for the purpose of this study, the BITSEA competence score was used to ascertain ASD risk.

The BITSEA includes an item that asks parents to rate how worried they are about their child’s development on a 4-point Likert scale, ranging from “not at all worried” to “very worried”. All parents in this cohort of high-risk children reported feeling worried to some degree regarding their child’s development (‘little worried’, $n = 14$, 50%; ‘worried’, $n = 10$, 35.7%; ‘very worried’ $n = 14$, 50%).

The Autism Diagnostic Observation Schedule (ADOS; Lord, Rutter, Dilavore & Risi, 1999). The ADOS is a standardised semi-structured play based observational tool considered a gold standard instrument to guide diagnostic evaluations of ASD in children 2+ years of age. The instrument consists of a series of structured and semi-structured presses for interaction, accompanied by coding of specific target behaviours and general ratings of the quality of behaviours. The ADOS consists of four modules, one of which is selected for administration based upon the child’s expressive language ability. Modules 1-3 were used in the current study (Module 1: $n = 8$, Module 2: $n = 12$, Module 3: $n = 8$). The ADOS algorithm provides diagnostic cut-offs for autistic disorder, ASD, and non-ASD. Higher scores on the ADOS are indicative of greater abnormality. The ADOS requires specialist training and takes approximately 40-60 minutes to administer. The ADOS has demonstrated strong psychometric properties (Lord, Rutter, Dilavore & Risi, 2008). A revised version of the ADOS was released in 2012 (ADOS-2; Lord et al., 2012), but it was not available at time of data collection for this study.

CARS2-ST is a behavioural rating scale based on clinician observations of unstructured activities in children 2+ years of age. The CARS2-ST includes items drawn from five prominent systems for diagnosing autism. Based on the child’s combined score from the 15 items, the child can be classified with mild, moderate, or severe autism, or no autism, with higher scores indicating more severe forms of ASD. The CARS2-ST takes approximately 20 minutes to administer and can be used by professionals such as physicians, special educators, school psychologists, speech pathologists, and audiologists. The CARS2-ST has shown sound psychometric properties (Schopler et al., 2010).

**Procedure**

All parents provided informed consent and appropriate ethics approvals were obtained from the Human Research Ethics Committee of Queensland University of Technology prior to conducting the study. Parents were invited to participate in the study through distribution of a research flyer at paediatric appointments, allied health intervention sessions, early education centres, special education schools and through autism organisation mailing lists and websites. All parents and children participated in two testing sessions, 12 months apart. Both initial and follow-up testing sessions involved completion of all the instruments, including the ABII-C, ESAT, M-CHAT, BITSEA, ADOS, and CARS2-ST. Children who enrolled in the study prior to their second birthday ($n=2$) attended an additional testing session close to their second birthday to complete the ADOS and the CARS2-ST. Total testing time varied from 45 minutes to 90 minutes depending on the child’s level of engagement and ability. Administration of instruments was randomly assigned and counterbalanced. Half of the parents completed the parent-report instruments ($n=12$) first, and half of the parents and children were administered the clinician-administered instruments first.
(n=16). The order of completion of the parent-report and clinician-administered instruments was randomly assigned. All children were diagnostically evaluated by independent practitioners for ASD between initial and 12-month screening. A follow-up telephone interview at 24 months was conducted with all parents to confirm stability of screening and diagnostic outcomes.

**Results**

**Reliability and Validity**

Internal consistency, $\alpha = .91$ and twelve-month test-retest reliability, $r = .95$, was excellent. With the exception of the BITSEA, the ABII-C total scale score was significantly strongly correlated with all instruments at both initial and 12-month follow-up, $r’s > .79$ (see table 1 for the correlation coefficients between instruments).
Table 1

*Correlations Between the ABII-C and Established Instruments*

<table>
<thead>
<tr>
<th></th>
<th>M-CHAT</th>
<th>ESAT</th>
<th>BITSEA</th>
<th>CARS2-ST</th>
<th>ADOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial screen</td>
<td></td>
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<tr>
<td>ABII-C</td>
<td>.81*</td>
<td>.86*</td>
<td>-48</td>
<td>.73*</td>
<td>.83*</td>
</tr>
<tr>
<td>M-CHAT</td>
<td>.86*</td>
<td></td>
<td>-55</td>
<td>.74*</td>
<td>.83*</td>
</tr>
<tr>
<td>ESAT</td>
<td></td>
<td></td>
<td></td>
<td>.73*</td>
<td>.69*</td>
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<tr>
<td>BITSEA</td>
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<tr>
<td>CARS2-ST</td>
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<tr>
<td>12-month follow-up</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>ABII-C</td>
<td>.82*</td>
<td>.79*</td>
<td>-18</td>
<td>.87*</td>
<td>.72*</td>
</tr>
<tr>
<td>M-CHAT</td>
<td>.92*</td>
<td></td>
<td>-47</td>
<td>.81*</td>
<td>.84*</td>
</tr>
<tr>
<td>ESAT</td>
<td></td>
<td></td>
<td></td>
<td>.85*</td>
<td>.71*</td>
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<tr>
<td>BITSEA</td>
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<tr>
<td>CARS2-ST</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>.78*</td>
</tr>
</tbody>
</table>

* p<.05. ABII-C = Autistic Behavioural Indicators Instrument; ADOS = Autism Diagnostic Observation Schedule; BITSEA = Brief Infant Toddler Social Emotional Assessment; CARS2-ST = Childhood Autism Rating Scale- Second Edition-Standard version; ESAT = Early Screening for Autistic Traits; M-CHAT = Modified Checklist for Autism in Toddlers.

**Diagnostic Outcomes for Screen-positive Cases**

Of the 26 (92.9%) screen-positive cases on the ABII-C at initial assessment, 24 children were diagnosed with ASD at 12-month follow-up, yielding a positive predictive value (PPV) of .92 (95% CI: .74-.99). The remaining two children who screened positive were reported to have a formal diagnosis of speech and language impairment and developmental profiles symptomatic of ASD. Of the two screen-negative cases at initial assessment on the ABII-C, both children were regarded to display neurotypical development. At 12-month re-test, 25 (89.3%) children screened positive on the ABII-C. Of these children, 23 had received a DSM-5 (APA, 2013) ASD diagnosis. The remaining two children were the same children who had also screened positive at initial assessment. Of the three children who screened negative, one child was a girl who had received a DSM-5 (APA, 2013) ASD Severity level 1
diagnosis. The remaining two children were regarded to show neurotypical
development.

Table 2 presents the correct and incorrect classifications of children on the
ABII-C and the established instruments at both initial screen and at 12-month-
follow-up. With the exception of the CARS2-ST, there were no significant
differences in classification accuracy between the ABII-C and established measures.
The CARS2-ST significantly classified fewer children as ASD at both initial screen,
z = -2.24, p > .05 and at 12-month follow-up, z = -3.20, p > .05.

Table 2

<table>
<thead>
<tr>
<th>Measure</th>
<th>Initial screen</th>
<th>12-month follow-up</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Correct (%)</td>
<td>Incorrect (%)</td>
</tr>
<tr>
<td>ABII-C</td>
<td>26 (92.2)</td>
<td>2 (7.1)</td>
</tr>
<tr>
<td>M-CHAT</td>
<td>24 (85.57)</td>
<td>4 (14.3)</td>
</tr>
<tr>
<td>ESAT</td>
<td>25 (89.28)</td>
<td>3 (10.78)</td>
</tr>
<tr>
<td>BITSEA</td>
<td>25 (89.28)</td>
<td>3 (10.78)</td>
</tr>
<tr>
<td>CARS2-ST*</td>
<td>19 (67.86)</td>
<td>9 (32.14)</td>
</tr>
<tr>
<td>ADOS</td>
<td>25 (89.28)</td>
<td>3 (10.78)</td>
</tr>
</tbody>
</table>


Table 3 presents the characteristics of the children who were misclassified on
the instruments at initial screen and at 12-month follow-up. While results were not
significant, for some children, different screen positive or negative outcomes were
reached on some of the instruments.
Table 3

*The Characteristics of the Children Who Were Misclassified on the Instruments at Initial Screen and at 12-month Follow-up*

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Age</th>
<th>Gender</th>
<th>ABII-C T1</th>
<th>ABII-C T2</th>
<th>M-CHAT T1</th>
<th>M-CHAT T2</th>
<th>ESAT T1</th>
<th>ESAT T2</th>
<th>BITSEA T1</th>
<th>BITSEA T2</th>
<th>CARS2-ST T1</th>
<th>CARS2-ST T2</th>
<th>ADOS T1</th>
<th>ADOS T2</th>
<th>ADOS T1</th>
<th>ADOS T2</th>
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<td>I</td>
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<td>C</td>
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<td>ASD 1</td>
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<td>C</td>
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<tr>
<td>ASD 1</td>
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</table>

*Note:* T1 = Initial screen, T2 = 12-month follow-up; SLI = Speech and Language Impairment; TD = Typical Development; ASD 1 = Autism Spectrum Disorder, Severity level 1; ASD = Autism Spectrum Disorder, Severity level 2; ABII-C = Autistic Behavioural Indicators Instrument; ADOS = Autism Diagnostic Observation Schedule; BITSEA = Brief Infant Toddler Social Emotional Assessment; CARS2-ST = Childhood Autism Rating Scale- Second Edition- Standard version; ESAT = Early Screening for Autistic Traits; M-CHAT = Modified Checklist for Autism in Toddlers.
Agreement Between the ABII-C and Established Instruments

Table 4 presents the level of agreement between the instruments on ASD diagnostic classification at both initial screen and 12-month follow-up. At both initial and 12-month retest screen, there was significant agreement between the ABII-C and the established measures ranging from $\kappa = .28$ to $\kappa = .78$.

Table 4

<table>
<thead>
<tr>
<th>M-CHAT</th>
<th>ESAT</th>
<th>BITSEA</th>
<th>CARS2-ST</th>
<th>ADOS</th>
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<td>$p$</td>
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<tr>
<td>Initial screen</td>
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<td></td>
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</tr>
<tr>
<td>ABII-C</td>
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<td>.015</td>
<td>.65</td>
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<td>.65</td>
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<td>.139</td>
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<tr>
<td>ABII-C</td>
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<tr>
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<td>.65</td>
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<tr>
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<tr>
<td>CARS2-ST</td>
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The Effect of Age and ASD Symptom Severity on ABII-C Classification

A logistic regression was performed to assess whether ABII-C classification, after controlling for age and diagnostic status (ASD or non ASD), significantly predicted the children who would be classified as ASD. The full model was significant, $\chi^2(2, n = 28) = 5.873, p =.05$. The Hosmer and Lesmeshow test indicated...
a good fit, $\chi^2 = 4.04, p = .67$. The model as a whole explained between 18.9% (Cox and Snell R Square) and 38.3% (Nagelkerke R square) of the variance in ABII-C classification and correctly classified 89.3% of children. The strongest predictor of ABII-C classification was diagnostic status (ASD or non ASD), $p = .029$, recording an odds ratio of 3.57 (95% CI [46.82 – 59.23]). This result indicated that children with ASD were 3 times more likely than children without ASD to screen positive on the ABII-C. Age was not a significant predictor on ABII-C classification, $p = .435$.

To assess the impact of ASD symptom severity on the likelihood of ABII-C classification, degree of symptom severity, categorised by more (DSM-5 ASD severity level 3) and less (DMS-5 ASD severity level 1 or 2) severe presentations, and non ASD were entered as predictors. The full model was significant, $\chi^2(2, n = 28) = 6.64, p = .036$. Degree of ASD symptom severity did not significantly predict the children who would be classified as ASD, $p = .999$.

**Discussion**

This study is the first prospective examination of the ABII-C, a combined parent-clinician informant ASD screening instrument, to establish initial psychometric properties. Results show the potential importance of combining parent-clinician ratings to improve ASD screening outcomes. The ABII-C was the only screening instrument to correctly predict all of the children who went on to receive a best-estimate clinical DSM-5 (APA, 2013) ASD diagnosis or to be regarded to display neurotypical development. While the single informant screening instruments were shown to provide independent contributions in the prospective identification of children with ASD, results show the potential for the same child to reach different screen positive or negative outcomes as a function of screening instrument rather than the presence or absence of ASD symptoms. The differences in screening
outcomes between instruments for the same child could be influenced by informant source differences. While it is difficult to clearly ascertain the portion of misclassification risk that would be influenced by informant source differences, and a number of other factors, including the selection of ASD symptoms to be measured and the cut-off criteria used on the screening instrument may also influence instrument sensitivity and specificity (Garcia-Primo et al., 2014), results show that combining information from parent and clinician-rated instruments may reduce the potential for misclassification that could be associated with informant source differences. Study outcomes may be important in informing changes to the way we screen children for ASD.

While the ABII-C also detected the two children whose parents reported developmental concerns and who had a formal diagnosis of speech and language impairment, the ABII-C is not intended to screen more broadly than for ASD. These two children were also classified on all of the other established instruments and could be regarded to display incipient features of ASD that may reach diagnostic threshold at a later stage in their development. This result demonstrates the importance of long term follow-up screening studies to provide more information on the prognostic outcomes of screen negative and positive cases. As now recognised under the revised DSM-5 (APA, 2013) diagnostic criteria, some children with ASD may not manifest the full range of ASD symptoms to reach diagnostic threshold until later in development, where social demands exceed the child’s capacity (APA, 2013).

The ABII-C total scale score demonstrated excellent internal consistency, test-rest reliability and was strongly correlated with the established ASD specific instruments (M-CHAT, ESAT, CARS2-ST, ADOS), at both initial screen and 12-month follow-up. The non ASD specific instrument (BITSEA), was not significantly
correlated with any of the ASD specific instruments at either screening times. This result is not surprising given that the BITSEA does not measure symptoms within core ASD dimensions. However, the BITSEA was in good agreement with the ABII-C, M-CHAT, ESAT, and ADOS on the classification of children as ASD, at both initial and 12-month screen. This result suggests that, while the BITSEA measures different symptoms when compared to the ASD specific instruments, children with ASD may display early social, emotional and behavioural problems and delays in competence that could also predict an eventual ASD diagnosis.

With the exception of the CARS2-ST, which demonstrated high misclassification, the ABII-C was in moderate to good agreement with the established measures on the classification of children as ASD at both initial and 12-month screening. Predictive accuracy of ASD diagnostic classification for the established instruments, excluding the CARS2-ST, was above 90%. This high level of accurate detection and predictive success may in part reflect an elevated risk status of the sampled children. The ASD recurrence rate in this cohort of siblings was considerably higher than expected. Recurrence rate in siblings, at its highest rate, has been estimated to be 18.7% (Ozonoff et al., 2011). In this sample, 24 out of the 28 children went on to receive a best-estimate clinical DSM-5 (APA, 2013) ASD diagnosis. It is suggested the recurrence rate in this study is not a true recurrence rate estimate in siblings, rather, a likely reflection of a treatment or diagnostic seeking cohort of participants and high risk siblings who may have been more likely to have traits of ASD compared to a low risk sibling cohort. Parents of children in this study predominately reported feeling ‘worried’ to ‘very worried’ on the BITSEA regarding their child’s development.
The combined parent-clinician informant screening instrument, the ABII-C, did not significantly improve predictive accuracy compared to the existing instruments, with the exception that it was better than the CARS2-ST. It is hypothesised that this result may be influenced by the characteristics of this high-risk sample. Very few children did not go on to eventually receive an ASD diagnosis, and of these few children, half of them are suspected of having incipient ASD. In addition, this cohort of siblings has an elevated risk for ASD, possibly improving the accurate detection and predictive success of all of the instruments. Given the potential for single informant screening instruments to reach different screening outcomes depending on informant source, and the importance to combine informant ratings from parents and clinicians to improve the distinction of infants and toddlers with and without ASD (Wiggins et al., 2012), it may be premature to discount a combined parent-clinician informant ASD screening instrument.

While the ABII-C demonstrated very high sensitivity in this preliminary prospective investigation, it is acknowledged this could be at the risk of producing low instrument specificity. Only four out of the 28 children did not eventually receive an ASD diagnosis and the base-rate of ASD in this sample would be significantly higher than in the general population. It is acknowledged that this is a limitation of the study as instrument specificity could not be calculated and the results may not generalise outside a high risk infant sibling cohort. ASD symptom severity was not found to significantly increase the likelihood of classification on the ABII-C. However, IQ, adaptive functioning and speech and language assessment outcomes are required to understand any potential influence on ABII-C classification. Future research in a larger cohort of children from an unselected population of the ABII-C in children under 24 months of age is required to establish
the full range of psychometric properties of the ABII-C. Future research could explore the use of critical items, adjusted cut-off scores and a weighted scoring system. Future research could also compare the ABII-C with the toddler version of the ADOS (ADOS-2; Lord et al., 2012), the revised scoring algorithms of the ADI-R (Kim, Thurm, Shumway & Lord, 2013), and the M-CHAT-R/F, which have since been released.

Continued efforts are required to improve the accuracy of ASD screening instruments. However, attempts to improve early identification and diagnosis may still be burdened by diagnostic process and very early intervention efficacy. In order for early detection methods to yield the implied benefits for children with ASD, efficient diagnostic processes need to be implemented and intervention in children under the age of two years needs to be validated. The development of ASD screening instruments is therefore one, albeit critical, component to achieving the broader goal of improving the potential for improved outcomes for children with ASD.

Conclusion

The ABII-C, a combined parent-clinician informant screening instrument, correctly predicted all children who went on to receive either a best-estimate clinical ASD diagnosis or to be regarded as displaying neurotypical development. This result shows the potential for a combined parent-clinician informant ASD screening instrument to improve the accuracy and stability of screening outcomes for children with ASD. Future research is required to further explore the contributions a combined parent-clinician informant approach on ASD screening instruments could have on improving screening techniques and outcomes for children with ASD.
Chapter 9: General Discussion

The overall aims of the research program were to examine the assessment and diagnostic practices and challenges that influence the timing of ASD diagnosis and to adapt a single informant ASD screening instrument into a combined parent-clinician informant screening instrument. The five papers presented in this thesis address the aims of the research program. Given the specific findings of each of the studies have already been discussed in their respective papers, this chapter will present an integration of the key research findings. This chapter will demonstrate how this research program contributes valuable information to the body of knowledge regarding universal attempts to improve the timing of ASD identification and diagnosis and improving early behavioural detection methods for ASD. The final sections of this chapter will present the strengths, limitations, future directions and overall conclusions of the research program.

9.1 Integration of Key Findings

Five papers were presented in this thesis to address the two overarching research questions including: 1) ‘What practitioner factors impact ASD diagnostic evaluations?’; and 2) ‘Does a combined parent-clinician informant screening instrument improve ASD detection?’ The first study in this research program examined the practitioner reported factors that likely interact to influence the timing of ASD diagnosis and that may contribute to the potential of a diagnostic gap. The final four studies in this research program contributed toward the adaptation of a
single informant ASD screening instrument into a combined parent-clinician informant ASD screening instrument.

9.1.1 Examination of practitioner reported factors that influence the timing of ASD diagnosis.

The first aim of the research program was to examine the assessment and diagnostic practices and challenges that influence the timing of ASD diagnosis in Australia. A number of practitioner reported factors may impact ASD diagnostic evaluations and suggest the potential of a diagnostic gap in Australia. These results are important as they provide initial clues on where attempts could begin to support improvement to the timing of ASD diagnosis in Australia. Specifically, attempts to reduce the average length of a diagnostic gap may need to focus on: 1) reducing waiting periods; 2) improving practitioner training and confidence in diagnostic evaluations of children under the age of three years; and 3) increasing the availability of reliable and valid standardised instruments for use in toddlers. These findings imply that some of the potential barriers to timely ASD diagnosis in Australia could be overcome with improved diagnostic processes.

A potential improvement to the diagnostic process could involve a remodelling of the current common pathway to ASD diagnosis. To reduce the portion of the diagnostic gap that is attributed to waiting periods, an alternative streamlined diagnostic evaluation process could be implemented. Figure 9.1 presents a proposed remodelling of the most common diagnostic pathway (top panel) to an alternative streamlined diagnostic pathway (bottom panel). Under this streamlined approach, the general practitioner could prepare a dual referral to both the allied health practitioner and the paediatrician or psychiatrist for concurrent ASD evaluation.
Figure 9.1. A proposed remodelling of the most common diagnostic pathway to an alternative streamlined diagnostic pathway. OT = occupational therapist.

It is likely that waiting periods would continue to have an impact on the average length of a diagnostic gap. However, there is potential for these waiting periods to occur concurrently, thereby reducing the overall total length of the gap. There may also be the potential for multidisciplinary assessment to be completed while children remain on the wait list for paediatric or psychiatric review, reducing the overall total length of a diagnostic gap further. A number of systemic, demographic, practitioner and child factors may continue to interact to have an
additive contribution to influencing the length of a diagnostic gap. There is also the potential for families to be exited from the process if either of the dual referrers indicated that the child did not meet criteria for ASD. If viable, this proposed alternative streamlined diagnostic evaluation process could be implemented more quickly than other possible solutions that likely need to include legislative change to increase government support diagnostic evaluations, increasing practitioner numbers and providing ASD specific training and resources.

Improving the timing of referral of children for comprehensive diagnostic evaluation could also help to reduce the average length of a diagnostic gap. Notwithstanding any potential influence of sociodemographic or systemic factors, if children could begin their diagnostic evaluation before their third birthday, there may be the potential for final ASD diagnosis to be achieved around this time. In Australia, if the average age of final ASD diagnosis were to reduce from the current reported age of 49 months (Bent et al., 2015), down to around 36 months of age, there could be the potential to reduce the average length of a diagnostic gap by up to 13 months. In other developed countries, similar attempts to aim for final ASD diagnosis around the time of the third birthday could also yield a reduction to the average length of a diagnostic gap. However, attempts to improve the timing of children for ASD diagnostic evaluation will require concurrent attempts to improve general practitioner detection of early ASD symptomatic profiles or their active response to parental concerns.

The true prevalence and magnitude of a diagnostic gap is likely difficult to quantify and potentially varies considerably from one child to another due to variant symptom onset. Until such a time that a definitive test for ASD becomes available, and as long as the early identification of a symptomatic ASD profile is reliant on the
prospective surveillance of accumulating behavioural markers across the first few years of life (Barbaro & Dissanyake, 2010), it is reasonable to assume that a diagnostic gap will remain. However, it is the current average length of the diagnostic gap that the recommendations of this research aim to reduce.

9.1.2 Examination of a combined parent-clinician informant ASD screening instrument.

The second aim of this research program was to adapt a single informant ASD screening instrument, the ABII, into a combined parent-clinician informant ASD screening instrument, the ABII-C. The overall outcomes from studies 2 through 5 provide initial evidence for the added value a combined parent-clinician informant screening instrument may have on improving ASD screening outcomes. The combined informant ABII-C was the only screening instrument that prospectively identified all of the children displaying symptomatic ASD profiles and who went on to receive a best-estimate clinical ASD diagnosis or to be regarded as showing neurotypical development. While this result is preliminary, it may have implications for changing the way we screen children for ASD. Stepping away from a single informant ASD instrument, in favour of a combined informant instrument, could have the potential to reduce misclassification and improve the stability of screening outcomes.

Results showed that although single informant screening instruments can provide independent contributions to the detection of symptomatic ASD profiles, they could be at increased risk of misclassification due to the potential for impartial symptom measurement within core ASD domains. This result was consistent with previous research (Le Couteur et al., 2008; Lemler, 2012; Wiggins & Robins, 2008). Results demonstrated the potential for the same child with ASD to reach a different
screen positive or negative outcome as a result of the instrument that was used rather than the presence or absence of a symptomatic ASD profile. While it is difficult to draw firm conclusions as to the reason for these discrepant screening outcomes between the instruments, a portion of this result could be influenced by environmental and informant source differences that are present during screening procedures. Specifically, discrepancies in the environmental structure and time sample used to measure the presence of ASD symptoms, differences in the relationship with the child, and disparities in level of knowledge of ASD symptoms and child development between parents and practitioners.

Results from this research program build further support for the role of ASD specific screening instruments in identifying children displaying symptomatic ASD profiles. The accuracy of the screening instruments in correctly classifying and prospectively identifying children across the full spectrum of ASD suggest previously documented difficulties in detecting children displaying less severe symptomatic ASD profiles (Kleinman et al., 2008; Scambler et al., 2001) may be an artefact of measurement limitations. While children with more severe ASD presentations displayed higher scores on the screening instruments, symptom severity did not significantly impact the likelihood of ASD classification on either the ABII, ABII-PQ or ABII-C. Results from study 5 provide further evidence of the stability of symptom expression in children with ASD under the age of three years (Zwaigenbaum et al., 2015a). In study 5, children displayed symptomatic ASD profiles that were stable across a 24-month period of time and that correctly predicted an ASD diagnosis at both the initial and at the 12-month follow-up screen. Although these outcomes suggest that a discrete screening process could accurately identify children with symptomatic ASD profiles, it is possible that participant
characteristics, including the potential for increased parental knowledge of ASD symptoms, older participant child age and increased ASD risk status, may have influenced this result. It is also acknowledged that the political context of this study, in particular the link between diagnosis and government subsidised support, could have influenced some results, including diagnostic stability.

Recursive screening practices have been shown to improve ASD detection, particularly for those children who can display minimal signs of ASD followed by an increase in symptoms after 36 months of age (Chawarska et al., 2014). This pattern of ASD symptom manifestation later on in development is now recognised in the DSM-5 (APA, 2013). The developmental emergence and accumulation of ASD symptoms across time, necessitate developmental surveillance in combination with the availability of either a single instrument that can recursively measure the same set of symptoms that emerge in both mild to severe variants of ASD across the first few years of development, or multiple instruments that have high sensitivity across the full spectrum of ASD but that are to be used at specified ages. The ABII and ABII-PQ were both shown to potentially measure symptoms that are stable between two and six years of age and to accurately classify children across the full range of ASD presentations in this age range. The ABII-C is comprised of the ABII and ABII-PQ. These results could extrapolate to the ABII-C. If this were shown to be the case, the ABII-C may have potential as a recursive screening instrument to detect children displaying symptomatic ASD profiles up to the age of six years. In this thesis, a recursive application of the ABII-C was not evaluated, but is suggested for future research.

While misclassification was low on the ABII, ABII-PQ and ABII-C, any degree of misclassification on screening instruments carries inherent risks and
therefore caution should be exercised. However, screening can help to identify children who are already displaying deviant developmental trajectories and therefore are in need of intervention and evaluation. Although the magnitude of gains associated with early intervention can vary, are not universal to all children with ASD, and are unclear in the long-term, the importance of educating and informing parents of potential developmental deviance and providing evidence-based ASD specific intervention to address symptoms early has already been argued to have the potential to outweigh the cost of denying children and their families the benefits that can follow early detection and intervention (Koegel et al., 2014a). It is acknowledged that there may be a portion of parents who do not want to undergo screening or pursue formal diagnostic evaluation following a positive screen, or engage in intervention. Some parents can report perceived stigmatisation associated with the provision of an ASD diagnosis (Gray, 1993; Kinnear et al., 2016). Some parents can also view intervention as an attempt to normalise or change their child’s behaviour, inferring atypicality and an emphasis on viewing ASD from a negative perspective (O’Dell & Brownlow, 2015). While it is important to respect the autonomy of parents, it is also important that parents are informed stakeholders in their child’s development and are accurately informed of the presence of a symptomatic ASD profile. Developing a collaborative relationship between parents and their practitioners is important in discussions around the presence of an ASD profile to work toward mutual promotion of the child’s wellbeing (Graff, 2015; Moon, 2010).

Although this preliminary trial of the ABII-C has shown promise in the prospective identification of children with ASD, until the full range of psychometric properties are available, it remains under research development and is not recommended for clinical use at this time. Nevertheless, important steps have been
achieved in providing initial validation of the ABII-C and of its individual parent (ABII-PQ) and clinician (ABII) components. This research program has provided initial information on convergent and concurrent validity, reliability, and instrument sensitivity. These are important initial steps in the process of instrument development and evaluation to demonstrate the ABII-C, and its individual components, can measure current conceptualisations of ASD symptoms and correctly identify children diagnosed with ASD under the new DSM-5 (APA, 2013) symptom criteria. While the individual components of the ABII-C have had preliminary evaluation of their specificity, the ABII in a previous program of research (Ward & Gilmore, 2010) and the ABII-PQ in this program of research, the next phase of ABII-C evaluation will need to involve examination of instrument specificity.

Screening children to detect symptomatic profiles of ASD to initiate pre-diagnostic ASD specific intervention could be a future direction (Bradshaw et al., 2015). However, until government funded access to pre-diagnostic intervention becomes available, and until the efficacy and long-term outcomes of very early ASD specific intervention is shown, screening children to improve the timing of referral for comprehensive diagnostic evaluation will likely remain an aspirational goal. Improving the timing of referral involves many critical steps that extend beyond the development of a highly accurate screening instrument. Multiple barriers will likely impede integration of screening instruments into Australian primary health-care settings and further examination, government funding and support to improve uptake and reduce time constraints will be required (Roux et al., 2012). Although implementation of screening instruments, particularly instruments such as the ABII-C that include a practitioner-administered component, could be viewed as increasing already time constrained health-care services, the potential benefits arguably
outweigh the cost associated with the short administration time. In addition to this, the ABII-C was designed to be used by a range of child health practitioners, including psychologists, occupational therapists, speech pathologists, nurses, and could also be used by early child educators, such as kindergarten and day-care teachers, and therefore, there may be potential for using the ABII-C outside of already time constrained medical settings.

9.2 Theoretical Contribution

This research program provides valuable insight into the practitioner reported factors that may contribute to the potential for a diagnostic gap in Australia, and has added to the field by potentially advancing early behavioural detection methods for ASD. However, it is acknowledged that the outcomes of the thesis predominately make a practical rather than theoretical contribution. In saying this, the thesis may provide a contribution by adding to our understanding of how ASD is currently operationalised. Outcomes from this thesis may also add to our understanding of ASD as a spectrum disorder, with varying degrees of symptom severity, that now fall under a single broader diagnostic category in the DSM-5 (APA, 2013).

Although the additive combination of symptomology within core ASD domains on the ABII, ABII-PQ and ABII-C, correctly identified a high proportion of children with ASD, children with ASD displayed varying clusters of behavioural indicators. Also, although the cut-off score on each of the instruments demonstrated high sensitivity in correctly classifying children across the full range of mild to severe variants of ASD, children with ASD scored varying degrees of the additive presence of symptoms. Children with ASD were therefore not rated to display identical symptom profiles, indicating variability in symptoms and severity. While others have argued this variability demonstrates the need for ASD to not be viewed
as a single disorder (Geschwind & Levitt, 2007), symptom variability occurred within common core ASD domains. This result could provide support for changing the conceptualisation of ASD away from three distinct disorders to a single disorder with varying symptom severity ratings.

Outcomes from this research program suggest the inclusion of sensory symptomatology in recent conceptualisations of ASD is important to help guide ASD detection and classification. Up until the release of the DSM-5 (APA, 2013) diagnostic criteria, sensory symptomology did not form part of the required symptoms to reach diagnostic threshold. The inclusion of sensory symptoms in the DSM-5 (APA, 2013) may improve the sensitivity of the symptom criteria, particularly in younger children. Sensory symptoms have been shown to be amongst some of the earliest emergent signs of ASD (Bryson et al., 2007; Zwaigenbaum et al., 2005). The ABII, ABII-PQ and ABII-C all include a sensory scale to measure the presence of sensory symptoms. In study 2 of the research program, the increased presence of sensory symptomology distinguished children with an autism spectrum diagnosis from children regarded to have neurotypical development. In studies 2 through 5 of the program of research, high instrument sensitivity was demonstrated for the ABII, ABII-PQ, and ABII-C, when the detection of a symptomatic ASD profile used the combined presence of sensory, social attention and behavioural symptoms. These results may add to our understanding of the importance of combining symptoms across core ASD domains, rather than reliance on a single core domain to guide detection of symptomatic profiles. The findings from the program of research may also help to guide further refinement of existing screening instruments to include the combined presence of symptoms within core ASD domains to improve accurate symptom detection and prospective identification.
9.3 Practical Implications

The outcomes from this research program have important practical implications for understanding some of the required steps involved in the broader goal of improving the timing of ASD identification and access to intervention. The results show the potential for the ABII-C to detect children across the full autism spectrum from two to six years of age. However, results suggest that the implied benefits of early detection on a screening instrument like the ABII-C, could be lost, due to the additive effects of a number of practitioner and systemic factors that influence the timing of ASD diagnosis. Study outcomes highlight the importance of supporting timelier access to diagnostic evaluations, in conjunction with investment in practitioner training and resources to improve practitioner knowledge and confidence. These changes will likely require legislation reform to invest in the improvement of ASD diagnostic evaluations in Australia.

Reliance on diagnostic confirmation to access government supported evidence-based ASD specific interventions is likely to remain a barrier for some children with ASD and impede the benefits of early detection methods. Results suggest Australian practitioners rarely make a diagnostic recommendation in children under the age of three years. This result implies many Australian children with ASD would be accessing evidence-based ASD specific interventions for the first time well after the time at which these interventions have been shown to be most effective (Perry et al., 2013; Smith et al., 2015). Although evidence elsewhere suggests children with ASD are accessing some form of intervention prior to final ASD diagnostic confirmation and are reaching good outcomes (Monterio et al., 2016), the delivery of evidence-based ASD specific interventions is likely to maximise prognostic outcomes for children with ASD (Wong et al., 2014, 2015). Additionally, access to government
supported pre-diagnostic intervention is not yet available for all Australian children, and although the proposed NDIS will make provisions for pre-diagnostic intervention for children assessed as having developmental delay within the next two to three years, the delivery of evidence-based ASD specific interventions could be delayed until final ASD diagnostic verification.

The findings from this program of research may have important implications in informing future directions for screening instruments. Results show the method of relying on single informant data to guide ASD detection could be flawed. Research outcomes suggest implementation of a standardised method of integration of scores from parent and clinician rated instruments could advance screening practices. An additive scoring model, which combined equally weighted scores from both instruments to provide an overall total score and used a pre-determined cut-off to signify ASD risk, was identified to be a highly sensitive scoring procedure in both the accurate classification and prospective identification of children with ASD. Results from the research program suggest a weighted additive scoring model, where parent and clinician scores within core ASD domains are weighted differentially, could improve instrument sensitivity further. It is proposed that a weighted additive scoring method may extend more broadly than to ASD screening instruments. Though this suggestion is speculative, this scoring method could also potentially be explored in standardised parent and clinician rated instruments that are used to guide diagnostic evaluations for other developmental disorders and disabilities.

Combining parent and clinician rated ASD symptoms in a standardised screening instrument may pave the way forward for improving early behavioural detection methods. While it is possible the future will see biomedical testing as an early detection method for ASD or predictive algorithms that combine biomedical
and behavioural data, detection based on the presence of behavioural markers will likely be required not only in the lead up to development of such approaches, but also after. It is likely that biomedical testing is still some years off, and restrictions of access to such tests are likely to occur on a global scale as a function of sociodemographic factors. Thus, screening instruments that detect behavioural markers of symptomatic ASD profiles will be required for many years to come. The outcomes from this program of research may have the potential to inform and improve current screening practices and the timing of ASD identification.

9.4 Strengths, Limitations and Future Research Directions

This section will draw together the overall strengths and limitations of the research program and make suggestions for future research directions. The individual papers provide descriptions of the strengths and weaknesses of the individual studies.

9.4.1 Strengths.

The first strength of the research program is that it sought to contribute toward addressing the broader goal of improving the timing of ASD identification by making a parallel attempt to concurrently identify the factors that may contribute to a diagnostic gap in Australia and improving an existing ASD screening instrument. Outcomes imply that improvements to ASD screening instruments may not immediately reduce the length of a diagnostic gap and a number of practitioner reported factors will also need to be addressed.

A second strength of the research program is that it included psychologists as survey respondents in the examination of the practitioner reported factors that impact ASD diagnostic evaluations. This is an important contribution to updating our understanding of the process of diagnosis for children with ASD in Australia, as psychologists form an integral role in the multidisciplinary assessment that informs
ASD diagnostic recommendation (AHPA, 2015). A third strength of the research program was the elicitation of information from practitioners regarding gold standard instrument usage in their routine clinical practice. While best practice guidelines recommend the use of gold standard instruments to inform ASD diagnostic evaluations (AABASD, 2011; AAP, 2006; Volkmar et al., 2014), their use is not mandated and therefore cannot be inferred in clinical settings. Previous examinations have found low rates of use within clinical settings (Randall et al., 2016; Skellern, 2005; Wiggins et al., 2006), which may contribute to the length of a diagnostic gap. This research program suggests that, while these instruments are reportedly being used in diagnostic evaluations of children for ASD through a partnership between medical and allied health practitioners, it may be practitioner perceptions of the limitations of these instruments that are impacting on practitioner use in younger children as well as resource or time constraints.

The greatest strength of the research program is its contribution to the advancement of early behavioural detection methods for ASD. This research program has shown a combined parent-clinician informant ASD screening instrument could improve ASD detection. This research program demonstrated the potential for single informant screening instruments to be at increased risk of misclassification errors. It is difficult to clearly ascertain the portion of misclassification risk that is influenced by informant source differences and a number of other factors, including the selection of ASD symptoms to be measured and the cut-off criteria used on the screening instrument, may also influence instrument sensitivity and specificity (García-Primo et al., 2014). However, results show that combining information from parent and clinician-rated instruments may reduce the potential for different screen outcomes for the same child as a function of
informant source differences rather than the presence or absence of a symptomatic ASD profile.

A further strength of the research program includes initial validation of the method of symptom measurement employed on the ABII-C to guide the prospective identification of children across all severity level ratings of ASD. The ABII-C measures symptoms that are regarded to be amongst some of the earliest distinguishing markers of ASD within core domains, and establishes ASD risk on the additive presence of these combined symptoms. The high accuracy of this method of symptom measurement, in combination with the combined parent-clinician information method of symptom measurement, yielded very high instrument sensitivity. While it is acknowledged that full psychometric evaluation and longitudinal follow-up that extends beyond 24 months are required to understand the true screening accuracy of the ABII-C, results from this program of research provide initial clues on how to begin to improve screening instruments to reduce the risk of misclassification. An additional strength of this research program is that the results provide initial information on instrument validation with the new diagnostic criteria, not only for the ABII, ABII-PQ and ABII-C, but also for the established instruments used in the research program including the ADOS (Lord et al., 1999), CARS2-ST (Schopler et al., 2010), M-CHAT (Robins et al., 1999), ESAT (Dietz et al., 2006; Swinkles et al., 2006) and BITSEA (Briggs-Gowan & Carter, 2006).

The overall strength of the research program is that it has identified the potential for improvements to ASD symptom measurement to guide ASD detection and begins to delineate required changes to improve the timing of ASD diagnosis in Australia. These improvements may not be specific to ASD instruments or ASD diagnosis and could extend more broadly to other standardised instruments that are
used to support the diagnosis of other developmental disorders and disabilities. The difficulties inherent to ASD diagnosis may extend to other developmental disorders and disabilities and may not be a unique problem to Australia. Results could therefore generalise beyond ASD diagnosis and Australia. While the magnitude of gains associated with improvements to the very early detection of ASD may be limited for the time being, and dependent on much broader legislative change, there may be the potential to reduce the average length of a diagnostic gap in Australia and elsewhere. Any method that can improve the accurate early detection of ASD is regarded as a success as it may help toward supporting children with ASD to access intervention sooner.

9.4.2 Limitations.

Despite the important contributions the research program makes, a number of limitations need to be acknowledged. While the specific limitations of each individual study have been detailed in their respective papers, a review of the limitations common to the research program will now be documented. First, a number of factors may limit the generalisability of results from each of the studies. Participants were predominately recruited through settings that likely service diagnostic or treatment seeking parents that could be described as educated, medium to high income parents from a Caucasian background. A selection bias may also be present in the data. Although a response rate cannot be established for the individual studies within the thesis, it is likely that a number of participants who were approached did not participate and that parents and practitioners may not have been informed of the research. The recruitment of children from selected populations in studies 2 through 5 also limits the generalisability of results. Compared to an unselected population, the base rate of ASD in the studies was significantly higher,
which may influence how each of the instruments performed in regard to the sensitivity and specificity of their cut-off scores. The instruments could potentially perform differently in an unselected population and further research is required in this sample of children to determine if alterations to instrument cut-off scores are required.

Second, there is the potential for variation in how best-estimate clinical ASD diagnosis was reached for the children with ASD in the research program. All diagnostic evaluations were completed by practitioners in clinical practice. Although this means that all children who were diagnosed with ASD had received a verified ASD diagnosis, and are therefore formally identified as having ASD in Australia, it is a limitation that the exact procedures used for reaching these verified diagnoses are unknown. Also, although diagnostic confirmation letters were part of the inclusion criteria for studies 2, 4 and 5 to confirm child ASD diagnosis, study 3 relied on parent-report of ASD diagnosis and there is no method to confirm these diagnoses as respondents were anonymous. It is acknowledged that collection of information on assessment and diagnostic evaluation procedures would have provided further information on participant characteristics and further instrument validation if assessment outcomes were available. In order to minimise any impact of potential variations in assessment and diagnostic evaluation procedures, a standardised diagnostic evaluation method across all children would have been ideal. This was outside the scope of this thesis.

Third, the low rate of inclusion of parents and children without an ASD diagnosis limits psychometric evaluation procedures. While it was important to establish the sensitivity, reliability and validity of the combined parent-clinician informant ASD screening instrument the ABII-C, in both the accurate measurement
of ASD symptoms and detection of children with ASD, inclusion of a neurotypical control group in studies 2, 4 and 5 would have strengthened the results of the thesis. Inclusion of a neurotypical control group in study 5 would have enabled calculation of instrument specificity and positive and negative predictive values. It is acknowledged that an instrument with very high sensitivity can be at risk of low specificity. While the individual components of the ABII-C have been shown to have well balanced instrument sensitivity and specificity, the ABII in a previous examination (Ward & Gilmore, 2010), and the ABII-PQ in study 3 of the research program, a measurement of ABII-C specificity is required in order to fully understand its screening capabilities.

Fourth, although high-risk infant studies provide an increased opportunity to observe actual cases of ASD and are therefore a ‘fruitful’ population to recruit for prospective investigations (Dixon et al., 2011, p.199), their outcomes may not be generalisable to the general population (Zwaigenbaum et al., 2015c). Infants of siblings with ASD display a unique profile compared to low-risk children. Compared to children from the general population, infant siblings display an increased genetic risk of having ASD (Ozonoff et al., 2011), an increased risk of broader traits of ASD (Chawarska et al., 2014), and an increased risk of developmental delays and deficits (Iverson & Wozniak, 2007; Le Couteur et al., 1996). While there is currently no evidence to suggest these unique characteristics of high-risk siblings mean they display a unique early symptomatic profile compared to low-risk children who go on to be diagnosed with ASD, caution has been issued when translating outcomes to other populations (Zwaigenbaum et al., 2015c).

Fifth, the recruitment of high-risk siblings of children already diagnosed with ASD was a limitation due to the potential influence risk-status may have on parent
Parents of high-risk infants may have heightened vigilance and be more astute in their detection of developmental deviance and ASD symptoms, particularly with subtle symptoms, compared to parents of low-risk children (Ozonoff et al., 2009). Parents of high-risk infants may also experience higher degrees of worry regarding their child, which in turn can increase vigilance and detection of developmental problems that may otherwise have gone undetected by a parent of a child with neurotypical development (Glascoe, 1999). To overcome the limitations associated with a high-risk cohort of infant siblings of children with ASD, a general population cohort of children in a longitudinal investigation from birth to age of diagnosis would be a strong methodological design. However, given the estimated prevalence of ASD in the general population is approximately one in every one hundred children (Williams et al., 2014a), a very large-scale study is necessary to address this question.

Sixth, while inter-rater reliability has previously been established for the ABII (Ward & Gilmore, 2010), it is a limitation that inter-rater reliability was not measured in this research program and this may reduce the strength of the results as it has not been established whether multiple raters would score ASD indicators the same across the instruments. ASD screening instruments are designed to be completed by multiple raters and therefore, a measurement of the agreement between raters is an important stage of instrument evaluation. In this study, all ratings were completed by the same evaluator. A rate effect may therefore be present in the data.

A final limitation to the program of research is that it has not been able to provide validation of the ABII-C, or it its individual components, the ABII and ABII-PQ, in their intended age range. The ABII-C, ABII and ABII-PQ, are all intended to be used to screen children from 12 months of age. Despite efforts to recruit 12 month
old infants, very few children who were enrolled in the research program were under
the age of 24 months. Older child age of participants in studies 2 through 5 also
limits attempts to provide validation of an ASD screening instrument for use in
children under the age of 24 months.

9.4.3 Future research.

Directions for future research specific to the individual studies have been
outlined in their respective papers. This section will therefore provide a broader
overview of proposed future research. During the progression of the research
program new versions of the ADOS (Lord et al., 1999) and ADI-R (Rutter et al.,
2003), for use in children from 12 months of age, became available, and new
diagnostic criteria were released in the DSM-5 (APA, 2013). Future research could
investigate whether the recent availability of instruments for use in children from 12
months of age, such as the ADOS-2 (Lord et al., 2012) and revised ADI-R
algorithms (Kim et al., 2013), and changes to the diagnostic criteria in the DSM-5
(APA, 2013), have impacted the timing of diagnosis in Australia. Given the
outcomes from study 1 of the program of research showed many factors influence the
timing of ASD diagnosis in Australia, it would be anticipated that the availability of
these new instruments and criteria in isolation may not significantly contribute to
reducing the average length of a diagnostic gap.

Future examination is required to help to delineate all of the barriers that
impede the timing of ASD diagnosis. It is likely that improvements to the timing of
ASD diagnosis will require the combination of a number of methods that include but
may not be limited to: improved accuracy of early detection methods such as
screening instruments; increased uptake of screening instruments in clinical practice
to guide timely referral for diagnostic evaluation; consideration of a dual referral for
concurrent allied health assessment and paediatric or psychiatric evaluation; reduced waiting periods for diagnostic evaluation; improved practitioner training to align the timing of achievable clinical diagnosis from two to three years of age with the actual timing of diagnosis at this age; and equitable access to timely diagnostic evaluation for all children. It is unlikely that all of these factors can be concurrently improved in the near future. In the interim, future research could begin to investigate whether these factors are weighted equally in their potential to improve the timing of ASD diagnosis, or whether improvements to a single or combination of two or more factors could optimise the magnitude of gains.

Given the possible negative ramifications associated with a diagnostic gap for children with ASD, future research could examine the potential for a diagnostic gap for children with other developmental disorders and disabilities. Systemic, practitioner and child factors may also impact the timing of diagnosis for other developmental disorders and disabilities that do not have overt symptoms or genetic markers. Delays to diagnosis for children with other developmental disorders and disabilities could be associated with similar negative outcomes that have already been documented for children with ASD. Compared to parents of children with down syndrome, which can be diagnosed immediately or within days of birth, parents of children with fragile X syndrome can face a delay to diagnosis that can range up to 11 years, increasing parental distress and frustration (Abbeduto et al., 2004). The average age of diagnosis for children with developmental delay is over four years of age, which can also delay their access to intervention that could help to improve their developmental outcomes (Mann et al., 2008). Identification of the factors that may delay: parent expression of concerns to general practitioners; practitioner response to parental concerns; identification of symptomatic profiles; diagnostic evaluations; and
intervention is of great importance to improving the lives for all children with developmental disorders and disabilities and their families.

It is important that future attempts to improve early detection methods for ASD are conducted alongside attempts to develop and validate the efficacy of very early ASD specific interventions. Any potential benefit of an early detection method will be limited if early detection does not result in access to effective intervention. At this current time, effective ASD specific interventions are thought to be available from two years of age (Boyd et al., 2010; Wong et al., 2014, 2015). Emerging evidence is showing that ASD specific intervention from as young as six months of age can be of benefit to improving the developmental trajectories of children displaying symptomatic profiles of ASD (Rogers et al., 2014). These outcomes suggest that ASD specific intervention in children displaying ASD symptomatic profiles under the age of two years could be implemented before thresholds for ASD diagnosis are met.

Given that any new screening instrument requires ongoing development, validation and evaluation (Dixon et al., 2011) the ABII-C will require future research to further examine and establish the full range of its psychometric properties. First, the ABII-C needs to be trialled in a cohort of children within its intended age range. Second, given the ABII-C includes items that measure ASD symptoms that are thought to begin to emerge from as young as six months of age, a trial in this cohort of infants would be of interest to determine whether the ABII-C could be used in this very early age. Third, given that screening instruments are typically evaluated in regard to their sensitivity and specificity and positive and negative predictive values (Dixon et al., 2011; Garcia-Primo et al., 2014), further screening studies are necessary using the ABII-C in a sample of children from non-selected populations,
including children with neurotypical development and children who have signs of other developmental delays and disabilities. Fourth, to provide further instrument validation, the clinician-administered and parent-report versions of the ABII-C could be compared with the newly released ADOS-2 (Lord et al., 2012) and revised ADI-R algorithms (Kim et al., 2013). While the ABII-C is a screening instrument and is not designed to provide the same level of comprehensive assessment as these instruments, comparative analysis would contribute to further establishing convergent and construct validity. Fifth, inter-rater reliability needs to be established. Multiple large scale general population based prospective longitudinal investigations are recommended to rigorously evaluate the ABII-C. These studies are required in order to support the ABII-C as an ASD screener. Until such a time that these studies can be conducted and outcomes independently replicated, it is acknowledged that the ABII-C is an instrument that remains under research development.

Future ABII-C instrument refinement could include exploration of weighted scoring procedures, critical items and adjustment to severity cut-off scores to ascertain level of ASD risk, ranging from low to high. Given the importance of observing children in multiple contexts and environments to inform evaluations of ASD (Hepburn & Moody, 2011), development of a derivative early educator scale to be incorporated into the ABII-C could be examined. Future research could examine recursive screening using the ABII-C, to determine if there is an optimal age for use, whether a continuous rather than discrete screening process improves detection, and to provide further information on test-retest reliability and stability of screening outcomes over longer follow-up periods. Given the recent release of the M-CHAT-R/F, which has shown improved sensitivity in the detection of toddlers with ASD, future research could compare the ABII-C with the M-CHAT-R/F and explore
whether an ABII-C 2-stage screening process improves its psychometric properties. Future research could also examine whether the additive scoring model employed in the ABII-C, or a weighted additive scoring model, could be used to combine data from the ADOS (Lord et al., 1999) and ADI-R (Rutter et al., 2003) and other biomedical data to help guide ASD diagnostic evaluations. This standardised method of combining scores from parent and clinician rated instruments could be further explored in instruments that are used to guide the evaluation of other developmental delays and disabilities.

Given the multiple barriers that have already been implicated in impeding screening during routine health-care check-ups (Gillis, 2009), future research could further examine the use of screening instruments by other child health practitioners, such as nurses, psychologists, occupational therapists, speech pathologists, and early childhood educators, such as day care and kindergarten teachers, and how to best integrate information from these multi-informants in ASD screening procedures. Early childhood educators could be in a unique position to be trained to conduct developmental surveillance combined with recursive screening, an idea that warrants future examination.

9.5 Summary and Conclusions

This program of research provides initial clues on how to begin to address the broader goal of improving the timing of identification of children with ASD. Outcomes show the potential for improvements to both the screening and diagnostic process. These improvements could contribute toward supporting children with ASD to access intervention and diagnostic evaluations sooner. Results suggest the potential for a diagnostic gap for many children with ASD in Australia. With final diagnostic confirmation currently a pre-requisite to access government supported
intervention in Australia, this result suggests many children with ASD may not access ASD specific evidence-based interventions until well after the time it becomes available and effective. Outcomes implicate a number of practitioner and systemic factors in influencing the length of a diagnostic gap in Australia. These factors may not be unique to Australia and the findings may be applicable elsewhere as they echo previously identified trends.

The outcomes from this research program have contributed toward the further advancement of early detection methods. Screening instruments are believed to be increasingly important in supporting the early detection of children displaying symptomatic ASD profiles. The results from this research program suggest possible changes to the way screening instruments currently measure behavioural indicators for ASD to reduce the risk of misclassification. This program of research shows the potential for a combined parent-clinician informant ASD screening instrument to improve early detection methods for ASD. However, results from this program of research also imply improvements to the timing of ASD identification extend far beyond the development of a highly accurate ASD screening instrument. Outcomes suggest that even with high rates of uptake in clinical settings of an accurate screening instrument, unless broader changes to improve the constellation of factors that impact on the timing of ASD diagnosis occur, or until access to pre-diagnostic ASD specific intervention is supported and validated, the benefits of early detection methods may remain limited.

The implementation of very early ASD specific intervention in symptomatic infants may be a future direction to maximise prognostic outcomes for children displaying signs of being on an ASD trajectory. Pre-diagnostic intervention could provide the opportunity to deliver intervention in children already displaying deviant
developmental trajectories during a developmental period where neuroplasticity is highest (Reichow et al., 2012). This potential to intervene before a formal ASD diagnosis could be reached forms one reason why it is important to continue to improve the accuracy of ASD screening instruments to ensure methods to detect symptomatic infants are available upon validation of these very early interventions. However, given that final diagnostic confirmation will remain important to ensure delivery of evidence-based ASD specific interventions, the benefit of ASD screening instruments may be in supporting the earlier referral of children for diagnostic evaluation, so that initial ASD evaluations occur as close to possible to the time a reliable and valid diagnosis could be achieved.

A screening instrument that could be used recursively in combination with developmental surveillance methods, could help to guide the accurate referral of children for diagnostic evaluation by the time of their second to third birthday. Improving the timing of referral for diagnostic evaluation could form an initial step to reducing the average length of a diagnostic gap and improving the timely access of children to ASD specific interventions. This thesis sought to provide initial validation of an ASD screening instrument, the ABII-C, that could have the potential to meet this need. The ABII-C is a unique ASD screening instrument in that it combines a parent and clinician rated screening instrument into a single instrument that seeks to prospectively identify children with ASD on the basis of the additive presence of unique primary combined behavioural ASD indicators.

Universally, children with ASD are being diagnosed much later than they could and should be. Attempts to reduce the average length of a diagnostic gap are needed and could help to improve prognostic outcomes for individuals with ASD. While the outcomes from this thesis provide initial clues on how to improve the portion of the
gap that may be influenced by the weaknesses associated with existing screening instruments and practitioner and systemic related factors, much more is to be done to improve the lives of children with ASD and their families.
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responsibilities/disability-and-carers/program-services/for-people-with-disability/is-my-child-eligible


Swinkels, S.H., Dietz, C., Daalen, E., Kerkhof, I.H., Engeland, H., & Buitelaar, J.K.


Zwaigenbaum, L., Bauman, M., Choueiri, R., Fein, D., Kasari, C., Pierce, K., …


Appendix A

Diagnosis of Autistic Spectrum Disorders Practitioner Survey

Please note: Autistic Spectrum Disorders (ASD) include Autistic Disorder, Asperger’s Syndrome, Pervasive Developmental Disorders – Not otherwise Specified

1) What is your profession? ☐ Paediatrician ☐ Psychiatrist ☐ Psychologist

2) How many years have you been practicing? ☐ 0-4 ☐ 5-9 ☐ 10-14 ☐ 15-19 ☐ 20+

3) What best describes your type of practice? ☐ Private ☐ Public ☐ combined

4) What best describes your practice setting? ☐ Large City ☐ Provincial city ☐ Rural/Remote

5) What is your practice location?
☐ Queensland  ☐ Victoria
☐ New South Wales  ☐ Western Australia
☐ Tasmania  ☐ South Australia
☐ Australian Capital Territory  ☐ Northern Territory

6) Have you undergone additional training or professional development specific to the assessment and diagnosis of young children with ASD? ☐ Yes ☐ No

7) On average, how many children are you referred for assessment/diagnosis of ASD?
☐ 1 per month ☐ 2-3 per month
☐ 1 per week ☐ 2-3 per week
☐ >3 per week

8) What is the age range of children you see who are referred for assessment/diagnosis of ASD?
☐ 0-3 Years ☐ 3-5 Years
☐ 5-8 Years ☐ 8-12 Years
☐ 12-17 years ☐ 17+ Years
9) What age range of children are you predominately referred for further assessment/diagnosis of ASD?
☐ <12 months
☐ 12 - 18 months
☐ 19-24 months
☐ 25 – 30 months
☐ 31-36 months
☐ >37 months

10) a) What is the average time it takes for you to complete the assessment?
   ☐ 1 hour
   ☐ <4 hours
   ☐ <6 hours
   ☐ <10 hours
   ☐ >10 hours

11) Do you find that you require more time to diagnose ASD than other Developmental Delays and difficulties? □ Yes □ No

12) Do you have children on a wait list? □ Yes □ No

13) What is the average length of time children are on the wait list?
   ☐ <1 week
   ☐ < 2 weeks
   ☐ < 1 month
   ☐ >1 month

14) Do you follow a standardised protocol of assessment? □ Yes □ No

15) Which best describes your protocol for assessment
   ☐ developed your own protocol
   ☐ follow protocol outlined in National Autism Plan for Children

16) What methods do you usually use when diagnosing ASD? (Please tick all that apply)
   ☐ Non standardised structured/unstructured interview
   ☐ Standardised structured interview (e.g. Autism Diagnostic Interview-Revised - ADI-R).
   Please specify measure ________________________
   ☐ Non standardised clinical observations across 1 session
   ☐ Non standardised clinical observations across 2 or more sessions
   ☐ Standardised observational method (e.g. Autism Diagnostic Observation Schedule - ADOS or Childhood Autism Rating Scale -CARS)
   ☐ Clinical judgment
   ☐ DSM-IV-TR diagnostic criteria
   ☐ Referral for Multidisciplinary assessment reports (e.g. Psychologist, Speech Pathologist, Occupational Therapist)
   ☐ Standardised Autism Specific parent/teacher questionnaires (e.g. Australian Asperger’s Scale, Gilliam Asperger’s Disorder Scale - GADS, Gilliam Autism Rating Scale - GARS)
   ☐ Observational /descriptive information from teachers/day care professionals.
   ☐ Cognitive assessment
   ☐ Communication, speech and language assessment
   Please specify measures used ________________________
17) Which are you most likely to use when making a diagnosis? Please tick one box only
☐ Clinical judgment
☐ Clinical observations
☐ Parent report
☐ Standardised Structured interview
☐ Standardised observational measure
☐ DSM-IV-TR Diagnostic Criteria
☐ Combination of the above
Please Specify__________________________

18)

<table>
<thead>
<tr>
<th></th>
<th>Often</th>
<th>Sometimes</th>
<th>Occasionally</th>
<th>Not at all</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you had to change the diagnosis prescribed to a child earlier on in the course of their development to ASD? If so, what was the initial diagnosis?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you had to change the diagnosis prescribed to a child earlier on in the course of their development from ASD to a different diagnosis</td>
<td></td>
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<tr>
<td>Have you adopted the ‘watch and wait’ strategy for diagnosis (i.e. holding off on a formal diagnosis and diagnosing later on in the course of development because it is unclear if the child has ASD)?</td>
<td></td>
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<tr>
<td>Have you ever had a child who does not meet DSM-IV-TR criteria for ASD but your clinical judgment would say otherwise? If this happens, would you diagnose this child with ASD?</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Have you ever had a child who does meet DSM-IV-TR criteria for ASD but your clinical judgment would say otherwise? If this happens, do you diagnose this child with ASD?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you feel confident in your training/expertise to correctly detect and diagnose ASD?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
19) If you have had to change the diagnosis prescribed to a child earlier on in the course of their development to ASD what was the initial diagnosis most likely to be?
☐ Speech and Language Impairment
☐ Global Developmental Delay
☐ Intellectual Impairment
☐ ADHD
☐ Sensory Processing Disorder
☐ Other:

20) If you have had to change the diagnosis prescribed to a child earlier on in the course of their development from ASD to a different diagnosis what was the initial diagnosis most likely to be?
☐ Speech and Language Impairment
☐ Global Developmental Delay
☐ Intellectual Impairment
☐ ADHD
☐ Sensory Processing Disorder
☐ Other:

21) Please circle the number on the scale that best describes your level of agreement from 1=strongly disagree to 3=neutral to 5=strongly agree

<table>
<thead>
<tr>
<th>Diagnosis of children under age 2 is difficult</th>
<th>STRONGLY DISAGREE</th>
<th>Neutral</th>
<th>STRONGLY AGREE</th>
</tr>
</thead>
<tbody>
<tr>
<td>I am more confident in prescribing a definitive diagnosis of ASD to children over 3 years of age</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSM-IV-TR diagnostic criteria are useful in diagnosing ASD in children under 3 years of age</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSM-IV-TR diagnostic criteria are applicable to children under 3 years of age</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>There are reliable screeners/early detection tools to identify children with possible ASD under age 2</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening for ASD should become standard practice</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>It would be beneficial if a screening/early detection tool was available that could be used by GP’s and early educators to detect children who may warrant further investigation of ASD</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assessment measures need to be quick to administer to reduce time demands on health practitioners</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assessment measures need to be quick to administer to reduce financial demands on families</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In clear-cut cases, I would be more likely to diagnose ASD without using any standardised measures.</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observational measures can be more reliable than retrospective parent report</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>It is often difficult to discriminate children</td>
<td>1 2 3 4 5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
with a specific language disorder from children with ASD

| Diagnosing ASD based on the presence of ASD specific symptomology would help make a definitive diagnosis | 1 | 2 | 3 | 4 | 5 |
| Diagnosing ASD based on the earliest presenting symptomology (primary deficits) would improve the age of diagnosis | 1 | 2 | 3 | 4 | 5 |
| Diagnostic criteria and measures that rely on identifying secondary deficits associated with ASD (i.e. those deficits that occur later on in the course of development and that cannot be assessed early on in life e.g. delays in language) would delay diagnosis. | 1 | 2 | 3 | 4 | 5 |
| There is a need for an observational measure that is inexpensive, quick to administer and that detects ASD based on the presence of primary deficits that are specific to ASD | 1 | 2 | 3 | 4 | 5 |
**Appendix B**

**Autistic Behavioural Indicators Instrument (ABII)**

<table>
<thead>
<tr>
<th>Subscale</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Social Attention Subscale</strong></td>
<td></td>
</tr>
<tr>
<td>1. Duration of Gaze to non-social stimuli – picture of a flower</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seconds</td>
</tr>
<tr>
<td></td>
<td>&lt;5 seconds</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>(a) Affect</td>
<td>1</td>
</tr>
<tr>
<td>2. Duration of Gaze to social stimuli – picture of known human face</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seconds</td>
</tr>
<tr>
<td></td>
<td>&lt;5 seconds</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>(a) Affect</td>
<td>0</td>
</tr>
<tr>
<td>3. Duration of Gaze to non-social stimuli – picture of a flower</td>
<td></td>
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<tr>
<td></td>
<td>Seconds</td>
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<tr>
<td></td>
<td>&lt;5 seconds</td>
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<td></td>
<td>Positive</td>
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<td></td>
<td>0</td>
</tr>
<tr>
<td>(a) Affect</td>
<td>0</td>
</tr>
<tr>
<td>4. Duration of Gaze to social stimuli - picture of unknown human face</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Seconds</td>
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<tr>
<td></td>
<td>&lt;5 seconds</td>
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<tr>
<td></td>
<td>Positive</td>
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<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>(a) Affect</td>
<td>0</td>
</tr>
<tr>
<td>5. Preference for picture of social versus non social picture</td>
<td>Social</td>
</tr>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>6. Preference for picture of known versus unknown face</td>
<td>Known</td>
</tr>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>7. Preference for shared engagement with primary caregiver versus solitary play</td>
<td>Shared engagement</td>
</tr>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>8. Preference for solitary play or joint attention with primary caregiver by following caregiver’s head turn to object</td>
<td>Solitary Play</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>9. Preference for play or joint attention with primary caregiver by following caregiver’s eye gaze to object</td>
<td>Solitary Play</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>+ 19 (a)</td>
<td>0</td>
</tr>
<tr>
<td>+20 (a)</td>
<td>0</td>
</tr>
<tr>
<td><strong>TOTAL Social Attention Subscale Score</strong></td>
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310
### Sensory Subscale

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<tbody>
<tr>
<td><strong>10.</strong> Duration of gaze to a visually interesting toy in one continuous eye gaze.</td>
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<tr>
<td><strong>11.</strong> Preference for sensory exploration versus typical play with visually interesting toy.</td>
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<tr>
<td><strong>12.</strong> Preference for sensory exploration or typical play with common toy.</td>
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<tr>
<td><strong>13.</strong> Duration of tactile exploration of fabric</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Smooth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(b) Rough</td>
<td></td>
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<tr>
<td>(c) Fluffy</td>
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<td>(d) TOTAL</td>
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<tr>
<td><strong>14.</strong> Preference for tactile exploration versus play with a common toy</td>
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<tr>
<td><strong>15.</strong> Total Frequency of mouthing objects</td>
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<tr>
<td><strong>16.</strong> Hypo-responsiveness – lack of response to sensory stimuli or hyper responsiveness – exaggerated response to sensory stimuli</td>
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<tr>
<td><strong>To be scored in Social Attention Subscale</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solitary = 1</td>
<td></td>
<td></td>
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<tr>
<td>Caregiver = 0</td>
<td></td>
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<tr>
<td><strong>TOTAL Sensory Subscale Score</strong></td>
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</table>

### Behavioural Subscale

Record each behavioural protest and duration

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<tbody>
<tr>
<td><strong>17.</strong> Total frequency of behavioural protests</td>
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<tr>
<td><strong>18.</strong> Total duration of behavioural protests</td>
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<tr>
<td><strong>TOTAL Behavioural Subscale Score</strong></td>
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### Total ABHI Scale Score

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<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Total Social Attention</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>+ Total Sensory</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>+ Total Behavioural</strong></td>
<td></td>
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</tr>
<tr>
<td><strong>TOTAL ABHI Scale Score</strong></td>
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</table>
### Appendix C

#### Autistic Behavioural Indicators Instrument – Parent Questionnaire (ABII-PQ)

<table>
<thead>
<tr>
<th>Subscale</th>
<th>Response</th>
<th>Total Social Attention Subscale Score</th>
<th>Sensory Subscale</th>
<th>Behavioural Subscale</th>
<th>Total ABII-PQ Scale Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Social Attention Subscale</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Do/Did you find it difficult to gain your child’s attention?</td>
<td>No 0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes 1</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2. Do/Did you find it difficult to direct your child’s attention toward an object?</td>
<td>No 0</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Yes 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Do/Did you find that your child preferred to look away from human faces?</td>
<td>No 0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Do/Did you find that your child smiled when looking at human faces?</td>
<td>Yes 0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Do/Did you find your child preferred to play with objects rather than play with you or other individuals?</td>
<td>Yes 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No 0</td>
<td></td>
<td></td>
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<tr>
<td>6. Do/Did you find your child made few attempts to show you things?</td>
<td>Yes 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No 0</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>7. Do/Did you find your child smiled more at objects and toys compared to people?</td>
<td>Yes 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No 0</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>TOTAL Social Attention Subscale Score</strong></td>
<td>0</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Sensory Subscale</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>8. Do/Did you find your child was sensitive to Noise</td>
<td>Yes 1</td>
<td></td>
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<tr>
<td></td>
<td>No 0</td>
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<tr>
<td></td>
<td>Touch</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Smells</td>
<td></td>
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<tr>
<td></td>
<td>Tastes</td>
<td></td>
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</tr>
<tr>
<td>9. Do/Did you find your child preferred to touch, mouth or look at toys rather than play with them in a typical fashion</td>
<td>Yes 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No 0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Do/Did you find your child did not react or respond to noise?</td>
<td>Yes 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No 0</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>TOTAL Sensory Subscale Score</strong></td>
<td>0</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Behavioural Subscale</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>11. Do/Did you find your child difficult to soothe</td>
<td>No 0</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Yes 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Do/Did you find your child had difficulties in emotional regulation</td>
<td>Yes 1</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>No 0</td>
<td></td>
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<tr>
<td><strong>TOTAL Behavioural Subscale Score</strong></td>
<td>0</td>
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<tr>
<td><strong>Total Social Attention</strong></td>
<td>0</td>
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<tr>
<td><strong>Total Sensory</strong></td>
<td>0</td>
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<tr>
<td><strong>Total Behavioural</strong></td>
<td>0</td>
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</tr>
<tr>
<td><strong>TOTAL ABII-PQ Scale Score</strong></td>
<td>0</td>
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</tbody>
</table>
Appendix D

Dear Ms Samantha Ward

A UHREC should clearly communicate its decisions about a research proposal to the researcher and the final decision to approve or reject a proposal should be communicated to the researcher in writing. This Approval Certificate serves as your written notice that the proposal has met the requirements of the National Statement on Research involving Human Participation and has been approved on that basis. You are therefore authorised to commence activities as outlined in your proposal application, subject to any specific and standard conditions detailed in this document.

Within this Approval Certificate are:

* Project Details
* Participant Details
* Conditions of Approval (Specific and Standard)

Researchers should report to the UHREC, via the Research Ethics Coordinator, events that might affect continued ethical acceptability of the project, including, but not limited to:

(a) serious or unexpected adverse effects on participants; and
(b) proposed significant changes in the conduct, the participant profile or the risks of the proposed research.

Further information regarding your ongoing obligations regarding human based research can be found via the Research Ethics website [http://www.research.qut.edu.au/ethics/](http://www.research.qut.edu.au/ethics/) or by contacting the Research Ethics Coordinator on 07 3138 2091 or ethicscontact@qut.edu.au

If any details within this Approval Certificate are incorrect please advise the Research Ethics Unit within 10 days of receipt of this certificate.

<table>
<thead>
<tr>
<th>Project Details</th>
</tr>
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<tbody>
<tr>
<td><strong>Category of Approval:</strong> Human non-HREC</td>
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<tr>
<td><strong>Approved From:</strong> 14/12/2009</td>
</tr>
<tr>
<td><strong>Approval Number:</strong> 0900001353</td>
</tr>
<tr>
<td><strong>Project Title:</strong> The early detection of Autistic Disorder using the Autistic Behavioural Indicators Instrument (ABII)</td>
</tr>
<tr>
<td><strong>Chief Investigator:</strong> Ms Samantha Ward</td>
</tr>
<tr>
<td><strong>Other Staff/Students:</strong> A/Prof Karen Sullivan, Dr Linda Gilmore</td>
</tr>
<tr>
<td><strong>Experiment Summary:</strong> Investigate the utility of the Autistic Behavioural Indicators Instrument.</td>
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<table>
<thead>
<tr>
<th>Participant Details</th>
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<tbody>
<tr>
<td><strong>Participants:</strong> Approximately 20 parents</td>
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<tr>
<td><strong>Location/s of the Work:</strong> QUT</td>
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<table>
<thead>
<tr>
<th>Conditions of Approval</th>
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<tbody>
<tr>
<td><strong>Specific Conditions of Approval:</strong> No special conditions placed on approval by the UHREC. Standard conditions apply.</td>
</tr>
</tbody>
</table>

RM Report No. E801 Version 3
University Human Research Ethics Committee
HUMAN ETHICS APPROVAL CERTIFICATE
NHMRC Registered Committee Number EC00171

Date of Issue: 19/1/10 (supersedes all previously issued certificates)

**Standard Conditions of Approval:**
The University’s standard conditions of approval require the research team to:

1. Conduct the project in accordance with University policy, NHMRC / AVCC guidelines and regulations, and the provisions of any relevant State / Territory or Commonwealth regulations or legislation;

2. Respond to the requests and instructions of the University Human Research Ethics Committee (UHREC);

3. Advise the Research Ethics Coordinator immediately if any complaints are made, or expressions of concern are raised, in relation to the project;

4. Suspend or modify the project if the risks to participants are found to be disproportionate to the benefits, and immediately advise the Research Ethics Coordinator of this action;

5. Stop any involvement of any participant if continuation of the research may be harmful to that person, and immediately advise the Research Ethics Coordinator of this action;

6. Advise the Research Ethics Coordinator of any unforeseen development or events that might affect the continued ethical acceptability of the project;

7. Report on the progress of the approved project at least annually, or at intervals determined by the Committee;

8. (Where the research is publicly or privately funded) publish the results of the project in such a way to permit scrutiny and contribute to public knowledge; and

9. Ensure that the results of the research are made available to the participants.

**Modifying your Ethical Clearance:**
Requests for variations must be made via submission of a Request for Variation to Existing Clearance Form (http://www.research.qut.edu.au/ethics/forms/hum/var/var.jsp) to the Research Ethics Coordinator.

Minor changes will be assessed on a case by case basis.

It generally takes 7-14 days to process and notify the Chief Investigator of the outcome of a request for a variation.

Major changes, depending upon the nature of your request, may require submission of a new application.

**Audits:**
All active ethical clearances are subject to random audit by the UHREC, which will include the review of the signed consent forms for participants, whether any modifications / variations to the project have been approved, and the data storage arrangements.

End of Document
Appendix E

PARTICIPANT INFORMATION FOR QUT RESEARCH PROJECT

The early detection of Autistic Spectrum Disorder

QUT Ethics Approval Number 0900001353

Research Team Contacts

<table>
<thead>
<tr>
<th>Research and PhD student</th>
<th>Dr Karen Sullivan</th>
<th>Dr Linda Gilmore</th>
</tr>
</thead>
<tbody>
<tr>
<td>Samantha Ward</td>
<td>Principal Supervisor</td>
<td>Associate Supervisor</td>
</tr>
<tr>
<td>School of Psychology &amp; Counselling – Faculty of Health – QUT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phone: 3902 1572</td>
<td>Phone: 3138 4609</td>
<td>Phone: 3138 9617</td>
</tr>
<tr>
<td>Email: <a href="mailto:samantha@steppingstonesforlife.com.au">samantha@steppingstonesforlife.com.au</a></td>
<td>Email: <a href="mailto:karen.sullivan@qut.edu.au">karen.sullivan@qut.edu.au</a></td>
<td>Email: <a href="mailto:l.gilmore@qut.edu.au">l.gilmore@qut.edu.au</a></td>
</tr>
<tr>
<td><a href="mailto:s24.ward@student.qut.edu.au">s24.ward@student.qut.edu.au</a></td>
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</tbody>
</table>

Description

This project is being undertaken as part of a PhD research project by Samantha Ward at Queensland University of Technology.

The purpose of this research project is to investigate the early detection of Autistic Spectrum Disorder, investigate current diagnostic practices amongst health care professionals who are involved in the early assessment and diagnosis of young children with Autistic Spectrum Disorders (ASD) and establish the utility of an Autism Specific instrument (Autistic Behavioural Indicators Instrument – ABII; Ward & Gilmore, 2010) in detecting young children with Autism.

The researcher requests your assistance in completing a practitioner questionnaire that will investigate current diagnostic practices amongst health care professionals.

Participation

Your participation in this project is voluntary. If you do agree to participate, you can withdraw from participation at any time during the project without comment or penalty. However, as no names will be recorded on questionnaires, it will not be possible to withdraw your questionnaire once it has been submitted to the researchers. Your decision to participate will in no way impact upon your current or future relationship with QUT.

This specific study will be investigating current diagnostic practices amongst health care professionals who are involved in the early assessment and diagnosis of young children with Autistic Spectrum Disorders (ASD).

Your participation will involve completing an online questionnaire or the enclosed Questionnaire, which will take approximately 15 minutes to complete.

Expected benefits

It is expected that this project will not benefit you directly. However, your contribution to the research will have long-term benefits for children with Autism and their families because the results may facilitate earlier identification and diagnosis, and consequently result in earlier entry into appropriate intervention programs.

Risks

There are no risks beyond normal day-to-day living associated with your participation in this project.

Confidentiality

All comments and responses are anonymous and will be treated confidentially. The names of individual persons are not required in any of the responses.

Consent to Participate

The return of the completed questionnaire is accepted as an indication of your consent to participate in this project.

Questions / further information about the project

Please contact the principal researcher, Samantha Ward, if you have any questions or if you require further information about the project.

Concerns / complaints regarding the conduct of the project

QUT is committed to researcher integrity and the ethical conduct of research projects. However, if you do have any
concerns or complaints about the ethical conduct of the project you may contact the QUT Research Ethics Unit on 3138 5123 or email ethicscontact@qut.edu.au. The Research Ethics Unit is not connected with the research project and can facilitate a resolution to your concern in an impartial manner.

Thank you for helping with this research project. Please keep this sheet for your information.
Appendix F

PARTICIPANT INFORMATION FOR QUT RESEARCH PROJECT

The early detection of Autistic Spectrum Disorder

QUT Ethics Approval Number 0900001353

Research Team Contacts

| Samantha Ward | Dr Karen Sullivan | Dr Linda Gilmore |
| Research and PhD student | Principal Supervisor | Associate Supervisor |
| School of Psychology & Counselling – Faculty of Health – QUT |

Phone: 3902 1572  Phone: 3138 4609  Phone: 3138 9617
Email: samantha@steppingstonesforlife.com.au  Email: karen.sullivan@qut.edu.au  Email: l.gilmore@qut.edu.au

s24.ward@student.qut.edu.au

Description

This project is being undertaken as part of a PhD research project by Samantha Ward at Queensland University of Technology.

The purpose of this project is to establish the utility of an Autism Specific instrument (Autistic Behavioural Indicators Instrument – ABII; Ward & Gilmore, 2010) in detecting young children with Autism. Study 1 of the research will establish the utility of the ABII in correctly identifying Autism in 12 – 18 month old infants who are identified as “high risk” for Autism. The research will also investigate whether the ABII is more accurate in predicting and identifying young children with Autism compared to other measures that are currently being used. Study 2 of the research will establish the utility of the ABII in correctly identifying Autism in 2-6 year old children who have received a formal diagnosis of ASD and investigate retrospective parental accounts of their diagnostic experiences to help establish the measures used to diagnose their children and the average age of diagnosis.

The research team requests your assistance including your child in the research project.

Participation

Your participation in this project is voluntary. If you do agree to participate, you can withdraw from participation at any time during the project without comment or penalty. Your decision to participate will in no way impact upon your current or future relationship with QUT.

For study 1, you and your child’s participation will involve undergoing a series of screening tools and parent report instruments for Autism Spectrum Disorders and a developmental assessment across 2 separate sessions. The parent report measures will ask you questions regarding the development of your child. For example, “does your child turn to look at you when you call their name?”. These sessions will be either when your child is aged 12 months and 18 months (if you have enrolled in the study prior to 12 months), when your child is aged 18 and 24 months (if you have enrolled in the study prior to 18 months) or when your child is 24 months and 30 months (if you have enrolled in the study prior to 24 months). Each of these sessions will vary in length depending on the number of instruments being used. It is anticipated that each session will, on average, be approximately 1-2 hours in length.

For study 2, you and your child’s participation will involve undergoing a Screening tool, parent report instruments for Autism Spectrum Disorders and diagnostic experiences across 1 session which will, on average, be approximately 1 hour in length. The parent report measures will ask you questions regarding the development of your child. For example, “does your child show interest in playing with a variety of objects?”.

You will be asked to provide a photograph of yourself for use in this research. This photograph is required for a number of items on one of the measures that are included in the research, where your child’s gaze to a photograph of a primary caregiver is recorded. This photograph will only be used for this research and will either be destroyed or returned to you upon completion of the study.

The sessions will be held at Stepping Stones for Life Psychology, a child and adolescent psychology clinic.

Participation in this project will not result in a diagnosis of Autistic Spectrum Disorder. This is because a comprehensive assessment of your child’s development will not be conducted and the assessments being used are for screening rather than diagnostic purposes. However, a list of paediatricians, psychologists and early intervention services will be provided. It is recommended that, if at any time you have concerns regarding your
child’s development, you consider contacting these services for recommendations regarding the assessment of your child.

**Expected benefits**

You and your child may benefit from participation in this research if you choose to receive feedback regarding your child’s motor (fine and gross), language (receptive and expressive), and cognitive development, if their performance suggests developmental delay. Early identification of potential developmental delay will facilitate earlier intervention for you and may improve their developmental outcomes. It is also expected that this project will have long-term benefits for children with Autism and their families because the results may facilitate earlier identification and diagnosis, and consequently result in earlier entry into appropriate intervention programs.

**Risks**

If you have chosen to receive feedback regarding your child’s development, and results from a standardised measure of child development indicates that your child may be displaying developmental delay, there is a potential risk of discomfort for parents when receiving this information. However, early detection of developmental delay would facilitate early intervention for your child. In the event that this does occur, information regarding diagnostic, clinical and intervention services will be provided.

There are therefore some risks beyond normal day-to-day living associated with your participation in this project, as you may experience some discomfort if you choose to receive feedback regarding your child’s development, and if their performance indicates potential delays in development. However, it is considered that this small risk of discomfort is outweighed by the potential benefit of facilitating early diagnosis QUT provides for limited free counselling for research participants of QUT projects, who may experience discomfort or distress as a result of their participation in the research. Should you wish to access this service please contact the Clinic Receptionist of the QUT Psychology Clinic on 3138 0999. Please indicate to the receptionist that you are a research participant.

**Confidentiality**

All comments and responses are anonymous and will be treated confidentially. The names of individual persons are not required in any of the responses. To help in recording your child’s responses a second researcher may be present in the room during some of your child’s session. However, you will still be able to participate in the project without the presence of a second researcher if you are not comfortable with this.

**Consent to Participate**

The researcher would like to ask you to sign a written consent form (enclosed) to confirm your agreement to participate.

**Questions / further information about the project**

Please contact the researcher named above to have any questions answered or if you require further information about the project.

**Concerns / complaints regarding the conduct of the project**

QUT is committed to researcher integrity and the ethical conduct of research projects. However, if you do have any concerns or complaints about the ethical conduct of the project you may contact the QUT Research Ethics Unit on 3138 5123 or email ethicscontact@qut.edu.au. The Research Ethics Unit is not connected with the research project and can facilitate a resolution to your concern in an impartial manner.

*Thank you for helping with this research project. Please keep this sheet for your information.*
CONSENT FORM FOR QUT RESEARCH PROJECT

The early detection of Autistic Spectrum Disorder

QUT Ethics Approval Number 0900001353

Research Team Contacts

Samantha Ward  Dr Karen Sullivan  Dr Linda Gilmore
Research and PhD student  Principal Supervisor  Associate Supervisor

School of Psychology & Counselling – Faculty of Health – QUT

Phone: 3902 1572  Phone: 3138 4609  Phone: 3138 9617
Email: samantha@steppingstonesforlife.com.au  Email: karen.sullivan@qut.edu.au  Email: l.gilmore@qut.edu.au
s24.ward@student.qut.edu.au

Statement of consent

By signing below, you are indicating that you:

• have read and understood the information document regarding this project
• have had any questions answered to your satisfaction
• understand that if you have any additional questions you can contact the research team
• understand that you are free to withdraw at any time, without comment or penalty
• understand that you can contact the Research Ethics Unit on 3138 5123 or email ethicscontact@qut.edu.au if you have concerns about the ethical conduct of the project
• agree to participate in the project
• agree to have your photograph taken

☐ understand that the project may include the presence of a second researcher
☐ agree to be contacted by the researcher or other individual’s from QUT in the future for follow up research.

Name  ____________________________________________________________

Signature  _________________________________________________________

Date  ____________________________________________________________

Please return this sheet to the investigator.
Appendix G

The early detection of Autistic Disorder using the Autistic Behavioural Indicators Instrument (ABII)

Research Team Contacts

<table>
<thead>
<tr>
<th>Samantha Ward</th>
<th>Dr Karen Sullivan</th>
<th>Dr Linda Gilmore</th>
</tr>
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<tbody>
<tr>
<td>Research and PhD student</td>
<td>Principal Supervisor</td>
<td>Associate Supervisor</td>
</tr>
<tr>
<td>School of Psychology &amp; Counselling</td>
<td>School of Psychology &amp; Counselling</td>
<td>School of Learning &amp; Professional Studies</td>
</tr>
<tr>
<td>Phone: 3902 1572</td>
<td>Phone: 3138 4609</td>
<td>Phone: 3138 9617</td>
</tr>
<tr>
<td>Email: <a href="mailto:samantha@steppingstonesforlife.com.au">samantha@steppingstonesforlife.com.au</a></td>
<td>Email: <a href="mailto:karen.sullivan@qut.edu.au">karen.sullivan@qut.edu.au</a></td>
<td>Email: <a href="mailto:l.gilmore@qut.edu.au">l.gilmore@qut.edu.au</a></td>
</tr>
<tr>
<td><a href="mailto:s24.ward@student.qut.edu.au">s24.ward@student.qut.edu.au</a></td>
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Description

This project is being undertaken as part of a PhD research project by Samantha Ward at Queensland University of Technology.

The purpose of this project is to establish the utility of an Autism Specific Parent Questionnaire (Autistic Behavioural Indicators Instrument – Parent Questionnaire ABII-PQ; in detecting young children with either a diagnosis of Autism or typical development.

The research team requests your assistance including your child in the research project.

Participation

Your participation will involve completing an anonymous online questionnaire or the enclosed Questionnaire, which will take approximately 10 minutes to complete.

Expected benefits

It is expected that this project will not benefit you directly. However, your contribution to the research will have long-term benefits for children with Autism and their families because the results may facilitate earlier identification and diagnosis, and consequently result in earlier entry into appropriate intervention programs.

Risks

There are no risks beyond normal day-to-day living associated with your participation in this project.

Confidentiality

All comments and responses are anonymous and will be treated confidentially. The names of individual persons are not required in any of the responses.

Consent to Participate

The return of the completed questionnaire is accepted as an indication of your consent to participate in this project.

Questions / further information about the project

Please contact the principal researcher, Samantha Ward, if you have any questions or if you require further information about the project.

Concerns / complaints regarding the conduct of the project

QUT is committed to researcher integrity and the ethical conduct of research projects. However, if you do have any concerns or complaints about the ethical conduct of the project you may contact the QUT Research Ethics Unit on +61 7 3138 5123 or email ethicscontact@qut.edu.au. The Research Ethics Unit is not connected with the research project and can facilitate a resolution to your concern in an impartial manner.
Appendix H

ADDRESSING THE NEED FOR EARLY IDENTIFICATION AND DIAGNOSIS OF AUTISM DISORDER

Early Behavioural Indicators for Autism

The identification of behavioural indicators of Autistic Disorder, that reliably differentiate Autism from other developmental disorders and delays, will enable more accurate screening for Autism at an early age.

The researcher needs you...

To help improve the age of diagnosis and timing of early intervention for Autism, and in doing so, ensuring that all children have the best possible chance to reach their full potential.

Who is needed?

• Study 1: Children 11-48 months whose parents have concerns regarding their development.
• Study 2: Children aged 2-12 years who have a diagnosis of Autistic Spectrum Disorder

What does participation involve?

• Undergoing Autism screening tools and parent report forms.
• Study 1: 2 visits to a clinic over a 12 month period for approximately 1-2 hours each and 24 month telephone follow up.
• Study 2: 1 visit to a clinic for approximately 1-2 hours.

For more information & to enroll in this study, please contact:

Samantha Ward at
Stepping Stones for Life Psychology
Phone: 3902 1572
Email: samantha@steppingstonesforlife.com.au
or
s24.ward@student.qut.edu.au

Research
Addendum to Chapter 7: Combining parent and clinician ratings of behavioural indicators of autism spectrum disorder improves diagnostic classification

This addendum to the results section of Chapter 7 provides an alternative way to display the results of table 2.

Table 2

Agreement (Kappa) between the Autism Behavioural Indicators Instrument (ABII) and ABII Parent Questionnaire (ABII-PQ)

<table>
<thead>
<tr>
<th>ABII-PQ</th>
<th>Subscale</th>
<th>Positive</th>
<th>Negative</th>
<th>Agreement (%)</th>
<th>κ</th>
<th>p</th>
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<tbody>
<tr>
<td>Total Scale</td>
<td>Positive</td>
<td>44</td>
<td>3</td>
<td>45 (88.2)</td>
<td>.19</td>
<td>.184</td>
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<tr>
<td></td>
<td>Negative</td>
<td>3</td>
<td>1</td>
<td></td>
<td></td>
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<tr>
<td>Social Attention</td>
<td>Positive</td>
<td>47</td>
<td>0</td>
<td>48 (94.2)</td>
<td>.38</td>
<td>.001</td>
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<tr>
<td></td>
<td>Negative</td>
<td>3</td>
<td>1</td>
<td></td>
<td>.04</td>
<td>.341</td>
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<tr>
<td>Sensory*</td>
<td>Positive</td>
<td>24</td>
<td>26</td>
<td>26 (50.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>0</td>
<td>1</td>
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<tr>
<td>Behavioural*</td>
<td>Positive</td>
<td>28</td>
<td>23</td>
<td>23 (45.1)</td>
<td>.05</td>
<td>.265</td>
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<tr>
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n = 51. *Significant difference between instruments on ASD classification derived using z statistic, p <.05.