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EARLY DIAGNOSIS METHODS FOR AUTISM SPECTRUM DISORDER: A SYSTEMATIC REVIEW

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PsyD Clinical Dissertation Signature Page

This Clinical Dissertation, written under the direction of the student's Clinical Dissertation Chair and Committee and approved by Members of the Committee, has been presented to and accepted by the faculty of the Clinical Psychology PsyD Program in partial fulfillment of the requirements for the degree of Doctor of Psychology. The content and research methodologies presented in this work represent the work of the student alone.

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Abstract

Objective: This systematic review aimed to comprehensively synthesize existing literature on early detection methods for Autism Spectrum Disorder (ASD) in children birth to 3 years, that lead to an effective and reliable early diagnosis in children 2 to 3 years of age.

Methods: A systematic search was conducted across multiple electronic databases, including PubMed, Scopus, and PsycINFO following PRISMA guidelines. Studies reporting on early detection methods for ASD in infants and toddlers within ages 0 to 3 years that lead to early diagnosis of children ages 2 to 3 years were eligible for inclusion. Data extraction and quality assessment were performed, and relevant studies were synthesized to provide insights into the accuracy, validity, and clinical utility of each early ASD diagnosis method.

Results: The initial search yielded a total of 648 articles, of which 4 studies met the inclusion criteria. The identified studies encompassed various diagnostic approaches, including behavioral assessments, neuroimaging techniques, genetic markers, and screening instruments. Findings suggest that early detection of ASD is feasible, with promising tools and methodologies available for use within the specified age group. However, the accuracy and reliability of these methods vary, highlighting the need for continued research and refinement of diagnostic tools.

Conclusion: Early diagnosis of ASD in children prior to the age of 3 is crucial for initiating timely interventions and improving long-term outcomes. This systematic review underscores that while there is a diversity of early detection methods available, only 4 studies illustrate the

effectiveness of early detection methods for diagnostic accuracy before the age of 3. Nonetheless, further research is warranted to enhance the precision and clinical applicability of these approaches. Research examining if early detection methods lead to early diagnosis is lacking, this area of research is needed to facilitate early interventions and understand the developmental trajectory of ASD during early childhood development. Additionally, this study confirms the ongoing health disparities and cultural gap in research connected to early diagnosis of ASD. Future research needs to include a more culturally diverse population and address how to incorporate biomarkers for ASD as a component of early diagnosis accuracy.

Introduction

Statement of the Problem

Autism Spectrum Disorder (ASD) can be reliably diagnosed at 24 months old and sometimes as early as 18 months (Centers for Disease Prevention [CDC], 2020). The American Academy of Pediatrics recommends that all children be screened for autism at 18 months and at 24 months, yet only about half of primary care practitioners screen for autism (Hyman & Levy, 2019). A diagnosis of autism can typically be made by age 2, however the average age at diagnosis in the United States is more than 4 years old (Hyman & Levy, 2019). Delay in evaluation and diagnosis can result in delaying early intervention implementation and in turn, lead to poor long-term outcomes (Zuckerman et al., 2017). There is a plethora of studies on early intervention methods however research on early diagnosis methods in it's infancy. While early intervention helps increase positive long-term outcomes, it is necessary to determine and utilize effective early evaluation and diagnosis of ASD when possible.

Research Question and Aims

This study plans on answering the following research question: What are the effective early detection methods for ASD in children from birth to 3 years of age that leads to an early diagnosis prior to the age of 3? This question utilizes the Population, Intervention, Comparison, Outcomes and Study (PICOS) approach mentioned previously (Ukwaja, 2020). The following aims helped to answer research question:

Aim 1: Identify early detection methods for diagnosing children with ASD prior to the age of 3.

Aim 2: Identify and analyze how cultural consideration and health disparities factors are attended to within the early detection and diagnostic accuracy research.

Aim 3: Compare the diagnosis methods to determine which diagnosis method is most effective for early diagnosis of ASD in children 2-3 years.

Research Design

This systematic review adhered to Muka et al.'s (2020) structured approach, which provides researchers with a detailed, sequential model for conducting a thorough research study. Furthermore, the review was conducted and reported in accordance with the guidance outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, as articulated by Page et al. (2021).

Definition of Terms

Autism spectrum disorder (ASD) - "a complex developmental condition involving persistent challenges with social communication, restricted interests, and repetitive behavior" (Jadhav & Schaepper, 2021).

Biomarker - "an objective way to identify and measure biological abnormalities for diagnostic purposes" (Jensen et al., 2022).

High-risk - a child that is at a higher likelihood for autism, can be due to having an older sibling with autism or complications during pregnancy or at birth, or higher parental age (CDC, 2022).

Early identification/detection - "identification of risk of autism prior to the age of 3" (Okoye et al., 2023)

Early diagnosis - diagnosis of autism prior to the age of 3 (Okoye et al., 2023)

Review of the Literature

Introduction

There is limited research on early diagnosis methods of ASD. However, the existing studies highlight three primary methods of early diagnosis within the birth to three years of age range: 1. Clinical imaging 2. Two-tiered or more screening and 3. Home video analysis. While these three diagnosis methods are the most prevalent, they are not the only diagnosis methods utilized. The purpose of this literature review is to identify the existing research on early ASD detection methods and how they can lead to early diagnosis methods for ASD. Before going into the literature on early detection and diagnosis it is important to have an understanding of what Autism is, the historical development of the diagnosis, and the defining features of autism.

Overview of Autism

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that is characterized by deficits in social, communication, and motor skill functioning, as well as stereotyped and repetitive patterns of behavior (American Psychiatric Association [APA], 2013). The Centers for Disease Control and Prevention (CDC) has shown an increase in prevalence rates. Approximately 1 in 36 children in the U.S. are diagnosed with ASD (CDC, 2020), which is an increase from 2018 where 1 in 44 children were diagnosed with ASD (CDC, 2018). Additionally, the CDC states that boys are more than 4 times as likely to be diagnosed with ASD than girls (CDC, 2019). It is important that clinicians and parents understand the factors that have contributed to increased prevalence of ASD so that they are aware of ways in which

they may be able to prevent or reduce the impact of related risk factors, when possible. Some theories suggest that ASD diagnoses have increased due to various environmental factors (Karimi et al., 2017), whereas other possibilities include increased sophistication of early diagnosis methods, which leads to detection of otherwise undiagnosed cases (Aspril & Johns Hopkins Bloomberg School of Public Health, 2020). In order to support efforts to understand the trend of increasing prevalence rates in recent years, it is important to examine the ways in which ASD is assessed and diagnosed.

To date, much of the research on ASD has focused on early intervention methods for ASD, but few studies on the early diagnosis methods for ASD have been conducted. According to Brian, Zwaigenbaum, & Ip (2020), symptoms of ASD may begin to appear in the first two years of life. However, some symptoms that affect the child's ability to function socially, at school, at home, or in other areas of life may not develop until after their second year of life. Although current treatments vary, most interventions focus on managing behavior and improving social and communication skills to enable optimal social functioning and independence (Fombonne, 2020; Holbrook & Israelsen, 2020; Smith et al., 2021). Clinician-led assessments of ASD remain the gold standard for diagnosis of ASD and is the only legal standard for an official ASD diagnosis (Elder et al. 2017; McCarty & Frye, 2020). Diagnostic criteria for ASD were revised in 2013 with the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), which delineates two core ASD symptoms: persistent social and communication deficits and the presence of restricted, repetitive patterns of behaviors

and/or interests, and sensory differences (APA, 2013). Additionally, ASD severity, which categorizes the impact of symptoms on the individual's adaptive functioning, is now considered in the diagnostic process (APA, 2013). Advances in ASD science have challenged the traditional conceptualizations of ASD as a discrete phenotype, in which particular genes or set of genes are responsible for the development of ASD (Lyall et al., 2017). Instead, clinicians, and researchers are seeing that ASD exists along a continuum of neurodiversity (Kapp et al., 2013) in which clinicians can incorporate multiple different diagnosis methods to assist in a definitive ASD diagnosis. Today, it is required to have expert clinical judgment when evaluating the presence of significant impairment(s) in the core symptom areas of ASD, thus determining the presence (or absence) of ASD (Elder et al. 2017) and planning the optimal therapeutic approach/intervention.

Severity varies for individuals with ASD. Some individuals with ASD demonstrate symptoms that cause mild impairment, whereas others are profoundly impaired (APA, 2013). Although the spectrum of severity in ASD is well-defined, the range of ASD symptoms can be classified into broader categories of core symptoms as well as secondary symptoms within each severity spectrum (Elder et al. 2017). Secondary symptoms can include conditions such as intellectual impairment, which occurs in approximately 50% of patients with ASD (Matson & Shoemaker, 2009), self-injury, aggressiveness toward others, sleeping disorders, eating disturbances, and seizures (Elder et al. 2017). It is important to note that manifestation of ASD symptoms can alter throughout the lifespan (Elder et al. 2017). For instance, language

difficulties and hyperactivity which is often seen in younger children can shift into mood dysregulation, relational problems, and hypoactivity in adolescence and young adulthood (Hofvander et al., 2009). In summary, characterizing and diagnosing ASD can be challenging, but progress has been made in refining the diagnostic processes. Earlier knowledge of the diagnosis can help support better outcomes for the individual and the family (Elder et al. 2017; Malik-Soni et al., 2021).

While it is believed that early intervention strategies lead to better outcomes for children with ASD, early intervention is predicated on early diagnosis. Furthermore, it is unknown what interventions can be used within the first year of life and how effective these may be, as there are few studies on both early intervention and detection of ASD in infants under the age of one. Therapeutic strategies that start before reliable early diagnosis haven not been evaluated, which is why it is important to analyze the effectiveness of the current studies on early diagnosis methods of ASD to assist with early intervention. If clinicians and pediatricians know the various and effective methods of early diagnosis of ASD and researchers adequately disseminate their findings the information can be used to provide an early diagnosis, which can change the diagnosis age to before 2 years, then they may be more likely to implement early interventions, which in turn may lead to better long-term outcomes for children with ASD. To do this, researchers must first identify the current early diagnosis methods and assess their effectiveness in accurately diagnosing ASD and properly disseminate the information so that both clinicians and parents can have access.

Diagnostic Criteria for Autism Spectrum Disorder

Diagnostic criteria for ASD have differed over time, and thus relevant literature typically reflect the criteria that were current at publication. Substantive changes occurred for ASD diagnostic criteria between the DSM-IV-TR and DSM-5. Within the DSM-IV-TR, ASD was split into 5 subtypes: 1. Autistic Disorder, 2. Asperger's Disorder, 3. Childhood Disintegrative Disorder, 4. Rett Syndrome, 5. Pervasive Developmental Disorder, Not Otherwise Specified (PDD-NOS). Within the DSM-IV-TR behaviors associated with autism were divided into three groups: Social, Communication, and Repetitive behaviors. It is important to know that to qualify for an ASD diagnosis within the DSM-5, behaviors associated with autism are divided into two groups rather than three as seen in the DSM-IV-TR. Rett Syndrome, a genetic disorder that occurs exclusively in females and is caused by a specific mutation in the MECP2 gene, is no longer considered a type of Autistic Spectrum Disorder although it has many autistic characteristics. All of the other previous DSM-iv subtypes are included in the single overarching DSM-5 class Autism Spectrum Disorder. In the DSM-5 the difficulty with communication skills group seen in the DSM-IV-TR diagnostic criteria is now included either in social skills or repetitive behaviors depending on which dimension is affected. However, language impairment can now be given as a specifier for an ASD diagnosis within the DSM-5. An ASD diagnosis based on the DSM-5 consists of the following observable behaviors:

1. Difficulty with social skills

Individuals with ASD might not respond to social cues or understand how to behave in different social situations. They might have trouble with picking up on and understanding nonverbal communication, like facial expressions and eye contact.

2. Restricted or repetitive behaviors and interests:

   For individuals with ASD this may be seen in routines and rituals, like eating the same things, wanting to keep the same schedule, or taking a similar route. Individuals with ASD may also have intense interests, like wanting to talk only about planes or a favorite book.

Another significant change for ASD in the DSM-5 is the inclusion of the supercategory of "Neurodevelopmental Disorders," under which ASD is now located. Previously, ASD was found under "Disorders Usually First Diagnosed in Infancy, Childhood, and Adolescence" under the subcategory of Pervasive Developmental Disorders. The new organizational placement emphasizes the significance of the neurobiological foundations for ASD.

Brain Structures Involved in Autism Spectrum Disorder

ASD is thought to be a complex neurodevelopmental condition that emerges within the first three years of life and is defined by deficits in social skills and communication in addition to stereotyped repetitive behavior. Understanding how each brain region is affected also helps us understand the cognitive and behavioral processes of people with ASD. It is also helpful to

know what brain regions are responsible for particular ASD symptoms and behaviors in order to help clinicians, researchers, and parents understand what behaviors and functions might be impacted and therefore what to look out for when making a diagnosis of ASD.

While the literature is still limited in information about the neurobiology and neuroanatomy of ASD in the early developmental period, existing research demonstrates that the cerebral cortex, amygdala, hippocampus, temporal lobe, glial cells, and cerebellum are all affected in individuals with ASD (Donovan & Basson, 2017). The cerebral cortex is responsible for movement, sensation, future planning, and social behavior. When this region is altered and connections do not form properly or are forming more often we may see differences in these functions for people with ASD (Casanova et al., 2002; Amina et al., 2020). The amygdala is the region of the brain that is responsible for emotions, survival instincts (fight or flight), and memory (Schumann et al., 2004). For children and adolescents with ASD, this region of the brain is often too large yet smaller in adults with ASD (Schumann et al., 2004). Increased activity in the amygdala may be one reason why people with ASD report high levels of anxiety (Herrington et al., 2017; Herrington et al., 2016). Additionally, diminished amygdala function has been repeatedly associated with deficits in social intelligence, motivation and perception, particularly among individuals with ASD (Chevallier et al., 2012). The hippocampus is responsible for the formation of memories and in many of those who have ASD it is found that their hippocampus is bigger which may be the reason why those with ASD can hold on to enormous amounts of detail on a fixed interest (Richards et al., 2020). Deficits in the hippocampus may also be reasons for why those with ASD cannot remember the proper social

rules they were once taught. The temporal lobe is responsible for auditory processing, visual input, semantics of language, and verbal memory. Dysfunction in this region, specifically the fusiform gyrus, can be reasons for why people with ASD avoid eye contact due to impaired face processing (Pierce et al., 2001). The cerebellum is responsible for coordination of motor control, balance, sensory integration, and emotion regulation (Gold & Toomey, 2018). It is found that about half of individuals with ASD have a smaller number of Purkinje cells which are located in the cerebellum. Purkinje cells are responsible for the release of the inhibitory neurotransmitter GABA (Rogers et al., 2013). This can be the reason for the decreased capacity for motor learning in children with ASD (Rogers et al., 2013).

Aside from understanding brain function, it is important to understand the theories behind the behavioral patterns associated with ASD. Literature suggests that behavioral observation is the main criterion for ASD diagnosis at this time, due to ASD being behaviorally defined (CDC, 2020). However, with biomarker and genetic studies increasing this can change how we diagnose ASD.

Observable Characteristics Associated with Autism

As researchers and clinicians have learned more about ASD, there have been specific observable characteristics that clinicians look out for when diagnosing ASD. Since many of the methods that will be mentioned in the literature review utilized behavioral observation and coding to confirm an Autism diagnosis, it is important for us to understand the significance of these observable characteristics and why they are present in individuals with ASD. It is also

important to see how our understanding of the development of ASD behavioral patterns have shifted and evolved over the years by expansive research and better understanding of autism in and of itself. Knowing the basis of these various observable characteristics will help us gain a sense of how people may conduct behavioral observations and why certain behavioral patterns are predominant in people on the Autism spectrum. Additionally, ASD is thought to have a genetic basis however, there have been no studies that are able to identify a single gene that causes ASD. Finding a single gene may be difficult to pinpoint because there may be multiple genes at play in ASD, as it is expressed differently for different individuals. While no one knows the exact root of autism, that has not stopped researchers and clinicians from speculating and hypothesizing various reasons as to why certain observable behavioral patterns develop in children that are on the autism spectrum.

Lack of Eye Contact

One of the most common characteristics of ASD is atypical eye gaze and contact (Madipakkam et al., 2017). For many typical developing children, a lack of eye contact is usually a sign of social indifference (Massachusetts General Hospital, 2017). It is believed that for those with Autism, eye contact causes them to feel a significant amount of stress and discomfort (Massachusetts General Hospital, 2017). Madipakkam et al. (2017) found that shift in eye gaze away from another's eyes is done unconsciously in those with ASD. Madipakkam et al. (2017) suggest that this lack of eye contact may occur prior to behavioral patterns of ASD and can be helpful in the early diagnosis of ASD.

Selective Mutism

In the DSM-IV and DSM-5 Selective Mutism (SM) is described as an anxiety diagnosis in which individuals are not able to speak when expected to during social interaction in certain social situations, but are able to speak in other situations (5th ed.; DSM–5; American Psychiatric Association, 2013). While SM is a distinct diagnosis from ASD, the two are commonly found to be comorbid (Steffenberg et al., 2018). Steffenberg et al. (2018) conducted a retrospective study looking at the prevalence of ASD among those diagnosed with SM and found that ASD has a high occurrence within SM families. It was also found that among the patients who exhibited SM within the home, all but one also had an ASD diagnosis (Steffenberg et al., 2018). Additionally, a study done by Suzuki et al. (2020) suggests that ASD tendency often occurs in people with SM. Knowing that SM and ASD have a strong association with one another can help us when establishing effective early diagnostic methods by incorporating some form of communication assessment that is relevant to a child 2 years or younger.

Sensory Hyper- and Hyposensitivity

It is common for individuals with ASD to have atypical responses to one or more sensory stimulations (Bogdashina, 2014). Individuals may experience hypersensitivity to sensory stimuli. This may take the form of hypervision, hyper hearing olfactory hypersensitivity, hypertactile, vestibular hypersensitivity, and/or proprioceptive hypersensitivity (Robertson & Cohen, 2017; Jussila et al., 2020). Conversely, individuals with ASD may experience hyposensitivity to sensory stimuli. This may result in hypovision, hypohearing,

hypotaste/smell, hypotactility, vestibular hyposensitivity, and/or proprioceptive hyposensitivity (Robertson & Cohen, 2017; Jussila et al., 2020).

Visual Sensory Perception

Some children with ASD may experience hypersensitivity or hyposensitivity to visual stimuli in the form of hypervision or hypovision. Hypervision means that the individual can detect the smallest particles and typically dislike bright lights and air particles (Robertson & Cohen, 2017; Jussila et al., 2020). Whereas an individual with hypovision means that they can only see the outline of an object (Robertson & Cohen, 2017).

Auditory Sensory Perception

Another form of hypersensitivity or hyposensitivity may be in response to an auditory stimuli. For those with hyperhearing, the quietest auditory sound may trigger them (Jussila et al., 2020). Individuals with hyperhearing tend to be very light sleepers and are startled by unpredictable and sudden sounds and will typically avoid situations in which sounds are present (Robertson & Cohen, 2017; Jussila et al., 2020). Whereas, individuals with hypohearing will seek out sounds, and may create sounds to satisfy their craving (Robertson & Cohen, 2017).

Tactile Sensory Perception

Hypertactility and hypotactility are present when individuals are responding to tactile stimuli. For those that experience hyperactivity, they do not enjoy the sensation of touch and can be triggered by even the slightest touch. They often do not like their hands being washed or

cutting of nails or hair. For those with hypotactility, these individuals are not able to feel certain forms of tactile stimulation or even pain (Robertson & Cohen, 2017).

Oral Sensory Perception

When individuals' sense of taste is affected they may experience either hypertaste or hypotaste. For individuals with with hypertaste, they may be picky eaters due to many tastes being too strong or aversive for them (Robertson & Cohen, 2017; Jussila et al., 2020). Most individuals with hypertaste avoid trying new foods and will typically stick to the same meal (Robertson & Cohen, 2017). For individuals with hypotaste, these individuals are typically wanting to put everything in their mouth and may experience excessive drooling and constantly have their mouth open (Robertson & Cohen, 2017).

Olfactory Sensory Perception

Hypersmell or hyposmell is present in individuals that have issues surrounding their olfactory sensory perception. For individuals with hypersmell, they are not able to tolerate even the slightest smell, even though those around them may be unaware of a smell. This hypersmell may prevent an individual from eating regardless of how hungry they may be. On the other hand, hyposmell may draw an individual to places with strong odors (Robertson & Cohen, 2017) due to their craving for smells (Jussila et al., 2020).

Vestibular Sensory Perception

The vestibular sensory system is responsible for managing balance and spatial orientation in regards to balance (Robertson & Cohen, 2017; Jussila et al., 2020). When a

person experiences vestibular hypersensitivity they may exhibit difficulty walking or crawling on uneven surfaces or changing direction (Robertson & Cohen, 2017; Jussila et al., 2020). They prefer their feet always touch the ground and may show anxiety or fear when their feet have to leave the ground. For those that have vestibular hyposensitivity they crave movements where their body is off balance and will enjoy movements like vigorously rocking back and forth or spinning/swinging round and round and will not feel nausea or dizziness (Robertson & Cohen, 2017; Jussila et al., 2020).

Proprioceptive Sensory Perception

The proprioceptive system is located in our muscles and joints and provides us with a sense of body awareness (Jussila et al., 2020). For those with proprioceptive hypersensitive they may hold their body in atypical positions and may exhibit frustration manipulating small objects (Jussila et al., 2020). For individuals with proprioceptive hyposensitivity, these individuals have difficulty in body awareness and may constantly bump into objects/people, drop things, fall over, and struggle with supporting their own body or holding objects (Robertson & Cohen, 2017; Jussila et al., 2020).

Restricted and Repetitive Behaviors

When a child with autism is responding to a lack of or heightened sensory stimuli, this causes the child exhibit behaviors that are labeled restricted and repetitive behaviors (RRBs) (Robertson & Cohen, 2017; Jussila et al., 2020). Repetitive movements are a diagnostic characteristic of ASD and it is important to understand why these behaviors are occurring

(Ravizza, Solomon, Ivry, & Carter, 2013). While some behaviors may be a result of hyper- or hyposensory reactions, there is little known about the etiology of RRBs (Ravizza et al., 2013). RRBs in ASD do not only include atypical sensory responses but also include stereotyped movement, repetitive use of objects and speech, restricted interests, and insistence on sameness. Each child has a different presentation of these RRBs but it is important to understand that across all children with ASD some presentation of RRBs is observed and is a defining diagnostic characteristic (Turner-Brown & Frisch, 2020).

Clinical Imaging

Clinical imaging of the brain is important for both early detection and diagnosis of ASD as ASD is a disorder that is heavily associated with a difference in the brain structure that alters one's functioning (Hashem et al., 2020). It is important to understand the biomarkers for ASD and how to effectively detect these biomarkers. ASD biomarkers refer to the differences in the neurological and biological functions and structures in individuals with ASD compared to typically developing individuals (McPartland, 2020). Several types of biomarkers are defined, including: 1. Diagnostic biomarker, which detects or confirms the presence of a condition, 2. Predictive biomarker, which gives information about the effect of a therapeutic intervention, 3. Prognostic biomarker, which provides information about a person's overall outcome regardless of intervention (Califf, 2018).

Additionally, there are also specific time periods in development during which these biomarkers can be present within the birth to 3 years period. Prior to birth there may be prenatal

(predictive) biomarkers which are found in utero while the baby is still developing in the mother's womb. According to Xu et al. (2020), prenatal genetic testing (PGT) for ASD is available through clinical genetic services and may inform parents about their unborn child's risk for ASD allowing parents to arrange for early diagnosis and interventions. However it is important to note that genetic testing alone cannot predict a future diagnosis of ASD, there needs to be the presence of behavioral indicators of ASD as well. Next, there are very early (predictive) biomarkers that are typically detected between birth and 24 months of age and indicate the possibility of a future diagnosis of ASD. Klin (2018) discusses the ways in which numerous studies have been found that identify predictive biomarkers as early as 2 months and how this is useful in the future diagnosis of ASD at the age of 2 years. Lastly there are early diagnostic biomarkers which present themselves at the age of 2 years for children with ASD (Frye, 2019).

According to Bosl, Tager-Flusberg, & Nelson (2018) it is difficult to find specific biomarkers relevant to the early detection of ASD because of the various presentations of this disorder. However, through the use of electroencephalograms (EEG) as a means of functional brain imaging, we can start to gain a better picture and understanding of the differences in the brain of a person who is diagnosed with ASD. This may lead to a possible means for early detection of ASD. Bosl et al. (2018) found, through the use of EEGs, that key digital biomarkers could be extracted from the EEG measurements. These findings are especially significant for ASD diagnosis and early detection because they allow for early intervention. While there is no

cure for ASD, with the implementation of early intervention, the reduction of the presenting symptoms of ASD is possible and possibly, for some individuals, they may no longer meet the criteria for an ASD diagnosis (Leadbitter et al., 2021).

Additionally, Gabard-Durnam et al. (2019) tested infant participants who were either at low familial risk of ASD or high familial risk for ASD, high risk was determined based on having a sibling with ASD. Gabard-Durnam et al. (2019) gathered EEG measurements from an undisclosed number of infants at 3, 6, 9, 12, 18, 24, and 36 months. Their findings showed that EEGs recordings of the frontal lobe within the first 12 months of life have the strongest prediction of the later development of ASD, but frontal EEG power closer to the diagnostic age of 3 did not provide useful predictors of an ASD diagnosis. Gabard-Durnam et al.(2019) analyzed specific frequency bands and found that changes within the delta and gamma power, which is the amount of activity in a certain frequency, was a strong factor in differentiation between infants with and without a future diagnosis of ASD.

Both studies led by Bosl et al. (2018) and Gabard-Durnam et al. (2019) illustrate the potential for the utilization of EEG during the period of early brain development to strengthen early detection of ASD prior to the emergence of behavioral patterns of ASD. Bosl et al. (2018) and Gabard-Durnam et al. (2019) highlight the importance of utilizing EEGs within the first 12 months of life because the atypical brain development leading to ASD symptoms typically occur prior to the atypical behaviors of ASD.

In addition to the use of EEGs, functional magnetic resonance imaging (MRI) was utilized to detect the brain differences among low familial risk and high familial risk ASD 6-month-old infants in a study done by Emerson et al. (2017). This study found that utilizing a functional MRI in order to create functional creativity matrices at 6 months can accurately predict a future ASD diagnosis (Emerson et al., 2017). It was also seen that the use of functional MRIs have a higher ability to accurately detect ASD in 6-month-olds than solely utilizing a behavioral screener with this age group (Emerson et al., 2017).

Two-Tiered Screening

Dietz et al. (2006) performed a study in which they implemented a two-stage screening protocol for ASD among 31,724 infants 14-15 months. Initially the infants were prescreened by a physician utilizing the 4-item Early Screening of Autistic Traits Questionnaire (ESAT; Swinkels, Dietz, Van Daalen, Kerkhof, Van Engeland & Buitelaar 2006). When an infant screened positive they were then observed and evaluated during an hour and a half home visit conducted by a trained psychologist using the 14-item ESAT.

Khowaja et al. (2018) looked into the differences between implementing a level 1 screening (Modified Checklist for Autism in Toddlers, Revised with FollowUp; Robins, Fein, & Barton, 2009) versus a combined screening utilizing level 1 and level 2 (Screening Tool for Autism in Toddlers and Young Children). The goal of their study was to reduce the high rate of false positive ASD diagnoses in toddlers. This study included 109 toddlers ranging from 16 to 30 months of age who screened positively for ASD in a level 1 screening. Level 1 screening

included the Modified Checklist for Autism in Toddlers, Revised with follow up (M-CHAT R/F). All 109 toddlers were given a level 2 screening which included the Screening Tool for Autism in Toddlers and Young Children (STAT). The STAT is an interactive screening tool that assesses four behavior domains: 1. Play 2. Requesting 3. Directing attention 4. Imitation. When exhibiting a positive score on the STAT, a diagnostic evaluation was conducted that included the Mullen Scales of Early Learning, Vineland Adaptive Behavior Scales-II, Behavioral Assessment System for Children-2, Autism Diagnostic Interview, Revised or Toddler ASD Symptom Interview, Childhood Autism Rating Scale-2, Autism Diagnostic Observation Schedule, first and second editions (ADOS(- 2), and parent report of developmental history. Results showed that implementing a two-tiered screening for ASD in toddlers (16 - 30 months) did reduce the rate of false positives. This study shows that solely relying on M-CHAT ratings for detection of ASD is not a clinically significant way of properly detecting ASD. There needs to be the addition of further testing to ensure that the positive score for ASD on the M-CHAT is truly indicative of an ASD diagnosis when additional assessment is conducted.

Home Video Analysis

The use of home video analysis appears to be a common method used to identify the presence of the social and repetitive behaviors commonly found in ASD. The presence of repetitive movements is a key feature in people with ASD. Purpura et al. (2017) "conducted a retrospective analysis of video-clips taken from home videos to compare the frequency and the duration of Repetitive Movement Episodes (RMEs) in a sample of 30 children equally

distributed among the three groups." The three different groups of infants ages 6 - 12 months were broken down into: 10 infants with ASD, 10 infants with Developmental Delay (DD), and 10 infants with Typical Development (TD). ASD and DD diagnoses were given to these children when they were between the ages of 3 and 4. Purpura et al. (2017) found a range of repetitive movement in the children with ASD that mainly involved bilateral Repetitive Movement Episodes (RMEs) utilizing fingers, hands, arms, and lower limbs. There were no patterns found for the children with DD and TD. When it came to unilateral RMEs there was no significant difference found between children with ASD and DD/TD. These findings are significant in that they show that a high rate of bilateral RMEs exhibited during infancy may be indicative of an ASD diagnosis. These findings helped identify types of movements that were typical in children with ASD and differentiated from children with DD and TD. Another study done by Costanzo et al. (2015) also utilized home videos retrospectively examined possible predictive behaviors that are symptomatic of ASD. The study found that home videos are more reliable than parent recall because of the presentation of factual and real time observations of events and behaviors exhibited by the child. The videos allowed the observer to accurately evaluate the child's behaviors and symptoms relative to ASD diagnostic criteria.

Fusaro et al. (2014) assessed the usefulness of applying a gold-standard diagnostic instrument, the Autism Diagnostic Observation Schedule-Generic (ADOS), to help assess brief and unstructured home videos. Authors collected 100 publicly accessible YouTube videos of children ages 1 to 15 years with an ASD diagnosis (n=45) and without (n=55). Videos were

scored by non-clinical raters using the ADOS. Fusaro et al. (2014) found that use of the ADOS by non-clinical raters provided high classification accuracy and high inter-rater reliability. The authors also found that a majority of the behaviors identified in items in the ADOS were exhibited in the videos and provided a good amount of content for the rater to utilize. Review of the literature in this field shows a number of studies utilizing home video analysis as a means for early detection of ASD. These studies would be important to include in a systematic review and meta-analysis in order to determine the efficacy of the home video analyses and the effectiveness of the use of home video analysis amongst the general population.

Identification of High-Risk Versus Diagnosis of Autism Spectrum Disorder

Rysavy and Murph (2015) report the differences in identifying high risk of autism and providing a formal diagnosis and how they are two distinct stages in the process of understanding and addressing ASD. Rysavy and Murph (2015) report that the identification of high risk often involves early screening and assessment tools designed to flag potential signs of ASD in individuals. This initial step is crucial for both early diagnosis and early intervention and support, as it enables professionals to recognize behavioral patterns or developmental delays that may indicate a heightened likelihood of autism. High-risk identification is more about signaling a need for further evaluation rather than making a definitive diagnosis. Rysavy and Murph (2015) report that identifying a child for high risk of autism may not provide the information needed to implement appropriate intervention that a diagnosis of autism would provide.

Providing a diagnosis of autism is a more comprehensive and conclusive process (Okoye et al., 2021). Obtaining a formal diagnosis of autism typically involves a thorough evaluation by a multidisciplinary team of professionals, such as psychologists, speech therapists, and developmental pediatricians. The diagnostic process entails a detailed examination of a person's behavior, communication skills, social interactions, and developmental history. Moreso, the diagnostic processes for an early diagnosis is even more complex and entails the diagnostic team to be familiar with the current assessment tools appropriate in establishing a diagnosis prior to the age of 3 (Steiner et al., 2016). Formal diagnostic criteria, such as those outlined in the DSM-5, are often used to determine whether an individual meets the criteria for an autism diagnosis and a formal diagnosis is crucial for developing tailored interventions and accessing appropriate support services that address the specific areas of impairment (Okoye et al., 2021). Therefore, identifying a high risk of autism is an initial step that involves recognizing potential indicators and prompting further evaluation, while providing a diagnosis is a more comprehensive process that involves a thorough assessment by a qualified team of professionals. Both stages are essential for understanding and addressing the unique needs of individuals with autism, enabling early intervention and appropriate support to enhance their well-being and developmental outcomes (Okoye et al., 2021, Rysavy & Murph, 2015).

Importance of Early Diagnosis

Miller et al. (2020) conducted a study on the characteristics of toddlers with early diagnosis versus later diagnosis. The authors found that an early diagnosis of autism is crucial

for early intervention because it allows for prompt and targeted support to be implemented during a critical period of developmental plasticity. Additionally, while identifying high risk is an essential first step, a formal diagnosis provides a more comprehensive understanding of the individual's condition, allowing for specific and tailored interventions. Research highlights several reasons why early diagnosis is needed for effective early intervention:

Timely Access to Intervention Services

According to Okoye et al. (2023), a formal diagnosis of ASD enables families to access specialized intervention services promptly. Early intervention programs are designed to address the specific challenges associated with autism, focusing on areas such as communication, social skills, and behavior. Grzadzinski et al. (2021) reports that for some parents, receiving an early diagnosis of their child's ASD makes them more likely to access intervention and support for their child. The sooner these interventions begin, the greater the potential for positive outcomes.

Tailored and Targeted Interventions

MacMillan (2021) reports having an early diagnosis allows professionals to design interventions that are specifically tailored to the individual's needs. MacMillan (2021) explains how a comprehensive evaluation can help to identify a child's unique needs and how individuals with autism may present with varied strengths and challenges. This can then be used as the foundation for developing interventions that address the core symptoms of ASD that are identified in the assessment utilized for the formal diagnosis of ASD (MacMillian, 2021).

Establishing Individualized Education Plans (IEPs)

Rubenstein et al. (2017) report that in many educational settings, a formal diagnosis is required to develop an IEP. An IEP outlines specific educational goals, accommodations, and support services tailored to the individual's needs, ensuring a supportive learning environment. For a child with ASD, an IEP can provide them with the accommodations and supports that can help them succeed in school (Rubenstein et al., 2017). Additionally, obtaining an early diagnosis of ASD allows for a child to develop an IEP at the start of their educational journey and can provide them with better academic outcomes than children who had an IEP implemented at a later age (Rubenstein et al., 2017).

Essentially, while identifying high risk is a crucial first step, an early autism diagnosis is essential for unlocking the full potential of early intervention. It provides the necessary foundation for targeted and individualized support, maximizing the effectiveness of interventions during a period of significant developmental influence.

Significance and Proposed Impact

While research on early diagnosis methods of ASD is growing, there is not a consensus as to which method is the most effective in early diagnosis of ASD. This systematic review sought to shed light on the effectiveness of the methods in order to inform future research. Knowing which of the current methods is most effective at early ASD diagnosis has the potential to lead to better long term outcomes of people living with ASD.

Clinical Implications

Research is showing strong evidence that in order for children with ASD to have a better prognosis it is crucial that there is early diagnosis which can lead itself to early intervention and therapy (Dorobantu, 2020). With more research on the early diagnosis of ASD it is imperative that clinicians are aware of the various methods of diagnosis and that parents and their children have the access to these diagnosis methods. With the knowledge we gain from clinical imaging, home video analysis, and/or multi-level assessments clinicians can properly advise parents of the early interventions that are clinically significant in the treatment of ASD.

Methodology

Overview of the Methodology

The specific goal of this systematic review was to identify all prior research in which early detection approaches resulted in a formal diagnosis of ASD prior to the age of 3. According to Ukwaja (2020), it is important to put thoughtful and intentional effort into formulating the review/research question when conducting a systematic review, so that you are gathering the correct studies that pertain to your question. Ukwaja (2020) suggests, when formulating the review question it is recommended to follow the PICOS statement; i.e.:

- Participant - children birth to 3 years of age, inclusive of both male and female (assigned at birth), and all ethnicities
- Intervention - the type of early detection methods: Home video analysis, Clinical imaging, and Two or more tiered screening
- Comparator condition - the interventions will be compared against each other; between group comparisons
- Outcomes - Formal Diagnosis of ASD
- Studies - Experimental Studies, Randomized Controlled Studies, Studies that have no control group, and Case Studies

By having a clear, concise, and targeted research question I am better able to pinpoint the studies needed for the systematic review (Ukwaja, 2020).

Murlow (1994) describes the rationale for a systematic review is to break down large amounts of information into smaller and more manageable pieces to better understand the state of the literature for a given topic. Therefore, this systematic review showcases the current state of published literature on the early detection and diagnosis methods of ASD prior to the age of 3.

Research Question and Aims

The research question this study aimed to answer is: What are the early detection methods for ASD in children from birth to 3 years of age that lead to early diagnosis prior to 3 years of age? This question utilizes the PICOS approach mentioned previously (Ukwaja, 2020). The following aims will help to answer this proposed research question:

Aim 1: Identify early detection methods used for diagnosing children with ASD prior to the age of 3.

Aim 2: Identify the cultural consideration and health disparities within the early detection and diagnosis of ASD.

Aim 3: Compare the diagnosis methods to determine which diagnosis method is most effective for early diagnosis of ASD prior to the age of 3 years.

Inclusion and Exclusion Criteria

The following criteria were utilized to select studies that were included in the systematic review.

Participant Criteria

Studies that had a sample population that range from birth to 36 months were included. ASD onset is determined to be at 3 years of age (Mandell, Novak, & Zubritsky, 2005) therefore, for the purpose of this study I focused on studies that included a sample population that was in the early detection age range which would be from birth to 36 months and the early diagnosis age of 2-3 years. I did not exclude participants based on other demographic factors such as sex, race, socioeconomic status, and comorbid disorders.

Exclusion Criteria

Studies that did not provide data on early diagnosis methods or where participants were outside of the birth to 3 years age range were not included in this study. Additionally, studies with incomplete information or those for which the full text could not be accessed were also excluded.

Procedures

Search Strategies

I conducted a comprehensive search of published peer-reviewed literature using the following databases: PsycINFO, Pubmed, and SCOPUS. During the literature search I consulted with a librarian to help determine the correct search terms. I searched for subject headings and key terms related to early diagnosis of autism. For instance, when looking for studies that were

on autism I searched: “Autism Spectrum Disorders”, “Autistic Traits”, autism*, and ASD. For a comprehensive list of all the search terms utilized refer to Appendix A.

Study Selection Process

Study selection was done using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Appendix B). Once the database searches were conducted, I utilized Zotero, a citation and article management program, to collect, organize and store the articles. After removing the duplicate studies, I was left with 557 studies. I then conducted a title review in which I looked at the title of the study and determined its relevance. After conducting the title review, 250 studies were excluded because the title indicated the study was not specific to autism. After removing the 250 studies I successfully obtained the full text manuscript for the remaining 301 studies. Of the 301 studies fully reviewed, 223 were excluded because the participants were outside the studies targeted age range. Of the remaining 78 studies 74 assessed the effectiveness of screening for ASD detection, but did not provide an official diagnosis. This left me with 4 studies, see Appendix B for the prisma flow diagram that illustrates this process.

Data collection process

I gathered the data on how each early detection method was conducted in order to establish early diagnosis for ASD. To do this I pulled the following data out from each study:

1. The qualitative description of the method(s) used
2. The number of participants included in the study

3. The age of the participants
4. The composition of the groups studied (if applicable)
5. The statistical data on the methods used (PPV, NPV, sensitivity, specificity)
6. The results and the number of early diagnoses of ASD made

Risk of Bias

The systematic review approach was assessed for risk of bias based on guidelines outlined by the Cochrane Handbook for Systematic Reviews of Interventions (Cochrane Collaboration, 2008) and utilizing the Risk of Bias Assessment Tool for Systematic Reviews (ROBIS; Whiting et al., 2016). According to Cochrane, multiple types of bias need to be considered (i.e., selection bias, performance bias, detection bias, attrition bias, and reporting bias) and there are 7 evidence based domains (i.e., random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias) that need to be addressed (Cochrane Collaboration, 2008). When assessing for each type of bias Cochrane recommends utilizing a "Risk of bias" table that lists out the types of bias paired with the correlated evidence based domain (Cochrane Collaboration, 2008). The ROBIS was utilized for this systematic review and addresses four domains: (1) study eligibility criteria; (2) identification and selection of studies; (3) data collection and study appraisal; (4) synthesis and findings (Whiting et al., 2016)

Results

Syntheses of Systematic Literature Review

The primary goal of this systematic review was to analyze prior research in which early identification approaches resulted in a formal diagnosis of ASD. This review identified and synthesized a small body of literature that provided information on early detection methods of ASD that lead to a formal diagnosis of ASD prior to the age of 3 years.

Early Diagnosis Methods

Four studies met the inclusion criteria in which early detection methods provided a method for diagnosis of ASD at the age of 36 months or earlier (n = 4). A total of 4 different early diagnosis methods were utilized (a) two-tiered screening (n = 1); (b) clinical imaging (n = 1); (c) use of a screener with addition to a follow-up (n = 1); (d) surveillance (n = 1). Table 2 represents an overview of the diagnostic methods employed in each study.

Khowaja et al. (2018), established a two-tiered screening approach for early ASD detection and diagnosis, involving the Modified Checklist for Autism in Toddlers, Revised with Follow-Up (M-CHAT-R/F) as a Level 1 screening tool and the Screening Tool for Autism in Toddlers & Young Children (STAT) as Level 2 screening tool. Khowaja et al. (2018) had an initial sample size of 109 toddlers that screened positive for ASD in the M-CHAT-R/F and were followed up. In the follow up, parents of children who screened positive on the M-CHAT were offered a free diagnostic evaluation and were asked if they would participate in the level 2 screening, the STAT.

Haweel et al. (2021) introduced a clinical imaging method for early diagnosis of ASD involving task-based functional magnetic resonance imaging (TfMRI) to observe the impact of audio stimuli on 100 toddlers aged 12 to 40 months at the time of TfMRI acquisition. In their study, Haweel et al. (2021) paired the use of the TfMRI with a technique called discrete wavelet transform (DWT) to help them focus on the most important parts of the brain activity. Then, they use a computer program, deep learning 2D CNN network, to decide if someone has ASD or not based on these highlighted brain features.

Kleinman et al. (2008) utilized the Modified Checklist for Autism in Toddlers (M-CHAT) to identify the toddlers that were at risk for ASD with the addition of a follow-up phone call to determine the need for further diagnostic evaluation. Kleinman et al. (2008) utilized a participant sample of 3,793 toddlers that were identified at risk for ASD with the designation of low-risk (n=3,309) and high-risk (n=484). These 3,793 toddlers were re-assessed with the M-CHAT. When a phone call follow up was conducted, a total of 203 children were identified for a diagnostic evaluation.

Lastly, the fourth study utilized a surveillance approach to assist in the early diagnosis of ASD. Barbaro et al. (2022) introduced a developmental surveillance methodology for the early diagnosis of ASD employing the Social Attention and Communication Surveillance-Revised (SACS-R) and the Social Attention and Communication Surveillance-Preschool (SACS-PR) tools. The investigation encompassed two distinct phases. During Phase 1, participation was extended to toddlers aged 11 to 30 months, resulting in the identification of 13,511 eligible toddlers. From this pool of eligible subjects, 327 toddlers were deemed to be at a high risk for

ASD based on their SACS-R scores and were subsequently referred for ASD diagnostic evaluation. Among these high-risk toddlers, 240 underwent comprehensive ASD diagnostic assessments.

Outcome and Study Findings

Each of the four studies utilized a different early detection method to arrive at an ASD diagnosis by the age of 3 years. Khowaja et al., (2018) identified a two-tiered screening method for early diagnosis of ASD . Kleinman et al. (2007) examined the efficacy of utilizing a screener plus telephone follow-up in the early diagnosis of ASD among children 16 to 30 months. Haweel et al. (2021) assessed the efficacy of the use of TfMRI for early diagnosis of ASD Lastly, Barbaro et al. (2022) utilized a developmental surveillance method for early diagnosis of ASD.

Two-Tiered Screening

As mentioned earlier, Khowaja et al. (2018) identified a two-tier screening method for early diagnosis of ASD which consisted of a level 1 screening, M-CHAT-R/F, paired with a level 2 screening, STAT. When the M-CHAT-R/F is marked with three or more items this indicates risk of ASD and a follow-up is needed to be completed by the parent. The STAT assesses four behavioral domains: 1 = play, 2 = requesting, 3 = directing attention, and 4 = imitation. The study had a sample of N=109 toddlers who screened positive on the level 1 screening, M-CHAT-R/F. The 109 toddlers were then administered the STAT prior to a

diagnostic evaluation. The diagnostic evaluation consisted of the Mullen Scales of Early Learning (Mullen, 1995, the Vineland Adaptive Behavior Scales-II; Sparrow et al., 2005), the Behavioral Assessment System for Children-3 (Reynolds and Kamphaus, 2004, the Autism Diagnostic Interview, Revised (Lord et al., 1994), the Toddler ASD Symptom Interview (Barton et al., 2012), the Childhood Autism Rating Scale-2 (Schopler et al., 2010) the Autism Diagnostic Observation Schedule, first and second editions (Lord et al., 1999, 2012), and a parent report of the child's developmental history.

For the data analysis, Statistical Package for the Social Sciences (SPSS) was utilized to assess sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). The sample size was then split (N=54, N=55) for two separate analyses. A receiver operating characteristic (ROC) analysis was performed on the first half of the sample to determine optimal scoring cutoffs for the alternative total score. The alternative STAT total scores were determined utilizing the discriminant function analysis (DFA), which equally weighed all 12 STAT items. The items with the greatest discriminatory power accounted for the alternative total score (Khowaja et al., 2018). The second half of the sample size then had the alternative scoring applied.

Screener Plus Telephone Follow-up

Kleinman et al. (2007) utilized the Modified Checklist for Autism in Toddlers (M-CHAT) on 3,793 children ages 16 to 30 months to examine the efficacy of the early diagnosis of ASD. The M-CHAT is a 23 item yes/no parent report checklist (Robins et al., 1999). Among the 3,793 children that were administered the M-CHAT, 2,469 were identified as

eligible for re-screening and a telephone follow up was given. Data was collected on 1,416 participants for the re-screening.

Clinical Imaging

Haweel et al. (2021) identified a clinical imaging early diagnosis method consisting of a task-based function magnetic resonance imaging (TfMRI). A TfMRI is a diagnostic imaging technique used for observing the effects of a disease or condition on the functional activity of the brain (Haweel el al., 2021). Haweel et al. (2021) selected participants from the “Biomarkers of Autism at 12 Months: From Brain to Overgrowth to Genes" data set obtained through the national database for autism research (NDAR: http://ndar.nih.gov). Haweel et al. (2021) selected a dataset consisting of 100 toddlers (50 ASD and 50 typically developing (TD)) aged 12 to 40 months at the time of the TfMRI acquisition. This study utilized a fMRI block-related design, this method consists of several discrete on-off periods, with the "on" representing a period of stimulus presentations, and the "off" referring to a state of rest or baseline (U.S. Department of Health and Human Services). Haweel et al. (2021) utilized three audio stimuli: complex forward speech, simple forward speech, and backward speech. These three audio stimuli were played on repeat in an alternating pattern separated by silence blocks within a 6 minute 20 second duration.

The TfMRI of the 50 ASD toddlers responding to speech tasks in sleep showed hypoactivation of the bilateral superior temporal gyrus, bilateral primary auditory cortex, cingulate gyrus, and angular gyrus whereas the 50 TD toddlers showed typical left-brain dominance. The ASD group exhibited a loss in the left hemisphere lateralization which supports

the authors' hypothesis that the failure of proper language development and neural circuitry is a crucial indicator of ASD. Haweel et al. (2021) found that efficient extraction and reduction of input feature dimensionality yields higher diagnostic accuracy.

Developmental Surveillance

Barbaro et al. (2022) identified a developmental surveillance method for early diagnosis of ASD through the use of the Social Attention and Communication Surveillance-Revised (SACS-R) and the Social Attention and Communication Surveillance-Preschool (SACS-PR). Barbaro et al. (2022) utilized two phases in their study. As part of the eligibility requirements, toddlers in phase 1 were within the 11-30 month age range. 13,511 eligible toddlers were identified and out of these eligible toddlers, 327 were identified as high risk for ASD based on the SAC-R and were referred for ASD diagnostic testing. 240 out of the 327 high risk toddlers underwent the ASD diagnostic testing.

Study and Participant Demographics

Four studies were included in this study, three studies were conducted in the United States and one in Australia. When combined, these four studies included 17,513 participants. However, due to attrition and lack of follow-up, the overall number of participants that were reported receiving or not receiving a diagnosis were 697, across all 4 studies. Table 2 illustrates the number of participants in each study that have been diagnosed and not diagnosed with autism. Out of the 697 participants, a total of 462 were given an ASD diagnosis.

Analysis of Participants

The breakdown of the various demographic data provided by each study is depicted in Tables 1, 3, and 4. Among the four studies, out of the 4,359 participants, 1,863 are female and 2,282 are male. Out of the 4,359 participants sex demographics were not reported for 214 participants. Ethnicity demographics were reported by three out of the four studies. The data reported across the three studies included the following ethnicities: African, Asian, Middle Eastern, Latino, White, Mixed Race, Indigenous, or unspecified (Table 3). Lastly, annual income was only reported by two of the studies, Kleinman et al. (2008) reported that their participants had an average household income of $40,000 - $60,000. While the Barbaro et al. (2022) reported that out of 357 participants, 32 participants had an annual income of less than $33,214, 25 participants had an annual income between $33,216 to $52,195, 43 participants had an annual income between $52,196 to $71,175, 40 participants had an annual income between $71,176 to $90,155, 33 participants had an annual income between $90,156 to $109,135, 30 participants had an annual income between $109,136 to $128,115, 15 participants had an annual income between $128,116 to $147,095, 11 participants had an annual income between $147,096 to $166,075, 37 participants had an annual income above $166,075, and 78 participants did not report their annual income.

Comparison of Diagnosis Methods

When analyzing the four studies, Barbaro et al. (2022), provided the most accurate early diagnosis based on the detection methods utilized. Barbaro et al. (2022) had 75% rate of

diagnostic. Alone, the SACS-R exhibited high diagnostic accuracy, with an 83% positive predictive value and 99% negative predictive value .The specificity was notably high at 99.6%, accompanied by a moderate sensitivity of 62%. However the inclusion of the SACS-PR resulted in a substantial increase in estimated sensitivity to 96% Additionally, the prevalence of autism was determined to be 2.0% (1 in 50) between 11 and 30 months of age, with a slightly higher prevalence of 3.3% (1 in 31) between 11 and 42 months of age.

As table 2 depicts, the four studies each use different diagnosis strategies: clinical imaging, screening plus a follow-up, surveillance, and, two-tiered screening. No two studies have utilized the same methods to engage in early diagnosis. However, two studies utilized the M-CHAT with one utilizing the M-CHAT and the other using the M-CHAT-R/F.

Reduction of False Positives

Table 5 depicts the psychometric data for all of the testing measures used in the four studies. Results for Khowaja et al. (2018), found that higher scores on the STAT, using both published and alternative scoring methods, related to higher severity of ASD symptoms and lower cognitive and adaptive functioning in children with ASD. It was also found that implementation of a two-tiered screening process allows for a reduction of false negative and false positive ASD early diagnosis. This study reports adequate accuracy or area under the curve (AUC = 0.73), based on a 0.70 threshold for the STAT.Which means that 73% of the time there was accurate detection yielding adequate accuracy. When looking at seven items on the STAT

(two directing attention, two play, two requesting, and one imitation), this had the strongest discriminatory power for ASD diagnosis which yielded a good accuracy (AUC= 0.81).

Kleinman et al., (2007) found the administration of a telephone follow-up reduces the risk of false positives and improves the positive predictive value. The results of the study suggest the M-CHAT can be effective in early diagnosis of ASD in children 16 to 30 months. Kleinman et al. (2007) suggest the implementation of a Level 2 screen may add to the reduction of false positive diagnoses, especially with a low-risk sample.

Barbaro et al. (2022) discussed the reduction of false negatives rather than false positives. They utilized the addition of SACS-R+PR in order to reduce the rate of false negatives among their participants. They found that the use of the SACS-R+PR increased the sensitivity from 62% to 96%. When adding the SACS-PR to the SACS-R, the SACS-R+PR psychometrics data provides evidence of high diagnostic accuracy between 12 and 42 months of age with a PPV of .78, NPV of .99, sensitivity of .96, and specificity of .99.

Haweel et al. (2020) provided only the sensitivity and specificity data. The authors also provided the AUC = .80. In order to verify the diagnostic accuracy of their proposed method Haweel et al. (2022) conducted an independent testing of 20 participants from the same study. The resulting accuracy, sensitivity, and specificity rates were found to be 75%, 71%, and 77%, respectively.

Risk of Bias Assessment for Systematic Reviews

The ROBIS (Whiting et al., 2016) was utilized to assess risk of bias of this systematic review. Data for this risk assessment is reported in Appendix C and shows that for domain 1: study eligibility, has low concern for risk. This study employed significant efforts to precisely articulate the review question and objectives. Additionally, there was a deliberate effort to predefine and rationalize comprehensive eligibility criteria, ensuring strict adherence throughout the review process. The other three domains: identification and selection of studies, data collection and study appraisal, and synthesis and findings, had high concern for risk. The review's limitation of focusing on just three databases may have resulted in the omission of certain eligible studies. Additionally, bias could have been introduced during data collection or risk of bias assessment processes. These factors collectively suggest that the synthesis is prone to producing biased results. This susceptibility is attributed to several factors, including the neglect of potential biases within and/or across studies, inadequate consideration of significant between-study variation, methodological shortcomings, and concerns arising from incomplete or unclear reporting of findings.

Discussion

The aim of this systematic review was to analyze prior research in which early identification approaches resulted in a formal diagnosis of ASD. This review identified and synthesized a small body of literature on the early diagnosis methods for ASD. Four methods were identified: two-tiered screening, clinical imaging, use of a particular screener with addition to a follow-up, and surveillance. Although various studies have examined the use of screeners and biomarkers for early detection, most of these studies have demonstrated whether their application directly results in an early ASD diagnosis. All the included reviews reported multiple factors that were important for early diagnosis of ASD, and no single factor was identified as a key barrier or facilitator. Each diagnostic method was different, but utilized a two-factor approach to determine an early ASD diagnosis.

In the four studies reviewed it was found that the key factors for effective early diagnosis included pre-screening to identify high risk in addition to follow-up to ensure early diagnosis was accurate and to assess for false positives and negatives. Parent participation was also crucial as they needed to follow through with appointments and bring their toddlers in for further evaluation.

Pre-Screening

Early diagnosis of autism is crucial for initiating timely interventions and support, significantly influencing long-term outcomes for individuals on the autism spectrum and in order for early diagnosis to be accurate, pre-screening is needed to identify infants and toddlers

at risk, both low and high risk. Pre-screening plays a pivotal role in this process by identifying potential signs and risk factors in children at an early age. The significance of pre-screening lies in its ability to detect subtle developmental differences and behavioral patterns that may indicate the presence of ASD. By conducting screenings during well-child check-ups or routine medical visits, healthcare professionals can observe and assess a child's communication skills, social interactions, and behavior, offering an initial indication of developmental trajectories.

The importance of pre-screening becomes evident in the context of the "wait-and-see" approach. Some developmental differences associated with autism might not be immediately apparent or may be mistaken for typical variations in early childhood behavior. Pre-screening allows for the identification of red flags that warrant further evaluation, enabling healthcare providers to recommend comprehensive assessments when needed. Early detection through prescreening facilitates timely access to specialized services and intervention programs tailored to the unique needs of children with ASD. This proactive approach empowers families with the knowledge and resources necessary to navigate the complexities of autism, fostering early intervention strategies that can enhance developmental outcomes and improve the overall quality of life for individuals on the autism spectrum.

Parental Participation

A major factor in attrition within the studies was due to parents not bringing their child for the additional evaluation(s)/assessment(s). All four of these studies indicate a moderate to notable attrition rate, where children do not return for necessary follow-up. However, none of

these studies investigated the reasons behind parents' inability to follow up. As previously noted in the literature (Makino et al., 2017), parental engagement is a critical factor. Therefore, emphasis needs to be placed on understanding the barriers impeding parental engagement. Healthcare providers, including psychologists, must assume a crucial responsibility in comprehending and tackling these barriers. Conducting qualitative research involving interviews with parents to ascertain participation barriers becomes imperative for creating and implementing intervention strategies. Studies on parental stress indicate family members and parents who do not have ample support and guidance can experience severe levels of stress, especially regarding the process of ASD diagnosis (Elder, Brasher, Alexander, 2016). This can cause parents and family members to not engage in the proper follow up needed to ensure proper diagnosis and treatment of ASD.

Follow-up

The importance of follow-up in the early diagnosis of autism cannot be overstated, as it serves as a foundation in the continuum of care for individuals on the autism spectrum (Okoye et al., 2023). Early diagnosis lays the groundwork for timely and targeted interventions, but it is through systematic and consistent follow-up that the full benefits of early identification are realized. Kleinman et al. (2007) found that the incorporation of a telephone follow-up reduce the rates of false positive ASD diagnoses in their participants. Follow-up assessments allow healthcare professionals, educators, and families to track the progress of a child with autism, ensuring that interventions are responsive to the individual's evolving needs (Elder et al., 2017).

Early diagnosis provides a starting point for intervention, but the developmental trajectory of a child with autism is dynamic and can vary widely. Follow-up assessments play a critical role in providing a formal diagnosis and understanding how the child responds to interventions, identifying initial areas of limitation, areas of improvement, and addressing emerging challenges (Okoye et al., 2023). This iterative process allows for personalized adjustments to intervention strategies, ensuring that the support provided remains finely tuned to the child's unique strengths and difficulties.

In addition to monitoring developmental progress, follow-up is instrumental in identifying and managing any co-occurring conditions or associated challenges that may emerge over time. Autism often presents with a spectrum of symptoms, and follow-up assessments enable healthcare professionals to comprehensively address the diverse needs of individuals with autism. By tracking and addressing issues such as communication difficulties, sensory sensitivities, or behavioral challenges, follow-up contributes to a more holistic and tailored approach to care (Elder et al., 2017, Okoye et al., 2023).

Within an educational context, consistent follow-up is equally vital. It enables educators to gauge the effectiveness of educational interventions, adapt teaching strategies, and provide ongoing support that aligns with the child's learning style (Rubenstein et al., 2017). This collaborative approach, involving healthcare providers, educators, and families, fosters a comprehensive and integrated support system that maximizes the potential for positive outcomes in the developmental journey of individuals with autism (Fulceri et al., 2023). In essence, follow-up is the cornerstone that transforms early diagnosis into a sustained and

impactful continuum of care, promoting the well-being and growth of individuals on the autism spectrum. Overall consistent follow-up is needed at all the stages involved with an autism diagnosis, pre-screening, screening, diagnostic evaluation, intervention, and schooling.

Diversity within Early Diagnosis Methods

` Out of the four studies looked at in this systematic review, only three studies reported ethnicity demographics and only two studies reported socioeconomic status. Additionally, in the studies that did provide ethnicity demographics we see that a majority of the participants are white/caucasian. This lack of diversity in the research feeds into the eurocentric bias that research has been known to have (Torres, 2023). It is important that with our population's ethnic makeup trending to where now people of color are the majority, it is important that our research reflect that.

The lack of diversity in early diagnosis research for autism represents a significant gap in understanding and addressing the diverse experiences of individuals across various demographic and cultural backgrounds (de Leeuw et al., 2023). Much of the existing research predominantly focuses on populations that do not adequately represent the full spectrum of individuals with autism. This lack of diversity can impact the accuracy and applicability of diagnostic tools and intervention strategies, as these may not be culturally sensitive or may overlook certain manifestations of autism that are more prevalent in specific communities (de Leeuw et al., 2023).

Furthermore, the absence of diversity in research hinders our ability to uncover potential cultural nuances in the expression of autism symptoms. Different cultural contexts may influence how individuals and families perceive and interpret developmental differences, potentially leading to variations in help-seeking behaviors and diagnostic patterns (Kang-Yi et al., 2018) Failure to account for these cultural differences may contribute to delayed or missed diagnoses, preventing timely access to crucial interventions and support services (de Leeuw et al., 2023).

The underrepresentation of diverse populations in early autism diagnosis research not only limits the generalizability of findings, but also perpetuates disparities in access to resources and support (Aylward et al., 2021). Recognizing and addressing these gaps is essential for developing more inclusive and effective diagnostic strategies that consider the full spectrum of human diversity, ensuring that individuals from all backgrounds receive equitable and timely care for autism spectrum disorder.

Health Disparities in ASD Early Detection and Diagnosis

Early diagnosis of ASD is a crucial step in ensuring timely interventions and support for individuals and their families (Elder et al., 2017). However, people of color, those with low socioeconomic status, and other marginalized groups often face barriers that impede their access to accurate and timely diagnosis (Alyward et al., 2021).

Healthcare providers and psychologists are essential in breaking down obstacles and promoting a fair diagnostic process for marginalized communities. Their pivotal role involves

actively addressing and removing barriers that hinder access to healthcare services, ensuring that diagnostic procedures are conducted in a manner that is unbiased and considerate of the unique challenges faced by individuals from marginalized backgrounds. This includes adopting culturally sensitive approaches, providing education, and advocating for policies that promote inclusivity and equal access to diagnostic resources, ultimately contributing to a more equitable healthcare system.

Healthcare providers and psychologists need to prioritize cultural competence and sensitivity in their practices. Understanding the cultural nuances, communication styles, and behaviors within different communities is paramount. By recognizing that the manifestations of ASD can vary across cultures, professionals can ensure that diagnostic criteria are interpreted accurately. Cultural competence also involves acknowledging the influence of cultural stigmas surrounding developmental differences and mental health, which can impact the willingness of families to seek evaluation. It is also imperative that researchers include a more diverse population to help provide healthcare providers and psychologists with insight into what these barriers are and how to effectively dismantle these barriers.

Limited access to healthcare services often hinders marginalized individuals from obtaining timely diagnosis. Healthcare providers must actively collaborate with community organizations and governments to establish accessible and affordable healthcare options for underserved populations. Telehealth services, mobile clinics, and partnerships with local community centers can help bridge the gap between these communities and diagnostic resources.

Raising awareness about ASD within marginalized communities is vital. Healthcare providers and psychologists can contribute by organizing educational workshops, webinars, and informational sessions that address myths, misconceptions, and the benefits of early diagnosis. These efforts can empower families to overcome skepticism, stigma, and cultural barriers, leading to increased acceptance of the diagnostic process.

Marginalized communities often grapple with layers of complexity when confronted with the introduction of another marginalized identity within their midst, such as Autism. The process of understanding and accepting Autism within these communities involves navigating a web of cultural implications that extend far beyond the confines of individual experiences.

In communities of color, the diagnosis of Autism can pose unique challenges. Firstly, there may be cultural stigmas attached to disabilities that have deep historical roots. Some cultures place a strong emphasis on physical and mental resilience, which can make it particularly difficult for individuals and families to accept a diagnosis that falls outside these traditional expectations. Additionally, some communities may view disability as a reflection of family shortcomings, leading to feelings of shame and embarrassment.

The cultural implications of Autism in communities of color are also intricately tied to cultural norms, beliefs, and social expectations. In some cases, there might be a lack of awareness or understanding about Autism within these communities, leading to misperceptions and misconceptions about the condition. This can further complicate the process of seeking support and resources, as families may face resistance or skepticism from their own cultural networks.

Moreover, the interplay between family dynamics and cultural expectations plays a significant role in the way Autism is perceived and handled within marginalized communities. The diagnosis of a family member with Autism can sometimes lead to intra-family shame and negative implications within their cultural communities. Families may grapple with feelings of isolation and fear of judgment, which can deter them from seeking the necessary support and resources. The pressure to conform to cultural norms and maintain a positive image within the community can add a layer of complexity to the already challenging journey of understanding and embracing Autism.

Therefore, when people within marginalized communities face the reality of Autism they must navigate multifaceted layers of cultural implications, ranging from stigma and misperceptions to intra-family shame. As healthcare providers and psychologists, it is essential to promote awareness, education, and open dialogue within these communities to foster acceptance, understanding, and support for individuals with Autism and their families, ultimately breaking down barriers and fostering inclusivity. In addition to creating diagnosis and intervention methods that encompass the needs of these communities.

A collaborative interdisciplinary approach is essential for facilitating early diagnosis in marginalized communities. Healthcare providers, psychologists, educators, speech therapists, and social workers should collaborate to create a comprehensive evaluation process. This team-based approach can ensure that all aspects of an individual's development are considered, leading to a more accurate diagnosis.

Creating a supportive environment within communities is crucial for overcoming barriers to early diagnosis. Healthcare providers and psychologists can facilitate support groups, parent networks, and peer mentorship programs. These initiatives provide families with emotional support, information sharing, and a platform to discuss their experiences, fostering a sense of belonging and empowerment.

Overall, healthcare providers and psychologists play a pivotal role in promoting equitable early diagnosis of Autism Spectrum Disorder within marginalized communities. Through cultural competence, accessible healthcare, awareness initiatives, tailored assessment tools, and collaborative efforts, these professionals can dismantle barriers and ensure that all individuals, regardless of their socioeconomic status, ethnicity, or cultural background, have equal access to timely and accurate diagnoses. By prioritizing these strategies, we can work towards a more inclusive and just diagnostic process for everyone.

Early Diagnosis with high risk children

There is no one cause of ASD, in fact there have been many factors identified that put a child at higher risk of developing ASD. It is also important to understand that these factors can be environment, biological, and/or genetic (CDC, 2022). While we do not have much understanding as to the etiology of ASD there is evidence to suggest that certain factors may put a child at greater risk of developing ASD. The CDC (2022) identifies several factors that determine risk of ASD. These factors include: (1) Having a sibling with ASD, (2) Having

certain genetic or chromosomal conditions, such as fragile X syndrome or tuberous sclerosis, (3) Experiencing complications at birth, and (4) Being born to an older parent.

This study sheds light on the need for more research on effective early diagnosis methods for autism. Apparent behavioral signs of ASD are not typically present in the first six months of life (Ozonoff et al., 2010). Hence, the need for more studies that incorporated clinical imaging into the early diagnosis process to provide the gap in the early identification of risk and more importantly, high risk in infants prior to 6 months. Studies of high-risk infants suggest an emergence of ASD behavioral symptoms in the second half of the first year of life, which may include poor or delayed motor development and control, feeding and sleeping difficulties, and/or excessive passivity or reactivity (Anagnostou et al., 2014; Zwaigenbaum et al., 2015). Additionally, symptoms in the core domains of ASD typically emerge between 12 and 24 months (Tanner & Dounavi, 2021). It is important to understand that behavioral signs vary and that there is no one sign that is able to confirm or rule out an ASD diagnosis. Therefore, the need for early detection and diagnosis methods that rely on the use of identification of biomarkers for ASD can help to close the gap that this variance in behavioral signs poses on early diagnosis of autism.

Additionally, early diagnosis of autism holds significant importance, even in cases where behavioral symptoms typically manifest around the age of 24 months. Detecting autism at an early stage allows for timely intervention and support, which can greatly enhance the developmental outcomes and overall quality of life for individuals with ASD. While overt behavioral signs might not be evident in the early months of life, there are often subtle markers

and atypical developmental patterns that can be identified by trained professionals. Utilizing these early diagnosis methods identified in these four studies which can assist in pinpointing these subtle indicators and initiating appropriate interventions, such as behavioral therapies and educational strategies, before the onset of more pronounced symptoms. This can allow individuals with ASD to benefit from enhanced cognitive, social, and communication development. Moreover, early diagnosis empowers families with the knowledge and resources to better understand their child's needs and access tailored interventions, fostering a more supportive and inclusive environment for their growth. Ultimately, the early diagnosis of autism establishes a foundation for optimized developmental trajectories and improved long-term outcomes.

Zwaigenbaum et al. (2015) suggests that when developmental surveillance indicates a possible risk for ASD, further in-depth assessment is needed. This is seen in the Kowaja et al. (2018), where the authors do the STAT in addition to a more formal diagnostic evaluation to ensure the validity of the diagnosis and to ensure a true positive diagnosis. Additionally, vigilance is needed from both clinicians and parents for children with known risk factors, because the overall prevalence of ASD is higher in these children. This study found that in order to ensure reliable early diagnosis of ASD, ASD-focused assessments should include a standardized measure of ASD symptoms, a parent questionnaire (i.e., M-CHAT-R/F) or, in communities where trained personnel are available, an interactive tool (e.g., STAT) could be used at the start of identification of risk (Zwaigenbaum et al., 2015).

Research shows that children who meet scoring criteria according to a standardized ASD symptom measure, or whose clinical presentation indicates a high level or risk and suspicion, should proceed to a diagnostic assessment, either by a community pediatrician or a specialized team (Rojas-Torres et al., 2020; Zwaigenbaum et al., (2015). When identified as high-risk, children should be referred immediately for local early intervention services (e.g., infant development, speech-language therapy, occupational therapy, targeted preschool support), depending on level of need and the local service model, pending a diagnostic assessment. In order to ensure the proper intervention referrals, diagnosticians and clinicians need to be adequately informed of the areas of impairment in the child and the appropriate early interventions that meet the needs of the child and family (Miller et al., 2021).

Clinical Implications

The results of this review shows early diagnosis among infants/toddlers from birth to three years of age is possible. This review highlights four different approaches to early diagnosis. These studies show the need for more research within early diagnosis methods for ASD. While there are several studies on screeners and biomarkers, a majority of these studies did not investigate effective and accurate early diagnosis of ASD. They simply examine the question, “Does my child have the risk of developing autism?” While it is important to know whether a child is at risk, it is more important to know which diagnostic methods can be utilized to determine if a child definitively has ASD or if they just present with characteristics of ASD as this can help in early intervention. This lack in the research is why I was only able to identify

four studies that looked at early diagnosis for autism prior to the age of 3. Within these four studies, some clinical implications identified include: (1) Implementation of early diagnosis methods for high risk children; (2) The use of early diagnosis methods to help in the early intervention of ASD; (3) Incorporation of early diagnosis methods within pediatrician visits; (4) Providing parental and family support.

Early Diagnosis and Early Intervention

Research highlights the importance of receiving an early diagnosis of ASD followed by implementation of early intervention (Volkmar, 2014; Rotholz et al., (2017). However, Oswald et al., (2017) found that, despite early parental concerns, children in the ASD group were diagnosed later than children in the developmentally delayed group. Additionally, late diagnosis has been associated with increased parental stress which can delay early intervention and decrease the potential for positive outcomes (Elder, 2016). Early intervention is crucial as studies have found that when an intervention is implemented prior to the age of 48 months there are significant gains in the areas of cognition, adaptive behaviors, and language development (Vivanti & Dissanayake, 2016). Additionally, researchers have found correlation in the implementation of early interventions in ASD and improvements in activities of daily living skills and social behavior (Remington et al., 2007). Therefore, literature suggests that early diagnosis paired with early intervention are crucial in creating a more positive quality of life for children with ASD (Remington et al., 2007, Elder, 2016, Vivanti & Dissanayake, 2016).

Towle et al. (2020) found “the earlier, the better” has implications for continued efforts for early identification and treatment, and there is a clear rationale for involving families with children with ASD as early as possible in terms of support and advocacy skills that involvement with the intervention systems affords. Most children with ASD will require educational services, vocational services, and adult support services, therefore, the earlier caregivers learn what their children’s needs are, what services they benefit from, and how the service systems work, the more able they will be to make informed decisions that support optimal development for their child (Tolmie et al., 2017). Additionally it is important for clinicians to be able to have a good understanding of the different early interventions in order to provide parents and families with the needed information and guidance to ensure they are making the appropriate choice for their child (McCormack et al., 2020).

The connection between early diagnosis and early intervention in autism is pivotal in shaping the developmental journey of individuals on the autism spectrum (Elder et al., 2017). Early diagnosis enables the identification of subtle markers and atypical behaviors that might not yet be manifest as overt symptoms. Hence, it is crucial for healthcare practitioners, including psychologists, to possess knowledge about efficacious early diagnostic approaches that can be applied to infants and toddlers who exhibit high-risk indications or display these subtle markers and atypical behaviors associated with autism. This early identification serves as a gateway to timely and targeted interventions, as it allows professionals and families to implement appropriate strategies during a critical period of brain plasticity. Early intervention capitalizes on the brain's heightened receptivity to learning and adaptation, maximizing the

potential for positive outcomes. By tailoring interventions to the individual needs of the child and addressing core challenges related to communication, social interaction, and behavior, early intervention can effectively mitigate the impact of autism-related difficulties. As a result, children are equipped with essential skills and strategies that foster their cognitive, emotional, and social growth. The synergy between early diagnosis and intervention not only accelerates progress but also establishes a solid foundation for lifelong learning and development, empowering individuals with autism to achieve their full potential.

Incorporation within Pediatrician Visits

Pediatric Health Providers (PHPs) play a vital role in the timely identification of ASD and have the potential to impact the age at which a diagnosis is made (James & Smith, 2020). To maximize their influence on reducing the age of diagnosis, James and Smith (2020) propose that PHPs should possess a comprehensive grasp of the intricate aspects of the disorder. This includes recognizing the unique traits of individuals with ASD who might be overlooked or diagnosed later in life. It is equally important for PHPs to integrate methods for early diagnosis into regular check-ups for children displaying high risk factors or early indications of ASD. Furthermore, PHPs need to be well-versed in the array of effective early screening techniques to identify initial warning signs for ASD. By gaining a more refined understanding of the subtle distinctions within ASD, particularly for infants and toddlers, and becoming familiar with different avenues of detection, PHP are likely to enhance their screened practices and be more

attuned to early diagnosis of ASD. Consequently, this can contribute to decreasing the age in which children are referred for a full diagnostic evaluation of ASD.

For many children, pediatricians are the "first line of defense" in regards to identifying ASD symptoms and warning signs (Crais et al., 2014). The American Academy of Pediatrics (AAP) recognized this in 2007 by publishing updated autism screen guidelines that recommend ASD specific screening be conducted at both 18- and 24-month well-visits utilizing validated and standardized screening tools (Johnson & Myers, 2007). Within the AAP recommendation is the notion that early screening of ASD by pediatricians can help reduce the age that children are referred for formal evaluation, which can reduce the age of diagnosis and expedite the implementation of appropriate interventions.

Providing Familial and Parental Support

Familial and parental involvement is crucial for the successful development of a child with ASD. Families and parents play a vital role in implementation of interventions and providing guidance and learning for their child with ASD. Research shows that there appears to be some variation in how families react to a diagnosis (Kang-Yi et al., 2018), for example, some parents express relief after finally receiving a conclusive diagnosis after prolonged periods of uncertainty (Abbott, Bernard, Forge, 2013). However, some parents experience the grieving process: denial, anger, depression, and acceptance, when faced with a child's diagnosis of ASD (Elder & Alessandro, 2009). It is important for clinicians to note, once parents and families have accepted a diagnosis, it is common for them to search for a cure (Elder, Brasher, & Alexander,

2016). During this phase, parents and families are particularly vulnerable and can fall prey to false claims of "cures" from a variety of sources, many of which are found on the internet. Hence, it holds significance for healthcare professionals to recognize this potential risk and offer parents and families the necessary assistance and direction for the effective implementation of suitable interventions.

Rabba et al, (2019) suggests that a collaborative partnership between parents and professionals is important and more so empathetic professionals. Additionally, parents are seeking education and knowledge about autism and professional support that is tailored to their individual needs may be what some families require in order to ensure their follow through with diagnosis and treatment recommendations (Rabba et al., 2019). Empathetic professional support may be what some families require at this vulnerable time to foster confidence and generate a feeling of competence in their ability to provide care and support to their child as they progress through the ASD diagnosis process, interventions, and treatment. In the Rabba et al. (2020) study, parents identified a need for a streamlined approach post-diagnosis. Specifically, access to one key person who assisted in clarifying concerns, providing direction, and generally debriefing with them about the diagnosis would have been beneficial. Therefore, while it is crucial to provide support in the diagnosis processes it is also imperative that this support carries through post-diagnosis (Rabba et al., 2019).

As we move toward earlier detection and diagnosis of autism Rabba et al. (2019) note that it is important to better understand this unique population of parents to ensure that professionals are equipped to provide better support that may positively impact the child and

family's future. For example, if parents are able to understand autism and feel reassured that they can handle what is to come at the time of diagnosis this may help them begin early intervention sooner. Rabba et al. (2019) highlights the importance of understanding the impact of early diagnosis of ASD on families and parents, to ensure that professionals are able to adequately address their needs and provide support throughout the process.

Ward et al. (2016) examined practitioner's views of assessment and diagnosis of autism and found that the majority (92%) of clinicians prefer to "watch and wait" rather than provide a diagnosis, especially when children are very young. Ward et al. (2016) suggests that this is one of the key reasons behind later diagnosis. Hesitance to diagnose by professionals may leave parents waiting and wondering what to do. This contributes to late diagnosis and may contribute to parental stress, delays in early intervention, and subsequently poor developmental trajectory for their child. It is imperative that diagnosticians and clinician be better equipped to assess and deliver an early ASD diagnosis confidently with sensitivity and compassion at an early age (Rabba et al., 2019).

Limitations

Early diagnosis of ASD is a complex endeavor that confronts several significant limitations within current research. One substantial challenge is the inherent heterogeneity of ASD, encompassing a wide range of behavioral and developmental manifestations (Masi et al., 2017). This diversity poses difficulties in identifying consistent and specific markers that could reliably indicate the presence of autism at a very young age. Additionally, the absence of a

definitive biological or neurological marker for autism makes it challenging to establish a universally applicable diagnostic tool (Wang et al., 2023). Moreover, the reliance on behavioral observations and standardized assessments, while valuable, may not fully capture the subtle nuances of ASD in its earliest stages. Furthermore, issues related to access to specialized diagnostic services and the potential for overdiagnosis or underdiagnosis further complicate the pursuit of accurate early detection. Thus, the field of early autism diagnosis research grapples with intricate obstacles that necessitate innovative approaches and interdisciplinary collaboration to advance our understanding and capabilities in identifying ASD in its earliest forms.

There has been growth in the field of ASD research with the addition of many new diagnoses, as well as screening, biomarker, and intervention studies. This review focused on early diagnosis methods and while there are many studies on diagnosis methods of ASD, there are few studies on early diagnosis methods for ASD. I sought to find a broad range of ASD early diagnosis methods, however, the literature search produced only four studies on early diagnosis methods. It is also noteworthy to mention within the literature there were a wide range of studies on biomarkers and screeners. However, due to the goal of this study being to determine and finding early diagnosis methods for ASD these studies were excluded from the review.

Research Gaps

While there are a range of studies looking at identifying biomarkers and screeners or early diagnosis of ASD. The majority of studies currently do not demonstrate whether or not these methods actually recuse a definitive diagnosis. Studies have shown that there is a correlation on the timing of implementation of intervention and the impact on trajectories of children diagnosed with ASD (Brasher et al., 2020; Rojas-Torres et al., 2020). Ensuring a timely diagnosis allows for the implementation of early clinical and educational intervention, but also alleviated parental distress (Estes et al., 2019; McCafferty, P., & McCutcheon, J. 2021), which in turn impacts the outcome of the ASD diagnosis on the child (Zeng et al., 2020). Therefore, it is imperative that future research emphasizes the importance of identifying effective and efficacious early diagnosis methods for ASD to help ensure early intervention which can not only reduce parental stress but also improve the trajectory of the ASD diagnosis on the child (Miller et al., 2021).

Future Directions

An ASD diagnosis typically relies on a collection of both behavioral observations conducted by a qualified clinician in addition to parental report on the developmental history and current presentation of the child. While clinical signs are important, it is also important for researchers to look at the neurological and biological signs that can help aid in early diagnosis of ASD. In recent years, efforts have been made to identify ASD diagnostic markers through this study some of the research include, eye tracking technologies (Vacas et al., 2022), structural

and functional neuroimaging studies (Ayoub et al., 2022), and various biomedical technologies (Shen et al., 2020). When searching the databases for early diagnosis methods for ASD, there was an abundance of studies on biomarkers and screeners, it would be helpful for future ASD research to conduct a systematic review and meta analysis focusing on biomarkers or screeners to help assess their validity, reliability, and efficacy of these identified biomarkers and screeners and how they can potentially influence and aid in early ASD diagnosis.

McCarty and Frye (2020) suggest that developing biomarkers that could be used in conjunction with the screening methods proposed by the AAP is another method for improving the efficiency of the diagnostic process. Therefore, biomarkers that could (1) identify risk for determining which children should be screened, (2) be used as a secondary screen, and/or (3) confirm the behavioral observations of diagnostic tests, which could potentially aid in early diagnosis and intervention (McCarty & Frye, 2020). McCarty and Frye (2020) highlight five types of biomarkers. Biomarkers at prenatal and presymptomatic stages can be used to help identify risk in order to focus behavioral screening tools while biomarkers at the diagnostic stage can be used to verify diagnosis once behavioral symptoms develop.

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emphasizes the importance of identifying effective and efficacious early diagnosis methods for ASD to help ensure early intervention which can not only reduce parental stress but also improve the trajectory of the ASD diagnosis on the child (Miller et al., 2021).

It would also be helpful for researchers to develop, conduct, and implement more studies on early diagnosis methods, as these are related to the research on early intervention methods for ASD. It is also important for future studies on early diagnosis methods to identify ways in which the method addresses comorbid diagnoses. As seen in the current literature, various methods have been employed for early diagnosis of ASD, including two-tiered screening, clinical imaging, and surveillance techniques. Two-tiered screening is often initiated during routine pediatric check-ups and typically involves the use of standardized questionnaires or observations to identify early signs of autism. While this approach offers a cost-effective and accessible means of early diagnosis, it may lack sensitivity and specificity, leading to false positives and false negatives. A more objective approach is, clinical imaging, particularly functional magnetic resonance imaging (fMRI) and electroencephalography (EEG). Clinical imaging offers a more objective and neurobiological perspective by examining brain structure and function. However, its applicability in widespread screening is limited due to high cost and the need for specialized equipment. Surveillance methods, which entail continuous monitoring of a child's developmental milestones and behaviors. This can provide longitudinal data for early autism diagnosis, but may not capture subtle signs in a timely manner. To optimize early diagnosis, a combined approach, incorporating elements of two-tiered screening, clinical imaging, and surveillance, may prove most effective in identifying at-risk children and

facilitating early intervention, potentially improving long-term outcomes for those with autism spectrum disorder. Further research is needed to determine the most accurate and cost-effective combination of these methods in early autism diagnosis.

Conclusion and Recommendations

This study highlights the importance of early diagnosis. While major advances have been made in the ASD field of research, more research on early diagnosis methods is needed. As previously mentioned, ASD is a lifelong condition and families must adapt their focus on therapies as their child grows into adulthood. Early diagnosis can allow for families to learn this shift early on in their child's life and help implement early intervention methods to help decrease the severity of ASD symptoms as their child advances in age.

Given that ASD is a condition that spans an individual's entire life, families need to adapt their approach to support their child's evolving needs. This includes transitioning from childhood-centered interventions to those appropriate for adolescence and adulthood. Early diagnosis serves as a pivotal factor in facilitating this transition. By identifying ASD at an early point in a child's life, families are better equipped to recognize the nuances and complexities of the condition. This recognition enables them to proactively shift their focus towards implementing suitable interventions that cater to the child's developmental stage.

One of the most significant advantages of early diagnosis is its potential to initiate early intervention methods. These interventions, when applied during the crucial developmental phases, have the capacity to mitigate the severity of ASD symptoms. As the child advances in

age, these interventions can contribute to improved cognitive, social, and communicative skills, thereby enhancing their overall quality of life. This underscores the importance of early diagnosis as a foundational step that empowers families with the information needed to make informed decisions and provide the most effective support for their child's long-term development.

Additionally, early diagnosis of ASD serves as a compass guiding families toward a path of understanding and implementing effective support. It equips families with the knowledge and tools to navigate the unique needs and challenges their child might face. By identifying ASD traits at a young age, families can access a range of evidence-based interventions, such as applied behavior analysis (ABA), speech and language therapy, occupational therapy, and social skills training. These interventions are most effective when started early, during the critical developmental years, enabling children to build essential skills to help empower them to successfully navigate and thrive in this world that is built for neurotypical and able bodied individuals.

For many years, autism has predominantly been viewed through a medical lens, focusing primarily on its diagnostic criteria, neurological underpinnings, and therapeutic interventions (Krcek, 2013). While this approach has undoubtedly advanced our understanding of ASD and provided essential support for individuals with the condition, there is a growing recognition that a more comprehensive perspective is needed. It is increasingly imperative to shift the paradigm towards a social lens that acknowledges the profound impact of societal attitudes, inclusivity, and acceptance on the lives of autistic individuals (Goering, 2015). Embracing a social lens

invites us to consider how environmental factors, societal norms, and stigmatization affect the well-being and opportunities of those with ASD. It calls for a broader discussion on fostering inclusive communities, promoting neurodiversity, and respecting the unique strengths and challenges of autistic individuals, ultimately striving for a world where differences are celebrated and accommodated rather than pathologized.

Furthermore, the journey of learning to adapt to an autism diagnosis is a transformative experience for families. While the concept of seeking a cure may seem alluring, it's important to recognize that autism is not a disease; it's a neurological variation that shapes an individual's perceptions, interactions, and talents. Embracing this reality and focusing on adaptation encourages families to celebrate their child's unique strengths and abilities, fostering an environment of acceptance and support. It helps families shift their perspective from trying to change their child to seeking ways to facilitate their child's growth and self-expression.

Adaptation also has a broader societal impact. Embracing and accommodating neurodiversity contributes to creating more inclusive communities that value the contributions of all individuals, regardless of their neurological makeup. Families that choose adaptation over cure often become advocates for autism awareness and inclusivity, promoting understanding and empathy among peers, educators, and neighbors (Seligman & Darling, 2017). This ripple effect enhances the quality of life not only for the individual with autism but for the entire community.

Early diagnosis of ASD serves as a cornerstone for families, providing them with a roadmap to navigate the unique challenges and opportunities that come with raising a child with

ASD. It enables families to access specialized interventions and therapies that are tailored to their child's needs, fostering effective communication, social interaction, and behavioral management skills. Moreover, early diagnosis contributes to a deeper understanding of ASD as a neurological variation rather than a disorder, helping to dispel misconceptions and reduce stigma surrounding it.

Psychologists and healthcare providers play a crucial role in empowering individuals with ASD to lead successful lives. By offering comprehensive assessments and personalized interventions, they can help individuals harness their strengths and overcome challenges. Collaborative efforts between professionals, families, and individuals with ASD can create a holistic support system that nurtures personal growth and development. Additionally, psychologists and healthcare providers can guide families in adapting to the unique needs of their child with ASD. By offering guidance on effective communication strategies, behavior management techniques, and advocacy skills, they empower families to create inclusive environments that foster independence and self-advocacy in their child. This approach not only enhances the quality of life for individuals with ASD but also contributes to a more inclusive and empathetic society that values neurodiversity.

While early diagnosis of ASD has its benefits, it is crucial to recognize that the methods used for early diagnosis of ASD can disproportionately place a heavier burden on individuals from communities of color, those with limited socioeconomic resources, and other minority populations. This is a result of the intersection of various systemic inequalities. The established diagnostic criteria often lack cultural considerations, leading to the misinterpretation of

behaviors and communication styles that may differ across diverse communities. This can result in underdiagnosis or misdiagnosis, depriving individuals of timely interventions. Limited access to healthcare resources within these communities further exacerbates the issue, causing delays in receiving proper assessments and support services. Moreover, cultural stigma surrounding developmental differences and mental health can dissuade families from pursuing evaluations, perpetuating disparities in early diagnosis. Effectively addressing these challenges necessitates a multi-faceted approach that recognizes the unique experiences of marginalized groups, rectifies biases in diagnostic methods, enhances accessibility to healthcare, and promotes awareness to counteract stigma.

In conclusion, this study highlights that while considerable progress has been achieved in the realm of ASD research, the domain of early diagnosis remains an area demanding further investigation. Early diagnosis is instrumental in enabling families to tailor their approach to the evolving needs of individuals with ASD. By leveraging timely and accurate diagnosis, families can implement early interventions that have the potential to significantly influence the trajectory of the condition, leading to improved outcomes and a better quality of life for those affected by ASD and more importantly, allowing individuals and families to learn to live successfully with ASD. Additionally, it is important for researchers to identify ways in which early ASD diagnosis methods and interventions can be accessible to everyone and ensure that identified barriers are eliminated to ensure proper evaluation, assessment, and intervention for children and families dealing with an Autism diagnosis.

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Tables and Figures

Table 1

Participant Demographics

Study	Male	Female	Not Reported	Total Number of Participants
Barbaro et al. (2022)	n = 279 (78.2%)	n = 78 (21.8%)	n = 0	N = 357
Haweel et al. (2021)	Not Reported	Not Reported	Not reported	N = 100
Khowaja et al. (2018)	Not reported	38.5%	Not Reported	N = 109
Kleinman et al. (2007)	n = 2,003	n = 1,743	n = 47	N = 3793

Table 2

Study Information

Study	Detection Methods	Geographic Location	Age Range	Diagnosed with ASD	Not Diagnosed with ASD	Total Participants
Barbaro et al. (2022)	Social Attention and Communication Surveillance-Revised (SACS-R) Social Attention and Communication Surveillance-Preschool (SACS-PR)	Australia	11-30 months	n = 268	n = 89	N = 357
Haweel et al. (2021)	Task-based fMRI (TfMRI)	United States	12-40 months	n = 50	n = 50	N = 100
Khowaja et al. (2018)	Modified Checklist for Autism in Toddlers, Revised with Follow-Up (M-CHAT-R/F), Screening Tool for Autism in Toddlers & Young Children (STAT)	United States	16-30 months	n = 64	n = 45	N = 109
Kleinman et al. (2008)	Modified Checklist for Autism in Toddlers (M-CHAT) and Telephone follow-up interview	United States	16-30 months	n = 80	n = 51	N = 131

Table 3

Participant Ethnicity Demographics

Study	White/ Caucasian	African	Asian or Middle Eastern	Hispanic	Indigenous	Mixed Race	Unspecified or Not Reported	Total
Barbaro et al. (2022)	Mother: n = 246 (68.9%) Father: n = 230 (64.4%)	Mother: n = 6 (1.7%) Father: n = 8 (2.2%)	Mother: n = 74 (20.7%) Father: n = 64 (17.9%)	Not Reported	Mother: n = 4 (1.1%) Father: n = 3 (0.8%)	Mother: n = 6 (1.7%) Father: n = 5 (1.4%)	Mother: n = 8 (2.2%) Father: n = 34 (9.5%)	N = 357
Haweel et al. (2021)	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	N = 100
Khowja et al. (2018)	37.6% n = 41	44.0% n = 48	Not Reported	Not Reported	Not Reported	Not Reported	19.4%	N = 109
Kleinman et al. (2007)	72% n = 146	2.5% n = 5	1.5% n = 3	3% n = 6	Not Reported	Not Reported	21% n = 43	N = 203

Table 4

Annual Family Income

Study	< $33,214	$33,216 - $52,195	$52,196 - $71,175	$71,176 - $90,155	$90,156 - $109,135	$109,136 - $128,115	$128,116 - $147,095	$147,096 - $166,075	> $166,075	Not Reported	Total
Barbaro et al. (2022)	n = 32 (9.0%)	n = 25 (7.0%)	n = 43 (12.0%)	n = 40 (11.2%)	n = 33 (9.2%)	n = 30 (8.4%)	n = 15 (4.2%)	n = 11 (3.1%)	n = 37 (10.4%)	n = 78 (21.8%)	N = 357
Haweel et al. (2021)	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	N = 100
Khowja et al. (2018)	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	N = 109
Kleinman et al. (2007)	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	N = 3793

*Kleinman et al. (2007) reported an average household income of $40,000–$60,000.

Table 5

Psychometric Data

Study/Testing measure	PPV	NPV	Sensitivity	Specificity
Barbaro et al. (2022) - SACS-R	.83	.99	.62	1.00
Barbaro et al. (2022) - SACS-R+PR	.78	.99	.96	.99
Haweel et al. (2021) TfMRI	Not Reported	Not Reported	.84	.76
Khowaja et al. (2018) - M-CHAT-R/F	.48	.99	.85	.99
Khowaja et al. (2018) - STAT (24 - 35 months)	.86	.92	.92	.85
Khowaja et al. (2018) - STAT (14 - 23 months)	.68	.97	.93	.83
Kleinman et al. (2007) - M-CHAT	.36	Not Reported	2/6 critical item score = .77 (77%) and 3/23 item score = .92 (92%)	2/6 critical item score = .43 (43%) and 3/23 item score = .27 (27%)
Kleinman et al. (2007) - M-CHAT and telephone interview	.74	Not Reported	Not Reported	Not Reported

Appendices

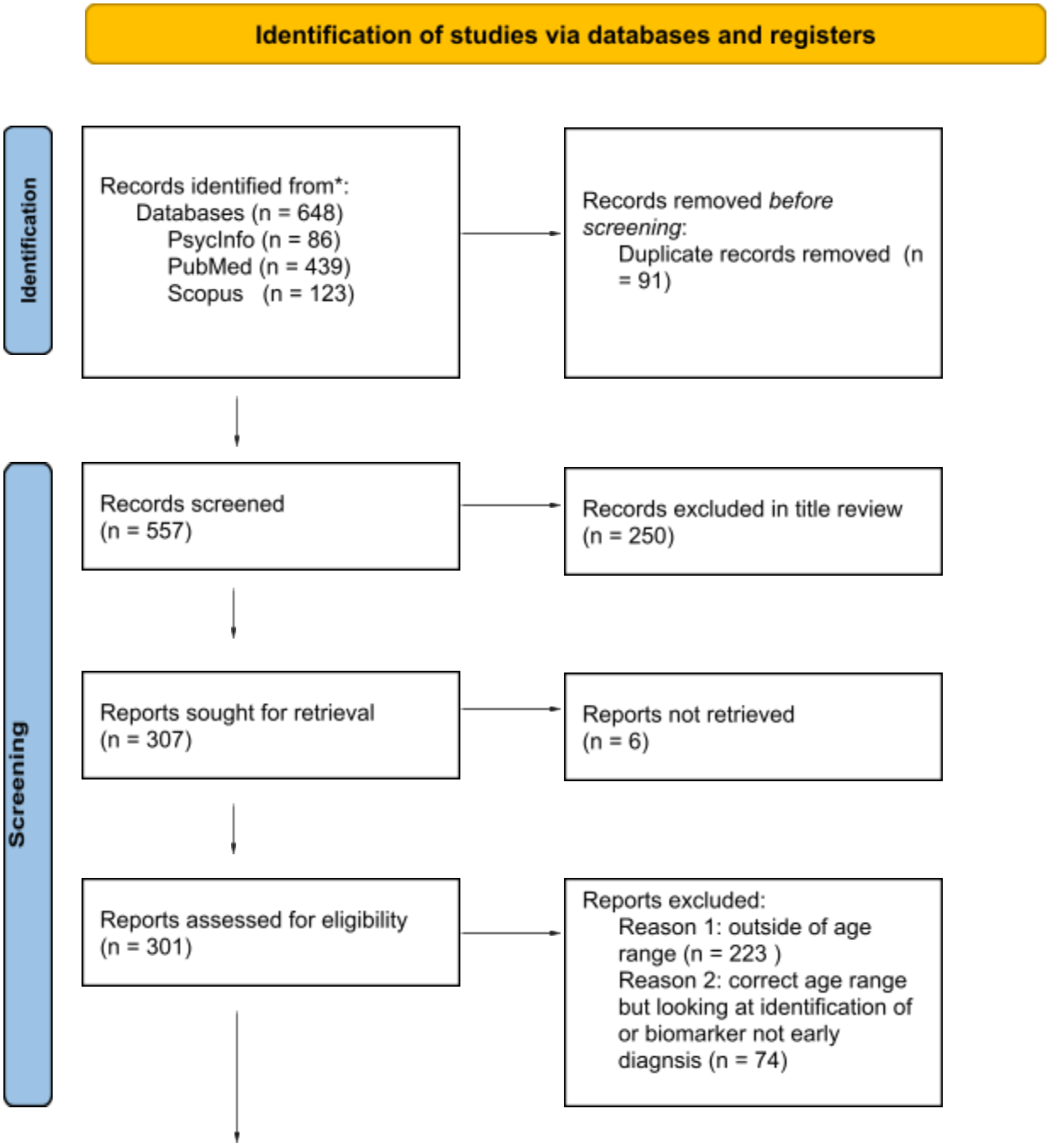
Appendix A

Key Search Terms

Category	Terms Searched
Autism	“Autism Spectrum Disorders" "Autistic Traits" autis* ASD
Methods	"Magnetic Resonance Imaging" "Functional Magnetic Resonance Imaging" "Tomography" "Electroencephalography" "Evoked Potentials" “MRI” “magnetic resonance imaging” “CT Scan” “computerized tomography” “EEG” “electroencephalogram” “eye scan” “tiered screening” “multi-tiered screening” “multitiered screening” “home video analysis” “eye gaze” “functional MRI” “FMRI” “Evoked Potential” “EP” “Auditory Brainstem Response” “Hearing test” “Event Related Potential” “ERP”
Diagnosis	“Early Diagnosis” “Early Detection”

Appendix B

Prisma Flow Diagram



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020

Appendix C

Risk of Bias Assessment Tool for Systematic Review

Domain	Rating	Reasoning
Domain 1: Study Eligibility Criteria	Low concern	Considerable effort was made to clearly specify the review question and objectives, and to pre-specify and justify appropriate and detailed eligibility criteria that have been adhered to during the review
Domain 2: Identification and Selection of Studies	High concern	Some eligible studies are likely to be missing from the review due to only looking at three databases
Domain 3: Data collection and Study Appraisal	High concern	Some bias may have been introduced through the data collection or risk of bias assessment processes.
Domain 4: Synthesis and Findings	High concern	The synthesis is likely to produce biased results, because (i) potential biases were ignored (within and/or across studies), (ii) important between-study variation was not accounted for; (iii) there were important inadequacies in the methodology; or (iv) findings are incompletely reported in a way that raises concerns.

From: Whiting, P., Savović, J., Higgins, J. P., Caldwell, D. M., Reeves, B. C., Shea, B., Davies, P., Kleijnen, J., Churchill, R., & ROBIS group (2016). ROBIS: A new tool to assess risk of bias in systematic reviews was developed. Journal of clinical epidemiology, 69, 225–234.