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Applying Informatics to Autism Spectrum Disorder: From Screening to Early Intervention

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By

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An abstract of
A thesis submitted to the Faculty of the
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Abstract

Applying Informatics to Autism Spectrum Disorder: From Screening to Early Intervention

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Background: According to CDC's Autism and Developmental Disabilities Monitoring Network (ADDM) 1 in 68 children are affected with ASD in the United States. As the impact of ASD continues to grow, it is necessary to understand how primary care physicians can better identify the signs of ASD, diagnose ASD, and ultimately increase access to early intervention services. Early intervention services shows substantial evidence to improve developmental outcomes for those with ASD. Whether the use of information systems enables this effort, is important to understand, as the steady growth in ASD is regarded as a significant public health concern.

Key Aims and Methods: The overall goal of this thesis is to better understand how integrating technology with traditional ASD practices can increase access to early intervention services. The first aim is "Are healthcare providers leveraging technology to increase completeness and accuracy of ASD screening and diagnosis?" The second aim is "Are healthcare providers that use integrated technology for ASD diagnosis, able to screen, evaluate, and diagnose for ASD at a younger age when compared to healthcare providers that use traditional modalities? To achieve these aims, a literature review was conducted.

Results: Literature review confirmed that leveraging technology to screen and assess children for ASD increased timeliness, completeness, and accuracy. Improving screening practices subsequently reduces the burden on specialists and increases access to early intervention services for those accurately diagnosed with ASD. Although the second aim could not be answered definitively, this literature review reinforces the knowledge around how integrating technology with traditional screening modalities could potentially decrease age of diagnosis through evidence showing how technology has expedited processes involved, such as screening and diagnostic evaluation.

Conclusion: There is an apparent need to expedite ASD screening, evaluation and diagnosis to subsequently increase access to early intervention services, as evidence shows early intervention greatly improves quality of life. Although there is some information pertaining to how technology can improve processes involved with diagnosis, knowledge surrounding how technology affects age of diagnosis is lacking. These findings show evidence of methods that can be applied to use technology to lower the age of ASD diagnosis.

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Table of Contents

Introduction 3
Problem Statement 5
Purpose Statement 6
Key Aims: 6
Significance Statement 7
Review of Literature 8
Introduction 8
Autism Spectrum Disorder 8
Screening 9
Diagnostic Assessment 12
Mobile and Telemedicine Technology 15
Methodology 18
Introduction 18
Results 21
Introduction 21
Study Characteristics 21
Web Based Screening 21
Machine Learning 22
mHealth 23
Analysis of Major Themes 23
Tables 25
Discussion 27
Introduction 27
Key Findings 27
Limitations 29
Implications 31
Recommendations/Next Steps 32
Conclusion 33
References 37

Introduction

Autism Spectrum Disorder (ASD) is a group of "developmental disabilities that can cause significant social, communication, and behavioral challenges" (Christensen et al., 2016). According to the Centers for Disease Control and Prevention's (CDC) Autism and Developmental Disabilities Monitoring Network (ADDM), as of 2014, 1 in 68 children are affected with ASD in the United States. This is an increase in prevalence from 2007 when ADDM estimated that 1 in 150 children were affected with ASD (Christensen et al., 2016). Although it is not clear as to whether the increase in prevalence is due to an increase in awareness of ASD and diagnosis guidelines or an increase in ASD incidence, the steady growth in ASD prevalence is regarded as a significant public health concern (Oberleitner et al., 2005).

An autism diagnosis is needed to provide early intervention services, which shows substantial evidence to improve developmental outcomes (Daniels, Halladay, Shih, Elder, & Dawson, 2014). Early intervention is defined as the critical period of when a child's language and cognitive development are the most easily influenced (Mazurek et al., 2014). However, even though children with ASD can be diagnosed as early as 24 months, the average age of diagnosis is after 48 months, which lessens the potential benefits of intervention, that influence quality of life (Gordon-Lipkin, Foster, & Peacock, 2016). To improve the impact of ASD on the health of the public, it is important to understand how to streamline the processes involved in screening and diagnosis of ASD and increase the number of children with access to early intervention services prior to 48 months.

Public health informatics, by definition, is "the systematic application of information and computer science and technology to public health practice, research, and learning" (Richards,

n.d.). The guiding principles of public health informatics are based on information systems that are aimed at improving the health of populations versus an individual, information systems that prevent disease and injury "by altering the conditions or the environment that put populations at risk" (Magnuson & Fu, 2013, p. 11), and exploring prevention at various points along the causal chain of disease, injury, or disability regardless of the social, behavioral, or environmental context (Magnuson & Fu, 2013). These guiding principles are at the foundation of public health informatics and have been used in developing systems that can aid in assessing population health and developing intervention strategies based on data. Population health is defined as "the health outcomes of a group of individuals, including the distributions of outcomes within the groups"(Lobb & Colditz, 2013). This is applicable to the methodologies discussed in this thesis, such that, the health outcomes of those with ASD have an indirect impact on the larger population. Informatics may provide a tool for streamlining ASD screening, diagnosis, and access to early intervention, which would reduce the age of diagnosis and improve outcomes of intervention services; for both the group of individuals and the individuals within the group. Technology integration such as mobile health and mobile telemedicine are possible solutions for bridging the service gap using informatics. The World Health Organization (WHO) defines mobile health (mHealth) as "medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless devices." (Kay, Santos, & Takane, 2011). WHO defines mobile telemedicine (telemedicine) as "the communication or consultation between health professionals about patients using the voice, text, data, imaging, or video functions of a mobile device" (Kay et al., 2011). Further examining the existing barriers of ASD diagnosis and how informatics solutions may have an impact on these will provide further education and understanding as to how

informatics solutions can better public health and enable access to improved outcomes.

Problem Statement

As ASD prevalence has increased, the demand for services has as well. Currently, the number of certified professionals is not able to keep up with the demand, which has created longer waiting lists and further delays in diagnosis (Gordon-Lipkin et al., 2016). This service gap between those needing services and those able to provide said services has been noted as cause for public health concern(Oberleitner et al., 2005). Delays in diagnosis reduce access to early intervention services, the potential impact of those services, and the potential quality of life for those diagnosed with ASD (Daniels et al., 2014). Reduction in the potential quality of life subsequently has an impact on public health by the burden imposed on those individuals throughout the population with ASD. Information technology has been shown to make improvements in delays when integrating with the M-CHAT-R/F and ADOS modules (Brooks, Haynes, Smith, McFadden, & Robins, 2016; Wall, Kosmicki, Deluca, Harstad, & Fusaro, 2012). How mobile and telemedicine can further assist timely diagnosis and access to early intervention services needs to be examined as a possible solution to help fill the void in services. Further reducing diagnostic timelines by using technology increases access to providers and services, which may directly increase access to early intervention services, which is proven as the best predictor or improving health outcomes (Mazurek et al., 2014).

Streamlining screening, diagnosis, and access to intervention through informatics applications impacts public health in addition to the individual benefits, through collection of timely data, which provides insight. The ability to compile individual-level data and transform it into usable, aggregate data can help public health in better understanding ASD, what improves

ASD outcomes, and how to lessen the burden on the health of the community. As new technologies continually emerge, it will be important to understand how integrated technologies can further assist data collection and inform prevention activities utilized through mobile health and telemedicine. Mobile health and telemedicine have the potential to improve geographic and logistical limitations that increase delays and time between initial screening and receipt of diagnosis. If delays in diagnosis do not improve, the gap in service between first concern and receiving an ASD diagnosis will continually decline, adversely affecting public health.

Purpose Statement

The purpose of this thesis is to examine the use of technology and how it affects screening, diagnosis, and access to early intervention services for children with ASD. This thesis will explore how mobile health and telemedicine technology can support ASD diagnosis from initial concern to early intervention services. The predicted outcome is that utilizing mobile and telemedicine technology will reduce the average age of diagnosis of ASD and subsequently increasing access to early intervention services. Examining this topic increases understanding as to how using informatics can improve public health by improving health of individuals and populations. The overall goal is to better understand how integrating technology with traditional ASD screening and diagnosis practices can increase access to early intervention services.

Key Aims:

1. Are healthcare providers using technology to increase completeness and accuracy of ASD screening and diagnosis?
2. Are healthcare providers, that use integrated technology for ASD diagnosis, able to

screen, evaluate, and diagnose ASD at a younger age when compared to healthcare providers that use traditional modalities?

Significance Statement

Determining whether integrated information systems have an impact on ASD diagnosis services is critical to public health because the burden of ASD has been shown to decrease when access to early intervention services is available (Daniels et al., 2014). Access to early intervention services is largely dependent on physicians providing screening at 18 and 24-month well-child visits, referral for further evaluation, and the ability of healthcare providers to reliably diagnose ASD, without delay. When delays occur in screening and diagnosis, the access to early intervention services and the possibility of improved outcomes, is missed (Daniels et al., 2014).

As the number of children needing ASD screening, diagnosis, and services increases, and the disparity in certified professionals does not improve, the application of information technology is important to consider as a means to improve outcomes for those with ASD (Oberleitner & Laxminarayan, 2004). Informatics has the ability to do this through using technology to reduce barriers that prevent providers from screening, assessing, and ultimately diagnosing children with ASD; as well as, barriers that prevent parents from accessing care for their children. How mobile and telemedicine technology can further improve the state of ASD diagnosis is important to examine as it has direct implications on the health of the population.

Review of Literature

Introduction

The goal of this literature review is to build the knowledge base surrounding information solutions as they pertain to ASD diagnostic timelines. The following literature review examines existing research pertaining to ASD for young children, with the emphasis of expediting diagnostic timelines and accessing early intervention. The review will examine current processes and how integrating technology can expedite screening, diagnostic assessment, and access to early intervention services for children at risk for ASD. First, the review will discuss the overall diagnostic process for ASD and its current state. Second, it will review the most widely used ASD screening currently and potential technological improvements. Third, the review will examine the current diagnostic observation tool and method and how using machine learning has been used as a potential solution to increase timeliness. Last, the review will examine possible mobile and telemedicine technology and how they could potentially impact ASD diagnosis by reducing barriers that prevent early intervention.

Autism Spectrum Disorder

Currently, no medical markers exist for ASD. Thus, the ability to diagnose ASD early is largely dependent on identifying behavioral markers (Kosmicki, Sochat, Duda, & Wall, 2015). Particular behavioral markers signal healthcare providers that the child may have ASD and that further evaluation is necessary following screening (Kosmicki et al., 2015). The current "gold standard" for diagnosing ASD is done through a multi-disciplinary team (MDT) (Falkmer,

Anderson, Falkmer, & Horlin, 2013). The MDT diagnosis ASD through behavioral examination using instruments that have been designed to assess and measure impairments in areas meeting the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) criteria for ASD.(Kosmicki et al., 2015) The DSM-V identifies impairments in both "communication and social interaction" and "restricted interests and repetitive behaviors" as the two core domains for ASD (Kosmicki et al., 2015). Diagnosing ASD is a long process due to the MDT approach that is used to assess the "historical, behavioral, and parent-report information" (Falkmer et al., 2013). From the time a child is initially screened for ASD to receiving a diagnosis can take 13 months or longer in the United States, due to the time requirements of various instruments, the need for in-person appointments, and the rise in the number of children needing assessment (Falkmer et al., 2013). The delay in diagnosis from the time of initial screening has been a significant impediment to receiving early intervention services, which has shown to be beneficial to the quality of life and improving potential developmental outcomes (Daniels et al., 2014; Kosmicki et al., 2015). Increasing access to early intervention services can be done through optimizing the process from screening to receipt of diagnosis. In order to expand access to early intervention, diagnosis must be made at a younger age. Thus, reducing the age of diagnosis has become a priority of the field (Klin, Klaiman, & Jones, 2015).

Screening

The American Academy of Pediatrics (AAP) recognized the need for routine screening of ASD in 2006. The AAP recommended that all children in the United States should be screened for ASD at 18 and 24-month well-child visits and whenever a parent informs the provider that they have concerns related to their child's development (Corsello, Akshoomoff, & Stahmer, 2013).

Following the AAP recommendation, significant effort has been put into implementing recommended screening for ASD at physicians' offices (Brooks et al., 2016). However, most children with ASD are not diagnosed until they are 48 months or older when a diagnosis can occur as early as 24 months. (Kosmicki et al., 2015). This is a significant delay in services and negatively affects potential outcomes, increasing the burden of ASD on the population affected. As the weight of ASD continues to grow, it is important to understand how primary care physicians can better detect ASD through using technology to facilitate screening, thus, enabling earlier referral for early intervention services and improving overall outcomes.

Screening for and identifying ASD is the first step in an integrated, multidisciplinary, diagnostic approach. In order to obtain an ASD diagnosis, the child must undergo a developmental screening and a comprehensive diagnostic evaluation. Various tools exist for screening and diagnostic evaluation of ASD due to the lack of a universal tool (Falkmer et al., 2013). Although there is not a standardized screening or diagnostic tool that is universally used, evidence has shown that a highly reliable diagnosis involves a procedure that must have a "standardized parent interview and a standardized observational measure in combination with clinical judgment."(Corsello et al., 2013). The most widely used screening tool for ASD is the Modified Checklist for Autism in Toddlers-Revised, with Follow-Up Interview (M-CHAT-R/F) (Weitlauf, Vehorn, Stone, Fein, & Warren, 2015). The M-CHAT-R/F is a screening tool, which physicians use to screen children for ASD based on parent's answers. Often times, parents are the first to notice signs and symptoms associated with ASD. Subsequently, the M-CHAT-R/F uses a series of informative questions that, based on the parent's answers, can indicate whether or not the child should be evaluated further by a specialist ("How Is Autism Diagnosed?," n.d.). The questionnaire consists of 20-items that are filled out via paper and pencil. The questions are

concerning the child's skills and behaviors, currently, in a yes/no format. If the child fails 3-7 of the questions, the parents are referred for a follow-up interview. The preliminary follow-up interview is designed to gather additional information related to the failed questions. (Weitlauf et al., 2015). If the child failed 8 or more items on the initial questionnaire or continues to fail 2 or more questions on the preliminary follow-up interview, then the child is considered to have sufficient risk and is referred for further evaluation.

Although the M-CHAT-R/F is recommended by the AAP there are still significant disparities that further delay screening and diagnosis using this tool. Losses to follow up after the initial assessment is a particular issue that the M-CHAT-R/F faces. While parents fill out the first portion of the assessment at the physician's office, long wait periods or lack of follow up may occur for the subsequent portions, leading to inaccurate and incomplete screenings. Geographic disparities, in addition to inefficient screening processes, compound negative outcomes by further delaying diagnosis due to cultural differences in healthcare perception (Brooks et al., 2016). Children who live in rural areas have been shown to receive a diagnosis later than children who do not live in rural areas.(Mazurek et al., 2014). Current screening practices are conducted on paper in the physician's office, which creates a barrier to patients who cannot get their children to the providers office for both logistical (i.e. can't take time off of work, busy schedules, etc.) and geographic limitations. Thus, what is needed is a solution to provide access to screening and evaluation services that can be delivered quickly, produce accurate results, and be done from anywhere.

In a study conducted by Brooks et al. 2016, a web-based M-CHAT-R/F was administered to parents, in an urban setting, with the assistance of mobile technology, an iPad (tablet). Conducting the M-CHAT-R/F by electronic means was found to reduce scoring errors, expedited

the screening process by automatically initiating follow-up as needed, and was deemed more favorable by users. The web-based format of the M-CHAT-R/F was found to increase follow-up for the interview portion of screening. The paper-based M-CHAT-R/F had 35.1% of follow-up interviews not conducted, and the web-based M-CHAT-R/F had only 3.1% of follow-up interviews not conducted. The paper based M-CHAT-R/F is reliant upon phone interviews for the follow-up portion, whereas, the web-based leads the follow-up interview immediately following the screening, if necessary (Brooks et al., 2016). Additionally, the completeness of the M-CHAT-R/F was significantly higher for the web-based versus the paper-based modalities. The increase in completeness and timeliness is one example of how providing access to M-CHAT-R/F screening, via the web, enables usability and decreases existing barriers. Additionally, providing web-based screening allows parents to complete the screening away from the provider's office, as well as, encourages parents to fill out the questions in their entirety (Brooks et al., 2016). The results of the increase in completeness and reduction in time are indicative that using technology to reduce diagnostic timelines is of significant importance to public health.

Diagnostic Assessment

Following a screening indicative of possible ASD, a child is referred for a diagnostic evaluation to evaluate further the behavioral markers that were noted (Kosmicki et al., 2015). One of the most universally used diagnostic clinical assessments for ASD is a 4 module program called the Autism Diagnostic Observation Schedule (ADOS) (Kosmicki et al., 2015). The ADOS is widely used for finalizing a clinical diagnosis due to its “high degree of clinical utility and diagnostic validity” (Wall et al., 2012). The ADOS is a formal behavioral observation tool used by

clinicians, following a patient history interview with parents. The ADOS must be performed by a trained clinician and further assesses communication, social skills, play, imaginative use of materials, and restricted/repetitive behaviors (Wall et al., 2012). The four modules are independently conducted through semi-structured activities, with each module tailored to a specific subset of individuals based on pre-assessment language and developmental levels (Wall et al., 2012). Each individual is assessed with the module most indicative of his or her level of language development. Module 1 is tailored for individuals "with little or no language" and consists of 10 activities and 29 items (Wall et al., 2012). Due to the lower level of language requirement, Module 1 is typically used when younger children are being assessed (Wall et al., 2012). Module 2 is used for children who have some flexible speech but are not fluent and consists of 14 activities with 28 items (Wall et al., 2012). Module 3 is aimed for "verbally fluent children whom playing with toys is age appropriate" and consists of 13 activities and 23 items(Wall et al., 2012). Module 4 is for assessing individuals with the highest level of development, such that, it is intended for verbally fluent individuals over the age of 12 and consists of 10-15 activities with 31 items (Wall et al., 2012). A certified professional must run each module and including scoring, can take from 60-90 minutes (Wall et al., 2012). Additionally, increases in time between testing and receipt of diagnosis can occur if additional professionals must re-score the individual to account for variance in inter-rater reliability, leading to delays as long as 13 months from initial ADOS assessment and diagnosis (Kosmicki et al., 2015; Wall et al., 2012). Delays in diagnosis are exacerbated by the need for the ADOS to be scored by a professional following observation in a clinical facility, which are usually located in major metropolitan areas which creates barriers to access (Wall et al., 2012). The delay in diagnosis is further compounded when geographic and logistical barriers exist (Kosmicki et al.,

2015; Wall et al., 2012). Much like the M-CHAT-R/F's limitations, the number of those needing assessment outweighs the number of certified professionals (Wall et al., 2012). Therefore, further delays beyond screening with the M-CHAT-R/F exist and processes to expedite this process through using technology must be examined as a solution to increase access to early intervention services.

In a study by Wall et al., 2012, for module 1 and a preceding study by Kosmicki et al. 2015, for modules 2-3, machine learning was used to evaluate the ADOS to determine whether there is a computational and statistical method that would enable earlier diagnosis of children with ASD. Machine learning is defined as "the field of study that gives computers the ability to learn without being explicitly programmed"(Bell, 2014). In the module 1 study, which is most relevant to toddler evaluation, 612 individuals with an autism classification and 11 individuals with a non-spectrum classification were included. 16 alternative classifiers (AC) were constructed by performing machine learning analyses using the Waikato Environment for Knowledge Analysis (WEKA) on the 29 items in module 1. WEKA is "a collection of machine learning algorithms for data mining tasks" (Eibe Frank, Mark A. Hall, and Ian H. Witten, 2016). This was used to classify those on the autism spectrum and those who were considered non-spectrum. Classifiers were then cross validated to utilize the one with the best sensitivity, specificity, and accuracy(Wall et al., 2012).

Wall et al., 2012, found that the use of machine learning algorithms alongside the ADOS program decreased the number of behaviors needed to sufficiently detect ASD risk. Only 8 of the 29 behavior items in module 1 were needed to sufficiently classify autism with 100% accuracy (Wall et al., 2012). In the preceding study conducted by Kosmicki et al., it was found that only 9 of the 28 behaviors in module 2 and 12 of the 28 behaviors in module 3 were needed, with

98.27% and 97.66% accuracy, respectively (Kosmicki et al., 2015). Much like the M-CHAT-R/F, delivering the ADOS has geographic and logistical hurdles, in addition to the long waiting lists to see a certified professional that contributes to further diagnostic delays (Kosmicki et al., 2015). Based on the reduction in the number of behavioral items/markers needed for a reliable diagnostic assessment of ASD, by the assistance of technology, suggests that evaluating the role of information systems ability to lower the average age of diagnosis is justified (Kosmicki et al., 2015).

Mobile and Telemedicine Technology

Not much information is available on existing mobile health technologies as they relate specifically to ASD, but there is evidence that fewer behaviors are needed to develop an accurate diagnosis of ASD when integrating screening and diagnostic assessment with technology (Kosmicki et al., 2015). Both research on the electronic versions of the M-CHAT-R/F and the ADOS have shown that integrating technology with current modalities can reduce diagnostic procedure timelines, increase completeness, and improve accuracy. Wall et al., in conjunction with these results, suggested that there is a need to examine how integrating mobile health approaches may further shorten evaluation and diagnostic processes as a means to facilitate intervention services earlier than under current practices. Mobile technology can aid in the facilitation of screening, but can also increase the access to telemedicine, subsequently increasing access to diagnostic evaluation. Integrating mHealth technology (mobile and mobile telemedicine) in conjunction with the "Web-based M-CHAT-R/F" and "ADOS-with machine learning" solves logistical and geographic issues that increase delays in accessing early

intervention services.

Telemedicine is another form of mHealth that has the potential to transform diagnostic evaluation of ASD. Telemedicine allows access for families in rural areas, concerning both screening and diagnostic evaluation. Additionally, this would reduce the barrier imposed by the shortage in specialized professionals needed to conduct diagnostic evaluations, especially for those living in rural areas. Connecting patient and providers via mobile telemedicine would circumvent the challenge of specialized providers not being readily available to meet the high demand (Kay et al., 2011). Another solution that telemedicine provides is to provide subspecialty consultations for specialized professionals part of a multi-disciplinary team (Gordon-Lipkin et al., 2016). With high demands and busy schedules, teleconferencing would enable interactive interprofessional consultations that could otherwise cause delays. Additionally, a study conducted by Reese et al., 2015, preliminarily showed data that integrating telemedicine reduced barriers for accessing diagnostic services, in addition to cost, for those in rural and underserved areas. Integrating mobile and telehealth technologies into ASD screening and diagnostic procedures has the potential to improve public health by possibly increasing access to early intervention services through reducing barriers to care (Brooks et al., 2016).

Currently, in the United States approximately 1 in 68 children are diagnosed with ASD, however, only 43% of children receive a comprehensive evaluation by 36 months (Jenco, 2017). Increasing the number of children who have access to early intervention services is essential to improving the quality of life following an ASD diagnosis. This is a public health issue, such that, increasing the proportion of young children with ASD who are screened, evaluated, and enrolled in special services in a timely manner is a maternal, infant, and child health goal of Healthy People 2020 (“Maternal, Infant, and Child Health | Healthy People 2020,” n.d.). As technology

advances, it is important to understand how it can support the achievement of public health goals through integration with traditional modalities. The purpose of this thesis is to examine the use of technology and how it affects screening, diagnosis, and access to early intervention services for ASD. This thesis will explore how mobile health and telemedicine technology can expedite ASD diagnosis from initial concern to early intervention services to better support the goal of reducing age of diagnosis.

Methodology

Introduction

Relevant ASD literature was reviewed to develop an understanding of previous, current, and potential future developments (i.e. universal screening tool, web-based screening, mobile screening, and tele-intervention) from the initial screening for ASD all the way to receipt of diagnosis. A literature search was conducted to identify relevant literature about ASD, screening for ASD, early intervention, and technology integration as it relates to ASD or related behavioral health fields (i.e. pervasive developmental disorders). The materials and methods used for this study are shown in Table 1. The search terms are included but were not limited to those noted in Table 1.

Table 1: Literature Review Search Terms

Materials and Methods	
Literature Search	● PubMed ● Google Scholar ● PMC ● Web of Science
Search Terms	Autism Spectrum Disorder, Autism, Screening, Modified Checklist for Autism in Toddlers, With Follow Up - Revised, M-CHAT, Autism and Technology, Autism and Informatics, mHealth, mobile health, telehealth, telemedicine, ADOS, DSM-V, Early Intervention, web based, mobile health technologies, telehealth technologies.
Other Sources	Autism Speaks, CDC, American Academy of Pediatrics

The literature search was primarily conducted using PubMed for peer reviewed literature pertaining to ASD screening and diagnosis. The most relevant search terms were Autism Spectrum Disorder in combination with screening, diagnosis, mhealth, telehealth, and M-CHAT; PubMed Search results were further narrowed by publication date of 2000- 2017; full text

availability; Infant-23 months; and in the United States. Search terms for mobile health, informatics, and telehealth were also included; yielding 480 results. Other sources of literature, including Grey Literature, yielded an additional 10 results. Identifying specific articles that addressed the questions the investigator sought to ascertain through this literature review further narrowed the organization. Ultimately, narrowing of relevant literature resulted in 89 records that were useful in overall research, with 25 included in literature review analysis. The organization process is shown in Figure 1.

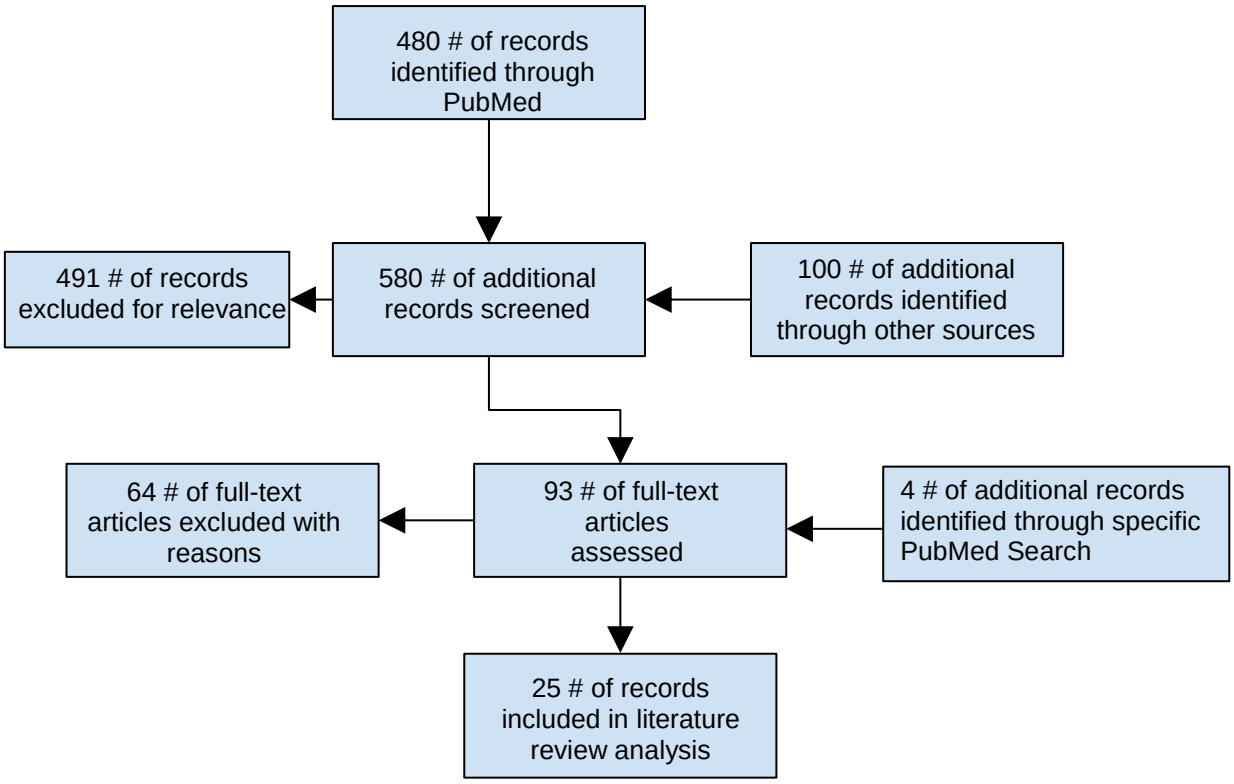

Figure 1: Organizational structure used for the literature search conducted in PubMed.

There was a significant difference in the amount of literature available pertaining to ASD and screening when compared to information available relating to informatics solutions and ASD. Due to the large number of articles from the PubMed search pertaining to ASD, articles were eliminated for relevance to the topic of enhancing early intervention access as a means to improve public health. When conducting a search for ASD as it relates to web based screening, a separate search was conducted. The search was done in PubMed for "Use of Digital Modified Checklist for Autism in Toddlers". This yielded 1 result, but 97 similar articles. Of the 97 similar articles, 4 were deemed relevant (i.e. they covered subject matter pertaining M-CHAT modalities that utilized technology for screening for ASD).

The information that was taken from the selected articles was used to ascertain how screening and diagnostic evaluation modalities are currently used, how they have been supported or enhanced by a technological process, and how these methods could integrate with mHealth to further enhance current processes. In reviewing all articles relating to screening for ASD using the M-CHAT-R/F, they were categorized by modality: paper and web-based. Sensitivity, completeness, accuracy and PPV were categorized between the articles to determine if informatics truly enhanced the current processes. This same process was conducted for the diagnostic assessment using the ADOS. When reviewing information relating to potential use of mHealth and telemedicine, patterns were examined for how utilizing mHealth and telemedicine have been used or suggested to better achieve access to early intervention services.

Results

Introduction

The initial literature review screening consisted of 580 articles relating to Autism Spectrum Disorder in combination with screening, diagnosis, mhealth, telehealth, and M-CHAT. However, many of the articles were easily discounted due to lack of relation (i.e. genetic tests for ASD, comorbidities, siblings of children with autism, etc.) The articles selected needed to address screening, diagnosis, and/or access to early intervention services for a child in their toddler years. Additionally, the articles relating ASD to informatics needed to discuss how technology can impact screening, diagnosis, and/or access to early intervention services. The final literature review consisted of 93 full text articles. Following review, 25 of the reviewed resources were utilized in the literature review. The articles that were selected for the final review needed to address the M-CHAT screening tool, the ADOS diagnostic assessment, and/or information relating to accessing early intervention services. Additionally, informatics articles needed to discuss web based modalities, machine learning, and/or mHealth (mobile and telemedicine) integration.

Study Characteristics

Web Based Screening

The paper based M-CHAT-R/F is a validated screening tool, where the web-based modality is not currently validated (Brooks et al., 2016). When the M-CHAT was revised in 2014 and combined with the follow-up interview, sensitivity decreased, specificity increased, and PPV

increased (Robins et al., 2014). The literature review was not conducted to determine the validity of the M-CHAT-R/F, which has been proven, but to determine if implementing the M-CHAT-R/F with technological assistance would further enhance screening efficiency.

Following the American Academy of Pediatrics (AAP) recommendation to screen all children for ASD at their 18 and 24-month well child visits, specialized professionals could not keep up with the increased demand (Wise, Little, Holliman, Wise, & Wang, 2010). The increased demand was not only due to the increase in ASD prevalence, but also due to the number of children being referred for further evaluation following overly sensitive screening (Monteiro et al., 2015). In order to improve the accuracy of children referred for further evaluation and to reach the number of children needing services, consensus was reached through review that enhancements need to be made to the current processes (Wise et al., 2010).

Machine Learning

The literature review examined how implementing machine learning alongside the ADOS for diagnostic evaluation for children at risk for ASD, shortens time to diagnosis (Wall et al., 2012). Although multiple articles pertaining to ADOS evaluation were reviewed, there was limited information available pertaining to machine learning alongside the ADOS. The information pulled from the studies is evidence to further build the knowledge surrounding reducing diagnostic timelines.

In studies by Kosmicki et al. and Wall et al. machine learning using ADOS data from the Autism Genetic Resource Exchange (AGRE), which is a repository of families with at least one child with ASD, as the input for classification (Wall et al., 2012). Both studies utilized machine learning for individuals diagnosed with an autism classification by the ADOS and utilized those

who were classified as non-spectrum as controls. Wall et al. specifically studied toddler-aged children. The findings from these studies were mirrored in other studies, however, they were not specifically referring to the ADOS and were excluded.

mHealth

Review of relevant mHealth articles as they relate to enhancing public health and reducing barriers were examined. Of the articles that were reviewed, they were utilized to build associations and develop insights as they relate to reducing ASD diagnostic timelines through the use of mobile devices and tele-consultations. The articles that were examined compared in-person diagnostic assessment with teleconferencing observation. The articles were reviewed to determine accuracy of diagnosis via telemedicine in comparison with traditional, in person assessments.

Analysis of Major Themes

In the study conducted by Harrington et al. web based screening was implemented via a mobile tablet to deliver the M-CHAT-R/F in an urban clinic. After using retrospective analysis to compare the paper based modality (N=197, M_{age}=23.1 months) to the web based modality (N=176, M_{age}= 22.1 months), the web based modality was found to improve the current processes (Harrington, Bai, & Perkins, 2013). Of the parents who completed the web-based version on the mobile device, 97.14% did not need help completing the web based mobile M-CHAT and among those who had previously filled out a paper-based M-CHAT (N=92), 78% preferred the web based mobile version. Usability and user satisfaction are important measures when determining whether the enhanced screening would have buy-in from parents and

physicians, which in turn can more broadly impact public health usability. Additionally, the difference between the modalities showed a statistically significant difference (P=.005) in the number of children classified as being at risk. The web based M-CHAT classified 3 % as at risk, and the paper M-CHAT classified 10% at risk. This could potentially be due to the increased completion of the follow up portion of the web based M-CHAT-R/F. The follow-up portion of the M-CHAT-R/F reduces the false positive rate and is essential to the accuracy of the M-CHAT-R/F(Robins & Dumont-Mathieu, 2006). This is evidence that web based M-CHAT-R/F screening will aid in controlling over referral as a means to reduce the burden on specialized professionals and increase access to early intervention services for those accurately diagnosed.

The literature review revealed that there is substantial evidence that the web-based modality strengthens the utility of the M-CHAT-R/F. By comparing the different attributes studied in the literature, it is apparent that screening children for ASD, when using a web-based modality, reduced high sensitivity (over referral), increased PPV (children referred who were later diagnosed with ASD), increased user satisfaction (filling out the M-CHAT), and increased completeness for follow up in various studies (Table 2). However, it is important to note that each variable was not examined within each study. Additionally, two of the web based modalities utilized mobile technology (tablets in waiting room).

Implementing machine learning alongside the ADOS substantially reduced the number of behavioral markers needed to accurately diagnose ASD, from 29 to 8 (Wall et al., 2012). The selected algorithm, for each individual module, further enhanced diagnostic timeliness, while maintaining sensitivity, specificity, and accuracy (Wall et al., 2012) (Table 2). This has potential to significantly reduce the 13-month timeline from evaluation to diagnosis, not including the time between screening and referral. However, this did not solve barriers due to geographic

locations, especially for those living in rural areas, that compounds the large gap between concern and diagnosis (Reese et al., 2013). Utilizing telemedicine as a means to enhance diagnostic assessment using the ADOS was reviewed by Reese et al. where it was determined that when assessing for ASD through the use of interactive video conferencing, on average across all of the ADOS items, the same result was achieved as in person assessment 71.07% (SD =12.74) of the time. This result is further evidence that telemedicine has the potential to be utilized to bridge the gap between providers and those needing diagnostic assessment, as the results were not significantly different across modalities (in person versus video conferencing).

Tables

Table 2: Represents measurable outcomes to support use of technology for ASD screening and diagnostic assessment.

Reference	Outcome
Brooks et al., 2016	Data analyzed using Statistical Package for Social Sciences (SPSS). Paper based M-CHAT-R/F (n=2042), web based M-CHAT-R/F (515). No significant difference based on modality (paper M = 1.41, SD = 2.05; web based M= 1.33, SD = 1.86), P=.46. Significant association with screening modality and missing data at the Follow-up screening, $\chi 2(1, N = 427) = 32.11$, P< .001. Paper based resulted in 35.1% missing follow-up, web based resulted in 3.1% missing follow-up. 58.5% increase in number of cases screened per month when using web based screening versus the paper based screening, which is larger than what would be accounted for by an 8.5%.
Campbell et al., 2017	Accuracy increased for screening results from 54% to 92% (38% increase, 95% CI 14%-64%). Appropriate action increased from 25% to 85% (60% increase, 95% CI 35%-85%). 90% of physicians rated using the digital version as an improvement from the paper version and improved assessment.
Corsello et al., 2013	ADOS had strong specificity and sensitivity for Autism vs. Not Autism and ASD vs. Non Spectrum
Harrington et al., 2013	Electronic M-CHAT-R/F (n=176), paper M-CHAT-R/F (n=197). Retrospective review used for the paper modality comparison. The electronic screening "at-risk" frequency (3%) was significantly different from the paper screening (11%). 99% of parents completing the electronic screening rated it

	as " good" or "excellent". The electronic screening lowered false at risk screens and false not-at-risk screens. Parent's user satisfaction was higher for the electronic version than the paper version.
Kosmicki et al., 2015	Module 2: 9 of 28 behaviors sufficient to detect ASD risk with 98.27% accuracy using Logistic regression algorithm, 98.9% sensitivity, 98.58% specificity. Module 3: 12 of the 28 behaviors are sufficient to detect ASD risk with 97.66% accuracy using LibSVM algorithm. 100% sensitivity, 98.9% specificity. Greater than 55% reduction in the number of behaviors with negligible loss of accuracy.
Reese et al., 2013	Ratings were compared between in person raters (InP) and videoconference (IVC) rates. No significant difference in reliability of diagnostic accuracy, observations, or parent satisfaction when using videoconferencing for the ADOS. All items on the ADOS were not significantly different, when compared using Z-tests for each item, except for item A7 ($z=2.6$, $p=0.009$) between InP and IVC. When both raters were in the same setting(InP vs InP; IVC vs IVC);(72.24%; SD=11.55%), their average agreement across all items, did not differ significantly from when raters were in different settings(InP vs IVC); (71.07%; SD=12.74%).
Robins et al., 2014	Children whose total score was ≥3 initially and ≥2 after follow-up had a 47.5% risk of being diagnosed with autism spectrum disorder (ASD; confidence interval [95% CI]: 0.41–0.54) and a 94.6% risk of any developmental delay or concern (95% CI: 0.92–0.98). This did not include follow up portion of screening. Children were diagnosed 2 years younger than the current national average age of diagnosis.
Sturner et al, 2016	The goal of this study (N=98) was to evaluate the feasibility, validity, and reliability of the M-CHAT/F by PCPs with online prompts at the time of a positive M-CHAT screen. PPV improvement from M-CHAT alone (0.77; [95% CI]: 0.68-0.85) to M-CHAT with follow up (0.90; [95% CI]: 0.84-0.96); P=.0. Reduced false positive screens by 71%. Primary care pediatricians aided by electronic decision support during routine well-child care, yielded results that are as accurate as, and timelier than, those produced by specially trained clinicians.
Wall et al., 2012	Module 1: 8 of 29 behaviors sufficient to detect ASD risk with 100% accuracy using ADTree algorithm, 100% sensitivity, 94% specificity.

Discussion

Introduction

All of the methods examined throughout this review have the potential to reduce the gap in service that increases time between initial concern and diagnosis. However, it is important to note that more research needs to be done. Screening, diagnostic assessment, and access to early intervention services are not currently able to keep up with the modern world. Using technology has shown beneficial to expediting current processes. Once further research has built upon the current knowledge base of aforementioned methods, implementation could potentially transform the continuum of care for ASD.

Key Findings

There are two key aims to be achieved by this thesis as a means to reach the overall goal to better understand how integrating technology with traditional ASD practices can increase access to early intervention services. The first aim is to answer the question of "Are healthcare providers using technology to increase completeness and accuracy of ASD screening and diagnosis?" The second aim was to answer the question of "Are healthcare providers, that use integrated technology for ASD diagnosis, able to screen, evaluate, and diagnose for ASD at a younger age when compared to healthcare providers that use traditional modalities?" To achieve these aims, a literature review was conducted.

Screening, using the M-CHAT-R/F was examined to better understand how technology can enhance timeliness, completeness, and accuracy. Throughout the studies that compared the

web based/electronic version of the M-CHAT-R/F with the paper based modality, technology did in fact improve timeliness, completeness, and accuracy. Importantly, user satisfaction appeared to increase with the ease of use of the electronic version. Although user satisfaction increased when utilizing the web based modality, parents often found it difficult to fill out the survey when holding their child in the waiting room or having to place their children in their lap. This is an incentive to have physicians refer parents to the links to use on their mobile phones, and then they could fill it out at their leisure.

Machine learning alongside the ADOS showed evidence for increasing timeliness by requiring less behavioral identifiers to accurately predict ASD diagnosis, without reducing accuracy. The ADOS is a time and resource intensive process, but when the proper algorithms were implemented, time and resources needed were reduced(Wall et al., 2012). Additionally, when utilizing videoconferencing for means of ADOS observation, logistical and geographical limitations were reduced while maintaining accuracy. The ADOS is limited by the need for a specialized professional to perform the assessment, the time it takes for the assessment, and wait lists due to resource limitations. Implementing machine learning and videoconferencing with ADOS processes reduced limitations imposed by lack of specialized professionals, logistical, geographical, and time intensive limitations.

Timeliness, completeness, and accuracy are important measures to assess, as they are key performance indicators in public health surveillance (Jajosky & Groseclose, 2004). These performance measures are important when evaluating screening and diagnosis for the time it takes to screen and evaluate children at risk, completeness of screening and diagnosis, accuracy of ASD risk, and referral for early intervention services following; as well as, in terms of data

collection. Data collection is important for informing public health programs by monitoring trends, identifying high risk populations, and monitoring early intervention effectiveness(Jajosky & Groseclose, 2004). By increasing timeliness, completeness, and accuracy of information collected for ASD diagnosis as a means to accessing early intervention services, public health can make better informed decisions and better tailor programs to reduce the bottleneck effect in the public sector, as well as, improve potential quality of life for those with ASD throughout the US population.

Ultimately, reducing the time involved with screening and diagnostic assessment, increases access to early intervention services. This literature review has shown how technology not only able to reduce diagnostic timelines, increase completeness, and accuracy, but also it has shown how technology can enhance user experience of the processes involved. By increasing user experience of the processes involved, buy in subsequently increases. User acceptability is vital to increasing support for both research to validate processes involved and future implementation. Technology has shown to be a potential solution to increasing access to screening, diagnostic assessment, and early intervention services; which has a positive impact on the health of communities and strengthens the knowledge base of how informatics improves public health.

Limitations

The literature review was somewhat limited when finding relevant material for informatics solutions and ASD. This limited the amount of review that was able to be done in reference to technology used to enhance ASD screening and diagnostic assessment methods. Of the

information that was available, limitations to the amount of research concerning rural populations was apparent. It is important to note that increasing access, is only being assessed for those with access to a primary care physician and/or to cellular service/internet connectivity. Individuals that do not have access to health care, regardless of locale, will not benefit from the use of technology; as well as, individuals who do not have access to Internet connectivity, will not benefit from the use of technology to solve logistical and geographical barriers.

Social desirability bias is a limitation when reviewing self reporting tools, such as the M-CHAT-R/F. Web based modalities depersonalize the questionnaires, such that, respondents feel they can be more candid in their responses (Aday & Cornelius, 2006). This allows the web based modality to retain the benefit, while the parents may perceive this as less personal and respond the same or more honestly(Yama, Freeman, Graves, Yuan, & Karen Campbell, 2012). Although the potential for social desirability bias must be addressed as a limitation to the differences in the paper and web based modalities, it is believed that the impact was minimal, as was evidenced by Brooks et al. which saw no significant differences in screen-positive rates based on modality alone.

A limitation to implementation of machine learning alongside the ADOS, is acceptability as well as the issue of implementation science. Implementation science can be defined as “the use of strategies to adapt and use evidence-based interventions in targeted settings to sustain improvements to population health”(Lobb & Colditz, 2013). Parents may be less likely to accept a diagnosis delivered by the use of an algorithm, regardless of accuracy being 100% for module 1. An algorithm, although able to make the same diagnosis requires complete and accurate data, therefore, is only useful when all of the information has been acquired and entered accurately

and in its entirety. This creates the potential for parent hesitancy, such that, they might question the validity of the data. The need for the physician will remain essential in ASD screening and diagnosis, as they play a critical role in follow up interview and relaying diagnostic results, which also may reduce parental hesitancy. Implementation science is essential to understanding how to strategize the discussed solutions to apply methodologies on a broad basis and impact population and public health. Evidence of the benefits of technology as a means to improve ASD practices and their impact on population health is a limitation at this time and is a potential issue for acceptability. Learning how to better implement these methodologies will be essential in future research and uptake of these technological solutions.

Implications

The solutions discussed throughout this literature review have the potential to help lay the groundwork to create informatics solutions for other public health programs, as well as, improve population health (group of children with ASD and the individual lives among the group). Public health informatics often builds comprehensive frameworks which then can be applied to additional areas, as long as there is applicability, support and end user buy-in. Following further examination and research to build the evidence surrounding the proposed solutions, potential implementation strategies must be examined. Public health informatics involves seeing the individual components (i.e. web based screening, machine learning w/ diagnostic assessment, video conferencing) while being able to see the big picture (increasing access to early intervention). Should the solutions discussed become widely accepted, their applicability to other programs, as a means to better public health as a whole, would be important to examine. By

building the knowledge surrounding public health informatics as it relates to ASD screening, diagnostic assessment, and early intervention services-- additional programs could benefit by reviewing the literature and utilizing transferable applications to enhance their public health programs. As technology continues to evolve it is vital to public health to leverage solutions to transform methods involved to reach programmatic objectives more efficiently.

Recommendations/Next Steps

The methods described throughout the literature review have shown potential for enhancing ASD screening, evaluation, and diagnosis when integrated with technology. Utilizing all three methods (mobile, web based M-CHAT, ADOS w/machine learning, and telemedicine for observation) has the potential to create a systematic solution to reducing age of diagnosis. All of the individual components have shown to be positively impacted by the use of technology. Employing all of the discussed solutions as an interdependent system could potentially further solve timelines between the steps to diagnosis. If screening, diagnostic assessment, and referral for services were employed in a system that is interdependent, alerts could trigger the next step involved in diagnosis. An informatics system employing all of the processes would allow members of a multi-disciplinary team to be informed of all steps and where the patient was in the process-- possibly increasing efficiency through increased knowledge/data sharing. It will be important for the solutions to have the ability to integrate with existing electronic health records (EHR) that are utilized by providers. Integrating all solutions into an EHR network would enable greater data sharing and collection possibilities to further enhance the continuum of care and public health. Reducing the wait time from initial concern to receipt of diagnosis is the main

issue identified discussed in this review, but how data can be collected and utilized to increase the knowledge base and to better inform decisions would be the next step.

Conclusion

The first aim of the review was to determine if healthcare providers are using technology to increase completeness and accuracy of ASD screening and diagnosis. Review determined that--no, health care providers are not using technology to increase completeness and accuracy of ASD screening and diagnosis. However, review found that *when* technology has been used alongside current screening and diagnostic assessment processes, completeness and accuracy does increase. The second aim of the review was "Are healthcare providers, that use integrated technology for ASD diagnosis, able to screen, evaluate, and diagnose ASD at a younger age when compared to healthcare providers that use traditional modalities?". It was determined that those who used technology, although a limited number, were able to screen and evaluate children at a younger age compared to those who used traditional modalities. However, it is important to note that the review did not determine whether age of diagnosis was ultimately reduced. The caveat of this determination is that the number of providers using technology to screen and evaluate children for ASD diagnosis is extremely limited. However, based on the information that was collected it is evident that technology does reduce the time involved with current processes and reduces barriers that increase delays. The evidence found by researching the key aims provides substantial support for accomplishing the overall goal to better understand how integrating technology with traditional ASD screening and diagnosis practices can increase access to early intervention services.

Providers used technology as a means to speed diagnosis and provide increased access to

early intervention services for children. This was done by implementing web based screening, machine learning with diagnostic assessment, and telemedicine (video conferencing). All of these solutions provided support for how technology can increase access to early intervention services. Web based screening, in conjunction the M-CHAT-R/F, demonstrated how technology could simplify a current process. The paper based M-Chat requires humans scoring, which introduces the potential for error. The electronic M-CHAT is automatically scored, and therefore, does not incorrectly score a child as "at risk", unless determined not at risk through follow up interview. This reduction in the number of children incorrectly being referred would create a reduction in children who are being screened a second time, lessening the wait time between screening and diagnosis because there wouldn't be such an influx of children needing to be unnecessarily screened.

Mobile devices, such as tablets and smartphones, enable parents to access M-CHAT screening either on their phone before the appointment or in the waiting room at the physician's office on a tablet. Providing the tablet version of the M-CHAT ensures access for those who do not have a smart phone or Internet access at home. Providing the mobile, web-based version allows for increased completeness, flexibility, and accuracy (reducing human error by parent and provider). Providers who used web based screening with automated risk assessment were able to accurately and completely identify children at risk for ASD at a younger age than those who do not (Harrington et al., 2013). The average age of those diagnosed in the United States is 4.5; whereas, the average age of diagnosis for those included in studies using a M-CHAT-R/F is 2 years below the average age in the U.S. (Robins et al., 2014). However, the average age of diagnosis, using the web based M-CHAT cannot be determined at this time.

Machine learning enhanced current practices for diagnostic assessment of ASD using the

ADOS. Although the current practices are shown to be effective, they are time consuming and prohibitive(Wall et al., 2012). Using machine learning alongside the ADOS achieved high classification accuracy utilizing only a small subset of the behavior items. Machine learning algorithms were able to reduce the number of items that needed to be scored while maintaining accuracy and a low rate of false positives(Wall et al., 2012). By reducing the number of items that could potentially need to be on the ADOS module exam, the time involved in the activities of the exam could subsequently be reduced. Machine learning has shown to be a suitable enhancement to the ADOS for diagnostic assessment, but needs further examination for how algorithms can be refined, potentially leading to more rapid results in the future.

In conclusion, technologically enhanced ASD screening and diagnostic assessments create an opportunity for both providers and individuals to facilitate increased access to early intervention services. The role of the individual among the group of those affected is important in better understanding how to improve ASD throughout the population. Population health not only examines the group of individuals affected, but also those within the group. Better identifying how to improve the potential outcomes for the individual in the clinical setting is useful when determining how to strategically improve the health outcomes of the population, as those in the public sector require are disproportionately affected. Increasing evidence through data collection will enhance public health programs by increasing the knowledge used to inform decision makers. ASD is regarded as a public health challenge and therefore, needs to be addressed on a small and wide scale to determine the best possible solutions that influence outcomes. By increasing evidence through data collection that supports the use of technology, acceptability will potentially improve and the applicability to the population level will as well. This review shows how increasing use of innovative technologies within current practice can

increase screening, improve diagnostic timelines, and reduce barriers to care. Further utilizing technology to close the gap between time of initial concern and diagnosis is essential to facilitating early intervention as a means to improve long term prognosis in today's fast paced world. Additional research needs to be done to validate proposed methods; as well as, discover additional optimizations. The ability of informatics to improve ASD diagnosis, from screening to early intervention, is evident. The applicability of the proposed solutions to public health are apparent through evidence based research, however, further research must be conducted to further validate potential solutions to overcoming the ASD public health challenge.

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