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To Screen or Not to Screen for ASD Universally is Not the Question: Why the Task Force Got it Wrong

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There is widespread agreement across the American Academy of Pediatrics (AAP)^{1, 2}, expert panels^{3, 4}, parents and autism advocacy organizations⁵, as well as the U.S. Department of Health and Human Services Interagency Autism Coordinating Committee⁶ that early identification and intervention for toddlers with autism spectrum disorder (ASD) is a very high public health priority and that universal early screening in pediatric populations is an essential tool for early ASD risk detection. The AAP guidelines to implement universal early screening for autism¹ as standard of care is one of the most positive and successful public health policies ever created for children affected by autism. Indeed, such a policy has led to the regular detection and treatment of autism by the 2nd birthday in cities with systematic screening programs^{7–11}. Early screening by pediatricians is becoming commonplace in the US and is objectively successful³. Studies show that using standardized screening tools is the most accurate approach to early at-risk autism detection, even as compared to pediatrician judgment and surveillance^{12, 13}. Private and public resources and research have together resulted in the development of early screening approaches that, when implemented, can detect ASD 2–3 years sooner^{7–11} than the national average of 4 years of age¹⁴. Implementing ASD screening as standard-of-care is particularly important for children from low SES and minority backgrounds who are consistently overlooked and under-detected and as a result have a later age of first diagnosis and delayed access to services relative to other children¹⁵. Early detection importantly allows for intervention to begin earlier, which is considered essential to achieving the best outcomes^{16–18}. Research

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suggests that individuals with positive outcomes, including gains in IQ, adaptive skills, and reduction in ASD core symptoms, as well as those with optimal outcomes who no longer meet criteria for ASD over time, are more likely to have been identified and treated before age 3 years¹⁹.

In the midst of this major accomplishment and advance over the past when ASD children commonly went undetected and untreated for years across childhood, the US Preventive Services Task Force (or Task Force) released its own views about early universal screening for ASD.

The US Preventive Services Task Force Recommendation Statement

Earlier this year, the USPSTF, referred to here as “Task Force”, released a report on ASD screening that stated: “Current evidence is insufficient to assess the balance of benefits and harms of screening for autism spectrum disorder (ASD) in young children for whom no concerns of ASD have been raised by their parents or a clinician²⁰.” In essence, the Task Force failed to recommend universal screening for ASD in the general pediatric population, because it claims there is insufficient evidence of its benefits (but later admits its “harms” are minimal). Additional details regarding the Task Force report are summarized in Figure 1.

The Task Force statement about “harms”

The statement carries the sense that universal early screening may actually do harm since the noted benefits do not outweigh “harm.” Yet, at the same time, the Task Force notes that early universal screening has been repeatedly demonstrated to be effective in detecting ASD (see³) and in fact does little to no harm. The report states: “The USPSTF found that the harms of screening for ASD and subsequent interventions are likely to be small based on evidence about the prevalence, accuracy of screening, and likelihood of minimal harms from behavioral interventions.” Surprisingly, the potential benefits of universal ASD screening, as we illustrate in Figure 2, was not fully considered in the report.

The Task Force statement about “benefits”

The Task Force did not clearly define what it meant by benefits, improvement, and outcomes. The Task Force suggested only vague metrics of changes in educational, behavioral, functional or IQ measures in order for them to pronounce that the “evidence is sufficient.” In reality, the potential benefits of ASD early identification and treatment range from tangible and easier to document impacts such as changes in IQ or social behavior, to more systemic changes that may impact the health, functioning, and well being of the entire family unit (see Figure 3). Truly understanding treatment response and outcome in ASD is thus a complex issue because, beyond the treatment itself, outcome is related to a range of factors including a child’s underlying genetics as well as family, educational, social, economic and cultural environmental factors. Precision medicine that takes such information into account is only beginning to be considered in ASD²¹. Improvements can happen both proximally and distally: in social engagement, school preparedness, language expression, language reception, and in the child’s everyday life experiences at home and in public places and school. All such improvements are legitimate changes in response to treatment. Changes

are also moderated by changes in stress levels for both the child and parent that change as the result of success (or failure) in response to treatment. It is through this complex lens that the benefits of early detection and subsequent treatment should be considered along with the acknowledgement that many of the potential impacts of early treatment are not easily or quickly captured.

Furthermore, ASD is a complex, heterogeneous disorder and the potential benefits of early detection and subsequent treatment are equally complex and heterogeneous. For example, the report does not delineate which autism subgroups would suffice as evidence that early identification and treatment has benefit. Those with low IQ or high IQ; those with known genetic abnormalities or those without genetic abnormalities; those with only verbal deficits; or those with verbal and nonverbal deficits; early onset or later onset autism, or all individuals with autism? ASD biological and phenotypic heterogeneity is considerable^{22–26}. Some individuals possess good verbal skills and may go to college, while others may remain nonverbal their entire lives²⁷. Some have rare genetic mutations with strong biological impact, while others do not²⁸. Some children with ASD may show normal visual attention levels to social images, while other may show highly abnormal attention levels²⁹. It is thus not surprising that in response to treatment, different biological, genetic, and behavioral subgroups show different outcomes. In one recent study only toddlers with low levels of object interest at baseline showed changes in communication ability post treatment³⁰.

The Task Force statement about “children for whom no concerns have been raised by their parents or clinical provider”

The Task Force report, as per its mission, focuses on “children for whom no concerns have been raised by their parents or clinical provider.” Whether intended or not, this phrasing may lead to the impression that universal screening may wrongly identify autism before it exists, begins, or has caused a visible challenge for the child or family. Just because a toddler has not yet been understood by parents and pediatricians to have autism, does not mean the child does not already have autism. In general population based screening research³¹ as well as research by others that utilize baby sibling cohorts³², ~80–100% of toddlers identified as ASD at very early ages (12–24 months) retain that diagnosis across longitudinal follow-up.

The selective focus on children for whom no concerns have been raised also implies that toddlers identified as having ASD via universal screening are in some way different from toddlers identified via parent and pediatrician concern. Currently, aside from the fact that they are generally younger³³, there is no scientific evidence to suggest that ASD toddlers detected via universal screening are clinically different than other ASD toddlers. For example, in a universal screening study⁷, toddlers identified as ASD in the general population around age 17 months were found to have a mean total score of 16.8 on the Autism Diagnostic Observation Schedule (ADOS), which signifies fairly symptomatic levels of ASD. This high ADOS score is in alignment with scores from other studies wherein toddlers were identified not based on a general population screen, but on parent or physician concern (i.e., “clinic referral sample” see³⁴). Another screening study directly compared toddlers that were referred for evaluation based on detection through universal screening to toddlers referred based on clinician concern. Results indicated equivalent ADOS scores at

the time of intake between both groups of toddlers³⁵. Thus, current research illustrates that children identified through universal early screening are not more or less symptomatic than children identified by parent or clinician concern.

It is also important to keep in mind that screening tools were designed to aide non-expert clinicians in quickly determining if there is a developmental concern, and by definition, should identify delays prior to parent or clinician concern. As we mention elsewhere in this article, pediatricians are not consistently able to detect ASD when it is in fact present^{12, 13}. Ignoring this fact creates confusion regarding the purpose and utility of screening tools and undermines the interpretation of research regarding screening tools. The purpose of screening is to increase the efficiency of early identification in clinical practice.

The Task Force research recommendations

Research recommendations focus on determining whether or not the very early identification that is achieved via universal screening is associated with improved health outcomes. Several designs are proposed such as randomized clinical trials (RCTs) comparing outcomes in early screened and identified children to outcomes in wait-listed, less intensely treated, or “alternatively” treated children. Another suggestion includes using quasi experimental designs (e.g., step wedge design) in regions with low screening rates to compare early screening at 12 to 18 months with later screening or case-finding on educational, IQ, and other outcome measures at age 6 years. However, we contend that it would be unethical to randomly withhold early screening (which is accurate, easy, quick, inexpensive and can be done by anyone anywhere) or normal levels and types of treatment from some toddlers in a community while others in that same community get early screening, early identification, early services, and high quality early intervention. Furthermore, the simple and brief research suggestions in the report do not address the multiple complicating services and intervention issues discussed above having to do with heterogeneity, subgroups, different underlying biologies, and different family and environmental factors.

The Task Force missed a key clinical issue

A key concept in this discussion is that while universal screening is an essential step in the health care process for ASD, it merely creates the opportunity for early treatment and services. Screening in and of itself does not determine the quality and benefits of such treatment. Some early screened and identified children get into treatment quickly, while parents of others are reluctant to act; some early screened and identified children opt for high quality, evidence-based ABA treatment, while the parents of others opt for alternative therapies with unknown impact. Many parents, regardless of how their child was first identified, find the services and intervention landscape daunting and often somewhat confusing; parents follow diverse paths. The most important issue, therefore, is not screening, but what happens next. Thus, the Task Force is sending the country in the wrong direction down a path of experiments of screen vs non-screen, or early vs late screened, instead of the right direction which is research identifying clinically useful and practical services and interventions tailored to the diverse and yet specific needs of early identified toddlers based on biological subtypes; behavioral, cognitive, social and language symptom level and abilities; and a child’s family, community, and cultural beliefs. In short, missing in

the report and the field at large is clinically translatable research on services and interventions that aim to maximize the outcome benefits of early identification for the heterogeneous ASD population.

Conclusions about the Task Force report

The overall tenor of the report implies that health care policy on early universal screening should be held in question until extensive research resources are expended that compare outcomes of screened and non-screened (or late screened) children. However, the proverbial horse is out of the barn: Early screening is commonplace in the US (approximately 50% of pediatricians use standardized screening tools at well-baby visits to detect ASD³⁶), and is objectively successful³. Early screening is largely accurate, easy, quick, inexpensive and can be done by anyone anywhere; important help and services can begin early for identified toddlers and young children. The Task Force's non-endorsement of universal early screening could unintentionally have a chilling effect on this major accomplishment. Withholding or delaying universal early screening from toddlers in order to satisfy vague research ideals is considered by many to be untenable³⁷.

An Expanded View of the Benefits of Universal ASD Screening

Results from molecular and postmortem studies provide striking evidence that the biology of autism begins in prenatal and early postnatal life³⁸⁻⁴². Numerous genetic⁴³⁻⁴⁸, genomic⁴⁹, and animal model⁵⁰⁻⁵³ studies also underscore this early biological onset of autism. After birth, pediatricians and family medicine practitioners are commonly the first professionals to encounter autism as the symptoms slowly reveal themselves with increasing clarity across the next 2 years of life^{54, 55}. Prospective and retrospective studies find that in some cases warning signs are present by or even before the 1st birthday⁵⁶⁻⁵⁹. Universal screening therefore provides the opportunity to detect a disorder that is undeniably present and observable across the first 2 years of life.

In decades past, however, pediatricians and family medicine practitioners did not have access to reliable screening tools for recognizing autism risk in infants and toddlers, leaving many children undetected and untreated often for years. For example, the California Department of Developmental Services released a report noting that children with ASD born in 1987 started receiving treatment services around age 7 years⁶⁰. Another study published 10 years ago noted that only 8% of pediatricians systematically screened for autism⁶¹, citing a lack of access to reliable screening tools as a primary reason⁶¹. Parents were often frustrated and confused by the lack of answers and support from professionals, and had few resources to help their child⁶². Moreover, without systematic early identification, researchers could not easily study early development and devise novel early treatment approaches, dramatically slowing the pace of early treatment research. Indeed, in a review of published early intervention studies across a 9-year period from 1998 to 2006 for children ages 5 years and younger, researchers found only a meager 22 studies, averaging approximately 2.4 studies per year⁶³.

Fortunately this bleak situation changed considerably in the past decade as remarkable progress has been made in early screening and detection of infants and toddlers in the

general population^{3, 7, 9–11, 64}. Research has demonstrated that ASD can be detected as young as 12 months^{7, 65}, and routinely by 18–24 months^{9, 10, 66} using parent report screening tools at well baby check-ups. In fact, one cohort of toddlers with ASD detected using the Communication and Symbolic Scale Developmental Profile Infant/Toddler Checklist (CSBS DP IT Checklist)⁶⁷, an early developmental screen (i.e., a “broadband screen”) that detects delays in social communication, expressive and receptive language and symbolic functioning, began receiving behavioral treatment by age 17 months⁷.

Routine Screening for ASD Facilitates Detection of All Delays

Although developed in the spirit of ASD detection, most screening tools are also highly accurate at detecting general developmental delays. For example, when the Modified Checklist of Autism in Toddlers Revised (M-CHAT-R) is used with a follow-up interview further probing parents about responses, the positive predictive value is ~0.45 for ASD specifically, but >0.90 for all developmental delays including ASD^{9, 10, 68}. In other words, a failed score is a valid cause for a concern of developmental delay. Within this context, the risk of false positives is low, resulting in relatively few unnecessary evaluations or undue parent stress, as some type of early intervention service is likely warranted and beneficial. Recent research has also suggested the use of general developmental screening (e.g. PEDS or ASQ) to assess for a range of developmental delays, with the use of an autism specific instrument as a second tier screen for children that fail the initial general development screen may be a useful approach to accurately target autism screening within busy pediatric settings^{69, 70}.

Screening is Rapid and Simple

Most screening tools are easy, relatively quick, and cost-effective to implement in ordinary community settings. For example, both the CSBS DP IT Checklist and the M-CHAT-R can be completed by parents in approximately 5–10 minutes^{7, 9, 11}. Additional time (~10 minutes) could be required to further probe failed positive screens (about 8% of all cases screened), as is currently recommended as best practice with the M-CHAT-R¹⁰. These additional interview minutes are an important step in the M-CHAT process in particular because such follow-up conversations considerably reduce false positives and open the opportunity for parent-clinician dialogue. Most parent report screening tools are available in multiple languages and easily implementable in underserved communities⁷¹. Their clinical value has been demonstrated and is currently billable. Thus, a child with autism can be screen-detected even by those who are not experts in autism and who might otherwise not recognize the presence of symptoms for months or years. This is extremely important as the prevalence of autism is now reported to be 1 in 68¹⁴ and screening is the easiest, quickest and most cost-effective means of identifying such large numbers by non-autism experts in pediatric and community health settings throughout the US.

Screening Improves Clinician Awareness and Knowledge

Following induction into a screening program, 87% of pediatricians reported that using a screening tool ultimately heightened their awareness of autism and developmental delays⁷. In that same study 96% of pediatricians reported that using a screening tool overall enhanced their clinical practice⁷. It is thus not surprising that standardized screening has been shown

to improve detection relative to clinical judgment alone. One study showed that when pediatricians rely on clinical judgment rather than formal screening to identify children at risk for ASD, as many as 50% of children with ASD who could have been identified on a positive screen at 18 or 24 months were missed. Thus, when only clinical judgment is used, most true toddlers with ASD will experience a potential delay in access to treatment¹³. In an experimental study in the Netherlands an early detection screening program was implemented and compared to a control site that relied on general surveillance and referral methods and found that the early screening program led to toddlers with ASD being identified 21 months earlier than cases from the control sites³³. In another study utilizing focus groups to understand what physicians need to do to improve well child care, physicians stated that formal screening with standardized questionnaires aids them in knowing when to prioritize developmental concerns⁷².

Screening Reduces Disparities in Access to Services

Unfortunately, in the absence of systematic screening, families from underserved populations are more likely to be evaluated and identified with autism at later ages than other children^{14, 15} resulting in a disparity in access to services. A survey of pediatricians in California found that most pediatricians felt Latino and African American families were less informed about ASDs than White families⁷³. Many pediatricians also admitted having more difficulty assessing children from primarily Spanish speaking families due to language and cultural differences⁷³. These findings are consistent with a recent study that conducted ASD screening in state licensed daycares serving low-income populations that led to the identification of ASD in 3% of the children (mean age of 50 months)⁷⁴. Importantly, *none* of these children had been previously identified. Fortunately, such disparities can be reduced by universal screening. For example, a recent study found that using one of several versions of the M-CHAT reduced the usual disparities observed in the age of first evaluations for underrepresented populations⁷¹. These data reinforce the idea that relying on parents to raise concerns or simple surveillance by physicians is not an effective method of identification and may have the most adverse consequences for the most vulnerable populations.

Screening May Strengthen Parent-Pediatrician Relationships

Using a standardized screening tool gives physicians a starting point for difficult conversations about delays in development and for responding to parent concerns. Proactive response to parent concerns by physicians can result in a 1 year reduction in age of treatment initiation according to a study of parental concern for autism⁷⁵. Often parents with concerns about their child's development experience stress when uncertainty and questions remain unaddressed by professionals⁷⁶. Most parents are greatly relieved to have an explanation for their child's behavior and it is not surprising that more rapid diagnoses are associated with higher levels of satisfaction in parents⁷⁷. In short, early screening improves standard of care for parents as well as children.

Screening Enables Interventions To Begin Far Sooner

The primary purpose of early screening is autism risk detection and referral for follow-up evaluation and rapid treatment. Screening and detection are independent of what happens next for the child and family. Thus, screening enables further steps to be taken but does not

determine what they will be. It is essential to separate screening success and treatment success. It is misleading for the Task Force to entangle screening and screening-related policy with the separate question of what happens next to the child with ASD and how successful different services and treatments may be.

Early screening does enable help, services and interventions to begin far sooner than was the case a decade ago. In fact, early screening studies in combination with increased autism awareness have ushered in a new era for services research aimed at improving a wide range of services and treatment approaches for ASD toddlers and their families that did not exist a decade or two ago^{78, 79}. Early identification of ASD has opened doors to resources and research aimed at developing novel early social and communication treatments^{80–82}, developing age-appropriate curriculum and assessments^{83, 84}, as well as developing early preschool peer inclusion programs⁸⁵. Such treatments have been demonstrated to improve cognitive and behavioral capacities in many individuals when started at early ages^{78, 79}. Early detection also has the capacity to impact family functioning by providing information that equips families to seek early support and parent training, raise community awareness, and ultimately increase understanding of how best to help toddlers and young children with autism and their families to improve long-term outcomes.

Thus, the rapid progress in research detecting and diagnosing ASD at earlier and earlier ages has opened up a wide range of important areas for progress and improvement in “what happens next,” ranging from improvements in the daily lives and experiences of affected toddlers and services for the child and parents to improvements in multiple ability areas and reductions in negative experiences and behaviors (see Figure 3).

Early Screening Improves our Ability to Understand Early Development in ASD

Evidence of ASD as a disorder with very early, likely prenatal (biological) onset, highlights the first few years of life as critical periods of development. Despite the crucial importance of this period in ASD, historically, scientists knew very little about the behavioral and biological development during the first years of life due to the absence of early screening and detection. In the past decade, however, early screening and detection approaches, such as the 1-Year Well-Baby Check-Up Approach⁷, have transformed early developmental research opportunities and provided a rich array of scientific and clinical information about early development in ASD^{86–89}. Many studies of very young toddlers with ASD have found unusual trajectories of brain growth^{87, 90–100} and axonal^{101–106} and functional connectivity^{107, 108} in multiple regions including the cerebral cortex, amygdala, cerebellum and striatum. Greater overgrowth of the amygdala in particular is related to worse social symptoms^{95, 109} and associated with circulating immune markers in toddlers with ASD¹¹⁰. Diffusion tensor imaging (DTI) studies¹⁰⁶ find evidence of excess axon connectivity and electroencephalogram (EEG) studies¹⁰⁸ excess functional over-connectivity very early, by the first year and second years of life; after that early age, there appears to be an abnormally slow rate of further axon development and greater connectivity abnormality tends to be associated with worse later ASD social symptom outcome. One new functional magnetic resonance imaging (fMRI) study of early language in ASD found strikingly reduced brain activation to speech in 1 and 2 year olds with ASD who later had a poor language outcome

by 3–4 years, but very strong brain activation to language at 1–2 years in infants with ASD with a later good language clinical outcome²². Such studies, and our now deepened understanding of the neural heterogeneity of ASD, its relation to clinical phenotype, and the promise of prognostic biomarkers, would not have been possible without the early screening program employed⁷.

In sum, the success of systematic early screening for ASD is clear, and the numerous benefits of early screening tools far outweigh the minimal harms (see Figure 2). This sound foundation of research and widespread professional and public acknowledgement of the importance and success of early screening has established early screening for autism as a public health priority and a standard of care for pediatricians.

Very Early Treatment Has The Greatest Potential To Alter Brain Function And Improve Outcome

One of the fundamental motivations for the early screening and treatment of autism is the knowledge that the human brain undergoes a profound period of establishing and refining neural connections during prenatal life and the first three postnatal years¹¹¹. These first three years, when autism can be detected and treatment started, are the single most transformative period in all of human postnatal brain development. Neural circuits grow from simple ones supporting only the most basic functions to astonishingly complex ones that rapidly enable higher-order cognitive, social, behavior, learning, and language abilities (see Figure 4). Ideally, detection and treatment should begin by or before this time. For example, synaptic density in the human prefrontal cortex, the brain region centrally involved in higher-order social behavior, doubles between birth and 1–2 years in age¹¹². Synaptic density in language areas, such as Wernicke's and Broca's areas, also doubles and peaks shortly thereafter by age 3 years¹¹³. The time period following a peak in synapse number is characterized by a phase of refinement where effective connections are strengthened, and weak ones die away. This important developmental step, namely the construction of specific adaptive neural circuits and the pruning of excess (unused or maladaptive) synapses, is thought to be largely dependent on input from the environment^{114, 115}. If an at-risk toddler is identified and behavioral treatment begins either before or while brain connections are being established, it is likely that brain function for that toddler stands the best chance of being optimized, rather than if treatment begins after mature but faulty circuitry is already established. It is for this very reason that the early identification and treatment of autism is essential.

Additional evidence highlights the importance of the first years of life as an optimal time window for early brain plasticity in human infants and toddlers. In a rare example, Nelson and colleagues (2007)¹¹⁶ studied the outcomes of infants reared in an impoverished institution in Bucharest Romania, some of whom were placed in foster care after various periods of time. Results indicated that institutionalized infants placed into foster care at an early age (by 18 months) had a mean developmental quotient that was 14 points *higher* than infants placed in foster care at later ages (after 30 months). The infants who were selected for either institutionalization or foster care placement were randomly selected and the main difference between the infant groups was the depth and complexity of environmental

stimulation (institution, low stimulation vs foster care, higher stimulation). Although ethical considerations prevent parallel studies in the field of autism, it is at least theoretically clear that treatment could have a massive, perhaps even a preventative impact if started at or prior to 18 months. However, treatment started at this early age can only be achieved if clear and standardized methods of early identification are systematically followed across the nation. Fortunately, as the Task Force statement acknowledges, there are scores of studies documenting that ASD can be detected reliably between 18–30 months in the general population^{9, 10, 117}, and new studies show it is even possible at 12 months^{7, 8, 11, 65, 118}.

Finally, the animal model literature clearly demonstrates that the mammalian brain undergoes enormous changes in response to environmental enrichment during early development¹¹⁹. New neurons can appear in the dentate gyrus in the hippocampus, a brain region critical for learning and memory^{120–122}. Synapse^{123, 124} and dendrite numbers can be increased¹²⁵, as can myelin density¹²⁶ and capillary volume^{124, 127}. In addition to significant changes in brain structure and morphology, social environmental enrichment has been shown to change social communication behaviors in animals as well¹²⁸.

Why is treatment started around the 1st to 2nd birthday ideal?

Starting treatment for ASD between 1–2 years is ideal for several reasons. First, as articulated above, new circuits, particularly in frontal cortex, are being formed rapidly during that time, generating the opportunity to shape effective connections while they are actually forming, rather than after many circuits are already formed such as at three years or later (see right side of Figure 4). Second, interventions for ASD prior to 1 year in age have not been empirically tested in large, randomly assigned samples. Thus 1 year is the youngest possible age that validated interventions could theoretically be implemented. Third, around the 1st birthday, an explosion of new skills emerge in toddlers: walking¹²⁹, talking¹³⁰, bi-manual manipulation of objects¹³¹, and engaging in shared attention with others¹³². In short, children become highly interactive with their environment and the people in it at this age, making them ready to engage in treatment, even those toddlers that have not mastered the aforementioned skills. Fourth, naturalistic, developmental behavioral interventions (NDBIs) such as Pivotal Response Training^{133, 134}, ESDM⁸³ and JASPER¹³⁵ are available for use, and ideally suited for the early treatment of toddlers with ASD. Such treatment approaches have demonstrated efficacy in young populations⁷⁹, are highly interactive, easily implemented in naturalistic settings such as the home or playground, utilize highly natural contingencies (e.g., offering access to a doll if a child says the word “doll”), and utilize shared control between treatment provider and child which enhances a toddler’s interest in engaging in activities. Such play-based naturalistic treatments are enjoyable for both parents and professionals alike - for more information about NDBIs, see¹³⁶.

Ongoing Treatment Studies Utilizing Toddlers with ASD Detected by General Population Screening

Randomized control trials provide evidence of improved outcomes of toddlers detected from the general population through autism screening^{137, 138}. For example, in a unique RCT pilot study, Baranek and colleagues followed sixteen families with a toddler at-risk for ASD

detected around the 1st birthday using a general population screening tool named the 1st Year Inventory¹³⁷. Toddlers were randomly assigned to a parent intervention named Adapted Responsive Teaching (ART), or referred to general community early intervention services. Level of community service uptake, changes in language and parent interaction styles were tracked. Results indicated greater utilization of community services in the control group, but greater change in child language and parent interaction style and improved social abilities in the ART treatment group¹³⁷.

In another RCT study, Wetherby and colleagues (2014) tracked treatment outcomes in a combined cohort: approximately half of the toddlers were those who failed a screening tool at their pediatrician's office, the CSBS IT Checklist, while the other half were referred due to parental or physician concern. The combined cohort received a diagnosis of ASD at a mean age of 19 months and subsequently randomly assigned to either an individualized or group based parent administered treatment¹³⁸. Results indicated significant positive change in social communication, receptive language, and other skills in toddlers who received the individualized treatment. Other RCT studies that contained toddlers under age 2 years, although not detected via screening programs per se, report encouraging positive changes following early identification treatment tailored to meet the learning styles and needs of the ASD population. One such study utilized the Early Denver Start Model (ESDM) that focuses on enhancing social interaction and language, among other skills, noted that not only were significant gains in developmental quotient and language skills found following treatment⁸³, but gains were also associated with normalized patterns of brain activity¹⁶. Specifically, toddlers with ASD that received ESDM treatment showed increased cortical activation when viewing faces relative to the toddlers with ASD that did not¹⁶. For a review of recent treatment studies see^{78, 79}.

Overall, current research continues to bolster the fact that standardized screening tools can detect ASD at very young ages, and that toddlers make substantial gains in early intervention. Again, it is important to stress that future research may be misguided in continuing to evaluate if early screening is beneficial relative to surveillance alone as recommended by the Task Force. Rather, the field is already in a prime position to discover ways to refine and individualize early intervention and further improve outcomes for early-detected toddlers with ASD.

Summary and Conclusions

The Task Force report concludes by “advocating for more research”, which is laudable. It also agrees with the field at large that early screening tests can detect ASD among children ages 18 to 30 months for whom there is no prior concern. The report also urges randomized clinical trials in order to more rigorously establish treatment effects, noting there are many types and modalities of treatment. Public opinion was acknowledged, although its impact on the report appears modest. It also acknowledged that recommendations of other organizations were largely in support of early screening, but noted that its United Kingdom counterpart, the UK National Screening Committee, explicitly does not recommend universal screening for ASD in children under age 5 years¹³⁹. The direct impact of such a myopic recommendation is unclear, but it is worth noting that the median age of ASD

diagnosis in the UK is 55 months, with only ~10% of children being identified prior to age 3 years - a statistic that largely hasn't changed across the past decade¹⁴⁰.

By contrast, the widespread concern in the U.S. for the health and well being of children with ASD and the recognition that it begins in the first years of life has led to a concerted effort to identify and help children with ASD and their families at early ages. There has been a sea of change: The past lack of awareness for and benign neglect of children with ASD and their families is gone and replaced by early screening, identification, help and treatment. Because of early detection and treatment a significant proportion of children with autism are now able to integrate within normal settings of school, grocery stores, and playgrounds.

The lack of Task Force support for this nearly national consensus effort should not diminish the effort or progress towards early detection via screening or other methods in general pediatric populations. Reducing the consistency of universal early screening will do far more harm than good for children with autism, parents and families, teachers, and pediatricians and other developmental health care providers. The Task Force report incorrectly implies that where there is no concern, there is no autism, and disregards the idea that screening tools are used to establish whether or not there may be developmental concerns. Such tools have been embraced by the medical community as evidenced by endorsement from the AAP¹. Simply relying on parent or pediatrician concern, places an alarming amount of responsibility on individuals that are not always experts in the area of autism. Adopting the use of a standardized screening tool allows for a routine procedure to assess for delays and start a discussion between the parent and provider about potential delays. The benefits and utility of standardized screening tools clearly outweigh the potential harms of waiting to identify ASD through non-standardized methods of surveillance.

If we apply the same yardstick of examining the ratio of benefits/harms to the Task Force that they have applied to universal autism screening, then it is incumbent on them to demonstrate that, on balance, waiting to identify ASD when it eventually comes to the attention of parents and practitioners is more beneficial than harmful as a standard of care. We assert that it is not. In fact, it could unintentionally encourage a lack of monitoring in the clinic that may ultimately do harm and offers little to no benefits.

We do agree, however, with the Task Force that RCTs have a valuable place in science and can be leveraged to understand the factors that lead to the best outcome in ASD. However, the right direction for ASD research is to conduct RCTs to compare different approaches for providing help, services, and treatments for autism at all early ages and regardless of how the child is identified –whether via an early screen, public awareness or a concerned pediatrician, parent or teacher. There is a critical need to enhance interventions (help, services, treatments) so they are tailored to varying age of initial clinical detection and autism subtype.

In sum, early screening is an effective clinical tool for early detection of ASD or risk for ASD. The benefits of early detection —whether via screening or other paths such as parental or professional concern— are many (Figures 2 and 3) and, contrary to the Task Force opinion, far outweigh harms. Early detection, regardless of method: (a) leads to early ASD

identification, treatment, and services, (b) increases physicians' awareness and knowledge of delays, (c) reduces disparities in access to services between low and high SES families, (d) facilitates treatment during a crucial and singular time of life when intervention could have the greatest impact on brain development, (e) can lead to important non-treatment ancillary services for parents and toddlers with ASD following early identification that they would not occur if early screening were to once again disappear, (f) is ethically required since the disorder is already in progress, can be detected, and effective treatments are available, (g) makes possible the RCT research we recommend on early interventions following early detection, (h) makes possible studies that elucidate the heterogeneous biological and behavioral development of ASD during arguably the single most important period in early postnatal human life, (i) makes possible discovery of early biomarkers of the disorder, prognosis, and treatment responsiveness^{22, 25, 29, 141}, and (j) through such biology and biomarker studies, may one day lead to identification of powerful biotherapeutics that target specific neural subtypes and biological mechanisms and/or identification of etiological factors and means of prevention.

Given the wealth of benefits of early detection, and as a result, access to early intervention, the lack of support for early ASD universal screening by the Task Force is incomprehensible. There is an obvious disconnect between the current research and the Task Force conclusion despite their acknowledgement that early screening can detect cases of ASD and that early intervention does lead to clinical improvement. The Task Force's narrow interpretation of the available literature because toddlers that participated in treatment studies were not necessarily detected as the result of screening, should be interpreted as just that: namely, narrow. Instead, it is imperative to continue and expand early screening in all communities, especially in those that currently have too few early services for toddlers with ASD, and provide all families with access to the best possible care.

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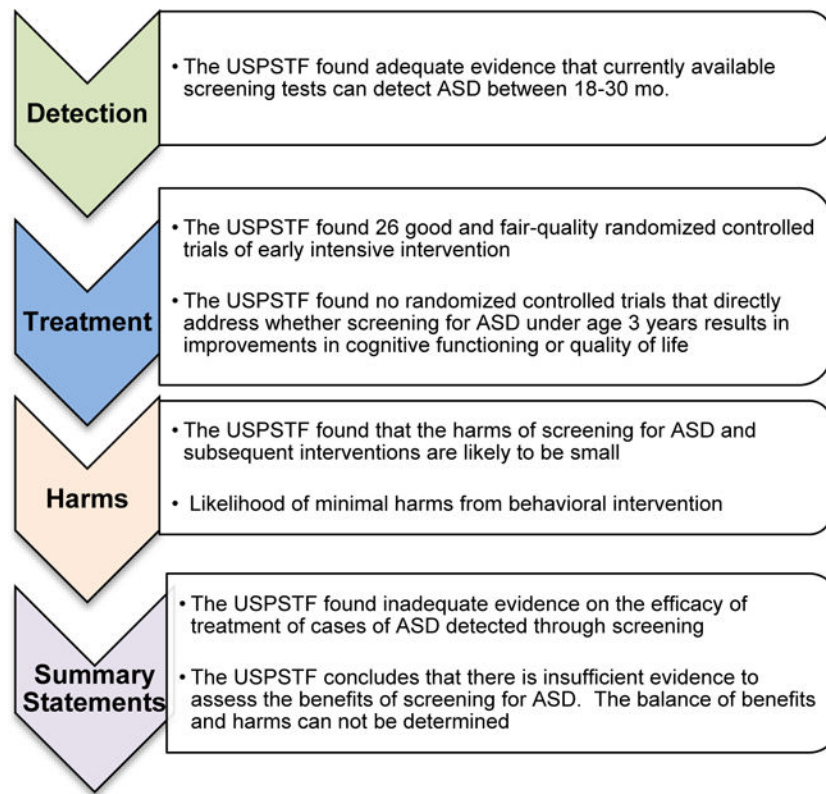


Figure 1. Overview of key features of USPSTF ASD Screening Recommendation Statement²⁰.

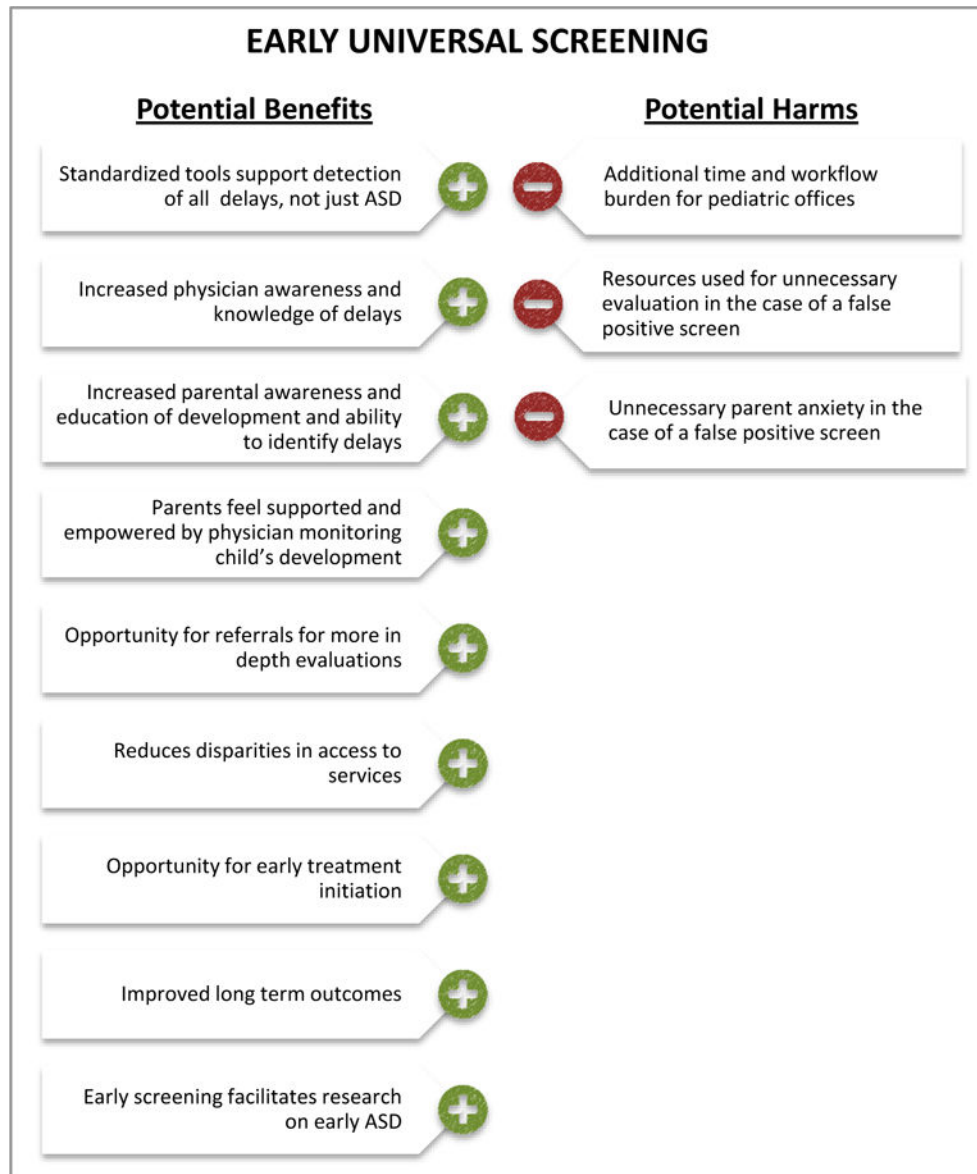


Figure 2. Illustration of the balance of potential benefits and harms of engaging in universal early screening for ASD. As illustrated in the figure, the potential benefits outweigh potential harm.

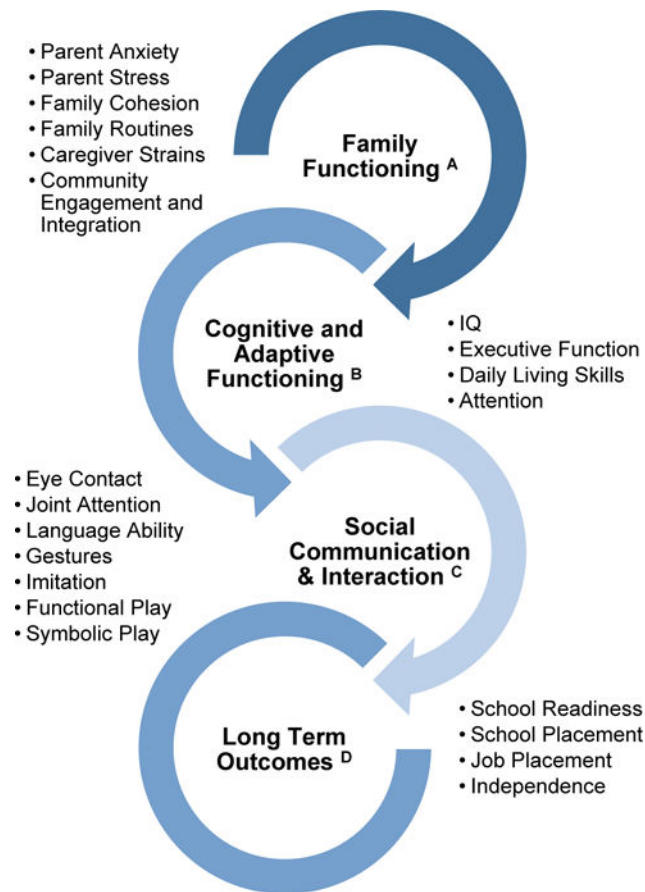


Figure 3.

Areas of known (B,C) and theoretical (A, D) improvement following early intervention. Early detection enables services to begin sooner which in turn leads to many areas of change for a child with ASD and their family. Early treatment can impact family functioning, the child's cognitive and adaptive functioning, social communication and interaction, and ultimately long-term outcome.

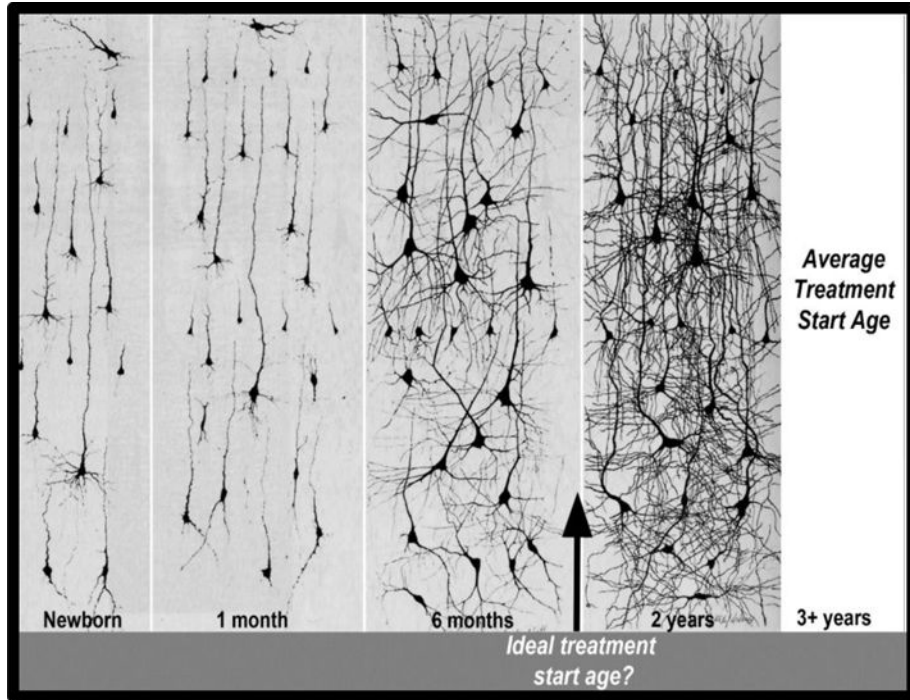


Figure 4. Golgi-stained sections highlighting the size and dendritic arborization of brain cells in the anterior portion of the middle frontal gyrus at different ages. As illustrated in the figure, the normal newborn has sparse neural circuitry, and then, with increasing age, there is a tremendous increase in the complexity of neural circuitry that is illustrated by the great increase of dendritic arbors from birth to 2 years. The figure highlights the ideal age for intervention might be prior to 2 years. The figure also highlights that most ASD children start treatment well after much circuitry is already formed. Adapted from Courchesne and Pierce (2005a) which was previously adapted from Nolte (1993), whose figure combined panels from Conel, 1939; 1941, 1951 and 1959.