

# Early Identification and Interventions for Autism Spectrum Disorder: Executive Summary

**AUTHORS:** Lonnie Zwaigenbaum, MD,<sup>a</sup> Margaret L. Bauman, MD,<sup>b</sup> Roula Choueiri, MD,<sup>c</sup> Deborah Fein, PhD,<sup>d</sup> Connie Kasari, PhD,<sup>e</sup> Karen Pierce, PhD,<sup>f</sup> Wendy L. Stone, PhD,<sup>g</sup> Nurit Yirmiya, PhD,<sup>h</sup> Annette Estes, PhD,<sup>i</sup> Robin L. Hansen, MD,<sup>j</sup> James C. McPartland, PhD,<sup>k</sup> Marvin R. Natowicz, MD, PhD,<sup>l</sup> Timothy Buie, MD,<sup>m</sup> Alice Carter, PhD,<sup>n</sup> Patricia A. Davis, MD,<sup>o</sup> Doreen Granpeesheh, PhD, BCBA-D,<sup>p</sup> Zoe Mailloux, OTD, OTR/L, FAOTA,<sup>q</sup> Craig Newschaffer, PhD,<sup>r</sup> Diana Robins, PhD,<sup>s</sup> Susanne Smith Roley, OTD, OTR/L, FAOTA,<sup>s</sup> Sheldon Wagner, PhD,<sup>t</sup> and Amy Wetherby, PhD<sup>u</sup>

<sup>a</sup>Department of Pediatrics, University of Alberta, Edmonton, Alberta, Canada; <sup>b</sup>Department of Anatomy and Neurobiology, Boston University School of Medicine, Boston, Massachusetts; <sup>c</sup>Division of Developmental and Behavioral Pediatrics, University of Massachusetts Memorial Children's Medical Center, Worcester, Massachusetts; <sup>d</sup>Department of Psychology, University of Connecticut, Storrs, Connecticut; <sup>e</sup>Graduate School of Education & Information Studies, University of California Los Angeles, Los Angeles, California; <sup>f</sup>Department of Neurosciences, University of California San Diego, La Jolla, California; <sup>g</sup>Departments of Psychology, and <sup>h</sup>Speech and Hearing Sciences, University of Washington, Seattle, Washington; <sup>i</sup>Department of Psychology, Hebrew University of Jerusalem Mount Scopus, Jerusalem, Israel; <sup>j</sup>Department of Pediatrics, University of California Davis MIND Institute, Sacramento, California; <sup>k</sup>Yale Child Study Center, New Haven, Connecticut; <sup>l</sup>Genomic Medicine Institute, Cleveland Clinic, Cleveland, Ohio; <sup>m</sup>Harvard Medical School and Massachusetts General Hospital for Children, Boston, Massachusetts; <sup>n</sup>Department of Psychology, University of Massachusetts, Boston, Massachusetts; <sup>o</sup>Integrated Center for Child Development, Newton, Massachusetts; <sup>p</sup>Center for Autism and Related Disorders, Tarzana, California; <sup>q</sup>Department of Occupational Therapy, Thomas Jefferson University, Philadelphia, Pennsylvania; <sup>r</sup>A.J. Drexel Autism Institute, Drexel University, Philadelphia, Pennsylvania; <sup>s</sup>USC Mrs T.H. Chan Division of Occupational Science and Occupational Therapy, Los Angeles, California; <sup>t</sup>Behavioral Development & Educational Services, New Bedford, Massachusetts; and <sup>u</sup>Department of Clinical Sciences, Florida State University College of Medicine, Tallahassee, Florida

## ABBREVIATIONS

ASD—autism spectrum disorder

DSM-5—*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*

M-CHAT—Modified Checklist for Autism in Toddlers

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Autism spectrum disorders (ASDs) are neurodevelopmental disorders characterized by impaired social communication skills and isolated areas of interest.<sup>1</sup> The current prevalence of these disorders is estimated to be 1 in 68,<sup>2</sup> and recent estimates of the risk of recurrence in families with at least 1 child diagnosed with ASD are 10% to 19%.<sup>3–5</sup> Advances have been made in identifying genetic variants that can account for biological vulnerability to ASD,<sup>6,7</sup> although recent studies examining patterns of heredity implicate environmental factors and potential gene-by-environment interactions.<sup>8</sup> Although the exact etiology remains unknown in most families, some researchers suggest that the pathogenesis of the disorder begins during prenatal life.<sup>9,10</sup> It is likely that ASD is heterogeneous in its etiology as well as in its clinical presentation.<sup>11</sup>

The American Academy of Pediatrics has recommended screening for ASDs at 18 and 24 months of age,<sup>12</sup> but recent research suggests that atypical behaviors may be detectable in some children at even younger ages.<sup>13,14</sup> However, we are still learning how the timing and developmental course of early ASD symptoms vary across children and how best to detect such symptoms across the continuum of children seen in community practice. In addition, reports<sup>15</sup> that early intervention can improve developmental and behavioral outcomes in infants and toddlers have lent urgency to identifying children across the autism spectrum at an earlier age. Advances in genetic, neuroimaging, and other neurobiological research have also raised the potential of biomarker screening. Given the progress in these areas, a review of the current state of the science on early identification, screening, and intervention of ASD was warranted.

These issues were the focus of an international, multidisciplinary panel of clinical practitioners and researchers with expertise in ASD and developmental disabilities. A meeting of the panel was convened in Marina del Rey, California in October, 2010, to develop best practice standards for early identification, screening, and early intervention for ASD in very young children and to identify priorities for future research. To complement previously published reports, our literature review on early identification and screening for ASD focused on children aged  $\leq 24$  months, whereas our review of intervention studies focused on children aged  $\leq 36$  months. The panel reached consensus in 3 areas:

- What are the earliest signs and symptoms of ASD in children aged  $\leq 24$  months that can be used for early identification?
- How can we optimize developmental course and outcomes through ASD screening programs for children aged  $\leq 24$  months?
- What interventions have shown efficacy in children with ASD aged  $< 36$  months?

## METHODS

Before the conference, participants were assigned to 1 of 3 working groups, each comprising 7 to 10 experts and focusing on the early identification of ASD, early screening, and early interventions and outcomes. The Early Identification group comprised Drs Stone, Yirmiya (co-chairs), Chawarska, Estes, Hansen, McPartland, and Natowicz. The Early Screening group comprised Drs Fein, Pierce (co-chairs), Baranek, Davis, Newschaffer, Robins, and Wetherby. The Early Intervention and Treatment Outcome group comprised Drs Choueiri, Kasari (co-chairs), Buie, Carter, Charman, Granpeesheh, Mailloux, Mesibov, Smith Roley, and Wagner.

To inform the work of each group, literature searches were conducted on Medline to identify relevant articles for each topic (the specific search terms are provided in the other articles in this supplement to *Pediatrics*<sup>16–18</sup>). Search results were complemented by additional publications identified by working group members. Although the search strategy was comprehensive, selection of articles was not systematic, which is an important limitation. A scoping approach, with some discretion by consensus of the multidisciplinary expert working group, was used instead to select articles of highest relevance and methodologic quality. Articles were assigned to working group members for review.

During the conference, each group presented a synthesis of the current literature and offered draft recommendations for discussion, modification, and ratification by all attendees. Electronic voting was used to express opinions and guide consensus building. A modified nominal group technique was used to review the recommendations, with consensus reached by  $\geq 1$  round of voting. A total of 18 to 21 participants voted on 28 statements, and 16 statements received solely agree or strongly agree votes. The number of statements was condensed

to 25 during the writing process. The first statement pertains to the literature review as a whole, with subsequent statements specific to each of the 3 sections. Some of the statements summarize the state of the literature, whereas others are in the form of recommendations for research needed to deal with outstanding questions or aimed at addressing important clinical practice issues.

More recent peer-reviewed research was subsequently incorporated to ensure that the final article reflected the most recent literature. The search for each topic (ie, early identification, screening, intervention) was updated by using the same strategy to add articles published to December 31, 2013. Evidence tables and text references were updated, and the working group reviewed and approved the final wording of the summary and recommendations.

We recognize that transition to recently published criteria for ASD as delineated by the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5),<sup>1</sup> may recast diagnostic boundaries, at least to some degree.<sup>19,20</sup> At this point, it is probably too soon to tell how the revised diagnostic criteria will affect the identification and management of the ASDs, but it is likely that key principles regarding best practice and the “state of the science” from previous research will apply to DSM-5–defined ASD.

## RESULTS

Consensus statements are summarized in Tables 1, 2, and 3 and are discussed in detail in the other articles of this supplement to *Pediatrics*.<sup>16–18</sup> These other articles include tables summarizing the original research articles that support the recommendations.

## DISCUSSION

Early diagnosis and intervention can have a significant positive impact on the developmental outcomes of children with

ASD<sup>21,22</sup> and can also improve parental well-being by addressing concerns and reducing the stress associated with untreated ASD and co-morbid behavioral challenges.<sup>23</sup> Moreover, the human brain undergoes a profound period of establishing and refining connections between neurons during the first years of life. For example, synaptic density in the human prefrontal cortex (ie, the brain region centrally involved in higher order social behavior) peaks between 1 and 2 years of age.<sup>24</sup> Synaptic density in language areas, such as Wernicke’s and Broca’s areas, peaks shortly thereafter by age 3 years. A period of refinement occurs after peaks in synapse number, during which effective connections are strengthened and weak ones die away. This important developmental step, namely the construction of specific neural circuits and the pruning of excess (unused) synapses, is believed to depend largely on input from the environment.<sup>25</sup> Thus, early identification and intervention either before or while brain connections are being established may enable optimal prognosis.

The present review highlights the constellation of ASD-related symptoms emerging by the second year of life, the potential utility of clinical screening to facilitate early identification, and the growing number of empirically supported interventions for very young children. Considerable progress has been made over the past decade in delineating the ASD phenotype during the first 2 years of life, providing a solid foundation for early diagnosis. Moreover, there have been parallel advances in intervention research, ensuring that early diagnosis can lead to substantially improved outcomes. However, much work remains to be done to ensure that children across the ASD spectrum can benefit from clinical and therapeutic advances and that promising model programs can retain their effectiveness when implemented

**TABLE 1** Consensus Statements on Early Identification of ASD

No.	Statement	Key Messages
1.	Evidence indicates substantial heterogeneity in the presentation and natural history of clinical features associated with ASDs. This heterogeneity has ramifications for the interpretation of research literature as well as for clinical practice	<ul style="list-style-type: none"> <li>Given the marked clinical and etiologic diversity among individuals with ASD, it is not surprising that early manifestations and developmental course vary as well</li> <li>Methodologic differences (eg, prospective versus retrospective designs, measurement strategies) may affect comparability across published studies</li> </ul>
2.	There is evidence that reduced levels of social attention and social communication, as well as increased repetitive behavior with objects, are early markers of ASD between 12 and 24 mo of age. Additional potential markers include abnormal body movements and temperament dysregulation	<ul style="list-style-type: none"> <li>Evidence supporting this statement is summarized in Table 1 of the article on early identification by Zwaigenbaum et al<sup>16</sup></li> <li>“Strong evidence” refers to replicated findings in multiple prospective samples from independent research groups (with further support from retrospective studies)</li> <li>“Potential evidence” refers to at least 1 finding from a prospective sample, without replication, or inconsistent findings</li> </ul>
3.	Reliable behavioral markers for ASD in children aged < 12 mo have not yet been consistently identified	<ul style="list-style-type: none"> <li>Evidence supporting this statement is summarized in Table 2 of the article by Zwaigenbaum et al<sup>16</sup></li> <li>Differences in social attention (as indexed by gaze orienting), motor development, and general behavior (passivity versus irritability) have been reported as early as age 6 to 9 mo in some children later diagnosed with ASD</li> <li>However, overt, clinically apparent differences in social communication have not yet been identified before 12 mo of age</li> </ul>
4.	Developmental trajectories may also serve as risk indicators of ASD	<ul style="list-style-type: none"> <li>Prospective studies assessing HR infants at multiple ages have suggested that time course (rather than just cross-sectional differences) in language and cognitive development, social communication, and patterns of gaze orienting may predict a subsequent ASD diagnosis</li> </ul>
5.	Caution should be exercised in drawing conclusions about early risk markers of ASD from studies that do not include individual-level outcome data	<ul style="list-style-type: none"> <li>Some studies report group differences between HR and LR infants</li> <li>If diagnostic outcomes are not reported at an individual level (ie, if it is not known which HR infants were later diagnosed), group differences are not necessarily related to ASD</li> </ul>
6.	Caution should be exercised in generalizing findings from studies of HR infants	<ul style="list-style-type: none"> <li>Findings from HR samples might not generalize to the general population due to differences in research design (eg, ascertainment) and biology</li> </ul>
7.	Research about early markers of ASD should include diverse HR and LR samples	<ul style="list-style-type: none"> <li>Although most current prospective studies involve younger siblings of children with ASD, studies of other HR infants (eg, premature infants) might also inform the field</li> <li>In addition, it is essential that findings from HR samples be validated in LR (ie, community) samples</li> </ul>
8.	Future research should aim to identify: (1) early markers that can be measured in routine clinical practice; (2) early biological processes; and (3) combined approaches	<ul style="list-style-type: none"> <li>There have been advances in technology-dependent risk markers (eg, eye tracking) that could have future utility in community settings, although early detection still depends on features that can be observed by parents and clinicians</li> <li>There is much promise from emerging research on biomarkers, however, both alone and in combination with behavioral markers</li> </ul>

HR, high-risk; LR, low-risk.

across a broad range of family and community contexts.

There is now robust evidence across a diversity of study designs that behavioral signs of ASD can be detected in the second year of life. Highly replicated findings point to impairments in social attention (eg, reduced response to name) and social communication (eg, reduced joint attention behaviors), as well as atypical object use (eg, repetitive actions such as tapping and spinning) and abnormal visual atten-

tion, emerging by 12 to 18 months of age in children subsequently diagnosed with ASD. Other potential early markers which have been less extensively studied but that may also contribute to identifying at-risk toddlers include unusual body movements, atypical emotional regulation, and reduced motor control. Although research to date has not yet identified clear behavioral markers of ASD in infants aged < 12 months, evidence is growing that developmental trajectories (ie, change

over time) in early social orienting and language and cognitive skills beginning as early as 6 months can be predictive of ASD.<sup>26,27</sup> Thus, longitudinal studies of at-risk infants (eg, those with an older sibling with ASD), as well as those detected early in the general population, may be particularly informative. Such studies have the added advantage of including the potential to evaluate both biological and behavioral markers, the combination of which may further aid in early identification. Future longitudinal

**TABLE 2** Consensus Statements on Early Screening of ASD

No.	Statement	Key Messages
1.	Evidence supports the usefulness of ASD-specific screening at age 18 and 24 mo	<ul style="list-style-type: none"> <li>Evidence supporting this statement is summarized in Table 1 of the article by Zwaigenbaum et al<sup>17</sup> on early screening.</li> <li>ASD screening before age 24 mo may be associated with higher false-positive rates than screening at age <math>\geq 24</math> mo</li> <li>Broadband screening in children aged <math>&lt; 24</math> mo can also assist in early detection of ASD</li> </ul>
2.	Siblings of children with ASD are at elevated risk for ASD and other developmental disorders and thus should receive intensified surveillance	<ul style="list-style-type: none"> <li>With risk of ASD as high as 18%,<sup>4</sup> and of milder symptoms and/or developmental delays at <math>\geq 15%</math>,<sup>16</sup> siblings of children with ASD are high-risk group</li> </ul>
3.	Children identified through ASD-specific screening should be immediately referred for diagnostic evaluation and appropriate intervention	<ul style="list-style-type: none"> <li>The potential benefits of a positive screen will be realized only if followed by consistent referral and timely access to specialized assessment and intervention services</li> </ul>
4.	The long-term stability of ASD diagnosis in children $\geq 24$ mo of age is well established	<ul style="list-style-type: none"> <li>Evidence supporting this statement is summarized in Table 2 of the article by Zwaigenbaum et al<sup>17</sup></li> <li>Emerging data suggest that ASD diagnoses before 24 mo of age are stable, although further research is needed, particularly involving children identified via early screening</li> </ul>
5.	Barriers to ASD-specific screening in the health care system need to be identified and removed to facilitate rapid diagnosis and early intervention	<ul style="list-style-type: none"> <li>Reported barriers include insufficient time and/or reimbursement and other logistic challenges (eg, disruption of work flow, lack of office-based systems for making referrals)</li> <li>Health care provider beliefs regarding the potential benefits and risks can also influence participation in screening programs</li> </ul>
6.	Methodologically rigorous research in ASD-specific screening should be a high priority	<ul style="list-style-type: none"> <li>Recommendations for future research include applying current screens in large diverse community samples to maximize generalizability, assessing clinically relevant outcomes (eg, age of diagnosis), follow-up of both screen-positive and screen-negative children, and more detailed sample characterization to better understand what factors may influence accuracy of screening</li> </ul>
7.	There are several additional priorities for future ASD screening research	<ul style="list-style-type: none"> <li>Considerations for future research also include incorporating combined broadband and ASD-specific screening, randomized designs, repeat screening, use of technology, biomarkers, and examining factors that may influence screening uptake and outcomes.</li> </ul>

research would benefit from the use of both high- and low-risk comparison groups, to ensure that risk profiles adequately distinguish between ASD and other developmental disorders, rather than just ASD and typical development.

Our review of published research evaluating ASD screening tools (Table 3) supports current American Academy of Pediatrics' recommendations of ASD screening in the second year.<sup>28</sup> These

tools include both those targeted at ASD-specific behaviors (eg, the Modified Checklist for Autism in Toddlers [M-CHAT]) as well as measures targeting a broader range of delays (eg, the Communication and Symbolic Behavior Scales Infant/Toddler Checklist). Data from large community-based samples suggest that ASD screening by using the M-CHAT (specifically, its current version [revised, with follow-up])<sup>29</sup> or the Infant/Toddler Checklist<sup>30</sup> can

identify children with ASD earlier and with greater sensitivity compared with open-ended questions regarding parental concerns and thus offers advantages over general developmental surveillance. There is some support for the potential utility of ASD screening before 18 months of age. For example, a positive screen on the Infant/Toddler Checklist at 12 months (as part of the First Year Check-Up model)<sup>31</sup> was associated with a positive predictive value of 0.75 for ASD or other developmental delays but with considerable loss to follow-up (based on the  $\sim 1$  in 7 screen-positive children who were ultimately seen for diagnostic assessment).

Other ASD screens targeting this younger age group have shown some promise. For example, the Early Screening of Autistic Traits questionnaire can identify ASD as early as 14 months but with a low case detection rate and presumably low sensitivity,<sup>32</sup> and the First Year Inventory may detect some children with ASD at 12 months but also with only modest sensitivity.<sup>33</sup> Further research on ASD screening for this age group is needed. It is also recognized that younger siblings of children with ASD are at substantial risk for the disorder (with estimated recurrence as high as 18.7%),<sup>4</sup> as well as other developmental challenges,<sup>34</sup> and thus warrant additional monitoring. It is also important to take into consideration what populations have been investigated for currently available screens (Table 3) and the degree to which this analysis may influence generalizability to other contexts. For example, community pediatric practices can be a highly informative setting to assess the screening properties of particular measures in children without specific risk factors but may not fully reflect the diversity (eg, socioeconomic, ethnic) of a true population sample. Screening must be linked to timely referral for additional evaluation

**TABLE 3** Consensus Statements on Early Intervention and Outcomes of ASD

No.	Statement	Key Messages
1.	Current best practice interventions for children aged <3 y with suspected or confirmed ASD should include a combination of developmental and behavioral approaches and begin as early as possible	<ul style="list-style-type: none"> <li>• Evidence supporting this statement is summarized in Table 1 of the article by Zwaigenbaum et al<sup>18</sup> on early intervention</li> <li>• Behavioral interventions (ie, based on applied behavioral analysis) use evidence-based principles to systematically change behavior</li> <li>• Developmental models of intervention use developmental theory to design approaches to target ASD-related deficits</li> <li>• In practice, many empirically supported interventions for children aged &lt;3 y blend features of both approaches</li> </ul>
2.	Current best practice interventions for children aged <3 y with suspected or confirmed ASD should have active involvement of families and/or caregivers	<ul style="list-style-type: none"> <li>• Active family involvement is consistent with best practices of interventions for children aged &lt;3 y</li> <li>• Parents and caregivers can capitalize on teachable moments as they occur, provide learning opportunities during daily routines, and facilitate the generalization of learned skills across environments</li> </ul>
3.	Interventions should enhance developmental progress and improve functioning related to both the core and associated features of ASD, including social communication, emotional/behavioral regulation, and adaptive behaviors	<ul style="list-style-type: none"> <li>• Targeted early interventions have been associated with improvements in early functional domains relevant to ASD, specifically in joint attention and other aspects of social communication, imitation, and functional and symbolic play</li> <li>• Comprehensive interventions for young children with ASD have also led to improvements in adaptive functioning</li> </ul>
4.	Intervention services should consider sociocultural beliefs of the family and family dynamics and supports, as well as economic capability, in terms of both the delivery and assessment of factors that moderate outcomes	<ul style="list-style-type: none"> <li>• Respect for the perceptions, priorities, and preferences of family members is an important “family-centered” tenet to keep in mind when working with children with ASD</li> <li>• Service provider training should promote cultural competence, and families should be provided with culturally appropriate program materials</li> <li>• Cultural as well as socioeconomic factors may present barriers to accessing services</li> </ul>
5.	Intervention research should include socially and culturally diverse populations and evaluate familial factors that may affect participation, acceptability, and outcomes of therapeutic approaches as well as willingness to participate	<ul style="list-style-type: none"> <li>• Recruitment to intervention research should emphasize social and cultural diversity, to maximize generalizability and applicability of the interventions being studied</li> </ul>
6.	Future research should prioritize well-defined sampling strategies, rigorous investigative design, fidelity of implementation, and meaningful outcome measurements	<ul style="list-style-type: none"> <li>• Future directions include: identifying characteristics of children and families who would benefit most from particular interventions and systematically varying components of multifaceted intervention programs to identify critical ingredients</li> <li>• Randomized controlled trials are generally the optimal design, although other designs can be informative, especially at the feasibility stage</li> <li>• Intervention studies should include measures that are responsive to change and index relevant areas of functioning</li> </ul>
7.	Research is needed to sort the specific active components of effective interventions	<ul style="list-style-type: none"> <li>• These might include (but are not limited to): the type of treatment provided; agent implementing the intervention(s) (parent, therapist, teacher, or combination); consistency of service provision across environments and between providers; and duration of treatment and hours per week</li> </ul>
8.	Adopting a common set of research-validated core measures of ASD symptoms that can be used across multiple sites will facilitate comparisons across studies of children with ASD aged <3 y	<ul style="list-style-type: none"> <li>• Outcome measures do not need to be identical across studies, but agreement on a subset of standardized instruments to use, which may assess changes in cognitive function, core autism symptoms, and adaptive and language behavior, would facilitate future comparisons</li> </ul>
9.	Future research should examine biological and behavioral heterogeneity as moderators of individual responses to interventions	<ul style="list-style-type: none"> <li>• Subtypes of individuals with ASD need to be identified to understand the cause of their disorder, the associated neurobiologic mechanisms at work, and to be able to offer more directed interventions depending on the biological (and/or behavioral) subtype when known</li> </ul>
10.	Intervention providers should monitor for medical disorders that may affect a child's response to an intervention and refer to appropriate health care providers as indicated	<ul style="list-style-type: none"> <li>• Medical factors such as seizures, sleep disruption, and gastrointestinal symptoms may affect daytime functioning and should thus be considered as possible moderators of treatment response</li> </ul>

for risk-positive children as well as prompt access to interventions targeted to specific, identified functional concerns while diagnostic status is

being clarified. Earlier research suggests only a modest increase in ASD screening in pediatric practice<sup>35</sup>; the routine implementation of diagnostic

measures could be enhanced, however, by providing administrative support to assist with processing completed screens and facilitating subsequent

referrals.<sup>31,36</sup> Placing screening in the broader context of ASD assessment may also help engage community physicians.<sup>37</sup> Additional barriers, including third-party reimbursement, lack of monitoring systems to track positive screening results, and challenges accessing early intervention services, need to be addressed to enhance incorporation of recommended screening practices into routine care for community practitioners.

Although some studies have reported that screening can identify children with ASD earlier and more consistently than routine inquiry about parental concerns,<sup>31</sup> none has examined whether interventions offered to children with ASD identified solely according to screening yield improved outcomes. Indeed, screening effectiveness is generally assessed with respect to classification accuracy (ie, sensitivity and specificity) rather than clinically meaningful outcomes (ie, changes in developmental trajectories related to earlier initiation of intervention), an important focus for future ASD screening research.

Considerable progress has also been made in developing and evaluating ASD intervention models specific to the needs of children <3 years of age. Several groups have adapted treatments initially designed for older preschool-aged children with ASD by integrating best practice in behavioral teaching methods into a developmental framework based on current scientific understanding of how infants and toddlers learn. The central role of parents has been emphasized, and interventions are designed to incorporate learning opportunities into everyday activities, capitalize on “teachable moments,” and facilitate the generalization of skills beyond the familiar home setting. Although some trials were limited to 8- to 12-week outcome data, enhanced outcomes associated with some inter-

ventions (eg, the Early Start Denver Model) were evaluated over periods lasting as long as 2 years.<sup>21</sup>

Although no studies to date have directly compared intervention models in children with ASD aged <3 years (even for older children, such studies are rare), there is clear evidence that interventions initiated at this early age can lead to marked improvements in targeted skills (eg, social communication, imitation)<sup>38,39</sup> as well as more global improvements in cognitive and adaptive functions.<sup>21,40</sup> Although additional research is needed to further optimize existing models (eg, to differentiate the specific active ingredients), accumulating evidence indicates that toddlers with ASD benefit from early, diagnosis-specific interventions, thus placing greater urgency on the need to ensure broader dissemination and uptake of evidence-based practices beyond initial research settings. Recent data<sup>41</sup> that such interventions not only improve adaptive and social behaviors but also lead to normalized patterns of brain activity in response to viewing faces further emphasize the potential to improve long-term neurodevelopmental trajectories. Efforts to implement effective research programs in formats that can reach larger numbers of children through innovative training approaches (eg, an Internet-based distance learning model for Early Start Denver Model therapists) have also been encouraging.<sup>42</sup>

### STUDY LIMITATIONS

The recommendations outlined in the present article (and discussed in greater detail in the other articles comprising this supplement<sup>16–18</sup>) were informed by a review of the published literature as well as consensus of our expert group. However, it is important to acknowledge that the selection of articles for review by the working groups was not systematic. A scoping approach was instead used to select

articles of highest relevance and methodologic quality; it is possible that this process excluded key references that might have further informed the recommendations.

### FUTURE DIRECTIONS

Whereas better and earlier characterization of behavioral symptoms should continue to be a significant focus of research (especially those early characteristics that can be more easily applied in clinical practice), the active search for underlying biological markers should remain a high priority. Promising findings from neuroimaging<sup>43–45</sup> and neuroelectrophysiology<sup>46</sup> studies may also guide future biomarker-based strategies. For example, the observation of enlarged brain volume early in life could be useful in some cases. In addition, the pursuit of biologic examination of cord blood, placenta, maternal blood, and amniotic fluid, when available, may provide useful and more feasible resources for defining very early indicators of atypical neurologic development and might ultimately lead to more specific treatment modalities.

Although disturbances in sensory processing have not always been considered a core feature of ASD, atypical sensory processing is frequently reported by parents, therapists, teachers, and patients themselves. With the publication of the DSM-5 in May 2013, unusual sensory responses were included in the restricted and repetitive interests/behaviors domain, thus acknowledging that these symptoms play a role in ASD.<sup>47</sup> More recently, imaging and neurophysiologic studies have reported abnormalities in the white matter microstructure of the brain in children with sensory-processing disorders.<sup>48,49</sup> How disorders of sensory processing<sup>50</sup> (including modulation and integration of sensory information) influence many of the behaviors, and potentially some of the core features of ASD,<sup>51</sup>

remains poorly understood and will be an important area for future research; understanding these mechanisms could have important implications for early diagnosis and treatment.

There is a growing appreciation that ASD is heterogeneous in its causes, underlying neurobiology, and clinical presentation and that the “autisms” comprise a continuum of signs and symptoms, many of which may change over time, either as the result of age or therapeutic interventions or both. Currently, we have little understanding of the natural life history of ASD and how the clinical changes in any individual patient may be reflective of underlying neurobiological mechanism(s) not yet defined. Large-scale longitudinal studies designed to follow up cohorts of well-characterized individuals over time and examine the interplay between biological processes and subsequent experiences could generate new insights to help better individualize treatment strategies.

When considering research related to intervention outcomes, a more concerted focus should be placed on the investigation of those children with ASD who make dramatic progress, some of whom eventually “lose” their diagnosis (ie, the optimal outcome),<sup>52</sup> and those who, despite well-designed, high-quality programs and strong family support, fail to make any significant improvement. Defining the differences between these 2 groups could potentially provide important information relative to the underlying causes of these subsets of children and, furthermore, what specific interventions should be tailored to which type of child. Other indices of heterogeneity (eg, symptom severity, variation in cognitive and language levels, comorbid behavioral and medical conditions) should be more explicitly considered in future studies to help better understand

variation in intervention outcomes. It will also be essential that we learn more about how such diversity can affect the effectiveness of early detection and screening, and how this information can help us to develop multipronged strategies that lead to earlier diagnosis across the autism spectrum.

The potential effects of co-morbid medical conditions on the behavior, developmental progress, and general well-being of children with ASD are becoming increasingly apparent and warrant careful consideration, even in the context of early intervention. The autism community has begun to appreciate that a variety of medical conditions (including gastrointestinal disorders, sleep, airway obstruction related to enlarged tonsils and adenoids, and obesity) can—and do—occur among children with ASD and, when present, can negatively affect developmental progress and quality of life. Furthermore, some of the behaviors frequently associated with ASD (eg, stereotypies, aggression, self-injury) are often related to the pain and discomfort associated with these underlying medical conditions. It will be important to determine the prevalence of these co-morbid conditions; to identify their presenting symptoms, which may differ from those seen in typically developing children; and to effectively treat these conditions in concert with other interventions.

Future research related to early identification, screening, and intervention should address the impact of social and cultural beliefs and values, family expectations, stresses and involvement, and outcome goals. Belief systems among service providers may influence utilization of early detection and screening and referral to specialized assessment and interventions.<sup>53</sup> Belief systems among families regarding social behavior and development, in addition to ear-

lier experiences with health care providers, can influence communication regarding early risk markers and participation in screening programs. Cultural beliefs, as well as family dynamics and socioeconomic circumstances, can also influence a family's effective engagement in intervention programs and thus may ultimately affect outcomes.<sup>54</sup> Future research should take into account the diversity of beliefs and world views among families and consider how to adapt early detection, screening, and intervention strategies to minimize health disparities or systemic practices that marginalize historically underserved groups to ensure that barriers and health care disparities are overcome. The goal of treatment is early detection, diagnosis, and access to effective interventions for all children across the autism spectrum.

## ACKNOWLEDGMENTS

The conference chairs and working groups acknowledge the preconference contributions of individuals who were unable to attend the conference, including Grace Baranek, PhD, OTR/L, FAOTA, Tony Charman, PhD, Katarzyna Chawarska, PhD, and Gary Mesibov, PhD. We also acknowledge the efforts of Katherine F. Murray, BSN, RN, Massachusetts General Hospital for Children, in coordinating the forum and subsequent conference report process, and Sifor Ng in the conference report process.

The meeting and consensus report were sponsored by the Autism Forum. An important goal of the forum is to identify early indicators of ASDs that may lead to effective health care services. Autism Forum programs are developed under the guidance of its parent organization, the Northwest Autism Foundation. For this project, the Autism Research Institute provided financial support.

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Drs Zwaigenbaum and Bauman initiated a literature review, co-chaired the meeting that generated the consensus recommendations outlined in this article, and drafted the initial manuscript; Drs Choueiri, Fein, Kasari, Pierce, Stone, and Yirmiya co-chaired the working groups that conducted the literature review, generated initial recommendations that were discussed at the consensus meeting, and provided critical input to subsequent drafts of the manuscript; Drs Estes, Hansen, McPartland, Natowicz, Buie, Carter, Davis, Granpeesheh, Mailloux, Newschaffer, Robins, Smith Roley, Wagner, and Wetherby were members of the working groups that reviewed selected publications, contributed to recommendations, and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

[www.pediatrics.org/cgi/doi/10.1542/peds.2014-3667B](http://www.pediatrics.org/cgi/doi/10.1542/peds.2014-3667B)

doi:10.1542/peds.2014-3667B

Accepted for publication Aug 3, 2015

Address correspondence to Lonnie Zwaigenbaum, MD, Autism Research Center, Glenrose Rehabilitation Hospital, Room E209, 10230 111 Ave, Edmonton, AB, Canada T5G 0B7. E-mail: lonniez@ualberta.ca

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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**FINANCIAL DISCLOSURE:** Dr Zwaigenbaum was the site Principal Investigator of a study sponsored by SynapDx (he received operating funds but no honoraria). Drs Fein and Robins are co-owners of M-CHAT, LLC, which licenses use of the Modified Checklist for Autism in Toddlers in electronic products. Dr Stone is the author of the Screening Tool for Autism in Two-Year-Olds and receives a share of royalties from sales of this instrument. The authors received an honorarium as well as travel expenses from Autism Forum for contributing to the expert panels.

**FUNDING:** Sponsored by the Autism Forum under the guidance of the Northwest Autism Foundation and with the support of the Autism Research Institute.

**POTENTIAL CONFLICT OF INTEREST:** The authors have indicated they have no potential conflicts of interest to disclose.

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*Pediatrics* 2015;136;S1

DOI: 10.1542/peds.2014-3667B

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