

## **Question 1 Draft Updates for the IACC 2011 Strategic Plan**

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### **When Should I Be Concerned?**

#### **What is new in the research area and what have we learned this past year?**

The prevalence of autism continues to rise according to the most recent ADDM Network data that indicates nearly 1% of children have an ASD diagnosis, reflecting an increase of 57% over a four year period. Importantly, the mean age at diagnosis did not change significantly over this time period with most children not diagnosed until age 3 to 5 years. A second study from the large National Survey of Children's Health using very different study methods from those used in the ADDM project also reported a prevalence of ASD of approximately 1% of children (Kogan et al., 2009).

Research from three important studies over the past year has pointed to the importance of factors that place children at increased risk for ASDs. Findings indicate the role of underlying genetic disorders and prenatal risk factors that when present, may warrant screening and early follow up and in some instances, more specific medical work up. First, an evidence-based review of a large clinical series of patients with ASD and with other developmental disorders concluded that chromosomal microarray resulted in considerably higher diagnostic sensitivity for genetic testing than did G-banded karyotyping, particularly for submicroscopic deletions and duplications (Miller et al., 2010). Second, a study by Johnson et al., found that very preterm birth (<26 weeks gestational age) was associated with a much higher risk of developing ASD, with a prevalence of 8% diagnosed by age 11. While early gestational age has been identified as a risk factor for ASD, previous studies have lacked the power to examine children born at such vulnerable gestational ages. A third study of 7.9 million children in California showed that older fathers and mothers were more likely to have a child with autism as compared to younger parents (Grether, et al. *American Journal of Epidemiology*. November 2009). Evidence is also accumulating on the developmental trajectory for autism. A 2010 prospective study showed little deviation between children who eventually developed autism and typically developing children up to age 6 months, after which time measurable differences emerged (Ozonoff et al., 2010). Importantly, while a decrease in developmental trajectory of skills was found in the majority of children, it was not identified by most parents, suggesting current limitations in the use of parent-identified early markers of ASD in the first year of life. Also, Klin et al., found that as compared with typically developing toddlers, toddlers with ASD paid more attention to stimuli in which sound and motion were synchronous. This difference in sensory processing may be connected to the tendency for people with ASD to focus on the mouth over the eyes in conversation.

Two important studies highlighted work on the barriers to early screening and diagnosis. Evaluation of the implementation of the AAP recommendations for developmental surveillance was conducted in 17 diverse pediatric practices and demonstrated reasonable success in implementing ongoing screening (85% of practices screened patients at recommended screening ages), but that pediatric practices experienced challenges in referral for medical subspecialty care and early intervention (King et al., 2010). A second study (Norris and Lecavalier, 2010) evaluated the diagnostic sensitivity of the various parent/care-giver autism Level 2 screening scales for children older than 3 years—beyond the AAP-

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recommended screening ages—and concluded that even in this older age group, while some tests performed well, overall, more scientific evidence is needed for these instruments.

**What gaps have emerged since last year?**

Recent data (Shattuck et al., 2009; Giarelli et al., 2010) show that girls are diagnosed with ASD at a later age than are boys. Examination of the 2009 autism portfolio analysis of currently funded research shows that studies in girls and minority racial/ethnic/socioeconomically disadvantaged populations remains a gap area. While the authors speculate on reasons for this disparity, including different clinical manifestations of ASD by gender and cultural differences in accepted or anticipated behaviors in girls relative to boys, gender should be included as an important disparity factor in studies examining barriers to early screening and diagnosis.

There are important ethical, legal and social issues implications resulting from the study by Miller et al., particularly relating to screening for genetic and other markers for autism and other developmental disorders. There is a diverse range of opinions in the autism community on early screening for autism ranging from strong support for developing biologic prenatal screening methods to concerns that such efforts may lead to selected terminations of fetuses showing genetic or other biomarkers of increased risk. It is imperative that autism research proceed with the appropriate precautions and safeguards and that the concerns of the autism community are reflected in this process. At this point, the state of the science is focused on improving early screening in the first years of life to identify risk for an ASD in order to initiate early intervention to reduce or prevent the development of disabling symptoms and promote positive skill development.

The study by King et al. highlights the need for a clearer understanding of the challenges and barriers to screening and referral. Studies are needed to determine the factors that lead to implementing screening and referral programs that successfully serve children with ASD and their families. Studies should include factors relating to the clinical practice, availability and collaboration among community-based services, and information needs of parents, other caregivers, and early educators.

There is a lack of reliable and valid screening and diagnostic tests for use in international, resource-poor settings. Early screening and diagnosis when coupled with inexpensive, parent-guided interventions is an important potential prevention strategy in such settings.

Research is needed to identify effective methods for identifying children at higher risk for ASDs, such as the extremely preterm children and children with a sibling with an ASD, in community screening efforts. Although the AAP recommends ongoing developmental and autism-specific screening in the first few years of life, establishing risk profiles indicating the need for heightened monitoring of development among some children warrants investigation to improving early identification.

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### What new research opportunities and research objectives have emerged?

- o Conduct at least one study to determine the positive predictive value and clinical utility (e.g., prediction of co-occurring conditions, family planning) of chromosomal microarray genetic testing for detecting genetic diagnoses for ASD in a clinical setting, by 2010.
- o Conduct at least five (ancillary or dedicated) studies of the ethical, legal, and social implications (ELSI) of autism research, including at least one study regarding the potential impact of future prenatal genetic testing and at least one study regarding the need and clinical utility of genetic testing and genetic counseling as part of a standard diagnostic ASD assessment. Ensure the inclusion of both individuals on the autism spectrum and family members as distinct stakeholder groups in these studies.
- o Revise Short-Term Objective C to better define the screening and referral system and the targeted health disparities: Conduct at least three studies to identify barriers to implementation of and access to screening, diagnosis, referral and early intervention services among diverse populations, as defined by socio-economic status, race, ethnicity, and gender of the child.
- o Revise Short-Term Objective B to include 'gender' as a population qualifier and 'resource-poor international settings'.
- o Revise Long-Term Objective A to "Identify behavioral and biological markers that separately, or in combination, accurately identify, before age 2, one or more subtypes of children at risk for developing ASD and evaluate whether these risk markers or profiles can improve early identification through heightened developmental monitoring and screening by 2014."

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**Comment [OARC1]:** The Subcommittee felt this issue warranted more discussion by the full Committee

### New References

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