2013 IACC Strategic Plan Update - Question 1 Draft

"When Should I Be Concerned?" – Volunteer drafter – John Robison and OARC

Introduction

The aspirational goal of the first Question is to identify children at risk for autism spectrum disorder (ASD) before behavioral symptoms of ASD fully manifest. When originally framed, Question 1 was directed toward identifying at-risk children by the age of 24 months to facilitate the greatest chance of successful early intervention. Scientific advances since then have shown that, in infants who have an older sibling with autism who are therefore at high genetic risk for ASD, symptoms of autism begin to emerge as young as 6 months of age in infants who later develop ASD. These new findings suggest that it may someday be possible to screen for children at risk for ASD before the onset of the full syndrome. This progress in screening potential highlights the challenges that remain for this Question, which include validating whether the early symptoms identified in infant siblings who later develop ASD can be used as a screening tool in other high risk populations (e.g. very low birthweight infants) and/or in the general population.

New research suggests that existing screening tools, such as the Modified Checklist for Autism in Toddlers (M-CHAT with the follow-up interview, which is typically not utilized)[1] and the Infant-Toddler Checklist[2] can be effectively used by pediatricians and other community providers. The M-CHAT shows promise as an ASD screen between 18 – 36 months of age, and the Infant-Toddler Checklist shows promise as a broadband screen for communication that can catch children with autism between 12 and 24 months. There remains a great need for the development of efficient and cost effective screeners below 18 months of age, as well as more efficient methods of deploying developmental and ASD screening in community settings, including evaluation of effective parent-professional communication strategies for coping with concerns, referrals, follow-up evaluations for services and diagnosis, and linkage to appropriate services and supports. In addition, the development of culturally sensitive diagnostic tools that can be more easily used in both clinical and research settings is urgently needed.

Many of the advances in the screening and diagnosis area have been on development and refinement of screening tests. Moving forward, more attention needs to focus on innovations in diagnostic tools. Finally, there has been a growing awareness of the need for better tools to diagnose adults on the ASD spectrum and to provide meaningful assessments of functioning, which is an issue that is captured in an objective in Question 6 of the IACC Strategic Plan, but may involve adaptation of tools that are currently used to diagnose children.

The 2009 Strategic Plan, with revisions added in 2010 and 2011, identified a total of 9 objectives to address research gaps pertaining to Question 1, including 6 short-term and 3 long-term objectives. Issues addressed in the Question 1 objectives include the identification of behavioral or biological markers that can predict ASD risk, development and adaptation of screening and diagnostic tools for use in diverse populations, studies to understand the reasons for health disparities, the development of standardized behavioral or biological measures for diagnosis and detection of treatment response, and a workshop to explore the ethical legal and social

implications of ASD research. The overall budget recommended for all 9 objectives under Question 1 was $151.235M.

Progress Toward the Strategic Plan Objectives

The 2011-2012 IACC ASD Research Portfolio Analysis reviewed projects funded by both government agencies and private foundations from 2008 – 2012. From 2008-2012, the total funding devoted to projects that address Question 1 was $186.771M, and if just the years since the publication of the first IACC Strategic Plan in 2009 are considered, the funding for Question 1 related projects was $157.65M. On average for each year from 2009-2012, the funding levels for this Question were 35% higher than the 2008 level ($29M) that preceded publication of the Strategic Plan. Also in years 2009-2012, 11% of the total funding went toward core research projects that were not aligned with the research gaps covered by the 9 objectives in Question 1.

Of the nine specific objectives under Question 1, four objectives addressing development of screening and diagnostic tools, identification of risk biomarkers and a workshop on ethical issues, met or exceeded the recommended budget and fulfilled the recommended number of projects. Three objectives, concerning determining the utility of genetic tests and developing measures of heterogeneity and symptom severity, partially met the recommended budget and had a number of projects underway, while one objective on understanding the reasons for disparities in screening and diagnosis, was far below the recommended budget and number of projects. One objective, on studies to understand if early diagnosis leads to early intervention and better outcomes, did not have any funding or projects, though some of this type of research may be covered in projects that are categorized elsewhere.

Over the past 5 years, good progress has been made toward developing tools and practices for more effective screening and diagnosis. With repeated screening at 6, 12, and 18 months, the potential now exists to identify as many as 95% of children with ASD by the age of 24 months; however, community-based research is needed to confirm this. While this capacity represents a remarkable scientific advance, the practical application of existing screening tools must be improved. The clinical reality is that currently only about 20% of children with ASD are being identified early, which means that screening capabilities that have been observed in academic settings have not fully made the transition to use in a community setting[3]. Barriers to the broader deployment of advanced screening and diagnostic tools is their cost and the expertise required to administer the tests. Also, repeat screenings at 6 month intervals beginning at 6 months of age are not being done in practice, despite demonstrated efficacy of the technique with at-risk infants[4]. In addition, it appears that in practice, children who are identified in early screens are not always being referred for diagnosis and early intervention, even though there is now strong evidence to suggest the benefit of early intervention[5–7]. Thus, we need to better understand the barriers that are preventing caregivers from seeking a diagnostic evaluation after a child fails an autism screener and to identify strategies that will help caregivers navigate the pathway from screening to diagnosis to entry into early intervention. Until this gap between screening and intervention is closed, the potential impact of ASD screening on improving outcomes for individuals with ASD will not be realized. More needs to be done to raise awareness in the practitioner community of the current capabilities and benefits of early, repeated screenings, early diagnosis and early intervention. Although not the scope of a research plan, a major stumbling block is the capacity crisis that exists – both in terms of

professionals to refer to for evaluation and for services and supports. Along these lines, we need more complete data to estimate the population of children with ASD and other developmental delays who are likely to need early intervention services so that a truly coordinated early identification process is possible where the family has access to timely evaluation and services and supports (A note for Question 5).

While there has been some progress in understanding the prevalence of ASD in diverse communities, with recent results now suggesting that apparent differences in autism prevalence in minority populations are due to diagnostic differences[8,9], there is still a gap in understanding the reasons for disparities in access to screening, diagnosis, referral, and early intervention services. While this was an area targeted by the IACC in the 2009 Strategic Plan, much more work is needed to address this gap.

An area of groundbreaking research for Question 1 has been on the detection of ASD risk in high risk infants (infant siblings) as young as 6 months of age. Among infant siblings, differences in both white-matter tracts and posture and have been observed in 6-month-old infants who are later diagnosed with ASD[10,11]. Differences in the developmental trajectories of visual attention to social stimuli have also been identified as a marker of those infant siblings who later developed ASD; a decline in visual attention to the eyes from 2 to 6 months of age is seen in infants who are later diagnosed with ASD[12]. These exciting results suggest new potential screening tools, like existing tools, must now be validated in other high risk populations and the general population and, if proved efficacious, modified for broader use in order to be beneficial to the wider community. A step toward this goal will be determining if these markers which have been studied in siblings of children with ASD can also be used to identify risk in children without family history of ASD.

At the molecular level, there has been significant progress in identifying genetic differences in ASD. Mutations associated with genetic risk for ASD can now be identified in about 30% of individuals diagnosed with ASD (see Chapter 3 for details). This rate of genetic identification today is substantially greater than five years ago, and further progress is anticipated. In order for these genetic markers to be useful from a screening perspective, they too will need to be validated in more general populations. Such an advance could also help address the issue of adult diagnosis. It is noteworthy that the overwhelming majority of screening and diagnostic tools are developed for and studied in infants and children, but there is a dearth of tools that can be used effectively in adults. More effort needs to be focused on developing, adapting and validating screening and diagnostic tools for use across the lifespan.

Advances in capabilities to detect ASD early create a variety of legal, ethical, and social concerns, and the IACC Strategic Plan update of 2011 recommended that a workshop be held to address these issues. NIH, the Autistic Self-Advocacy Network and Autism Speaks all held workshops that either directly or partially addressed this topic, fulfilling the original objective. Still, continued attention to this topic is warranted as the legal, ethical and social implications of ASD screening will continue to evolve in response to changing technologies.

Progress Toward the Aspirational Goal:
Children at Risk for ASD Will Be Identified Through Reliable Methods Before ASD Behavioral Characteristics Fully Manifest.

Tools have begun to emerge that have the potential capability to detect children at risk for ASD before the full manifestation of behavioral symptoms, which is the aspirational goal of this Question. The challenge that remains is to develop practical, cost effective tools, validate and adapt these tools for use in a variety of diverse populations, support the development of the needed provider workforce, and deploy these tools so that this capability becomes a clinical reality across communities. Additionally, the link between screening and referral to intervention remains weak, but must be strengthened for the realization of the aspirational goal. Even when early screening takes place and at-risk children are identified, almost half the children are not progressing through the system to diagnosis and early intervention and face major roadblocks in the ultimate goal of accessing needed services and supports as early as possible. Future work should focus on identifying and removing the cultural and logistical impediments to following up on a screen that has found a risk for ASD.

In terms of continued screening tool development, there is a need for increased investigation of risk factors in the 0-12 month age group. Currently there is no combination of genetic and behavioral markers in this age group that are reliable indicators of ASD risk. Also, the focus of the search for biomarkers has been on behavior and genetics, but this focus needs to be broadened to include a number of physiologic markers as well (i.e. sleep, EEG, autonomic measures, and gastrointestinal (GI) function). In addition, in the period prior to the development of language skills, biomarkers such as early motor tone, symmetry, and joint attention should be further considered. For greater accuracy, emphasis should be placed on both direct observation and parent report.

In order to increase community usefulness of established tools, more investment is needed for community-based studies with larger sample sizes that will increase knowledge of disparities among various groups in access to screening and in applicability of screening tools. New technologies such as portable device applications, Electronic Health Records (EHRs), and video tasks will also be important for the development of innovative screening methods and screeners that could be used for diagnosis in children and adults. Finally, rigorous validation of existing tools is necessary so the community will know which ones are reliable in which populations.

The true realization of the aspirational goal is dependent on progress on the other Questions of the Strategic Plan. While all the Questions are interrelated, the success of screening and diagnosis depends most heavily on the existence of effective interventions (Question 4) and services (Question 5) for all those identified, including those with mild or moderate levels of disability. In addition, while the aspirational goal of Question 1 focuses on early diagnosis in children, there is also a need to greatly strengthen efforts to develop and adapt diagnostic tools for use in adult populations, which is addressed in Question 6 of the Strategic Plan.

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