2013 IACC Strategic Plan Update – Draft Conclusion – Prepared by Tom Insel, OARC and John Robison

Progress

The *2013 Strategic Plan Update* details the progress that has been made on the scientific questions and investment recommendations of the IACC Strategic Plan. Of the 78 specific Plan objectives, 72 have fully met or partially met the recommended budget. Overall, approximately $1.5B in public and private research funding has been dedicated to ASD projects over the past 5 years, with an average funding increase of 39% across the Strategic Plan Questions for the period following its initial release in 2009. This increased investment has brought forth a range of scientific advances at all levels of the Plan.

The state of the science has dramatically changed in the ASD field since 2008. While biological differences in individuals with ASD were hypothesized earlier, now there are data demonstrating specific changes in the genome and epigenome, gene expression, cell structure and function, brain connectivity, and behavior that are connected to ASD. Over the past 5 years, genetic studies have revealed that genetic variation ranging from changes in single bases to alteration of large regions of DNA or even extra chromosomes can contribute to ASD risk, and that both inherited and spontaneous mutations can play a role. Several environmental factors have emerged as potential contributors to ASD risk in the past five years, including: prenatal maternal infection, preterm birth, advanced maternal and paternal age at conception, short inter-pregnancy interval, and use of certain prescription medications by mothers during pregnancy, as well as some data suggesting that exposure to air pollution, pthalates and pesticides during pregnancy may also increase risk. Vitamin intake during pregnancy has been identified as a possible protective factor against ASD risk. Both the genetic and environmental data now point to early months of gestation as a critical period in the developmental course toward ASD.

Advances in screening and diagnosis tools now provide the theoretical capability to identify 95% of children with ASD before the age of 24 months. New research on eye-tracking patterns, white matter tract development, and posture control also suggest the possibility of detecting ASD as early as 2-6 months of age. This ability for early ASD detection, however, will only become a reality if efficient, cost effective tools can be designed around these new capabilities. It will also be critical to ensure that following an early diagnosis, there are effective early interventions available. Recent clinical trials of behavioral interventions have begun to provide the evidence base needed to support the widespread use of these advances in the community, but more needs to be done to make these therapies affordable and scalable to large community settings, and efforts are needed to increase the number of children who progress from identification in early screens to diagnosis and early intervention.

Comment [sd1]: Add examples

Some of the most promising research on interventions for ASD have emerged from studies of animals with mutations that cause autism in people. While these studies, which show reversal of symptoms in adulthood as well as development, may not translate to humans with sporadic autism, they provide a pathway for developing treatments for the core symptoms of ASD. Clinical trials in toddlers have demonstrated the value of early intervention, with changes in brain EEG activity as well as behavior. Several trials are currently underway, with 175 projects identified in the portfolio analysis ranging from exploratory trials of novel interventions to tests

of currently used treatments. Over the past five years, a large clinical network has been developed, several pharmaceutical companies have become engaged in ASD research, and new technologies have emerged that may prove transformative. This field still requires standardized, sensitive outcome measures and biomarkers that can both stratify the heterogeneous ASD population and serve as rapid indicators of clinical response.

Recent studies have revealed sobering information regarding the tremendous service needs within the community, with data showing that young adults transitioning out of the educational system frequently lose their services access and often have limited opportunities for employment and independent housing. While more data is needed on the needs of adults with ASD so that services can be more appropriately targeted, there is already an opportunity to collect data on the effectiveness of current services, and in some cases, to do comparative studies that could begin to make improvements in services for adults in the near term.

One of the most encouraging signs of progress has been the increased research infrastructure over the past 5 years, helping the scientific community embrace a culture of data integration and sharing. Several large scale government funded research centers, privately funded efforts, and some public-private collaborative projects have been built in the past five years . The National Database for Autism Research (NDAR), a hub that stores and shares aggregate data, from exomes to images, has grown to over 70,000 human subjects. Efforts such as the NIH Neurobiobank and the Autism Brain Net have been established to try to rebuild and expand the supply of available brain and other tissue samples for ASD and brain disorder research. In addition, the Interactive Autism Network (IAN) and Autism Genetic Resource Exchange (AGRE) give families the opportunity to share data that can be accessed by researchers, and new models of more rapid, interactive clinical trials can be supported by these kinds of resources, expanding the possibilities for future research.

Relative to many other areas of biomedical research, ASD science is still a young field. While the past five years have seen rapid growth and substantial scientific progress, the Committee recognizes the large gap that still remains between advances made in research settings and practical benefits that are ready to be delivered to individuals and families living with ASD today. We remain far from the aspirational goal of research to yield tangible improvements in quality of life for people with ASD across all settings and communities. An intensified effort will be needed to ensure that recent promising discoveries are rapidly translated into clinical practice and services that will improve quality of life for individuals with ASD.

In conducting this review, the Committee recognized several core needs that spanned across multiple areas on the research portfolio:

- **Scaling Up**: Many of the screening tools, interventions and services approaches that have been developed to date are effective in research settings, tested in small groups. In order for these tools and approaches to have the potential to impact the community, they must be scaled up to be useable in the full range of community settings.
- **Population Inclusion**: Screening tools are frequently tested in the siblings of ASD children. Children with no family history of ASD, adolescents, and adults must all be considered in future screening tool development. For other studies, most subjects have mild disability and are in areas with good access to medical care. It is vital that subjects across the full range of ASD disability, across all periods of the lifespan, and from

underserved populations are included so that tools developed will have broad applicability.

- **Research to Practice**: In the arenas of interventions and services, there are already many practices that are being utilized within the community, and there are interactive networks of individuals and families available, providing an opportunity to study the use of these interventions and services in a real-world setting. More academic and community partnerships and new clinical trial approaches are needed to leverage these resources and gain valuable insight into what works well in the community.
- **Leveraging Existing Infrastructure**: In the past five years, both public and private resources have been invested in establishing infrastructure for surveillance, clinical research, environmental studies, and data sharing. To fully utilize these resources and gain the maximum value from these investments, agencies and organizations should consider building new studies onto these existing resources.
- **Applying Strategies from Other Fields:** Science and services research are advancing in other fields. Over the past five years, there has been much success in learning about ASD biology from research on related disorders. Similarly, ASD researchers may be able to adopt successful strategies from other disease fields to solve issues such as how to detect trace chemicals in small biosamples effectively or how to effectively reach underserved populations with tools and services. Finally, the data collected by longitudinal studies and the data available through NDAR need to be exhaustively analyzed.
- **Standardized Outcome Measures**: In order to truly determine the effectiveness of interventions and the outlook across the lifespan, measurements of outcomes that are responsive to interventions and quality of life measures that can help determine the effectiveness and impact of services must be identified and standardized.

Future Directions

History may show that the past five years marked an inflection point for our understanding of ASD. Increased investments, especially from private sources, improved resources for research, and many new scientists entering this field all provide hope that recent progress will accelerate. Many new areas of science, from microbiomics to social prosthetics, may transform our understanding of ASD and provide entirely new tools for interventions. One of the greatest challenges will be finding the right balance between science that can immediately improve quality of life for individuals with ASD and science that offers a deep understanding of ASD with the promise of prevention or cure. The ASD community is not of one mind on how to set this balance, with some focused on identifying the causes of ASD so that ASD prevalence can be reduced in future generations and others focused on inclusion and acceptance, passionately opposed to the goals of prevention and cure. In the near term, science can serve both goals as we develop a deeper understanding of the many forms of ASD and enhance interventions that can offer individuals with ASD opportunities for independence and participation in the community.

Prepared for IACC Conference Call December 13, 2013

This document is for discussion purposes only and does not reflect the decisions of the IACC