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2013 IACC Strategic Plan Update - Question 7 Draft

What Other Infrastructure and Surveillance Needs Must Be Met? - Volunteer drafter – Alison Singer

Introduction:

The aspirational goal for Question 7 is to "develop and support infrastructure and surveillance systems that advance the speed, efficacy and dissemination of ASD research". The original strategic plan, launched in 2009, was structured around only six Questions. In 2010, the IACC recognized that grouping the topics of research infrastructure and workforce, as well as ASD surveillance, into a separate chapter would highlight these issues that are critically important to research success and help the committee track investments and evaluate progress in this area in the same organized, rigorous manner that is used in the rest of the plan. Over the past 5 years, a total of $158M dollars has been invested in building and maintaining the ASD research infrastructure to support needed research and surveillance efforts. Many of the original infrastructure needs identified in 2009 have been accomplished, but ongoing funding is critical in order to develop, maintain, and build on these valuable new resources.

Progress Towards the Strategic Plan Objectives:

The IACC ASD Research Portfolio Analyses reviewed projects funded by both government agencies and private foundations from 2008-2012. From 2009-2012, the total funding devoted to projects pertaining to Question 7 was $158.03M. On average for each year from 2010-2012, the funding levels for this Question were doubled from the 2009 level ($15.8M) and the number of funded projects was also more than twice as high. Additionally, in years 2009-2012, 27% of the total funding went toward core research projects that were not aligned with the research gaps covered by the 16 objectives in Question 7.

Of the 16 specific objectives under Question 7, 8 objectives addressing basic and clinical data sharing and dissemination, workforce expansion, and model-systems resources met or exceeded the recommended budget and fulfilled the recommended number of projects. Four objectives, concerning documenting the services available in each state, expanding biobanks, and expanding surveillance infrastructure partially met the recommended budget and had a number of projects underway. Four more objectives did not have any funding or projects. Two of these objectives, focused on a needs assessment for database linkage, and a funding mechanism for rapid replication remain high-priority. The objective concerning development of a web-tool for prevalence estimates was fulfilled through a project outside of the autism portfolio, and the intent of the objective to disseminate best practices in service provision through "Promising Practices" papers was not completed, but may have been superseded by

other types of best practice dissemination methods, so the objective in its current form was not viewed by the committee as a high priority to continue.

Infrastructure:

Over the past five years there has been a significant rise in data sharing among researchers, increased availability of biological samples, expanded surveillance efforts, substantial investment in building the ASD research workforce and major improvement in research dissemination.

Databases have been developed to house and provide researchers with access to valuable research data collected from those affected by autism as well as neurotypical subjects. In addition, in 2011 the NIH Office of Autism Research Coordination developed and launched a new database, the IACC Portfolio Analysis Web Tool, that gathers data on all federal and nonprofit supported ASD research-related projects together into one place, enabling broad public access to detailed information about these projects, as well as searching, sorting and graphics to facilitate further analysis and monitoring of progress over time.

The Interactive Autism Network (IAN), developed by the Kennedy Krieger Institute is a tool designed to match scientists with research subjects to enhance the pace of research. The IAN network has also greatly facilitated rapid research on issues of symptom severity and intervention. For example, in 2011 when the issue of autistic wandering was brought to the IACC's attention, a study involving over 1200 children was completed in only 3 months utilizing the IAN database that indicated that almost 50% of children with ASD had wandered. (Anderson et al., 2012). In conjunction with this rapid study, a new ICD-9 code to track autistic wandering was almost immediately implemented and the AAP issued new guidelines that included wandering in patient-family anticipatory guidance, alerting parents of children with ASD to the prevalence of wandering so that they could take preventative measures.

The National Database for Autism Research (NDAR) funded by NIH is a rich resource that includes genomic data and imaging studies as well as other types of data for use in ASD research. NDAR has become the standard data repository for the ASD research community. In January 2010, the NIH began including an expectation for data sharing in most of its awards, requiring that human subject data be deposited in a broadly accessible database. In 2012, 81% of NIH-funded human subjects grants were contributing data to NDAR. NDAR also supports data sharing from other funders of autism research including the Autism Science Foundation, the Centers for Disease Control, the Department of Defense, and the State of New Jersey. NDAR has also now linked to IAN and the Autism Speaks supported Autism Genetic Resource Exchange (AGRE) and Autism Tissue Program (ATP), enabling researchers access to data in those repositories.

Comment [sd1]: SFARI data not available yet, but will add in if available by time of publication

To date, NDAR has facilitated the sharing of data on 70,000 research subjects with much more expected in the next 24 months. Also, the rich "omics" and imaging datasets have been de-identified and now protected in the computational cloud, enabling unprecedented resources, techniques and computational software to be used collaboratively. The results of such efforts (e.g. omic alterations and imaging volumetrics) along with ontological concepts like IQ, language and executive function enable a layered approach across research disciplines to help drive scientific discovery. NDAR data have been cited in publications, and access requests have been substantial. Over 300 researchers at 75 laboratories from 10 countries have applied and been granted access to NDAR in 2013, which is a 300% increase over 2012.

Aggregated data in NDAR, its federated partners and the labs sharing data are available to the general public (see NDAR Query). NDAR now supports harmonized receipt of all human subjects research data with clinical, imaging, omics, proteomics, EEG, eye tracking, and task-based fMRI specifically supported. Figure 1 provides a summary of the data now available in NDAR.

(Table) Number of Research Subjects Shared Through NDAR

	2009*	2013
Total	**2,500**	**70,000**
Omics	**2,500**	**18,500**
Images	**0**	**2,400**

Figure 1.* *Essentially all data being shared in 2009 were contained in the Autism Speaks AGRE and ATP data repositories. By 2013, NDAR had dramatically expanded the data available in all categories.*

Comment [DJH 2]: We began sharing in 2010 so it seems more appropriate to show only 2009 and 2013. I can add 2011 if needed.

(Table) Number of Research Subjects Shared Through AGRE

	2009	2013
Total	**4,000**	**70,000**
Omics	**3,200**	**18,500**
Images	**0**	**2,400**

Figure 2. The number of samples in the NIMH Genetics repository has increased to more than 27,000, many with extensive phenotypic/genotypic information. The NIMH repository has also started collecting IPS lines and fibroblasts. In terms of DNA, this represents a two-fold increase since 2008.

NIMH Genetics Repository Sample Summary

Phenotypic category	# Subjects with DNA/LCL/CPL[1] samples	#Subjects with samples and phenotypic[2] data in	# Total affected cases in distribution (independent	#Multiplex families (Trios)	# Subjects with fibroblast lines (iPSC[6]) in distribution

		distribution[3] (% non-caucasian[4])	cases[5])		
Autism (2013)	28,288	15,676 (17%)	6,278 (4,222)	1,553 (3,387)	21 (25)
Autism (2012)	27,240	14,628 (17%)	5,938 (3,906)	1,530 (3,179)	0 (0)
Autism (2011)	25,890	9,822 (24%)	4,252 (2,479)	1,431 (1,860)	0 (0)
Autism (2010)	23,421	8,601 (20%)	3,842 (2,128)	1,386 (1,630)	0 (0)
Autism (2009)	19,824	6,434 (19%)	3,001 (1,598)	1,125 (1,209)	0 (0)
Autism (2008)	14,887	6,434 (19%)	3,001 (1,598)	1,125 (1,209)	0 (0)

Figure 3. Summary of sample number and type for Autism specific samples included in the NIMH Genetics Repository. [1] LCL, Lymphoblastoid Cell Line; CPL, Cryopreserved Lymphoblasts [2] Phenotypic data includes clinical interviews, DIGS (Diagnostics Interview for Genetics Studies) & DSM variables. Samples include unaffected family members. [3] Distributions are NIMH sample collections with phenotypic data available for distribution to authorized investigators. [4] Non-Caucasians include Black, Hispanic, American Indian and Asian. [5] Subjects are unrelated. [6] Induced pluripotent stem cell lines produced by NGRR Stem Cell facility.

Unfortunately, brain tissue samples have actually declined over the past five years due to a freezer malfunction at Harvard in 2012 that resulted in the loss of more than half of the existing samples. This year, only 9 new ASD brains were added to the repositories. Despite these challenges and setbacks, there is a concerted effort both publicly and privately to increase the number of brain tissue samples. In 2013, NIH launched a new NIH Neurobiobank initiative. This repository will collect and standardize brain tissue samples for research on ASD as well as other brain disorders. The initiative includes a publication to increase awareness of brain donation, "Why Brain Donation? A Legacy of Hope." In addition, a group of private funders including the Autism Science Foundation, the Simons Foundation, Autism Speaks, and the Nancy Lurie Marks Foundation recently launched the Autism BrainNet, a multi-site effort to increase the numbers of ASD-specific brain samples. Their efforts will also include an ASD-specific outreach and education plan to encourage tissue donation.

Surveillance:

Updated estimates published in 2012 from the Centers for Disease Control and Prevention's ASD and Developmental Disability Monitoring Network (ADDM) indicate that 1 in 88 children is diagnosed with an ASD spectrum disorder. The ADDM network has been the primary U.S. surveillance initiative, including 12 sites, and data are now available over multiple years, which

enables researchers to examine prevalence trends as well as characteristics that are changing in the population and average age at diagnosis. The ADDM infrastructure has laid the foundation to expand surveillance to younger children in 6 ADDM sites. In addition, ADDM investigators have initiated data linkage and analytic projects to better understand characteristics of the population of children with identified ASD. These include evaluations of perinatal characteristics, parental age, medication use, participation in the juvenile justice system, hazardous air pollutant exposures, phenotypic characteristics, and changes in prevalence over time, among others. The ADDM Network has established a system to provide updated ASD prevalence estimates and has enabled a better understanding of the needs of the community. In addition to ADDM, the National Survey of Children's Health (NSCH), using telephone survey methodology, reported ASD prevalence estimates that were surprisingly consistent with ADDM estimates (Van Naarden Braun, Pettygrove et. Al. 2007). More recently, Autism Speaks supported a population-based screening effort to evaluate the potential for children with ASD to be missed by current methods. Future needs include continued use of surveillance to describe the most current and changing population of children with ASD and to better understand the functional status of individuals meeting diagnostic criteria for ASD and needs of adolescents and adults with ASD.

Comment [I[3]: What about need for population based epi (now underway in SC), studies of incidence (recently reported in UK), and resolving questions about reasons for rising prevalence?

Despite tracking of the age of diagnosis and other changes over time, there has been minimal progress in reducing the age of diagnosis. As the prevalence of ASD increases, there has been a greater number of children identified with ASD: specifically those with ASD without intellectual disability and among racial and ethnic minority groups. Children without intellectual disability or with fewer ASD characteristics tend to be identified at later ages. Thus, while more children are being identified, much work needs to be done to identify children with ASD and other developmental delays earlier and more equitably so that all of those in need of services can be connected to appropriate services and supports as early as possible. The surveillance infrastructure may present opportunities for more in depth data collection related to services, treatment, and co-occurring conditions to complement data currently collected and identify opportunities for improving diagnosis and treatment of children with ASD.

Future efforts must focus on encouraging more families from diverse backgrounds to participate in ASD research, join registries, and donate biological samples. As the ability to collect and link data grows, it is crucial to also pay greater attention to issues of privacy, security and ethical use of data.

Progress Towards the Aspirational Goal:

Progress towards the Question 7 aspirational goal to "develop and support infrastructure and surveillance systems that advance the speed, efficacy and dissemination of ASD research" has been rapid over the past 5 years. As demonstrated by the above tables, the numbers of shared subjects and samples have doubled at minimum, and in some cases increased by orders of magnitude. This increase in resources to study advances the speed and efficacy of ASD research. The sharing of these resources through initiatives such as NDAR, IAN, and AGRE demonstrate effective dissemination of resources, and fuel the cycle of increased research speed and efficacy. In terms of research infrastructure, the aspirational goal will be met as long as current support is continued and current momentum is maintained.

Surveillance systems have also progressed over the past 5 years, with the caveat that despite tracking of the age of diagnosis and other changes over time, there has been minimal progress in reducing the age of diagnosis. As the prevalence of ASD increases, there has been a greater number of children identified with ASD: specifically those with ASD without intellectual disability and among racial and ethnic minority groups. Children without intellectual disability or with fewer ASD characteristics tend to be identified at later ages. Thus, while more children are being identified, much work needs to be done to identify children with ASD and other developmental delays earlier and more equitably so that all of those in need of services can be connected to appropriate services and supports as early as possible. The surveillance infrastructure may present opportunities for more in depth data collection related to services, treatment, and co-occurring conditions to complement data currently collected and identify opportunities for improving diagnosis and treatment of children with ASD.

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