Question 7 Draft Updates for the IACC 2011 Strategic Plan

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

Question 7. What other Infrastructure and Surveillance Needs Must be Met?

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

Data sharing

This year, the Autism Informatics Consortium (AIC) was formed with the goal of accelerating scientific discovery by making informatics tools and resources more useful to, and usable by, autism researchers. The consortium is charged with identifying information technology solutions, harmonizing major informatics frameworks, and developing standards in the field for working with research data. The consortium is comprised of representatives from both public and private institutions that are responsible for the development of major autism informatics tools and resources. Current members include Autism Speaks (Autism Genetic Resource Exchange), Kennedy Krieger Institute (Interactive Autism Network), Simons Foundation and Prometheus Research (Simons Foundation Autism Research Initiative), and the National Institutes of Health (National Database for Autism Research). The AIC held its first workshop on August 26-27, 2010 at the NIMH offices in Rockville, MD. In attendance were representatives from 12 major research institutions. The objective of the meeting was to explore short term (1-2 years) and intermediate term (2-5 years) priorities for increasing the utility and harmonization of major autism research informatics resources, identify ways to best pursue those priorities, and determine ways to measure progress toward achieving them.

Considerable progress has been made on the input of data to the National Database for Autism Research created by the NIH. Data are now available to researchers from over 10,000 participants enrolled in studies of ASD. Access to the data is through a NDAR supported web portal which supports queries from multiple databases simultaneously.

Biobanking

There has been considerable progress in the growth of a number of major biobank repositories:

The Autism Treatment Network (ATN), a collaboration among 14 academic medical centers providing clinical services for children with ASD, collects and stores common, extensive phenotypic data on children with autism in a central patient registry. This year the ATN was funded by the National Institute of Mental Health to collect DNA, plasma, and urine from four of the 14 sites as a beginning step toward establishing a comprehensive biorepository for the ATN. One goal of establishing the repository is to provide a platform for conducting comparative effectiveness research that can utilize biomarkers to predict response to treatments.

The Simons Simplex Collection, supported by the Simons Foundation Autism Research Initiative (SFARI) , was established to develop a permanent research repository of detailed phenotypic and genetic information on 3000 simplex families with a child with an ASD. Nearly 2000 families have been enrolled as of November 2010 with the goal of completing enrollment by the summer of 2011. (Fischbach and Lord, 2010)

The Autism Genome Project, a collaborative effort between Autism Speaks and a number of other organizations is focusing on identifying genes associated with the risk for ASD. The AGP consists of 120 scientists from more than 60 institutions representing 11 countries. The biobank now includes 23,101 samples with 5,814 probands.

The Autism Genetic Resource Exchange (AGRE) is a program of Autism Speaks to advance genetic research in autism spectrum disorders. Genetic biomaterials and clinical data are obtained from multiplex families (i.e., families with more than one member diagnosed with an ASD). The biological samples, along with the accompanying clinical data, are made available to AGRE-approved researchers. There are over 10,000 samples in the AGRE repository on individuals with ASD and their family members (include 4240 on probands.) About half of the sample in AGRE are also represented in the AGP

[OARC to provide information on NIH intramural biobanks]

Surveillance

One area which has progressed is the establishment of systems to identify and monitor the prevalence of ASDs in the US. The ADDM Network (CDC, 2009) and report from the National Survey of Children's Health (Kogan et al., 2009) reported ASD prevalence of around 1% of children. Of great concern was the average increase of 57% from 2002 to 2006 in 10 areas of the US covered by the ADDM Network (CDC, 2009) with 45% of the children ever having an autistic disorder diagnosis in 2002 and 47% in 2006. While some of the increase was attributed to improved identification of particular subgroups such as Hispanic children and children without cognitive impairment; a true increase in risk is also possible. (CDC, 2009) Several other recent studies have also indicated that multiple identification factors contribute to, but do not fully explain the rising ASD prevalence (Hertz-Picciotto and Delwiche, 2009; Saemundsen, 2010; King and Bearman, 2009; Rice et al., 2010; Van Meter et al., 2010; Mazumdar et al., 2010). Concerted efforts are now needed to evaluate the reasons behind these changes.

Information and Communication Dissemination

Of particular importance is the rapid translation of research findings as they apply to intervention and the dissemination to families and practitioners in the community in a way that is easy to access and understand. There have been several reviews of intervention quality and effectiveness (http://www.impaqint.com/files/4-content/1-6-publications/1-6-2-project-reports/finalasdreport.pdf) (Lang et al., 2010) and several states have formed task forces or councils for ASD and other DD services and have compiled service plans based on the current state of knowledge. http://www.aucd.org/template/event.cfm?event_id=2456&id=547&parent=547

Research Workforce Development

[OARC to provide information… opportunity and gap left by ending of ARRA funds…]

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What gap areas have emerged since last year?

Data sharing

The AIC identified several short term and long term priorities for increasing the utility and harmonization of major autism research informatics resources, identifying ways to best pursue those priorities, and determining ways to measure progress toward achieving them. Examples of gap areas identified include the need for improved options for data federation, query interfaces and languages, genetic visualization tools, file and data set management, data quality and validation rules and algorithms, data dictionaries and ontologies, standardizing GUID usage. procedures for maintaining phenotype resources with associated biospecimens (imaging, genetics, etc) , defining a core (clinical) phenotype battery, working with publishers of copyrighted assessments, and addressing concerns about intellectual property.

During 2010, the Affordable Care Act was passed with an unprecedented call to transition record keeping to Electronic Health Records (EHRs). The development of EHRs provides an opportunity to consider the use of EHRs for data collection and analyses related to the service needs of people with ASDs. Of course, important privacy issues need to be considered and addressed before these types of data could be more routinely collected and utilized as part of EHRs.

Biobanking

In the absence of biological markers, current approaches for stratification of individuals with ASD into clinically meaningful subgroups have relied on behavioral characteristics. However, the variability of behavioral, medical, and developmental concerns that affect individuals with ASD has made it extremely difficult to predict which treatments work best for which individuals. The integration of biologic information into phenotype selection algorithms can help to guide the development and evaluation of more targeted and effective therapeutics and significantly improve the prediction of a therapeutic response. To this end, there is a need for the establishment of a robust network of clinical research sites offering clinical care in real-world settings that can collect and coordinate standardized and comprehensive diagnostic, biological (e.g. genotype), medical, and treatment history data that would provide a platform for conducting comparative effectiveness research and clinical trials of novel autism treatments. Currently, there is a need high-throughput screening tools to quickly evaluate gene-environment interactions relevant to ASD. Lack of progress in this area has made identification of potential exposures of interest difficult and driven by anecdotal evidence.

Surveillance

Moving forward, there is a need to maintain the sites so that early prevalence and population characteristics can be compared over time. A particular challenge is keeping consistency in the number of sites with four-year funding cycles and different numbers of sites funded based on availability of funds. In addition, completeness of data collection is hindered in some sites by the lack of access to educational records for surveillance purposes. Despite these challenges, the ADDM Network has maintained a core of approximately 12 sites with multiple prevalence years completed. There is now a need to go further to understand how multiple identification and potential risk factors have influenced

the increasing estimates of ASD prevalence. Further analyses of existing datasets are needed to examine any relationship between changes in ASD prevalence and changes in potential risk factors in the population. Surveillance cohorts also provide the opportunity for communities and policy makers to use these data for resource allocation in addition to characterizing population-based identification patterns and gaps. Surveillance data can also be used to better characterize the population of children identified with an ASD by select characteristics such as level of cognitive impairment, subtypes as diagnosed by community professionals, diagnostic features, associated conditions, degree of impairment by clinician rating. Expansion of surveillance efforts are to improve early identification and to understand functioning and outcome of individuals with an ASD as adults.

Communication and Information Dissemination

There have been several reviews of intervention quality and effectiveness and several states or agencies (Governor's councils, task forces, Department of Education, etc.) have developed plans for ASD and other DD services based on the current state of knowledge. This information and these plans should be easily accessible to other communities. Right now, there are many public and private resources which work to compile services and supports information; however, finding this information can be challenging.

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Focusing more on the issue of translating research into practice, the IACC Services Subcommittee Workshop on November 8, 2010 called for research that is meaningful to teachers and family members, and conducted in non-clinical settings to better simulate the settings in which children with ASD are being served. This will help to ensure that students with ASD receive high quality special education services.

The Agency for Health Research and Quality (AHRQ) has ongoing efforts to related to translation of research into practice. This work includes identifying sustainable and reproducible strategies (1) to help accelerate the impact of health services research on direct patient care and (2) to improve the outcomes, quality, effectiveness, efficiency, and/or cost effectiveness of care through partnerships between health care organizations and researchers. To further address the challenges around dissemination of research findings, AHRQ developed a "knowledge transfer framework" which encompasses three major stages—knowledge creation and distillation, diffusion and dissemination and end user adoption, implementation and institutionalization. While this work is not specific to autism, it may provide a useful framework to guide autism research translation efforts.

Research Workforce Development

The on-going investment in developing research expertise and facilitating careers in autism research is needed, especially in the emerging areas of health services research, translational research, and international collaborative studies.

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The pharmaceutical industry is making a substantial investment in drug-related research for ASDs. One large company has efforts specifically devoted to drug discovery for autism and other major

pharmaceutical companies have active trials or are in the research planning phase. There are also some smaller biotech/pharmaceutical companies that have active trials (phase I-IV) in clinicaltrials.gov specifically for autism or fragile-x and autism. (Is this strictly a workforce development issue, or is it more broadly about the expansion of the field in the direction of therapeutics development? Also this sounds like progress rather than a gap, so should it move to earlier section on progress?)

What new research opportunities and research objectives have emerged?

Revise Objective B: Conduct an annual "State of the States" assessment of existing state programs and supports for people and families living with ASD by 2011, *IACC Recommended Budget: $300,000 each year.* Revise Objective D: Establish and maintain an international network of biobanks for the collection of brain, fibroblasts for pluripotent stem cells, and other tissue or biological material, by acquisition sites that use standardized protocols for phenotyping, collection, and regulated distribution of limited samples by 2011. This includes support for post-processing of tissue such as genotyping, RNA expression profiling, and MRI. Protocols should be put into place to expand the capacities of ongoing large-scale children's studies to collect and store additional biomaterials, including newborn bloodspots, promoting detection of biological signatures. Support should also be provided to develop an international web-based digital brain atlas that would provide high resolution 3D images and quantitative anatomical data from tissue of patients with ASD and disease controls across the lifespan, which could serve as an online resource for quantitative morphological studies by 2014.

IACC Recommended Budget for establishing biobanks by 2011: $10,500,000 over 2 years. IACC Recommended Budget for maintaining biobanks: $22,200,000 over 5 years.

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Research Resources

New Objective:

A. Establish a robust network of clinical research sites offering clinical care in real-world settings that can collect and coordinate standardized and comprehensive diagnostic, biological (e.g. DNA, plasma, fibroblasts, urine), medical, and treatment history data that would provide a platform for conducting comparative effectiveness research and clinical trials of novel autism treatments by 2012.

B. Create an information resource for ASD researchers (e.g. PHEN-X Project) to share information to facilitate data sharing and standardization of methods across projects. This includes common protocols, instruments, designs and other procedural documents and should include updates on new technology and links to information on how to acquire and utilize technology in development. This can serve as a bidirectional information reference, with autism research driving the development of new resources and technologies, including new model systems, screening tools, and analytic techniques by 2013.

Deleted: Revise Objective M: Support 10 "Promising Practices" papers that describe innovative and successful services and supports being implemented in communities that benefit the full spectrum of people with ASD, which can be replicated in other communities by 2015 and make these available on the "ASD Services and Supports" web portal. *IACC Recommended Budget: $75,000 over 5 years.* ¶

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Deleted: <#> programs and funding mechanisms that expand the research workforce, enhance interdisciplinary research training, and recruit early career scientists into the ASD field by 2013. *IACC Recommended Budget: $5,000,000 over 3 years.* ¶

Comment [c2]: How does NDAR and AIC fit into this?

C. Provide resources to centers or facilities which develop promising vertebrate and invertebrate model systems and make these models more easily available or expand the utility of current model systems, and support new approaches to develop high throughput screening technologies to evaluate the validity of model systems by 2013.

D. Create an information resource for ASD service providers, researchers, families, and people with an ASD which serves as a portal to obtain the most recent evidence-based reviews and plans for intervention, services, and support by 2012.

Comment [c3]: Offered as a revision to Obj E

E. Conduct a meeting in 2011 that will establish standards for data collection on phenotyping and imaging protocols (other aspects??)

References

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