The Interagency Autism Coordinating Committee

2010 STRATEGIC PLAN

for Autism Spectrum Disorder Research

DEPARTMENT OF HEALTH & HUMAN SERVICES·USA

IACC
INTERAGENCY AUTISM
COORDINATING COMMITTEE

About the IACC

The Interagency Autism Coordinating Committee (IACC) was established by Congress under the Combating Autism Act of 2006 (CAA) to provide advice to the Secretary of Health and Human Services (HHS) and coordinate all efforts within HHS concerning autism spectrum disorders (ASD).

As mandated by law, the IACC has a membership composed of federal officials from agencies involved in autism research and services and public members, including people with ASD, parents of children and adults with ASD and members of the autism advocacy and research community. The diversity of the committee ensures that a broad range of views and opinions is reflected and discussed in a public forum.

Under the CAA, the IACC is required to: (1) Develop and annually update a strategic plan for ASD research, (2) develop and annually update a summary of advances in ASD research, and (3) monitor federal activities related to ASD.

In completing the first IACC Strategic Plan for Autism Spectrum Disorder Research in 2009 and releasing this first update of the plan in 2010, the IACC has laid out a framework for the pursuit of critical biomedical and services research. Through activities such as public meetings and workshops, publication of an annual Summary of Advances in ASD Research, dissemination of information regarding ASD research and IACC activities, gathering of public input and coordination of federal activities related to autism, the IACC continues in its effort to provide guidance to the Department of Health and Human Services and to reach out to the broader autism community to find ways to work together to help people with autism and their families.

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For more information about the IACC, see: www.iacc.hhs.gov

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Preface

With recent reports that autism spectrum disorder (ASD) is becoming increasingly prevalent – now estimated to affect about 1 percent of children in the United States – efforts to accelerate the research field take on even greater urgency.

In developing the 2010 Strategic Plan for ASD Research, the Interagency Autism Coordinating Committee (IACC) updated the previous Plan to highlight the most pressing research needs and opportunities for the field today. The Plan, which must be annually updated in accordance with the Combating Autism Act (CAA) of 2006, provides a blueprint for autism research that is advisory to the Department of Health and Human Services and serves as a basis for partnerships with other agencies and private organizations involved in autism research and services. In the process of developing the 2010 update of the Plan, the committee collected feedback from scientists, advocacy groups, research funding organizations, and members of the public to guide their efforts to refine the first version released in 2009.

"On this first update of the Plan, the IACC really put its shoulder to the wheel, adding not only new objectives but a new chapter, as well," said Dr. Thomas Insel, M.D., IACC Chair and Director of the National Institute of Mental Health (NIMH), part of the National Institutes of Health (NIH).

These substantial revisions, which include the addition of a new chapter on infrastructure, came after a year-long process in which the IACC conducted a comprehensive analysis of current ASD research funding and summarized major research advances in the previous year. The IACC also revised the 2009 Plan based on public input through a formal Request for Information, a Town Hall meeting, and other public comments. During a two-day workshop, invited panelists considered all of this information as they made recommendations for the update.

During the updating process, the IACC heard the need for more research on adults, more focus on non-verbal people with ASD, and the need for better infrastructure for research – from biological specimen repositories to better surveillance. The 2010 Strategic Plan addresses these needs and has developed additional objectives with recommended budgets for the research.

ASD research has become a national priority, receiving a massive surge in funding through the American Recovery and Reinvestment Act (ARRA) of 2009. With greater financial resources and the 2010 Strategic Plan to direct future work, researchers have been given the tools to make great strides in understanding ASD, developing potential interventions, and improving quality of life for people with ASD and their families.

The Interagency Autism Coordinating Committee (IACC) Strategic Plan for Autism Spectrum Disorder Research

Introduction

Two decades ago, autism was a little known, uncommon disorder. Today, with prevalence estimates increasing at an alarming pace, autism is emerging as a national health emergency. Autism is now recognized as a group of syndromes denoted as autism spectrum disorder (ASD). The most recent Centers for Disease Control and Prevention (CDC) prevalence estimates of ASD for children are 1 in 110 (CDC, 2009). These estimates, more than ten-fold higher than two decades ago, raise several urgent questions: Why has there been such an increase in prevalence? What can be done to reverse this alarming trend? How can we improve the outcomes of people already affected, including youth and adults?

Approaches to ASD diagnosis have evolved as more has been learned about the disorder. Currently, ASD is diagnosed on a combination of behavioral characteristics of impairment in verbal and nonverbal communication skills and social interactions, and restricted, repetitive, and stereotyped patterns of behavior, and these can range in impact from mild to significantly disabling. Adequately addressing these conditions requires sophisticated educational and therapeutic approaches. Some people with ASD also have a range of medical conditions including, but not limited to: motor and sensory impairments, seizures, immunological and metabolic abnormalities, sleep problems, and gastrointestinal symptoms.

The cost of ASD to affected people, families, and society is enormous. A great majority of adults with ASD struggle with ongoing and mostly unmet needs for employment, housing, services, and supports. Compounding these stressors, families with a child with autism typically lose income, possibly as a result of one parent leaving the workforce in order to care for and meet the special health and educational needs of the child (Montes & Halterman, 2008). The cost to society of ASD is currently estimated to be $35-$90 billion annually, the higher estimate being comparable to Alzheimer's disease (Ganz, 2007; Järbrink & Knapp, 2001). Although research on ASD has expanded over the past decade, there remains an urgent need for continuing research support.

It is imperative that resources be devoted to research commensurate with the public health need. Specifically, we need research that deepens our understanding of ASD, including the complex genetic and environmental factors that play a role in its causation; development of improved ASD diagnostic approaches and treatments; and science to enhance the level of services and supports available to people with ASD, their families and caregivers. With current scientific knowledge and tools, we have unprecedented potential for discoveries that will improve the quality of life for people with ASD.

In response to the heightened societal concern over ASD, Congress passed the Combating Autism Act (CAA) of 2006 (P.L. 109-416). Through this Act, Congress intended to rapidly increase, accelerate the pace, and improve coordination of scientific discovery in ASD research. The CAA requires the Interagency Autism Coordinating Committee (IACC) to develop and annually update a Strategic Plan for ASD research, including proposed budgetary requirements.

Driven by both the sense of urgency and a spirit of collaboration, the IACC developed an initial Strategic Plan for ASD Research in 2009 and revised it in 2010 in accordance with the CAA. The Plan and its revisions were developed through extensive and iterative input from members of the public, academic, and advocacy communities. In developing and revising the Strategic Plan, the IACC:

- Identified recent investments and accomplishments in ASD research.
- Assessed the strengths, weaknesses, opportunities, and gaps in the ASD research enterprise.
- Gathered ideas for research opportunities from a diverse group of stakeholders.
- Convened four scientific workshops and solicited input from the public and non-government research sponsors to identify research opportunities.
- Convened expert workgroups to recommend research objectives and strategies.
- Convened programmatic and agency experts to develop and recommend professional judgment budget estimates for each objective in the Plan.
- Convened a scientific workshop to review and revise the Strategic Plan in 2009.

The Strategic Plan incorporates this array of input in two main sections. First, the foundation of the Plan – vision, mission, core values, and crosscutting themes – is described. The remainder of the Plan is organized around seven critical questions asked by people and families living with ASD.

- **When should I be concerned?**
- **How can I understand what is happening?**
- **What caused this to happen and can this be prevented?**
- **Which treatments and interventions will help?**
- **Where can I turn for services?**
- **What does the future hold, particularly for adults?**
- **What other infrastructure and surveillance needs must be met?**

Each question is followed by a brief discussion of what we currently know and need from research, an aspirational goal, research opportunities and objectives. This framework was chosen by the IACC to emphasize the need for consumer-focused research that addresses the most pressing questions of people and families living with ASD, and to link these questions to specific research efforts.

Vision Statement

The Strategic Plan will accelerate and inspire research that will profoundly improve the health and well being of every person on the autism spectrum across the lifespan. The Plan will set the standard for public-private coordination and community engagement.

Mission Statement

The purpose of the Strategic Plan is to focus, coordinate, and accelerate high quality research and scientific discovery in partnership with stakeholders to answer the urgent questions and needs of people on the autism spectrum and their families.

Core Values

The IACC adopted these core values and emphasized their importance for the Strategic Plan development and implementation:

Sense of Urgency – We will focus on what steps we can take to respond rapidly and efficiently to the needs and challenges of people and families affected by ASD.

Excellence – We will pursue innovative basic and clinical research of the highest quality to protect the safety and advance the interests of people affected by ASD.

Spirit of Collaboration – We will treat others with respect, listen to diverse views with open minds, discuss submitted public comments, and foster discussions where participants can comfortably offer opposing opinions.

Consumer-focused – We will focus on making a difference in the lives of people affected by ASD, including people with ASD, their families, medical practitioners, educators, and scientists. It is important to consider the impact of research on the human rights, dignity, and quality of life of people with ASD from prenatal development forward.

Partnerships in Action – We will value cross-disciplinary approaches, data sharing, teamwork, and partnerships with clearly defined roles and responsibilities.

Accountability – We will develop SMART (Specific, Measurable, Achievable, Realistic, and Time-bound) research objectives aligned with funding priorities and develop systems for evaluation, assessing impact, and course corrections.

Crosscutting Themes

The Strategic Plan for ASD Research is designed to highlight the most promising research ideas, while appreciating the inherent unpredictability of research. These ideas form the basis for the research opportunities and objectives of the Strategic Plan. In the process of gathering ideas from ASD stakeholders for this Plan, certain themes emerged repeatedly. These themes are highlighted here to emphasize their importance across the framework.

Heterogeneity: Although certain core features are present at varying degrees among all people with ASD—i.e., social impairments, communication difficulties, and stereotyped behaviors—considerable heterogeneity exists as well. In the context of ASD, the term heterogeneity refers to the constellation of behavioral and medical conditions and symptoms that may accompany the disorder. The spectrum includes people with ASD who are nonverbal and cannot live independently, and others who find gainful employment and live independently. There is little reason to assume that this spectrum identifies a single disorder. Rather, the spectrum encompasses a range of disorders. The heterogeneity of ASD poses both challenges and opportunities to researchers: challenges, because there are likely to be many different causal factors and trajectories for ASD subtypes, and opportunities, because recognition of the variety of ASD phenotypes can lead to more appropriate diagnosis, more precisely targeted treatments, and increased public awareness about the diversity inherent in ASD. Heterogeneity has a profound impact on the priorities and tactics of ASD research, because any given study must either focus on a particular focal point on the spectrum, or must be sufficiently complex and resourced to encompass a broader range along the spectrum. Acknowledging heterogeneity also has implications for intervention. With multiple causes and symptoms, there likely will be multiple ways and approaches to intervene (e.g., medical, behavioral, nutritional). In so doing, the ASD field will be more strategically positioned to determine what works best for which people.

Prevention: It is critical for research to identify the methods and approaches that can be used to prevent the challenges and disabilities of ASD. Additionally, if one views ASD as a biological disorder triggered in genetically susceptible people by environmental factors, then prevention can include prevention of new cases of ASD through the identification and elimination of environmental causes. What is essential for ASD research is to develop the state of knowledge to a level similar to what is now available in fields such as cardiology. No longer do we need to wait for someone to suffer a heart attack before providing life-saving treatments. Rather, early interventions are applied upon the

detection of risk factors so as to preempt these more serious consequences. Having sound research on the risk factors and the environmental triggers for ASD ultimately may allow us to achieve the goal of prevention: preventing the development of the disorder in some people at risk or reducing the degree of severity in those affected.

Earlier Detection: ASD is a developmental brain disorder that is currently diagnosed by the observation of core behavioral symptoms. As with many neurodevelopmental disorders, brain dysfunction may precede abnormal behavior by months or even years. However, without biomarkers to detect people either with or "at risk" for ASD during pre- or neonatal periods, diagnosis must rely on behavioral observations long after birth. As a result, intervention efforts may miss a critical developmental window. Until recently, most children with ASD in the United States (U.S.) did not receive a diagnosis until school age, and diagnosis was further delayed among disadvantaged or rural populations (Mandell et al., 2007). It is critical that the field enhance methods for detecting ASD earlier in life and across diverse populations, in order to bring about earlier intervention. Furthermore, a recurrent theme expressed during the scientific workshops for the Plan was the need for biomarkers to identify ASD risk before the behavioral manifestations and the delayed developmental trajectory are established.

Lifespan Perspective: Historically, ASD has been characterized as a disorder of childhood. Although most people with ASD will not outgrow their diagnosis, their symptoms will change in form and severity over time. There was great support during the development of this Plan for more research on ASD in older people, especially the need for practical strategies for increasing the quality of life and functioning of adolescents and adults with ASD. As people with ASD advocate for themselves and expand our knowledge of their experiences and needs, they become partners in the research effort.

Data Sharing: Data sharing allows researchers to: (a) validate the research results of other investigators; (b) pool standardized information collected by many different researchers to facilitate rapid progress; and, (c) use data collected by others to explore hypotheses not considered by the original investigators. The expectations for data sharing have increased with the recognition that larger samples are needed to answer many research questions and with the sense of urgency for making progress. Databases for neuroimaging scans and genomic sequence are already proving important for ASD research. Wide adoption of a standardized data sharing system like the National Database for Autism Research

(NDAR) can provide the necessary infrastructure to combine important research participant data and thereby propel ASD research forward.

Resources: In addition to data sharing, research often depends on the availability and quality of research resources, such as access to scientific instruments and repositories of biospecimens. An important resource, paradoxically, is the identification, assessment, and collection of biospecimens from people who do *not* have the disorder, as a basis for comparison. Such comparison groups serve a critical role in interpreting ASD research and findings. Moreover, human resources such as adequate numbers of well-trained researchers and administrators are vital to these efforts. This need cannot be understated. Attracting a cadre of rigorously trained researchers, including those outside the ASD research field, will foster innovative ideas and inter-disciplinary approaches**.**

Public-Private Partnerships: A strength of current ASD research is the degree of private involvement and investment in research funding from advocacy groups and committed stakeholders. In addition, the amount of research dollars awarded by the U.S. government for ASD research has grown rapidly over the past ten years. There is currently a great willingness on the part of government agencies and private organizations to collaborate on the development and implementation of the Strategic Plan for ASD Research. In fact, the Strategic Plan is built on the premise that the public and private sectors will work collaboratively to better leverage resources to advance the research opportunities and objectives put forth in the Plan.

Community Engagement in ASD Research: People with ASD, their families, their educators, their caregivers, and advocacy organizations have vital roles to play in shaping, participating in, and disseminating research. Their insights and perspectives are needed in order for interventions and services to be developed that will have maximal impact and have the strongest evidence and means for real-world uptake and utilization. Strategies are needed to gain and use the first-hand experience of people with ASD, their families, and caregivers.

1. WHEN SHOULD I BE CONCERNED?

- **What are the early signs of ASD?**
- **Are there typical characteristics that are part of an ASD diagnosis?**
- **How do variations in symptoms and severity create challenges in early diagnosis of ASD?**

What do we know?

A child's caregivers are often first to identify the signs of ASD. In the classic case, there may be delays or plateaus in a child's attainment of developmental milestones, such as the use of gestures, responding to name, or the onset of speech and pretend play. In other cases, the first signs of ASD occur in young children who appear to regress after they seem to have been developing normally. Current diagnostic criteria and classifications of ASD represent progress in identifying a core set of developmental symptoms that, in the past, might have been attributed to other disorders because of more narrowly defined ASD evaluation criteria.

The diagnosis of ASD can be reliably made by age three, because the core symptoms emerge by that time. However, most children eventually diagnosed with ASD exhibit signs of abnormal development well before the age of two. Recent studies of children at high risk because of the presence of a sibling with ASD suggest that many cases of autism can be detected by 12 months of age using simple behavioral tests, such as response to calling the child's name or ease of engaging the child in jointly looking at an object (Landa, Holman, & Garrett-Mayer, 2007). Nevertheless, the average age of diagnosis is 5 years (Wiggins, Baio, & Rice, 2006). A number of screening tools have been developed for detecting autism for children of varied ages and different levels of clinical variability. There are tools available for parents and caregivers, including a video glossary of early "red flags" of ASD in young children developed to help families and professionals learn how to identify subtle differences in development that may indicate areas of concern (Wetherby et al., 2007). In terms of diagnosis, there is emerging evidence that tools can be developed with sufficiently high sensitivity and specificity to support epidemiologic and risk factor studies.

Nationwide, there has been an effort to improve early identification of children with ASD to improve their functioning and outcomes. A recently published randomized, controlled trial demonstrated how a comprehensive developmental behavioral intervention for toddlers with ASD led to improvements in cognitive and adaptive behavior, thereby emphasizing the importance of early identification of and intervention for young children with ASD (Dawson et. al., 2010). Various public campaigns, including the CDC's "Learn the Signs. Act Early," have been initiated in recent years to raise awareness about the importance of early identification of developmental delays, including those associated with ASD. The American Academy of Pediatrics recommends screening children for ASD at 18 and 24 months with a standardized screening tool.

What do we need?

Most cases of autism and related disorders are not diagnosed until after a child's third birthday and sometimes not until adulthood, yet early intervention can have a critical influence on the future course of ASD. Moreover, many children from culturally, linguistically, and other diverse groups may have limited access to assessment services leading to delays in diagnosis (Mandell et al., 2009). Several issues have limited the use of early interventions. It remains difficult to diagnose ASD in very young children because there is considerable healthy variation in the age at which infants and toddlers reach typical developmental milestones (e.g., speech) and delays do not always indicate the presence of a disorder. The diagnosis of an ASD in a person of any age is currently based on behavioral and cognitive signs, reflecting abnormal brain development, but not on detection of brain or other biological differences that may be present before the emergence of the behavioral or cognitive signs. The discovery of reliable biomarkers could potentially identify people with ASD, or infants who will subsequently develop or are already developing subtle signs of ASD.

Children with ASD develop along different trajectories, some show abnormal behavior soon after birth, others develop normally for the first year or longer and then regress while others appear to later improve significantly. Greater clarity is needed in identifying these different trajectories and greater consistency is needed in applying their definitions. Healthcare and other early care and education providers may not have received training in recognizing the early warning signs of ASD. Pediatricians may not have received training on using existing screening tools at well check-ups as recommended by the American Academy of Pediatrics and some caregivers may be unaware of the early warning signs of ASD or where to access services, leading to delays in diagnosis.

Although families are eager for guidance, more research is needed to better answer the question of when developmental variation should become cause for concern. We need studies that test both new and current diagnostic and screening methods and that integrate both developmental and biologic approaches in community-based settings. In particular, studies need to be designed to validate methods in underrepresented minorities and disadvantaged populations. Such studies could increase our understanding of barriers to diagnosis and access to services. Taken together, earlier identification coupled with increased access to interventions and services could reduce disparities in health care and service provision, and ultimately improve outcomes for people with ASD.

Scientific studies of ASD require the reliable diagnosis of participants but this can be a time consuming and labor intensive process. Therefore, streamlined diagnostic approaches that facilitate the enrollment of research participants are needed. Researchers also need ASD measures that are easy to administer and are sensitive to changes in clinical status. With regard to heterogeneity, identifying characteristics that are specific to certain ASD subpopulations could potentially identify neurobiological and genetic markers and improve our understanding of more global causal and intervention mechanisms.

ASPIRATIONAL GOAL: CHILDREN AT RISK FOR ASD WILL BE IDENTIFIED THROUGH RELIABLE METHODS BEFORE ASD BEHAVIORAL CHARACTERISTICS FULLY MANIFEST.

Research Opportunities

- Valid and reliable ASD screening instruments and approaches, including general developmental screening instruments for use in community settings to identify a wide range of people, including younger children, adolescents, adults, people with co-occurring medical conditions, and people with subtle characteristics, who require diagnostic evaluation.
- Sensitive and efficient clinical diagnostic tools for diagnosing ASD in widely diverse populations, including underrepresented racial and ethnic groups, females, younger, older age groups, people with co-occurring medical conditions.
- ASD measures that are easy to administer and sensitive to incremental changes in both core and associated ASD characteristics. Such measures can be used to help track the clinical course of people with ASD, monitor responses to interventions, and provide information about the broader autism phenotype.
- Detailed criteria for specific ASD sub-types in order to better describe the variations in characteristics and severity and study how these variations relate to underlying pathology, intervention strategies, and outcomes.
- ASD subpopulations and associated biobehavioral markers that provide early indication of ASD risk and opportunities for appropriate early intervention.
- Protocols for genetic testing in routine clinical practice in order to identify people at risk for ASD. Identification of people with genetic variations associated with ASD will facilitate intensive studies of ASD subpopulations with shared genetic risk factors to characterize common phenotypic and biological features.
- Inclusion of ethical considerations into the diagnosis and screening processes, including consideration of the implications of genetic testing.
- Addressing barriers to the use of screening and diagnostic tools in minority populations and in community settings, including training programs for professionals.

Short-Term Objectives

A. Develop, with existing tools, at least one efficient diagnostic instrument (e.g., briefer, less time intensive) that is valid in diverse populations for use in large-scale studies by 2011. *IACC Recommended Budget: $5,300,000 over 2 years.*

B. Validate and improve the sensitivity and specificity of new or existing screening and diagnostic tools, including comparison of general developmental screening versus autism-specific screening tools, in both high risk and population-based samples through studies of the following community populations that are diverse in terms of age, socio-economic status, race, ethnicity, characteristics of ASD, and general level of functioning by 2012. *IACC Recommended Budget: $5,400,000 over 3 years.*

New Objective:

C. Conduct at least three studies to identify reasons for the health disparities in accessing early screening and diagnosis services by 2012. *IACC Recommended Budget: $2,000,000 over 2 years.*

New Objective:

D. Conduct at least two studies to understand the impact of early diagnosis on choice of intervention and outcomes by 2015. *IACC Recommended Budget: $6,000,000 over 5 years*.

Long-Term Objectives

A. 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 by 2014. *IACC Recommended Budget: $33,300,000 over 5 years.*

B. Develop at least five measures of behavioral and/or biological heterogeneity in children or adults with ASD, beyond variation in intellectual disability, that clearly relate to etiology and risk, treatment response and/or outcome by 2015. *IACC Recommended Budget: $71,100,000 over 5 years.*

C. Identify and develop measures to assess at least three "continuous dimensions" (i.e., social reciprocity, communication disorders, and repetitive/restrictive behaviors) of ASD symptoms and severity that can be used by practitioners and/or families to assess response to intervention for people with ASD across the lifespan by 2016. *IACC Recommended Budget: $18,500,000 over 5 years.*

***Note:** Objectives in boxes labeled "New Objective" are either entirely new additions to the 2010 Strategic Plan or significantly modified objectives from the 2009 Strategic Plan. Objectives from the 2009 Strategic Plan that did not change or that have been slightly modified for clarification purposes are unmarked.*

2. HOW CAN I UNDERSTAND WHAT IS HAPPENING?

- **What is happening early in development?**
- **Are there known biological differences that help explain ASD symptoms?**
- **Can subgroups of people with ASD help us understand the etiology of ASD symptoms?**

What do we know?

Researchers, clinicians, and families have long posed questions about the possible biological bases of ASD. Clinicians classify ASD as a developmental brain disorder based on the behavioral features required for diagnosis. Little evidence exists, however, for a specific neurological abnormality beyond reports of an exuberant and transient pattern of brain or head growth (Akshoomoff, Pierce, & Courchesne, 2002; Dawson et al., 2007; Hazlett et al., 2005). While much of the current science suggests that the behavioral features of ASD result from atypical brain structure, wiring or connections, there is no proven neural variance associated with ASD. Nevertheless, there are some promising leads, and projects are underway that have the potential to provide biological signatures of some forms of ASD.

The development of sophisticated imaging methods has enabled researchers to accurately visualize many aspects of brain structure and functioning. For example, many children and adults with ASD perceive and analyze the visual information conveyed by facial expression differently than do other people (Spezio et al., 2007). Other researchers have employed magnetic resonance imaging (MRI) methods to investigate differences in brain anatomy between people with and without ASD, and have found differences in the density of white and gray matter, in some cases linked to specific symptoms of ASD (Craig et al., 2007).

Subsets of people with ASD have been reported to have experienced regression (i.e., the loss of previously acquired language, social, and developmental skills). The phenomenon is poorly understood and may co-occur with medical conditions common to people with ASD such as epilepsy. Recent studies have sought to understand the relationship between regressive symptoms, co-occurring disorders such as epilepsy, and the etiology of ASD.

Regression is not unique to people with ASD and the loss of language skills (acute language regression) can occur in people without the disorder. In one study, researchers found that children with acute language regression (who did not have ASD) were more likely to have associated seizures or epilepsy than were children with regressive autism (which includes language regression, as well as the loss of other social and developmental skills). This suggests that there are different subtypes of language regression and may help to understand the phenomenon and its relationship to ASD (McVicar, et al., 2005).

Currently, the frequency of language regression is unknown in either children with ASD or the general population. Previous studies of regression have been hampered by delayed referral for

evaluation after the onset of regressive symptoms (McVicar, et al., 2005).

A few hypotheses regarding how disruptions of the immune system might contribute to ASD and other neurodevelopmental disorders have emerged in recent years. Some recent findings suggest that the immune system differences of parents and their children may affect early brain development and the onset and fluctuation of symptoms in some children with ASD (Pardo, Vargas, & Zimmerman, 2005). For example, some research indicates that maternal autoantibodies directed at fetal brain tissue could interfere with normal brain development (Braunschweig et al., 2008). While such medical symptoms may not be entirely specific to ASD, treating may have significant impact on quality of life, symptom severity, and level of functioning.

Better understanding of the biology of genes linked to ASD and their functions can also provide insight. Recent studies have shown that the MeCP2 gene (mutations in which can cause Rett Syndrome) is involved in forming connections at the synapse. Genes regulated by the Fragile X Syndrome gene, FMR1, also directly affect synapse function by controlling signaling of the neurotransmitter glutamate. In addition, a 2008 study found that the two genes that cause tuberous sclerosis complex (TSC) impair the formation of axons. Recently, several groups reported remarkable success with targeted therapies in animal models of these disorders showing the ability to reverse the underlying neuroanatomical and even behavioral deficits in the adult (Dolen et al., 2007; Ehninger et al., 2008; Guy et al., 2007). Understanding how MeCP2, TS1, FMR1, TSC1 and TS2TSC2 regulate the growth and function of neurons may help scientists understand related disorders like autism.

What do we need?

Exploring the biological basis of ASD requires access to biospecimens of people with and without ASD. Some progress has been made to establish the necessary infrastructure for the collection and preservation of post-mortem tissue from people with ASD. Nevertheless, the tissues currently available are insufficient for the needs of researchers. Educational campaigns, through contact with healthcare providers and the internet, may be useful to increase public awareness. New technology is expanding biological research beyond post-mortem tissue. For example, it is now possible to create pluripotent stem cells from skin fibroblasts of individual patients to create neuronal cell lines for study.

One of the greatest barriers to progress in determining the biological bases of ASD has been the heterogeneity of the spectrum. A clear need exists to advance understanding of the many phenotypes of ASD, including studies that link genotype to phenotype, investigations of natural and treated history, analyses of genetic interaction with environmental exposures, and studies of co-occurring behavioral and medical conditions. Different autism phenotypes may have different etiologies. There is a need to combine genotyping and functional analysis to better understand the contribution of specific genotypes with functional or structural subtypes. To determine the earliest discernable onset of ASD, experts have expressed the need for an intensive, multidisciplinary study

starting at early ages that examines biomedical, neurodevelopmental, and behavioral trajectories of children with ASD. A parallel multidisciplinary analysis of typically developing children and children with non-ASD developmental disorders would be especially enlightening, as limited normative information is currently available. An evaluation of differences in the interplay of biology and environmental exposures for children with and without ASD is also needed. Understanding early trajectories may lead to targeted interventions aimed at mitigating behavioral and medical challenges and improving outcomes through adulthood.

Another understudied arena of ASD research is gender differences. Many studies of autism preferentially enroll males, which, due to a 4:1 increased prevalence, are easier to recruit. Without additional information about the biological features of ASD in females, it remains unclear whether the course of ASD is similar and whether currently used interventions are appropriate for females. It is critical to determine how sex is related to etiology, protective factors, diagnosis, and trajectory. In addition, many studies of autism preferentially enroll higher functioning individuals who do not have cognitive impairment, because of their ability to cooperate and participate in study related tasks. However, these individuals represent only a subset of all individuals with autism and lessons learned from them may or may not be generalizable to all individuals with ASD. Priority must be made to develop studies looking at the underlying etiology of non verbal individuals and to understand the impact of and etiology of co-occurring language and cognitive impairment.

ASPIRATIONAL GOAL: DISCOVER HOW ASD AFFECTS DEVELOPMENT WHICH WILL LEAD TO TARGETED AND PERSONALIZED INTERVENTIONS.

Research Opportunities

- Multi-disciplinary, longitudinal, biobehavioral studies of children, youths, and adults beginning during infancy that characterize neurodevelopmental and medical developmental trajectories across the multiple axes of ASD phenotype and identify ASD risk factors, subgroups, co-occurring symptoms, and potential biological targets for intervention. Such studies could include:
    - High-risk siblings of children, youths, and adults with ASD, children without a family history of ASD, and typically developing children.
    - Multi-disciplinary assessments of brain imaging, metabolic and immune markers, microbiomics, electrophysiology, and behavior.
- Research on females with ASD to better characterize clinical, biological and protective features.
- Human and animal studies that examine immune, infectious and environmental factors in the occurrence of ASD.

- Research on the unique strengths and abilities of people with ASD with evaluation of functional and biological mechanisms behind social, linguistic, and cognitive profiles.
- Research on individuals with ASD who are nonverbal and /or cognitively impaired
- Research targeting the underlying biology of co-occurring syndromes and co-occurring conditions.
- Prospective research on children with language regression, both with and without autistic regression, including potential underlying genetic and other risk factors including seizures and epilepsy.

Short-Term Objectives

A. Support at least four research projects to identify mechanisms of metabolic and/or immune system interactions with the central nervous system that may underlie the development of ASD during prenatal-postnatal life by 2010. *IACC Recommended Budget: $9,800,000 over 4 years.*

B. Launch three studies that specifically focus on the neurodevelopment of females with ASD, spanning basic to clinical research on sex differences by 2011. *IACC Recommended Budget: $8,900,000 over 5 years.*

C. Identify ways to increase awareness among the autism spectrum community of the potential value of brain and tissue donation to further basic research by 2011. *IACC Recommended Budget: $1,400,000 over 2 years.*

New Objective:

D. Launch three studies that target improved understanding of the underlying biological pathways of genetic conditions related to autism (e.g. Fragile X, Rett syndrome, tuberous sclerosis complex) and how these conditions inform risk assessment and individualized intervention by 2012. *IACC Recommended Budget: $9,000,000 over 5 years.*

New Objective:

E. Launch three studies that target the underlying biological mechanisms of co-occurring conditions with autism including seizures/epilepsy, sleep disorders and familial autoimmune disorders by 2012. *IACC Recommended Budget: $9,000,000 over 5 years.*

New Objective:

F. Launch two studies that focus on prospective characterization of children with reported regression, to investigate potential risk factors by 2012. *IACC Recommended Budget: $4,500,000 over 5 years.*

*****Note:** Objectives in boxes labeled "New Objective" are either entirely new additions to the 2010 Strategic Plan or significantly modified objectives from the 2009 Strategic Plan. Objectives from the 2009 Strategic Plan that did not change or that have been slightly modified for clarification purposes are unmarked.*

New Objective:

G. Support five studies that associate specific genotypes with functional or structural phenotypes, including behavioral and medical phenotypes (e.g., nonverbal individuals with ASD and those with cognitive impairments) by 2015. *IACC Recommended Budget: $22,600,000 over 5 years.*

Long-Term Objectives

A. Complete a large-scale, multi-disciplinary, collaborative project that longitudinally and comprehensively examines how the biological, clinical, and developmental profiles of individuals, with a special emphasis on females, youths, and adults with ASD, change over time as compared to typically developing people by 2020. *IACC Recommended Budget: $126,200,000 over 12 years.*

New Objective:

B. Launch at least three studies which evaluate the applicability of ASD phenotype and/or biological signature findings for performing diagnosis, risk assessment, or clinical intervention by 2015. *IACC Recommended Budget: $7,200,000 over 5 years.*

***Note:** Objectives in boxes labeled "New Objective" are either entirely new additions to the 2010 Strategic Plan or significantly modified objectives from the 2009 Strategic Plan. Objectives from the 2009 Strategic Plan that did not change or that have been slightly modified for clarification purposes are unmarked.*

3. WHAT CAUSED THIS TO HAPPEN AND CAN THIS BE PREVENTED?

- **Is there something in my genetic or family history that poses a risk for ASD?**
- **What environmental exposures pose risks for the development of ASD?**
- **How might genetics and the environment interact to influence the occurrence of ASD?**

What do we know?

As with many complex disorders, causation is generally thought to involve some forms of genetic risk interacting with some forms of non-genetic environmental exposure. The balance of genetic risk and environmental exposure likely varies across the spectrum of ASD. The greatly increased concordance of strictly defined autism in monozygotic (identical) twins (70 - 90%) compared to dizygotic (fraternal) twins (0-10%) argues for the importance of genetic factors (Bailey et al., 1995; Steffenburg et al., 1989). Moreover, there are subpopulations of those diagnosed with ASD that have a known genetic mutation, often associated with a genetic disorder, such as Fragile X syndrome, Rett syndrome, or tuberous sclerosis, understanding of which has led to identification of possible pharmaceutical interventions. In many cases the same genetic variation does not result in an ASD phenotype, suggesting possible genetic or environmental modifiers that could be important intervention targets.

Using new technology that reveals gaps and extra copies in DNA sequences, researchers have found that some people with ASD have deletions and duplications of genetic material not found in their parents' DNA (Sebat et al., 2007). Recent genetics research has identified common genetic variations (e.g., Wang et al., 2009; Weiss et al., 2009), changes in chromosomal structure in specific genomic regions, (Marshall et al., 2008; Kumar et al., 2008; Weiss et al., 2008) and rare mutations in genes all associated with synaptic connectivity (Alarçon et al., 2008; Bakkaloglu et al., 2008; Durand et al., 2007; Jamain et al., 2003; Laumonnier et al., 2004.; Strauss et al., 2006). Some of these findings have contributed to new hypotheses about the inheritance of ASD. In families with just one affected member, spontaneous deletions and duplications may be causal factors of ASD. However, what causes these spontaneous deletions and duplications is not clear and could be due to environmental exposures.

Taken together, rare genetic mutations, chromosomal abnormalities and sub-microscopic deletions and duplications of genetic material are involved in at least 10% of ASD cases, yet individually each abnormality is found in no more than about 1-2% of cases (Abrahams & Geschwind, 2008). Since common genetic variations confer only modest increase in risk, this suggests that the genetic factors in ASD may involve many different genes and interactions between genes and environment. Possible models include: many additional rare genetic mutations to be discovered; multiple common genetic variations each conferring a small increased risk; and, many forms of ASD with different genetic contributions, both common and rare in the population. There is growing recognition that the

same genetic contributions can lead to a wide variety of different phenotypes across individuals. As one good example, deletions and duplications in chromosomal region 16p11 have been associated with a broad range of phenotypes, including disorders outside the autism spectrum. The factors responsible for this variability in disease phenotypes remain to be defined.

Researchers are working to better understand the interaction of genetic vulnerability with developmental experiences, such as a specific environmental exposure. While gene-environment interactions have been hypothesized to play a role in many medical disorders, these interactions have been difficult to prove or disprove beyond statistical tests showing that some genetic subgroups have a greater response to some environmental factor. Epigenetics is one mechanism by which it is thought that environmental factors may be influencing gene expression, and now molecular tools are allowing researchers to gain insight into epigenetic phenomena that may be contributing to a variety of disorders, including ASD (Baccarelli and Bollati, 2009; Nagarajan et al., 2008).

While genetics maps the sequence of DNA, epigenetics maps the modifications of the structure of DNA due to proteins or other factors that bind to the DNA helix. DNA is essentially linear text that gets "read" into RNA that in turn codes for proteins. Epigenetic modifications do not change the text but they highlight or redact large sections of text, changing how it is read. Epigenetic modifications consist of biochemical "tags" that attach to the DNA in different places, leading to the "silencing" or "activation" of genes. The pattern of epigenetic silencing or activation of genes can differ between genders, between species or between generations, and can change during specific time windows in development or in response to environmental cues. It is thought that the addition or removal of epigenetic tags from DNA is one mechanism by which developmental experience (i.e. exposure to physical or emotional stimuli) can cause long-term biological and behavioral effects. In the past year, the first maps of the human epigenome have provided the first comprehensive look at where and how nature and nurture may interact (Lister et al., 2009).

Progress in identifying environmental factors which increase autism risk has been made recently (Eskenazi et al., 2007; Palmer et al., 2006; Palmer, Blanchard, & Wood, 2009; Rauh et al., 2006; Roberts et al., 2007; Windham et al., 2006), although this area of research has received less scientific attention and far fewer research dollars than genetic risk factors. Environmental factors may be pertinent not only to brain development but also to chronic systemic features of at least some subgroups of ASD. An Institute of Medicine (IOM) workshop held in 2007 summarized what is known and what is needed in this field (Forum on Neuroscience and Nervous System Disorders, Institute of Medicine, 2008). Numerous epidemiological studies have found no relationship between ASD and vaccines containing the mercury based preservative, thimerosal (Immunization Safety Review Committee, 2004). These data, as well as subsequent research, indicate that the link between autism and vaccines is unsupported by the epidemiological research literature. However, the IOM report acknowledged that the existing population-based studies

were limited in their ability to detect small susceptible subpopulations that could be more genetically vulnerable to environmental exposures.

Of note, the Committee receives many public comments that reflect concerns about vaccines as a potential environmental factor in autism. Some members of the public are convinced that the current data are sufficient to demonstrate that vaccines do not play a causal role in autism and argue against using limited autism research funds to do additional vaccine studies when many other scientific avenues remain to be explored. At the same time, those who believe that prior studies of the possible role of vaccines in ASD have been insufficient argue that investigation of a possible vaccine/ASD link should be a high priority for research (e.g., a large-scale study comparing vaccinated and unvaccinated groups). A third view urges shifting focus away from vaccines and onto much-needed attention toward the development of effective treatments, services and supports for those with ASD.

In addition, a number of other environmental factors are being explored through research because they are known or suspected to influence early development of the brain and nervous system. Recent studies suggest factors such as parental age, exposure to infections, toxins, and other biological agents may confer environmental risk. These findings require further investigation and testing, some of which is ongoing through the CADDRE Program, the Norwegian cohort study, the CHARGE study, the EARLI study, and the Children's Centers for Environmental Health and Disease Prevention supported by NIEHS and the Environmental Protection Agency (EPA).

What do we need?

Although most scientists believe that risk factors for ASD are both genetic and environmental, there is considerable debate about whether potential environmental causes, genetic precursors, or interactions between genes and environmental factors should be the highest priority for research aimed at identifying the causes of ASD. To date, few studies have ruled in or ruled out specific environmental factors. There are reports of associations of ASD with exposure to medications, maternal antibodies, toxicants, and infections prenatally or postnatally, however these observations need to be the subject of additional study. It is still not known whether any specific factor is necessary or sufficient to cause ASD. Similar to other disease areas, advancing research on the potential role of environmental factors requires resources and the attraction of scientific expertise. Bringing this to bear on autism will help define the environmental factors to study, as well as the best approach for staging studies to examine environmental factors, interaction between factors, and between individual susceptibility and various environmental factors.

For example, some researchers believe that it is important to study a large number of exposures, or classes of exposure, that are known to affect brain development. Others support more tightly focused studies of one exposure or a limited number of exposures, with greatest biologic plausibility for interacting with known or suspected biologic or genetic ASD risk factors. In addition, it is also important to design

studies that assess environmental exposure during the most relevant exposure windows: pregnancy and early development. In doing this research, it will be important for the field to develop sound standards for identifying and claiming that environmental factors contribute to ASD, as it is for genetics.

Research studies on risk factors can be pursued through several means. Smaller, focused studies are needed for hypothesis testing and to provide insight for replication studies. Similar to other health outcomes research for relatively rare conditions, case-control studies can be an effective first line of inquiry. The CHARGE and CADDRE (SEED) studies are good examples of this approach where environmental exposures and biological pathways, along with genetics, are being examined. Other existing cohorts could also be identified and used for epigenomic as well as traditional genomic and environmental studies.

To address public concerns regarding a possible vaccine/ASD link, it will be important for the IACC to continue to coordinate with the National Vaccine Advisory Committee (NVAC), a Federal advisory committee chartered to advise and make recommendations regarding the National Vaccine Program.

Epigenomics provides a ready mechanism for understanding how genes and environment may act jointly to affect autism risk. Studies are needed to investigate whether candidate environmental exposures alter epigenetic mechanisms that modify the expression of suspected autism susceptibility genes or genomic regions. Such studies should incorporate examination of time or stage of development as an important factor determining the impact of environmental agents on epigenetic programming. Finally, studies are needed to understand how changes in epigenetic tags in response to environmental stimuli could lead to specific phenotypic characteristics associated with autism.

Another approach for studying risk factors for ASD requires large sample sizes to disentangle the many possible genetic and environmental factors that contribute to and help explain ASD and the frequently co-occurring conditions. For other complex disorders, large DNA collections, i.e. >20,000 samples, have been necessary to detect the full genetic risk architecture. There are no genetic repositories of this size for ASD. Similarly, large birth cohort studies, in which biological samples have been collected throughout pregnancy and early postnatal life may be essential for detecting the interplay of environmental exposures and genetic factors that lead to ASD. As a complement to these large-scale studies, research on critical sub-populations that may be at higher risk could provide leverage in identifying genetic and environmental risk factors.

ASPIRATIONAL GOAL: CAUSES OF ASD WILL BE DISCOVERED THAT INFORM PROGNOSIS AND TREATMENTS AND LEAD TO PREVENTION/PREEMPTION OF THE CHALLENGES AND DISABILITIES OF ASD.

Research Opportunities

- Genetic and epigenetic variations in ASD and the symptom profiles associated with these variations.
- Environmental influences in ASD and the symptom profiles associated with these influences.
- Family studies of the broader autism phenotype that can inform and define the heritability of ASD.
- Studies in simplex families that inform and define de novo genetic differences and focus on what role the environment might play in inducing these differences.
- Standardized methods for collecting and storing biospecimen resources from well-characterized people with ASD as well as a comparison group for use in biologic, environmental and genetic studies of ASD.
- Case-control studies of unique subpopulations of people with ASD that identify novel risk factors.
- Monitor the scientific literature regarding possible associations of vaccines and other environmental factors (e.g., ultrasound, pesticides, pollutants) with ASD to identify emerging opportunities for research and indicated studies.
- Better understanding environmental and biological risk factors during pre- and early post-natal development in "at risk" samples.
- Cross-disciplinary collaborative efforts to identify and analyze biological mechanisms that underlie the interplay of genetic and environmental factors relevant to the risk and development of ASD, including co-occurring conditions.
- Convene ASD researchers on a regular basis to develop strategies and approaches for improving data standards and sharing, understanding gene – environment interactions, improving the speed of replication of findings, and enhancing the translation of research on potential causative factors to prevention and treatment studies.
- Measures of key exposures for use in population and clinic based studies and standards for sample collection, storage, and analysis of biological materials.
- Studies of behavioral, developmental, and medical variations across those with ASD who share common genetic factors.
- Studies of clinically meaningful subgroups to examine common genetic and environmental factors, as well as unique epigenomic signatures.

Short-Term Objectives

A. Coordinate and implement the inclusion of approximately 20,000 subjects for genome-wide association studies, as well as a sample of 1,200 for sequencing studies to examine more than 50 candidate genes by 2011. Studies should investigate factors contributing to phenotypic variation across individuals that share an identified genetic variant and stratify subjects according to behavioral, cognitive, and clinical features. *IACC Recommended Budget: $43,700,000 over 4 years.*

B. Within the highest priority categories of exposures for ASD, identify and standardize at least three measures for identifying markers of environmental exposure in biospecimens by 2011. *IACC Recommended Budget: $3,500,000 over 3 years.*

C. Initiate efforts to expand existing large case-control and other studies to enhance capabilities for targeted gene – environment research by 2011. *IACC Recommended Budget: $27,800,000 over 5 years.*

D. Enhance existing case-control studies to enroll racially and ethnically diverse populations affected by ASD by 2011. *IACC Recommended Budget: $3,300,000 over 5 years.*

New Objective:

E. Support at least two studies to determine if there are subpopulations that are more susceptible to environmental exposures (e.g., immune challenges related to infections, vaccinations, or underlying autoimmune problems) by 2012. *IACC Recommended Budget: $8,000,000 over 2 years.*

New Objective:

F. Initiate studies on at least 10 environmental factors identified in the recommendations from the 2007 IOM report "Autism and the Environment: Challenges and Opportunities for Research" as potential causes of ASD by 2012. *Estimated cost $56,000,000 over 2 years.*

Long-Term Objectives

A. Conduct a multi-site study of the subsequent pregnancies of 1,000 women with a child with ASD to assess the impact of environmental factors in a period most relevant to the progression of ASD by 2014. *IACC Recommended Budget: $11,100,000 over 5 years.*

B. Identify genetic risk factors in at least 50% of people with ASD by 2014. *IACC Recommended Budget: $33,900,000 over 6 years.*

***Note:** Objectives in boxes labeled "New Objective" are either entirely new additions to the 2010 Strategic Plan or significantly modified objectives from the 2009 Strategic Plan. Objectives from the 2009 Strategic Plan that did not change or that have been slightly modified for clarification purposes are unmarked.*

C. Determine the effect of at least five environmental factors on the risk for subtypes of ASD in the pre- and early postnatal period of development by 2015. *IACC Recommended Budget: $25,100,000 over 7 years.*

D. Support ancillary studies within one or more large-scale, population-based surveillance and epidemiological studies, including U.S. populations, to collect data on environmental factors during preconception, and during prenatal and early postnatal development, as well as genetic data, that could be pooled (as needed), to analyze targets for potential gene/environment interactions by 2015. *IACC Recommended Budget: $44,400,000 over 5 years.*

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4. WHICH TREATMENTS AND INTERVENTIONS WILL HELP?

- **When should treatments or interventions be started?**
- **What are the medical issues I need to know about?**
- **How do I know that treatments are both safe and effective?**

What do we know?

Although autism is defined and diagnosed by deficits in core behaviors, accumulating evidence suggests that the breadth of this disorder extends well beyond the behavioral diagnosis. There is increasing recognition that the multiple systemic issues in children with ASD may influence vulnerability, onset, and severity of symptoms and behaviors. The systemic component of autism supports the possibility that both the core behaviors and medical issues have a convergent mechanistic basis that if identified, could provide new insights into treatment targets, candidate genes, and strategies for prevention.

A wide range of treatment and intervention options are available for children and adults with ASD that can target core symptoms, ameliorate associated symptoms, and prevent further disability. For example, interventions such as speech therapy facilitate language development, pragmatic communication and social interaction. Occupational therapy can improve functioning in everyday activities (e.g., eating, bathing, and learning) as well as sensory integration. Both types of therapy can promote the development of life skills, which help people with ASD to gain more independence. People with ASD can benefit from adaptive technologies, such as the use of keyboards and computers that promote expressive communication skills, and visual representation tools such as the Picture Exchange Communication System (PECS) that assist those with little or no language to communicate more effectively. For pre-school and school age children, public school systems and private schools can provide essential interventions including curricula that are individualized to the child, testing for cognitive and academic strengths and weaknesses, and special education services with lower teacher to student ratios, to name a few. For all of these interventions, there is a range of improvement, with some people making profound gains and others showing little response. We do not know how to predict which people will benefit from any of the available treatments.

Of the numerous behavioral interventions currently in use, little scientific evidence from randomized controlled trials (RCT) supports their efficacy. Behavioral therapies, such as Applied Behavior Analysis (ABA) based therapies, which use the principles of reinforcement and repetition, have been used since the 1960s and have been studied most extensively. Controlled trials have shown ABA to be effective for improving social skills and language when provided for at least 25-40 hours per week for 2 years (Lord & McGee, 2001). Efficacy is greatest when behavioral interventions are used early, but improved skills have been reported with adolescents and adults (McClannahan, MacDuff, & Krantz, 2002; Weiss & Harris, 2001).

Medications to improve some of the symptoms associated with autism have been studied. However, thus far, no medication has been shown in controlled trials to enhance social behavior or communication. In 2006, risperidone became the first Food and Drug Administration (FDA)-approved pharmacologic therapy for certain symptoms of autism. First introduced in 1993 as medication used to treat symptoms of schizophrenia, risperidone has now been shown to be effective as a treatment of irritability and aggression seen in some children with ASD. Selective serotonin reuptake inhibitors have had mixed results in decreasing certain repetitive and stereotyped behaviors (Kolevzon, Mathewson, & Hollander, 2006; King et al., 2009). Other biological and pharmacological treatments that have been investigated in small studies and may warrant fuller attention include omega-3 fatty acids, memantine, oxytocin, and pioglitazone (Ammiger et al., 2007; Chez et al., 2007; Hollander et al., 2007; Boris et al., 2007).

There are other treatments in wide use that have not been studied in randomized controlled trials. These include nutritional supplements and diets (e.g., probiotics, mitochondrial cocktails, CoQ10, carnitine, and gluten-casein free diets), and chelation. One such treatment, the neuropeptide secretin, that had been reported to improve symptoms of ASD, was studied in a placebo-controlled trial and found to be ineffective (Esch & Carr, 2004). Some parents and therapists suggest that these treatments are effective, that recovery is possible, and that further studies are needed. Others are concerned that these treatments involve more than minimal risks and urge caution before recommending large-scale studies.

What do we need?

Safe and effective interventions are needed across the lifespan, from early development shortly after the detection of risk or diagnosis, through childhood, school age, adolescent, adult, and senior phases of life. Going forward, research needs to be balanced between two poles. On the one hand, we need novel, targeted interventions based on an understanding of the molecular mechanisms of ASD. These interventions, analogous to ongoing efforts in cancer and cardiovascular research, will require a successful commitment to earlier elements of this Strategic Plan. On the other hand, we need rigorous studies to develop and safely test the efficacy of current interventions, identifying which elements are most effective in reducing or ameliorating symptoms for which persons. Intervention research should collect information about the mode of delivery, intensity, duration, and dose as well as unique characteristics of the people with ASD (e.g., behavioral, biological, genetic) in an effort to develop more personalized interventions, treatments, services and supports, and help inform basic research about additional targets for study. This research will require large-scale multidisciplinary randomized controlled trials.

The identification of biomarkers, for instance, in plasma, saliva, cerebrospinal fluid (CSF), or tissue is necessary to provide insights into targeted treatment strategies designed to improve or reverse autistic symptoms as well as insights into preventive measures. Further, if biomarkers present in children with ASD

are found to be present in infants and toddlers at high risk of developing autism, targeted intervention strategies to normalize these biomarkers could be tested for potential to arrest or reverse the symptoms and progression of autism.

Decision makers (people with ASD, families, clinicians, and payors) frequently lack critical information about which treatment is best for an individual person. While there are many interventions in wide use, the field lacks comparative studies of their value or how these various interventions should be staged or combined. Comparative effectiveness research yields information from head to head comparisons of interventions or policies that, when combined with a personalized approach, can inform decision makers about health care choices. This approach, already helpful for cardiovascular and cancer research, needs to be developed to inform ASD interventions.

Special attention is needed on treatment of co-occurring medical issues, developing pharmacological treatments, and testing interventions that are in wide use, (e.g., nutritional supplements) but for which little rigorous efficacy data exist (Levy & Hyman, 2003). Medical issues, such as gastrointestinal symptoms and sleep disorders, may influence the effectiveness of interventions designed to affect the core symptoms of ASD. Similarly, interventions that focus on medical issues may also affect or reduce core symptoms. Animal models and/or cell lines relevant to autism are needed to develop new or test existing pharmacological agents for ASD, understand the mechanisms of action, and serve as a first-step in testing drug safety. Such model systems research may be crucial in leveraging the pharmaceutical industry to develop medications that target the core symptoms of ASD.

While some people with ASD have been reported to show marked improvement, little is known about the characteristics of these people or the types of interventions they have received that may help to explain these changes. Studies of these people may provide an opportunity for discovering important clues with regard to risk factors and intervention strategies for specific ASD subgroups.

***ASPIRATIONAL GOAL*: INTERVENTIONS WILL BE DEVELOPED THAT ARE EFFECTIVE FOR REDUCING BOTH CORE AND ASSOCIATED SYMPTOMS, FOR BUILDING ADAPTIVE SKILLS, AND FOR MAXIMIZING QUALITY OF LIFE AND HEALTH FOR PEOPLE WITH ASD.**

Research Opportunities

- Large scale studies that directly compare interventions and combinations of interventions (e.g., pharmaceutical, educational, and behavioral interventions) to identify what works best for which people and how much it will cost.
    - Best practice models that are being used in community-based ASD intervention programs.
    - Clinical trials that assess the safety and efficacy of widely used interventions that have not been rigorously studied for use in ASD populations.
    - Studies in diverse populations.
- Interventions that improve functioning and quality of life for people with ASD across the lifespan, including older children, adolescents, and adults with ASD.
- Early interventions that aim to prevent the development of ASD in very young "at risk" children and reduce family burden.
- Innovative treatments that specifically target core symptom clusters unique to ASD.
- Development of emerging technologies, such as assisted communication, that provide opportunities for people with ASD to become more engaged in the community.
- Animal models and/or cellular lines that can be used to test efficacy and/or safety of ASD interventions and treatments.
- Strategies that facilitate rapid translation of promising basic scientific discoveries and community practices into clinical research and trials.
- Methods of treating co-existing medical or psychiatric conditions and assess how such treatments affect ASD symptoms and severity.
- Interventions that may enhance neural plasticity and adaptive brain reorganization in children, adolescents, and adults with ASD thereby promoting significant improvement of ASD.
- Outcome studies of the effectiveness of behavioral, developmental, and cognitive therapies and approaches.
- Methods for measuring changes in core symptoms of ASD from treatment.
- Dissemination research (coordinated with subsequent goals) to ensure that evidence-based interventions are implemented in diverse communities with fidelity and efficiency.

- Investigation of the use of medications to control challenging behaviors in people with ASD, particularly adults.

Short-Term Objectives

A. Support at least three randomized controlled trials that address co-occurring medical conditions associated with ASD by 2010. *IACC Recommended Budget: $13,400,000 over 3 years.*

B. Standardize and validate at least 20 model systems (e.g. cellular and/or animal) that replicate features of ASD and will allow identification of specific molecular targets or neural circuits amenable to existing or new interventions by 2012. *IACC Recommended Budget: $75,000,000 over 5 years.*

C. Test safety and efficacy of at least five widely used interventions (e.g., nutrition, medications, assisted technologies, sensory integration, medical procedures) that have not been rigorously studied for use in ASD by 2012. *IACC Recommended Budget: $27,800,000 over 5 years.*

D. Complete two multi-site randomized controlled trials of comprehensive early intervention that address core symptoms, family functioning and community involvement by 2013. *IACC Recommended Budget: $16,700,000 over 5 years.*

New Objective:

E. Convene a workshop to advance the understanding of clinical subtypes and treatment personalization (i.e. what are the core symptoms to target for treatment studies) by 2011. *IACC Recommended Budget: $50,000.*

New Objective:

F. Launch five randomized controlled trials of interventions including biological signatures and other measures to predict response, and monitor quality of life and functional outcomes, in each of the following groups:

- Five trials in infants and toddlers by 2013. *IACC Recommended Budget: $30,000,000 over 5 years.*
- Three randomized controlled trials of interventions for school-aged children and/or adolescents by 2013. *IACC Recommended Budget: $18,000,000 over 5 years.*
- Three trials for adults by 2014. *IACC Recommended Budget: $18,000,000 over 5 years.*

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Long-Term Objectives

A. Complete at least three randomized controlled trials on medications targeting core symptoms in people with ASD of all ages by 2014. *IACC Recommended Budget: $22,200,000 over 5 years.*

B. Develop interventions for siblings of people with ASD with the goal of reducing risk recurrence by at least 30% by 2014. *IACC Recommended Budget: $6,700,000 over 5 years.*

New Objective:

C. Conduct at least one study to evaluate the safety and effectiveness of medications commonly used in the treatment of co-occurring conditions or specific behavioral issues in people with ASD by 2015. *IACC Recommended Budget: $10,000,000 over 5 years.*

***Note:** Objectives in boxes labeled "New Objective" are either entirely new additions to the 2010 Strategic Plan or significantly modified objectives from the 2009 Strategic Plan. Objectives from the 2009 Strategic Plan that did not change or that have been slightly modified for clarification purposes are unmarked. .*

5. WHERE CAN I TURN FOR SERVICES?

- **What types of services and supports should I seek and where can I find them?**
- **What is my state or local government doing to provide services for ASD?**
- **What is the cost of services and how will it be paid?**

What do we know?

To fulfill the mission to "profoundly improve the health and well being of every person on the autism spectrum across the lifespan," scientific discoveries must be implemented in communities and supported by public policy. The gap between knowledge and action can only be overcome by an aggressive focus on engaging families, people with ASD, and the services community in the research process, disseminating research findings into the community, eliminating barriers to services and helping people with ASD and their families identify which services are needed.

The communities in which children are diagnosed vary tremendously in their ability to meet the needs of people with ASD (Shattuck & Grosse, 2007). Local school districts vary in their ability to identify and provide appropriate educational and related programs for children with ASD (Mandell & Palmer, 2005; Palmer et al., 2005). States vary in the policies they have developed to organize, finance and deliver care. The professional infrastructure or capacity is often inadequate to provide timely diagnosis, appropriate care, services and supports, and assure health and safety.

While remarkable improvements have been made during the last three decades in understanding the best ways to identify, assess, educate and support people with autism and their families, these improvements rarely enter community practice. In fact, some have suggested that the lag between research and practice is close to 20 years. When proven-efficacious services are implemented in community settings, they often do not result in the same positive outcomes (i.e., they are efficacious in research settings, but not effective in community practice). The reasons for this lag and ways to improve services only recently have become an area of research in autism.

Another important issue for service delivery is that community needs far outpace the state of research. Most autism services research has focused on behavioral interventions for young children. Behavioral interventions for youth and adults, as well as community supports that address quality of life (as opposed to core symptoms) for people with autism and their families have almost no traditional evidence base to support them. Yet these types of services are some of the most requested and most needed. Providers and policy makers must therefore make decisions in the absence of evidence. Local resources, advocacy, and creativity about existing funding streams all may affect what services get funded, by whom, and for whom.

These differences in policies, resources and organization result in marked differences in the prevalence of ASD across geographic areas, the types of services and support that are received, availability of appropriate lifespan

transition opportunities, and the associated costs (Fujiura, Roccoforte, & Braddock, 1994; Ganz, 2007; Järbrink, Fombonne, & Knapp, 2003; Mandell et al., 2008; Ruble et al, 2005; Stahmer & Mandell, 2007). In general, children with ASD have a much more difficult time accessing appropriate services than children with other special healthcare needs (Krauss et al., 2003). Data are still lacking on how these differences in policy and infrastructure relate to the differences in services used, and in turn how these differences affect outcomes for children and families, and adults with ASD.

What do we need?

People with ASD and their families need assistance navigating complex service systems to find the most appropriate services and supports. Providers and people with ASD and their families need help choosing and implementing evidence-based services that are effective and sustainable. Policy makers and payers for services, including private insurers and school districts, need assistance creating organizational structures and financial incentives so that high-quality interventions are institutionalized. Equally important, services researchers and community organizations must collaborate to quickly and efficiently develop much-needed services and supports for underserved groups among people with ASD, and to test widely-used, safe, and promising services that may not have much evidence to support them.

Strategies to educate people with ASD and their families about the best ways to obtain appropriate services and supports should be developed and tested. Methods for simplifying the process by which people access services also are needed, with a focus on improving collaboration across the many agencies that provide services to people with ASD. This is especially important for traditionally underserved groups whose members often are diagnosed late (or not at all), and who are even more likely than other people with ASD to receive inappropriate or inadequate services.

An initial part of this process is the assessment of needs and costs. Services for developmental disorders are financed largely by federal, state and local agencies in both the health care and education sectors. Because there are significant regional differences in ASD resources, describing this varied landscape across states and localities in the U.S. will provide important baseline data for those with ASD and policymakers so they can appropriately seek and plan for services respectively. Research can also define the cost-effectiveness of evidence-based practices and thereby provide the data needed by various payers and policymakers.

Observational studies of current practice can play an important role in understanding how best to address questions surrounding services and supports. They can identify malleable barriers and appropriate points of intervention, and provide a baseline against which to measure future progress. Because service systems vary greatly from place to place, these types of studies also can take advantage of the natural experiments that occur as systems struggle to respond to the needs of people with ASD.

Experimental studies are more difficult to design and conduct in this area of science than they are for traditional intervention trials; yet are key to understanding the best ways to improve community services. Designs such as those used in comparative effectiveness research, where both groups receive intervention (rather than having a "treatment as usual" control), will be critically important to satisfy ethical and practical concerns. Because the unit of analysis for many of these studies is the provider or system, rather than the person with ASD, large-scale network studies and quasi-experimental designs will also yield information.

Families, people with ASD, and communities can be empowered to become partners in research that can in turn inform policy. Research must include services that are built upon principles of self-direction and self-determination, and emphasize quality of life across the ASD spectrum. All people with ASD, their families, and support systems should have the services and supports they need and desire throughout the lifespan to lead productive lives in the community, and to reach their fullest potential.

ASPIRATIONAL GOAL: COMMUNITIES WILL ACCESS AND IMPLEMENT NECESSARY HIGH QUALITY, EVIDENCE-BASED SERVICES AND SUPPORTS THAT MAXIMIZE QUALITY OF LIFE AND HEALTH ACROSS THE LIFESPAN FOR _ALL_ PEOPLE WITH ASD.

Research Opportunities

- Development and effective dissemination of evidence-based community practices for people with ASD across the spectrum and lifespan.
- Comparative effectiveness studies of services and supports for people with ASD across the spectrum and lifespan.
- Studies that characterize current ASD diagnostic and service utilization patterns in community settings, examine the relationship between the likelihood of a diagnosis and services availability for ASD, and evaluate services and intervention outcomes across the spectrum and lifespan.
- Development of a coordinated, integrated, and comprehensive community-based service delivery system for people with ASD.

Short-Term Objectives

A. Support two studies that assess how variations and access to services affect family functioning in diverse populations, including underserved populations, by 2012. *IACC Recommended Budget: $1,000,000 over 3 years.*

New Objective:

B. Conduct one study to examine how self-directed community-based services and supports impact children, youth, and adults with ASD across the spectrum by 2014. *IACC Recommended Budget: $6,000,000 over 3 years.*

New Objective:

C. Implement and evaluate two models of policy and practice-level coordination among state and local agencies to provide integrated and comprehensive community-based supports and services that enhance access to services and supports, self-determination, economic self-sufficiency, and quality of life for people with ASD across the spectrum and their families, with at least one project aimed at the needs of transitioning youth by 2015. *IACC Recommended Budget: $10,000,000 over 5 years.*

Long-Term Objectives

A. Test four methods to improve dissemination, implementation, and sustainability of evidence-based interventions, services, and supports in diverse community settings by 2013. *IACC Recommended Budget: $7,000,000 over 5 years.*

B. Test the efficacy and cost-effectiveness of at least four evidence-based services and supports for people with ASD across the spectrum and of all ages living in community settings by 2015. *IACC Recommended Budget: $16,700,000 over 5 years.*

New Objective:

C. Evaluate new and existing pre-service and in-service training to increase skill levels in service providers, including direct support workers, parents and legal guardians, education staff, and public service workers to benefit the spectrum of people with ASD and promote interdisciplinary practice by 2015. *IACC Recommended Budget: $8,000,000 over 5 years.*

*****Note:** Objectives in boxes labeled "New Objective" are either entirely new additions to the 2010 Strategic Plan or significantly modified objectives from the 2009 Strategic Plan. Objectives from the 2009 Strategic Plan that did not change or that have been slightly modified for clarification purposes are unmarked.*

6. WHAT DOES THE FUTURE HOLD, PARTICULARLY FOR ADULTS?

- **What will my family member be like when he/she gets older?**
- **What is known about adults with ASD and how can I plan for the future?**
- **How does American society support people with ASD?**

What do we know?

An overarching goal of ASD research is to enable people with ASD to lead fulfilling and productive lives in the community. We are in critical need of information about the current landscape of long-term outcomes for all people with ASD across the spectrum. The lack of knowledge about adults with ASD and their lifetime support needs has repeatedly arisen as a critical issue when stakeholders are queried about their most fundamental concerns. Longitudinal studies designed to capture the range of possible outcomes for people with ASD are best suited to inform public policy decision-making, service and support delivery, and funding strategies. It is also important to improve public understanding of ASD in adults, including older adults, so that they may receive support from the communities where they live. Efforts to improve public awareness and community supports help foster acceptance, inclusion, and appreciation of people with ASD.

ASD poses economic and social costs for people with ASD, their families, and society at large. Although ASD symptoms vary greatly in character and severity, autism occurs in all ethnic and socioeconomic groups and affects every age group. Some scientists and economists have estimated that the combined direct and indirect costs to provide lifelong supports for all Americans with ASD exceeds $35 billion, and that each person accrues approximately $3 million in costs over his or her lifetime (Ganz, 2007). Families often report incurring large debts related to medical and educational services not covered through public programs or medical and dental insurance. Many families find the transition from the education system, where services are mostly obligatory, to the developmental disabilities and vocational systems, where services are optional, difficult to understand and manage. This fragmentation of service systems impedes access to services, especially for youth transitioning to adulthood, as well as during other periods of transition. In addition to financial challenges, ASD can lead to emotional hardships for people with ASD and their families throughout life.

What do we need?

Although considerable research has focused on the earliest phase of ASD, through early screening, improved diagnostics and early intervention, far less effort has addressed the adolescent, adult, and older adult phases of life. Minimal guidance exists for people with ASD across the spectrum and their families about the trajectories of ASD across the lifespan. Although the general assumption is that children who possess expressive and receptive language skills and coping strategies and who do not demonstrate significant challenging behaviors can sometimes excel as adults, while children who do not currently

possess typical expressive language skills and who engage in significant challenging behavior will grow up to need long-term, 24/7 supports and services, the evidence base for these ideas is lacking. Scientists have not yet identified key prognostic factors or detailed information about how adults across the spectrum with ASD function, where they are, and how they are best supported.

More research is needed to tailor treatments, interventions, and services and supports to the evolving needs of adolescents transitioning to adulthood, and adults across the spectrum with ASD, with an emphasis on principles of self-determination. There is a need to address co-occurring conditions and developmental changes that coincide with transitions such as adolescence to adulthood, to better assess functional outcomes, and to integrate standardized quality-of-life measures for adults across the spectrum with ASD living in community settings. Factors that contribute to improved quality of life and health outcomes in adulthood are virtually unknown.

A number of other areas raise serious concerns. There is little information about the number of adults with ASD within the criminal justice system. Some adults with ASD may not be diagnosed, or may have been mis-diagnosed. Although issues surrounding the direct support workforce are well documented, we do not know if they differ respective to adults with ASD. Community integration and access to individualized, quality adult supports and services are problematic across the United States, and long waiting lists for subsidized community-based services persist. Many services are available only to people who meet institutional level of care requirements. Additionally, there is scant research on the use and safety of psychopharmaceutical medications in adults with ASD.

***ASPIRATIONAL GOAL*: ALL PEOPLE WITH ASD WILL HAVE THE OPPORTUNITY TO LEAD SELF-DETERMINED LIVES IN THE COMMUNITY OF THEIR CHOICE THROUGH SCHOOL, WORK, COMMUNITY PARTICIPATION, MEANINGFUL RELATIONSHIPS, AND ACCESS TO NECESSARY AND INDIVIDUALIZED SERVICES AND SUPPORTS.**

Research Opportunities

- Studies of the scope and impact of the spectrum of ASD in adults, including diagnosis of ASD in adulthood, needs during critical life transitions, and quality of life.
- Longitudinal studies that follow carefully characterized cohorts of the broad spectrum of adults with ASD and their families into adulthood in order to better understand their needs during critical life transitions, and to identify and track risk and protective factors that account for improved quality of life and health outcomes.
- Projects that increase coordination across State and local delivery systems to improve access to services and supports, particularly those that focus on transitioning youth and adults with ASD.

- Improved understanding of the challenges associated with accessing community housing for people with ASD.

Short-Term Objectives

New Objective:

A. Launch at least two studies to assess and characterize variation in the quality of life for adults on the ASD spectrum as it relates to characteristics of the service delivery system (e.g., safety, integrated employment, post-secondary educational opportunities, community inclusion, self-determination, relationships, and access to health services and community-based services) and determine best practices by 2012. *IACC Recommended Budget: $5,000,000 over 3 years.*

New Objective:

B. Evaluate at least one model, at the state and local level, in which existing programs to assist people with disabilities (e.g., Social Security Administration, Rehabilitation Services Administration) meet the needs of transitioning youth and adults with ASD by 2013. *IACC Recommended Budget: $5,000,000 over 3 years.*

New Objective:

C. Develop one method to identify adults across the ASD spectrum who may not be diagnosed, or are misdiagnosed, to support service linkage, better understand prevalence, track outcomes, with consideration of ethical issues (insurance, employment, stigma) by 2015. *IACC Recommended Budget: $8,400,000 over 5 years.*

New Objective:

D. Conduct at least one study to measure and improve the quality of life-long supports being delivered in community settings to adults across the spectrum with ASD through provision of specialized training for direct care staff, parents, and legal guardians, including assessment and development of ASD-specific training, if necessary, by 2015. *IACC Recommended Budget: $7,500,000 over 5 years.*

Long-Term Objectives

New Objective:

A. Develop at least two individualized community-based interventions that improve quality of life or health outcomes for the spectrum of adults with ASD by 2015. *IACC Recommended Budget: $12,900,000 over 5 years.*

*****Note:** Objectives in boxes labeled "New Objective" are either entirely new additions to the 2010 Strategic Plan or significantly modified objectives from the 2009 Strategic Plan. Objectives from the 2009 Strategic Plan that did not change or that have been slightly modified for clarification purposes are unmarked.*

New Objective:

B. Conduct one study that builds on carefully characterized cohorts of children and youth with ASD to determine how interventions, services, and supports delivered during childhood impact adult health and quality of life outcomes by 2015. *IACC Recommended Budget: $5,000,000 over 5 years.*

New Objective:

C. Conduct comparative effectiveness research that includes a cost-effectiveness component to examine community-based interventions, services and supports to improve health outcomes and quality of life for adults on the ASD spectrum over age 21 by 2018. *IACC Recommended Budget: $6,000,000 over 5 years.*

New Objective:

D. Conduct implementation research to test the results from comparative effectiveness research in real-world settings including a cost-effectiveness component to improve health outcomes and quality of life for adults on the ASD spectrum over age 21 by 2023. IACC Recommended Budget: $4,000,000 over 5 years.

***Note:** Objectives in boxes labeled "New Objective" are either entirely new additions to the 2010 Strategic Plan or significantly modified objectives from the 2009 Strategic Plan. Objectives from the 2009 Strategic Plan that did not change or that have been slightly modified for clarification purposes are unmarked. .*

7. WHAT OTHER INFRASTRUCTURE AND SURVEILLANCE NEEDS MUST BE MET?

- **What infrastructure systems need to be supported, strengthened, or built to support this plan?**
- **How can we ensure that resources and data are shared to support the scientific research process?**
- **How can we ensure that findings are communicated to the public in a responsible and timely manner?**
- **How can we improve autism surveillance efforts?**

What do we know and what do we need?

Current infrastructure may be insufficient to adequately support the research programs outlined in this plan. Additional investment in infrastructure is necessary to collect and share data among researchers, to encourage and enable individuals with ASD and their families to participate in research, and to improve the speed with which findings are disseminated and the extent to which findings are translated into practice and policy.

Data Sharing:

In 2006, the National Institutes of Health (NIH) launched the National Database for Autism Research (NDAR) to improve sample sizes and enable researchers to share data for increased analyses. The NIH-supported national Autism Centers of Excellence (ACE), as well as the grants funded under the "Research to Address the Heterogeneity in Autism Spectrum Disorders" Request for Applications as part of the American Recovery and Reinvestment Act (ARRA), receive funding contingent upon acceptable plans and means for data sharing. Incentives are needed, however, to encourage data submission by other researchers. It will also be necessary to link other significant ASD databases with NDAR. In addition, databases that collect information and coordinate recruitment of people with ASD and their families to participate in research studies need to be enhanced and expanded. Programs to support contribution of data for recruitment, healthcare, education, social services and administrative databases, like the Interactive Autism Network (IAN), should be encouraged. Collecting information about people with ASD will facilitate the study of whether early diagnosis, entry to services and type of intervention affects the course of ASD over time. Multiple data sources from existing research or service systems (e.g., education, Medicaid, etc.) currently operate in isolation. Compiling and sharing data from existing data sources need to address data standardization as well as important privacy and ethical issues. Methods for merging such databases and linking investigator-recruited samples to these merged databases have been used in other populations and in specific locales with success and need to be further developed.

Biobanking:

Many in the field have highlighted the need to establish nationally coordinated strategies for the collection and preservation of post-mortem tissue from

both people with and without ASD. The existing brain and tissue bank resources must be expanded to meet the high and continuously increasing demand for post-mortem tissue by scientific investigators. More well-preserved brains are needed from people at various stages of development and particularly from those with few co-occurring disorders. Additional matched controls are needed, as well, to supplement the limited supply in existing repositories.

In addition, it will be necessary to develop methods, standards and protocols for collecting and storing other biological specimens such as blood and urine which might be used to study biological differences or signatures, and skin fibroblasts for creation of pluripotent stem cells.

Surveillance:

Autism surveillance provides important estimates on the numbers of children affected with ASD and helps describe the characteristics of the people with autism spectrum disorders in the general population. Surveillance must be sustained over a period of many years in order to track trends in prevalence estimates over time, and is an essential building block for population-based research — providing clues about potential risk factors that warrant further study. Surveillance provides important data regarding early identification of children with autism, and informs education and health systems regarding areas in which programs can be modified in order to improve early identification and intervention. Surveillance data also provide critically important information for communities to use when planning for services.

In 2007, CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network published the first and most comprehensive summary of autism prevalence estimates in the United States (CDC, 2007). These data showed that between 1 in 100 to 1 in 300 (with an average of 1 in 150 children) were identified with ASD. In October 2009, investigators from HRSA and CDC reported that ASD occurs in an estimated 1.1% of children 3 to 17 years, based on parent-report during the National Survey of Children's Health (NSCH), sponsored by HRSA (Kogan et al., 2009). Updated estimates from CDC's ADDM Network, published in December 2009, confirmed that approximately 1% of children were identified with an ASD (between 1 in 80 to 1 in 240 children with an average of 1 in 110) (CDC, 2009). There was an increase of 57% in identified ASD prevalence from 2002 to 2006 in multiple areas of the US. While these data provide important information for service planning, and begin to help us understand that the increases are not fully accounted for by improved identification, many questions related to the multiple causes of ASD increases remain.

There are a number of areas in which prevalence studies could be improved, including the continued estimation and evaluation of prevalence in the same population over time; assessment of ASD prevalence in the context of other neurodevelopmental disorders; further analyses of existing datasets to examine the multiple identification and potential risk factors as they vary by prevalence; collection of data beyond core ASD symptoms, including genetic data and co-occurring medical, dental, and behavioral conditions; and expansion of studies across ages.

Supporting international autism surveillance activities, prevalence estimates, and epidemiologic research will also be important, in order to compare prevalence estimates and epidemiologic characteristics across countries.

Communication and Dissemination:

Research data regarding autism is now being published at a rapid rate. It is critical that new findings are communicated promptly and appropriately to the public so that research findings can be better translated into practice as appropriate. Effective translation is important so that new findings can be utilized to improve risk assessment and implementation of individualized interventions to reduce the disabling symptoms and promote a positive developmental trajectory as early as possible. Additional attention needs to be paid to improving the communication channels between scientists, practitioners, people with ASD and their families.

There is also need to build a system for rapid replication studies concerning key findings. In addition, there is still not agreement about meaningful subtypes or about how to individualize treatment. As more professionals become involved in autism research, there is a need for organized input from established scientists to provide guidance and expertise.

In addition, it will be necessary to identify and address the wide range of ethical and clinical issues related to the diagnosis, assessment, and communication of genetic, environmental, and clinical risk for autism.

Research Workforce Development:

In order to accomplish the necessary research in the field of autism, it will also be important to develop an adequate scientific workforce. While much autism research is already underway, there are several areas of research that are new and growing, including interdisciplinary research, where additional researchers will be needed in the coming years. In fiscal year 2009, there were 92 trainees (graduate students and postdoctoral fellows) supported by specific NIH training and fellowship grants to study autism. These are in addition to the trainees supported on more than 300 NIH research grants focused on autism. The continued expansion and development of this research workforce will be essential to fulfilling the goals laid out in the IACC Strategic Plan.

ASPIRATIONAL GOAL: DEVELOP AND SUPPORT INFRASTRUCTURE AND SURVEILLANCE SYSTEMS THAT ADVANCE THE SPEED, EFFICACY AND DISSEMINATION OF AUTISM RESEARCH.

Short-Term and Long-Term Objectives

A. Conduct a needs assessment to determine how to merge or link administrative and/or surveillance databases that allow for tracking the involvement of people living with ASD in healthcare, education and social services by 2009. *IACC Recommended Budget: $520,000 over 1 year.*

B. Conduct an annual "State of the States" assessment of existing state programs and supports for people and families living with ASD by 2009. *IACC Recommended Budget: $300,000 each year.*

C. Develop and have available to the research community means by which to merge or link databases that allow for tracking the involvement of people in ASD research by 2010. *IACC Recommended Budget: $1,300,000 over 2 years.*

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 developing fibroblast repositories to produce pluripotent stem cells. Protocols should be put into place to expand the capacities of ongoing large-scale children's studies to collect and store additional biomaterials, promoting detection of biological signatures. *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.*

New Objective:

E. Begin development of a web-based toolbox to assist researchers in effectively and responsibly disseminating their finding to the community, including people with ASD, their families, and health practitioners by 2011. *IACC Recommended Budget: $400,000 over 2 years.*

New Objective:

F. Create funding mechanisms that encourage rapid replication studies of novel or critical findings by 2011.

****Note:** Infrastructure objectives that appeared in the 2009 Strategic Plan were moved from other chapters to Question 7.*

Objectives in boxes labeled "New Objective" are either entirely new additions to the 2010 Strategic Plan or significantly modified objectives from the 2009 Strategic Plan. Objectives from the 2009 Strategic Plan that did not change or that have been slightly modified for clarification purposes are unmarked

New Objective:

G. Develop a web-based tool which provides population estimates of ASD prevalence for states based on the most recent prevalence range and average identified by the ADDM Network by 2012. *IACC Budget Recommendations: $200,000 over 2 years.*

New Objective:

H. Create mechanisms to specifically support the contribution of data from 90 percent of newly initiated projects to the National Database for Autism Research (NDAR) and link NDAR with other existing data resources by 2012. *IACC Recommended Budget: $6,800,000 over 2 years.*

New Objective:

I. Supplement existing ADDM Network sites to use population-based surveillance data to conduct at least 5 hypothesis-driven analyses evaluating factors that may contribute to changes in ASD prevalence by 2012. *IACC Recommended Budget: $660,000 over 2 years.*

New Objective:

J. Develop the personnel and technical infrastructure to assist states, territories, and other countries who request assistance describing and investigating potential changes in the prevalence of ASD and other developmental disabilities by 2013. *IACC Recommended Budget: $1,650,000 over 3 years.*

New Objective:

K. Encourage 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.*

New Objective:

L. Expand the number of ADDM sites in order to conduct ASD surveillance in younger and older age groups; conduct complementary direct screening to inform completeness of ongoing surveillance; and expand efforts to include autism subtypes by 2015. *IACC Recommended Budget: $16,200,000 over 5 years.*

New 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. *IACC Recommended Budget: $75,000 over 5 years.*

*****Note:** Infrastructure objectives that appeared in the 2009 Strategic Plan were moved from other chapters to Question 7.*

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Research Resources

Below is a list of currently available resources for conducting ASD research. It includes government and non-government resources spanning topics such as genetics, bioinformatics, brain and tissue samples, and animal resources, as well as resources related to surveillance, prevalence, and services.

Government Resources

Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE)

http://www.cdc.gov/ncbddd/autism/caddre.html

> *Regional centers of excellence for ASD and other developmental disabilities which are currently conducting the largest U.S. study of ASD risk factors*

CDC Autism and Developmental Disabilities Monitoring (ADDM) Network

http://www.cdc.gov/ncbddd/autism/addm.html

> *A surveillance network that provides data about ASD prevalence and describes the population of children with ASD*

National Children's Study

www.nationalchildrensstudy.gov/

> *A population-based study of environmental influences on child health and development that could be used to investigate the relationship between genetic and environmental risk markers and ASD diagnosis*

NDAR (National Database for Autism Research)

http://ndar.nih.gov

> *A secure bioinformatics platform for scientific collaboration and data-sharing between ASD investigators*

NDAR Data Definition

http://ndar.nih.gov/ndarpublicweb/standards.go

> *A data definition of ASD research terminology*

NICHD Brain and Tissue Bank

http://medschool.umaryland.edu/BTBank/

A brain tissue repository to support and enhance the acquisition and distribution of tissue samples from deceased individuals diagnosed with intellectual and developmental disabilities for use in research studies

NIF (Neuroscience Information Framework)

http://nif.nih.gov

NeuroLex is a dynamic lexicon to improve communication among neuroscientists about their data

NIH Pediatric MRI Data Repository

http://nih-pediatricmri.org

A multi-site longitudinal study used technologies (anatomical MRI, diffusion tensor imaging [DTI], and MR spectroscopy [MRS]) to map pediatric brain development

NIMH Center for Collaborative Genetic Studies

http://nimhgenetics.org/

A repository of biospecimens from individuals with mental illnesses such as schizophrenia, bipolar disorder, autism spectrum disorders, depression, and obsessive compulsive disorders

NIMH Genetics Repository

http://nimhgenetics.org

A repository to produce, store, and distribute clinical data and biomaterials such as DNA samples and cell lines (includes subjects with ASD)

NITRC (Neuroimaging Informatics Tools and Resources Clearinghouse)

http://www.nitrc.org

A neuroimaging tools repository, NITRC facilitates finding and comparing neuroimaging resources for functional and structural neuroimaging analyses

Non-Human Primate Atlas of Gene Expression through Development

http://www.blueprintnhpatlas.org/nhp

An atlas mapping the expression of particular genes to specific neuroanatomical locations across several timepoints in development in the rhesus monkey

Non-Government Resources

AGRE (Autism Genetic Resource Exchange)

http://www.agre.org

A repository for biomaterials and associated phenotype and genotype information from over 1,000 individuals with an ASD diagnosis and their families

Autism Genome Project

http://www.autismspeaks.org/science/research/initiatives/autism_genome_project.php

A study to find the genes associated with inherited risk for autism

Autism Tissue Program

http://www.brainbank.org

An ASD brain tissue repository

Autism Treatment Network

http://www.autismspeaks.org/science/programs/atn

A network of hospitals and physicians dedicated to developing a model of comprehensive medical care for children and adolescents with autism

Baby Siblings Research Consortium

http://www.autismspeaks.org/science/research/initiatives/babysibs.php

A consortium studying the infant siblings of children with ASD in order to identify early behavioral and biomedical markers of the disorder

IAN (Interactive Autism Network)

http://www.ianproject.org

An online registry of over 35,000 people who have or are related to those with ASD

ISAAC (Internet System for Assessing Autistic Children)

http://www.autismtools.org/index.cfm

A web-based application for administering and managing health research projects/studies and the associated data

RedCap

http://project-redcap.org

Two secure, web-based applications (REDCap and REDCap Survey) designed to support data capture for research studies

SFARI (Simons Foundation Autism Research Initiative)

https://sfari.org/simons-simplex-collection/

A repository of genetic samples and phenotypic data from families where parents without ASD give birth to a child with the disorder

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