

The Interagency Autism Coordinating Committee

2009 STRATEGIC PLAN

for Autism Spectrum Disorder Research



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Preface

In January 2009, the Interagency Autism Coordinating Committee (IACC), a federal government advisory panel, released its first blueprint for autism research. The IACC Strategic Plan for Autism Spectrum Disorder Research advises federal agencies and Congress on needs and opportunities for research investigating autism, a complex developmental disorder that affects 1 in 150 children.

"This plan will help fill the gaps between what we know about autism and what we need to do to help affected families and communities," said Thomas Insel, M.D., chair of the IACC and director of the National Institute of Mental Health, part of the National Institutes of Health. "This document marks a significant achievement in that it is the product of a truly collaborative effort involving the IACC, scientists, advocacy groups, and the public."

In establishing the IACC, the Combating Autism Act of 2006 mandated that the body develop and annually update a strategic plan for autism research. The IACC, composed of both federal and public members, developed the plan through an extensive process engaging a wide range of federal agencies and public stakeholders.

The IACC convened four scientific workshops to identify research opportunities as well as expert workgroups to recommend research objectives. The committee also sought extensive public input on ASD research priorities through means such as town hall meetings and Requests for Information. The resulting plan reflects a diversity of views and the breadth of research that will be required to address the needs of people with ASD and their families.

The Interagency Autism Coordinating Committee 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 6.7 per 1,000 (1 in 150) (CDC, 2007). 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 this initial Strategic Plan for ASD Research, which is focused on the unique needs of people with ASD and their families, as well as other consumers of these efforts. The Strategic Plan was developed through extensive and iterative input from members of the public, academic, and advocacy communities. In developing 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.*

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 six critical questions asked by people and families living with ASD:

- I. When should I be concerned?**
- II. How can I understand what is happening?**
- III. What caused this to happen and can this be prevented?**
- IV. Which treatments and interventions will help?**
- V. Where can I turn for services?**
- VI. What does the future hold?**

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 six-question 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 six-question 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 can increase 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 that being

implemented by 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.

I. WHEN SHOULD I BE CONCERNED?

- What are the early warning signs?
- Are there typical characteristics that are part of an ASD diagnosis?
- How much variation is there in symptoms and severity associated with ASD?

What do we know?

A child's primary 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 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. Some children at risk may also begin to experience co-occurring medical symptoms. Recent studies of children at high risk because of a family history of 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).

A number of screening tools have been developed for detecting autism for children of varied ages and different levels of clinical severity. A video glossary of early red flags of ASD in young children has been 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.

What do we need?

Most cases of autism and related disorders are not diagnosed until after a child's third birthday, and yet early intervention can have a critical influence on the future course of ASD. At least five issues have limited the use of early interventions. First, 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). Delays do not always indicate the presence of a disorder. Pediatricians recognize that most children who are slow to walk or talk will catch up in the second year.

Second, 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.

Biomarkers can potentially identify people with ASD, or infants who will subsequently develop or are already developing subtle signs of ASD, so that providers can initiate

intensive early intervention strategies to address or possibly preempt developmental delay.

Third, children with ASD develop along different trajectories. Some show normal 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 consistency in applying their definitions.

Fourth, healthcare and other service providers may not have received training in recognizing the early warning signs of ASD nor use existing screening tools at well check-ups. For example, the American Academy of Pediatrics has recommendations for pediatricians. Fifth, parents and caregivers may be unaware of the early warning signs of ASD, 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 with or at risk for ASD will be identified by 24 months and receive appropriate interventions

Research Opportunities

- ASD screening instruments and approaches for use in community settings to identify people 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 and older age groups.
- ASD measures that are easy to administer and sensitive to incremental changes in both core and associated ASD symptoms.

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 symptoms 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 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 bioethics considerations into the diagnosis and screening processes, including consideration of the implications of genetic testing.

Short-Term Objectives

- 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.*

- Validate and improve the sensitivity and specificity of new or existing screening tools for detecting ASD through studies of the following community populations that are diverse in terms of age, socio-economic status, race, ethnicity and level of functioning by 2012. *IACC Recommended Budget: \$5,400,000 over 3 years.*
 - School aged children
 - General population (vs. clinical population)

Long-Term Objectives

- Identify a panel of biomarkers that separately, or in combination with behavioral measures, 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.*
- 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.*
- Identify and develop measures to assess at least three continuous dimensions of ASD symptoms and severity that can be used by practitioners and/or parents to assess response to intervention for people with ASD across the lifespan by 2016. *IACC Recommended Budget: \$18,500,000 over 5 years.*

II. HOW CAN I UNDERSTAND WHAT IS HAPPENING?

- **What is happening early in development?**
- **Are there known biological differences that help explain ASD symptoms?**
- **Are there subgroups of people with ASD that have been identified?**

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 many scientists believe that the behavioral features of ASD result from atypical brain wiring or connections in synapses, they have not reached a consensus on a specific 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 magnetic resonance imaging (MRI) 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 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).

Frequently, people with ASD experience co-occurring behavioral and medical symptoms. In the case of the immune system, a number of hypotheses concerning how disruptions might contribute to ASD and other neurodevelopmental disorders have emerged in recent years. Some recent findings suggest that the immune systems 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, research on the effect of maternal antibodies, proteins produced as part of the immune response, on an array of fetal brain proteins suggested that in some cases maternal antibodies could interfere with normal brain development (Braunschweig et al., 2008). These questions have been receiving increasing attention in recent years but it is too early for clear answers. While such medical symptoms may not be entirely specific to ASD, treating them may have significant impact on quality of life, symptom severity, and level of functioning.

Exploring the neural 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.

What do we need?

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 medical conditions.

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 would be especially enlightening, as limited normative information is currently available. An evaluation of differences in environmental exposures between 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 whether the gender ratio is accurate and whether gender is related to protective factors, diagnosis, and trajectory.

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 cannot satisfy the high demand and the continuously increasing demand for post-mortem tissue by scientific investigators. Currently, the numbers of well-preserved brains, and the specimens include a number of varying co-occurring conditions and are of limited developmental range. Furthermore, there are few matched controls available for the resources in the existing repositories.

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.
 - An international public-private collaboration to expand current postmortem brain and other tissue resources (e.g., skin fibroblasts) to increase the acquisition, quality, type and availability of biomaterials relevant to studying the pathology of ASD.
 - Research on the unique strengths and abilities of people with ASD.
- Short-Term Objectives**
- Establish an international network of biobanks for the collection of brain and other tissue (e.g., skin fibroblasts) with acquisition sites that use standardized protocols for phenotyping, collection and distribution of tissue by 2011. *IACC Recommended Budget: \$10,500,000 over 2 years.*
- 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.*
 - Launch three studies that specifically focus on the neurodevelopment of females with ASD by 2011. *IACC Recommended Budget: \$8,900,000 over 5 years.*
 - Identify ways to increase awareness among the autism spectrum community of the potential value of brain and tissue donation to further basic research. *IACC Recommended Budget: \$1,400,000 over 2 years.*

Long-Term Objectives

- Complete a large-scale, multi-disciplinary, collaborative project that longitudinally and comprehensively examines how the biological, clinical, and developmental profiles of children, 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.*
- Maintain an international network of biobanks and support continued collection of brain and other tissue. *IACC Recommended Budget: \$22,200,000 over 5 years.*

III. 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?
- How might genetics and/or the environment influence the occurrence of ASD?
- Could an exposure to something in the environment lead to the development 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. 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 research has revealed additional mutations of specific genomic regions (15q21 and 16p11) (Marshall et al., 2008; Weiss et al.,

2008). 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, these genetic structural abnormalities account for 10-20% of ASD cases, yet individually each abnormality accounts for only 1-2% of cases (Abrahams & Geschwind, 2008). This suggests that the genetic factors in ASD may involve many rare mutations. Possible models include: (a) additional genetic mutations to be discovered; (b) multiple genetic variations each conferring a small increased risk; and, (c) many forms of ASD with different genetic contributions.

Progress in identifying susceptibility genes has been made possible due to collaborations and resources, both public and private, including: the National Institute of Mental Health (NIMH) Center for Collaborative Genetic Studies; the Collaborative Programs of Excellence in Autism (CPEA) co-sponsored by NICHD and the National Institute on Deafness and Other Communication Disorders (NIDCD); the National Institute of Environmental Health Sciences (NIEHS) Childhood Autism Risks from Genetics and the Environment (CHARGE) study; the Autism Genetic Resource Exchange (AGRE) sponsored by Cure Autism Now (CAN) with a large consortium of researchers assembled by Autism Speaks/National Alliance for Autism Research; CDC's Centers for Autism and Developmental Disabilities Research and Epidemiology (CADDRE); the Norwegian cohort study supported by the

National Institute of Neurological Disorders and Stroke (NINDS); and the Simons Foundation Collection.

In addition, existing research resources in toxicology could be tapped to provide important infrastructure for studying some forms of environmental risk.

Research on environmental risk factors is also underway. An Institute of Medicine workshop held in 2007 summarized what is known and what is needed in this field (Institute of Medicine of the National Academies, 2007). 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 research literature. Some do not agree and remain concerned that ASD is linked or caused by vaccination through exposure to Measles Mumps Rubella (MMR), imposing challenges to a weakened immune system, or possibly due to mitochondrial disorder.

Public comment to the Committee reflected opposing views on vaccines as a potential environmental cause. Those who are convinced by current data that vaccines do not play a causal role in autism argue against using a large proportion of limited autism research funding toward 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 agents are being explored through research that 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, 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. While there are reports of associations of ASD with exposure to medications or toxicants prenatally, and to infections after birth, 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 focus 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 would be for genetics.

To address public concerns regarding a possible vaccine/ASD link, it will be important over the next year for the IACC to engage the National Vaccine Advisory Committee (NVAC) in mutually informative dialogues. The NVAC is a Federal advisory committee chartered to advise and make recommendations regarding the National Vaccine Program. Communication between the IACC and NVAC will permit each group to be informed by the expertise of the other, enhance coordination and foster more effective use of research resources on topics of mutual interest. Examples of such topics include: studies of the possible role of vaccines, vaccine components, and multiple

vaccine administration in ASD causation and severity through a variety of approaches; and assessing the feasibility and design of an epidemiological study to determine whether health outcomes, including ASD, differ among populations with vaccinated, unvaccinated, and alternatively vaccinated groups.

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.

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

- Genomic 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 gene differences and the role of the environment 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.

- Environmental and biological risk factors during pre- and early postnatal 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 understanding gene – environment interactions.
- Exposure assessment -- efficient and accurate measures of key exposures for use in population and clinic based studies and standards for sample collection, storage, and analysis of biological materials.

Short-Term Objectives

- Initiate studies on at least five 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 2010.
IACC Recommended Budget: \$23,600,000 over 2 years.
- 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.
IACC Recommended Budget: \$43,700,000 over 4 years.

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

Long-Term Objectives

- 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.*
- 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.*
- Identify genetic risk factors in at least 50% of people with ASD by 2014. *IACC Recommended Budget: \$33,900,000 over 6 years.*
- Support ancillary studies within one or more large-scale, population-based surveillance and epidemiological studies, including U.S. populations, to collect nested, case-control 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.*

IV. 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 autistic children 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), which are based on 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). 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 (Amminger 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., 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, rigorous scientific studies are needed to develop and safely test the efficacy of comprehensive interventions, and to identify 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 RCTs.

The identification of biomarkers, for instance, in plasma, saliva, 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 autistic children 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.

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 preventing the disabilities associated with ASD.

Research Opportunities

- Large scale studies that directly compare interventions and combinations of 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.
- 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 symptom clusters unique to ASD.
- 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 methods 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.
- Test safety and efficacy of at least five widely used interventions (e.g., nutrition, medications, medical procedures) that have not been rigorously studied for use in ASD by 2012. *IACC Recommended Budget: \$27,800,000 over 5 years.*
- 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.*

Short-Term Objectives

- Launch at least four research projects that seek to identify biological signatures that measure significant changes in ASD core symptoms across the lifespan by 2010. *IACC Recommended Budget: \$12,700,000 over 4 years.*
- 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.*
- Conduct five randomized controlled trials of early intervention for infants and toddlers by 2011. *IACC Recommended Budget: \$16,700,000 over 5 years.*
- Launch three randomized controlled trials of interventions for school-aged and/or adolescents by 2012. *IACC Recommended Budget: \$15,600,000 over 5 years.*
- 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.*

Long-Term Objectives

- 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.*
- 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.*

V. 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 interventions and how will it be paid?**

What do we know?

Discovery of new diagnostic tests and efficacious interventions is necessary but not sufficient to reach the bold vision for this Strategic Plan. 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 clinical practice and supported by public policy. The gap between knowledge and action can only be overcome by an aggressive focus on engaging families and the services community in the research process, disseminating research findings into the community, eliminating barriers to services and helping people and 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). 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 to these people. The professional

infrastructure or capacity is often inadequate to provide timely diagnosis, appropriate care, and assurance of health and safety.

These differences in policies, resources and organization result in marked differences in the treated prevalence of ASD across geographic areas, the types of services and support that are received, availability of appropriate lifespan transition opportunities, and the associated financial costs to families (Fujiura, Rocciforte, & 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 care 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 care received, 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 help address these challenges, a new health services research field of implementation science is emerging to: (a) evaluate the effectiveness of interventions in community settings; (b) identify the most effective means of disseminating research into widespread clinical practice; and, (c) define the best ways for research to inform policy on ASD services and supports. Integral to success will be community engagement in shaping, participating, and disseminating ASD research.

An initial part of this process is the assessment of needs and costs. Care for developmental disorders is 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 policy makers 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.

In addition to disseminating best practices from ASD treatment and intervention research studies to community settings, so called bench to bedside translation, the other kind of translation, bedside to bench, could take and test promising community practices in rigorously designed research trials. Using a participatory action model, families, people with ASD, and communities can be empowered to become partners in research that can in turn inform policy.

ASPIRATIONAL GOAL:
Communities will implement high quality, evidence-based and cost effective services and supports across the lifespan for people with ASD.

Research Opportunities

- Annual “State of the State” review of policies, services and supports for people with ASD and their families.
- Effective dissemination of evidence-based practices for people with ASD at the community level.
- Cost-effectiveness studies of interventions and services for people with ASD across the 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.
- Improved and coordinated methods for tracking trends in ASD prevalence across the lifespan of diverse populations.

Short-Term Objectives

- Initiate a “State of the States” assessment of existing state programs and supports for people and families living with ASD by 2009. *IACC Recommended Budget: \$630,000 over 2 years.*
- Support two studies that assess how variations and access to services affect family functioning in diverse populations by 2012. *IACC Recommended Budget: \$1,000,000 over 3 years.*

Long-Term Objectives

- Test the efficacy and cost-effectiveness of at least four evidence-based services for people with ASD of all ages in community settings by 2015. *IACC Recommended Budget: \$16,700,000 over 5 years.*
- Test four methods to improve dissemination of effective interventions in diverse community settings by 2013. *IACC Recommended Budget: \$7,000,000 over 5 years.*

VI. WHAT DOES THE FUTURE HOLD?

- **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 for adults with ASD. Longitudinal studies designed to capture the range of possible outcomes for adults with ASD are best suited to inform public policy decision-making, service and support delivery, and funding strategies. Also it is important to improve public understanding of ASD in adults, including older adults, so that they may receive support from communities to help them lead fulfilling and productive lives. Efforts to improve public awareness and community supports could help foster acceptance, inclusion, and appreciation of people with ASD.

ASD poses economic and social costs for people, their families, and society at large. Although ASD symptoms vary greatly in character and severity, the disorder 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 care for all Americans with ASD during their lifetimes exceeds \$35 billion,

and that each person accrues approximately \$3 million in costs over his or her lifetime (Ganz, 2007). Families often incur large debts related to medical and educational services not covered through public programs or medical and dental insurance. In addition to financial challenges, ASD can lead to emotional hardships for people and their families throughout life.

What do we need?

Although considerable research has focused on the earliest phase of ASD, through optimized diagnosis and early intervention, far less effort has addressed the adolescent, adult, and older adult phases of life. Minimal guidance exists for individuals and families about the trajectories of ASD across the lifespan. Although the general assumption is that higher functioning children can sometimes excel as adults, and children with more narrowly defined autistic disorder grow up to become adults who are lower functioning, the evidence base for these ideas is lacking. Scientists have not yet identified key prognostic factors or detailed information about how adults with ASD currently function and how they are best supported.

There are a number of areas in which prevalence studies could be improved: continued estimation and evaluation of prevalence in the same population over time; assessment of ASD prevalence in the context of other neurodevelopmental disorders; collection of data beyond core ASD symptoms, including genetic data and co-occurring medical, dental, and behavioral conditions; and expansion of studies across ages.

More research is needed to tailor treatments, interventions, services and supports to the evolving needs of school-age children, adolescents transitioning to adulthood, and adults with autism. There is a need to address co-occurring conditions and developmental changes that coincide with transitions from adolescence to adulthood, to better assess functional outcomes (e.g., school-to-work, independent living, access to healthcare, including oral health care) in older people, and to develop improved quality-of-life measures for adults with ASD that assess dimensions other than intelligence and language skill. There is little information about the number of adults with ASD within the criminal justice system.

Finally, merging and analyzing health care, education, and social services administrative databases that include 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. 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.

ASPIRATIONAL GOAL: Advances in intervention, education, and services will support and enable people on the autism spectrum to lead fulfilling and productive lives in the community.

Research Opportunities

- Longitudinal studies of both people with ASD and their families to follow trajectories that account for clinical, psychosocial and biological heterogeneity.
- The scope and impact of ASD in adults, including how to diagnose ASD in adulthood, their needs during critical life transitions, assessment of functional and legal outcomes, family relationships, and co-occurring health issues.
- Use of existing administrative databases for information relevant to diagnosis, course, interventions and long-term outcomes for ASD.

Short-Term Objectives

- 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.*
- Launch at least two studies to assess and characterize variation in adults living with ASD (e.g., social and daily functioning, demographic, medical and legal status) by 2011. *IACC Recommended Budget: \$5,000,000 over 3 years.*
- Conduct at least two clinical trials to test the efficacy and cost-effectiveness of interventions, services and supports to optimize daily functioning (e.g., educational, vocational, recreational, and social experiences) for adolescents, adults, or seniors living with ASD by 2012. *IACC Recommended Budget: \$8,000,000 over 5 years.*
- 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 health care, education, and social services by 2009. *IACC Recommended Budget: \$520,000 over 1 year.*

Long-Term Objectives

- Develop at least two community-based interventions with individual specificity that improves outcomes, as measured by educational, occupational, and social achievements by 2015. *IACC Recommended Budget: \$12,900,000 over 5 years.*
- Develop and have available to the research community means by which to merge or link administrative databases that allow for tracking the involvement of people living with ASD research in health care, education, and social services by 2018. *IACC Recommended Budget and Time Frame: To Be Determined.*
- Conduct a cost/benefit analysis on provision of services and interventions over the lifespan with regard to long-term benefits including employment, productivity, and the need for federal/state assistance. *IACC Recommended Budget: \$2,300,000 over 3 years.*

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