

QUESTION 4: WHICH TREATMENTS AND INTERVENTIONS WILL HELP?		
IACC Strategic Plan Objectives	Conclusions	Funding 2008-2012
<p>4.S.A Support at least three randomized controlled trials that address co-occurring medical conditions associated with ASD by 2010.</p> <p><i>IACC Recommended Budget: \$13,400,000 over 3 years</i></p>	<p>Funding: The recommended budget was met. Progress: More than 3 projects were funded, including trials of sleep, anxiety, seizure and gastrointestinal (GI) interventions, meeting the objective, but additional work will be needed in the future to fully address these conditions. Remaining Gaps, Needs, and Opportunities: Sleep issues, anxiety, hyperactivity and GI issues are key co-occurring medical conditions in patients with ASD. Although there is much more known today about sleep initiation than what was understood 5 years ago, there is little understanding of what interventions/treatments are effective for sleep maintenance or night awakening. There is not much known concerning anxiety treatments for those with ASD, and challenges exist regarding the adaptation of anxiety treatments from outside ASD patient groups. Research into interventions for hyperactivity may be transferred from populations outside of those with ASD (i.e., ADHD). Though there has been an increased awareness of gastrointestinal difficulties and common symptoms among people with ASD, little is known about the etiology of autism related GI issues. More research on the etiology of GI issues will be needed to develop appropriate treatments/interventions.</p>	<p>\$17,105,378</p>
<p>4.S.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.</p> <p><i>IACC Recommended Budget: \$75,000,000 over 5 years</i></p>	<p>Funding: The recommended budget was met and exceeded. Progress: More than 90 projects were supported to develop animal models. Remaining Gaps, Needs, and Opportunities: Planning Group members discussed whether the amount of investment in this area is appropriate when compared to investments in clinical trials and other later stage studies. Invited experts suggested that the current stage of scientific research in ASD requires pre-clinical research to identify targets from animal and cellular models. Similar to cancer treatment development pathways, which spanned 20-30 years, research in ASD must invest in model systems to understand the fundamental biology from which translation to the clinic can be built. The translational validity of research in non-human animals cannot be determined until human trials are conducted, thus the need for rapid progress to clinical studies in humans is important.</p>	<p>\$102,110,669</p>
<p>4.S.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.</p>	<p>Funding: The recommended budget was partially met, but more funding is needed. Progress: Several projects were funded in this area, but more work is needed, as this is an area of significant public interest. Remaining Gaps, Needs, and Opportunities: Experts discussed the best balance between developing new treatments and testing current treatments that lack evidence, especially when funds are limited and conclusive clinical trials are expensive. The group noted that interventions for minimally verbal children are needed; some projects on assistive communication technologies and robotics and speech processing technology to assist with social communication training are funded, but more are needed. There are other projects related to minimally verbal autism in objective 4SG. Small pilot studies on nutritional therapies (i.e., GFCF diet studies) have been conducted with inconclusive outcomes demonstrating the necessity for further exploration of nutritional interventions. Future emphasis on scientific investment in sensory integration and assisted technologies is needed.</p>	<p>\$8,946,921</p>

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<p><i>IACC Recommended Budget: \$27,800,000 over 5 years</i></p> <p>4.S.D Complete two multi-site randomized controlled trials of comprehensive early intervention that address core symptoms, family functioning and community involvement by 2013.</p>	<p>Funding: The recommended budget was met and exceeded. Progress: In 2011 and 2012, ~20 trials were supported, including a mix of trial sizes. Remaining Gaps, Needs, and Opportunities: There is a need for both small, pilot studies and larger, robustly powered studies in this area. Several larger studies in the past few years (i.e. Early Start Denver Model) have emerged, but most studies in this area are generally smaller than in other fields of medicine and therefore lack the power to be informative if negative or definitive if positive. This objective also cites “family functioning” and “community living”, which may have significant overlap with objectives in questions 5 and 6 of the Strategic Plan.</p>	<p>\$42,088,407</p>
<p><i>IACC Recommended Budget: \$16,700,000 over 5 years</i></p> <p>4.S.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.</p>	<p>Funding: The recommended budget was partially met. Progress: A workshop specifically targeted to this topic has not taken place, but other activities have partially addressed these issues. Remaining Gaps, Needs, and Opportunities: Autism Speaks held a workshop in December 2011 “<i>Outcome Measures for Clinical Trials with Individuals with ASD: Challenges and Opportunities</i>” that was focused on developing strategies for advancing clinical trials of medications for ASD core and associated symptoms. The EU-AIMS public-private consortium in Europe (and Autism Speaks) has focused on biomarkers for identifying subtypes as well as personalization of interventions for ASD. Joint meetings between EU-AIMS and the Foundation for NIH Biomarkers Consortium are ongoing to determine the opportunities for collaboration on identifying surrogate markers for treatment studies.</p>	<p>\$26,000</p>
<p><i>IACC Recommended Budget: \$50,000</i></p> <p>4.S.F Launch 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:</p> <ul style="list-style-type: none"> • Five trials in infants and toddlers by 2013. • Three trials in school-aged children and/or adolescents by 2013. • Three trials in adults by 2014. 	<p>Funding: The recommended budget has been partially met. Progress: The investment in projects under this objective is making good progress toward the recommended amount, with more than 20 projects funded in 2011 and 2012. Remaining Gaps, Needs, and Opportunities: Current projects in this area are restricted to small pilot studies, which are essential to establishing a foundation prior to expansion to larger scale work. Thus, increased investment in this area is important. It should be noted that most RCTs in the future will incorporate some aspect of biological signatures (thus potentially presenting a challenge to future coding of projects).</p>	<p>\$41,177,035</p>
<p><i>Total IACC Recommended Budget: 66,000,000 over 5 years</i></p>		
<p>4.S.G Support at least five studies on interventions for nonverbal individuals with ASD by 2012. Such studies may include:</p> <ul style="list-style-type: none"> • Projects examining service-provision models that enhance access to augmentative and alternative communication (AAC) supports in both classroom and adult service-provision settings, such as residential service-provision and the impact of such access on quality of life, communication, and behavior; • Studies of novel treatment approaches that facilitate communication skills in individuals who are nonverbal, including the components of effective AAC approaches for specific subpopulations of 	<p>Funding: The recommended budget has been met. Progress: 11-16 studies were funded in 2010-2012, but results will not be available for at least two years. Remaining Gaps, Needs, and Opportunities: The field of research on non-verbal patients with ASD is growing, yet still requires significant work and future investment. ASD research has historically concentrated on verbal individuals and adults, which highlights the need for increased research on minimally verbal populations.</p>	<p>\$9,580,403</p>

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<ul style="list-style-type: none"> people with ASD; and Studies assessing access and use of AAC for children and adults with ASD who have limited or partially limited speech and the impact on functional outcomes and quality of life. 		
<p><i>IACC Recommended Budget: \$3,000,000 over 2 years</i></p> <p>4.S.H Support at least two studies that focus on research on health promotion and prevention of secondary conditions in people with ASD by 2012. Secondary conditions of interest include weight issues and obesity, injury, and co-occurring psychiatric and medical conditions.</p>	<p>Funding: The recommended budget was partially met. Progress: A small number of projects were funded, but further work is needed to address some of the specific issues described in the objective. Remaining Gaps, Needs, and Opportunities: Overlap in interpretation between “co-occurring” and “secondary” conditions presents a challenge in evaluating this objective. There is likely overlap between projects that may fit this objective and those in 4.S.A. Areas of health promotion and prevention should be emphasized in this objective, as those are distinct from issues mentioned in other objectives in this Question. It was noted that 4SH’s emphasis on prevention and health promotion may also overlap with 5SD and 5LD on “health and safety and mortality” issues.</p>	<p>\$1,404,969</p>
<p><i>IACC Recommended Budget: \$5,000,000 over 3 years</i></p> <p>4.L.A Complete at least three randomized controlled trials on medications targeting core symptoms in people with ASD of all ages by 2014.</p>	<p>Funding: The recommended budget has only partially been met. Progress: 10-14 studies have been funded, and momentum within the pre-clinical phases of this objective is currently building. Remaining Gaps, Needs, and Opportunities: Though there is little evidence that CNS drug development in animals will translate to humans, either in terms of toxicity or efficacy, there is still a need for investment in well-established animal model studies to identify promising molecular, cellular, or systems targets before mounting randomized clinical trials in humans. However, existing drugs for other indications may be adapted to ASD without extensive pre-clinical work, and there is also evidence for proof of concept studies for ASD (particularly those addressing core symptoms). It is also critically important to develop appropriate outcome measures for use in trials.</p>	<p>\$9,715,095</p>
<p><i>IACC Recommended Budget: \$22,200,000 over 5 years</i></p> <p>4.L.B Develop interventions for siblings of people with ASD with the goal of reducing the risk of recurrence by at least 30% by 2014.</p>	<p>Funding: The recommended budget has only partially been met. Progress: Only a small number of projects has been funded, and the intent of the objective has not been met to date. Remaining Gaps, Needs, and Opportunities: Studies within this objective will emerge in the near future. Greater understanding of the mechanisms underlying sibling development of ASD will be key before any targeted early interventions may be developed for this population.</p>	<p>\$831,111</p>
<p><i>IACC Recommended Budget: \$6,700,000 over 5 years</i></p> <p>4.L.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.</p>	<p>Funding: The recommended budget was partially met. Progress: A small number (3-7) of studies of pharmacological interventions was funded. There exist many studies examining drugs that are in active use for ADHD that are now being adapted to ADHD-ASD patient groups. Remaining Gaps, Needs, and Opportunities: There currently is much need for greater understanding of drug efficacy in ASD populations.</p>	<p>\$6,475,421</p>
<p><i>IACC Recommended Budget: \$10,000,000 over 5 years</i></p> <p>4.L.D Support at least five community-based studies that assess the effectiveness of interventions and services in broader community settings by 2015. Such studies may include comparative effectiveness research studies that assess the relative effectiveness of:</p> <ul style="list-style-type: none"> Different and/or combined medical, pharmacological, nutritional, behavioral, service-provision, and parent- or caregiver-implemented treatments; Scalable early intervention programs for 	<p>Funding: The recommended budget has been partially met. Progress: 30-45 studies have been supported, exceeding the initial target. Considerable work has been done under this objective, but these projects do not cover the full scope of interventions in the community. Remaining Gaps, Needs, and Opportunities: Emphasis on both the evaluation of interventions in controlled/academic settings prior to community based studies and the translation of interventions to community-based settings is key. Understanding of “Type 2 Translation,” or transfer from academic settings to real-world settings, in research is important, considering barriers to transferring academic-based interventions to clinical groups and communities. Investment is still necessary in the academic setting before successful</p>	<p>\$25,239,169</p>

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<p>implementation in underserved, low-resource, and low-literacy populations; and</p> <ul style="list-style-type: none"> • Studies of widely used community intervention models for which extensive published data are not available. 	<p>translation to community-based interventions. For successful T2 translation to underserved communities, cost effectiveness and case coordination or case management is often helpful with uptake. This objective also overlaps considerably with objectives in Question 5. It is important to explore which supports are specifically executed at the community level (vs. home, schools, etc.), and to determine how they are best designed.</p>	
<p>Outcome measures should include assessment of potential harm as a result of autism treatments, as well as positive outcomes.</p>		
<p><i>IACC Recommended Budget: \$37,500,000 over 5 years</i></p>		
<p>Not specific to any objective</p>		\$44,566,554
<p>Total funding for Question 4</p>		\$309,241,132