

## QUESTION 4: WHICH TREATMENTS AND INTERVENTIONS WILL HELP?

IACC Strategic Plan Objectives	Conclusions	Funding 2008-2012
<p><b>4.S.A</b> 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>The recommended budget was met, and more than 3 projects were funded, but these projects are just a start on what needs to be done. Projects include trials of sleep, anxiety, seizure and GI interventions. However, more work is needed to address those co-occurring conditions more thoroughly and to address other co-occurring conditions. Sleep issues, anxiety, and hyperactivity are key co-occurring medical conditions in patients with ASD. Sleep is a primary concern from the clinical perspective with little understanding of what interventions/treatments are effective for sleep maintenance or night awakening. There is much more known today about sleep initiation than what was understood 5 years ago. Research into interventions for hyperactivity may be transferred from populations outside of those with ASD (i.e., ADHD). 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. Majority of what is known concerning gastrointestinal issues in ASD populations involves common complaints and symptoms—thus increased research on etiology of autism related GI issues will be needed to develop appropriate treatments/interventions.</p>	<p><b>\$17,105,378</b></p>
<p><b>4.S.B</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>The recommended budget was met and exceeded, and more than 90 projects were supported to develop animal models. 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 current stage of scientific research in ASD is still chiefly pre-clinical and greatly dependent on animal and cellular models. Similar to cancer and fragile X Syndrome treatment development pathways, which spanned 20-30 years, research in ASD must invest in model systems before findings may be successfully translated to clinical settings. At the same time, comprehensive “autistic animal models” are unlikely to exist, thus the need for continued clinical studies in humans is important.</p>	<p><b>\$102,110,669</b></p>
<p><b>4.S.C</b> 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><i>IACC Recommended Budget: \$27,800,000 over 5 years</i></p>	<p>The recommended budget was partially met and several projects were funded in this area, but more work and funding are needed, as this is an area of significant public interest. 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 important outcomes demonstrating the necessity for further investment in and exploration of nutritional interventions. There exists a need for these studies to be expanded into larger trials in the future as this is an area of great public interest. Future emphasis on scientific investment in sensory integration and assisted technologies is needed.</p>	<p><b>\$8,946,921</b></p>
<p><b>4.S.D</b> Complete two multi-site randomized controlled trials of comprehensive early intervention that address core symptoms, family functioning and community involvement by 2013.</p> <p><i>IACC Recommended Budget: \$16,700,000 over 5 years</i></p>	<p>The recommended budget was met and exceeded. In 2011 and 2012, ~20 trials were supported There was a mix of trial sizes. 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 that observed in other fields within medicine. 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><b>\$42,088,407</b></p>
<p><b>4.S.E</b> 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><i>IACC Recommended Budget: \$50,000</i></p>	<p>A workshop specifically targeted to this topic has not taken place, based on information that is currently available. Autism Speaks held a workshop in December, 2011 on related topics titled “Outcome Measures for Clinical Trials with Individuals with ASD: Challenges and Opportunities.” The Foundation for NIH Biomarkers Consortium is in the process of completing a project that aims to facilitate the development and validation of biomarkers in ASD for future drug design.</p>	<p><b>\$0</b></p>

<p><b>4.S.F</b> 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"> <li>• Five trials in infants and toddlers by 2013.</li> <li>• Three trials in school-aged children and/or adolescents by 2013.</li> <li>• Three trials in adults by 2014.</li> </ul>	<p>The recommended budget has been partially met. 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; however, more work is needed. 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. Most RCTs in the future will incorporate some aspect of biological signatures (thus presenting a challenge to future coding of projects).</p>	<p><b>\$41,177,035</b></p>
<p><i>Total IACC Recommended Budget: 66,000,000 over 5 years</i></p>		
<p><b>4.S.G</b> 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"> <li>• 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;</li> <li>• 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 people with ASD; and</li> <li>• 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.</li> </ul>	<p>The recommended budget has been met and 11-16 studies were funded in 2010-2012, but work needs to continue in this area. The field of research on non-verbal patients with ASD is growing, yet still requires significant work and future investment. ASD research is historically concentrated in high functioning individuals and adults, which highlights the need for increased research on lower-functioning and minimally verbal populations.</p>	<p><b>\$9,580,403</b></p>
<p><i>IACC Recommended Budget: \$3,000,000 over 2 years</i></p>		

<p><b>4.S.H</b> 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>The recommended budget was partially met and a small number of projects were funded, but further work is needed to address some of the specific issues described in the objective. 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><b>\$1,404,969</b></p>
<p><i>IACC Recommended Budget: \$5,000,000 over 3 years</i></p>		
<p><b>4.L.A</b> Complete at least three randomized controlled trials on medications targeting core symptoms in people with ASD of all ages by 2014.</p>	<p>The recommended budget has only partially been met. Ten-fourteen studies have been funded. Momentum within the pre-clinical phases of this objective is currently building. There is still a need for greater investment in well-established animal model studies in this area before translation to RCTs. It is expected that greater opportunity for this objective will be presented in the future as the science advances. Existing drugs for other indications may be adapted to ASD without extensive pre-clinical work, while there is also evidence of 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><b>\$9,715,095</b></p>
<p><i>IACC Recommended Budget: \$22,200,000 over 5 years</i></p>		
<p><b>4.L.B</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>The recommended budget has only partially been met and only a small number of projects funded. The intent of the objective has not been met to date. 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><b>\$831,111</b></p>
<p><i>IACC Recommended Budget: \$6,700,000 over 5 years</i></p>		
<p><b>4.L.C</b> 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>The recommended budget was partially met. 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. There currently is much need for greater understanding of drug efficacy in ASD populations.</p>	<p><b>\$6,475,421</b></p>
<p><i>IACC Recommended Budget: \$10,000,000 over 5 years</i></p>		
<p><b>4.L.D</b> Support at least five community-based studies that</p>	<p>The recommended budget has been partially met and 30-45 studies have been</p>	<p><b>\$25,239,169</b></p>

<p>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"> <li>• Different and/or combined medical, pharmacological, nutritional, behavioral, service-provision, and parent- or caregiver-implemented treatments;</li> <li>• Scalable early intervention programs for implementation in underserved, low-resource, and low-literacy populations; and</li> <li>• Studies of widely used community intervention models for which extensive published data are not available.</li> </ul> <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> Not specific to any objective</p>	<p>supported, exceeding the initial target. Considerable work has been done under this objective, but these projects do not cover the scope of interventions in the community. Emphasis on both pre-community evaluation of studies and translation 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 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 also 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><b>\$44,566,554</b></p>
<p><b>Total funding for Question 4</b></p>		<p><b>\$309,241,132</b></p>

**Aspirational Goals Discussion:** Overall, there currently exist many significant opportunities for growth in this question that were not available 5 years ago. Early Start Denver Model trials over the past 5 years have been crucial in the advancement of treatments, and future data is still forthcoming. There have also been growth in the past 5 years via Cognitive Behavioral Therapies for verbal children with ASD with higher IQ that have proven effective in treating anxiety and social skills. There is growing evidence of pharmaceutical drugs that may be effective in treating hyperactivity in children with ASD. While much progress is still needed, new opportunities are apparent in all of the objectives in this question. The field has shifted over the past 5 years where newer opportunities now exist due to the availability of more developed model systems—thus facilitating future translation of research toward effective interventions.