

**Summary of Strategic Plan Question 4 Working Group – Conference Call #2
September 30, 2016; 2:00pm EDT**

Welcome and Introductions

Working Group Members in Attendance:

Kevin Pelphrey – Chair
James Ball
Samantha Crane
Robert Ring
Timothy Buie
Connie Kasari
Beth Malow
Mustafa Sahin
Frederick Shic
Alice Kau
Alexander Leonessa

Working Group Members Absent

Geraldine Dawson
Tiffany Farchione
Melissa Harris
Elisabeth Kato
Louis Reichardt
Christy Kavulic
Alex Kolevzon
Elizabeth Laugeson
Nancy Minsheu
Samuel Odom
Phillip Strain
Denis Sukhodolsky
Zachary Warren

Follow Up from Call #1

- To follow up on a request from the first Question 4 conference call, more information on the variety of AIR-P subprojects addressing co-occurring conditions can be obtained from HRSA if the working group feels it would be helpful for drafting the chapter.

Discussion of Public Comments Received Through the Request for Information

- The public comments indicate there is a significant need for a clearinghouse of available, evidence-based interventions that can serve as resource to the community.
- The working group members were grateful for the large number of comments received, and they noted that the comments illustrate the heterogeneity in what the community needs regarding interventions. Many commenters asked to have specific interventions and therapies tested, indicating that there are many different areas that need to be addressed.

- There were a number of public comments submitted which suggested that early interventions should be prioritized. The working group members noted that in addition to early interventions, interventions for other age groups, including adolescents and adults, are also important. There may be interventions that work best in specific age-based subpopulations.
- One of the themes highlighted in the public comments addresses interventions for minimally verbal individuals. This area has started to be prioritized in response to a greater awareness of public needs and past comments; since 2013, the ACE program has made research efforts in this area.
- The working group members noticed the public comments reflect a significant amount of dissatisfaction with a lack of integration and unification between different areas of research on treatments and interventions.

Discussion of Research Progress

Topics may include: Pharmacological, behavioral/social, educational, occupational/sensory, and technology-based interventions that target either core symptoms, co-occurring symptoms, different subgroups, genders, and age groups. Also includes combination therapies and personalized approaches.

1. What are the most notable areas of recent progress in this Question's field of research? What new opportunities have emerged?

- Working group members noted progress in the following areas:
 - Interventions for minimally verbal individuals with ASD.
 - Parent-mediated interventions; however, depending on the type of intervention and age of child, different outcomes of trials have been seen, so this is an area that still needs significant attention.
 - Integration of technology with interventions; recent studies on augmentative and alternative communication (AAC) have expanded the field, and researchers have applied rigorous methodology.

2. What progress has been made in translating research into practice?

- In recent years, there have started to be more studies conducted in community settings (e.g. community centers and schools), including randomized controlled trials (RCT) that are of significant size. There is recognition that a community-based implementation science approach is gaining momentum, but more work in this area is needed.
- The working group members were encouraged by recent shifts in clinical development activities so that more studies are now focused on treating the core symptoms of ASD rather than peripheral symptoms. For example, there are clinical trials looking at the effect of oxytocin on social communication.

3. What are the most significant barriers to progress in this field?

- A significant barrier identified by the working group is the difficulty of putting together the large-scale clinical trials that are needed to achieve sufficient statistical power. Best practices for planning the size and design of trials need to be applied to studies of all kinds of therapeutic interventions. However, a key aspect to balance with the benefits of larger trials is the importance of developing highly personalized or contingent interventions tailored to specific needs.

- Another barrier the working group identified is the difficulty of understanding the heterogeneity that exists in the population of individuals with ASD. Better-defined subgroups are needed, along with adaptive and smart trial designs as well as additional detail to treatment methodology, allowing for the study of personalized intervention strategies in response to heterogeneity.
- There is concern that the lack of existing, validated clinical targets and endpoints is dampening the enthusiasm among funders across the funding landscape; funders see too much risk in studies when there is an absence of validated outcome measures.
- Regarding research on the use of digital tools for delivering interventions (e.g. games and apps), there is a lack of sufficient infrastructure to enable studies to use proper research strategy, to take into account the complexity of needs in ASD, and to address questions of accessibility. Part of the problem is that there is not a clear path from funding basic research on technologies to funding clinical trials of these technologies. More coordination between NSF and NIH to ensure a path for developing these technologies and interventions would be desirable.

4. What are the most pressing needs or evidence gaps that can be addressed through research?

- An overarching consensus of the working group is that more needs to be done to establish meaningful, agreed-upon outcomes. For example, meaningful outcomes would include whether an intervention improves an individual's real-life social interactions, such as meaningful friendships and relationships.
- There is a gap in understanding how to best determine the "active ingredients" of interventions, especially those that are critical to producing meaningful outcomes.
- The working group members noted the importance of developing standardized measures for meaningful outcomes measuring positive progress in the area of social interactions. For example, measures focusing on number and frequency of prosocial behaviors can produce different results than measures of the quality of friendships, time spent with friends, feelings of loneliness, attainment of social goals, etc.
- The variability in treatment response due to the heterogeneity of ASD necessitates the development of a "science of personalized medicine" to provide a framework for interventions and treatments.
- Regarding health issues, the heterogeneity of the variety of health issues being faced by individuals with ASD is challenging. There is a need to develop adequate, standard tracking tools to measure health progress over time. There is perhaps an opportunity for systems biologists to contribute expertise on how to standardize data collection in this area.
- In general, there is a need for more intervention research conducted in schools where the interventions are applied, rather than in clinics. In addition, there are currently very few studies about the academic skills of children with ASD (e.g. reading, math, executive function in the classroom).
- More intervention research needs to be conducted in low-resourced contexts, including the inclusion of more underrepresented groups.

5. Are there emerging areas of research that need additional support?

- The emerging areas of research identified by the working group included:
 - Methods for systematically incorporating feedback from individuals with autism into research plans, into the development of treatment programs over time, and into the determination of research funding priorities.
 - Methods for personalizing interventions to personal needs.

- Building an evidence base for what makes high-quality outcome measures; this should be of interest to drug companies, as it would help to de-risk research into therapeutics.
- The interface between medications and interventions (including the incorporation of AAC devices) and how to develop effective combination therapies tailored for individuals.
- Digital tools for delivering interventions.
- Methodologically rigorous, large-scale studies on the effectiveness of autonomous robotics for delivering training, and moving the use of robotics into clinical studies.
- Long-term studies in use of social robotics and how they can be used to augment behavioral interventions.
- Understanding heterogeneity in ASD to address GI and dietary problems.
- Mitochondrial differences and methylation in ASD.
- The inclusion of individuals with ASD and co-morbidities (such as epilepsy) in ASD studies.
- Assessment of individuals' microbiomes and metabolomes, including the pathways involved in these, how they might affect core ASD symptoms, and how they might be treated.
- Lesser addressed co-occurring conditions, including connective tissue disorders, for example.
- Studies on eating disorders in all ASD populations of all age groups, not only children.

Discussion of Services and Policy Changes

1. Are there any innovative programs or recent policy changes that have address some of the gaps or interests of this Question's research area?

- None were cited, but the working group expressed an interest in making recommendations that would better enable evidence-based interventions to reach more of the patient population.

2. Is there new research evidence that can inform the policy agenda?

- As more research is done to establish an evidence-base for interventions, dissemination of this information will help the community make more informed health care choices.

3. Are there opportunities for practice to more actively inform research?

- More should be done to enable the involvement of adults with ASD in clinical trial studies (rather than only neurotypical adults or children with ASD). For example, testing medications for co-occurring conditions can be safer in adults than in children, and it should be possible to consent populations of adults with ASD.
- Study design should incorporate feedback from patient populations. For example, sometimes interventions are tested at such a high intensity level that in practice they are not realistic for use in the real world, and input from individuals with ASD could be helpful in developing appropriate intensity levels.

4. What are the most significant services needs or gaps that are not being addressed by current policies and programs?

- There is a lack of sufficient funding, workforce, and coordination between agencies to accelerate clinical research on the use of robotics.

Discussion of Aspirational Goal

Based on the state of the field, is the **Question 4 Aspirational Goal** still appropriate?

Interventions will be developed that are effective for reducing both core and associated symptoms, for building adaptive skills, and for maximizing quality of life and health for people with ASD.

- Due to time limitations, the discussion of the Aspirational Goal will be on the agenda for the next Working Group 4 conference call.

Wrap up and preview of next call

- On the next call, the working group will discuss the development of objectives for Chapter 4.
- In the meantime, the Chairs of the working group will start to develop an outline for drafting the chapter.