Question 4: Which Treatments & Interventions Will Help?

Aspirational Goal: Develop a range of interventions that optimize function and abilities across the lifespan to achieve meaningful outcomes and maximize quality of life for people on the autism spectrum.

Introduction

The evolution of this aspirational goal reflects the progression of priorities in the autism community. Over the past several years, the IACC's focus has shifted from "preventing disabilities" (2009 IACC Strategic Plan), to encouraging "building adaptive skills" (2013 IACC Strategic Plan Update), and now continues to emphasize the construction of lifespan approaches and utilization of meaningful treatment outcomes for individuals living with ASD and their families. This change also recognizes the shifting landscape of treatment opportunities driven by exciting discoveries from cognitive neuroscience, which reveal breathtaking developmental reorganizations of brain structure, function, and connectivity in adolescence and young adulthood[1,2,3], adding new possibilities for intervention across the lifespan.

Since the *2013 IACC Strategic Plan Update*, there has been an explosion of behavioral intervention studies and several advancements in intervention science, including continued progress in the development of multiple intervention types. Key advances include improvements in community implementation of effective interventions, greater numbers of fully-powered randomized trials, comparative efficacy studies, and implementation science studies that consider child outcomes as well as best implementation practices. Additionally, the diversity of study participants has improved, as researchers more often strive to include underserved families as well as populations previously excluded or overlooked in ASD research, such as minimally verbal children and girls. There has also been great progress in brain-behavior measures as predictors of outcomes of interventions, as well as the development of adaptive interventions, recognizing that sequential and multiple interventions are often required to improve child outcomes. Finally, technology has been used more frequently, as a tool within an intervention (such as iPads for communication and storyboarding), to deliver interventions using telehealth methods, and to collect data in real time that can be used to guide intervention and gauge treatment response.

Intervention Types

The autism community continues to emphasize the importance of establishing evidence-based practices in interventions[4]. The concept of evidence-based practice is first based on the premise that there are interventions that have evidence of their positive and strong effects for individuals with ASD, and that practitioners (e.g., psychologists, speech pathologists, teachers) should therefore prioritize their use while working with families. Second, when strong evidence for an intervention or treatment to address a specific goal or outcome does not exist, the practitioner should try the intervention with the most evidence, although the empirical efficacy may fall below an established standard. Third, clinical and/or professional expertise plays a major role in selecting an intervention or practice to address a specific goal or more generalized outcomes and is especially useful for adapting the intervention for the individual with ASD when needed.

Behavioral Interventions

Behavioral interventions can be broadly categorized into 2 groups, focused intervention practices and comprehensive treatment models (CTMs). Focused intervention practices are defined as instructional or therapeutic approaches applied to an individual's goals (e.g., making social initiations to peers, reducing

self-injury), designed to produce outcomes related specifically to the goal, and are implemented over a relatively short period of time until an individual meets his or her specific goal. Meanwhile, CTMs are designed to address broader outcomes (e.g., increases in cognitive abilities, adaptive behavior, social and communication skills). CTMs consist of many focused intervention practices organized around a conceptual framework, are documented through treatment protocols, and exist over a more extended time period. Examples include the Lovaas Model[5] and Early Start Denver Model (ESDM)[6].

Practitioners use these two classes of interventions/treatments in different ways. They may select multiple focused intervention practices to build individualized programs for children, youth, and adults with ASD, or they may fully adopt a comprehensive treatment program in which the focused interventions and their use are already prescribed[7]. Although several CTMs have been shown to be efficacious, they may be implemented less often by practitioners than focused intervention practices[8,9]. The National Standards Project and the National Professional Development Center on ASD (NPDC) have conducted critical and rigorous reviews of the intervention research literature and identified sets of focused intervention practices that have evidence of efficacy[10]. The NPDC work specifically focused on practices that could be implemented in school and/or community settings. Similarly, deBruin and colleagues conducted a meta-analysis of school-based interventions in high schools, finding evidence of efficacy for many of the same focused intervention practices (i.e., antecedent-, video-, and consequent-based interventions)[11]. Other reviews have documented the efficacy of 1) school-based, focused interventions on challenging behavior, 2) the use of peer-networks to foster social engagement, 3) social skills training, and 4) academic interventions[12,13,14,15,16,17]. Research on the efficacy of several behavioral interventions continues today, including the Lovaas Model, ESDM, JASPER (Joint Attention, Symbolic Play, Engagement & Regulation), LEAP (Lifeskills and Education for Students with Autism and other Pervasive Behavioral Challenges), PRT (Pivotal Response Treatment), First Words Project, DIR/Floortime (Developmental, Individual-Difference, Relationship-Based), and STAR (Strategies for Teaching based on Autism Research)[5,6,18,19,20,21,22,23,24].

School-Based Interventions. It can take over a decade and a half for evidence-based interventions to become widely implemented in the community when developed in the laboratory. Thus, researchers are increasingly developing and testing interventions in school-based settings, with the added goal of sustaining the intervention beyond the study period. Two recent studies demonstrate that similar outcomes can be obtained in the community and the lab[25,26]. Both of these studies implemented Joint Attention, Symbolic Play, Engagement and Regulation (JASPER) aimed at improving core impairments in social communication, and noted sustainability of the intervention over a short-term follow up. As a whole, these and other findings highlight the effectiveness of teacher-implemented interventions in school settings on improving one of the core features of ASD and pave the way for more school-based intervention research.

Parent-Mediated Interventions. As diagnostic advances have made it possible to identify children with ASD at earlier ages, researchers have tested a number of parent-mediated interventions in order to meet the need for interventions that can be implemented as early as possible. Most of these are labeled Naturalistic Developmental Behavioral Interventions (NDBIs), a newly-vetted grouping of early interventions based on applied behavior analysis (ABA)[27]. Several recent studies have yielded significant improvements over earlier studies by comparing the experimental treatment to an active control group involving parent education but no hands-on coaching, versus comparing an experimental treatment to treatment as usual[28,29,30]. One conclusion of these recently-completed studies is that active hands-on parent coaching for social communication outcomes is more effective than parent education models where the same information is provided without active coaching. This conclusion is further supported by another recent study of toddlers at-risk for ASD, finding that initial gains in parent responsiveness did not sustain to the follow-up, speaking to the need for longer-term, more intense, or more hands-on

intervention[31]. A recent parent-mediated intervention study based on the DIR (Developmental Individual-difference Relationship-based model)/Floortime intervention approach suggests efficacy of this model for improving parent and child outcomes[22]. Researchers have also studied the benefits of parent group interventions, where groups of parents are coached to deploy interventions. In a recent study of the PRT approach, researchers found that parent group interventions yielded significant parent and child benefit[32]. While more cost effective than 1:1 therapy sessions, more research is needed to determine the generalizability and sustainability of parent group interventions to foster meaningful improvement in child behaviors, communication, and functioning.

Altogether, the foregoing studies add to the positive outcomes attained through parent-mediated interventions, but raise issues about meaningful outcomes (i.e., spontaneous versus prompted outcomes), and the specific "active ingredients" – or essential components - of treatment (i.e., hands-on coaching, dose, approach). In the future, researchers will need to better understand for whom an intervention works best, and why an intervention provides benefit. Understanding the mechanisms behind effective behavioral interventions helps researchers to identify the essential components of an intervention, making it possible to develop a repertoire of components that can be combined in various ways to customize treatment. Two recent studies suggest that parent synchronization (attuning of the parent's behavior to the child's attention) and mirrored pacing (following the child's lead) are important components or active ingredients of parent-mediated interventions[33,34].

Behavioral Interventions in Understudied Populations Developing interventions for minimally verbal children has been challenging in the past. A recent study tested whether JASPER combined with a behavioral language intervention with or without an augmentative and alternative communication (AAC) device facilitated greater spoken language over 6 months[30]. This study took an adaptive treatment approach, adjusting the treatment midway through the study based on an individual's progress. The results of this study suggest important implications about the treatment approach and timing of providing an AAC device in treating minimally verbal children with ASD.

Another under-studied group are girls with ASD. Recent studies find few developmental differences between preschool-aged boys and girls with ASD[35]. However, studies of older children find girls with ASD who have lower IQs also have more impairing symptoms of ASD than boys. In contrast, girls with higher IQs report better friendships and social skills, and fewer repetitive behaviors than boys[36]. School playground observations of girls with ASD find they are overlooked and neglected by their classmates in more subtle ways whereas boys with ASD are often overtly rejected[37]. In part, these differences between girls and boys with ASD are due to the ability of girls to camouflage their interaction difficulties[38]. These findings suggest that gender should be included as a tailoring variable when individualizing interventions for children with ASD.

Discoveries of neuroplasticity in the adult brain have opened new opportunities to consider autism interventions for use in adulthood. Very few studies of behavioral interventions have been performed in adolescents or adults with ASD, and most of these have focused on training adults to read social cues[39]. Executive and social brain networks exhibit the greatest rates of functional maturation during adolescence, establishing adolescence and young adulthood as a sensitive period for socio-emotional and self-control development[40]. These new findings suggest that the period from adolescence into young adulthood may offer an important new window of opportunity for individuals with ASD, their families, scientists, and clinicians to design novel approaches for improved outcomes and superior quality of life.

Medical Interventions

Pharmacological Treatments In contrast to the many behavioral intervention options available, only two drugs, risperidone and aripiprazole, currently have Food and Drug Administration (FDA) indication for

use in ASD, specifically for the symptom of irritability. There are no approved treatments for the core symptoms of ASD, which include social communication difficulties and restricted, repetitive patterns of behavior, interests, or activities. Although clinical trials of pharmacological interventions for core symptoms of ASD are now underway, they will require several years for completion, analysis, and reporting, thus there are few published findings to date. Advances in genetics and neurobiology have led to an increase in the number of clinical trials testing medical treatments for ASD. While the majority of such trials are testing pharmacological treatments, neurostimulation (discussed separately below) is also gaining momentum as a modality to alter brain activity and neuronal connectivity.

There has been an abundance of open label, single-center drug trials that report effectiveness in small samples. Unfortunately, many of these results were not replicated when tested in subsequent larger, randomized, placebo-controlled trials. Many of the drug trials in ASD exclude individuals with intellectual disability and very young children due to ethical and/or practical challenges. However, a mechanism-based intervention intended to improve core symptoms of ASD may be more effective if administered relatively early in life and may be most effective in those most severely affected. Thus, it is crucial that such individuals are included in upcoming trials. This will require researchers to carefully consider how interventions can be adapted to accommodate children or individuals with intellectual disability, and to identify age- and ability-appropriate outcomes and outcome measures. Additionally, researchers must ensure that parents and families are well-informed and actively engaged through all stages of the trial.

Many different genes may contribute to the susceptibility of developing ASD. This heterogeneity of underlying causal mechanisms makes it challenging to identify convergent molecular pathways and brain circuits involved in all individuals with ASD, although there has been recent progress. One promising target is oxytocin, a neuropeptide involved in social cognition that has been investigated in a number of ASD studies[41,42,43]. However, its molecular properties pose challenges for potential therapeutic use, thus further work is needed to determine the best doses and compare methods of delivery. Moreover, given the variation of oxytocin's effects based on behavioral context, studies aimed at understanding how oxytocin might enhance responses to evidence-based behavioral interventions is recommended[44].

Other randomized, placebo-controlled treatment trials have targeted additional mechanisms proposed to contribute to the pathophysiology of ASD, with varying successes[45,46,47,48,49]. However, larger trials are needed to validate these initial findings. Moreover, given the importance of context and a developmental perspective on ASD, it will be very important to conduct well-powered studies that combine pharmacological treatments with evidence-based practices including behavioral approaches, cognitive behavioral therapy, and social skills training.

Given that the rates of diagnosed ASD cases are rising and that there are no effective drugs to treat its core symptoms, it is imperative to further develop pharmacological treatments. Involvement of private companies will be crucial to help address this unmet need, including in industry-academic collaborations. Important private partners include the pharmaceutical industry, as well as those in software, electronics, and robotics development. As much as possible, multi-site, longer duration, placebo-controlled studies should be prioritized in order to produce more reproducible results, such that private industry will take on the challenges of conducting large Phase III registration studies.

Direct Brain Stimulation Transcranial magnetic stimulation (TMS) is a promising method for identifying neural mechanisms and treating aspects of altered brain function in ASD[50]. TMS can offer a non-invasive tool to study aspects of the altered physiology underlying ASD. Treatment strategies involve using TMS to modulate brain plasticity and network activity[51,52,53]. In particular, repetitive TMS (rTMS) can alter brain excitability and network activity beyond the duration of a stimulation session or treatment study, and is being examined as a treatment that could potentially reduce both core and associated ASD symptoms[54].

Recent studies have investigated whether neuromodulation via rTMS or transcranial direct current stimuli (tDCS) can induce neurophysiological and clinical benefits in individuals with ASD[55,56,57,58]. Preliminary results suggest that TMS might be of therapeutic value for improving core and associated symptoms of ASD. However, most studies to date have been based on small samples and employed open-label designs. There is a need for well-controlled, randomized trials with adequate sample sizes to better understand whether TMS is efficacious and safe and whether there are subgroups of individuals with ASD that might benefit from treatments based on TMS.

Technology-Based Interventions

Digital-based technology interventions for individuals with ASD have continued to increase in accessibility, breadth, and depth of use. Scientific evidence for the effectiveness of technology-based or technology-enhanced interventions has increased, with a larger number of randomized controlled trials (RCTs) appearing in recent years that highlight the breadth of technology applications in ASD research as well as their increasing rigor[59]. In the field of robotics, recent work has highlighted potential advantages of robots over human agents for accelerating several aspects of intervention research. Yet a number of challenges and gaps have been highlighted, which are also shared by speech generating devices, virtual reality, video games and computer-assisted instruction, mobile applications, and telemedicine[60,61,62]. It will be essential for future studies to address these challenges, as the development of interventions using digital technologies offers new opportunities to accelerate research progress. Furthermore, the proliferation of technology-based platforms purporting to help individuals with ASD points to a need for new, efficient, and scalable methods and infrastructure for evaluating technology-based interventions. Technology-based interventions have tremendous potential to benefit individuals on the autism spectrum in many ways, including by helping them improve social and communication skills and gain greater independence, all of which can improve the overall quality of life.

Precision Treatment Approaches

The prospect of precision medicine in ASD, i.e. specific, targeted treatments developed after gaining a better understanding of specific disease pathophysiology, is a tantalizing one. Genetically-defined disorders such as Rett Syndrome (RTT), Fragile X Syndrome (FXS) and Tuberous Sclerosis Complex (TSC) provide a unique opportunity to develop mechanism-based treatments for ASD. Thanks to basic science discoveries describing the molecular pathogenesis of these disorders, researchers have begun efforts to evaluate treatments targeting specific proteins in the implicated biological pathways[63]. In future work, biomarkers should be incorporated in order to help detect objective improvements in response to treatment and to identify optimal developmental periods to apply the treatment trials.

Advancement of new or reconceptualization of existing treatments into modular therapies (where therapies are organized into therapeutic modules that can be combined and reused in flexible arrangements) can provide finer granularity and more tractable opportunities for understanding change in individuals. Few examples currently exist that explore combinations of therapeutic modalities, although there are some studies in progress. This is an area of great need and can especially help address comorbidities, such as anxiety, aggression, and depression. Similarly, adaptive interventions, which incorporate more flexible study designs, can make more efficient use of existing clinical, research, and participant resources, providing more information to researchers and potentially greater benefit to participants. To encourage adoption, investment in study design methodology research (including dissemination of methods and development of trial design resources) will be of significant value.

<u>Outcome Measures & Biomarkers</u>

Over the past few decades, significant progress has been made in the development of new behavioral interventions and identification of novel drug targets aimed at reducing core and associated ASD symptoms and improving quality of life across the lifespan. A major challenge in determining whether new treatment approaches are efficacious has been the measurement of treatment response. Measurement of treatment response is particularly complex in ASD due to the heterogeneity resulting from an individual's symptom profile, sex, cognitive and language abilities, and development level. Moreover, many existing assessment measures were developed for screening and diagnosis and are not sensitive to assessing change in symptoms over time. Over the past several years, considerable effort has been directed toward evaluating which existing measures are suitable for clinical trials and for developing quantitative, objective, and sensitive measures of treatment response. Increasingly, the input of key stakeholders, including caregivers and persons on the autism spectrum, is solicited to ensure that outcome measures reflect the priorities and needs of persons for which the treatments are being developed. Several reviews and consensus statements have been published that have evaluated the appropriateness of existing parent report and observational measures for clinical trials, including measures of social communication, anxiety, and repetitive behaviors[64,65,66]. Studies validating observational measures of ASD symptom severity based on the Autism Diagnostic Observation Schedule (ADOS) have also been published[67], and a brief observational assessment of social communication change has also been recently developed[68].

Biomarkers of treatment success are needed, as are "stratification" biomarkers for matching people to the best treatment for them at the best time. Until it becomes possible to biologically measure treatment response, negative results from pharmacological and behavioral interventions will be difficult to interpret, and positive results may not definitively indicate the requisite dose or duration of treatment. Predictive biomarkers –those that help to match individuals to particular treatments– will help to create more precise treatments, and help individuals with ASD and their families to avoid wasted time and resources.

Biomarker Discovery

Initial efforts have focused on developing measures that are linked indirectly or directly to underlying neural circuitry, which can offer insight regarding whether the treatment is influencing specific aspects of neural circuitry, inform researchers of the neural mechanisms that might underlie the treatment effects, and predict treatment response. These measures include eye tracking, electrophysiological responses, and magnetic resonance imaging, among others. Such measures can also serve as an early efficacy signal that can detect response to treatment before changes in more distal measures such as language and social abilities are evident. Early efficacy markers can be used to identify which individuals are most likely to benefit from a given treatment and/or in adaptive study designs to indicate early in the trial whether modifications in the treatment (e.g. dose) should be made.

Eye tracking (ET) ET has great potential for acting as an early indicator of treatment efficacy by tracking changes in social attention[69]. While applications of ET to clinical trials and interventions are still relatively new, results have been encouraging and suggest that ET can be used as a method for measuring response across a wide range of treatments. Promising future directions for developing ET as a marker of change include: furthering data-driven, computational, and machine learning approaches towards subtyping and stratification with the autism spectrum and for improved discrimination between individuals with ASD and controls; the design of ET batteries with the express goal of treatment measurement; the adaptation and advancement of ET metrics in technology-driven/technology-interactive interventions, such as virtual reality, robotics, and simulators, as well as in novel adaptive paradigms designed to change gaze strategies; and advancement of methodological considerations including the promotion of big-data

studies, facilitation of replication, and increasing adherence to more rigorous and universal technical and methodological standards.

Electrophysiological measures Recent studies suggest that electroencephalography (EEG), a non-invasive measure that can record patterns of brain activity throughout the lifespan, offers promise as a metric of treatment response related to neural circuitry[70]. Children and adults with ASD have distinct electrophysiological signatures, offering the possibility of using such measures to detect treatment response. Furthermore, distinct EEG signatures have been found among genetic subtypes of individuals with ASD and related disorders which could be used in future clinical trials testing drugs that are targeted to individuals with ASD with specific genetic syndromes. In future work, prior to these measures being useful as potential biomarkers, it will be important to demonstrate their ability to reliably predict a signature of dysfunction at the individual subject level, as opposed to group averaged data.

Magnetic Resonance Imaging (MRI) MRI techniques, including functional MRI (fMRI) and Diffusion Tensor Imaging (DTI), have provided a wealth of information regarding the neurobiological underpinnings of ASD. Specifically, task-based fMRI studies have pointed to atypical social-brain functioning and activation in ASD, while resting-state functional MRI and DTI have pointed to deficiencies in integrative social information processing as indicated by white matter atypicalities and diminished long-range connectivity[71,72]. Despite the potential for brain imaging techniques to elucidate mechanisms underlying behavioral treatment response, few studies have directly used it for treatment monitoring or prediction of treatment efficacy. However, this appears to be rapidly changing, with several recent studies expanding on earlier work[73,74]. Considerable progress has also been made recently in regards to the use of brain imaging techniques for understanding *in vivo* pharmacological neural action in individuals with ASD. Altogether, these advancements are beginning to provide the context for expanding the scope and applicability of brain imaging techniques for monitoring treatment across the lifespan, including before the signs of ASD are overtly apparent. Given the many successes yielded from the application of MRI methods to the development of biomarkers in ASD and related fields, considerable opportunity exists for further research and development in this area.

Advances in Developing Measures of Treatment Response. Digital technologies, such as mobile devices, provide another approach for developing quantitative, objective, and sensitive measures of treatment response[75]. These tools provide opportunities to study biomarkers in combination with self-report data, often in more naturalistic contexts such as the home. The ability of technology-based systems, such as mobile applications, wearables, and internet resources, to automatically record and generate measures from will increasingly provide richer, denser, and more meaningful information to researchers. Novel analytic methods, such as machine-learning and computer vision analysis, can provide new insights into patterns of behavior. Although early in their development and application to ASD populations, such measures have the advantages of being scalable, objective, and feasible. Thus, studies that explore their utility as a method of treatment monitoring should be pursued. Additional emphasis should also be placed on transforming these signals into useful forms to maximally aid and personalize ongoing, real-world treatment of issues faced by individuals with ASD. As the understanding of these data streams matures, new methods and systems will need to be created to harness the power of this data and to manage the massive flows of information reaching data consumers.

Recently, a number of substantial investments have been made to support large, collaborative efforts aimed at validating biomarkers and outcome measures for use in ASD clinical trials. These consortia involve public-private partnerships among academia, advocacy and other nonprofit organizations, government, and industry with a goal of de-risking investments into pharmacological ASD trials and optimizing the success of such trials. These projects are examining a wide range of potential biomarkers and their relationships with observational and caregiver-report measures of behavior in large samples of individuals with ASD vs. typical development over time. Furthermore, regular communication, data-

sharing agreements, and shared measures across the existing consortia will increase the scientific utility of these investments. One example is ABC-CT (Autism Biomarkers Consortium for Clinical Trials), an NIH-, Foundation for the NIH-, and Simons Foundation-funded consortium of sites that aims to develop, validate, and disseminate objective measures of social function and communication for ASD with the ultimate goal of advancing these measures as markers and predictors of treatment response.

In sum, multiple laboratories are conducting studies to develop better ways of measuring treatment response. Continued investment in such studies will ensure that, as new behavioral and medical treatments are developed, we will have the capability of testing their efficacy. Such investments will also be essential for developing improved methods for identifying subgroups that are responsive to specific treatments and identifying neural mechanisms underlying treatment response.

Accelerating Research & Increasing Access to Evidence-Based Interventions

While research in interventions for individuals with autism has shown consistent growth and advancement, opportunities exist for accelerating the pace of research. First, high-quality intervention studies are expensive to conduct and require substantial specialized expertise to oversee. Additional investment in human and research infrastructure is likely to yield compounding gains in autism intervention research progress. Creating and sustaining networks of institutions, investigators, clinicians, and families committed to shared, large-scale implementation of interventions or experimental research will combat fundamental heterogeneity issues in ASD research, leading to more reproducible and robust scientific findings. These networks can be leveraged to promote testing of novel interventions, exploration of unique scientific perspectives, and commitment to a culture of non-exclusive innovation transcending traditional boundaries. Additional investment should focus on bridging gaps between scientific evidence and clinical and/or community applications of interventions.

Additional opportunities may emerge from standardization of reporting and protocols so as to facilitate aggregation or comparison of clinical trial data at meta-analytic levels. Examination of evidence at a higher analytical level may provide more comprehensive information about treatment effectiveness when clinical uncertainty is matched with appropriate variation along key implementation parameters. Similarly, sharing data at finer level of detail may additionally facilitate data mining investigations that may help to identify more streamlined assessment or nuanced precursors and predictors of treatment response.

Extra resources should be directed towards promoting the development of applied scientific tools, including more robust statistical methods, data mining techniques, basic science methods, laboratory techniques, and optimized pipelines for discovery. Additional resources could also be spent at the tail end of intervention science, on the wider dissemination of implementable discoveries. Examples would include encouraging Phase II transitions to Phase III trials, identifying appropriate industry partnerships to foster larger-scale intervention implementation, and *in vivo* studies of ongoing new intervention integration efforts. Incorporation of business and operations perspectives into autism research infrastructure development may help to optimize intervention deployment efficiency, enabling more studies to be conducted in a sustainable fashion. By focusing on practical barriers to ultimate treatment deployment (including insurance, provider adoption willingness, and marginal expenses), a more robust, efficient, and complete pipeline from idea to effective individual treatment can be realized.

Inclusion and Empowerment of Stakeholders in Intervention Research

Empowering individuals with ASD and their families to act as active directors in the research process can also accelerate scientific progress. Development of tools to help stakeholders manage and maintain research, educational, behavioral, and clinical records could help them better advocate for participation

in studies most relevant to their needs or most aligned with their personal goals. With a focus on usability and controlled data sharing, such tools could become interfaces by which information could be bi-directionally shared with researchers and relevant providers, reducing redundancy in information requests, streamlining study deployments, and reducing participant burden. Currently, several incarnations of such systems have been developed, including Microsoft HealthVault and Apple HealthKit. However, efforts towards tailoring interfaces, cross-platform interoperability, and common standards must be pursued so as to best meet the specific needs of the autism community, to prevent data from becoming unnecessarily locked to proprietary platforms or formats, and to better enable data exchange. Creation of user-friendly research registries that promote awareness of relevant ongoing intervention studies or technologies, that can be personalized by user preferences (including constraints on geography, participation characteristics, and study facets), that are updated regularly and managed in a sustainable fashion, and that facilitate connections between legitimate researchers and qualified research participants (with appropriate governance of privacy and participant rights) would further enable stakeholders to direct their research agenda. Adaptation of stakeholder-held records, including genomic information, for the purposes of creating an interface that would facilitate recruitment of participants with extremely specific characteristics (e.g. pharmacological trials targeting specific gene mutations) may be critical for appropriately powering highly-targeted studies and for providing stakeholders access to the most tailored and innovative science. Throughout these processes, the involvement and feedback from the autism community should be emphasized so as to provide continuous context for research endeavors.

Much more attention has recently been given to quality of life outcomes for addressing the needs of individuals with ASD, including: academic success, autonomy and self-sufficiency, financial stability, health and well-being, inclusion, independent living, meaningful employment with fair wages, pursuit of dreams, recreation and leisure, respect and dignity, safety, self-identity and acceptance, social connections, and subjective well-being. Using such outcomes allows professionals, parents, and individuals to develop intervention plans that will allow a person with ASD to advance daily in each of the quality of life indicators. Measuring such outcomes can occur both short- and long-term and can be developed based on the needs of the individual in terms of their level of skills, functioning and ability. When such indicators are maximized, the individual will be able to fully live a life maximizing long-term success.

Summary

While there have been several advances in the field of autism interventions, there is still much progress to be made. Researchers must continue to develop new treatments as well as adapt existing treatments for different settings and populations. Moving forward, there are several important issues to consider. First, it will be important to prioritize the understanding of the neurobiological basis and mechanisms underlying all therapeutic approaches. Second, researchers need to consider designs and recruitment strategies that allow for testing ways to maximize effectiveness and precise matching of treatment plans to individual needs and neurobehavioral profiles by combining therapeutic approaches. More robust, standardized outcome measures should be developed, including adaptive measures, predictive measures, biologically-based metrics, measures that address heterogeneity, and measures of practical outcomes that will help better target therapies to individual needs and goals. It is also necessary to ensure support for the entire intervention research pipeline including the training of the next generation of multidisciplinary intervention scientists. Finally, it is essential to strive to provide more tools to practitioners through translation of research to community-based practice and use of effective, novel dissemination strategies.

Objectives

Objective 1: Develop and improve pharmacological and medical interventions to address both core symptoms and comorbidities in ASD.

- Identify biomarkers that can help inform decisions about appropriate interventions and provide objective assessments of treatment response.
- Recruit more individuals for clinical trials testing pharmacological treatments for ASD.

Objective 2: Create and improve psychosocial, developmental, and naturalistic interventions for the core symptoms and comorbidities in ASD.

- Identify "active ingredients" of interventions in order to ensure sustained responses to treatments.
- Adapt interventions so that they can be deployed in a range of community settings.

Objective 3: Maximize the potential for technologies and development of technology-based interventions to improve the lives of people on the autism spectrum.

- Develop tools allowing individuals with ASD to track and direct their own treatment.
- Develop technology-based interventions that help people with ASD improve their social and communication skills, increase their independence, and in many other ways help improve their quality of their lives.
- Increase access to interventions by developing technology-based treatments that can be deployed outside of primary care or clinical settings.

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