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Development of the Observable Behaviors of Autism Spectrum Disorder Scale

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Abstract

Background: The objective of this research was to develop a caregiver-reported clinical outcome assessment (COA) measure designed to assess observable behaviors of children, ages 4 to 12 years, with autism spectrum disorder (ASD) for supporting labeling claims of treatment benefit. *Methods:* Development of the measure included a review of the literature and existing instruments, conceptual disease model development, concept elicitation focus groups, item generation, and cognitive debriefing interviews. *Results:* Predominant characteristics and behaviors of ASD identified by the literature and instrument reviews included sociability, communication deficits, stereotypy, inattention and hyperactivity, irritability, anxiety, and familial impact. In each of the 10 instruments reviewed, evidence of content validity was limited or nonexistent. Predominant themes arose across 8 major categories during concept elicitation. A total of 27 concepts were identified through focus group feedback and formed the basis for item development and cognitive pre-testing. Revisions to the items yielded a final version of a daily diary containing 21 items assessing observable behaviors and characteristics of ASD in children 4 to 12 years old. *Conclusions:* The Observable Behaviors of ASD Scale (OBAS) was developed as a self-administered, caregiver-reported measure containing 8 predominant themes. Items are scored on one of two 5-point ordinal categorical response scales, and the recall period for each item is "the past 24 hours." This research provides evidence that the OBAS is content valid for assessing treatment benefit, which was found to be lacking in other instruments.

Keywords

autism spectrum disorder, autism, observer-reported outcome, pediatric, child, caregiver-report

Introduction

Autism spectrum disorder (ASD) is a lifelong neurodevelopmental disorder that typically presents in childhood.[1-4] ASD is a broad clinical term encompassing autistic disorder, Asperger disorder, and pervasive developmental disorder not otherwise specified.[1,5-8] The *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (*DSM-5*), describes ASD using two dimensions: social communication and restricted and repetitive interests, activities, and behaviors.[9]

The prevalence of ASD has increased over the past 15 to 20 years. Current prevalence rates are 0.6%-0.9% in North America, 0.5%-1% in Europe, 0.5% in Australia, and 0.3% in Asia.[10-17] Many children with autism are treated with pharmaceutical therapies; however, there is little evidence to support a clinical benefit for most of these treatments.[18,19]

While numerous existing measures are available to diagnose and stage the severity of ASD, none of these tools are designed to assess treatment benefit. Although not developed to the standards described in the Food and Drug Administration's (FDA's) 2009 guidance on patient-reported outcomes (PROs), the Aberrant Behavior Checklist (ABC) Irritability subscale has been used to support product labeling for risperidone and aripiprazole.[3,20-23] The FDA PRO guidance makes clear that for a PRO measure to support labeling claims of treatment benefit, evidence obtained directly from the patient is essential for establishing the instrument's content validity. However, patients with ASD may suffer from cognitive deficits that prevent accurate self-reporting. Evidence such as behavioral expressions of ASD that are directly observed by a caregiver may be the most direct and feasible means for measuring treatment benefit. Currently, no disease-specific instrument exists in the published literature that has been designed to assess treatment benefit for key observable behaviors and characteristics associated with ASD from the perspective of a parent or caregiver that meets the FDA PRO guidance fit-for-purpose requirements. Specifically, evidence of direct input from the

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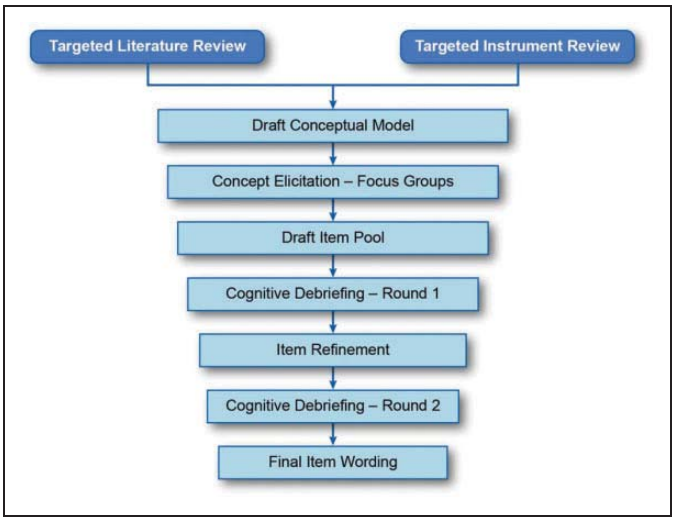

Figure 1. Qualitative steps in the OBAS development. OBAS, Observable Behaviors of ASD Scale.

intended respondent population to support content validity is either absent or not documented.

To address this unmet need, a caregiver-reported clinical outcome assessment (COA) suitable for supporting label claims of treatment benefit was designed to assess the observable behavioral expressions of children ages 4 to 12 years with ASD. The research methods follow best practice recommendations from the FDA PRO guidance, which extend to all COAs, and were conducted in a manner such that results are broadly applicable for use in therapeutic development programs and not specific to or in favor of any particular type of therapy.[24] Additionally, during the item development process, consideration was given to the intent that the newly developed COA be implemented on an electronic platform for use in future clinical studies. The data quality benefits of electronic technology for capturing daily COA data are well established.[25-28] This manuscript describes the methods, participants, and results of the instrument development process.

Patients and Methods

The Observable Behaviors of ASD Scale (OBAS) was developed through qualitative research methods including a targeted review of the literature and existing measures, conceptual disease model development, concept elicitation focus groups, item generation, and cognitive debriefing for finalization and refinement of draft items (Figure 1) and confirmation of the conceptual disease model.

Prior to any patient contact, this project was approved by an institutional review board. Written informed consent was obtained from all participants prior to the conduct of focus groups or interviews. Entry criteria are detailed within the section describing the concept elicitation methods. These same criteria were employed at the cognitive debriefing stage.

Targeted Literature and Instrument Reviews

To examine the concepts relevant to the assessment of ASD behavioral expressions, a targeted review of the literature was conducted, followed by a review of instruments, some of which were preselected based on precedent use in ASD. The primary objectives of the literature review were to aid development of a discussion guide for concept elicitation focus groups and to create a draft conceptual disease model denoting relevant concepts. In collaboration with two clinical experts, criteria were designed to target the identification of behaviors of ASD. Further, these clinical experts provided a review of the resulting conceptual disease model.

The review identified articles published since 2002 along with specifically identified seminal articles. The population included children, parents, and caregivers. Inclusion criteria included clinical trials, observational studies, longitudinal studies, naturalistic studies, cross-sectional studies, retrospective or prospective cohort analyses, systematic literature reviews, surveys, or instrument validation studies conducted with children aged 4 to 12 years. Only papers published in English were considered.

The objective of the instrument review was to identify and critically evaluate instruments that have been used to measure observable behaviors of ASD in a clinical setting. Resources for the reviews included PubMed, the PROQOLID reference database for subscribers, published instrument sources, and an internal reference database at RTI Health Solutions. Review of these instruments focused on evaluating each instrument in light of the FDA's guidance for industry on the use of PROs to support labeling claims.[20]

Concept Elicitation

To confirm and supplement concepts identified in the literature/instrument review for possible inclusion in the new COA, nine focus groups were conducted with caregivers of children aged 4 to 12 years diagnosed with ASD and a caregiver-reported history of observable hyperactive behavior. Recruitment criteria were established in consult with the two clinical neurologic disease experts. All caregivers assumed primary responsibility for their child with ASD (at least 4 nights a week or at least 2 weeks a month) and were able to read/write English. Caregivers of children with a physician diagnosis of mental retardation, developmental disability, and/or schizophrenia were ineligible. Participants were identified and recruited by qualitative research firms in Philadelphia, PA; Montgomeryville, PA; Raleigh, NC; and San Antonio, TX. The facilities utilized existing research databases to identify potential respondents in addition to advertisement via web, e-mail, and patient advocacy groups local to the firms. Focus groups were divided across three age categories of children (4-6 years, 7-9 years, and 10-12 years) to explore any age-dependent differences in behavior or characteristics and to ensure content relevance within each age group.

Each focus group was facilitated by two experienced moderators who followed a semistructured guide to target

the discussion. The guide was designed to ascertain caregiver observations of their child with ASD and included questions related to each reported behavior of ASD, followed by related consequences. A ranking activity was incorporated to ascertain the most important concepts from the perspective of these caregivers. Additionally, questions designed to explore both an appropriate recall period and response scale notions (ie, frequency, severity) were posed in preparation for item development.

A constant comparative analysis[29] was applied to identify dominant trends to confirm that an accurate reflection of each participant's views had been captured. All coding and analyses were conducted by the same researchers who conducted the focus groups. Saturation, defined as "the point when no new relevant or important information emerges," was monitored as part of the qualitative research efforts.[20] Saturation grids of thematic concepts were created to identify concepts endorsed across participants and groups that were meaningful, relevant, and directly observable. Results from the ranking activity were evaluated to further confirm endorsement of concept importance.

Item Generation

Draft items were generated based on concepts identified in the literature and focus group results with review by the clinical experts. Draft items met the following criteria:

- Capture only directly observable signs or behaviors associated with ASD
- Be generalizable across patient severity levels
- Have the potential to change with treatment and over time, not items suitable for diagnostic purposes only
- Use succinct caregiver-friendly wording to facilitate response (provide minimal cognitive load)
- Optimize questionnaire content with consideration for respondent burden and maximize response rates
- Relate naturally to the response options
- Meet best practice recommendations for developing new COAs for electronic administration

Cognitive Debriefing

Draft items were tested in two iterative rounds (3 sets per round, 1 set per age group) of cognitive debriefing interviews, conducted in Bala Cynwyd, PA; Tampa, FL; and Mount Laurel, NJ. All interviews were conducted using a semistructured discussion guide. Draft items were tested with each participant using a standard "think-aloud" method with directed probes to explore the question-answering cognitive process.

Participant feedback was used to confirm the relevance of the concepts and to refine question wording to improve comprehensibility. Following the first round of interviews, draft items and instructions were refined to address any potential problems. These modifications were tested during the second set of interviews, and additional refinements were noted. Response options were evaluated on an item-level basis, and the appropriateness of the recall period was continuously evaluated. Each interview offered an opportunity for participants to identify any missing concepts, contributing to the final measure's content validity.

Table 1. Predominant Characteristics and Behaviors of ASD From the Literature.[a]

Characteristic/ Behavior	Description
Sociability	Lack of interpersonal responses that allow for environmental adaptation through verbal and nonverbal communication, such as eye contact, speech content and intonation, facial affect, and motor movements
Communication deficits	Insufficient speech, underdeveloped language skills, joint attention (ie, alerting another to a stimulus via nonverbal means such as gazing or pointing), active vs passive
Stereotypy	Behaviors that are frequent and repetitive and manifested in movements, speech, routines, or rituals
Inattention and hyperactivity	Sustained attention problems, impulsivity
Irritability	Development of irritability, aggression toward others, and self-injurious behavior
Anxiety	Coping mechanisms, anxious behaviors
Familial impact	Caregiver and family burden

[a]Based on targeted review of the literature from 2007 through 2013.

Results

Literature Review

Results of the targeted literature review found that while specific behaviors manifest themselves in children with ASD, the variety and severity of these observable behaviors differ among individual children with ASD, particularly when the full spectrum of the disease is considered.

Predominant characteristics and behaviors of ASD identified by the literature review are presented in Table 1. The results of the literature review were used to create a draft conceptual disease model (Figure 2).

Instrument Review

Ten measures used to assess observable behaviors of ASD were reviewed against the recommendations of the FDA PRO guidance for a critical evaluation of their fit-for-purpose evidence as a measure of ASD treatment benefit in children aged 4 to 12 years (Supplemental Table S1).

Content validity is a key component of the FDA's review of COAs.[20,30] In each of the 10 instruments reviewed, evidence of content validity is limited or nonexistent. Specifically, there is no reported evidence of instrument content obtained through direct input from the intended respondent population, a critical requirement of content validity. While nearly all instruments have some evidence of convergent/divergent validity, fewer have demonstrated reliability, and only the ABC has data

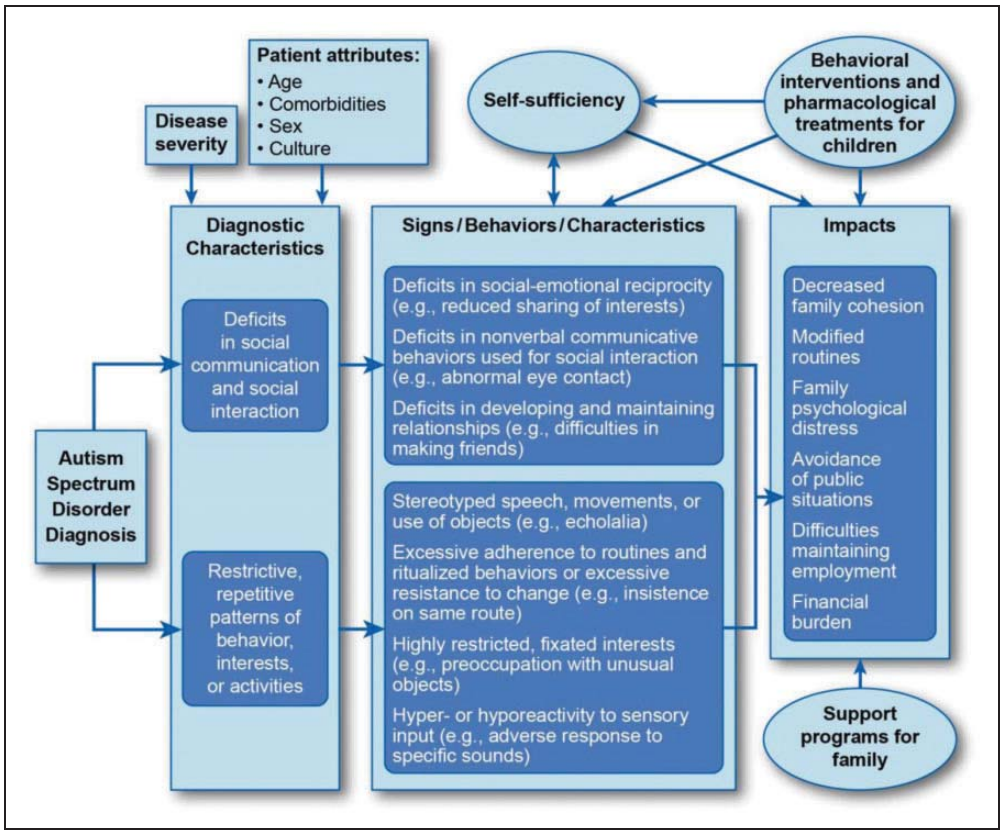

Figure 2. Conceptual disease model for ASD.

supporting its responsiveness among children with autism. Despite precedence for the irritability subscale of the ABC to support a claim of treatment benefit in ASD, documentation of content validity is extremely limited.

Concept Elicitation

A total of 56 parents of children diagnosed with ASD, ranging in age from 24 to 52 years, participated in the concept elicitation focus groups. Participants were predominantly white and female, and the majority of the children they were discussing were male. Table 2 presents characteristics of the participants.

Participants were asked to describe what alerted them that their child's development may warrant further investigation. What followed was a discussion of prominent behaviors their child displays related to their ASD. Predominant themes arose across 8 major categories or concepts (Supplemental Table S2) include behaviors associated with hyperactivity/inattention/impulsivity, aggression, irritability, repetitive behaviors, anxiety, issues surrounding socialization and communication, difficulties surrounding transitions and breaks in expected routines, and fixed interests. Results from the concept elicitation phase demonstrated saturation (Supplemental Table S3) and confirmed the concepts included in the draft conceptual disease model.

To assess relative importance, participants were asked to identify up to five ASD-related behavioral concepts that were most important for treatment to target. There was consistency in the endorsement of concepts across all 8 themes, which confirmed relevance across age groups. The relative importance of those concepts was unanimously supported. Of particular importance to parents were socialization and communication issues; behavioral expressions of frustration, irritability, and aggression; and anxiety.

Participants reported that the frequency of behavioral expressions of ASD varied while the relative severity of behaviors was consistent (ie, they either observed the behavior or did not). Participants described days in which they would notice a higher or lower frequency of those expressions. Parents noted that these daily fluctuations were directly observable, obvious, and easiest to recall over a 24-hour period.

Item Generation

A total of 27 concepts directly observable by parents were identified and formed the basis for item development and further testing (Supplemental Table S4).

Items endorsed by a majority of participants across the focus groups were drafted with the intent to assess directly observable behaviors related to the 8 concept themes. Although items addressing social/communication are not likely to change in the context of a clinical trial, they were included for further testing and to obtain additional feedback from cognitive debriefing participants because of the high degree of endorsement and ranking by focus group participants. Additionally, to increase

Table 2. Participant Characteristics: Concept Elicitation Focus Groups and Cognitive Debriefing Interviews.

	Focus Group Participants[a]				Cognitive Debriefing Interview Participants[a]				Combined Groups
	Age Cohort				Age Cohort				
Characteristic	4-6 y (n = 19)	7-9 y (n = 19)	10-12 y (n = 18)	Total (n = 56)	4-6 y (n = 4)	7-9 y (n = 8)	10-12 y (n = 9)	Total (n = 21)	(Total n = 77)
Participant age, y, mean (range)	34.6 (26-46)	40.0 (28-52)	39.9 (35-51)	38.1 (26-52)	30.3 (20-37)	38.0 (25-47)	40.4 (30-48)	37.6 (20-48)	38.0 (20-52)
Participant sex, n (%)									
Male	3 (15.8)	4 (21.1)	2 (11.1)	9 (16.1)	1 (25.0)	2 (25.0)	1 (11.1)	4 (19.0)	13 (16.9)
Female	16 (84.2)	15 (78.9)	16 (88.9)	47 (83.9)	3 (75.0)	6 (75.0)	8 (88.9)	17 (81.0)	64 (83.1)
Child sex, n (%)									
Male	16 (84.2)	16 (84.2)	13 (72.2)	45 (80.4)	2 (50.0)	4 (50.0)	6 (66.7)	12 (57.1)	57 (74.0)
Female	3 (15.8)	3 (15.8)	5 (27.8)	11 (19.6)	2 (50.0)	4 (50.0)	3 (33.3)	9 (42.9)	20 (26.0)
Participant education, n (%)[b]									
Less than high school	0 (0.0)	1 (5.3)	0 (0.0)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)
High school or equivalent (eg, GED)	2 (10.5)	1 (5.3)	2 (11.1)	5 (8.9)	2 (50.0)	2 (25.0)	1 (11.1)	5 (23.8)	10 (13.0)
Some college	6 (31.6)	5 (26.3)	5 (27.8)	16 (28.6)	0 (0.0)	3 (37.5)	3 (33.3)	6 (28.6)	22 (28.6)
Associate's or technical degree	1 (5.3)	3 (15.8)	3 (16.7)	7 (12.5)	0 (0.0)	0 (0.0)	2 (22.2)	2 (9.5)	9 (11.7)
College degree	9 (47.4)	6 (31.6)	4 (22.2)	19 (33.9)	2 (50.0)	2 (25.0)	2 (22.2)	6 (28.6)	25 (32.5)
Professional or advanced degree	1 (5.3)	3 (15.8)	4 (22.2)	8 (14.3)	0 (0.0)	1 (12.5)	1 (11.1)	2 (9.5)	10 (13.0)
Participant race/ethnicity, n (%)[b]									
Black	5 (26.3)	3 (15.8)	3 (16.7)	11 (19.6)	1 (25.0)	1 (12.5)	3 (33.3)	5 (23.8)	16 (20.8)
Hispanic or Latino	3 (15.8)	1 (5.3)	3 (16.7)	7 (12.5)	0 (0.0)	2 (25.0)	1 (11.1)	3 (14.3)	10 (13.0)
White	11 (57.9)	15 (78.9)	12 (66.7)	38 (67.9)	3 (75.0)	5 (62.5)	5 (55.6)	13 (61.9)	51 (66.2)
Child's diagnosis, n (%)[c,d]									
Autistic disorder (or autism)	18 (94.7)	16 (84.2)	12 (66.7)	46 (82.1)	3 (75.0)	5 (62.5)	7 (77.8)	15 (71.4)	61 (79.2)
Asperger syndrome	4 (21.1)	8 (42.1)	6 (33.3)	18 (32.1)	1 (25.0)	1 (12.5)	3 (33.3)	5 (23.8)	23 (30.0)
Pervasive developmental disorder	6 (31.6)	4 (21.1)	5 (27.8)	15 (26.8)	0 (0.0)	3 (37.5)	3 (33.3)	6 (28.6)	21 (27.3)
Child's comorbid diagnosis, n (%)[c,d]									
ADHD	4 (21.1)	6 (31.6)	7 (38.9)	17 (30.4)	1 (25.0)	2 (25.0)	7 (77.8)	10 (47.6)	27 (35.1)
Depression	0 (0.0)	0 (0.0)	1 (5.5)	1 (1.9)	0 (0.0)	0 (0.0)	3 (33.3)	3 (14.3)	4 (5.2)
Bipolar disorder or manic depression	0 (0.0)	0 (0.0)	1 (5.5)	1 (1.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.3)
Learning disability	2 (10.5)	6 (31.6)	8 (44.4)	16 (28.6)	0 (0.0)	3 (37.5)	5 (55.6)	8 (38.1)	24 (31.2)

Abbreviations: ADHD, attention deficit hyperactivity disorder; GED, General Educational Development test.
[a]While recruitment allowed for either a parent or caregiver to participate, all focus group and interview participants were parents of a child with ASD.
[b]Percentages do not equal 100 because of rounding.
[c]Participants could indicate more than one diagnosis.
[d]Self-reported diagnosis.

the generalizability of the measure for both verbal and nonverbal patients with ASD, items specifically assessing language skills were not included.

A recall period of the past 24 hours was applied to draft items to be tested during cognitive debriefing interviews based on participant feedback concerning the daily fluctuations of observable behaviors.

Cognitive Debriefing

A total of 21 parents of children diagnosed with ASD participated in two iterative rounds of cognitive debriefing. The majority of participants were female, white, and ranged in age from 20 to 48 years. Table 2 presents the demographic characteristics collected at screening.

In round 1 of cognitive debriefing, 30 items were tested addressing aspects of the 27 identified concepts with two candidate 5-point ordinal categorical response scales to assess frequency. The scales were matched to item stems asking "how often" or "how much of the time." At the conclusion of the first round of interviews, 4 items were either removed because participants did not interpret them as concepts directly observable or combined with a similar item to reduce redundancy identified by participants. Additional examples were added to 5 items to improve clarity. Between rounds 1 and 2, no changes were made to the response scales.

Twenty-six items were tested in round 2. Participant feedback further informed item reduction, along with a revised item order to facilitate a more intuitive flow of concepts. An additional 5 items were either removed because of issues with interpretation and/or generalizability across the full spectrum of the disorder or combined with a similar item to reduce any redundancy identified by participants. Further wording

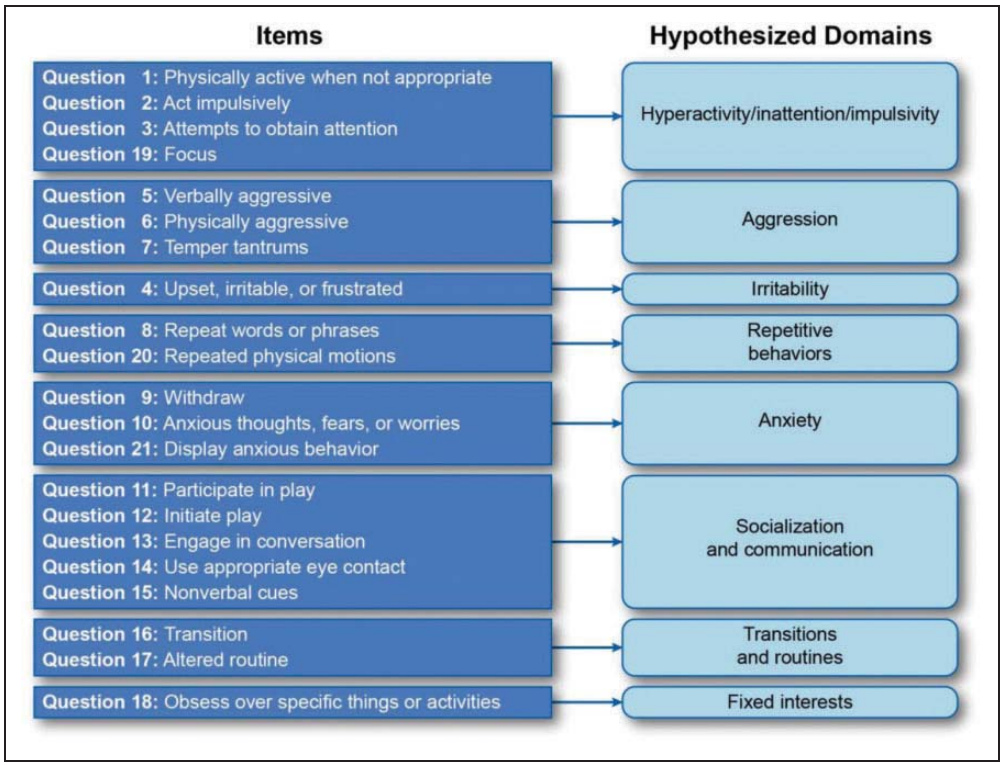

Figure 3. Conceptual framework. ASD, autism spectrum disorder.

revisions were implemented to improve instructions and item clarity. Based on participant difficulty responding to an item during round 2, changes were made to the question stem and coordinating response scale (ie, changing from "how much of the time" to "how often" and revising response scales accordingly) for one item (ie, did your child appear to obsess over specific things or activities?).

Participant endorsement of items across the two rounds confirmed content relevance. Participants identified no additional concepts as missing from the questionnaire, providing evidence to support content comprehensiveness.

Discussion

The OBAS was developed as a self-administered caregiver-reported scale assessing observable behaviors of children with ASD ages 4 to 12 years. It was designed for direct caregiver assessment without the influence of others and was intended to measure change due to treatment in a standardized manner. The 21-item OBAS (Figure 3) contains 8 concept themes (or hypothesized domains) including hyperactivity/inattention/impulsivity, aggression, irritability, repetitive behaviors, anxiety, socialization/communication, transition and routines, and fixed interests.

These concept themes were consistent across age categories, and the relative importance of these concepts was unanimously supported. Items are scored on one of two 5-point ordinal categorical response scales (ie, "how often"—18 questions, "how much of the time"—3 questions), and the recall period for each item is "in the past 24 hours."

The OBAS qualitative development process followed the principles outlined in the FDA PRO guidance, which are applied to the evaluation of all COAs to determine their "fit-for-purpose" in a given "context of use."[20,24] The OBAS's specific context of use is as a clinical trial measure of treatment benefit to the ASD patient population ages 4 to 12 years in support of product labeling. The qualitative research described here represents a critical component toward establishing the OBAS as a "fit-for-purpose" measure in this context. Specifically, as described in the FDA PRO guidance, the methods and results detailed provide qualitative evidence to support the content validity of this new measure. Direct input from the respondents—parents of children with ASD aged 4 to 12 years—was essential to ensure content completeness and relevance. Information gathered from the targeted literature and instrument reviews coupled with qualitative evidence collected from concept elicitation focus groups and cognitive debriefing supports the achievement of concept saturation. Further, the cognitive debriefing process confirmed content relevance and completeness (ie, no missing concepts were identified). The items included in the final OBAS all tested well within the context of the cognitive debriefing, including with participants who have lower levels of education. Respondents were easily able to read through each question and choose a response relevant to their particular child's behaviors. While the social/communications items were included for content completeness, it is unclear whether these concepts are likely to change within the context of a clinical trial. The response

scales were supported as meaningful to the manner in which parents observe behaviors of their child with ASD. Participants considered the past 24 hours an appropriate recall period. Because participants considered each new day (or 24-hour period) demanding and eventful for a caregiver, recall beyond 24 hours would risk response bias based on recent events.

The literature findings indicate an obvious unmet need for a caregiver-completed daily assessment of key ASD behaviors capable of detecting change with treatment and over time. The final OBAS covers concepts not currently assessed in the ABC, the only existing measure with a precedence to support ASD product labeling. Specifically, the OBAS contains items addressing the *DSM-5* concepts of transitions and routines, and fixed interests while the ABC does not. The OBAS covers additional concepts not contained in the *DSM-5* or the ABC that address aggression, anxiety, and socialization. Despite the generally satisfactory psychometric evidence for the ABC, documentation of the content validity is extremely limited, and the measure is clinician administered. The ABC is a lengthy scale (58 items) with a recall period of 4 weeks, much longer than this current research supports as appropriate and content valid. Further, the FDA PRO guidance states that recall periods that call for respondents to rely on memory—especially if they must recall over a long period of time, compare their current state with an earlier period, or average their response over a period of time—are likely to undermine content validity.

Of fundamental importance to this research was the determination of whether parents observed similar behavioral expressions across age groups or if individual, age-appropriate modules were necessary to assess children from 4 through 12 years of age with ASD. While specifics vary, parents of children across these age groups reported observing similar behavioral expressions. Cognitive debriefing participants could identify specific behaviors within their child, regardless of age, that were relevant to the concept focus of each of the 21 OBAS items. Therefore, age-specific modules of the OBAS were not deemed necessary.

Despite the rigorous methods employed, findings from the current study should be interpreted in the context of several limitations. While efforts were made to recruit caregivers of children with disorders across the ASD spectrum, the majority of study participants had children with autism. In these study participants, it is not uncommon for children to receive multiple diagnoses, making it difficult to get an accurate prevalence of specific conditions (eg, autism vs Asperger). Additionally, in the *DSM-5*, autism and Asperger are no longer separate disorders, falling now under one diagnosis code of ASD (299.00). In fact, Asperger is not even listed in the *DSM-5*, making it even more challenging to recruit ''discrete'' patient populations for future studies. It is unknown how well the sample included in the current study is representative of the overall ASD patient population. Future work may be warranted to confirm the concepts covered by the OBAS in an ASD sample of known diversity.

While the intention was to develop a caregiver-reported daily assessment of key ASD behaviors, all participants in this research were parents and nearly all were female. It is unclear how results would vary, if at all, for nonparents and/or males with primary caregiving responsibility; thus, further testing with nonparent and with male caregivers may be warranted.

Because the recruitment criteria for concept elicitation and cognitive debriefing required that parent participants reported observing some type of hyperactive behavior in their child, the generalizability of the OBAS for use in an ASD population without hyperactivity is uncertain. However, efforts were made to recruit a diverse sample in terms of sex, age, education, race, and child's severity and diagnosis across the spectrum. Further, the hyperactivity criteria did not lead to any noticeable loss of participants screening out because of lack of hyperactivity. Because the OBAS was designed to address concepts generalizable across both verbal and nonverbal patients with ASD, items specifically assessing language skills were not included. The OBAS may not be a comprehensive measure for nonverbal patients with ASD for assessing language skills. Finally, because refinements made after Round 2 of cognitive debriefing were not tested, future research may wish to conduct an additional set of cognitive debriefing interviews before moving to quantitative assessment of the instrument.

Conclusions

The methods employed provide clear documentation that the OBAS was developed in accordance with the FDA's PRO guidance for the purpose of assessing treatment benefit in relation to the observable behaviors of children aged 4 to 12 years with ASD.[20]

The next steps toward finalizing the OBAS for use in clinical trials are to pilot the OBAS and to collect quantitative evidence to confirm further the item content, to explore response scale distribution anomalies, and to establish subscale structure and determine a scoring algorithm. Also, quantitative evidence establishing important measurement properties such as internal consistency reliability, reproducibility, construct validity, and responsiveness will need to be gathered. Finally, it will be important to establish guidance for interpreting and defining a clinically meaningful change in scores for the OBAS.

Because of the well-documented benefits of electronic data capture, we recommend that any future use of the OBAS be conducted on an electronic platform appropriate for use by caregivers in an unsupervised setting (ie, at home as compared to in a clinic at a clinical study visit). Further assessment of the OBAS items for translatability and adaptation into additional languages and cultures is recommended prior to use outside the US.

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Declaration of Conflicting Interests

L.S.D. was an employee of Shire at the time the research was conducted and is now an employee of Pfizer. L.S.D. is a shareholder of Shire and Pfizer.

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Supplemental Material

Supplemental material is available in the online version of this article and at http://journals.sagepub.com/doi/suppl/10.1177/2168479016680258.

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