Qualitative Evaluation of the Autism Behavior Inventory: Use of Cognitive Interviewing to Establish Validity of a Caregiver Report Scale for Autism Spectrum Disorder

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Gahan Pandina
Janssen Research and Development
gpandina@its.jnj.com Corresponding Author
ORCID: https://orcid.org/0000-0003-0050-3575

Seth Ness
Janssen Research and Development

Jeremiah Trudeau
Janssen Research and Development

Sonja Stringer
Evidera Inc

Naomi Knoble
Evidera Inc

William R. Lenderking
Evidera Inc

Abigail Bangerter
Janssen Research and Development

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Abstract

Purpose: The Autism Behavior Inventory (ABI) is an observer-reported outcome scale measuring core and associated features of autism spectrum disorder (ASD). It was developed in alignment with the Food and Drug Administration’s patient-reported outcome guidance to address the need for instruments to measure change and severity of ASD symptoms.

Methods: Cognitive interviewing was used following extensive scale development to determine understanding and content validity of the scale prior to its use in a clinical trial. Interviews used a hybrid of the “think-aloud” and verbal probing approach, to assess ABI’s content validity and participant understanding of the instrument, including: (1) item clarity and relevance; (2) item interpretation; (3) appropriateness of response scales, and (4) clarity of instructions. Audio-recordings of the interviews were collected and transcribed for qualitative data analysis.

Results: More than 90% of caregivers of individuals with ASD indicated that they understood all but four items in the 70-item ABI, supported by qualitative analysis of responses. Caregivers were able to select an appropriate response from the options available and reported finding the examples helpful. Based on participant feedback from the first 38 interviews, instructions were simplified, 8 items were removed, and 10 items were reworded. The final revised 62-item scale was presented to an additional 12 caregivers, who reported readily understanding the instructions, response options, and item content.

Conclusions: Cognitive interviews with caregivers of a diverse sample of individuals with ASD confirm the content validity and relevance of the ABI to assess core and associated symptoms of ASD.

Background

Autism spectrum disorder (ASD) is a heterogeneous neurodevelopmental disorder characterized by social communication deficits (e.g., social reciprocity, nonverbal communication) and restrictive behaviors (RBs) resulting in significant functional limitations[1].

Performance-based assessments (e.g., Autism Diagnostic Observation Schedule, Second Edition) [2] and clinical interviews (e.g., Autism Diagnostic Interview–Revised) [3] are considered diagnostic “gold standard” measures, and parent-report measures are often included in these assessments. However,
few parent-reported instruments are available that measure core symptoms of ASD (i.e., social communication, restrictive behaviors) with brief recall periods appropriate for use in clinical trials [4-6]. In addition, instruments used for diagnostic purposes do not necessarily have sufficient sensitivity or specificity to detect responses to treatment[7, 8].

The Autism Behavior Inventory (ABI) was developed in alignment with the Food and Drug Administration’s (FDA) Patient-Reported Outcome (PRO) Guidance [9] as a web-based rating scale for completion by caregivers to assess core and associated symptoms of ASD[10] (Fig. 1). The ABI was tested with a sample of 144 caregivers of individuals with ASD and demonstrated robust psychometric properties (NCT02668991)[11]. The ABI (v1.0) comprised 73 items across five domains (i.e., social communication [SC], repetitive behavior [RB], mood and anxiety, self-regulation, and challenging behavior) (Fig. 2). Quantitative analysis and regulatory review of the instrument led to some proposed changes, such as adaptation or removal of items to ensure suitability for all age groups and verbal abilities and reduction of two response dimensions to a single response. Prior to the use of the instrument in a clinical trial it was important to ensure that respondents were able to understand and correctly interpret items, and that the instrument measured concepts relevant to the target group.

Therefore, content validation was conducted using cognitive interviewing with parents and caregivers of individuals with ASD to confirm comprehension and acceptability of changes to the instrument and to ensure understanding and completeness of the concepts contained in the items [9].

Cognitive interviewing is a process whereby an interviewer employs a variety of techniques to prompt a participant to verbalize the thought processes that occur when interpreting an item and producing a response. For example, the participant may be encouraged from the start of an interview to “think-aloud” and spontaneously describe their thoughts as they respond to the questionnaire. An alternative approach is to use verbal probing, where specific questions are asked by the interviewer in order to elicit the thinking processes driving the response to the instrument [12,13]. Use of probes can be helpful in cases where there is insufficient time for training in the “think-aloud” approach, and/or where participants find spontaneous description of their thought processes more challenging. Probes can be used throughout the task (Concurrent Probing), or can be used at the end
of completion of the scale (Cognitive Debriefing) [14]. Procedural flexibility is viewed as one of the most useful features of Cognitive Interviewing [15].

Cognitive interviews are recommended for use in content validation of patient or observer reported outcomes [16, 17]. They can provide qualitative and quantitative analysis of whether participants understand question items, both consistently across participants and in the way intended by the researcher [18]. The approach also enables assessment of whether items and domains are relevant and important to the target population.

The objective of this study was to further develop evidence for the content validity of the ABI through cognitive interviews with parents and caregivers of a heterogeneous group of individuals with ASD.

Methods
Study Design
This was a non-interventional, qualitative study consisting of interviews with parents and individuals who care for persons with ASD referred to as caregivers. The study design was structured-based on the recommendations of the International Society for Pharmacoeconomics and Outcomes Research Good Research Practices Task Force for establishing and reporting the content validity of PRO instruments to be used to support label claims [19], as well as the FDA PRO Guidance [9]. The FDA guidance indicates that evaluation of patient understanding through cognitive interviewing can contribute to evidence of content validity of items in the scale. A total of 50 participants across two rounds were recruited and interviewed from May 17, 2018 to July 11, 2018. Eligible participants were identified by an independent market research company via their proprietary databases, ASD advocacy support group network, and patient panels. Participants were required to be parents or caregivers of individuals with ASD aged 3 years or above, spends at least three hours per day with the person with ASD, and read and understand English.

Caregivers were recruited and stratified based on age of the child as well as on the child’s verbal ability (minimal verbal functioning vs. higher verbal functioning). For the purposes of this study, minimal verbal functioning was defined as either no language, or use of signs, single words or two/three-word utterances. Higher verbal functioning was defined as the ability to form simple and/or
full sentences. The aim was to achieve a balance across level of verbal functioning and age to adequately represent the broader population of individuals with ASD.

Institutional Review Board (IRB) approval of the study protocol and electronic informed consent were obtained prior to completion of any study procedures. The study was approved by Quorum IRB. 

Cognitive Interviews
For the purpose of these interviews a hybrid technique combining a “Think Aloud” approach with prompts as necessary were used to encourage verbalization of thoughts was utilized. A number of probe questions were asked, encouraging the caregiver to “think aloud”. Concurrent probing was used whereby the question was asked, followed by the caregiver answering the question and then the interviewer asking a probe question, if needed, and the caregiver responding.

Examples of Probes Used:
- Can you repeat this question in your own words?
- What does this mean to you?
- How did you get to that response?
- What were you thinking about as you determined your answer?
- Can you say a little more about that?
- Was this hard or easy to answer? Can you tell me why?
- Was this difficult or easy to understand? Can you say a little more about that?

Interviews were conducted via the web with the ABI presented on a shared screen using an online platform where caregiver participants and the interviewer could see and hear each other. Interviews lasted approximately 60–90 minutes and were audio recorded for transcription with study participants’ permission.

Trained interviewers carried out the interviews using the semi-structured interview guide. The interviews gathered participant feedback on the overall comprehension and clarity of the instructions, the individual items and examples, and item response options. Upon completion of the interview, participants were remunerated in the amount of $100 USD for their participation in the study.

Two rounds of interviews were conducted. The first round of interviews (round 1) was conducted with the 70-item version of the ABI, referred to as ABI_CI_v1.0. The study team, including professionals with clinical outcome assessment, clinical and ASD expertise, reviewed and discussed caregiver
feedback from round 1 interviews, which led to scale modification that were implemented in the second interview round (round 2). A revised 62-item version of the ABI was utilized in interview round 2 and is referred to as ABI_CI_v1.1.

Not all participants were asked every question in the interview guide, in order to maintain interview flow and participant rapport, and to manage time constraints given the length of the semi-structured interview guide. Interviewers prioritized the core ABI domains of SC and RB, and reviewed other ABI domains as time permitted, to ensure equivalent participant response coverage across all 5 domains.

Qualitative Analysis
Audio files were transcribed, and a quality-assurance check was performed, primarily to remove all personal health information found within the transcripts, and to correct any obvious transcription errors.

A content-analysis approach was used to analyze the cleaned transcripts using a coding dictionary and ATLAS.ti version 7.5.18 qualitative data analysis software[20]. Participant quotes were grouped and summarized by thematic code, and coding outputs were generated based on each utilized code. Frequencies of participant responses were calculated.

Results
Participant Demographic Characteristics
Sociodemographic characteristics of the sample of 50 caregivers and 50 individuals with ASD are presented in Table 1. The mean age of individuals with ASD as reported by their caregivers was 12.4 years (range 2–40 years). Among individuals with ASD, there were more males (n=33, 66%) than females ASD (n=17, 34%). Caregivers had a mean age of 42.3 years (range 26–49 years). Most caregivers were female (n=44, 88%), non-Hispanic (n=46, 92%), White (n=30, 60%), and married (n=26, 52%). Regarding caregiver level of education, more than half of the caregivers reported some college, but no degree (n=26, 52%), and nearly half of the caregiver sample reported being employed full-time (n=24, 48%).
Clinical characteristics of the individuals with ASD, as reported by caregivers, are found in Table 2. Most individuals with ASD were diagnosed by a psychologist/neuropsychologist/psychiatrist (n=23, 46%), or a pediatrician/primary care provider (n=15, 30%), and the majority received their diagnosis between the ages of two and three years (n=28, 56%). About half had fluent language ("speaks in full sentences," n=21, 42%), and the majority had at least one comorbid diagnosis (n=32, 64%). Most individuals with ASD (n=47, 94%) had had no significant changes in their condition in the past month, while three (6%) were reported to have had significant changes (two symptoms improved, one not known). For individuals with ASD still in school, the most commonly reported educational placements included regular classroom (n=13, 26%) and a self-contained classroom (n=9, 18%). Other than the higher proportion of females with ASD in our sample, these demographic and clinical characteristics are broadly similar to those of participants commonly reported and seen in clinical trials [21]
Table 2  
Clinical characteristics of individuals with ASD

| Characteristic                                                                 | Total (N = 50) |
|--------------------------------------------------------------------------------|----------------|
| **Age at Diagnosis, n (%)**                                                    |                |
| ≤ 3 years                                                                       | 31 (62)        |
| ≤ 9 years                                                                       | 16 (32)        |
| ≤ 14 years                                                                      | 3 (6)          |
| **Level of language, n (%)**                                                   |                |
| No language                                                                     | 4 (8)          |
| Puts signs or picture exchange together to make simple sentences                | 7 (14)         |
| Single words / 2- to 3-word utterances                                          | 10 (20)        |
| Uses simple sentences                                                           | 8 (16)         |
| Speaks in full sentences                                                        | 21 (42)        |
| Other conditions, n (%)                                                         |                |
| ADD/ADHD                                                                        | 12 (24)        |
| Anxiety                                                                         | 3 (6)          |
| Epilepsy/seizures                                                               | 2 (4)          |
| Global development delay                                                        | 2 (4)          |
| Intellectual disability/learning disability (e.g. math, reading)                | 8 (16)         |
| Sickle cell                                                                     | 1 (2)          |
| Speech disorder                                                                 | 1 (2)          |
| None                                                                            | 18 (36)        |
| Other: (e.g. behavior issues, insomnia)                                         | 3 (6)          |

ABI content validation

Overall Content Validity

Analysis of the transcripts across items was carried out to determine consistency of responses between caregivers, and confirmation that the item conveyed the intended meaning. Qualitative analysis involved identifying the experiences, description and perceptions that went into the respondents’ answers.

This analysis was used alongside qualitative analysis of whether respondents indicated an item was understood to determine whether wording changes, example additions, or item removal was appropriate.

The box below shows examples of the “think-aloud” responses for a specific item “Has difficulty being flexible” with the example “Has a hard time changing his/her mind. Responses demonstrate differences in approach with some participants (example 1&2) requiring minimum prompts to “think-aloud” and others (example 3&4) where the prompts were used to elicit responses (interview questions are in bold font).
Has Difficulty Being Flexible

Example 1 & 2: Participant spontaneously thinks out loud
001-003: Has difficulty being flexible—example, has a hard time changing his/her mind—yes, that is “very often”. That’s also (a response option of) “very often,” okay.
001-003: Yeah, she is very in a routine. If anything is out of place, the smallest thing will cause a meltdown. Like she knows now school is Monday through Friday, she knows that she gets up at the same time every day. Um, in terms of eating, that’s always been a little bit flexible, but other than that everything stays the same. So, like when—say, for instance, understand summer vacation, when the kids are out of school. She was upset that she couldn’t go to school, because I become a routine to her.

022-007: Has difficulty being flexible—has a hard time changing his or her mind. Uh, yeah, that would be “often”. That straightforward, too, you don’t need to change that at all. These kids are, you know, they just—things change and they I moving with it—that’s the best way I could say it.

Example 3 & 4 Participant requires more prompts to think out loud
001-005: Has difficulty being flexible. Example, has a hard time changing his or her mind.
What would you select for your answer, and why?
001-005: Um, I would answer “never”.
Never. And why is that?
001-005: Um, my son is not really hard to deal with, like when we need to go out, uh, like we need to go out, it’s like right even if he’s still watching TV, most of the time or most of the day he just watch TV, and when I tell him we need to go out somewhere, even though he act like he don’t understand, but when I try, start changing his clothes, put his shoes on, really seem to get upset. He just, um, he just let me take him to wherever.

002-010: Yes, I’m there. Has difficulty being flexible. Um, not really. Maybe once in awhile. I would say “sometimes” as.
Why would you say that? What’s your reason for that?
002-010: Because he, he knows the kind of society that we live in. He knows our day to day lives are constantly changin find myself doing is saying to him, this weekend, I don’t know, we’re singing at the, we sing in church. We’re singing a we’re singing at the 9:30, we’re singing at the 11:00, we’re, you know, I will basically have to tell him what’s going on, or when his father is working and where he will be, or if we’re able to go on vacation and where that might be. Um, and I fe the more I prepare him and communicate with him, the flexibility is better. So I will have to say to him, I know your violin Friday at 4:30, but your teacher, [name removed], needs you to come today at 3:30, and he’ll say but it’s on Wednesday yes, it’s Wednesday and we need to do it today, so let’s get ourselves together and get over there kind of a thing.

ABI Instructions
Participants were asked to comment on their impressions of the overall ABI instructions. Almost all participants that were asked to provide comments (n=36/37, 97%) stated the instructions were
“easy” and provided a good generalized overview of the questionnaire.

Are the instructions clear and easy to understand?

Some participants indicated more clarification was needed to clarify the two rating categories in the instructions. Six participants indicated that the term “dimension” could be changed to enhance understanding.

As a result, the term “dimension” was removed from the instructions, and the description of the “quality” response was reworded.

Recall period
Participants also provided feedback on the recall period of over the past 7 days. All participants who were asked to describe their understanding of the recall period (n=42) were able to successfully
explain it as intended, although there was some slight potential for confusion.

In order to clarify the recall timeframe, after the first round of the ABI interviews, the wording was modified from “over the past week” to “over the past 7 days”.

Response options
Participants were asked a series of follow-up questions to assess general understanding and conceptualization of the response options. For example, most participants (n=38/41; 93%) stated the response options for both domains were easy and clear and most stated they did not have any suggested changes. For those who had difficulty with the response scale (n=3/41; 7%), they indicated the option “with support” lacked clarity, the overall options were less clear than the frequency responses and had difficulty in differentiating “with support” vs. “with some reminders.”
There is no universal standard for participant comprehension, but with a clear, well-designed and simple instrument, a guideline of approximately 90% of respondents should be expected to understand the instructions, items, and response options[15]. In round 1 of interviews, 2 items in the SC domain and 1 item in the RB domain were understood <90% of the time. All items in the remaining domains were understood >90% of the time (Table 3).

Table 3
Percentage of caregivers’ understanding in core domains of SC and RB

| Domain                          | Understanding                     | Round 1 n (%) | Round 2 n (%) |
|---------------------------------|------------------------------------|---------------|---------------|
| Social Communication            |                                    |               |               |
| 1. Responds to familiar things, e.g., when a particular song is sung, when a familiar name is mentioned | 30/33 (85%) | Removeda      |
| 2. Shows appropriate affection towards familiar people | 32/33 (97%) | 12 (100%)     |
|   | Behavior                                                                 | Round 1     | Round 2     |
|---|--------------------------------------------------------------------------|-------------|-------------|
| 3. | Shows an interest in what other people are doing                         | 31/32 (97%) | 11/12 (92%) |
| 4. | Responds to attempts to initiate social interaction                      | 28/31 (90%) | 12/12 (100%)|
| 5. | Gives things to others in order to get help, e.g., brings you a box he/she can't open | 28/30 (93%) | 12/12 (100%)|
| 6. | Is flexible when playing with others or taking part in social activities | 30/31 (97%) | 10/10 (100%)|
| 7. | Is creative or imaginative in play or other activities, e.g., make believe play or has new or original ideas | 31/31 (100%) | 11/11 (100%)|
| 8. | Is able to take turns in conversation, e.g., responds to and builds on what has been said, using speech or signs or gestures | 29/31 (94%) | 11/11 (100%)|
| 9. | Directs facial expression towards other people to communicate feelings, e.g., gives eye contact, shows emotion on face | 31/31 (100%) | 10/10 (100%)|
| 10. | Offers information about his/her own thoughts or feelings, e.g., able to talk or sign about what he/she is thinking and feeling | 26/26 (100%) | 11/11 (100%)|
| 11. | Waves ‘hello’ and ‘goodbye’                                             | 27/27 (100%) | 11/11 (100%)|
| 12. | Uses common gestures, e.g., nods, shakes head                            | 27/28 (95%) | 11/11 (100%)|
| 13. | Combines gestures with vocalizations to enhance communication, e.g., uses actions and words to get point across | 25/25 (100%) | 11/11 (100%)|
| 14. | Use tone of voice appropriately, e.g., tone changes according to what he/she is saying | 25/26 (96%) | 11/11 (100%)|
| 15. | Responds to other people’s emotions, e.g., notices or comments on how others are feeling | 27/27 (100%) | 10/11 (91%)|
| 16. | Looks when he/she is called or praised                                   | 27/27 (100%) | 9/11 (82%)|
| 17. | Looks where another person is looking or pointing                         | 27/27 (100%) | 10/11 (91%)|
| 18. | Shows pleasure in shared interactions, e.g., enjoys doing things with people | 26/27 (96%) | 11/11 (100%)|
| 19. | Uses facial expressions that are appropriate to the situation, e.g., looks sad when someone is hurt, smiles when happy | 26/26 (100%) | 10/11 (91%)|
| 20. | Resists affection from familiar people                                   | 25/26 (96%) | 11/11 (100%)|
| 21. | Shows inappropriate affection towards unfamiliar people, e.g., hugging people that he or she does not know | 24/25 (96%) | 11/12 (92%)|
| 22. | Has difficulty interacting with peers, e.g., finds it hard to make and keep friends | 24/25 (96%) | 11/12 (92%)|
| 23. | Says socially inappropriate things OR makes inappropriate social approaches, e.g., will tell people they have a large nose, touches or strokes clothes or body parts | 26/27 (96%) | 10/11 (91%)|
| 24. | Attends to parts of sentences and misinterprets whole, e.g., focus on one or two words and misses the point | 14/22 (64%) | 7/11 (64%)a |

**Restrictive Behaviors**

|   | **Round 1** | **Round 2** |
|---|-------------|-------------|
| 25. | Gets upset over small changes in routine                                | 26/26 (100%) | 12/12 (100%)|
| 26. | Has difficulty being flexible, e.g., has a hard time changing his/her mind | 24/24 (100%) | 12/12 (100%)|
| 27. | Resists trying out new things, e.g., won’t go to new places, avoids new foods | 24/24 (100%) | 12/12 (100%)|
| 28. | Insists on doing things the same way each time                          | 23/23 (100%) | 11/12 (92%)|
| 29. | Is fixated on certain topics or activities and unable to move on         | 24/24 (100%) | 12/12 (100%)|
Items with <90% understanding were reworded or removed for round 2. In addition, if follow up comments from caregivers indicated confusion in response or similarity and overlap of items, these items were considered for removal or rewording.

Use of examples

The ABI contains some items with examples, which were included based on quantitative and qualitative feedback in previous rounds of instrument development. Caregivers provided feedback regarding the examples either spontaneously, or in response to a prompt. The overall response to the inclusion and utility of examples was positive. It was also confirmed that some items were appropriate and easily understood without examples. Some caregivers suggested other items for which an example might be helpful. These suggestions were discussed by the scale development team and, where appropriate, examples were added to items for round 2.

| Item | Main Observation | Round 2 Observations |
|------|-----------------|----------------------|
| 30.  | Has an unusually narrow range of interests | 21/24 (88%) 11/12 (92%)³ |
| 31.  | Repeats /echoes what others say, e.g., immediately repeats words or phrases | 23/23 (100%) 12/12 (100%) |

Item changes

Items changed as a result of the participant comments are shown in a tracking matrix (Table 4).

Changes included rewording of items, where participants indicated wording was confusing (e.g., attends to parts of sentences, shown below) or where follow up comments from participants indicated...
some differences in understanding from expected meaning. Other changes included the addition of an example or removal of an item. Changes were then presented and confirmed in round 2.

### Table 4

| Wording Presented in Round 1 | Final Wording Presented in Round 2 | Rationale |
|------------------------------|-----------------------------------|-----------|
| **Social Communication**     |                                   |           |
| Shows an interest in what other people are doing | Pays attention to or notices what other people are doing |           |
| Responds to attempts to initiate social interaction | Responds positively when others try to start social interaction |           |
| Combines gestures with vocalizations to enhance communication, e.g., *uses actions and words to get point across* | Combines body language with words or sounds to support communication, e.g., *uses actions and words to get point across* |           |
| Attends to parts of sentences and misinterprets whole, e.g., *focuses on one or two words and misses the point* | Attends to parts of sentences and misinterprets whole sentences, e.g., *focuses on one or two words and misses the point* |           |
| Resists affection from familiar people | Resists affection from familiar people e.g. pulls away from family members/close friends or rejects verbal displays of affection |           |
| Responds to familiar things, e.g., *when a particular song is sung, when a familiar name is mentioned* | Removed |           |
| **Restrictive Behavior**     |                                   |           |
| Has mannerisms or odd ways of moving her/his hands or fingers, e.g., flapping or moving fingers in front of eyes | Has mannerisms or odd ways of moving her/his hands or fingers, e.g., moving fingers in front of eyes |           |
| Makes repetitive movements, e.g., flapping arms, rocking body, rolling head | Makes repetitive movements, e.g., flapping arms, rocking body, rolling head, spinning or tapping objects |           |
| Attempts to harm him/herself | Behaves in a way that can cause injury to self, e.g., biting, picking skin, banging head |           |
| Has sensitivities to certain food textures | Is overly sensitive to certain food textures, e.g., refuses food that is too crunchy, or too soft |           |
| Has an unusually narrow range of interests | Has a very limited range of interests |           |
| Uses objects repetitively | Removed |           |
| **Mood and Anxiety**         |                                   |           |
| Is irritable and whiny, e.g., grouchy, moaning when unhappy | Is irritable, e.g., grouchy, cranky, moaning when unhappy |           |
| Worries about things, e.g., generally worries about minor things, making mistakes, going to school | Worries about minor things |           |
| Clings to adults or is too dependent on them | Clings to adults or is overly dependent on them |           |
| Complains about physical problems without a known medical reason, e.g., complains about aches and pains which may not be there | Removed |           |
| Looks worried or concerned, e.g., has a fearful worried expression | Removed |           |
| Gets upset when separated from a caregiver | Removed |           |
| **Challenging Behavior**     |                                   |           |
| Runs away | Runs or wanders away, e.g., does not stay in the place they should be |           |
| Is mean to animals, e.g., pulls pet’s tail, shoves, kicks | Removed |           |
Removal of items

In three cases, an item was removed because of participant difficulties with understanding. When considering removal, several factors were considered, including overlap with other items, comments from participants about suitability of an item for certain levels of verbal ability or age, number of responses at floor/ceiling, and perceived lower ability to detect change.

For example, “Uses objects repetitively” was removed because of the potential for differences in understanding by caregivers, and its similarity to other items in the domain. The item was combined with another item regarding repetitive and stereotypical behaviors in order to avoid confusion and reduce participant response burden (“Makes repetitive movements, e.g., flapping arms, rocking body, rolling head, spinning or tapping objects”).
"Response to familiar things" was removed due to reported ambiguity by some caregivers. In addition, the high level of endorsement of this item by caregivers in this study along with previous data, may leave little room for change in response to intervention.
The item “Complains about physical problems without a known medical reason” was reported by three caregivers of younger and older minimally verbal individuals as not relevant or applicable to their child and was therefore removed.

**Overall impressions**

When asked about overall impressions of the ABI, participants indicated the questions were applicable, straightforward, and presented in language that was respectful of caregivers for individuals with ASD. Examples of responses included the following:
Discussion

This study was designed to confirm the content validity and applicability of items in the Autism Behavior Inventory (ABI) for caregivers of individuals with autism spectrum disorder (ASD), with differing language ability and ranging in age, from 3 years to adult. Participants represented a diverse range of education levels. Most participants were mothers, consistent with expectations for primary caregivers of individuals with ASD.
Response to the first version of the ABI was positive with >90% of caregivers understanding all but 4 of the items presented. Caregivers also demonstrated understanding of the ABI item content consistent with each other and with the expectations of subject-matter experts (clinicians and scale development professionals with experience in ASD) through the “think-aloud” approach. The instructions were reportedly clear, although some caregivers expressed a preference for a frequency rating to be used throughout, caregivers reported that the response options were appropriate, and they were able to provide responses to items using the 4-point scale.

Simplification of the response scale to a single type of response option (frequency) was discussed within the development team, but subject matter experts indicated that the quality scale assessed a different measure of social communication ability that was not captured by frequency count only. Caregivers were more familiar with a frequency response option but were able to use the quality response option and found it appropriate in most cases.

The ABI contains a proportion of items with examples. These examples were added during the development of the instrument in cases where qualitative or quantitative analysis had indicated potential for misunderstanding. The use of examples was found to be especially helpful by caregivers to interpret items and provide an appropriate response, for example, making the scale seem less ‘clinical’ and more parent-friendly.

Caregivers reported the items and the survey as a whole to be relevant and appropriate to the individual with ASD, covering the kinds of behaviors that they were living with day-to-day. This was established through analysis of examples that caregivers gave of the relevance of behaviors to their child, and also through feedback given, sometimes spontaneously and in the opportunity for comments at the end of the interview. There were no suggestions of addition of items, and items such as sleep and food sensitivity which had been added in response to previous caregiver suggestions were validated by this group as being important items. Items in core and associated domains identified as valid in the ABI are also consistent with items and areas of importance identified in other qualitative studies of caregivers with ASD[8,22].

Limitations
As indicated, the sample over-represented females with ASD relative to the gender distribution within the general population of those with ASD (2:1 male:female in our sample vs. 5:1), and this may have impacted the interpretation of the items. Similarly, despite counterbalancing efforts, the sample was not robustly representative of minority populations. The study participants viewed an online pdf of the ABI rather than the actual web-based form itself, which may have impacted participant responses and did not provide electronic usability evaluation, though information on the usability and acceptability of the online version of the ABI has been reported elsewhere[23,24]. Finally, not all participants completed all items. However, it was ensured that a sufficient number of caregivers did complete items in each domain to be confident in the results, and a second round of interviews with the reduced scale enabled completion of more items by caregivers increased the robustness of findings.

Summary And Conclusions
In summary, the hybrid cognitive interview process, using spontaneous “think-aloud” and prompts was successful in eliciting responses and feedback on the ABI. Analysis of the responses resulted in a revised 62-item instrument assessing five domains of functioning that demonstrated content validity with caregivers of individuals with ASD. The results of the cognitive interviews demonstrate that the ABI instructions, items, item examples, and response options comprise a content valid caregiver-reported instrument aligned with instrument development methods described in FDA’s PRO guidance [9]. In response to caregiver feedback, minor adjustments were made to the ABI, specifically the simplification of the instructions, removal of some items, simplification of the phrasing of some items, and inclusion of some behavioral examples. This instrument can be considered content valid across a wide range of verbal ability for children and adults with ASD, and for caregivers of individuals with ASD. Additional psychometric evaluation data will support the ongoing development and validation of the ABI for use in clinical trials.

Declaration
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Conflicts of interest/Competing interests:
GP, AB, SN and JT are employees of Janssen Research & Development, LLC, and may hold company stock/stock options. SS and WRL are employees of Evidera, a business unit of Pharmaceutical Product Development, LLC, a paid consultant for this study. NK was an employee of Evidera at the time the work was conducted and the first draft of the manuscript was drafted, but is now with the FDA Division of Clinical Outcomes Assessment (DCOA).

Ethics approval:
Institutional Review Board (IRB) approval of the study protocol and electronic informed consent was obtained prior to completion of any study procedures. The study was approved by Quorum IRB

Consent to participate:
Electronic informed consent was obtained from all patients prior to completion of any study procedures.

Consent for publication:
Not applicable.

Availability of data and material (data transparency):
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

The Autism Behavior Inventory (ABI) v1.1 is available without charge for academic, research, and professional use, subject to terms and conditions. It can be downloaded in the USA from https://www.janssenmd.com/ (in the tools/psychiatry section) and accessed outside the USA via email request to autismbehaviorinventory@its.jnj.com.

Code availability:
Not applicable.

Authors' contributions:
All authors were involved in the analysis and interpretation of data, and critically revising the manuscript for important intellectual content. All authors agree to be accountable for all aspects of
the work and read and approved the final manuscript to be published. All authors meet ICMJE criteria and all those who fulfilled those criteria are listed as authors.

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**Figures**

**Figure 1**

Development of the 62-item version of the ABI v1.1 Fig 1 Footnote: ABI Autism Behavior Inventory, ASD autism spectrum disorder, TD typically developing.
Figure 2

Overview of the ABI domains Fig 2 Footnote: ABI Autism Behavior Inventory, ASD autism spectrum disorder