# Exploring Communication Ability in Individuals With Angelman Syndrome: Findings From Qualitative Interviews With Caregivers

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## Abstract

Communication deficits have a substantial impact on quality of life for individuals with Angelman syndrome (AS) and their families, but limited qualitative work exists to support the necessary content of measures aiming to assess communication for these individuals. Following best practices for concept elicitation studies, we conducted individual qualitative interviews with caregivers and clinicians to elicit meaningful aspects of communication for individuals with AS. Caregivers were able to discuss their child's specific communication behaviors within a large number of expressive, receptive, and pragmatic functions via numerous symbolic and non-symbolic modalities. These results aligned well with published literature on communication in AS and will be used to inform the design of a novel caregiver-reported measure. Future studies on communication in individuals with AS should focus on gathering quantitative data from large samples of diverse caregivers, which would allow for estimations of the frequency of specific behaviors across the population.

*Keywords:* Angelman syndrome, communication, qualitative methods, caregivers

Angelman syndrome (AS) is a rare, neurogenetic disorder caused by loss-of-function of the maternally inherited allele of the *UBE3A* gene (Sadikovic et al., 2014), resulting in deficits across multiple domains including communication, cognition, sleep, and mobility (Bonello et al., 2017; Buiting et al., 2016; Margolis et al., Bird, 2015). Individuals with AS experience high unmet clinical needs (Wheeler et al., 2017), although recent and ongoing preclinical studies are demonstrating exciting breakthroughs (Daily et al., 2011; Meng et al., 2015; Wolter et al., 2020). Understandably, deficits in expressive and receptive communication have a substantial impact on quality of life for these families (Wheeler et al., 2017; Zylka, 2020), and caregivers have identified communication ability as the most important area to target when evaluating efficacy for novel therapeutics (Willgoss et al., 2020). Unfortunately, there is a lack of communication measures

designed specifically for these individuals, and existing measures may not include appropriate content for this population based on the "striking and unusual communication profile" (Grieco et al., 2018; Pearson et al., 2019, p. 1272).

Most individuals with AS do not use words as a primary mode of communication (Alvares & Downing, 1998; Andersen et al., 2001; Calculator, 2013; Clayton-Smith, 1993; Micheletti et al., 2016; Pearson et al., 2019). Instead, people with AS often use alternative modalities like gestures, non-speech vocalizations, physical manipulations, sign language, and augmentative and alternative communication (AAC) devices (Alvares & Downing, 1998; Calculator, 2013; Didden et al., 2009; Grieco et al., 2018; Keute et al., 2020; Penner et al., 1993). Individuals with AS also may have more advanced receptive and pragmatic language skills that are seemingly unlinked to expressive language deficits or cognition (Jolleff & Ryan, 1993;

Micheletti et al., 2016; Penner et al., 1993). Taken together, the communication profile in individuals with AS is distinct from that of typically developing children, supporting the need for highly targeted and specific measurement tools.

A truly AS-specific measure would include all the communication functions identified by parents as being important to their lives, align well with models of communication development, and account for the different modalities used by individuals within this population. Thus, this study's main goal was to conduct formative concept elicitation interviews with caregivers to obtain detailed information on key concepts that are relevant for understanding parental perception of communication ability in individuals with AS. To inform patient-centered practices broadly in this work, our study team included parents and relatives of individuals with AS, who are listed authors (A.S., P.E., & J.P.).

## Methods

### Participants

#### Caregivers

Caregivers or parents of individuals with AS were eligible for the study if they were ≥ 18 years, had the ability to read, speak, and understand English, could provide informed consent, and had access to a telephone for interviews. Their child had to be at least 2 years of age, and caregivers had to report that their child's diagnosis of AS was molecularly confirmed (e.g., DNA methylation test, FISH, CGH, or sequencing). The caregiver also had to live with the individual with AS and reside in the United States.

Recruitment of caregivers was done in close partnership with an established patient advocacy organization, the Foundation for Angelman Syndrome Therapeutics (FAST). A recruitment invitation was posted to an existing Facebook page and circulated to other similar forums for parents of children with AS. Using snowball-sampling methods, FAST members could also distribute the recruitment flyer via email. Interested participants directly contacted the study team and were screened for eligibility.

Enrollment of caregivers was stratified by their child's age using four groups to ensure representation of communication across children, adolescents, and adults. Ages of the individuals with AS were grouped as follows: 2–7, 8–12, 13–17, and ≥ 18 years old. In addition to stratification by age group, we targeted recruitment to achieve a representative mix of the genetic mechanism of AS (chromosomal deletion, UBE3A mutation, paternal uniparental disomy [UPD], or imprinting center defect [ICD]). The identified genotype has important implications for both severity and symptom presentation of AS (Keute et al., 2020; Mertz et al., 2014). We also monitored caregiver race and ethnicity to support sample diversity.

The final sample included 22 caregivers of individuals with AS ($n = 6$ each for ages 2–7 and 8–12 years; $n = 5$ each for ages 13–17 and 18+ years), with one caregiver screened as eligible but lost to follow-up prior to their interview. Caregivers were on average 45.7 years old ($SD = 8.2$) and were predominantly mothers/stepmothers (86%; Table 1) with 73% (16/22) of caregivers identifying as non-Hispanic White, two caregivers as Black, two as Hispanic/Latino, one as Asian, and one as American Indian/Alaskan Native, meaning around one third of caregivers in our sample were non-White or Hispanic. All caregivers reporting having at least some college/university education, with 11 completing their undergraduate degree and six reporting postgraduate degrees.

#### Clinicians

To be eligible, clinicians were required to have an advanced degree in a communication-relevant field (e.g., speech-language pathology or augmentative and alternative communication (AAC) devices) and at least 2 years of experience working directly with individuals with AS. Eligible experts were identified by FAST study team members through their AS-specific networks and received a recruitment email from a member of the study staff. If an individual was interested in the study, they then contacted the study staff using the contact information in the recruitment email to obtain more information. Study staff conducted a screening visit, where eligibility of the clinicians were confirmed and additional demographics collected. After enrollment into the study, the qualitative interviews were scheduled and conducted.

In the final sample of six clinicians, five were women, average age 42.8 years, four had master's degrees and two had doctoral degrees. Of the individuals with Master's degrees, four indicated their title was speech-language pathologist (SLP) with one clinician reporting an additional title as complex communication needs specialist. The two

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**Table 1**

*Demographics for 22 Caregivers and Their Children With Angelman Syndrome Who Participated in the Concept Elicitation Interviews*

|  | n (%) |
|---|---|
| **Caregivers** | |
| Ethnicity | |
| Hispanic or Latino | 2 (9) |
| Race | |
| White | 18 (82) |
| African-American or Black | 2 (9) |
| Asian | 1 (5) |
| American Indian/Alaskan Native | 1 (5) |
| Caregiver relationship to child | |
| Mothers/Stepmothers | 19 (86) |
| Father/Stepfather | 2 (9) |
| Legal Guardian (female) | 1 (5) |
| **Individual with Angelman syndrome** | |
| Genotype | |
| Deletion Positive | 13 (59) |
| Mutation/UBE3A | 5 (23) |
| Imprinting (ICD) | 2 (9) |
| Uniparental Disomy (UPD) | 2 (9) |
| Gender | |
| Female | 12 (55) |
| Ethnicity | |
| Hispanic-Latino | 2 (9)[a] |
| Race | |
| White | 17 (77) |
| African-American or Black | 2 (9) |
| Asian | 1 (5) |
| Mixed Race | 2 (9)[b] |
| Age, years (*M/SD*) | 12.4/7.7 |

[a]One caregiver did not report their child's ethnicity.
[b]One caregiver reported their child race as American Indian/Alaskan Native and White; one caregiver reported their child's race as Asian and Native Hawaiian/Other Pacific Islander.

clinicians with doctoral degrees were faculty members at academic institutions. On average, clinicians had about 10.5 years of experience working with individuals with AS (median = 7 years; range = 4–30 years). All indicated they had experience with augmentative and alternative communication (AAC) devices. When asked about average caseloads, three clinicians reported seeing around five individuals with AS per year, and the other three reported upwards of 15 individuals per year.

## Interview Script Creation

After a review of the literature, semi-structured interview scripts were created for both caregivers and clinicians (see https://populationhealth.duke.edu/supplemental-files for copies of interview scripts utilized in this study). The caregiver interview script started with asking caregivers to describe the types of communication they see in their child on a typical day. Interviewers then queried around *why* and *how* individuals with AS communicate within expressive, receptive, and pragmatic communication functions. Caregivers were also asked about what would constitute "meaningful" changes in communication for their child. The resulting structure of the interview guide aligned with published models of communication development (Crais & Roberts, 1991; Paul, 2001) and existing communication measures (Didden et al., 2009; Quinn & Rowland, 2017). The wording of the questions reflected a strength-based approach ("How does your child …") in contrast to a deficit-based approach ("Does your child …"). This choice was deliberate and based on discussions with relatives of individual with AS, to allow caregivers to respond in an open-ended format.

The interview script for clinicians was developed in a similar fashion. Clinicians were asked to describe how individuals with AS typically communicate and what these individuals usually communicate about. Like the caregivers, clinicians were also asked about what constitutes meaningful changes in communication.

## Data Collection

The relevant institutional review board approved all study procedures prior to initiation, and their review conformed to recognized standards including the Declaration of Helsinki and the U.S. Federal Policy for the Protection of Human Subjects. Participants provided verbal consent prior to the interviews. Due to the rare nature of this condition and to ensure geographical representation, all interviews were conducted over the phone. Interviewers (M.M., N.L., & C.Z.) were trained in qualitative methods and on the specific interview guide, and were not formally a part of any AS-specific organization. With permission from study participants, interviews were audio recorded and transcribed. The interviews lasted 60–90 min, and interviewers took detailed field notes that were expanded immediately following

completion of the interview using a semi-structured debriefing form.

We planned to conduct approximately 20 interviews with caregivers (five caregivers in each of the four age groups), and 5 interviews with clinicians, understanding that more interviews might be needed to recruit caregivers of individuals with more rare genotypes. Based on initial review of our sample, we recruited one additional caregiver to ensure representation from UPD and ICD genotypes in each of the youngest age groups (2–7 and 8–12 years old). We chose to enroll caregivers and clinicians to provide complementary information; caregivers could talk in detail about their own child's communication in multiple settings (e.g., home, community) and over time, whereas clinicians could speak more generally across individuals they had worked with and their knowledge of AS, communication development, and communication disorders.

## Analysis

The goals of analysis were to (1) confirm the major communicative functions relevant to caregivers within expressive, receptive, and pragmatic communication, and (2) describe a wide breadth of communication behaviors within each function. Secondary goals were to examine the use of different modalities (e.g., verbal speech, gestures) and meaningful change in communication from the perspectives of caregivers and clinicians. It is important to note, that the goal of this analysis was not to speak to the frequency of specific communication behaviors in the larger population of individuals with AS or to identify developmental trends.

Thematic analysis was performed on all transcripts using the framework proposed by Nowell (Nowell et al., 2017). Thematic analysis is a method that is used for identifying, organizing, describing, and reporting themes (Braun & Clarke, 2006). Nowell's framework supports trustworthiness of thematic analysis specifically through well-structured procedures that support summarization of findings (Nowell et al., 2017). As fully described in Table 2, three analysts participated in the five phases of research including familiarization with the data, generating initial codes, searching for themes, reviewing themes, defining and naming themes, and producing reports (Nowel et al., 2017). The final codebook included 19 codes describing specific modalities ("words," "gestures," and "AAC Devices") as well as larger areas of communication ("expressive," "receptive," "pragmatic"). The broader communication codes also had related subcodes, representing more targeted communication functions (e.g., "expressive" => "refuse"; see https://populationhealth.duke.edu/supplemental-files for full codebook and descriptions of all codes). The goals of our analysis were primarily descriptive (and not interpretive), to report examples using the caregivers' own words.

Please note, we report frequency counts for specific aspects of the interview that every participant was queried about in the same way (i.e., meaningful change and number of words). For observable behaviors within a communication function, as is traditional for thematic analysis, we selectively and intentionally use semiquantitative terms (e.g., "a few", "many", "some"), when we want to reflect patterns seen in the data. Caregiver interviews were the primary data for analysis, clinician interviews were utilized to expand on and confirm concepts identified by caregivers. Thus, when we report data that was obtained from clinician interviews, this is specifically stated.

## Results

### Overview

Caregivers confirmed a number of communication functions relevant to individuals with AS and were able to describe a number of observable communication behaviors associated with each function. For ease of review, the results are organized by expressive, receptive, and pragmatic communication (Figure 1), with tables including additional quotations (Tables 3–5).

### Expressive Communication

Expressive communication was defined as specific communication interactions where the individual with AS was communicating something to their communication partner (most often, their caregiver).

#### Requesting

Caregivers reported that individuals with AS requested a variety of objects and activities, including food, attention, entertainment (i.e., music, TV shows), places (outside, pool, store, etc.), baths, and social games. Individuals with AS could be skilled at requesting a small number of things that they specifically enjoyed or that were

**Table 2**

*Thematic Analysis Approach of Qualitative Data to Support Trustworthiness of Findings*

| Phases of Thematic Analysis[a] | Methods utilized by study team to ensure trustworthiness |
|---|---|
| Phase 1: Familiarization with the data | • Data for this study included audio files, transcripts, and interviewer notes. These data were stored on a private, password protected server that was accessible by the analysts.<br>• Interviewers/analysts (subsequently referred to as analysts) took detailed notes during interviews to capture details such as duration of the interview, perceived attitudes about the questions asked, and any difficulty understanding concepts discussed.<br>• Following the interview, analysts completed semi-structured debriefing forms using audio files and interviewer notes in order to summarize findings at the individual participant level.<br>• Analysts memoed (Given, 2008) on all interview transcripts (including interviews they did not conduct) to underscore themes and patterns that emerge from the data. |
| Phase 2: Generating initial codes | • Analysts created the initial codebook, which was structured with deductive codes from the interview guide.<br>• NVivo12 was utilized to code the transcripts.<br>• An audit trail was begun to record subsequent code generation.<br>• Team meetings to discuss code generation were documented.<br>• Peer debriefing occurred regularly at bi-weekly study meetings to review patterns in the data, themes and general impressions with parents and relatives of individuals with Angelman syndrome. |
| Phase 3: Searching for themes | • As deductive codes were applied, inductive codes were identified through study team discussion and review of the data.<br>• Triangulation of new codes generated from different analysts were explored at regular meetings, and subsequently inductive codes were applied to all transcripts.<br>• Analysts pulled code reports from NVivo12 and then analysts memoed on all code reports to understand patterns and organize themes. |
| Phase 4: Reviewing themes | • Themes and subthemes were vetted by team members.<br>• Referential adequacy was checked by continuously returning to the data. |
| Phase 5: Defining and naming themes | • Discrepancies in coding were resolved through discussion within the analysts group and the larger study team, resulting in a refined codebook (documentation of these meetings occurred).<br>• Consensus was reached on defining and names of themes.<br>• Inter-rater reliability was examined and any conflicts in coding on individual transcripts were discussed (kappa range: 0.54-0.97).<br>• Peer debriefing and member checking occurred regularly at bi-weekly study meetings to review themes with parents and relatives of individuals with AS. |

(Table 2 continued)

**Table 2**
*Continued*

| Phases of Thematic Analysis[a] | Methods utilized by study team to ensure trustworthiness |
| --- | --- |
| Phase 6: Producing the report | • Analysts reviewed the code reports and wrote final analytical reports, including direct quotes from the transcripts assigned to each code.<br>• Thick descriptions of context were included within the reports, focusing on linkages across themes. For example, caregivers and clinicians reported that "motivation" played a role in their child's communication, and we specifically discuss motivation in terms of expressive, receptive, and pragmatic communication.<br>• Process of coding and analysis was described in detail & descriptions of the audit trail provided. |

[a]Based on the framework proposed by Nowell, L. S., Norris, J. M., White, D. E., & Moules, N. J. (2017). Thematic analysis: Striving to meet the trustworthiness criteria. *International Journal of Qualitative Methods, 16*(1), 1609406917733847. doi:10.1177/1609406917733847.
Given, L. M. (2008). *The SAGE encyclopedia of qualitative research methods* (Vols. 1-0). SAGE Publications. doi: 10.4135/9781412963909

motivating for them (e.g., their favorite food, a TV show, or a game they like to play). A few children could request specific things that were not in the same room or that they could not see.

For nonspecific communication attempts like crying, caregivers reported using context clues to help decipher what it is the child truly wanted. For example, caregivers mentioned they used context like the time of day or physical location (e.g., kitchen) to know that their child wanted food. "So, if it's 11:00 a.m. or 12:00 p.m. and she's fussing, then I know that she wants lunch." Caregivers also looked for confirmatory behaviors to help determine if their child's request was met (i.e., smiling, nodding yes, or squealing in excitement).

### Seeking Attention
Individuals with AS sought attention from their caregiver using sounds, their body, or their AAC device. For example, one caregiver of an individual who was ambulatory stated, "He will usually approach us and tap us, or pull on our pant legs if we're standing." Caregivers reported that their child would seek their attention before communicating a request.

### Requesting More of Something
Caregivers reported children requested "more" of something using different behaviors including reaching, pointing, vocalizations, specific signs/

gestures, or by using their AAC device. One caregiver said,

> I would usually ask him, "Do you want more?" and he'll either – he might do that little head nod thing with his body – "Yes" – or he might push his plate towards you. He might just reach for whatever it is.

Another caregiver reported use of symbolic language to request "more." "He makes the 'more' sign language. You sort of hit your two fists together in the front, and occasionally he will use the more button on his device or if he can see the item."

### Toileting
There was variation in the sample around observed communication behaviors about toileting. Some examples of communication around toileting included using an AAC device or tapping on their front or backside to share they needed to use the bathroom or needed a diaper change. There also was heterogeneity in the relevance of the concept to different families, which varied based on the priority caregivers placed on expressing needs around toileting (high/low), how intensely caregivers were reinforcing these skills with their child, and different levels of independence the individual had around toileting (being fully potty-trained vs. on a timed schedule vs. not being potty-trained). When clinicians were asked about this concept, they

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**Figure 1**

*Conceptual Model of Communication Ability Based on Themes Identified by Caregivers and Clinicians During Qualitative Interviews*
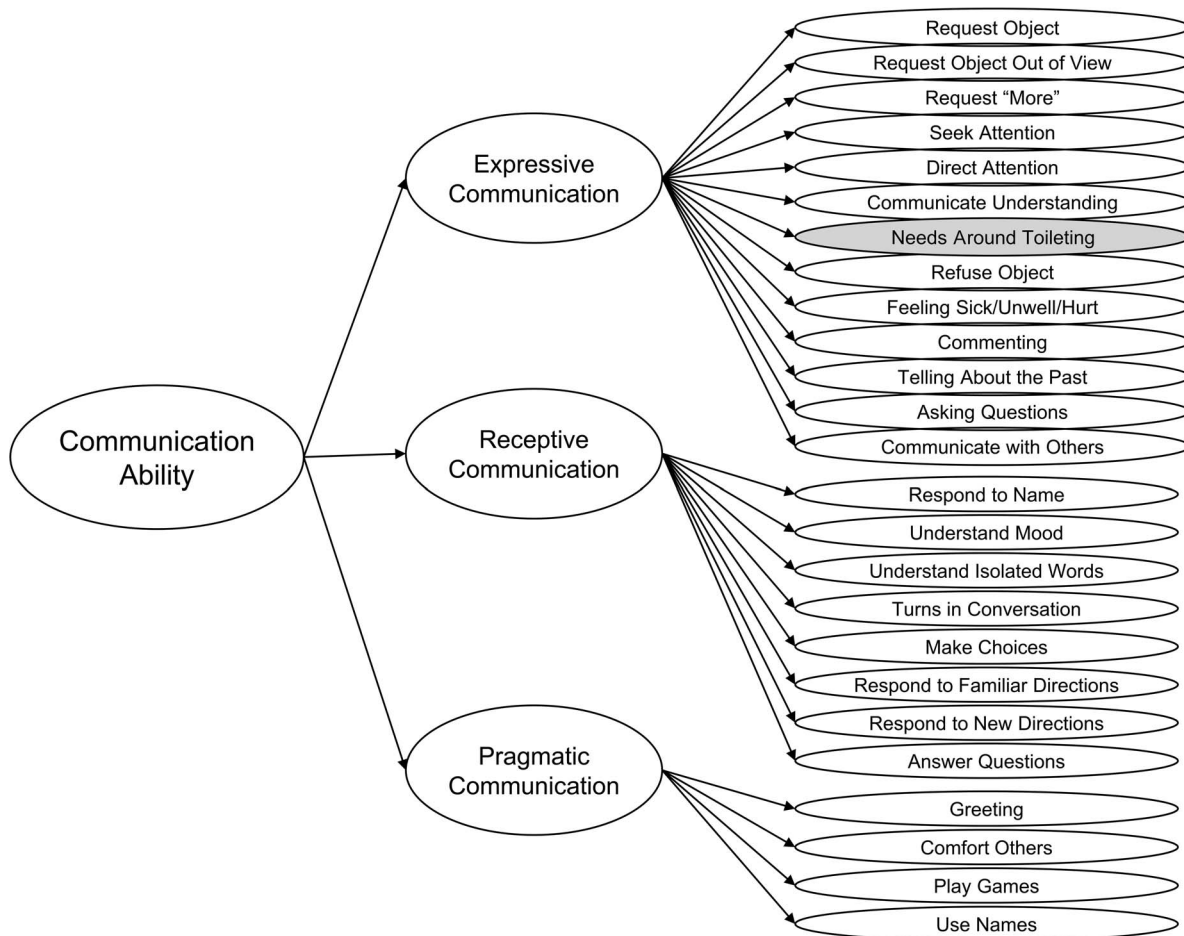


*Note.* The grey oval highlights a concept that may or may not be related to "communication ability." Please see text for more discussion.

reported that when nonsymbolic communication modalities were being used by the child, it is often not clear if the child was intentionally communicating or if the caregiver was identifying the individual's feelings of discomfort.

### Directing Attention

Caregivers reported individuals with AS using physical means to direct their attention. Examples of this included grabbing the caregiver's hand and bringing them to something, turning the caregiver's face, and handing something of interest to the caregiver. One caregiver said,

> She may point if she's wanting to show me on her iPad, she's watching kids at a water park, and she'll use her voice to get my attention and then point to that. If I still don't look because I'm doing something else or talking to someone, she may tap me and/or turn my head by pulling my chin to what it is she wants me to look at.

Other observed behaviors for directing attention included pointing to the object/action of interest and vocalizing/squealing ("ah ah!" or "eh eh!"). Some caregivers believed that their child could not direct attention or could not think of examples of directing attention.

### Refusal

Individuals with AS refused objects or activities for a variety of reasons and used a variety of different methods. The most common refusal

**Table 3**

*Conceptual Areas Representing the Expressive Communication Ability of Individuals With Angelman Syndrome Described by Caregivers and Clinicians*

| Expressive | Examples From Caregiver Interviews |
|---|---|
| Requesting an object | Well, she will kind of just start fussing and you kind of know what time of the day it is. So, if it's 11:00 a.m. or 12:00 p.m. and she's fussing, then I know that she wants lunch. Other times, if she sees you eating and she's hungry, then she kind of whimpers. |
| | Let's say I have a piece of string cheese and she will literally track it with her eyes and watch you pull it and put it into your mouth. And that's kind of her tracking it very intently. It's her way of saying that she would like some. |
| | So, she will do the banana sign with ASL [American Sign Language]...and then she uses sign language sign for chocolate. |
| | He touches his finger on his mouth if iPad is not next to him. Otherwise, he's gonna say, "I'm thirsty," "food." You know, "I want crackers." He gonna click that button a lot. So, that way we know if he's hungry. |
| Seeking attention | One of her things that she does to get attention is she'll come upstairs and she'll go for the thing that she knows she's not supposed to touch or do, and she'll just head for it, and then she'll just grab it, and then like have this wicked smile and then look at me. |
| | She'll get your attention really quick and she'll, like I said, she does this babble thing and then will do her hands. ... And other times, if she comes in the room, she'll get right in your face and look you in the eye and then she'll do the gesture or sign what she wants. Or another thing is when you're sitting there ... she'll take your face with her hand and move it so you look at her, or she'll tap you. |
| | How does she ask for attention? Well, she says "Look at me" [on her device]. That's extremely effective, but we worked hard to get to that—we worked hard to teach her that that's the most effective way. But, like I said, she has used that button 12,000 times, so that's a lot. And then, the other way would just be to grunt. "Eh." |
| Requesting "more" of something | I would usually ask him, "Do you want more?" and he'll either—he might do that little head nod thing with his body—"Yes"—or he might push his plate towards you. He might just reach for whatever it is. |
| | So she has a particular sound that she uses for I think more. She used to actually have a "more," like she used to say "muh" for "more." But then that's again, that's one that she's lost that we may hear again sometime or not. So she used to say more, like at least part of it. And now she's just kind of like, "Aaa. Aaa." But it's a particular "Aaa" that we know exactly what it means. |
| | He makes the "more" sign language. You sort of hit your two fists together in the front, and occasionally he will use the more button on his device or if he can see the item. |
| Expressing needs around toileting[a] | She actually pats the lower of her belly when she has to use the toilet. |
| | She has a button that says "Ladies' room, please."... She also will simply just get up and go because she has the ability to do that. She can just walk to the bathroom herself and go. She doesn't need anyone to take her, typically, if we're at home. |

(Table 3 continued)

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**Table 3**
*Continued*

| Expressive | Examples From Caregiver Interviews |
| --- | --- |
| Directing attention | If we're sitting at the kitchen table and he wants to direct my attention to the door because somebody's there, he can't do that. But if he wants me to activate or turn something on, he'll scoot over to it and tap on it. |
| | He'll come and get you if you're not sitting right there. His other thing—probably in the last year and a half—he's constantly—he takes my face, he pushes my face with his hands. He'll grab my face—lip or nose—turn my face towards whatever it is he wants to show you. |
| | If I'm not looking at her and she's sitting next to me, she'll make a sound. She may point if she's wanting to show me on her iPad, she's watching kids at a water park, and she'll use her voice to get my attention and then point to that. If I still don't look because I'm doing something else or talking to someone, she may tap me and/ or turn my head by pulling my chin to what it is she wants me to look at |
| Refusing an object | He'll either just push it away or walk away from you. He does not shake his head. We have not been able to get him to understand either to nod "yes" or to nod "no" on a consistent basis. So, if he doesn't want something, he'll just turn away from it or push it away. |
| | She will push it away with her hands or turn her head and not look back at you, or just crawl away. |
| | She does a sign for, "No I don't want it." She'll shake her head, "No." |
| | She'll put her hand up in the air to say stop. Sometimes she'll use one hand. I don't know what the term is why she may use two hands, but sometimes she'll put two hands up to let you know to stop or I don't want that. Like I said, she'll use a waving motion, for instance, if I don't understand what she wants to drink and say I pull out juice she'll wave her hands, or she'll take her straw out of the cup to indicate that she doesn't want what's in that cup. And then along with that, she'll do a no or a sound in disagreement. So, she'll do a host of things to let you know that I don't want that. |
| Commenting/ communicating understanding | Besides smiling, laughing, crying, he does have a confused face. If he's not sure about something, he kind of scrunches up his eyebrows and gives that "What's going on?" kind of look. |
| | He'll pull out the Tupperware container with a cookie in it, and I'll say, "You really want a cookie," and he will immediately—he'll hold that cookie in his mouth or in his hand and he'll just like "Huh," make a happy face, give me a sly smirk, and usually throws his arms up like, "Ha ha. I did it." So, that's right on the mark. His gesture and his movement was "I want this." That's totally easy to interpret. |
| | She'll say really funny things. She says, "That's my jam." If she likes a song, she says, "That's my jam." She says, "I think that's awesome," "I think that's silly." Sometimes, when she hasn't been really good, we'll say, "How was school today?" and she'll say, "Naughty." She's like, "Yeah, I'm not gonna lie. I'm naughty." I don't know. She comments—she has hundreds and hundreds of symbols on her talker to get her point across. I'm sure there are ways I can't think of. |
| Feeling sick or hurt | And if she's sick, if I'm not sure, sometimes that is the hardest thing for us to point out where she's sick at. If she's sick, I will ask her to show me so she will actually take her hand and point to the area where it's bothering her. |

[a]Expressing needs around toileting seemed less related to communication ability and more related to other abilities like motor skills (ability to walk to bathroom) and being independently potty-trained. Please see text for more discussion.

**Table 4**

*Conceptual Areas Representing the Receptive Communication Ability of Individuals With Angelman Syndrome Described by Caregivers and Clinicians*

| Receptive | Examples From Caregiver Interviews |
|---|---|
| Responding to name | When he was little, it was kind of like, "Yes, that's my name. That's my name." But now, I think it's more an anticipation. "Okay, you said my name. You're either gonna talk to me or tell me something that I wanna know." He's more curious as to what's gonna follow his name. |
| Answering questions | Familiar objects, you know, if I say "Where's your backpack" or "Where's your lunch bag" or "Where's your water cup," she'll go and get it for me or point and show me it's in the kitchen or something. |
| | So she mostly uses inflection in her voice. Sounds, questioning sounds. Most of the sounds that she uses, like "ah? ah?" She has, when she's very excited about something that I might ask her, like "Do you want to go to Legoland today?" She has said "Uh-huh" when shaking her head |
| | I can ask him questions, do you want to play Play-Doh, and he'll nod, or would you like a cookie, of course we always get a nod with that one, or sometimes, do you want to go see daddy, and he shakes his head no, he wants to stay with mommy. |
| Making choices | We actually put two or three food items or snacks in front of her and ask her to choose one, and we don't—we just set them there and then let her just pick it up. We tell her to pick it up, whichever one she wants, and that's what she does. |
| | He tells me on his device. If I'm giving him a choice, do you want grapes or strawberries, he will answer. |
| | I'll give her three choices for breakfast and she'll point to it or she'll just take it. And, like, this morning, she picked oatmeal. So, I had oatmeal, I had cold cereal and then I had a breakfast sandwich. As she picked oatmeal. |
| | I ask him, what does he want to play, and sometimes I say we can do Play-Doh, we can play with stamps, we can do tattoos, we can finger paint, Lite-Brite, so it's not necessarily just two choices, but I'll say, what do you want to play, tell me what you want to play, and he'll go to the play button in his iPad where a bunch of choices exist and he'll pick the thing that he wants to do. |
| Responding to directions | Like if I tell her no, she will normally stop doing what she is doing and back away from it. But other than that, there's no direction. |
| | If I say the word bath, he's off to the bathroom. He understands that. If I say, "It's time to put on your shirt." A lot of times he'll dunk his head down for me to put a shirt over his head, and then he'll put his arms through. Or if I say, "It's time for your shoes." Sometimes he'll, not consistently, but sometimes he'll give me a foot. |
| Understanding isolated words | I'll saying, something like, "I have to go to the store." And she'll go and get her shoes. |
| | We have no way of really understanding how much more he's understanding because he can't verbalize it or communicate it to us, but there's times where all of a sudden, we might be talking about something, and he. . .he will show that he knows what we're talking about, and it's just like, "Oh, okay. . ." |

(Table 4 continued)

Communication Ability in Angelman Syndrome

**Table 4**
*Continued*

| Receptive | Examples From Caregiver Interviews |
|---|---|
| Understanding mood | He had a hard time expressing or understanding feelings when he was younger. If you had a frown face on, and you were saying whatever he did was bad, he would just look at you and smile. He didn't recognize that you're making a frown face because you're upset about something.<br>It's like pretend I'm crying kind of thing, he say like, "No, stop." He knows Mommy's mad. So, he gonna run away and show things like Mommy's mad or something. He realize like tone of the voice. |
| Taking turns in conversation | Under a year old also, she would cough. It was one of the only sounds I think that she could make herself, so she and I would cough back and forth because it was, you know, like some kids start babbling and then the mom says "mamama," and then the baby does it. |

**Table 5**
*Conceptual Areas Representing the Pragmatic Communication Ability of Individuals With Angelman Syndrome Described by Caregivers and Clinicians*

| Pragmatic/ Social | Examples From Caregiver Interviews |
|---|---|
| Greeting | He usually jabbers at them, waves. He's big on waving and just making sounds to get their attention. If he is—a lot of times, when we're out in the community, he's in his chair, so the waving and the chatting—if he can get close to somebody, he will grab people and hang onto them while he's chatting away. If he's not in his chair, he will go up and just hug people, grab them and hug them, get in their face.<br>If I get her up from her nap, she's very excited to see me when I walk in the room. But, she'll bounce her body and she'll make happy noises. |
| Playing games | When he wants you to play peek-a-boo with him, he'll just take your hand and put your hand over your face. And, if you act like you don't know what you're saying, he might take your shirt and put it over his face—or a towel or something that's close by to let you know he wants to play peek-a-boo.<br>I'll put a blanket on her head. And she'll take it off. And I'll put it on again, and she'll take it off, and put it on again. And then, we've always done, for a long time, since gosh, she was five or six years old, we would do a vocal game where we do back and forth, where I mimic her. And sometimes she'll mimic, we'll go back and forth. And she'll say the sound again and I'll do it exactly like she does it. And we'll just go uh, uh, uh, uh. And that cracks her up. |
| Using names | If he want his sister, he gonna touch like "[name], [name], hi." So, he wants some attention from his sister or dad, he gonna point out their name, you know.<br>For like Dad, he'll do, "Dah." For Mom, well, he does "Mama" for Mom. For Sister, he'll do like "Sissa," like he'll tell like kind of like an S together. He calls, his grandmother's name is [name]" He calls her [name] like plain as could be. |
| Comforting others | She also is, if she sees other people upset, it can make her upset. That's both in real life and on TV. If she sees like kids crying out in public, she often is like, "Aaa. Aaa." And then she'll look at me, and then I have to tell her like, "They're gonna be okay." You know? |

behavior reported by caregivers was pushing an object away. Similarly, individuals with AS also might refuse something by walking/moving away from the object or person, whining, or fussing. Another example caregivers provided was use of a symbolic "no." One caregiver stated, "She does a sign for, 'No I don't want it.' She'll shake her head, 'No.'" We also heard caregivers discuss use of an AAC device to indicate refusal or use of a word/word approximation like "No" or "Nah." Caregivers could identify and discuss these nonsymbolic and symbolic forms of refusal and some reported they were working specifically to build and reinforce these skills.

### Commenting

Commenting was defined as remarks expressing opinions or reactions. Typically, comments that caregivers of individuals with AS identified were simple things like a laugh, smile, or vocalization to express happiness or excitement. Happy vocalizations came in the forms of shrieks or high-pitched babbles. Conversely, caregivers reported individuals with AS also made low-pitched vocalizations (i.e., whines, cries, or growls) or used facial expressions (scowling/frowning) to comment that they were unhappy or "displeased" with someone or something. In both cases, these reactions were used by the caregiver to identify their own understanding of the child's communication (e.g., to determine if they responded appropriately to a request). Some, not all individuals, were able to tell simple stories about something that happened in the past (using a device or gestures). For caregivers who could describe this type of communication, there often was significant interpretation that occurred on behalf of the communication partner using contextual cues. For example, on caregiver said,

> The cat coughed up a hairball in the middle of the floor and it was dark in the room, [the child] stepped in it and I heard her fuss and then she walked out, found me, held her foot up and pointed to it. And then she proceeded to show me exactly where the cat threw this hairball up at.

### The Importance of Communication Modality

Caregivers confirmed that individuals with AS used one or more of the following communication modalities: sounds/vocalizations, words or word approximations, signs or gestures (including modified gestures), and AAC devices. Caregivers reported that individuals with AS use these modalities across communication areas (e.g., expressive, receptive, and pragmatic) in varying degrees, and this was confirmed by clinicians. Some caregivers reported the use of multiple modalities within a specific function (e.g., using vocalizations, gestures, and body movements to seek attention). Individuals who could utilize symbolic forms of communication, like words/word approximations and AAC devices, were able to communicate more sophisticated messages, like answering open-ended questions, making requests for something out of view, or telling stories.

### Finger Point

Caregivers and clinicians reported the importance of the use of finger points in advancing communication skills across a number of functions. For example, individuals might reach toward a general area to let their caregiver know they wanted something or utilize a finger point:

> She's getting better with her pointing; we've been working on her with that because a lot of times it's just the hands opening and closing at a specific item to lets us know that she wants that item. Now, she's advanced to where she can finger point to that specific item.

### Words/Word Approximations

About half of caregivers reported that their child used words or word approximations; however, only four caregivers said their child had more than three words that they used consistently. Of note, only one child in the 2–7 age group used any words or word approximations. The most consistently used word/word approximation across all age groups was "mama." Caregivers also talked about words/word approximations that were "lost" over time. One caregiver stated, "She used to say 'dad' when she was younger but then about three years ago, she started saying mom, and she doesn't say dad anymore."

### AAC Devices

Use of an AAC device was common in our sample in at least some capacity, whether high tech (e.g., iPad with an app) or low tech (e.g., picture book).

Although we did not explicitly examine cohort effects, there were differences in device use between older and younger individuals with AS in this sample. For example, a caregiver of a child in the 2–7 years age group said, "He went through this huge spike of being able to communicate so much more with the introduction of the device." However, caregivers of adults with AS typically reported introduction later in life and less positive experiences: "Everybody was trying really hard to get him to use it. . . . It just didn't really click with him." When caregivers spoke about their child's level of mastery with the device, they mentioned various factors; how much modeling the support system was doing with the child, the child's motivation to use the device, the years using the device, the robustness of the device, and the child's fine motor abilities.

## Receptive Communication

Receptive communication is the process of understanding a message expressed by a communication partner. By definition, it is less directly observable than expressive communication. Thus, in describing examples of receptive communication, we focused on observable behaviors that indicated understanding after a specific prompt (Table 4).

### Responding to Name

Almost all caregivers reported their child would respond to their name in some fashion. Examples of other observed responses included physically coming to the caregiver, making a sound, looking up, or making eye contact with the communication partner. One caregiver said, "If you call him or say his name, he'll look up and look at whoever just said his name or called him. He will respond to that. He may make eye contact with you to see – 'What?'"

### Answering Questions

When asked to respond to a *yes* or *no* question (e.g., do you want to go to the park? Do you want a banana?), caregivers in our sample were able to report if their child could make a choice using at least one modality (e.g., a head nod, an informal gesture, or sound like clapping or squealing), but this behavior was less common than other functions. Other examples of responding to questions can be found in Table 4.

### Making Choices

Some caregivers in our sample said their child was able to consistently make personal choices, and caregivers reported using different methods to assist their child in making these choices. For example, one caregiver said,

> We actually put two or three food items or snacks in front of her and ask her to choose one . . . we just set them there and then let her just pick it up. We tell her to pick it up, whichever one she wants, and that's what she does.

Other caregivers reported that their child would utilize their device to make a choice.

> I'll say, what do you want to play, tell me what you want to play, and he'll go to the play button in his iPad where a bunch of choices exist and he'll pick the thing that he wants to do.

### Responding to Directions

Caregivers reported children understanding the word "no" (a very simple direction), with less frequent reports of understanding more complex directions. One caregiver shared examples of simple directions that their child follows, "If I say the word 'bath', he's off to the bathroom. He understands that."

Motivation played a role in caregivers being able to observe receptive communication behaviors, and could influence whether an individual with AS would respond appropriately to a communication partner and indicate understanding. One caregiver said,

> Like if she wants my cell phone and it's on the floor, I can say, "Hey, my cell phone's on the floor," and . . . she would go over and pick it up because she wanted it. But if I was like, "pick up your toy". . . she wouldn't do it.

### Understanding Isolated Words

Caregivers reported that individuals with AS were able to indicate their understanding of familiar words when overhearing their caregiver speak about something that mattered to them. For example, one caregiver was speaking about their child's love of their favorite food and how she

could not say the word aloud because the child would demand it immediately. Caregivers also reported that their child indicated name recognition by responding with excitement when someone mentioned the name of a person they like.

### Taking Turns in Conversation

Caregivers reported examples of their child taking turns in conversations and expressed enjoyment around these interactions with their child. For example,

> When [name] babbles, I talk back to her. I try to figure out what she's babbling what she goes, "Buh-buh-bub," or "Guh-buh-buh" and then point to something. I go, "Oh. So, you like this movie?" And she'll do the nod or not a nod and it's really cool.

Another caregiver provided an example of their child responding back to her with a question or comment: "If I say 'Dad,' … she might say, 'When? When will I see Dad?' Or [name] – if I say '[name],' she might say, 'When?' or she might say 'movie.' She likes to watch a movie with [name]."

### Pragmatic Communication

Social communication was described by both caregivers and clinicians as a strength of individuals with AS (Table 5). Caregivers reported their child greeted others and played familiar games (e.g., peekaboo). For older individuals, caregivers discussed their child's requests for familiar activities they may enjoy with others, like swimming. Other social communication functions that were described by caregivers included the use of specific names for people like siblings, cousins, or aids, using specific signs, symbols on their devices, or vocalizations. Some caregivers also reported that their child would comfort others if they noticed they were upset; although, this was only described by a small number of caregivers.

### Meaningful Change

Caregivers and clinicians all provided multiple answers for what would represent meaningful change; responses were aggregated into nine overlapping themes. The most frequently mentioned themes focused on complex communication, initiation of communication, communicating with people, verbal speech, and being able to communicate when hurt or sick. Examples of all themes can be found in Table 6.

Generally, caregivers and some experts mentioned that a meaningful change for an individual with AS would be gaining more complex communication skills. Some participants defined these skills in terms of more complex linguistic skills, like increased words per sentence or vocabulary. Other caregivers mentioned that this change could be independent of modality. The development of speech was also frequently mentioned by caregivers; however, most caregivers tempered these comments and suggested this goal was likely out of reach. For example, one caregiver expressed that a full vocabulary would be "amazing," but it was more important that their child used some words that "everyone could understand."

Initiating communication was also a popular theme, which was often discussed in terms of initiating communication on an AAC device. Caregivers wished that their child would initiate use of the device in multiple settings and for multiple reasons. Relatedly, one expert discussed meaningful change as a child understanding the value in communication. In their view, "increased association of using the device and receiving desired stimulus" would reflect this understanding.

Both caregivers and experts mentioned that the ability to communicate with other people (outside primary caregivers/family members/teachers) would be meaningful. Examples included more communication at school, with peers, with less familiar family members, or in other environments. Caregivers and experts also mentioned that social 'back-and-forth' conversation skills (i.e., "turn-taking") are really important to social well-being, even if this is entirely nonverbal.

## Discussion

To our knowledge, this is one of the first systematic, qualitative explorations of communication ability in individuals with AS from the perspective of caregivers with an explicit focus on future measurement development. Caregivers could clearly articulate how their child communicated in the areas of expressive, receptive, and pragmatic communication, supporting multiple relevant concepts that could be included in future measures (Figure 1). Caregivers in the sample also reported a spectrum of communication behaviors within the identified functions, indicating variability within this population.

Communication Ability in Angelman Syndrome

**Table 6**

*Themes Identified When 22 Caregivers and Six Clinicians Were Asked About Meaningful Changes in Communication for Individuals With Angelman Syndrome*

| Theme | Caregivers[a] | Clinicians[a] | Caregiver Quotations[b] |
|---|---|---|---|
| More complex communication (higher vocabulary, stringing words/symbols together, more back-and-forth dialogue) | 13 | 2 | It could be having some words like no and yes, or it could be something even more like—you know, the most meaningful change would be to have like a vocabulary of 1,000 or 2,000 words with verbs and, you know, the whole thing. |
| | | | If she could actually do more signs or better signs to use her fine motor skills better, if she added any vowel-consonant sounds for a word approximation, if she started describing even more on her talker, you know, great, she wants to go to the store. If she said she wants to go to the grocery store, or she wants to go to the store for bananas, just adding on top of any of the building blocks she already had would be immensely helpful. |
| More initiation of communication | 6 | 2 | I think meaningful change would be him taking more of the initiative to use pictures or an [device] rather than us initiating it and reminding him to use those things. |
| | | | What I would love to see is her be able to not so much always be responding to questions in terms of what she wants, but to be able to initiate communication. |
| Communication with other people | 4 | 4 | Connecting socially with others, I mean, other than us, just being able to have a conversation with someone else, connecting in that regard... |
| Verbal speech | 6 | 0 | I guess if she could speak, that would—She could actually use words. That would be the most profound. |
| | | | Obviously, I mean, the most meaningful change in communication would be speech, right. . . . Because that is ultimately—and it could just be having a hello and a goodbye, you know? That would be a wonderful meaningful change. |
| Communication around safety or feeling sick | 4 | 2 | I mean there's always the fear that your child will be abused, so there's like the sense that you want them to be able to tell if someone's hurting them. |
| | | | A meaningful change in communication, would just—sorry, this question gets me every time. Every time I think about communication. Just knowing what hurts. If something hurts, knowing what he needs. |

(Table 6 continued)

**Table 6**
*Continued*

| Theme | Caregivers[a] | Clinicians[a] | Caregiver Quotations[b] |
|---|---|---|---|
| Better motor skills to facilitate communication | 4 | 0 | I think it's not a cognitive impairment that keeps her from talking, it seems to me that it's a motor impairment. When she wants to talk, she knows what she wants to say, but she's not able to do it. |
| Communication success | 3 | 2 | I would really want him to be able to clearly state what his needs are and what his dislikes are, so I would like it if I could just say concretely if he could use his [device] and he could tell people "I want that" or "I don't like that" in a very consistent way or even build sentences like, "I want to go to the zoo," |
| Less aggressive communication | 2 | 2 | I think that's where a lot of his frustration comes from, the behaviors, is because it's kinda like stuck in his head but he can't get it out. |
| Expressing feelings | 2 | 1 | Like real communication, we do every day … feelings like missing, love. That kind of communication he can have besides just making requests or something, you know? |

[a]Frequency counts in columns 2 and 3 were calculated during rapid data analysis using data extracted via structured debriefing forms. These numbers are meant to support salience of each theme to caregivers and clinicians who participated in the interviews, but are not meant to represent overall prevalence in the population.
[b]Example quotations were pulled from caregiver interview transcripts to illustrate themes.

Our results support the unique communication profile of individuals with AS identified by previous research (Alvares & Downing, 1998; Calculator, 2013; Didden et al., 2009; Pearson et al., 2019; Quinn & Rowland, 2017). Data from both caregivers and clinicians confirmed the importance of considering alternative modalities used by individuals with AS when communicating. Words and word approximations were not common, and even when individuals used words (e.g., "mama"), they often did not rely on them for many communication functions. Any future measurement tool for this population must consider the implications of these alternative modalities and their ability to increase communication ability in the absence of verbal speech.

In the eyes of caregivers, meaningful changes in communication consisted primarily of improvements in language complexity with a focus placed on verbal speech. Caregivers also prioritized allowing their child to be more universally understood by others and to have more freedom of expression. Clinicians also discussed these themes. Almost all caregivers in our sample reported multiple changes that could be "meaningful," including behaviors that were very specific to the family situation. Thus, any future explorations of meaningful change in communication ability within clinical trials should allow for multiple areas of improvement.

It is important to note that recruitment occurred through collaboration with one patient advocacy organization. Strong partnerships with patient advocacy organizations are an invaluable asset to research done in rare disease populations but also have limitations (Pinto et al., 2016; Vat et al., 2017). In our study, we utilized a purposeful sampling approach, stratifying our enrollment by age group, and including specific recruitment targets for genotype and race/ethnicity with the goal of diversity across these variables. Although we met our prespecified targets for enrollment, our sample does not fully represent all subgroups of caregivers and individuals with AS. Importantly, our sample consists of caregivers with overall high levels of education and only two fathers and one female legal guardian. Future work should continue to carefully gather validity evidence with diverse samples.

## Conclusion

In this work, we describe caregiver identified communication behaviors within expressive, receptive, and pragmatic functions (Figure 1) and through numerous symbolic and non-symbolic modalities for individuals with AS, supporting the utility of caregiver report. These qualitative findings can be used to inform the development an AS-specific measure capturing communication from the caregiver's perspective for use in clinical trials. Future work should include also exploration of the frequency of communication behaviors in the larger population of individuals with AS, estimate developmental trajectories for communication, and confirm results in a larger sample of diverse caregivers.

## References

Alvares, R. L., & Downing, S. F. (1998). A survey of expressive communication skills in children with Angelman syndrome. *American Journal of Speech - Language Pathology, 7*(2), 14.

Andersen, W. H., Rasmussen, R. K., & Strmme, P. (2001). Levels of cognitive and linguistic development in Angelman syndrome: a study of 20 children. *Logopedics Phoniatrics Vocology, 26*(1), 2–9.

Bonello, D., Camilleri, F., & Calleja-Agius, J. (2017). Angelman Syndrome: Identification and Management. *Neonatal Network, 36*(3), 142–151. https://doi.org/10.1891/0730-0832.36.3.142

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology, 3*, 77–101. https://doi.org/10.1191/1478088706qp063oa

Buiting, K., Williams, C., & Horsthemke, B. (2016). Angelman syndrome - insights into a rare neurogenetic disorder. *Nature Reviews Neurology, 12*(10), 584–593. https://doi.org/10.1038/nrneurol.2016.133

Calculator, S. N. (2013). Use and acceptance of AAC systems by children with Angelman syndrome. *Journal of Applied Research in Intellectual Disabilities, 26*(6), 557–567. https://doi.org/10.1111/jar.12048

Clayton-Smith, J. (1993). Clinical research on Angelman syndrome in the United Kingdom: observations on 82 affected individuals. *American Journal of Medical Genetics, 46*(1), 12–15. https://doi.org/10.1002/ajmg.1320460105

Crais, E.R., & Roberts, J. E. (1991). Decision making in assessment and early intervention planning. *Language, Speech, and Hearing Services in Schools, 22*, 19–30. https://doi.org/10.1044/0161-1461.2202.19

Daily, J. L., Nash, K., Jinwal, U., Golde, T., Rogers, J., Peters, M. M., Burdine, R. D., Dickey, C., Banko, J. L., & Weeber, E. J. (2011). Adeno-associated virus-mediated rescue of the cognitive defects in a mouse model for Angelman syndrome. *PLoS One, 6*(12), e27221. https://doi.org/10.1371/journal.pone.0027221

Didden, R., Sigafoos, J., Korzilius, H., Baas, A., Lancioni, G. E., O'Reilly, M. F., & Curfs, L. M. G. (2009). Form and function of communicative behaviours in individuals with Angelman syndrome. *Journal of Applied Research in Intellectual Disabilities, 22*(6), 526–537. https://doi.org/10.1111/j.1468-3148.2009.00520.x

Given, L. M. (2008). *The SAGE encyclopedia of qualitative research methods* (Vols. 1-0). SAGE Publications. https://doi.org/10.4135/9781412963909

Grieco, J. C., Bahr, R. H., Schoenberg, M. R., Conover, L., Mackie, L. N., & Weeber, E. J. (2018). Quantitative measurement of communication ability in children with Angelman syndrome. *Journal of Applied Research in Intellectual Disabililities, 31*(1), e49–e58. https://doi.org/10.1111/jar.12305

Jolleff, N., & Ryan, M. M. (1993). Communication development in Angelman's syndrome. *Archives of Disease in Childhood, 69*(1), 148–150. https://doi.org/10.1136/adc.69.1.148

Keute, M., Miller, M. T., Krishnan, M. L., Sadhwani, A., Chamberlain, S., Thibert, R. L., Tan, W., Bird, L. M., & Hipp, J. F. (2020). Angelman syndrome genotypes manifest varying degrees of clinical severity and developmental impairment. *Molecular Psychiatry*. https://doi.org/10.1038/s41380-020-0858-6

Margolis, S. S., Sell, G. L., Zbinden, M. A., & Bird, L. M. (2015). Angelman syndrome. *Neurotherapeutics, 12*(3), 641–650. https://doi.org/10.1007/s13311-015-0361-y

Meng, L., Ward, A. J., Chun, S., Bennett, C. F., Beaudet, A. L., & Rigo, F. (2015). Towards a therapy for Angelman syndrome by targeting a long non-coding RNA. *Nature, 518*(7539), 409–412. https://doi.org/10.1038/nature13975

Mertz, L. G., Thaulov, P., Trillingsgaard, A., Christensen, R., Vogel, I., Hertz, J. M., & Ostergaard, J. R. (2014). Neurodevelopmental outcome in Angelman syndrome: genotype-phenotype correlations. *Research in Developmental Disabilities, 35*(7), 1742–1747. https://doi.org/10.1016/j.ridd.2014.02.018

Micheletti, S., Palestra, F., Martelli, P., Accorsi, P., Galli, J., Giordano, L., Trebeschi, V., & Fazzi, E. (2016). Neurodevelopmental profile in Angelman syndrome: More than low intelligence quotient. *Italian Journal of Pediatrics, 42*(1), 91. https://doi.org/10.1186/s13052-016-0301-4

Nowell, L. S., Norris, J. M., White, D. E., & Moules, N. J. (2017). Thematic analysis: Striving to meet the trustworthiness criteria. *International Journal of Qualitative Methods, 16*(1), 1–13. https://doi.org/10.1177/1609406917733847

Paul, R. (2001). *Language disorders from infancy through adolesence: Assessment and intervention* (2nd ed.). Mosby.

Pearson, E., Wilde, L., Heald, M., Royston, R., & Oliver, C. (2019). Communication in Angelman syndrome: A scoping review. *Developmental Medicine & Child Neurology.* https://doi.org/10.1111/dmcn.14257

Penner, K. A., Johnston, J., Faircloth, B. H., Irish, P., & Williams, C. A. (1993). Communication, cognition, and social interaction in the Angelman syndrome. *American Journal of Medical Genetics, 46*(1), 34–39. https://doi.org/10.1002/ajmg.1320460108

Pinto, D., Martin, D., & Chenhall, R. (2016). The involvement of patient organisations in rare disease research: A mixed methods study in Australia. *Orphanet Journal of Rare Diseases, 11*(2), 1–15. https://doi.org/10.1186/s13023-016-0382-6

Quinn, E. D., & Rowland, C. (2017). Exploring expressive communication skills in a cross-sectional sample of children and young adults with Angelman syndrome. *American Journal of Speech-Language Pathology, 26*(2), 369–382. https://doi.org/10.1044/2016_ajslp-15-0075

Sadikovic, B., Fernandes, P., Zhang, V. W., Ward, P. A., Miloslavskaya, I., Rhead, W., Rosenbaum, R., Gin, R., Roa, B., & Fang, P. (2014). Mutation update for UBE3A variants in Angelman syndrome. *Human Mutation, 35*(12), 1407–1417. https://doi.org/10.1002/humu.22687

Vat, L.E., Ryan, D. & Etchegary, H. (2017). Recruiting patients as partners in health research: A qualitative descriptive study. *Research Involvement and Engagement, 3*(15), 1–14. https://doi.org/10.1186/s40900-017-0067-x

Wheeler, A. C., Sacco, P., & Cabo, R. (2017). Unmet clinical needs and burden in Angelman syndrome: A review of the literature. *Orphanet Journal of Rare Diseases, 12*(1), 164. https://doi.org/10.1186/s13023-017-0716-z

Willgoss, T., Cassater, D., Connor, S., Krishnan, M. L., Miller, M. T., Dias-Barbosa, C., Phillips, D., McCormack, J., Bird, L. M., Burdine, R. D., Claridge, S., & Bichell, T. J. (2020). Measuring what matters to individuals with Angelman syndrome and their families: Development of a patient-centered disease concept model. *Child Psychiatry & Human Development, 52*(4), 654–668. https://doi.org/10.1007/s10578-020-01051-z

Wolter, J. M., Mao, H., Fragola, G., Simon, J. M., Krantz, J. L., Bazick, H. O., Oztemiz, B., Stein, J. L., & Zylka, M. J. (2020). Cas9 gene therapy for Angelman syndrome traps Ube3a-ATS long non-coding RNA. *Nature, 587*(7833), 281–284. https://doi.org/10.1038/s41586-020-2835-2

Zylka, M. J. (2020). Prenatal treatment path for Angelman syndrome and other neurodevelopmental disorders. *Autism Research, 13*(1), 11–17. https://doi.org/10.1002/aur.2203

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