Autism assessment in children with optic nerve hypoplasia and other vision impairments

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AIM This study examined the utility of standard autism diagnostic measures in nine children (aged 5-9y) with severe vision impairment and a range of social and language functioning.

METHOD The Autism Diagnostic Observation Schedule (ADOS) and the Autism Diagnostic Interview, Revised (ADI-R) were systematically modified and used to assess symptoms of autism in children with vision less than or equal to 20/800, the majority of whom had optic nerve hypoplasia. The results of the assessments, including analysis of symptom patterns, were compared with expert autism diagnoses.

RESULTS Modified autism measures demonstrated good agreement with clinical diagnoses. Symptoms found to be most and least reliable in discriminating autism from behaviors common to most children with congenital vision impairment are described. Comparisons of current behavior with parent-reported behaviors from a younger age suggested that some symptoms of autism in very young children who are congenitally blind may improve with age.

INTERPRETATION The ADOS and ADI-R are useful for clinical assessment and for advancing research efforts to understand autism symptoms in children with vision impairment. However, some autistic symptoms in very young children may change over time, and developmental changes should be closely monitored.

Symptoms suggestive of autism are often described in children with congenital vision impairment. Keeler first described autistic characteristics in five children with retinopathy of prematurity; similar reports have been described over the past 50 years. Fraiberg used the term ‘blindisms’ to describe repetitive, stereotyped behaviors common in congenitally blind children, such as eye rubbing, hand movements (flapping, posturing), rocking, and rhythmic swaying. Brown et al. described autistic features prevalent in congenitally blind children, including atypical exploration of new objects (touch, smell), pronoun reversal, limited imaginative play, and self-stimulatory motor behaviors. These stereotypic behaviors are not confined to those children with intellectual impairment. Clinicians and researchers have debated to what extent these characteristics can be attributed solely to congenital vision impairment as opposed to indicating an autism diagnosis. Most children with vision impairment have additional medical and developmental comorbidities which further complicate the diagnostic picture. This is particularly true in children with optic nerve hypoplasia (ONH), the leading ocular cause of vision impairment. Research addressing the prevalence and developmental course of autism symptoms in children with congenital vision impairment has been hampered by the lack of reliable and valid measures for assessing autism in this population.

Guidelines for autism intervention advise beginning treatment as early as possible; however, often, there is difficulty obtaining a comprehensive clinical assessment and appropriate services for children with vision impairment who also have autism. It is essential to identify and validate autism diagnostic tools so that clinicians can accurately diagnose autism in children with vision impairment and initiate appropriate interventions. Research to test typical autism interventions in children with vision impairment is minimal, consisting entirely of small case series, better consensus about appropriate methods of diagnosis of autism in this population will aid in the design of more rigorous intervention studies.

Investigators and clinicians have independently modified existing autism measures when assessing children with vision impairment. Modifications exclude items specific to visual responsiveness and adjust cut-off scores in the Childhood Autism Rating Scale, Autism Behavior Checklist, and Social Responsiveness Scale. However, the validity of modifications has not been tested, and they only address items that are directly vision dependent (e.g. eye contact) and not behaviors that may be an indirect result.

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DOI: 10.1111/dmcn.12264
of vision impairment. One published study of autism and vision impairment used retrospective chart data including the Autism Diagnostic Interview, Revised (ADI-R), but without information about whether modifications were made, or specific findings about the ADI-R symptom profile of children with vision impairment both with and without autism. No published studies of children with vision impairment have used the 'criterion standard' observational measure, the Autism Diagnostic Observation Schedule (ADOS; ADOS-2).

This pilot study systematically tested the utility of autism diagnostic measures in children with severe vision impairment with a range of social and language functioning. The objectives were (1) to determine if clinicians can reliably diagnose autism in children with severe vision impairment using modified ADOS and ADI-R measures; (2) to identify specific items on diagnostic measures that correspond with a clinical diagnosis of autism; and (3) to identify symptoms that may be common in all or most children with severe vision impairment and therefore could be less useful in diagnosing autism in this population.

METHOD
Participants
Nine children aged 5 to 9 years with severe vision impairment were recruited between May 2009 and September 2011 by a neuro-ophthalmologist at a major children’s hospital, where all data were collected. Inclusion criteria were that children must have severe vision impairment, be ambulatory and be English-speaking. Severe vision impairment was defined as best corrected visual acuity of 20/800 (meaning the ability to see at 20 feet what a person with typical vision can see at 800 feet) or worse. An experienced pediatric neuro-ophthalmologist assessed visual acuity using methods described previously. For children with limited communication, vision was assessed behaviorally and inclusion was based on an inability to fixate or pursue 6-inch toys as close as one foot. Since valid ADOS administration requires children to be ambulatory, children with significant motor impairment including cerebral palsy were excluded. In order to have an adequate sample to test the autism measures, the investigators purposefully selected individuals from a practice in which most of the blind children have ONH, a condition believed to predispose to autism. Seven children were congenitally blind as a result of ONH. One child developed optic atrophy after an infection at the age of 4 years. Another child developed vision impairment at the age of 5 years as a result of a head trauma that led to subretinal hemorrhages, retinal gliosis, and cataract. Significant medical history was abstracted from the medical record and participant characteristics are presented in Table I.

Measures
Autism Diagnostic Observation Schedule
The ADOS is a semistructured, standardized observational assessment of communication, social interaction, and play. After consultation with experts on children with vision impairment and approval from the publisher, specific modifications were made regarding (1) free play, where toys with interesting sounds and textures were added to the standard set; (2) the construction task, where an inset shape puzzle was substituted for the standard puzzle; (3) the description of picture, where a zoo scene with raised and textured pieces was substituted for the standard picture. The assessor named each animal as the child felt it, then used the standard ADOS prompts to ask the child to talk about the animals; and (4) telling a story from a book, where a Braille children’s book was substituted for the standard book.

The ADOS-2 was published after the children were assessed. It is functionally equivalent to the ADOS except for updated diagnostic algorithms; codes were transposed onto the ADOS-2 algorithms to compare algorithms for use with this population.

Autism Diagnostic Interview, Revised
The ADI-R is a semistructured, comprehensive diagnostic interview conducted with a parent or caregiver, focused on communication, reciprocal social interactions, and repetitive and stereotyped behaviors/interests. It includes symptoms occurring in the present as well as a retrospective report of symptoms at the age of 4 years. After consultation with experts on children with vision impairment and approval from the publisher, specific modifications were made regarding (1) the onset of symptoms, where symptoms other than vision impairment (developmental, communication, or social concerns) were focused on; and (2) items involving vision, where references to vision were deleted, but examples related to other sensory modalities were retained, or questions were modified to fit children with vision impairment (e.g. changing of 'what does s/he do if someone else smiles at her/him?' to 'what does s/he do if someone says something nice to her/him?').

Fourteen ADI-R items were modified; specific details are available in electronic supporting materials (see Data S1). Changes in scoring procedures for ADOS and ADI-R are discussed under 'Procedures'.

Developmental level
Since language level is critical in determining the appropriate ADOS module and in interpreting symptoms of autism spectrum disorder (ASD), and there are no measures of other aspects of development validated on children with vision impairment in this age group, assessment of children’s level of development focused on language. The ADOS was videotaped and transcribed. Mean length of

What this paper adds
• This study demonstrates the use of modified autism measures in children with vision impairment.
• An analysis of autism symptom patterns in congenital severe vision impairment is provided.
• Developmental changes in children with congenital severe vision impairment are shown.
utterance and additional information about language on
the ADOS was used to determine language phase, follow-
ing procedures outlined in Tager-Flusberg et al. This
rating provided an estimate of developmental functioning.

Procedures

Ethical approval for this study was provided by the Com-
mmittee on Clinical Investigations (IRB). After obtaining
informed consent, the modified ADOS and ADI-R were
administered and scored by the first author, a licensed
psychologist with research certification in both measures.
The first and third authors independently made a clinical
diagnosis of ASD based on the DSM-IV-TR criteria, using
clinical impressions obtained through independent review
of the child’s behaviors, play, and social interactions with
the therapist and the parent during the videotaped ADOS;
parent’s descriptions of the child’s current and prior behav-
iors elicited during the ADI-R; review of available records
provided by the parent; and clinical judgment about the
impact of other factors on any behaviors observed or
described, including, for example, the impact of vision
impairment, developmental delay, medical conditions, cul-
tural factors, or trauma history. Consensus of diagnosis was
reached if the psychologists initially disagreed on diagnosis.
Both psychologists are research-certified in the ADOS, and
have extensive clinical experience in the assessment and
diagnosis of autism in children with complex comorbid
developmental and medical conditions, including vision
impairment.

The ADOS was scored using standard procedures except
the following codes (‘0’ indicates non-autistic behavior):
(1) unusual eye contact and integration of gaze and other
behavior during social overtures were scored ‘N/A’ (coded
‘0’ in the algorithm); (2) responsive social smile was scored
‘0’ if the child smiled when the assessor talked to the child
in a friendly manner that did not imply physical touching;
(3) response to the child’s name was scored ‘0’ if the child
paused and clearly oriented to the assessor (e.g. turning
– eye contact was not required;
(4) pointing, requesting, showing, spontaneous initiation of
joint attention, language production, and linked non-verbal
communication were scored ‘0’ if all criteria for ‘0’ were
met except integration of eye contact; (5) response to joint
attention was scored ‘0’ if the child responded to the asses-
sor’s verbal cue of ‘look at that’! by orienting or verbaliz-
ing in an attempt to identify the object being referenced;
and (6) regarding unusual sensory interest in play material/
person, close visual examination or tactual exploration
(using the hands) to identify an object were not coded as
unusual sensory interests.

The ADI-R was scored using standard procedures except
the following codes: (1) direct gaze was scored ‘N/A’
(coded ‘0’ in the algorithm); (2) social smiling was scored ‘0’ if the child smiled in response to friendly verbalizations from others; and (3) pointing was scored ‘0’ if the child pointed to express interest – eye contact not required.

RESULTS
Developmental level
On the measure of expressive language, two children were rated as language phase 1 (pre-verbal communication), two children were rated as language phase 3 (word combinations), and five children were rated as language phase 4 (sentences). Table I identifies those children who had a previous history of developmental delay documented in their medical chart.

Clinical autism diagnosis reliability
The two clinicians agreed on seven of the children’s diagnoses (agreement rate 78%; kappa=0.55). In two cases, one clinician diagnosed pervasive developmental disorder not otherwise specified, and the other clinician diagnosed no ASD. The consensus diagnosis was no ASD in one case, and in the other pervasive developmental disorder not otherwise specified.

Relationship between scores on diagnostic tools and clinical autism diagnosis
Scores on the diagnostic measures were compared to the clinical diagnoses; see Tables II and III for results. The ADOS classification using the original algorithm (with modifications described above) matched the clinician diagnoses in all cases. Using the ADOS-2 algorithm, one child without ASD clinical diagnosis scored above the ADOS-2 autism cut-off.

The ADI-R classification, using the standard diagnostic algorithm focused on symptoms at the age of 4 years with the modifications described above, matched the clinician diagnoses in five out of nine cases. Using the ADOS-2 algorithm, one child without ASD clinical diagnosis scored above the ADOS-2 autism cut-off.

To discriminate between children with and without a clinical diagnosis of ASD, it was considered to have poor discrimination if 80% or more of the children with ASD scored ‘1’, ‘2’, or ‘3’. Table IV presents the individual items with ‘good’ and ‘poor’ discrimination for ADOS and ADI-R current behavior.

<table>
<thead>
<tr>
<th>Table II: Diagnostic classifications by child</th>
</tr>
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<tbody>
<tr>
<td>ASD</td>
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<tr>
<td>-----</td>
</tr>
<tr>
<td>1</td>
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<tr>
<td>2</td>
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<td>3</td>
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<td>4</td>
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<td>5</td>
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<td>6</td>
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<td>7</td>
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<td>8</td>
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<td>9</td>
</tr>
</tbody>
</table>

ASD, autism spectrum disorder; ADOS, Autism Diagnostic Observation Schedule; ADI-R, Autism Diagnostic Interview – Revised; PDD, pervasive developmental disorder – not otherwise specified.

Table III: Sensitivity, specificity, and diagnostic agreement of measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Children with ASD diagnosis exceeding cut-off (%)</th>
<th>Children with no ASD scoring below cut-off (%)</th>
<th>Agreement with clinical diagnosis (%)</th>
<th>Kappa statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADOS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>original algorithm</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>1.0</td>
</tr>
<tr>
<td>ADOS-2 algorithm</td>
<td>100</td>
<td>80</td>
<td>89</td>
<td>0.77</td>
</tr>
<tr>
<td>ADI-R standard algorithm</td>
<td>75</td>
<td>40</td>
<td>56</td>
<td>0.14</td>
</tr>
<tr>
<td>ADI-R current behavior</td>
<td>75</td>
<td>100</td>
<td>89</td>
<td>0.77</td>
</tr>
</tbody>
</table>

ASD, autism spectrum disorder; ADOS, Autism Diagnostic Observation Schedule; ADI-R, Autism Diagnostic Interview – Revised.

the age of 5 years. Using the current behavior score on the ADI-R and comparing it with the cut-offs for the diagnostic algorithm, ADI-R classification matched clinician diagnoses in eight out of nine cases (89% agreement; kappa=0.77). The following behaviors were abnormal based on parent report at the age of 4 years in all three children with congenital vision impairment who were not diagnosed with ASD, but were not abnormal in the non-congenital vision impairment group: reciprocal conversation, nodding head for ‘yes’, shaking head for ‘no’, spontaneous imitation of actions; imaginative play with peers; range of facial expressions; initiation of appropriate activities; group play with peers; social disorganization; circumscribed interests; repetitive use of objects or parts of objects; unusual sensory interests; hand and finger mannerisms; and other complex mannerisms.

Individual scoring codes were reviewed to determine which items best discriminated between children with and without a clinical diagnosis of ASD. Codes were considered to discriminate well if 75% or more of the children diagnosed with autism had a ‘1’, ‘2’, or ‘3’ score, and almost all children with no ASD diagnosis scored ‘0’. Codes were considered to have poor discrimination if 80% or more of the children with no ASD scored ‘1’, ‘2’, or ‘3’. Table IV presents the individual items with ‘good’ and ‘poor’ discrimination for ADOS and ADI-R current behavior.

DISCUSSION
This pilot study provides preliminary evidence in support of the clinical utility of the ADOS and the ADI-R in the evaluation of children with severe vision impairment. The data suggest specific symptoms that may be more reliable than others in discriminating autism from behaviors that may be common to all or most children with congenital vision impairment. These findings contribute to the limited literature on autism in children with vision impairment by utilizing a prospective (rather than a chart review) design as well as criterion standard observational and interview diagnostic measures, and detailing modifications so that findings can be replicated.
Experienced clinicians using slightly modified diagnostic tools demonstrated interrater reliability in the diagnosis of ASD in the majority of children assessed. Results of ADOS testing and current behavior ratings on the ADI-R corresponded closely with clinical diagnoses, although these were not independent since clinicians used ADOS and ADI-R results in reaching a diagnostic conclusion; this approach is similar to that used by Lord et al.26 in the original validation studies for the ADOS with sighted children.26 Blindness did not prevent the children without ASD from demonstrating levels of social engagement and social communication during the ADOS that clearly distinguished them from children with ASD. This study provides initial guidance regarding which symptoms may be most important in the diagnosis of autism in children with congenital severe vision impairment. Findings indicate that some symptoms suggestive of autism in sighted children do not distinguish children with ASD and vision impairment from children without ASD with vision impairment. Clinicians should be cautious about giving clinical significance to characteristics that were common in all or almost all congenitally blind children in the present study (thus showing limited specificity), such as repetitive or stereotyped finger or hand movements, repetitive interests or stereotyped behaviors, absence of pointing, limited range of facial expressions, undue sensitivity to noise, difficulty with imaginative play by parent report, and difficulty establishing age-appropriate friendships. Some of these symptoms (especially stereotyped behaviors) have also been found in other studies to be common in most children with congenital vision impairment.2,4,27 Given the frequency of stereotyped behaviors in children without ASD with vision impairment, the revised ADOS-2 algorithms (which include stereotyped behaviors in the total score), may be less appropriate for children with vision impairment than the original ADOS algorithm, which excludes these behaviors from the total score.

On the other hand, there were many symptoms of autism that had more reliable clinical significance in this sample because they were not present in the children with vision impairment who did not meet criteria for a clinical ASD diagnosis. Blind children in this age group without ASD were able to demonstrate appropriate responsiveness to social situations and appropriate social overtures such as shared enjoyment, offering comfort, and directing others’ attention. There were problematic behaviors reported almost exclusively in the blind children with ASD, and not in those without ASD, including aggression (toward family members and non-family members) and self-injury.

Another notable finding was that parents of several children with congenital vision impairment reported marked differences in their children’s behavior before and after the age of 5 years, with more autistic symptoms at the age of 4 years (the focus of the ADI-R interview) compared with present symptoms (at the age of 6–9y). As these children developed and became more comfortable fully exploring their environments, their reciprocal social and communicative behaviors increased dramatically, and their self-stimu-

### Table IV: Correspondence of clinical diagnosis with individual items

<table>
<thead>
<tr>
<th>Correspondence with diagnosis</th>
<th>Autism Diagnostic Observation Schedule item</th>
<th>Children with ASD diagnosis score 1, 2, or 3 (%)</th>
<th>Children with no ASD score 0 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>Frequency of vocalization directed to others (module 1)/amount of social ovetures (module 2)</td>
<td>75</td>
<td>80</td>
</tr>
<tr>
<td>Good</td>
<td>Shared enjoyment in interaction</td>
<td>75</td>
<td>80</td>
</tr>
<tr>
<td>Good</td>
<td>Response to name</td>
<td>75</td>
<td>100</td>
</tr>
<tr>
<td>Good</td>
<td>Response to joint attention</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Good</td>
<td>Quality of social ovetures</td>
<td>100</td>
<td>80</td>
</tr>
<tr>
<td>Good</td>
<td>Imagination/creativity</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Poor</td>
<td>Stereotyped/idiiosyncratic use of words or phrases</td>
<td>50</td>
<td>20</td>
</tr>
<tr>
<td>Poor</td>
<td>Pointing</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Poor</td>
<td>Facial expressions directed toward others</td>
<td>100</td>
<td>20</td>
</tr>
<tr>
<td>Poor</td>
<td>Unusually repetitive interests or stereotyped behaviors</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>

Autism Diagnostic Interview-Revised

| Good                         | Spontaneous imitation of actions                                                                         | 100                                           | 80                             |
| Good                         | Imaginative play with peers                                                                              | 100                                           | 80                             |
| Good                         | Showing and directing attention                                                                           | 100                                           | 80                             |
| Good                         | Seeking to share enjoyment with others                                                                    | 75                                            | 100                            |
| Good                         | Offering comfort                                                                                        | 75                                            | 100                            |
| Good                         | Appropriateness of social responses                                                                      | 75                                            | 80                             |
| Good                         | Response to approaches of other children                                                                 | 75                                            | 100                            |
| Good                         | Abnormal, idiiosyncratic, negative response to specific sensory stimuli                                  | 100                                           | 80                             |
| Good                         | Aggression toward caregivers or family members                                                           | 75                                            | 80                             |
| Good                         | Self-injury                                                                                              | 75                                            | 80                             |
| Poor                         | Imaginative play                                                                                        | 100                                           | 20                             |
| Poor                         | Friendships                                                                                             | 100                                           | 20                             |
| Poor                         | Undue general sensitivity to noise                                                                         | 100                                           | 20                             |

ASD, autism spectrum disorder.
latory and repetitive behaviors significantly decreased. Therefore, diagnoses of ASD in very young children with vision impairment may be less reliable than in sighted children and may not persist over time. This observation is consistent with research by Hobson and Lee,17 who re-evaluated nine congenitally blind children and sighted comparison children, all of whom were initially diagnosed with autism. Eight years after the initial diagnosis, only one of the nine blind participants met criteria for autism while all seven children in the sighted group continued to meet autism criteria. Additional research is needed to follow children with congenital vision impairment over time, with frequent assessments beginning in infancy, in order to identify common developmental trajectories in autistic symptoms. Measures such as those tested in this study would be especially helpful to allow delineation of changes in specific symptoms over time.

This is a preliminary study with a small sample size, and as such there are a number of limitations. The study does not attempt to determine the prevalence of ASD in children with severe vision impairment. Participants were not randomly selected, but rather chosen intentionally so as to provide a sample with a range of reported autistic-like symptoms and levels of developmental functioning to better test the utility of the autism measures. This preliminary evaluation of the utility of the modified autism measures was a first step toward being able to conduct robust research regarding ASD prevalence in this population. Subsequent research is needed to validate the measures in a larger sample, including children with a wider range of diagnoses and levels of vision impairment. Our study suggests that such a study may lead to modified ADOS and ADI algorithms and cut-offs for children with severe vision impairment.

All seven of the participants with congenital vision impairment had ONH. ONH is rarely isolated to vision impairment and the typical spectrum of associated clinical characteristics was represented in participants both with and without ASD in this study, including neuroradiographic abnormalities, endocrinopathies, and developmental delay. Autism can have multiple etiological pathways and associated clinical symptoms similar to ONH; however, it is difficult to know if the findings from this study can be generalized to children with isolated vision impairment.

The two participants with later-onset vision impairment were also the only participants with a diagnosis other than ONH. Neither participant demonstrated autistic symptoms. The small number of participants with later-onset vision impairment precludes drawing conclusions regarding differences between congenital and non-congenital groups. Qualitative clinical observations about the children with later-onset vision impairment suggested that they (1) used objects more in their play than the congenital vision impairment group; (2) oriented their face more toward the assessor when talking or listening; and (3) used gestures such as nodding the head for ‘yes’ and shaking the head for ‘no’, which were not observed in the children with congenital vision impairment. These preliminary observations suggest that the ADOS may be useful in conducting studies using a much larger sample of children with congenital versus later-onset vision impairment, matched for level of vision impairment; such studies would be helpful in better understanding the impact of early congenital blindness on the development of social interactions.

None of the children in the study, including the four diagnosed with an ASD by the study clinicians, had been previously diagnosed with ASD. Three of the four parents of children with ASD noted that they had considered the possibility of ASD based on the suggestion of other parents who had a child with ASD, or a school professional. However, none of the physicians or psychologists working with the children had made a diagnosis of ASD. This finding of underdiagnosis of ASD in children with vision impairment is consistent with suggestions of other researchers.12

In summary, this study found that modified autism diagnostic measures, including observational and parent interview measures, are useful in conducting diagnostic evaluations in children with severe vision impairment. Clinicians should be cautious of diagnosing autism in very young children with vision impairment, since it appears that symptoms may improve markedly over the course of development in at least some children. In addition, clinicians should be aware that some behaviors (e.g. stereotypes) seem to have poor specificity in children with congenital vision impairment, since they are exhibited by so many children in this population, and therefore should not be considered indicative of autism. Nonetheless, the autism measures were useful in ruling out autism in those children with vision impairment who had appropriate socially reciprocal interactions, and suggest a promising methodology for conducting more extensive studies about the prevalence and developmental course of autism symptoms in children with vision impairment. When diagnosing autism in children with vision impairment, clinicians are encouraged to include multiple sources of information in reaching a clinical judgment, including observational measures, comprehensive parent interviews, and naturalistic observations; use of modified standardized measures such as the ADOS and the ADI-R may prove useful as part of a comprehensive evaluation.

ACKNOWLEDGEMENTS
This research was supported in part by a grant from the Joseph Drown Foundation. The funder had no involvement in study design, data collection, data analysis, manuscript preparation, and/or publication decisions. The authors thank Ruth Rosner, Terese Pawletko, Pamela Garcia-Filion, and Adriana Anaya for their consultation and assistance with the study.

SUPPORTING INFORMATION
Additional supporting information may be found in the online version of this article:

Data S1. Recommended modifications to autism diagnostic interview–revised for children with vision impairments.
REFERENCES


