Systematic review and meta-analysis of the association of Autism Spectrum Disorder in visually or hearing impaired children

*Article* in Ophthalmic and Physiological Optics - March 2017

DOI: 10.1111/opo.12350

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Systematic review and meta-analysis of the association of Autism Spectrum Disorder in visually or hearing impaired children

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Keywords: Autism Spectrum Disorder, disability, hearing impairment, systematic review, visual impairment

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Abstract

Purpose: To determine whether there is an association with a congenital visual or hearing impairment (VI or HI) and Autism Spectrum Disorder (ASD) in children.

Methods: A systematic literature review was performed using nine relevant databases limited to peer reviewed articles in English between 1994 and January 2016. The search identified 1248 articles after duplicates were removed with subsequent screening of the abstracts excluding a further 1199, resulting in 49 full-text articles that were then independently assessed by five of the authors with a final 15 articles meeting the inclusion criteria. Bias assessment was determined through consensus of the first five authors. A meta-analysis of the included studies was performed to estimate the relative risk of ASD in the VI and HI groups compared to the general population based on reported prevalence rates in similar geographical regions. Overall prevalence rates for ASD were calculated from the combined studies in the VI and HI populations.

Results: The overall prevalence of ASD in VI and HI populations was 19% (95% CI 13–25%) and 9% (95% CI 6–12%) respectively. The overall risk-ratio of ASD was greater in the VI 31.0 times (95% CI 18.62–51.56; \( z = 13.21, \ p < 0.001 \) ) and HI groups 14.1 times (95% CI 3.41–58.62; \( z = 3.65, \ p < 0.001 \) ) compared to reported ASD prevalence in the general population.

Conclusion: There is a high association of ASD in VI or HI children and therefore these populations should be assessed for ASD in the presence of a visual or hearing disability.

Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder, affecting the development of social and communication behaviours.\(^1\)–\(^3\) ASD is a lifelong condition that impacts on the individual and their family’s quality of life\(^4\)–\(^5\) but with early intervention the long term outcomes can be significantly improved.\(^6\)–\(^7\) The prevalence rate of ASD in Australia is 0.6\%\(^8\) whilst in the UK and USA rates are closer to 1\% with a similar 4:1 male bias.\(^10\)–\(^11\) The lower prevalence rate in Australia may be due to differences in the referral and diagnostic pathways utilised by these countries.
establish in children with Visual Impairment (VI) or Hearing Impairment (HI) as they may not respond appropriately to social cues and consequently the diagnosis of ASD may be further delayed. This may be due to the difficulties with the methods used to diagnose ASD and/or masking of ASD by the pre-existing sensory impairment.5,15

Currently the term ASD is used to encompass: Autism, Pervasive Developmental Disorder – Not Otherwise Specified and Asperger’s syndrome, as specified by the Diagnostic and Statistical manual of Mental (DSM) disorders, DSM-V criteria.16 The diagnostic features of ASD include difficulty with reciprocal verbal and non-verbal communication and interactions with restricted or repetitive behaviours, interests and activities that are present in the early developmental period.1–3 Verbal communication deficits may range from absence of speech, to language developmental delay.17–19 Nonverbal communication deficits may include a lack of direct eye contact with atypical gestures, facial expressions, body orientation, or speech intonation20–22 coupled with a deficit in the development and understanding of reciprocal social and emotional understanding.1–3

Given the dependence on visual and auditory processing to engage with social interactions, children with congenital VI or HI may also have difficulties in developing their social and communication abilities23,24 leading to autistic like traits or behaviours.25,26 While congenital visual or hearing loss is not a direct cause of ASD, Mukkaddes et al.25 proposed that irrespective of the sensory impairment aetiology, developmental delay can occur with a greater risk of ASD associated with the severity of VI and mental ability. The impact of VI or HI on the development of social communication and appropriate behaviours may be sufficient to result in an association with ASD in these groups by reducing the salience of the visual (faces) and auditory (human voice) cues that are an important part of social human interaction. The superior temporal sulcus is implicated in the pathogenesis of ASD where elements that contribute to social interaction such as facial recognition, human voice27 eye-gaze28 and emotions29 are integrated.

Several studies have investigated the prevalence of ASD in children with VI25,26,28–32 or HI23,33,34 and report an association between VI and HI with ASD, however, it is unclear what level of association there is between VI or HI and ASD. One systematic review of the literature from 1948-2011 was unable to conclude if peripheral hearing loss was associated with ASD.34 Therefore, the aim of this review is to systematically review the recent literature on the prevalence of ASD in both VI and HI populations of children and compare the reported prevalence of ASD to comparative prevalence studies in the general population to estimate the relative risk of ASD in congenital VI and HI populations.

Materials and methods

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)35 publication standards when writing this report.

A systematic literature review was performed to critically evaluate the association between ASD in children with congenital VI or HI. The clinical diagnosis of ASD was in accordance with DSM-III-R, DSM-IV or DSM-V classifications during the literature review period (1994 to January 2016).16,36,37 The publication date of the DSM-IV in 1994 was chosen as the time-point for the beginning of the review as publications from this time would have used either of the diagnostic classifications for autism/ASD specified in these DSM versions that are encompassed by the current DSM-V definition. The studies included were all observational comprising: case series, retrospective cross-sectional studies and surveys. Table 1 lists the inclusion and exclusion criteria for studies included in this review.

Literature search strategy

All database searches were conducted on the 22nd January 2016. No subsequent searches were conducted after this date and grey literature was not sourced. The database searches were conducted in: Medline, Scopus, Web of Science, ProQuest, PubMed, Informit, Cochrane database of systematic reviews, Psychinfo and the Cumulative Index to Nursing and Allied Health Literature. The searches were performed by an experienced librarian. Publication date

Table 1. Inclusion and exclusion criteria for selection of the articles

Inclusion criteria
- HI: Mild hearing loss (minimum aided hearing threshold of ≥ 30 dB)
- VI: Visual acuity ≤ 6/21 (20/70) in the better eye with presenting correction, or visual fields no > 10° in radius from central fixation
- Original study reporting the proportion of participants under the age of 18 with ASD in either HI or VI children, acquired within the first 3 years of life
- Peer reviewed articles available in the public domain from 1994-January 2016 encompassing DSM-III to DSM-5 revisions or ICD-10 as diagnostic standards

Exclusion criteria
- Studies with participants with combined deaf-blindness
- Individual case reports
- Children with cochlear implants with a minimum hearing threshold of < 30 dB
- Non-English articles
- Prevalence not reported

restrictions were applied (1994–2016). Table 2 lists the search items used for the databases.

Data collection

All retrieved references were imported into EndNote ver 9.0 and duplicates removed. The original search of the databases yielded 1878 documents that were reduced to 1248 following duplicate removal. Each author screened the study titles and abstracts to identify those that were relevant to the aims of this review which were cross-checked with another author. This resulted in the exclusion of 1199 papers that did not assess prevalence in the study populations required. The remaining 49 full-text articles were then read by five authors (BD, PL, EM, BS and SS) who assessed each of these full-text articles against the inclusion criteria (Table 1). Any disagreement for final inclusion of the study in the review was settled by a consensus of opinion by these authors resulting in 15 final articles being included in the review. The 15 articles were analysed for bias independently by (BD, PL, EM BS and SS) and cross-checked between these authors (Figure 1).

Full-text articles were excluded if they studied the prevalence of a sensory impairment in an established ASD population, did not report prevalence, did not assess ASD following the diagnosis of a VI or HI or the population group were both deaf and blind (co-morbid sensory disability of deafblindness). To calculate an estimated relative risk ratio for ASD in the separate HI and VI populations, the prevalence rates in the general population were paired with studies in the same or close geographical location and matched with the best available prevalence rates for ASD in the age groups studied in the VI or HI populations. The broad geographical locations were Europe, North and South America and Asia. The main comparative prevalence rates were extracted from studies using a wide and diverse population base centred on either North America (New Jersey) or Europe (London). See Tables 3 and 4 for prevalence data used as a comparison to estimate the relative risk of association between ASD in the VI and HI populations.

Study selection

Fifteen studies were included in this review (Table 5) with eight studies containing only VI populations, five with HI and two studies with both HI and VI populations. There were seven cross-sectional and case series with one retrospective case note review. Ages of participants ranged from 3 to 18 years old, with the proportion of males ranging from 45.8 to 77.4%. Studies took place in the USA, the Netherlands, Turkey, the United Kingdom, Argentina, Canada, Italy, Sweden and Egypt. Diagnostic testing methods varied across the studies reflecting the varied nature of the diagnostic procedures in ASD. Only one study did not report on the methods used to diagnose ASD. Diagnostic methods used included the: Childhood Autism Rating Scale (CARS), Autism Diagnostic Observational Schedule, Autism Diagnostic Interview-Revised, Autism Behavioural Checklist (ABC) checklist for autism in toddlers, behaviour observation, interviews, review of case notes by developmental specialists, DSM-IV, parental interviews, Social Communication Questionnaire (SCQ), Vineland Adaptive Behaviour Scale (VABS), and social and communication repetitive and restricted behaviours (SCRR) as defined by the ICD-10. These diagnostic methods were in line with DSM-III to V, and ICD-10. Table 5 details the final included studies with the populations and diagnostic methods used.

Critical quality appraisal

The authors (BD, PL, EM, BS and SS) conducted the risk of bias assessment individually. Each appraisal of risk of bias was compared between these authors to reach a final

Table 2. Summary of Search terms associated with the natural language term used in this study (Words in bold were truncated to include variations in spelling and plurals). Searches were restricted to human and in the English Language from 1994–January 2016
overall bias conclusion. Bias assessment included: random sequence generation (selection bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other bias. Each study was assessed by consensus for bias as being high, medium or low risk (Figures 2 and 3).

Selection bias
The majority of the studies were conducted within a defined paediatric clinical population. van Gent et al. recruited their population solely from a mental health service, where these children had HI and mental health problems which

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**Table 3.** Autism Spectrum Disorder (ASD) prevalence data for Visually Impaired (VI) populations on the left with the study location and age range used as comparable prevalence rates for ASD in the general population without VI.

<table>
<thead>
<tr>
<th>Studies in the review</th>
<th>Country</th>
<th>Age (years)</th>
<th>Prevalence (%)</th>
<th>Comparable population study</th>
<th>Country</th>
<th>Age (years)</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ek et al.26</td>
<td>Sweden</td>
<td>4–17</td>
<td>41.46</td>
<td>Russell et al.52</td>
<td>UK</td>
<td>7.2–8.2</td>
<td>1.54</td>
</tr>
<tr>
<td>Ek et al.38</td>
<td>Sweden</td>
<td>5–18</td>
<td>46.15</td>
<td>Baird et al.10</td>
<td>UK</td>
<td>9–10</td>
<td>0.45</td>
</tr>
<tr>
<td>Fazzi et al.39</td>
<td>Italy</td>
<td>2–11</td>
<td>16.67</td>
<td>Skoneczna-Zydecka et al.61</td>
<td>Poland</td>
<td>4–7</td>
<td>0.53</td>
</tr>
<tr>
<td>Goodman et al.40</td>
<td>UK</td>
<td>4–11</td>
<td>17.65</td>
<td>Russell et al.52</td>
<td>UK</td>
<td>7.2–8.2</td>
<td>1.54</td>
</tr>
<tr>
<td>Jure et al.32</td>
<td>Argentina</td>
<td>2–18</td>
<td>15.00</td>
<td>Fombonne et al.59</td>
<td>Mexico</td>
<td>8</td>
<td>0.86</td>
</tr>
<tr>
<td>Justley-Neilson et al.41</td>
<td>UK</td>
<td>3–16</td>
<td>33.33</td>
<td>Russell et al.52</td>
<td>UK</td>
<td>7.2–8.2</td>
<td>1.54</td>
</tr>
<tr>
<td>Kancherla et al.23</td>
<td>USA</td>
<td>8</td>
<td>6.87</td>
<td>Bertrand et al.11</td>
<td>USA</td>
<td>6–10</td>
<td>0.61</td>
</tr>
<tr>
<td>Mukaddes et al.25</td>
<td>Turkey</td>
<td>7–18</td>
<td>11.67</td>
<td>Raina et al.60</td>
<td>India</td>
<td>1–10</td>
<td>0.17</td>
</tr>
<tr>
<td>Parr et al.30</td>
<td>USA</td>
<td>1–7</td>
<td>31.33</td>
<td>Bertrand et al.11</td>
<td>USA</td>
<td>3–5</td>
<td>0.55</td>
</tr>
<tr>
<td>van Naarden Braun et al.46</td>
<td>USA</td>
<td>8</td>
<td>7.98</td>
<td>Bertrand et al.11</td>
<td>USA</td>
<td>6–10</td>
<td>0.61</td>
</tr>
</tbody>
</table>
may have contributed to the high prevalence rate in this selected population. In other studies, the populations with VI were from a specific cause (optic nerve hypoplasia)\(^{30,38}\) or retinopathy of prematurity\(^{26}\) and only included those with the poorest vision and had high selection bias. The children recruited by Ahmed \(^{42}\) were self-selected by parents who were concerned about a delay in language development in their children and was classified as a medium bias.

### Detection bias

Detection bias was classified as medium in HI studies and low or medium in VI studies. Chilosi \(^{43}\) Ahmed \(^{42}\), Ek \(^{26}\), Fazzi \(^{39}\) and Mukkades \(^{25}\) were assessed as low risk because they used appropriate ASD diagnostic instruments such as the CARS, Autism Diagnostic Observation Schedule and the revised Autism Diagnostic Interview. Other studies were assessed as medium risk due to the use of less standardised instruments for assessing ASD. Variations in diagnostic criteria and methods may have resulted in an over or under representation of cases. No studies were assessed as high risk because assessors could not be masked to the ASD outcome.

### Attrition bias

Attrition bias was low risk for the majority of the included studies. A low risk of bias was associated with studies where the reported data totalled the number of subjects included in the study groups and when missing data, or losses to follow-up, was not ignored. Kancherla \(^{23}\), Szymanski \(^{33}\), Fitzpatrick \(^{44}\), van Naarden Braun \(^{45}\) and van Gent \(^{46}\) all reviewed and identified the diagnoses either retrospectively from archived data or from population-based data and therefore, attrition was a low risk in these studies.

### Reporting bias

The majority of studies had a low risk of reporting bias for both HI and VI groups. Participants were analysed in their respective groups, data reported equalled the study size and there was clear reporting of testing methods and results included in the studies. Medium risk of bias was indicated if there was unclear reporting of the methods used. Fitzpatrick \(^{44}\), van Naarden Braun \(^{45}\) and van Gent \(^{46}\) had a high risk of reporting bias as they could not access some records and/or had poorly detailed case notes that were not fully reported. These studies were assigned high risk as these factors may have underestimated the number of cases identified.

### Other bias

Other biases included possible confounding factors such as: premature births, co-occurring congenital malformations, intellectual disabilities and deviations from standard testing methods. The majority of the studies had a medium risk of bias, owing to these confounding factors\(^{23,26,41,44,46}\) as well as the use of non-standardised ASD assessments.\(^{30}\) High risk was assigned to Goodman and Minne\(^{40}\) due to Pervasive Developmental Disorder – Not Otherwise Specified not having a standardised diagnostic criterion.

### Descriptive aspects

There was a large heterogeneity between the studies included in the meta-analysis with respect to the age of the study groups. The overall age range of the VI included studies was from 3 to 18 years with the majority of the studies including children in the age range of 3–8 years\(^{32,38–41}\) with only one study including older children from 7 to 18 years.\(^{25}\) For the HI studies the age ranges were predominantly 3–6 years\(^{23,44}\) with one study including older children from 5 to 16 years.\(^{33}\) The age range of the study groups is important when evaluating the prevalence of ASD in these populations as the diagnosis of ASD may not be recognised at the time of diagnosis of the HI or VI\(^{23,44}\) thus studies incorporating older children were more likely to include children with a diagnosis of ASD.

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**Table 4. Autism Spectrum Disorder (ASD) prevalence data for Hearing Impaired (HI) populations on the left with the study location and age range used as comparable prevalence rates for ASD in the general population without HI**

<table>
<thead>
<tr>
<th>Studies in the review</th>
<th>Country</th>
<th>Age (years)</th>
<th>Prevalence (%)</th>
<th>Comparable population study</th>
<th>Country</th>
<th>Age (years)</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmed et al.(^{42})</td>
<td>Egypt</td>
<td>3–5</td>
<td>74.23</td>
<td>Bertrand et al.(^{11})</td>
<td>USA</td>
<td>6–10</td>
<td>0.61</td>
</tr>
<tr>
<td>Chilosi et al.(^{43})</td>
<td>Italy</td>
<td>1–16</td>
<td>5.00</td>
<td>Skonieczna-Zydecka et al.(^{61})</td>
<td>Poland</td>
<td>4–7</td>
<td>0.53</td>
</tr>
<tr>
<td>Fitzpatrick et al.(^{44})</td>
<td>Canada</td>
<td>0–18</td>
<td>2.04</td>
<td>Bertrand et al.(^{11})</td>
<td>USA</td>
<td>6–10</td>
<td>0.61</td>
</tr>
<tr>
<td>Kancherla et al.(^{23})</td>
<td>USA</td>
<td>8</td>
<td>5.48</td>
<td>Bertrand et al.(^{11})</td>
<td>USA</td>
<td>6–10</td>
<td>0.61</td>
</tr>
<tr>
<td>Szymanski et al.(^{33})</td>
<td>USA</td>
<td>5–17</td>
<td>1.84</td>
<td>Bertrand et al.(^{11})</td>
<td>USA</td>
<td>6–10</td>
<td>0.61</td>
</tr>
<tr>
<td>van Gent et al.(^{46})</td>
<td>Holland</td>
<td>10.2</td>
<td>23.65</td>
<td>Baird et al.(^{10})</td>
<td>UK</td>
<td>9–10</td>
<td>0.45</td>
</tr>
<tr>
<td>van Naarden Braun et al.(^{45})</td>
<td>USA</td>
<td>8</td>
<td>7.04</td>
<td>Bertrand et al.(^{11})</td>
<td>USA</td>
<td>6–10</td>
<td>0.61</td>
</tr>
</tbody>
</table>
In addition to the variations in age of the study groups there were some differences in the inclusion criteria for the VI and HI groups. For VI, the inclusion criteria ranged from no light perception\(^26,38\) to a lower threshold of best corrected monocular acuity of LogMAR 0.54.\(^23,45\) However, three studies did not report an exact visual acuity level and included those as ‘partially sighted to no light perception’,\(^39\) ‘partial congenital or acquired visual loss’\(^32\) or ‘mild/moderate to profound visual loss’\(^41\) in accordance with the ICD-10 definition of visual impairment.\(^54\) For the HI studies there was a greater concordance between the studies for the inclusion criteria of > 30 dB which is the clinical level of HI that requires a hearing aid. Two studies whose inclusion criteria included the 30 dB cut-off were included in the analysis: Szymanski \textit{et al.}\(^33\) with 27–40 dB and Ahmed \textit{et al.}\(^42\) with 25–36 dB.

The diagnosis of ASD may depend upon the consensus of clinical judgement from a multi-disciplinary team with the support of standardised clinical assessment instruments.\(^48,49\) There were a variety of methods used by the study groups to quantify the autistic nature of the cases such as the CARS.\(^25,26,42,43\) However, the CARS is limited because it does not take into account the relative weight of the three diagnostic domains and may overestimate the prevalence of ASD.\(^55\) This may account for the higher prevalence rates reported by Ahmed \textit{et al.}\(^42\) who found a 10% prevalence rate of ASD in their control comparison group.\(^42\) However, the Childhood Autism Rating Scale

### Table 5. Summary of studies included in the review

<table>
<thead>
<tr>
<th>Study</th>
<th>Case (N)</th>
<th>Study design</th>
<th>Age (years)</th>
<th>ASD diagnostic instruments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmed \textit{et al.}(^42)</td>
<td>HI (180)</td>
<td>Retrospective case series</td>
<td>3.00–4.75</td>
<td>CARS</td>
</tr>
<tr>
<td>Chilosi \textit{et al.}(^43)</td>
<td>HI (100)</td>
<td>Case series</td>
<td>0.67–16.00</td>
<td>Behaviour observation</td>
</tr>
<tr>
<td>Ek \textit{et al.}(^26)</td>
<td>VI (43)</td>
<td>Controlled population based</td>
<td>4–17</td>
<td>CARS, ADOS, ADI-R</td>
</tr>
<tr>
<td>Ek \textit{et al.}(^38)</td>
<td>VI (13)</td>
<td>Retrospective case series</td>
<td>5–15</td>
<td>Interviews, Case record review, Behavioural observation, ABC</td>
</tr>
<tr>
<td>Fazzi \textit{et al.}(^39)</td>
<td>VI (24)</td>
<td>Case series</td>
<td>2–11</td>
<td>Behavioural observation</td>
</tr>
<tr>
<td>Fitzpatrick \textit{et al.}(^44)</td>
<td>HI (785)</td>
<td>Retrospective case series</td>
<td>0–18</td>
<td>Case record review using DSM-IV</td>
</tr>
<tr>
<td>Goodman \textit{et al.}(^50)</td>
<td>VI (17)</td>
<td>Controlled population based</td>
<td>4–11</td>
<td>ABC</td>
</tr>
<tr>
<td>Jure \textit{et al.}(^32)</td>
<td>VI (38)</td>
<td>Cross-sectional</td>
<td>2–18</td>
<td>Clinical assessments, Developmental, Dimensional and Diagnostic Interview</td>
</tr>
<tr>
<td>Jutley-Neilson \textit{et al.}(^41)</td>
<td>VI (42)</td>
<td>Cross-sectional</td>
<td>3–16</td>
<td>VABS</td>
</tr>
<tr>
<td>Kancherla \textit{et al.}(^23)</td>
<td>VI (278)</td>
<td>Retrospective</td>
<td>8</td>
<td>Documentation of behaviours using DSM-IV criteria</td>
</tr>
<tr>
<td>Mukaddes \textit{et al.}(^25)</td>
<td>VI (308)</td>
<td>Controlled population based</td>
<td></td>
<td>ABC</td>
</tr>
<tr>
<td>Par et al.(^30)</td>
<td>VI (257)</td>
<td>Case series</td>
<td>7–18</td>
<td>ABC, CARS</td>
</tr>
<tr>
<td>Szymanski \textit{et al.}(^33)</td>
<td>HI (37 828)</td>
<td>Cross-sectional (national database)</td>
<td>5–17</td>
<td>Previous diagnosis in line with DSM-IV or IDEA</td>
</tr>
<tr>
<td>van Gent \textit{et al.}(^46)</td>
<td>HI (3750)</td>
<td>Cross-sectional</td>
<td>Mean 10.2</td>
<td>Parent and family interviews, Psychiatric interviews, self-reports using DSM-IV criteria</td>
</tr>
<tr>
<td>van Naarden Braun \textit{et al.}(^45)</td>
<td>VI and HI (5590)</td>
<td>Cross-sectional (survey)</td>
<td>8</td>
<td>Case record review using DSM-IV</td>
</tr>
</tbody>
</table>

(CARS) is superior to the Autism Behavioral Checklist (ABC) in distinguishing individuals with autistic disorders from other cases of development disorders. Other ASD assessment tools used in the studies included the Autism Diagnostic Interview-Revised, parent interviews, case note review, behavioural observation, Social Communication Questionnaire (SCQ), Vineland Adaptive Behaviour Scale (VABS), Social and Communication Repetitive and Restricted behaviours (SCRR) score and the Wechsler Intelligence Scale for Children (WISC). The Autism Diagnostic Observation Schedule allows for a structured assessment across diagnostic domains that can be applied to the developmental age of the individual. However, only one of the included studies used the Autism Diagnostic Observation Schedule to give a reliable index of ASD severity.

It is important to note that the assessment instruments have not been validated for children with a VI or HI. Therefore, some studies modified the procedures. For example, Fazzi et al. excluded the item VII (Visual Responsiveness) in the CARS and adjusted the scores to reflect the various degrees of autism. The included studies were completed in different monolingual countries although not all ASD assessment tools have been validated for each linguistic population - except the CARS for use with a Swedish population.

Prior to 2013, the DSM-IV was in use since its establishment in 1994. Most recent studies on ASD prevalence are in accordance to DSM-IV criteria. This review has included studies from 1994 when DSM-IV was first published, and align with the DSM-III-R to DSM-V criteria. However, studies such as van Gent et al. included cases that were diagnosed according to DSM-III criteria which were in use from 1980-1994 as well as cases diagnosed according to DSM-III-R and DSM-IV. As the DSM-V criteria for ASD came into effect in 2013, few of the included studies used the DSM-V criteria. In comparison to the DSM-III, which classified ‘Infantile Autism’ as a solitary diagnosis, the DSM-V takes a far broader definition of autism’s characteristics so that more individuals would meet an ASD diagnosis using DSM-V than with DSM-III. This could affect the reported prevalence rates of autism/ASD over time as the definition of ASD has evolved.
Statistical methods

All analyses were performed using Stata 14.1 (StataCorp LP, Texas, USA). A meta-analysis of cases (ASD) vs control (no ASD) in the VI or HI populations was performed using Stata’s `metan` command, with a random effects model to account for the heterogeneity between studies. Meta-analyses were also conducted using the prevalence data to determine the overall ASD prevalence among VI and HI populations.

The `metan` command pools studies to produce an overall effect estimate using inverse variance-weighted meta-analysis. Where there is excess variability between study results, random-effects models are used which typically produce more conservative estimates of the overall significance of the effect size. Such models typically assume that the effect observed in the studies are a random sample from a distribution of treatment effects with a given variance.

Prevalence rates were compared between the included studies reporting ASD and VI or HI with prevalence rates for ASD in the general population.10,11,59–63 Tables 3 and 4 list the included studies for VI and HI prevalence rates respectively with the details of the best matched comparison populations from which prevalence rates were compared to estimate the relative risk ratios (RR). See Figures 5 and 7. A p-value < 0.05 (two-tailed) was deemed to be statistically significant.

Results

Visual impairment meta-analysis

The overall prevalence of ASD in children with VI in the included studies was 19% (95% CI 13–25%) (Figure 4).

Ten studies were included in the random effects meta-analysis for ASD vs VI (Figure 5). VI was strongly associated with ASD, RR = 31.0 (95% CI 18.6–51.6), p < 0.001 (Figure 5). Heterogeneity $\chi^2 = 79.4$ (d.f. = 9) $p < 0.001$; I-squared (variation in risk ratio attributable to heterogeneity) = 88.7%; Estimate of between-study variance Tau-squared = 0.57. The highest association was found in Ek et al.,38 with RR = 103.1 (95% CI 56.6–187.8).

Hearing impairment meta-analysis

The overall prevalence of ASD in children with HI in the included studies was 9% (95% CI 6–12%) (Figure 6).

Seven studies were included in the random effects meta-analysis examining the association between ASD with HI. There was a significant association between ASD and HI (Figure 7) with a RR = 14.1 (95% CI 3.4–58.6), p < 0.001. Heterogeneity $\chi^2 = 477$ (d.f. = 6) $p < 0.001$; I-squared (variation in risk ratio attributable to heterogeneity) = 98.7%; Estimate of between-study variance Tau-squared = 3.61. The highest association was found in Ahmed et al.,44 with a relative risk of 135.8 (95% CI 85.4–215.8). When Ahmed et al.44 was excluded from the analysis the overall RR was still significant; RR = 9.7 (95% CI 2.1–45.2), $p < 0.001$ with a strong association of ASD and HI.

Discussion

This systematic review of studies into the prevalence of ASD with VI or HI shows a high association for both groups of children with either sensory impairment. The relative risk of association when compared to a comparative general population was 31 times greater in VI children with...
an overall ASD prevalence rate of 19%. The HI children’s relative risk of association was also significant with a 14 times greater prevalence of ASD compared to the comparative general population with an overall ASD prevalence rate of 9%. Ahmed et al.\textsuperscript{44} was the only study with a typical comparison group of children without a sensory impairment to compare prevalence data. Ahmed et al.\textsuperscript{44} reported an eight times greater prevalence of ASD in HI children compared to a typical comparison group which is similar to the 14 times higher prevalence rates reported for the HI studies in this review. When compared qualitatively to the prevalence of ASD in the general population of 0.6–1.0\%\textsuperscript{9,11,59–63} there is a greater likelihood of ASD in the presence of VI or HI. These findings strongly support the need for greater surveillance of ASD in children with congenital VI or HI.

This review does not evaluate the specific threshold of impairment where the risk of association increases. Therefore, all children with VI or HI as defined in the inclusion criteria should be screened for ASD at the earliest possible time point so that interventions can be implemented to facilitate the development of social and language skills. These findings add to growing data regarding risk factors and prevalence of ASD in specific populations. A recent systematic review of ASD in genetic syndromes\textsuperscript{64} has found associations of ASD in syndromes such as CHARGE,
Fragile-X, Downs, Williams and Noonans syndrome. The high association of ASD with VI or HI reported here is greater than other known risk factors for ASD such as epilepsy, premature birth (<28 weeks’ gestation) or antidepressant use in pregnancy.

Sensory integration is a key weakness for those with ASD and so a lack of visual or auditory cues would decrease their ability to recognise and integrate verbal and visual cues to help them develop a social picture. Currently evidence suggests that the superior temporal sulcus is atypical in ASD where there is sensory integration of both visual and auditory information and forms a key component of the social brain. The lack of input to the superior temporal sulcus via primary visual or auditory cortex is in line with current evidence that supports a significant role for the superior temporal sulcus in the pathophysiology of ASD.

Many causes of childhood VI or HI, apart from trauma, are associated with CNS malformations, cerebral palsy, Down’s syndrome or epilepsy. Among the study populations encountered, neurological comorbidities/intellectual disability are potential additional factors that may contribute to the diagnosis of ASD. Given the wide range of VI classifications and diagnostic criteria for ASD it is beyond the scope of this review to be able to infer an association of ASD with the degree of VI. This weakness could be addressed if a suitable diagnostic instrument could be developed for individuals with a range of VI. Further limitations of this report are the lack of prospective studies that could follow the risk of the development of ASD in congenital deaf or blind children. A further limitation was the exclusion of children with congenital deafblindness. One large study reports a higher risk of mental and behavioural issues including ASD in this population, however determining how ASD, deafblindness and intellectual disability are associated is not clear as tools for assessing ASD within these populations have not been fully developed to clearly identify ASD. Future systematic reviews may contribute to the associations of ASD with combined sensory and intellectual disability.

The best quality evidence was sourced for this review, and although higher quality evidence is lacking such as random controlled trials the results of this meta-analysis provides evidence for an increased association of ASD in childhood populations with VI or HI. Despite using random effects modelling, the results in this paper need to be interpreted with caution as the level of heterogeneity in several of the meta-analyses is high (p < 0.001). The source of the heterogeneity is largely methodological with differences in diagnostic criteria, measures of VI or HI and age and geographical location of the studies.

Conclusion

These findings suggest the importance of screening children for ASD who are born with, or develop vision or hearing loss early in life, as their underlying sensory disability may conceal ASD. However, appropriate diagnostic instruments will need to be developed that can assess ASD within populations with combined sensory and/or intellectual disabilities so that these individuals can be identified and receive the appropriate early interventions required to improve their long-term outcomes.

Acknowledgements

The authors would like to thank Nikki May from Flinders University Library services for help in conducting the

Figure 7. Forest plot showing the results of the random effects meta-analysis for the HI studies with ASD vs a comparable general population with ASD (Table 4). There was a significant association between ASD and HI (Figure 7) with a RR = 14.1 (95% CI 3.4–58.6), p < 0.001. Heterogeneity \( \chi^2 = 477 \text{ (d.f. = 6) } p < 0.001; I^2 = 98.7\% \). (HI: Hearing Impairment).
literature search. We thank the anonymous reviewers for their comments on improving this manuscript.

Disclosure

The systematic review was unfunded.

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ASD, visual and hearing impairment


