Early Screening for Autism

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Abstract

Significant progress has been made over the past two decades in the development of early screening instruments for autism spectrum disorder (ASD). Whilst it is possible prospectively to identify cases of ASD using screening instruments, few of the many available screening instruments have been well validated. The American Academy of Pediatrics, which advocates universal screening, and the UK National Institute for Health and Care Excellence (NICE), which does not, make very different recommendations. It is critical that those using screening instruments in clinical practice understand how to interpret data from published studies, in particular recognising the low positive predictive value of a single administration. Clinicians should receive training in how screening information is communicated to parents. As part of ongoing surveillance, completion of early autism screening instruments can provide valuable information on potential early emerging symptoms of ASD and other neurodevelopmental disorders.

Context for early screening

Until the 1990s it was rare for children to receive a diagnosis of ASD before the age of 3 or 4 years. Many children are now first identified in toddlerhood, although others, in particular those with average or above average language and cognitive abilities, are not diagnosed until school age or later (1). With the recognition that ASD is relatively common, and in many but not all cases can be identified early, there has been both growing clinical interest and research activity in the development of ASD-specific screening instruments (2,3). However, the research evidence base for early autism screening instruments is mixed and a critical observation would be that it would be better if we knew more about fewer screening instruments, rather than the somewhat inadequate information on validity that we do have available for an ever-increasing list of ASD screening instruments. The limitations of our knowledge, despite much optimism and advocacy within parts of the autism community, are highlighted by the very different positions on universal screening advocated by the US American Academy of Pediatrics – which advocates routine use of screening instruments at 18 and 24 month well-baby checks (4) – and the UK National Institute for Health and Care Excellence which, whilst recognising that screening instruments provide valuable information on early signs and symptoms, does not recommend universal screening (5) (see also Al-Qabandi et al., 2011 (6) for a critical review on early screening).

Issues in screening and surveillance

In relation to autism, screening and surveillance can be considered as being different but related activities involving the detection of impairments with a view to prevention or amelioration of disability. Screening is the prospective identification of an unrecognised disorder by the application of specific tests or examinations. Surveillance refers to the ongoing and systematic collection of data relevant to the identification of a disorder over time by an integrated health system. Surveillance involves a parent-professional partnership that combines the observations of parents with the knowledge of the professional and the deployment of specific tests. There is evidence that the use of screening instruments in combination with asking parents about their concerns improves the efficiency of an instrument (7). In this context, the use of specific screening instruments where there is some concern on the part of a parent or professional can be a useful adjunct to clinical judgement (5).

Several parameters of screening instruments are important in assessing their efficacy and utility.
(i) Sensitivity is the proportion of individuals with a disorder who have a positive screen result.
(ii) Specificity is the proportion of individuals without a disorder who have a negative screen result.
(iii) Positive predictive value (PPV) is the proportion of individuals with a positive screen result who have the disorder.

Sensitivity needs to be high to minimise missing cases of the disorder (avoiding falsely reassuring parents and professionals). Specificity needs to be high to minimise cases without the disorder being screen positive (avoiding falsely alarming parents and costly referral for in-depth assessment). When the sensitivity and specificity of a screen remain constant, the PPV is lower the rarer a disorder is within the population. Hence, PPV will be lower in population (low-risk) samples than in referred (high-risk) samples.

Prospective population screening studies

Whilst a number of large-population ASD screening studies have been conducted, with one exception (8) none have undertaken the long-term follow-up required in order to ascertain sensitivity fully, i.e. identifying cases missed by systematically re-visiting the whole sample at a later age point. Those studies that attempt to do so via a proxy route should be interpreted with appropriate caution.

The findings of the largest screening studies summarized in Table 1 focus on the PPV of the screening instruments. The Checklist for Autism in Toddlers (CHAT) (9) was developed specifically to assess the early social communication signs of impairments in joint attention and pretend play. Subsequent screening instruments cover a broader range of early-emerging ASD symptoms, including measuring other aspects of early social communication impairments (e.g. response to name, imitation) as well as repetitive behaviours (e.g. unusual finger mannerisms, restricted play) and sensory abnormalities (e.g. oversensitivity to noise).

Table 1. Prospective screening Sudies

Reference	Instrument	Age (Months)	Study design	Administration	Instrument parameters
Baird et al. (2000)	CHAT	18m	2-stage population screening (N = 16,235)	Parental questionnaire and health practitioner observation	Se = 0.38 (2-stage)[1] PPV = 0.59 (2-stage)
Dietz et al. (2006)	ESAT	14m	2-stage population screening (N = 31,724)	Health practitioner completes items following interview with parents	PPV ASD = 0.25 (2-stage) PPV DD = 0.68 (2-stage)
Robins et al. (2001)	M-CHAT	24m	2-stage combined high-risk and low-risk (N = 1,293)	Parent questionnaire + follow-up telephone call	PPV = 0.36 (1-stage) PPV = 0.68 (2-stage)
Kleinman et al. (2008)	M-CHAT	16-30m	2-stage combined high-risk and low-risk (N = 3,793)	Parent questionnaire + follow-up telephone call	PPV = 0.36 (1-stage) PPV = 0.74 (2-stage)
Robins (2008)	M-CHAT	16-27m	2-stage low-risk (N = 4,797)	Parent questionnaire + follow-up telephone call	PPV = 0.06 (1-stage) PPV = 0.57 (2-stage)
Chlebowski et al. (2013)	M-CHAT	16-30m	2-stage low-risk (N=18,989)	Parent questionnaire + follow-up telephone call	PPV = 0.06 (1-stage) PPV = 0.54 (2-stage)
Wetherby et al. (2004, 2008)	ITC	6-24m	Population screening (*n* = 5,385); multiple stage follow-ups	Parent questionnaire	PPV DD = 0.43 (6-8m) PPV DD = 0.79 (21-24m)

1 Data reported for the 2-stage, high-risk threshold

CHAT (Checklist for Autism in Toddlers); ESAT (Early Screening of Autistic Traits); M-CHAT (Modified- Checklist for Autism in Toddlers)

ITC (Infant Toddler Checklist); Se: sensitivity; PPV: positive predictive value; ASD: autism spectrum disorder; DD: developmental disorder

In all of these population (low-risk) studies, in order to minimise false positives from the first administration, a two-stage screening procedure has been adopted. Children who were initially screen positive received a second administration of the screen, usually within one month, most commonly via a follow-up telephone call. A number of important clinical recommendations emerge from these studies.

First, whilst several screening instruments report satisfactory positive predictive values (PPVs), this is only after re-administration a second time following an initial fail. In the recent large Modified-CHAT (M-CHAT) study of a population sample, the PPV at first administration was very low (6%) meaning that 94% of those toddlers who failed the initial screen did not go on to receive a diagnosis (10). This improved to 54% following the second administration. Several factors might explain the improvement in prediction following the repeat screening, including the following.

- The contact is by a knowledgeable researcher.
- Some maturation may have occurred in the interval.
- Parents are oriented to and notice behaviour they had not previously seen, following exposure to the initial screen.

Another point that emerges from several studies is that, whilst PPVs for detecting ASD are acceptable, at least from the two-stage administration, when the PPV is calculated based on detecting all neurodevelopmental disorders the values are higher still. A further additional caution is that early screening might not detect the 20%-30% of cases of ASD who undergo regression or loss of skills, most commonly between their first and second birthdays (11).

Two recent studies remind us that screening instruments do not act in isolation to improve early detection. Oosterling et al. (12) showed that, in combination, training health professionals in the early signs of autism and introducing use of the Early Screening of Autistic Traits (ESAT) screen (13) together with a clear referral and diagnostic pathway led to a reduction in mean age of diagnosis from 83 to 64 months and the proportion of cases diagnosed before the age of 24 months increased from 12.7% to 24.3%. Dereu et al. (14) provided training and introduced a new screening instrument, the CESDD (Checklist for Early Signs of Developmental Disorders), to day-care workers caring for children between 3 and 39 months of age. They reported a moderate sensitivity of 0.68 but a low PPV of 0.10. By being trained in the use of screening instruments and the early signs of ASD, health and education practitioners can develop their expertise to identify possible ASD cases and come to understand the benefits but also the potential limitations (e.g. false positives) of using the screening instruments.

Clinical issues in screening and surveillance

If screening is universal, for example at well-child check-up, the first recognition of some parents that something might be wrong may follow 'failure' of a screen and consequent discussion about their child's development with the professional involved. For a parent to make use of information about their child, the information first has to make sense and they have to be ready to agree on it. Recognition, belief and acceptance can be particularly difficult when the professional is giving completely unexpected information. One of the benefits of active, ongoing surveillance is the opportunity to discuss 'risk status' with parents and what it means when a particular child has a positive screening result for the condition. In practice, being screen positive does not constitute a diagnosis, even when tests have high positive predictive value. Rather, the initial screening process should be seen as the beginning of a dialogue between the parent and professional about the child's development, with additional assessments being couched as helpful checks towards achieving a definite conclusion as to whether the diagnosis should be made or not.

Screening results are sample-specific; the utility of any particular screening instrument and the application of any particular cut-point for identifying 'screen positives' depend both on the sample characteristics and on the intended purpose of screening. The choice of which screening instrument to use, and for which particular purpose, critically depends on the relative costs, in the broadest sense, of false positives and false negatives. It is also important to remember that these costs tend to

fall on different parties. False positives involve costly further investigation and parental anxiety. False negatives may deprive children of clinical and education resources or place the burden of provision entirely on parents.

Conclusions

The prospective screening studies conducted in the past decade have shown that it is possible prospectively to identify ASD from the age of 18 months or even earlier in the second year of life. The most common early signs captured by the screening are impairments or delays in early-emerging social communication behaviours such as response to name, joint attention and play behaviours, although sensory abnormalities or a restricted repertoire of play activities might also be early indicators of ASD. However, these early signs are neither universal nor specific to ASD as opposed to other neurodevelopmental disorders. In addition, one-stage screening has been shown to have low PPV with the attendant risk of over-referral, although PPV is increased to moderate but only marginally acceptable levels (~0.50 to 0.70) following a second well-managed administration. These findings suggest caution about recommending universal screening. However, screening instruments can be a useful adjunct to ongoing parent-practitioner surveillance. Whilst several promising ASD screening instruments have been developed, no studies to date have directly compared the efficacy of different screening instruments against one another. Clinicians looking to use screening instruments as part of their ongoing surveillance should choose those that have been tested most rigorously in populations similar to those seen in their clinical care (5).

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GP Comment.

What I learned from this paper?

1. There do exist a few validated screening tools for prospective suspicion and subsequent diagnosis. However, the cost implications of further tests in false positives may be overwhelmingly high.

2. A diagnosis made after the age of 3 years is enduring.

3. Further studies and data on adults with autistic spectrum disorder may be very helpful in the management of this condition.

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