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Fernell, Elisabeth, Wilson, Philip, Hadjikhani, Nouchine, Bourgeron, Thomas, Neville, Brian, Taylor, David, Minnis, Helen, and Gillberg, Christopher (2014) Screening, intervention and outcome in autism and other developmental disorders: the role of randomized controlled trials. *Journal of Autism and Developmental Disorders* . ISSN 0162-3257

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Deposited on: 3 March 2014

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LETTER TO THE EDITOR

Screening, intervention and outcome in autism and other developmental disorders – the role of randomized controlled trials

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ABSTRACT

We draw attention to a number of important considerations in the arguments about screening and outcome of intervention in children with autism and other developmental disorders. Autism screening in itself never provides a final clinical diagnosis, but may well identify developmental deviations indicative of autism – or of other developmental disorders – that should lead to referral for further clinical assessment. Decisions regarding population or clinic screening cannot be allowed to be based on the fact that prospective longitudinal RCT designs over decades could never be performed in complex developmental disorders, and we propose an alternative approach. Early screening for autism and other developmental disorders is likely to be of high societal importance and should be promoted and rigorously evaluated.

Health surveillance and screening for the purpose of identifying developmental disorders in young children – with a view to providing early intervention – are essential components of health visiting as well as of the activities of Child Health Centers (CHC). Screening for Autism Spectrum Disorders (ASD) in young children has been under debate in many countries during the last few years. The UK National Screening Committee has recently concluded that whole population screening for autism in children should not be offered (Allaby and Sharma 2011). In contrast, in the US, the Centers for Disease Control and Prevention (CDC), and the American Academy of Pediatrics have taken a different view (Johnson and Myers 2007), recommending universal screening for ASD at 18 and 24 months of age. The rationale provided for screening in the US, in broad terms, is that “the sooner ASD is identified, the sooner an intervention program can start.”

The UK report advocated caution regarding a national screening program for ASD in children under five years based on the fact that available randomized controlled trials (RCTs) did not provide sufficient evidence that screening programs and ensuing early intervention lead to significant improvements later in childhood, greater independence, *or improved vocational and social functioning in adulthood*. The report also emphasized that studies of the natural history of these conditions indicate that about a third of children who are given a diagnosis of autism at 20-23 months of age as a result of a screening program are likely to “lose” this diagnostic label by the age of four years, and that it is not clear whether these figures reflect the impact of early intervention (assuming it is effective), or over-diagnosis at 20-23 months of age.

We wish to draw attention to a number of important considerations in the arguments about screening and outcome of intervention in children with ASD and other developmental disorders.

Autism screening in itself never provides a final clinical diagnosis, but may well identify developmental deviations indicative of ASD – or of other developmental disorders – that should lead to referral for further clinical assessment.

There are reasonable guidelines for evaluating screening programs for “pathological” conditions. However, if there is a requirement that screening should only be implemented if there is RCT evidence that *intervention after screening* leads to clear improvement in long term outcomes (cf. *improved vocational and social functioning in adulthood* as argued by The UK National Screening Committee, see above), then – in the case of autism and other developmental disorders – one would have to wait 10 to 30 years before conclusions about efficacy of screening and of the intervention provided can be drawn. Maintaining the integrity of a RCT protocol is of course extremely difficult and costly over such long periods, though there are a few notable examples, such as trials of the Nurse-Family Partnership (Olds et al. 1998). Nevertheless, while it is clear that the full impact of early onset neurodevelopmental problems such as ASD and ADHD can only be appreciated in early adulthood, what we might learn from studies starting in 2013 may be obsolete in terms of informing clinical practice in the 2040s.

From a clinical point of view it is of great value to identify developmental disorders, including autism, early, in order to inform parents and staff in preschool settings about the child’s basic cognitive problems. Such information is necessary, for example, to aid understanding of the mechanisms behind tantrums and other behavior problems, and it will enable intervention to be adequately adapted.

ASDs are complex and heterogeneous conditions and should always be discussed in the context of the child’s general cognitive ability, particularly if there is a coexisting intellectual disability

and/or other associated disorders, such as epilepsy, language disorder or ADHD. Moreover, the heterogeneity also depends on the etiology of the ASD. There are almost as many causes as there are cases (Gillberg 2010). Therefore, there are specific challenges in studying outcome after intervention in children with ASD. RCTs may not always be the optimal – or only – design. The RCT provides the best study design in many types of intervention research, but it can have serious limitations when studying complex multifactorially determined developmental disorders such as ASD (Graham 2007; Rosenbaum 2010; Mesibov and Shea 2011). One has to note that the recent Cochrane report on the early intensive behavioral intervention for young children with autism spectrum disorders (Reichow 2012) also included non-randomized trials, showing that designs other than RCT can be of importance.

All future studies of interventions performed with children with ASD – and other Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations (ESSENCE) - require rigorous characterization of the child's type and severity of ASD, the associated developmental (e.g. intellectual and language), neurologic (e.g. epilepsy, muscular and motor) or psychiatric (e.g. ADHD, tics, anxiety and mood) disorders, and must take regard to the underlying (including genetic) medical etiologies.

Decisions regarding screening cannot be allowed to be based on the fact that prospective longitudinal RCT designs over decades could never be performed and here we propose an alternative approach. First, naturalistic studies, using the same rigorous design in respect of selection/documentation are needed. Existing cohort studies will allow us to characterize important intermediate outcomes, such as language delay, adaptive functioning, and educational attainment, to be used in shorter-term trials of screening. Some interim conclusions regarding the

efficacy of specific interventions can of course be also drawn on the basis of results obtained in quasi-experimental studies.

The key decision in implementation of a screening program for autism is not about the long-term effectiveness of treatments: there are already many programs in place; see Cochrane Database Systematic Review (Reichow et al. 2012). Rather it is about whether we should make organized and coordinated efforts to identify cases early rather than waiting until parents or schools are unable to cope with their child's problems. To assess the value of such an approach we could conduct randomized trials of screening, ideally using a cluster randomization approach which would require consent at institutional rather than individual level (Weijer et al. 2012). These types of studies would be relatively easy to deliver within the context of a national health service, as is the case in Sweden, UK, or Canada for example. The intervention should be based on an organized screening program, with screen-positive children at CHC undergoing a detailed assessment and then being offered a range of interventions linked to their difficulties. The comparison condition would be no screening program, but the same treatments should be available on request of treating clinicians. The outcome measures used in such a trial should be the surrogate measures identified in cohort studies – language delay, hyperactivity, dyspraxia/developmental coordination disorder etc – present at school entry and that are predictive of poor adult functioning.

Economic modeling based on existing datasets such as cohort studies could be used to generate information on the broader societal costs (in terms of education, criminal justice, health care) associated with these intermediate outcomes. This would allow estimates of the economic benefits associated with early intervention following screening to be generated.

In conclusion, we think that early screening for developmental disorders is likely to be of high societal importance and should be promoted and evaluated rigorously.

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