Early Detection and Intervention for ADHD

Abstract
ADHD is a high cost/high burden disorder. Early detection and intervention may prevent or ameliorate the development of the disorder and reduce its long term impact. Here we set out a rationale for an early detection and intervention programme. First, we highlight the costs of the condition. Second, we discuss limitations of the current treatments. We then outline the potential value of an early detection and intervention programme. We review evidence on predictors of poor outcomes for early ADHD signs and discuss how these might allow us to target early intervention more cost-effectively. We then examine potential barriers to engagement with at-risk samples. This leads to a discussion of possible intervention approaches and how these could be improved. Finally we describe the PEDIA (Programme for Early Detection and Intervention for ADHD) a five year programme of research supported by the National Institute for Health Research and conducted at the University of Southampton which aims to develop and evaluate a strategy for early intervention.

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ADHD is a high-burden condition: Attention Deficit/Hyperactivity Disorder (ADHD) is a debilitating mental health disorder which, although most frequently diagnosed in the school years, is now acknowledged to affect individuals across the lifespan, from the preschool period through to adulthood [1]. It is marked by symptoms of inattention, overactivity and impulsiveness that have an early onset, are age inappropriate, persistent and pervasive [2]. The UK National Institute for Health and Clinical Excellence (NICE) estimated that about 210,000 children aged 5-18 years are affected by ADHD in England and Wales [3]. In the long term childhood ADHD is associated with risk for delinquency, criminality, educational failure and mental illness creating a substantial burden to health care, social welfare and criminal justice systems [4]. The presence of comorbid diagnoses, such as Conduct Disorder (CD), increase the risk for a poor outcome. For instance, children with a comorbid CD diagnosis are at risk for greater and more diverse substance abuse [1] and delinquency [5] in adolescence. The associated costs are growing in many countries [6]. The burden associated with ADHD to paediatric clinics and social/education services is increasing [3,6] as the numbers of children attending services grows year on year, with preschoolers also being increasingly referred. The estimated annual cost associated with childhood and adolescent ADHD in the US in 2005 were approximately $14,600 per individual [7-8]. There are also substantial indirect costs associated with ADHD. For instance, family members of children with ADHD are likely to use medical services [9] and no account is taken of the costs due to family member stress [10]. Furthermore, children with ADHD suffer a wide range of impairments that impinge on social and health care systems at a number of levels (education, criminal justice, mental health, social services etc) [11]. It has been estimated that 45 percent of the young male prison population have ADHD ([12], see also [13] and [14]). In addition, adolescents with ADHD have more driving accidents [14].

Current ADHD treatment strategies are valuable but have drawbacks: Treatment for ADHD generally begins during the school years once the condition and its complications are well established [2]. Multi-modal approaches to the treatment of ADHD are recommended [15]. Pharmacological treatments are available and widely used [16] but there is still considerable unmet clinical need. Psychostimulant medication is the most common treatment for ADHD [15] however, despite its efficacy [17] it has a number of limitations. These include: (i) normalisation is rare [18]; (ii) tolerance may develop over time leading to the need for increased dosage [17]; (iii) long-term effects remain uncertain [19]; (iv) effects only occur during active treatment [20];
(v) although rarely serious, side-effects are common (sleep [21]; appetite [22]; growth [19,23];
(vi) parents often have reservations about medication use for behavioural control [24]; and (vii) on
its own, medication may not improve social and academic difficulties [25]. Currently available
non-pharmacological treatments include classroom-based behaviour modification and parent
training. These represent valuable alternatives to target these other deficits but offer less control of
ADHD symptoms [26].

**Could a Programme for Early Detection and Intervention for ADHD (PEDIA) offer a**
more cost-effective alternative to current treatments? There remains a need for the
development of new treatment strategies to bring about more generalised and long lasting
improvements in patients with ADHD. One approach to this would be to refine pharmacological
and non-pharmacological approaches to improve treatment outcomes in the school years. A more
radical alternative would be to implement a prevention-based approach built on early detection
and intervention. The goal of such a strategy would be to reduce the likelihood of the emergence
of ADHD, or its persistence, from its earliest manifestations. Through this it would aim to reduce
the long-term impairment for the individual and the long-term burden to families and society. A
rationale for such an approach was recently set out by Sonuga-Barke and Halperin [27]. Their
reasoning was that – “(i) rational treatment development involves identifying/targeting the causes
of a condition; (ii) causes of ADHD should be cast, not as static/fixed neuro-psycho-biologic
deficits, but rather in terms of underlying developmental processes; and (iii) targeting these
processes early can bring about fundamental alterations in the pathogenesis of ADHD, and thus
prevent or moderate the course of the disorder” ([27]; p 369). This developmental notion of
‘cause’ which gives emphasis to prodromal states and precursor processes as targets for
intervention, promotes the idea that intervening early “should be more successful than waiting
until outcomes are established and then trying to reverse the pathogenic process” ([27]; p 370).
While early intervention preventative approaches are less common for ADHD compared to other
disorder [28], the authors’ optimism that such approaches can alter developmental trajectories and
improve long term outcomes in ADHD is partly based on recent insights into brain plasticity in
developmental disorders [29], and the conditional nature of risk-disorder pathways. Brain
plasticity is greatest during early phases of development [30-31]. Furthermore, early interventions
may precede and prevent the establishment of strong behavioural habits in the child that
exacerbate patterns of impairment, and they may increase parents’ and families’ receptiveness and

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avoid the development of negative ADHD-related attitudes. Similarly, if effects can be established early on then complications associated with school failure can be avoided.

There are three prerequisites for the development of an effective early detection and intervention strategy. First, those in need of treatment need to be identified because, of those individuals who already have high levels of ADHD symptoms in the preschool period or who are in a prodromal state, not all will go on to have problems in later life. Second, we need to know how best to access and engage these “at risk” children and their families as many will be living in difficult circumstances and may be considered “hard to reach”. Third, we need to develop treatments that can effectively alter developmental pathways and reduce the risk for disorder in these cases.

Can preschoolers with high ADHD be identified reliably? ADHD is increasingly diagnosed during preschool, i.e. before the age of 5 [32-34]. It is unclear, however, whether these early cases represent early onset forms – or just early identification of the developmentally normal form. If they are early emerging forms, it is also unclear whether they are different from later forms and specifically whether they predispose to long-term difficulties. In considering preschool ADHD it is important not to over-pathologize, on the one hand [35], or to underestimate the clinical significance of early appearing symptoms and impairment [36], on the other. In general, preschool ADHD shares many features with later diagnosed ADHD: (i) Symptoms of preschool ADHD it is important not to over-pathologize, on the one hand [35], or to underestimate the clinical significance of early appearing symptoms and impairment [36], on the other. In general, preschool ADHD shares many features with later diagnosed ADHD: (i) Symptoms of preschool ADHD (inattention, overactivity and impulsiveness) cluster together [36]; (ii) This cluster is distinctive from, though overlapping with, symptoms of conduct problems [32,36-38]; (iii) The hyperactive-impulsive and inattentive symptom domain distinction is present in preschool [39], although inattention symptoms are the better predictors of difficulties [40]. Impairment in preschool ADHD is associated with developmental delay, deficient pre-academic skills deficits and problems with close relationships [41].

However, while for clinical purposes ADHD is seen as a category (with clear boundaries between the syndrome and its absence), a range of different data sources converge to suggest that the syndrome boundary represent differences in degree rather than kind [42-43]. Diagnostic thresholds are necessarily filtered through the expectations of individuals applying these standards, such as parents, patients, teachers or clinicians [44-45]. Given this, combined with the strong evidence for patterns of symptom increase, persistence, diminution and more general fluctuation across time [1,46], the concept of disorder onset in ADHD defined in terms of a rigid adherence to diagnostic criteria may not be useful in predicting future developmental
trajectories. This problem is exacerbated by the fact that the presence of the full diagnostic form of ADHD (in terms of symptoms) at any particular time may not correspond to the ‘onset’ of impairment. In view of this, an inclusive focus which includes sub-clinical and non-impairing forms seems the most appropriate starting point for an early intervention strategy. Furthermore, given the possible eventual clinical significance of sub-clinical problems manifested during the preschool years, effective early intervention strategies may need to include some element of universal screening. Screening assessment for ADHD is less developed than for other disorders [47]. In addition, the heterogeneity of developmental phenotypes further complicates the already difficult task of identifying risk factors because screening tasks should ideally identify predictors of later disorder and distinguish between different trajectories of disorder emergence and persistence. It is possible that screening tools will need to focus not only on symptoms but intellectual delay, neuropsychological deficits and the family environment.

Not all preschoolers with high levels of ADHD go on to have long term difficulties - Can we predict which ADHD children will do? Longitudinal studies show that high levels of preschool ADHD symptoms do not always persist into the school years and later in life [48-51], although more general patterns of impairment may persist even when ADHD symptoms diminish [52]. Early onset severe ADHD itself is a good predictor of ADHD later in life [53], as well as a risk for later conduct problems [54]. However, coercive cycles of parent-child interaction need also to be considered [55]. Given these patterns of continuity and discontinuity it becomes important to identify those factors that predict later problems. Early therapeutic resources can then be focused on those children who are at risk to go on to have later problems and whose condition is associated with significant societal burden. Currently there is insufficient evidence to provide a definitive assessment of different markers of persistence of ADHD and other problems in children with high levels of initial ADHD. This task is complicated by the complex and non-deterministic ways in which risk factors operate and the incomplete patterns of continuity from early phenotypic indicators to later disorder. At one level, certain genetic and pre-/peri-natal environmental factors have been shown to be significantly associated with the later emergence of ADHD [56]. Identifying these could in principle mean that intervention could be very early – even before ADHD itself appears. However, given their overall low predictive value and the fundamentally synergistic ways in which these risk factors operate, knowing about these factors is unlikely to help target early intervention strategies [57]. At a second level, early phenotypic risk factors may be more valuable, such as a hyperactive temperament [58], co-morbid dysfunctional mood
High risk individuals are also likely to be hard to reach and difficult treat. What are the barriers? If on the basis of a risk rating we could predict which children with ADHD symptoms in preschool go on to develop later problems, either in terms of ADHD itself or in other areas of functioning, we would need to be able to ensure that they received the help they need. However, it is known that many children in need of treatment do not receive it [63] and that there are many barriers to treatment take-up [28]. Unfortunately these barriers are likely to be correlated with many of the risk factors that are associated with a poor outcome, such as maternal mental health problems [55], so those children at most risk of poor outcomes are likely to be most difficult to access. The issue of barriers to treatment uptake has been explored in several studies, and a number of factors related to both parents/families as well as programmes have been highlighted. Factors related to the family/parents are often situational, such as lack of money, lack of time, competing work demands, no available transport facilities, or childcare issues [4]. However, often psychological factors act as barriers to treatment take-up, such as fear of stigmatisation, lack of confidence, shame/embarrassment, or fear of breaches of confidentiality. [64-67]. Treatment/programme factors include insufficient or inappropriate provision of information about the programme, insufficient programme availability or long waiting lists, or not accommodating for additional needs parents/families may have, such as literacy and language/cultural issues [68-70]. Keeping families within programmes will depend on the therapeutic working alliance [71-73]. Once in treatment and even with adequate take up preschool children at risk of long term outcome may also be more difficult to treat because of the presence of comorbid behavioural disorders and cognitive and linguistic impairments or the existence of negative and dysfunctional parenting and parental mental health in their homes [55,61,74].
levels of maternal ADHD symptoms limit the improvement of overactive symptoms shown by preschoolers after completing a parenting programme, suggesting that treatment of parental ADHD may be a prerequisite for the success of psychosocial interventions for childhood ADHD [74].

Are current preschool therapeutic approaches up to the job? How can they be improved?: Having identified and accessed children at risk for later ADHD, more efficacious treatments that are acceptable for use with preschoolers need to be developed. Psychostimulants remain a controversial option for preschoolers which appear less efficacious with preschoolers [75]. Side-effects may be more common [76]. Early intervention is likely to rely on developing effective non-pharmacological interventions appropriately tailored to the developmental period. Of non-pharmacological options, parent training programmes, such as Parent-Child Interaction Therapy [77] the Incredible Years [78] or the Triple P [79], are most popular with preschool [80]. However, as with older children with severe ADHD, effects on core symptoms are not compelling [81-83]. Nothing is known of whether either pharmacological or non-pharmacological approaches can alter trajectories and improve outcomes over the longer term for either full preschool ADHD or sub-clinical cases.

As such, the question remains as to how the preventative value of ADHD interventions can be optimized. Sonuga-Barke & Halperin [27] have argued that therapeutic approaches are likely to be more effective if they target the underlying pathophysiological processes that affect developing neural systems. Studies of working memory training in school-age children indicated an improvement of working memory and other cognitive domains, as well as a reduction in ADHD symptoms as rated by parents [84]. Working memory training can also be implemented with younger children [85]; however, it may be more effective if delivered as part of a parent training approach. In the New Forest Parenting Programme (NFPP) [86], a cognitive element is included targeting deficits in general self-regulation. Mother and child together undertake training exercises requiring attention, concentration, turn-taking, working memory and delay of gratification within everyday activities. This naturalistic teaching method provides opportunities for embedding training in everyday life. A recent trial reported large effects on core symptoms of ADHD [87]. Halperin and collaborators (unpublished) (personal communication), are developing a related approach (“Training Executive, Attention and Motor Skills; TEAMS”).

Given the pathophysiological heterogeneity of the disorder, training approaches need to target
different deficits. Operant techniques of fading and shaping may be an especially good way of altering incentive structures and improving delay behaviour [88].

**Future prospects - The PEDIA study:** The empirical study of early assessment and intervention in ADHD is in its infancy (cf. [41]). Existing approaches have produced clinical improvements [89], but we do not know the extent to which they alter negative developmental trajectories and improve long term outcomes. Methods for identifying ‘children at risk for ADHD’ need to be more fully developed. The Programme for Early Detection and Intervention for ADHD based at the University of Southampton (PEDIA) sets out to address these issues.

PEDIA has several aims: First, to develop a way of identifying preschool children with ADHD most at risk for a poor outcome, and to develop a risk index for poor outcome/high burden. This will be based on a prospective follow-up of a large sample of individuals who were identified as having pre-school ADHD but are now entering late adolescence or early adult life. As such, PEDIA will provide one of the first assessments of adult outcomes for preschool ADHD.

Second, an exploration of the barriers to engaging and working with the most difficult to reach and/or treat families using literature reviews and qualitative interviews with families and the professionals who work with them. Particular focus will be placed on gathering information on issues around accessing and attending parenting programmes, and facilitating continued engagement and attendance, as these are key challenges associated with this type of intervention [66, 81]. The impact of maternal ADHD and other mental health problems will also be explored further. This information will then provide the basis for an adaptation of the New Forest Parenting Programme so it can be used more effectively with high risk families and their children and improve outcomes for subgroups of ADHD preschoolers. An emphasis will be placed on trying to help those children with the most complex needs and where adult ADHD and other mental health problems occur within the family. In addition, specific elements targeted at assessing and enhancing parental motivation and readiness to change will be incorporated in order to increase attendance and treatment effectiveness. The adapted NFPP package will then be evaluated in a large scale multi-centre controlled trial to see if it is more effective (and cost-effective) with children at high risk for poor outcomes than a generic package recommended by NICE [3] and whether the benefits of the enhanced intervention extend across different settings and trial centres.

We believe that early identification and intervention strategies employing a certain element of universal screening represent an exciting basis for therapeutic innovation in ADHD, that may have the potential to alter underlying pathophysiological bases of negative developmental pathways.

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Whilst recognising the many challenges that are associated with this type of work, we believe programmes of research such as PEDIA represent a first step towards this goal. If it is successful the hope is that it can be widely implemented nationally and internationally leading to substantial health service savings over the life course and improvements in the wellbeing of children and the quality of life experienced by their families.

Expert Summary

In this article we set out the rationale for an early detection and intervention strategy for ADHD. We highlight the long term burden of ADHD to the individual patient, their family and their community and the potential benefit of an early intervention approach to reducing this burden. We argue that if such interventions can target the causal pathways which underpin ADHD then they may be able to alter developmental trajectories to reduce symptoms and associated impairment and therefore potentially reduce the need for later treatment. While of considerable potential value implementing such approaches will requires new and innovative ways to; (i) identify those preschool children at special risk of negative outcomes; (ii) encourage hard to reach children to participate in treatment (as these are often the very children at long term risk) and remove barriers to treatment success in these groups; and (iii) develop new treatment options for preschoolers that specifically target the developmental processes that underpin cognitive and motivational deficits associated with ADHD which could be integrated into more generic parent training approaches. The PEDIA study is an integrated set of five projects that attempt these issues to develop early intervention strategies for difficult to reach and hard to treat preschoolers with ADHD.
References


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17. The MTA Cooperative Group. A 14-Month Randomized Clinical Trial of Treatment Strategies for Attention-Deficit/Hyperactivity Disorder. *Arch Gen Psychiatry*, 56(12), 1073-1086 (1999).


43. Polderman TJC, Derks EM, Hudziak JJ, Verhulst FC, Posthuma D, Boomsma DI. Across the continuum of attention skills: a twin study of the SWAN.

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71. ADDISS. Parent Consultation Exercise Southport (2003).


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Many thanks in advance for your kind assistance.
Peer Review Paper


86. Sonuga-Barke EJS, Thompson M, Abikoff H, Klein R, Brotman LM. Nonpharmacological Interventions for Preschoolers With ADHD: The Case

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