

Interventions based on early intensive applied behaviour analysis for autistic children: a systematic review and cost-effectiveness analysis

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Declared competing interests of authors: none

Published July 2020

DOI: 10.3310/hta24350

Scientific summary

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Health Technology Assessment 2020; Vol. 24: No. 35

DOI: 10.3310/hta24350

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Background

Autism spectrum disorder (henceforth referred to as 'autism') is a lifelong neurodevelopmental condition characterised by impaired reciprocal social communication and a pattern of restricted, often repetitive, behaviours, interests and activities. As it is a spectrum condition, individual presentation is usually a combination of difficulties and strengths, which vary considerably. Those who are diagnosed in early childhood are typically those with more severe symptoms and appear more likely to have an intellectual impairment.

The prevalence of diagnosed autism in the UK is around 1% of the population and is higher (2%) in men than in women (0.3%). The relatively high prevalence of autism and the reduced ability of individuals to achieve their individual potential means that autism has significant economic and social impacts for individuals, their families and wider society. The estimated cost to the UK of supporting people with autism and related conditions has been estimated to be as high as £34B per year.

Early intensive applied behaviour analysis-based interventions, first described by Lovaas (Lovaas OI. Behavioral treatment and normal educational and intellectual functioning in young autistic children. *J Consult Clin Psychol* 1987;55:3–9), are a well-established, early intervention for autistic children. These principles promote a range of techniques (such as the breaking down of skills into their basic components) that emphasise discrimination, learning and positive reinforcement. This intensive approach is often delivered on a one-to-one basis for 20–50 hours per week.

Objectives

The aim of this study was to evaluate the clinical effectiveness and cost-effectiveness of early intensive applied behaviour analysis-based interventions for preschool autistic children based on current evidence.

The key objectives were to:

- evaluate the effects of early intensive applied behaviour analysis-based interventions in young autistic children by conducting a systematic review and individual participant data meta-analyses of data from all available comparative studies
- investigate potential study- and patient-level modifiers of treatment effect
- evaluate the cost-effectiveness of early intensive applied behaviour analysis-based interventions in young autistic children by developing a new economic model
- identify key uncertainties in the evidence base and highlight important areas for future research.

Methods

Individual participant data review and meta-analysis

A systematic review and individual participant data meta-analysis was conducted based on a prospectively agreed protocol and following recommended systematic review methods.

Relevant databases, including MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials, were searched to identify relevant studies.

Studies were included in the review if they recruited autistic children and compared early intensive (> 15 hours) applied behaviour analysis-based therapy with any other therapy. Studies of interventions delivered to parents rather than children were excluded. Non-comparative single-arm studies were also excluded.

Individual participant data were sought from all identified studies and, when received, were recoded to a common data dictionary. The individual participant data were then reanalysed in accordance with a prespecified analysis plan, using one- and two-stage meta-analytic models. A supplemental meta-analysis was also conducted to include studies that did not provide individual participant data.

Risk of bias in randomised controlled trials was assessed using the Cochrane Risk of Bias 2.0 tool and non-randomised controlled study designs were critically appraised using the Risk Of Bias In Non-randomised Studies – of Interventions (ROBINS-I) tool.

Economic evaluation

A new model was developed to evaluate the cost-effectiveness of early intensive applied behaviour analysis-based therapy in a UK context. Given that implementation of an effective early intensive intervention for young autistic children would likely impact across multiple sectors, the model considered several perspectives relevant for the UK. These included a health-care and social services perspective and a broader public sector perspective, which included costs falling on the education sector. The economic model used a 15.5-year time horizon, representing the period from diagnosis in early childhood to adulthood. Scenario analysis also explored a lifetime time horizon. Costs and health outcomes were discounted at a rate of 3.5% per annum. Costs were valued at 2016/17 prices.

The economic model drew on the individual participant data meta-analysis results to estimate the treatment effect associated with early intensive applied behaviour analysis-based therapy. The limited availability of appropriate effectiveness data, however, meant that this analysis was primarily exploratory, with a view to identifying key drivers of cost-effectiveness. The model structure was designed around the two most commonly recorded measures (cognitive ability and adaptive behaviour), and adopted a cohort approach to capture changes in these measures linking them to health-related quality of life and costs. Owing to the uncertainty in the long-term effects of early intensive applied behaviour analysis-based interventions, two scenarios were explored in the main analysis: an optimistic scenario, in which the observed benefits of early intensive applied behaviour analysis-based interventions were assumed to persist; and a pessimistic scenario, in which the proposed benefits dissipated over time.

Results

Systematic review and individual participant data meta-analysis

The review identified 20 studies comparing early intensive applied behaviour analysis-based interventions with alternative interventions (mostly 'eclectic' treatment or treatment as usual) and obtained 82% ($n/N = 654/800$) of individual participant data from published studies.

All included studies were at risk of bias on at least one domain in the Cochrane Risk of Bias or Risk Of Bias In Non-randomised Studies – of Interventions tools. Few studies were randomised. Most allocated interventions were based on parental preference. Outcome assessors were often not independent of treatment. In some studies, outcome data were missing or available for only one treatment group.

The meta-analyses of Vineland Adaptive Behaviour Scale composite score showed no clear evidence of a benefit of early intensive applied behaviour analysis-based intervention after 1 year (mean difference 2.93, 95% confidence interval -1.90 to 7.76 , $I^2 = 80\%$), but a seven-point difference in favour of the applied behaviour analysis-based intervention (half of a standard deviation) after 2 years, with less heterogeneity (mean difference 7.00, 95% confidence interval 1.95 to 12.06 ; $I^2 = 34\%$). Studies varied

substantially in their estimated mean differences, from 32 points in favour of early intensive applied behaviour analysis, to five points in favour of alternative interventions. In analyses of cognitive ability (intelligence quotient), results also favoured early intensive applied behaviour analysis-based interventions by around 10 points after 1 year (mean difference 9.16, 95% confidence interval 4.38 to 13.93; $I^2 = 0$) and 2 years (mean difference 14.13, 95% confidence interval 9.16 to 19.10; $I^2 = 15\%$). Evidence for other outcome measures, such as language development, was limited and meta-analyses were generally inconclusive. There was no evidence that the effect of these interventions varied with key characteristics of the children (such as baseline intelligence quotient), but data were limited.

Autism symptom severity was not measured in most studies and the results were too limited to be conclusive, with no clear evidence that early intensive applied behaviour analysis-based interventions had any effect. There were limited data on language (comprehension and/or expression) and challenging behaviours, with no statistically significant effects found. Adverse effects were rarely recorded in the individual participant data. Two included studies (by one group of authors) recalled that no adverse effects were observed, but adverse effects were not routinely collected in any of the included studies.

There was no evidence that any child- or study-level covariate moderated the treatment effect; however, there were very limited data on covariates, so only a subset of the planned analyses could be implemented.

Economic evaluation

Adopting a public sector perspective and making pessimistic assumptions about the long-term effectiveness, early intensive applied behaviour analysis-based interventions are associated with £58,940 in additional costs and generate 0.24 additional quality-adjusted life-years. The resulting incremental cost-effectiveness ratio was £189,122 per quality-adjusted life-year. When optimistic assumptions are made about the long-term effectiveness, scenario early intensive applied behaviour analysis-based interventions are associated with £58,496 in additional costs and generate 0.84 additional quality-adjusted life-years, with a resulting incremental cost-effectiveness ratio of £46,768 per quality-adjusted life-year.

Using National Institute for Health and Care Excellence decision rules to benchmark the results of the cost-effectiveness analysis and adopting a £30,000 per quality-adjusted life-year threshold, these results indicate that early intensive applied behaviour analysis-based interventions would need to generate either further benefits or cost savings to be considered cost-effective. In the pessimistic scenario, it would be necessary for early intensive applied behaviour analysis-based interventions to generate either a further 1.29 additional quality-adjusted life-years or produce £38,790 in additional cost savings to be considered cost-effective at a threshold of £30,000 per quality-adjusted life-year. In the optimistic scenario, these values fall to 0.47 additional quality-adjusted life-years or £14,066 in additional cost savings.

The results of the scenario analyses identified a number of drivers of value and showed that early intensive applied behaviour analysis-based interventions were more likely to be cost-effective if either the comparative benefits of therapy continued into adulthood, or it can have a significant impact on the type of school attended, as was observed in a small number of the effectiveness studies. The value generated by early intensive applied behaviour analysis-based interventions are, however, contingent on treatment effects persisting over a long period of time and it is much less likely that early intensive applied behaviour analysis-based interventions represent value for money if comparative benefits are realised only for a short period of time.

Limitations and uncertainties

A number of important limitations were identified in the studies included in the systematic review and individual participant data meta-analysis.

All of the included studies were at risk of bias on at least one domain, with the majority of studies at risk of bias on multiple domains. Randomisation was possible (as shown in a minority of studies), but rarely conducted.

The effect of therapy on many key outcome domains, including autism symptom severity, language development, challenging behaviours and education, remains uncertain because of the very limited data available for these outcomes.

The lack of long-term follow-up data in most studies means that, even when data were available (e.g. for adaptive behaviour score), the long-term effect of early intensive applied behaviour analysis-based interventions on these outcomes is uncertain, including the impact in later childhood and into adulthood.

These concerns carry through to the economic modelling and the results of the economic analysis should be interpreted in the context of these limitations. The restrictive focus on cognitive ability and adaptive behaviour scores means that other outcome measures, which plausibly affect both quality of life and costs, could not be included in the economic analysis.

Conclusions

Implications for service provision

Although individual participant data meta-analyses have shown small to moderate improvements in child cognitive ability and adaptive behaviour for early intensive applied behaviour analysis-based interventions relative to treatment as usual or eclectic approaches, all of the identified studies were at risk of bias, limiting the strength of conclusions that can be drawn from these results. Furthermore, results from individual studies varied considerably, with some showing no relative benefit of early intensive applied behaviour analysis-based interventions.

The concerns about bias in evidence of effects, together with the other limitations in the available evidence, mean that it is not possible to make strong judgements about the cost-effectiveness of early intensive applied behaviour analysis-based interventions. The restricted outcomes assessed in the research studies required the model to focus on cognitive ability and adaptive behaviour scores. This may mean that the results of the economic analysis do not fully reflect the impact of early intensive applied behaviour analysis-based interventions on outcomes and costs. Taken at face value, however, the results of the main economic analysis indicate that early intensive applied behaviour analysis-based interventions are unlikely to represent value for money, based on thresholds typically adopted by the National Institute for Health and Care Excellence.

The results of the economic analysis also highlighted the importance of assumptions made regarding the long-term effects of early applied behaviour analysis-based interventions, as this was the most significant driver of cost-effectiveness. Crucially, there are few reliable longer-term follow-up data from children who have received these interventions and therefore no clear evidence on whether or not any comparative benefits are retained through childhood and into adulthood.

Further implications of this research are constrained by the lack of high-quality evidence to support the clinical effectiveness and cost-effectiveness of early intensive applied behaviour analysis-based interventions. Service providers, families with young autistic children and those funding the provision of services in collaboration with the autism community need access to better evidence to decide how early intensive applied behaviour analysis-based interventions compare with other early interventions, and what the effective interventions are to achieve good outcomes for young autistic children in the short, medium and longer term.

Suggested research priorities

Researchers should consider carefully whether or not further evaluations of early intensive applied behaviour analysis-based interventions, compared with treatment as usual or eclectic approaches, are appropriate. The relative clinical effectiveness of other behavioural and developmental-social-pragmatic interventions lay outside the scope of this analysis, but many require substantially less resource to implement than early intensive applied behaviour analysis-based interventions and may represent better value. Future research should therefore focus on which interventions for young children currently have the best evidence of clinical effectiveness and cost-effectiveness, and which are worthy of further investigation.

Future studies of autism interventions should evaluate outcomes that matter most to autistic children and their families, including assessment of potential adverse effects or harms. Efforts to establish internationally agreed core outcomes and standardised measurements would be valuable, as would a priority-setting exercise involving the autism community.

A range of methodologies are likely to be required to address evidence gaps, particularly given the long-term time frames over which effects may operate. These might include intervention trials undertaken in developmental sequence, additional or structured follow-up of children recruited to existing effectiveness studies and the use of retrospective case-control analyses looking at any early intervention received.

Any future studies of comparative effectiveness should address the methodological limitations of the historical evidence base, as identified by this report. These would preferably be randomised controlled trials with prespecified outcome measures, collected by trained researchers blind to intervention received. Data should be collected on fidelity to treatment received. Data should be collected and, when possible, analysed for all randomised participants. Withdrawals should be carefully monitored, documented and reported. Preferably, independent groups who have no financial interest in, or strong views about, any of the interventions being evaluated should conduct new studies.

Study registration

This study is registered as PROSPERO CRD42017068303.

Funding

This project was funded by the National Institute for Health Research (NIHR) Health Technology Assessment programme and will be published in full in *Health Technology Assessment*; Vol. 24, No. 35. See the NIHR Journals Library website for further project information.

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 3.370

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, the Cochrane Library and Clarivate Analytics Science Citation Index.

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This report

The research reported in this issue of the journal was funded by the HTA programme as project number 16/104/15. The contractual start date was in July 2017. The draft report began editorial review in May 2019 and was accepted for publication in December 2019. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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