FACULTY OF HEALTH SCIENCES
UNIVERSITY OF COPENHAGEN

PSYCHIATRIC RESEARCH UNIT &
CHILD AND ADOLESCENT PSYCHIATRIC DEPARTMENT
REGION ZEALAND

PhD thesis

Ole Jakob Storebø

Social skills training for children with attention deficit hyperactivity disorder

– a Cochrane review, a randomized clinical trial, and an update of the Cochrane review

Academic advisors:
Erik Simonsen, Professor, MD, PhD, Dr.h.c.
Jesper Pedersen, MD, PhD
Per Hove Thomsen, Professor, MD, DMSc
Christian Gluud, MD, DMSc

Submitted: 29/10/11

PhD thesis

Social skills training for children with attention deficit hyperactivity disorder

- Cochrane review, a randomized clinical trial, and an update of the Cochrane review

Ole Jakob Storebø

"The important thing is not to stop questioning. Curiosity has its own reason for existing"

Albert Einstein

Author
Ole Jakob Storebø, Cand. Paed. Psych.
Child Psychiatric Clinic, Holbæk, Region Zealand

Principal supervisor
Erik Simonsen, Professor, MD, PhD, Dr.h.c., Psychiatric Research Unit, Region Zealand and Faculty of Health Sciences, University of Copenhagen

Project supervisor
Jesper Pedersen, MD, PhD, Child and Adolescent Psychiatric Department, Region Zealand

Co-supervisor
Per Hove Thomsen, Professor, MD, DMSc, Child and Adolescent Psychiatric Center, Risskov and Faculty of Health Sciences, University of Aarhus
Christian Gluud, MD, DMSc, Copenhagen Trial Unit Center, Center for Clinical Intervention Research, Rigshospitalet, Copenhagen University Hospital

Review committee
Chairperson: Anne Mette Skovgaard, Associate Professor, MD, DMSc, Research Unit, Child and Adolescent Psychiatric Centre and Faculty of Health Sciences, University of Copenhagen, Denmark
Niels Bilenberg, Professor, MD, PhD, Department of Child and Adolescent Psychiatry and Faculty of Health Sciences, University of Southern Denmark
Pål Zeiner, Senior Researcher, MD, PhD, Child and Adolescent Mental Health Research Unit, Oslo University Hospital, Norway

Public defense
Friday 27th April 2012

Preface

This thesis was carried out at the Child Psychiatric Clinic in Holbæk, Child and Adolescent Psychiatric Department, Region Zealand. The SOSTRA trial was financially supported by Region's Zealand University Hospital (RESUS), Region Zealand Research Foundation, and Psychiatric Research Unit, Region Zealand. Funding was also received from the Fru C. Hermansens Foundation, Slagtermester Max Wørzner and Inger Wørzners Foundation, and TrygFonden. I am grateful to the patients and their families who agreed to participate in the SOSTRA trial. They all contributed greatly, both by letting me know about their problems and also by agreeing to be interviewed twice about difficult areas of their lives.

Without the support of several other people, this thesis would not have been written. I would like to express my sincere gratitude to my mentors and all the others who supported me. I am very grateful to Medical Director of the Child and Adolescent Psychiatric Department in Region Zealand, Jesper Pedersen, MD, PhD, who first contacted me and gave me the chance to become a PhD student. He was also helpful in the process of implementing the trial in the clinic. I would like to thank staff nurse in the Child Psychiatric Clinic, Lotte Jensen for her valuable support in the first part of the project. I also want to thank Child and Adolescent Psychiatric Department, Region Zealand for the support of my research. I sincerely thank Prof. Erik Simonsen for accepting me as his student, and for his steady and encouraging support. He has been an inspiration to me, and I feel that his way of looking at combining clinical and research institutions as two independent, yet simultaneous bodies is valuable and sound. I am also grateful to Prof. Per Hove Thomsen for his valuable comments, and support in making funding applications. Christian Gluud, Head of the Copenhagen Trial Unit, taught me much about being a true researcher, generously sharing his knowledge about systematic reviews and randomised clinical trials, as well as the importance of meticulousness and attention to detail. I will also thank research associate Maria Skoog, Copenhagen Trial Unit, for here valuable feedback in the planning phase of the SOSTRA Trial and also her help with the Cochrane review. She has been like an informal mentor to me. Furthermore, I would like to thank senior statistician, Per Winkel, Copenhagen Trial Unit, for his help with the statistical analysis and valuable comments.

Many thanks to secretary Lone Krogh, Pernille Darling Rasmussen, MD, psychologist Kirsten Bach, student Katrine Søby, and student Kristoffer Levinsen for their help with the project. I will also thank secretary Dorit Mortensen, Psychiatric Research Unit, for her help with my manuscript and also secretary Lotte Rein, Child Psychiatric Clinic in Holbæk, for being my daily sparring partner.

I am grateful to all my colleagues at the Child Psychiatric Clinic in Holbæk especially the therapists in the intervention groups: the psychologists, Karen Christensen, Damaris Hansen, Lise Lotte Valentin Mortensen, and paedagogical consultant Tina Mancher.

I had a wonderful time in Toronto, Canada visiting Prof. Rosemary Tannock and her research laboratory, where I learned a lot about ADHD. It was a great opportunity to spend many hours in thought-provoking discussions about ADHD, and she kindly invited me to her home. I also visited Senior Researcher, Yael Shmueli-Goetz at the Anna Freud Centre in London, and I am particularly grateful for the knowledge gained on attachment, especially the Child Attachment Interview.

Last, but not least, I thank my children, Hannah and Tobias, and my wife Bente for being my rock, and a wonderful person who inspires such warm feelings.

Ole Jakob Storebø
March 2012

Guide to reading the thesis

This thesis is based on three papers that focus on social skills training for children and report a Cochrane systematic review and a randomised clinical trial.

The aim of the thesis is to make a qualified contribution to investigate the efficacy of social skills training for children with symptoms of attention deficit hyperactivity disorder (ADHD) and social problems. Empirical research, which forms the basis of the thesis, is described, followed by background research. The diagnoses and social competences of children with ADHD are then elaborated. A growing, global prevalence of this disease in children underlines the need for effective interventions. Different types of interventions for children with ADHD are presented, including pharmacological, psychosocial, and others. Furthermore, attachment seems to be associated with both social skills and ADHD, and naturally connected to the relationship problems of these children, the background of which is presented. A narrative review of the research on the association between ADHD and attachment is summarised. Social and emotional skills and social skills training are briefly elaborated upon. A systematic review of the efficacy for social skills training is much needed, and the background for the Cochrane review on social skills training undertaken in this PhD project is presented, followed by a description of the objective, methods, searching strategy, interventions, trial sequential analysis, quality assessment, and review results. The review underlines the need for more high-quality trials with low risks of systematic and random errors, and therefore we conducted the SOSTRA trial. The aim and framework of the SOSTRA trial are presented followed by a description of the methods, treatment samples, ethical considerations, and plans for the analysis. The difficulties of choosing the right measurement forms, how to avoid missing data, and how to perform the right sample size calculation in the SOSTRA trial are reflected upon and discussed. The results from the SOSTRA trial and the Cochrane review are then presented, followed by updated meta-analyses where data from the SOSTRA trial are included in some of the meta-analyses from the Cochrane review. Thereafter, the Cochrane review and the trial are discussed and concluded upon. Finally, reflections on the clinical implications and areas for future research are elaborated upon.

Objectives

The aim of the Cochrane review was to assess the beneficial and possible harmful effects of social skills training in children and adolescents with ADHD.

The first aim of the SOSTRA trial was to examine the effect of the combination of standard treatment plus social skills training and parental training, versus standard treatment alone on the outcome measures of ADHD core symptoms and social and emotional skills in children with ADHD. The second aim was to investigate whether the parent's own ADHD symptoms and the children's attachment patterns had any impact on influencing the effect of the treatment.

Table of Contents

List of papers

Paper 1: Storebø OJ, Skoog M, Damm D, Thomsen PH, Simonsen E, Gluud C. Social skills training for attention deficit hyperactivity disorder (ADHD) in children aged 5 to 18 years. Cochrane Database of Systematic Reviews 2011, Issue 12.

Paper 2: Storebø OJ, Pedersen J, Skoog M, Hove Thomsen P, Winkel P, Gluud C, Simonsen E. Randomised social skills training and parental training plus standard treatment versus standard treatment of children with attention deficit hyperactivity disorder - the SOSTRA trial protocol. Trials 2011, 12:18

Paper 3: Storebø OJ, Simonsen E, Winkel P, Gluud C. Social skills training for children with ADHD - the randomised SOSTRA trial. Submitted to PLoS ONE in October 2011.

List of abbreviations

ADHD: Attention Deficit Hyperactivity Disorder
APHRIS: A Priori Heterogeneity-adjusted Required Information Size
ASRS: Adult Self Report Scale
CAI: Children Attachment Interview
Conners CBRS: Conners Comprehensive Behaviour Rating Scales
DSM-IV: Diagnostic and Statistical Manual of Mental Disorders
K-SADS: The Schedule for Affective Disorders and Schizophrenia for School-aged Children
ICD-10: International Classification of Diseases
IQ: Intelligence Quotient
IS: Information Size
MD: Mean Difference
MTA: Multimodal Treatment study of ADHD
PHHRIS: Post Hoch Heterogeneity-adjusted Required Information Size
RCT: Randomised Controlled Trial
RIS: Required Information Size
SCQ: Social Communication Questionnaire
SD: Standard Deviation
SOSTRA Trial: Social Skills Training and Attachment Trial
SMD: Standard Mean Difference
TSA: Trial Sequential Analysis
WISC-III: Wechsler Intelligence Scale for Children

Background

Attention deficit hyperactivity disorder

Attention-deficit hyperactivity disorder (ADHD) is characterized by impulsive actions, attention difficulties, and hyperactivity at home and especially in the school setting (1;2). Children with ADHD not only have these problems but also have difficulty with social interaction with parents, peers, and teachers. A systematic review showing a survey of the international prevalence rates of ADHD found that 3% to 5% of all children suffer from ADHD (3). The determined prevalence is dependent on the classification system used, with boys being 2 to 4 times more likely than girls to be diagnosed with ADHD (4;5). In studies including the entire population, the difference between the sexes was considerably smaller, indicating under-diagnosis of girls with ADHD (6-8). ADHD is an inherited disease, and it seems the disease shares common genes and pathways for several neuropsychiatric disorders, e.g., autism and tics. This is consistent with the common clinical co-occurrence of ADHD with other such conditions (9). Beyond childhood, ADHD increasingly is discussed as a psychiatric disorder in adulthood, with high heterogeneity and comorbidity with other psychiatric disorders (4). Comorbid conditions include behavioural disorders, depression, anxiety, tics, learning difficulties, and verbal and cognitive difficulties (10;11). Children with ADHD have an increased risk of developing personality disorders and psychotic conditions, drug or alcohol abuse, and criminal behaviour (12;13).

These children often have seriously disturbed relationships with other people and struggle to develop and maintain friendships (14;15). Other difficulties involve affective components, such as motivation delay and mood regulation (4;16;17).

Diagnosis of ADHD

ADHD consists of 18 subgroups of symptoms, which are equal in both the International Classification of Diseases (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (18-20). However, there are different sub-diagnoses in both systems in which specific symptoms are identified. In the DSM-IV these subtypes are the ‘predominantly inattentive type’, ‘predominantly hyperactive-impulsive type’, or the ‘combined type’; the latter is the most common type (21). The symptoms must show up in two different settings, e.g. at home and in school for at least six months. The number of children referred to child psychiatric care with a suspicion of ADHD is increasing internationally (22-25).

Interventions for children with ADHD

Introduction

Children with ADHD are commonly treated with medication, which often has a good effect on their core symptoms. However, this treatment does not alleviate all of the children's social problems. The need for more specific treatment to address these children's social problems exists. It is crucial that the overall treatment also focuses on treating comorbid disorders and preventing the development of later disorders and illnesses. Some psychosocial treatments might alleviate both the ADHD symptoms and the social skills problems; behavioural/cognitive treatments, including social skills training, which are the best-documented (26).

Pharmacological interventions

A number of clinical trials have indicated that approximately 80% of children and adolescents with ADHD show clinically significant benefits from treatment with methylphenidate. The placebo effects from clinical trials are about 3% to 10%, leading to a relative risk reduction of up to 77%. Reviews have assessed the effect of methylphenidate and have shown clear positive treatment effects. However, several of these studies and reviews had biases and other limitations (27).

The most common drugs used for the treatment of ADHD in children and adolescents include methylphenidate, atomoxetine, and dexamphetamine (22;28). The functional mechanisms of the medications are not clearly known, but it is presumed that the effects on ADHD symptoms are related to the effect of the stimulants on dopaminergic and noradrenergic neurotransmission in the central nervous system (29).

Children and adolescents with ADHD often have difficulties when it comes to language, learning, and anxiety and have conflict-ridden interactions with parents and teachers, and little evidence shows that stimulant medications have an effect on these outcomes (29-32). In addition, adverse reactions are cause for concern, most commonly including headaches, sleeping problems, fatigue, and decreased appetite. However, these are reversible with the exception of decreased appetite, which in many cases continues through treatment (25). Serious adverse reactions affect 3% to 6% of children (26;33-35). There is evidence that dexamphetamine can affect children's sleep; cause dry mouth, thirst, weight loss, decreased appetite, stomach aches; and increases the risk of regressive, dependent behaviour and psychosis (22). Atomoxetine is associated with pain, nausea and vomiting, decreased appetite with associated weight loss, dizziness, and slight increase in heart rate and blood pressure (36). There is some evidence that methylphenidate also affects children's height and weight curves (37;38). Further, there have been reports of sudden death in children and adults treated with methylphenidate, but it is unclear if these deaths are directly related - more research is being conducted on this topic (39). Some research suggests that the combination of behavioural therapy (e.g. behavioural parent

training, school consultation, and direct contingency management) and pharmacotherapy might benefit most patients (26;40).

Psychosocial interventions

The best-documented non-medical methods of ADHD treatment are the behavioural/cognitive ones. These consist of behavioural training, social skills training, cognitive training, and different forms of expedient adjustment of the child's difficulties to the environment at home and at school (26;41). There is good evidence on the effect of behavioural treatment on children with ADHD (42). For cognitive treatment, on the other hand, there is no clear evidence, so it cannot be recommended either as an independent treatment nor in combination with medical treatment (43). We have identified four meta-analyses of social skills training for children with ADHD, two of which state that social skills training for children with ADHD has no effect (44;45) and the other two stating that social skills training for children with ADHD has a significant treatment effect (46;47). However, looking at the quality of this meta-analysis, all of their findings must be questioned due to several methodological weaknesses, as these latter reviews did not evaluate systematic errors (bias), and random errors (play of chance) in the included trials, making them questionable.

A Cochrane review by Zwi et al. found that parental training might have a positive effect on the behaviour of children with ADHD, but the ADHD symptom data are ambiguous and all the included studies were of poor methodological quality. The authors concluded that there is currently no evidence of parent training for children that could form practice recommendations (48).
Interventions that focus on improving function in school could be helpful (49).
One Cochrane review assessed family therapy; only two studies met the inclusion criteria of the review, but the findings differed and further research is needed (50).

Other interventions

In three Cochrane reviews, the effects of acupuncture, homeopathy, and meditation therapy on ADHD symptoms in children were assessed. Several trials were included, but no evidence supporting or refuting any of these interventions were found, indicating also the lack of research on these topics (51-53).

ADHD and family-theoretical considerations

The interventions follow the assessment of the child. However, an ADHD diagnosis does not give a sufficiently qualified basis for making a treatment plan for that specific child and its family. It is important to explore the severity and the comorbidity of psychological, behavioural,

and learning difficulties. The assessment of the child's difficulties should be a part of a wider programme with an evaluation of the whole family's situation. Thus, ideally the type of intervention offered each child should differ depending on the child's difficulties and family situation. There is both mild and severe ADHD and these children's social and relationship competences differ greatly. In this thesis, I focus on the attachment aspect as an important part of the development of the personality of these children. The whole interesting area of ADHD and genetics/biology could also have been elaborated in this thesis, as it is clearly associated to ADHD. However, I have chosen to focus on the attachment aspect, as this is associated with both ADHD and social skills competences, adding a review of the genetics aspect would have been too vast a subject of this paper. It must, however, be underlined that it is not possible to state whether the attachment problem is caused by the genetics aspect of ADHD, or if it is the other way around – i.e., the developmental problems are causing the ADHD disease. Most likely, it is a combination. Several studies have shown the association between attachment and social skills. In a study by Di Tommaso et al. it was found that secure attachment and social skills were related on several significant levels (54). Allan et al. showed that attachment insecurity predicted a decrease in social skills (55). Thus, it is relevant to examine the differences in attachment competences among children with ADHD and explore the association between ADHD and attachment, and furthermore to investigate how these profound interpersonal patterns can affect the efficacy of social skills training. There is much research investigating the association between ADHD and different kinds of comorbidity, but the question about ADHD and attachment has not been elaborated upon. Therefore, research that can say something about the child's ability to relate to other people is much needed.

Attachment and ADHD

The theory of attachment was formed by John Bowlby and Mary Ainsworth, and was founded via three articles by Bowlby (56-58). The different forms of attachment include *secure attachment*, *insecure dismissing, insecure preoccupied,* and *disorganised attachment* (59;60). Bowlby's theory of attachment has a biological focus because he claimed that the young child creates attachment with the caregiver as a survival instinct. The child searches for safety in relation to the mother, e.g. when he/she was hungry or afraid. The theory also has a developmental aspect because there is a stimulus for development in the attachment, exploration, and fear factors. The child's experience with the caretaker causes the development of so-called 'internal working models', which reflects the outer lived experiences on an inner level. The experiences with the social environment could create a securely attached child in whom the majority of internal working models are positive, or an insecure child in whom the majority of internal working models are negative (61).

A securely attached child can use the primary caregivers as a safe base from which it can move 'out in the world' on 'discovery trips'; later on, this child will meet 'the outside world' with

positive expectations and trust. An insecurely attached child will have negative expectations of its surroundings and will be marked by anxiety. It is important to stress that the problems with attachment competences can also be caused by inborn constitutional difficulties.

Brief narrative overview of the empirical literature on attachment and ADHD

The PsycINFO, Medline, and EMBASE databases were searched for relevant abstracts using the terms ADHD, randomized controlled trials (RCT), and attachment. ADHD terms also included minimal brain disorder, hyperactivity, and attention deficit disorder. RCT terms were used according to the highly sensitive RCT filter (62). Attachment terms included 'reactive attachment disorder', 'emotional attachment', 'empathy', 'parent-child-relations', 'object relations', etc. The complete search strategy is described in detail in Appendix.

The searches were conducted at two time points: the first search (May 2010) resulted in 71 records, nine of which were relevant; the second search (September 2011) resulted in 159 records, four of which were relevant. The 13 relevant studies were reviewed in detail (Table 1).

Table 1: ADHD and Attachment

First author	Article title	Year	Location	n	Design and sample source	Methods and measures
Niederhofer	Attachment as a component of attention deficit hyperactivity disorder	2009	Italy	101	Naturalistic, outpatient	• "Hyperscheme' • Parent-Child Reunion Inventory
Kissgen	Attachment representation in mothers of children with attention deficit hyperactivity disorder	2009	Germany	51	Naturalistic, outpatient	• DISYPS-KJ • Adult Attachment Projective
Lifford	Parent-child relationships and ADHD symptoms: A longitudinal analysis	2007	UK	194	Longitudinal design	• Child Behaviour Checklist • Child`s Report of Parental Behaviour Inventory
Johnston	Responsiveness in interactions of mothers and sons with ADHD: relations to maternal and child characteristics	2002	Canada and USA	136	Baseline characteristics	• Clinical interview • Observation from videotaped interactions
Green	Disorganized attachment representation and atypical parenting in young school age children with externalizing disorder	2007	UK	69	Naturalistic, outpatient	• Eyberg Child Behaviour Inventory • Manchester Child Attachment Story Task • Atypical Parenting/Expressed Emotions • Beck Depression Inventory
Finzi-Dottan	ADHD, temperament, and parental style as predictors of the child`s attachment patterns	2006	Israel	65	Naturalistic, outpatient	• Temperament Survey for Children: Parenting Ratings • Parents Report Questionnaire • Children`s Attachment Style Classification Questionnaire
Follan	Discrimination between attention deficit	2010	UK	107	Naturalistic, outpatient	• Clinical assessment • Semi-structured Interview

	hyperactivity disorder and reactive attachment disorder in school aged children					With Parents • Waiting Room Observation • Relationship Problems Questionnaire
Pinto	ADHD and infant disorganized attachment. A prospective study of children next-born after stillbirth	2006	UK and Sweden	53	Cohort	• Structured Clinical Interview • Antenatal assessment of maternal unresolved mourning • The Strange Situation test of infant security • Assessment of mother's ADHD symptoms in childhood (Wender Utah Rating Scale) • ADHD-RS
Clarke	Attention deficit hyperactivity disorder is associated with attachment insecurity	2002	Australia	38	Between-group comparison	• Demographic interview • The Revised Conners' Parent Rating Scale • The Separation Anxiety Test • The Self Interview • Family Drawing
Karabekiroglu	Parental attachment style and severity of emotional/behavioural problems in toddlerhood	2010	Turkey	103	Naturalistic, outpatient	• The Structured Clinical Interview for DSM-IV-TR • Beck Depression Inventory • Adult Attachment Scale • Instruments for Toddlers • Child Behaviour Checklist/2-3
Audet	Mitigating effects of the adoptive caregiving environment on inattention/overactivity in children adopted from Romanian orphanages	2011	Canada	142	Naturalistic, between-group comparison	• Child Behaviour Checklist/4-18 Preschool Behaviour Questionnaire • The Home Observation for Measurement of the Environment • Parent Interaction Style
Abdel-Hamid (conference abstract)	Attachment in adult patients with attention-deficit hyperactivity disorder	2010	Germany	39	Naturalistic, between-group comparison	Self-estimation measures
Bohlin (conference abstract)	Are attachment disorganization and inhibition independent predictors of symptoms of ADHD, externalizing problem behaviors and callous unemotional traits?	2010	Sweden	60	Longitudinal study	Attachment doll play procedure

Few empirical studies have focused on the association between ADHD and attachment. We found only 13 relevant studies in our searches. The following nine studies support that there seem to be an association between ADHD and attachment. In the Niederhofer study, 79 of the children were assessed as having an insecure attachment competence, while 22 were assessed as having secure attachment competence. There was a statistical significant relationship between insecure attachment and ADHD (63). In the study of Kissgen et al., there was a statistical significant association between mothers with insecure attachment competences and the risk of having children with ADHD (64). In the study by Clarke et al., 19 children with ADHD were compared with 19 controls and they found consistent statistical support for an association

between insecure attachment and ADHD (65). In the study by Pinto et al (2006) in which children were followed from the age of 0 to 7 years, a clear association between disorganised attachment at an early age and later ADHD symptoms were found (66). Finzi-Dottan found that children with the ADHD combined subtype and the hyperactive-impulsive subtype showed a higher level of anxious and avoidant attachment, and had parents who used a controlling parenting style (67). In the study by Audet et al., inattention/overactivity was examined over time in relation to caregiving in three matched groups with different levels of deprivation (68). Attachment was negatively predictive of inattention/overactivity in children with <19 months' deprivation but was unrelated to inattention/overactivity in children with >19 months' deprivation (68). In the study by Karabekeriroglu and Rodopman-Arman, the association between maternal and paternal attachment style and emotional and behavioural problem severity in toddlers were investigated. The result of this study showed that a maternal insecure attachment style was significantly associated with toddler hyperactivity (69). The association between ADHD and insecure attachment was clearly supported in two studies (70;71).

The following two studies did not support the view that there is an association between ADHD and attachment. The study by Johnston et al., in which mother-child interactions were observed, reported a connection between the mother's responsiveness and conduct problems but not in relation to children's ADHD symptoms. Green et al. found no association between ADHD symptoms and disorganised attachment, as >50% of the disorganised children did not have ADHD (72;73).

Two other studies showed other aspects of the relation between ADHD and attachment. Follan et al. tried to determine whether it was possible to discriminate between children with ADHD and children with reactive attachment disorder. The study concluded that it is possible to discriminate clearly between the two syndromes (74). Lifford et al. investigated the association between children's ADHD symptoms and the parent-child relationship. They found a difference between the mother or father's rejection of the child and the child's degree of ADHD symptoms. In short, the children's ADHD symptoms influenced mother-child rejection, whereas father-child rejection influenced the children's ADHD symptoms (75).

Overall, it seems that there is an association between ADHD and attachment, and this must be a topic of further research. Skovgaard also supports this in a study. She found that parent-child relationship problems identified by health nurses in the first 10 months of life were associated with a double increase in risk of a child disorder at the age one and a half years. Furthermore, she found that children with a parent-child relationship disorder had more than a ten fold risk of developing comorbid ADHD later on (76).
One must assume that children with ADHD also need a form of treatment that focuses on their ability to form relationships and on their social problems. Shmueli-Goetz et al. assessed 227

children using the Child Attachment Interview (CAI) (77). The population included both a referred sample and a non-referred sample. They found that 61% of the children in the non-referred sample had secure attachment patterns, while 29% had insecure attachment patterns. They also found that 26% of children in the referred sample had secure attachment patterns, while 74% had insecure attachment patterns.

Social and emotional skills

Social skills facilitate interaction and communication. Social rules are created, communicated, and changed both verbally and non-verbally. Developing such skills is part of the socialization process. Emotional skills concern the child's ability to process, manage, express, and control his or her emotions. Emotional self-regulation is an important aspect of resilience. Children who have effective strategies for dealing with disappointments, losses, and other upsetting events are much more likely to be able to bounce back from adversity than those who do not. Managing positive emotion is also important. Success both socially and academically depends on being able to control exuberance appropriately. Inability to regulate both positive and negative emotions has been associated with disorders such as ADHD and conduct disorder (78).
The immense difficulties children with ADHD develop with regard to social interaction with peers can be reinforced by the negative reactions to their disruptive behaviour. Therefore, a vicious circle can easily develop in which difficulties increase (79).

Social skills training

Social skills training aim to teach children how to regulate their behaviour according to normal social rules. This is a method of intervention, which can help children improve their social competences. Learning occurs via role-play exercises and games as well as homework involving parents and possibly teachers. The main elements of social skills training focus on an effort to change an individual's cognitive assessment of other people and social situations. The training focuses on the subtle cues in social interaction and on being able to recognize the emotional expressions of others (80;81). The programmes often include training parents and teachers. The treatment period is often relatively short, lasting from eight to 10 weeks, but it can last up to two years (82-85).

Paper 1: Evidence of social skills training: the Cochrane review

We performed a complete Cochrane review according to The Cochrane Handbook for Systematic Reviews of Interventions (86). After registering the title, we assembled a review team and developed a protocol that was published before the work with this review started (86;87).

Objective

To assess the beneficial and possible harmful effects of social skills training in children and adolescents with ADHD.

Method

We only included randomised clinical trials investigating social skills training alone or as an adjunct to pharmacological treatment. The participants were 5 to18 year-old children diagnosed with ADHD according to the DSM and ICD diagnostic systems. We considered all types of social skills training programmes in which the training focused on behaviour- and cognition-based efforts to improve social skills and emotional competences.

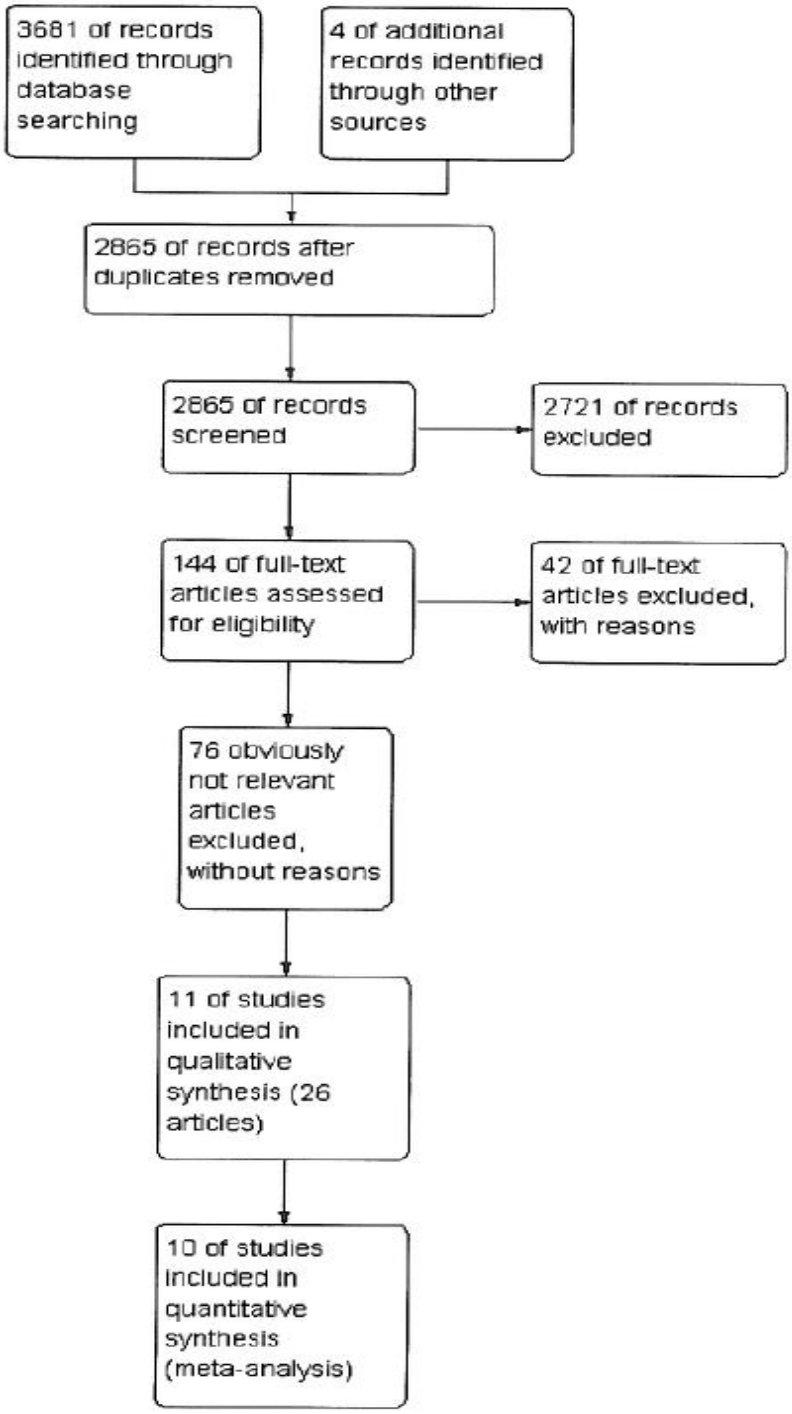
Outcomes

The predefined outcomes were social skills, general behaviour, ADHD symptoms, school performance and grades, participant and parent treatment satisfaction, and adverse outcomes.

Search strategy

We searched the following electronic databases: The Cochrane Central Register of Controlled Trials (CENTRAL, 2011(1)); MEDLINE (1948 to 9th week of 2011; searched on 2 March 2011);, EMBASE (1980 to 9th week of 2011; searched on 2 March 2011), Eric (1966 to 9th week of 2011; searched on 2 March 2011), Amed (1985 to 24th week of 2011; searched on 17 June 2011), PsycINFO (1806 to 9th week of 2011; searched on 2 March 2011), CINAHL (1980 to 9th week of 2011; searched on 2 March 2011), and Sociological Abstracts (1952 to 9th week of 2011; searched on 2 March 2011). We also searched International Clinical Trials Registry Platform for trials on 15 October 2010. We applied no language or date restrictions to the searches. We contacted 176 experts in the field for possible information about unpublished or ongoing randomised clinical trials and searched the Internet for conference abstracts; 15 of these experts replied via email.

Figure 1: Flow chart of the review process



The experimental interventions

In the 11 included trials, the experimental intervention had different names: social skills training, cognitive-behavioural intervention, multimodal behavioural/psychosocial therapy, behavioural therapy/treatment, behavioural and social skills treatment, and psychosocial treatment, all of which were considered eligible for inclusion in the review. The trials compared social skills training, parent training, and medication versus medication. In some of the trials, there were also teacher consultations. We included all the trials, with or without teacher consultations in the meta-analyses.

The control interventions

In all the trials there was a no treatment control group (no treatment or waitlist), and medical treatment was either offered to both the experimental and control groups or in none of these groups.

Data extraction

Two authors independently extracted data by using an appropriate data collection form. The data was entered into the Cochrane software: Review Manager. Differences were resolved by discussion. In cases where there were not enough data or unclear data in the published trial reports, nine of the authors were contacted and a request made to supply the missing information. Answers were received from five authors.

Heterogeneity-adjusted required information size and trial sequential analysis

Trial sequential analysis (TSA) is a tool for quantifying the statistical reliability of the data in a cumulative meta-analysis and gives a valuable overview of the number of participants needed to make a firm evaluation of a possible intervention effect (88-91). In traditional meta-analyses the risk of type 1 errors (rejecting the null hypothesis) is considerable larger than usually understood. When one thinks one is dealing with a type 1 error risk of 5%, the risk may in fact be 10% to 40%. This is due to sparse data and repetitive testing in accumulating meta-analysis (88-92).

Comparable to the 'a priory' sample size estimation in a single RCT, a meta-analysis should include an information size (IS) at least as large as the sample size of an adequately powered single trial to reduce the risk of random error. The TSA provides the required information size (RIS) in meta- analysis to adjust the significance level for sparse data and repetitive testing on accumulating data to avoid the increased risk of random error (91).

Multiple looks on accumulating data when new trials emerge leads to 'repeated significant testing', thus, use of conventional *P*-value criterion is prone to exacerbate the risk of random error (92;93). Meta-analyses not reaching the RIS are analysed with trial sequential monitoring

boundaries analogous to interim monitoring boundaries in a single trial (91). This approach will be crucial in pending updates of the review.

We calculated the a priori heterogeneity-adjusted required information size (APHRIS) (i.e., number of participants required to detect or reject a specific intervention effect in the meta-analysis) and performed trial sequential analysis for the primary outcome, teacher-rated social skills competences at end of treatment based on the following a priori assumptions.

1. The standard deviation of the primary outcome is 1.0
2. An anticipated intervention effect equal to Hedge's g 0.5
3. A maximum type I error of 5%
4. A maximum type II error of 20% (minimum 80% power) and of 10% (minimum 90% power)
5. A priori anticipated 50% heterogeneity (88-91)

We conducted TSA to assess the risk of type 1 error and to estimate how far we were from obtaining the required information size to discover or reject a certain modest intervention effect.

Subgroup analyses

We conducted three subgroup analyses to investigate whether there was a statistical significant difference between the subgroups.

Subgroup analysis 1: trials with ADHD and comorbidity compared to trials with ADHD and no comorbidity.

Subgroup analysis 2: trials with social skills training without parent training compared to trials with social skills training and parent training.

Subgroup analysis 3: trials with social skills training, parent training, and medication compared to trials with social skills training, parent training, without medication.

Sensitivity analyses

To test the robustness of the primary analyses we performed sensitivity analyses in each outcome.

We investigated if the effects were significantly affected by excluding the trial with the longest treatment duration; excluding the largest trial; and by conducting both fixed-effect and random-effects model analyses.

Quality assessment

Two of the review authors selected trials for inclusion and resolved any disagreements. The authors also independently assessed the risk of bias in all of the trials following the recommendations in The Cochrane Handbook for Systematic Reviews of Interventions (Tables 2 and 3)(86).

Table 2: Risk of bias table of the 11 included trials

Green = Low risk of bias

Yellow = Unclear risk of bias

Red = High risk of bias

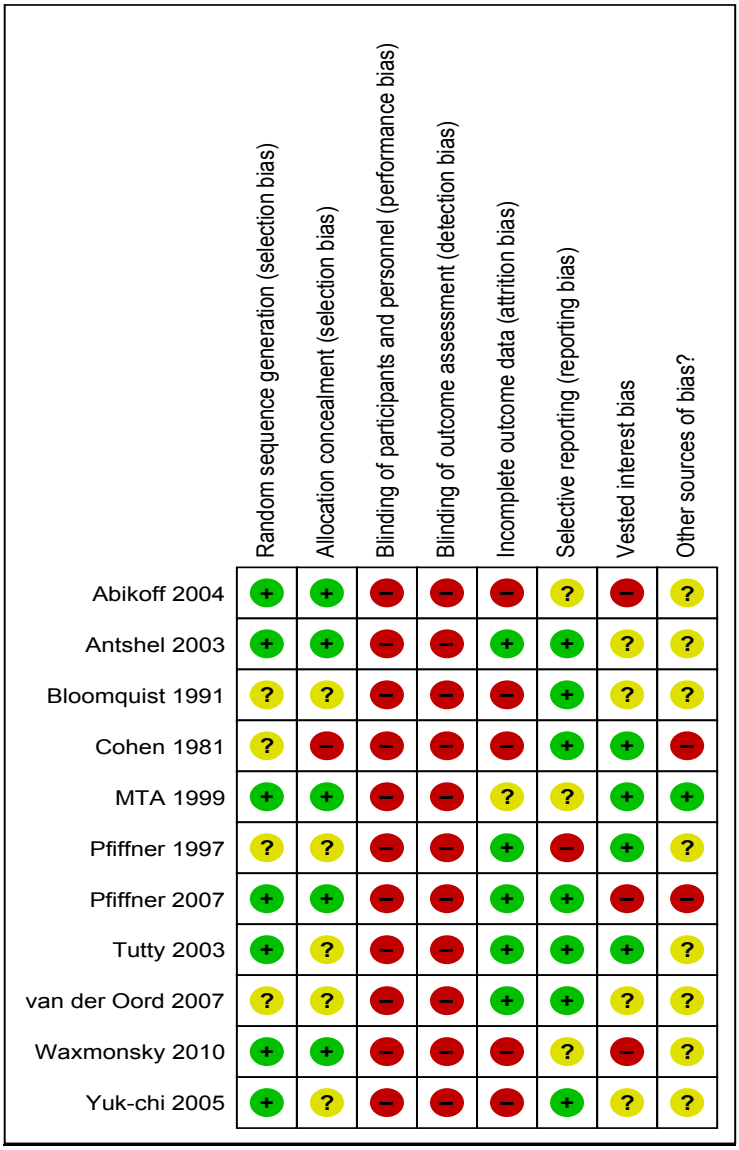
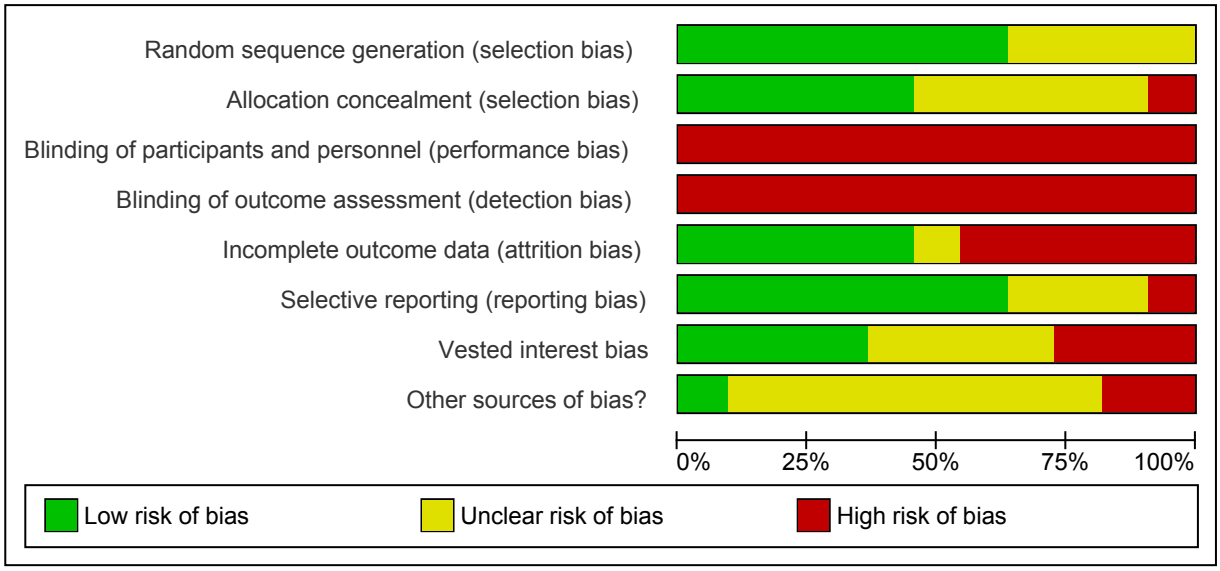


Table 3: Each risk of bias item presented as percentages across all included studies



Results of the Cochrane review

We identified 3,681 records after the database search. A total of 144 full text articles were considered for inclusion. Ultimately, 11 trials, including 747 patients, published in 26 articles were included in the review, and 10 of these trials were used in meta-analyses (Figure 1). All of the patients in the included trials were 5 to 12-year-old children with an ADHD diagnosis. Eight of the 11 included trials were carried out in the US, one in Canada, one in the Netherlands, and one in China.

Risk of bias in included studies

All the included trials were considered as high risk of bias as there were systematic errors (bias) in all of them (Table 2). More than half of the trials had systematic errors regarding generation of allocation sequence and allocation concealment. None of the trials had blinding of personnel and participants or on the outcome assessment. In the Cochrane Handbook of Systematic Reviews of Interventions, it is stated that there is no sufficiently well designed method to combine the results of trials with high, unclear, or low risk of bias. However, it is possible to perform meta-analysis when all the studies are low risk, all unclear, or all the studies are at high risk of bias, and to perform sensitivity analyses accordingly. We performed meta-analyses on all the trials. We also added an evaluation of our results following the GRADE system to ensure quality judgment about risk of bias, as well as other factors affecting the quality of evidence (86;94).

We performed meta-analyses on the teacher-rated, social skills, general behaviour, and ADHD symptom outcomes. We chose teacher rated as our primary analysis because the teachers, in some way, were more blinded than the parents, who were not blinded at all. We performed all

the subgroup analyses as described above, but found no statistical differences in these comparisons. We also conducted sensitivity analyses as described above and found no statistical differences. There were, however, significant differences between the three teacher-rated primary analyses; social skills, general behaviour, and ADHD symptoms and the three parents-rated secondary analysis; social skills, general behaviour, and ADHD symptoms. This difference is interesting and questions our decision of choosing the teacher-ratings as the primary analysis in this outcome. The parents might be more sensitive to the children's changes, however they are highly subjective, and therefore it is our opinion that the teacher ratings carry more validity.

Trial sequential analysis (TSA)

The primary analysis, teacher-rated social skills competences at the end of treatment, was further analysed with TSA. Using an 'a priory' assumption about the intervention effect being half of the standard deviation, the intervention effect barely reaches into the futility area, possibly signalling that there is no effect of social skills intervention on teacher-rated social skills competences at the end of treatment (Figure 2). In this 'a priory' assumption, however, there is a 20% risk of overlooking a true effect, and minimizing this risk to 10% gives a priori heterogeneity-corrected required information size (APHRIS) of 338 participants (Figure 3) before a firm conclusion can be made.

Using available data from this meta-analysis to calculate the required information size in the TSA yields a post hoc heterogeneity-corrected required information size (PHHRIS) of 504 participants before a firm conclusion can be drawn (Figure 4). The estimated effects size of MD 1.81 (95% CI -1.02. to 4.64) is low and not considered clinical relevant as none of the trials were low risk of bias. We chose an intervention effect of 4, which is more clinically relevant for social skills rating scales, and a potential likely heterogeneity of 25% (available data: 95% CI for $I^{2:}$ 0.00 to 0.59, mean: 0.00).

Both the 'a priory' and the 'post hoc' trial sequential analyses show that there is a need for more participants to make a firm conclusion as to whether social skills training benefits social skills competences.

Figure 2: TSA analysis of teacher-rated social skills competences at end of treatment with power of 80%.

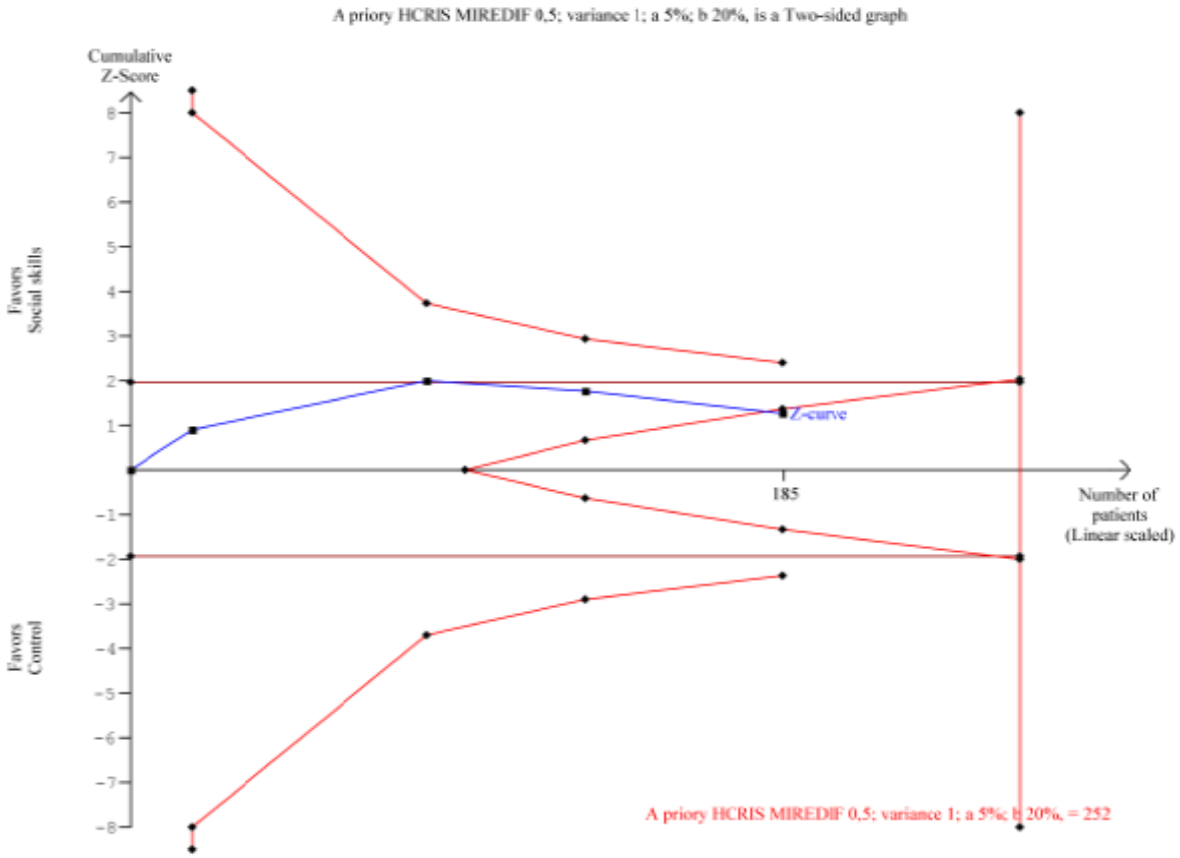


Figure 3: TSA analysis of teacher-rated social skills competences at end of treatment with power of 90%

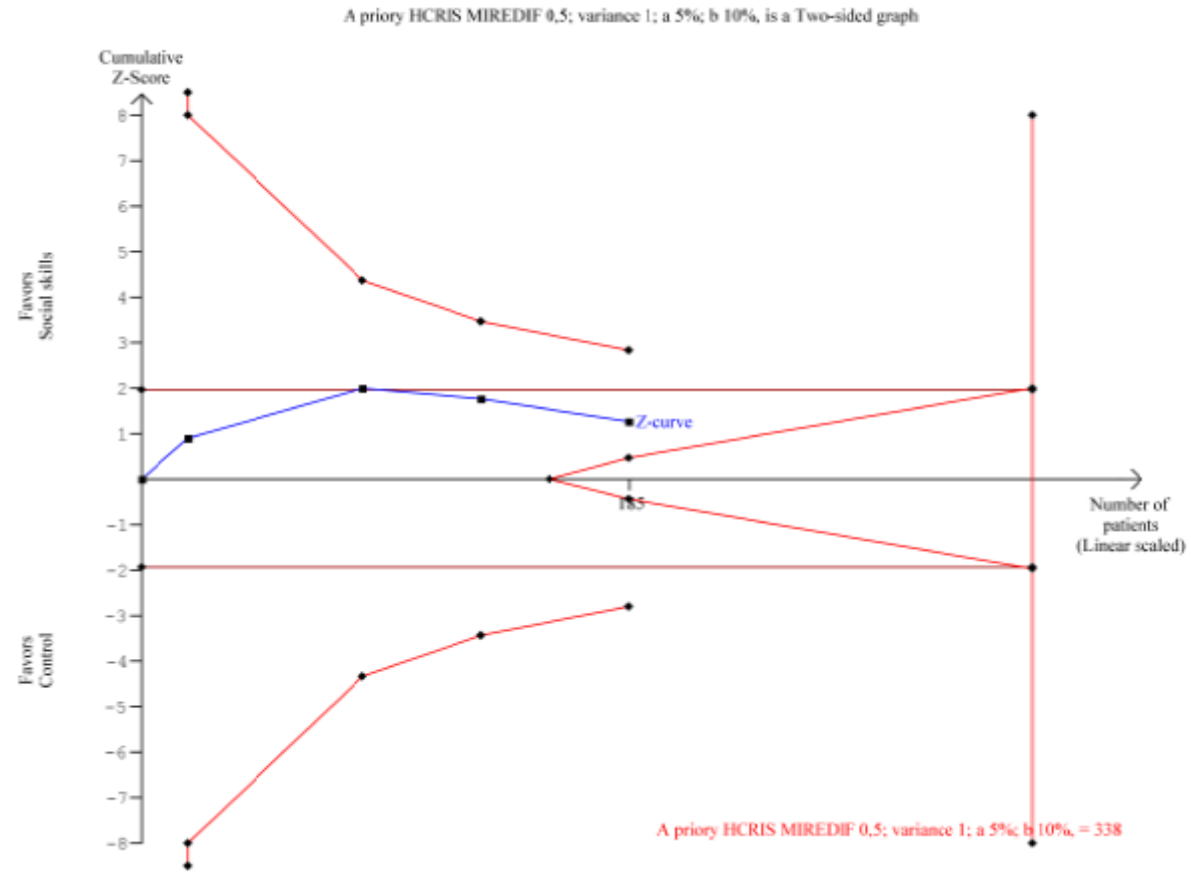
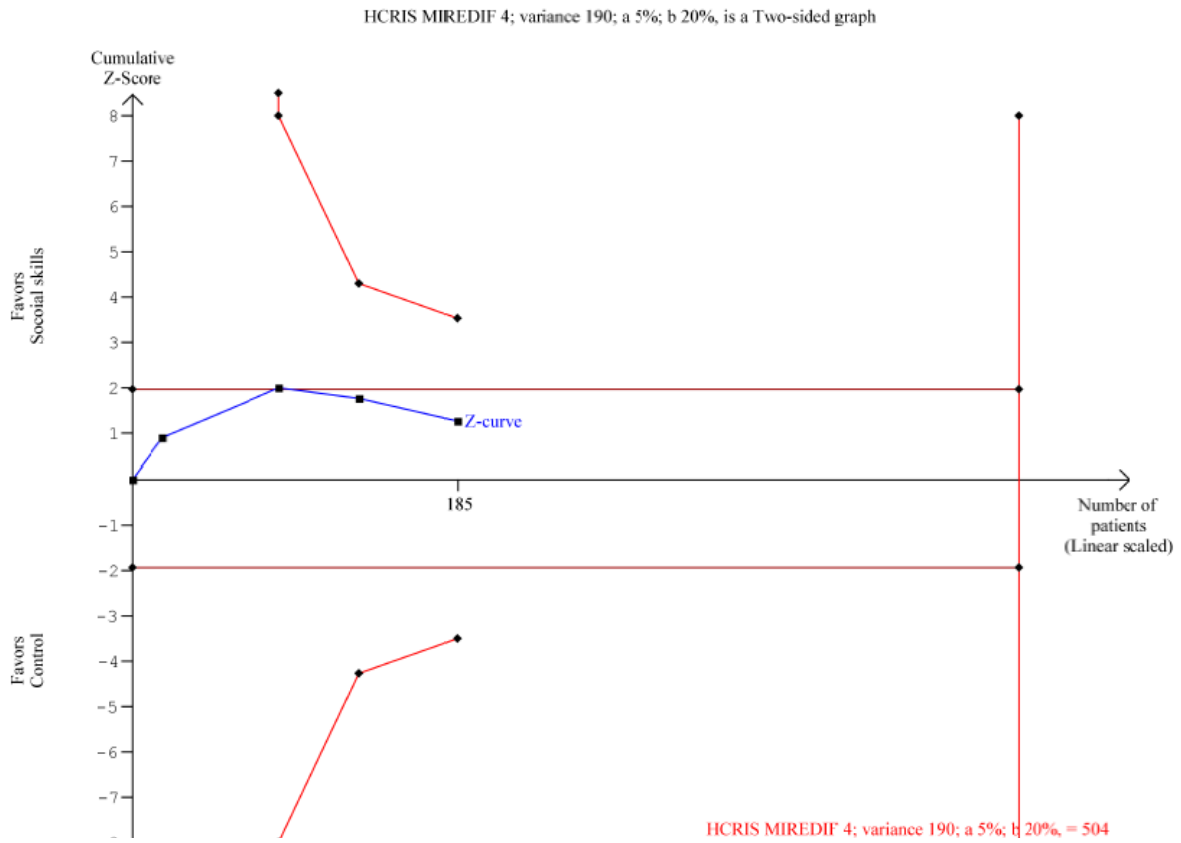


Figure 4: TSA based on available data - the teacher-rated social skills competences meta-analysis



The overall findings show no treatment effect in the social skills competences outcome (standard mean difference [SMD], 0.16; 95% confidence interval [CI], (-0.04 to 0.36), general behaviour (standard mean difference [SMD] 0.00; 95% confidence interval [CI] -0.21 to 0.21), and ADHD symptoms (SMD, -0.02; 95% CI, -0.19 to 0.16) (Table 4).

The conclusion of this review is that there is currently no evidence to support or refute social skills training for children with ADHD. There is a lack of trials with low risk of bias and with sufficient patients (Figures 2-4). There is a need for more high-quality trials with sufficient numbers of participants (95). The summary of findings in Table 4 shows the results in the most important findings; the two primary and the first secondary outcomes, these were the outcomes where it was possible to perform meta-analysis.

Table 4: Summary of findings

Social skills training compared to for No intervention

Patient or population: No intervention
Settings: all
Intervention: Social skills training
Comparison:

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk **Social skills training**				
Teacher-rated social skills competences at end of treatment all eligible trials SSRS		The mean teacher-rated social skills competences at end of treatment all eligible trials in the intervention groups was **0.16 standard deviations higher** (0.04 lower to 0.36 higher)		392 (5 studies)	⊕⊕⊖⊖ **low**	
Teacher-rated general behaviour at end of treatment all eligible trials		The mean teacher-rated general behaviour at end of treatment all eligible trials in the intervention groups was **0.00 standard deviations higher** (0.21 lower to 0.21 higher)		358 (3 studies)	⊕⊕⊖⊖ **low**	
Teacher-rated ADHD symptoms at end of treatment all eligible trials		The mean teacher-rated adhd symptoms at end of treatment all eligible trials in the intervention groups was **0.02 standard deviations lower** (0.19 lower to 0.16 higher)		515 (6 studies)	⊕⊕⊖⊖ **low**[1]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Lowered by one grade because of high degree of hetereogenity

Paper 2: The SOSTRA ADHD trial

Introduction

Based on the Cochrane review results, we performed a randomised clinical trial investigating the effect of social skills training in children with ADHD.

We tried to avoid some of the systematic errors we found in many of the trials included in the Cochrane review. We therefore developed a protocol with predefined primary and secondary outcomes, performed a sample size calculation, made a detailed plan for the analyses, used a central computer-generated randomisation procedure, properly concealed the allocation, and used blinded outcome assessors. The protocol was published before we embarked on the trial (96). We developed a manual and video-recorded social skills training module with a weekly 1.5-h intervention programme for both the child and the parents. The programme lasted for eight weeks and the treatment content included different forms of cognitive-behavioural techniques aimed at teaching the children more self-control and social skills. The control treatment consisted of a standard treatment of medication and consultations.

Aim

The primary purpose of the trial was to examine the effect of the combination of social skills training, parental training, and standard treatment versus standard treatment alone in 8–12-year-old children with ADHD. The secondary purpose was to examine the relationship between social skills and ADHD symptoms, the ability to form attachments, and parent's ADHD symptoms.

Method

The trial was constructed as a two-armed, parallel group, assessor-blinded superiority trial. The participants were randomised to either social skills training and parental training plus standard treatment or standard treatment alone.

The trial took place in the Child Psychiatric Clinic in Holbæk, Denmark. This clinic annually receives 200 children with a suspected ADHD disorder. The referrals come from general practitioners, specialists, the pedagogical and psychological advice centres in the municipality, psychologists in general practice, and others.

Participants

The inclusion period for the trial was from August 2009 to January 2011.

The records of 8 year to 12 year-old ADHD patients from visitation meetings were distributed to the primary investigator. Here, the inclusion and exclusion criteria were evaluated. If documented in the record that some of the exclusion criteria were fulfilled, the child was excluded. The families who wanted to participate were invited for assessment. They received a

letter with a brochure describing the research project and concrete dates for when the research assessment would occur. If the family did not want to participate, they were invited for an ordinary assessment later on.

Inclusion/exclusion

The children were screened according to the following inclusion criteria: ADHD diagnosis according to DSM-IV; 8–12 years of age at the start of assessment; and parents willing to participate in the trial, give consent for medication treatment, and understand and speak Danish. Exclusion criteria were schizophrenia or autism diagnosis according to the DSM-IV, violent or criminal children, verbal or non-verbal intelligence quotient (IQ) < 80, previously medicated for ADHD, and resistance to participating (Table 5).

Table 5: Inclusion and exclusion criteria of the SOSTRA trial

Inclusion	Exclusion
1) Parents interested in participating in parental groups in the Child Psychiatric Clinic in Holbæk	Patients with the following diagnoses according to DSM-IV: Schizophrenia
2) The patient (and parents) must understand and speak the Danish language to an extent where a translator is not needed in order to be able to complete the assessment and the treatment	2) Children with; Autism according to the DSM-IV *or a cut off score on both the SCQ questionnaires >15*
3) The parents must give informed consent to participate in the trial	3) Violent and criminal youngsters
4) The child must be 8–12 years of age at the start of the assessment	4) Children with a total verbal and non-verbal intelligence quotient (IQ) <80 according to the WISC-III
5) Both boys and girls can participate	5) Strong resistance from the child to participate
6) Children with a total verbal or non-verbal IQ >80 according to the WISC-III	6) Previously started medical treatment for ADHD
7) The children must fulfil research criteria for the diagnosis of ADHD according to the DSM-IV (1994): codes 314.00, 314.01, 314.02, or 314.9.	7) No informed consent
8) The parents must provide consent for medical treatment for their child, and there must be a clinical indication for medical treatment	

Assessment

The first author (OJS), who was trained to administer the K-SADS at a training course, administered the Schedule for Affective Disorders and Schizophrenia for School-aged Children (K-SADS). The children were screened at the time of entry using the K-SADS. This semi-structured interview includes algorithms from the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) in children and adolescents (97). The children were screened for autism and the parents completed the Social Communication Questionnaires (SCQ). Children with scores >15 on 2 SCQ questionnaires were excluded (98). The parents also completed the Adult Self-

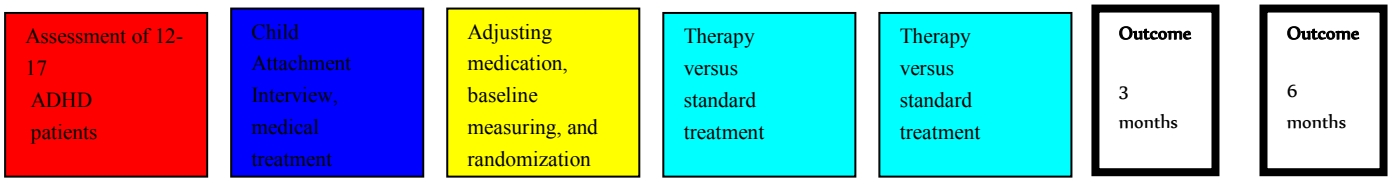
Report Scale (ASRS)(99) to screen for adult ADHD symptoms. Children who had not been subjected to the Wechsler Intelligence Scale for Children (WISC III test) (100) during the past three years were tested with the WISC III test by unit psychologists.

The parents were informed in advance that if their child did not fulfil all inclusion criteria and none of the exclusion criteria - a condition for participating in the trial - they were excluded from the trial. Unit clinicians fulfilled clinical assessment. All of the children were tested using the Children Attachment Interview (CAI) (101). A certified rater blinded to the treatment assignment scored this interview. The children's teachers completed the Conners 3 and the Conners Comprehensive Behaviour Rating Scale (CBRS) rating scales (102;103).

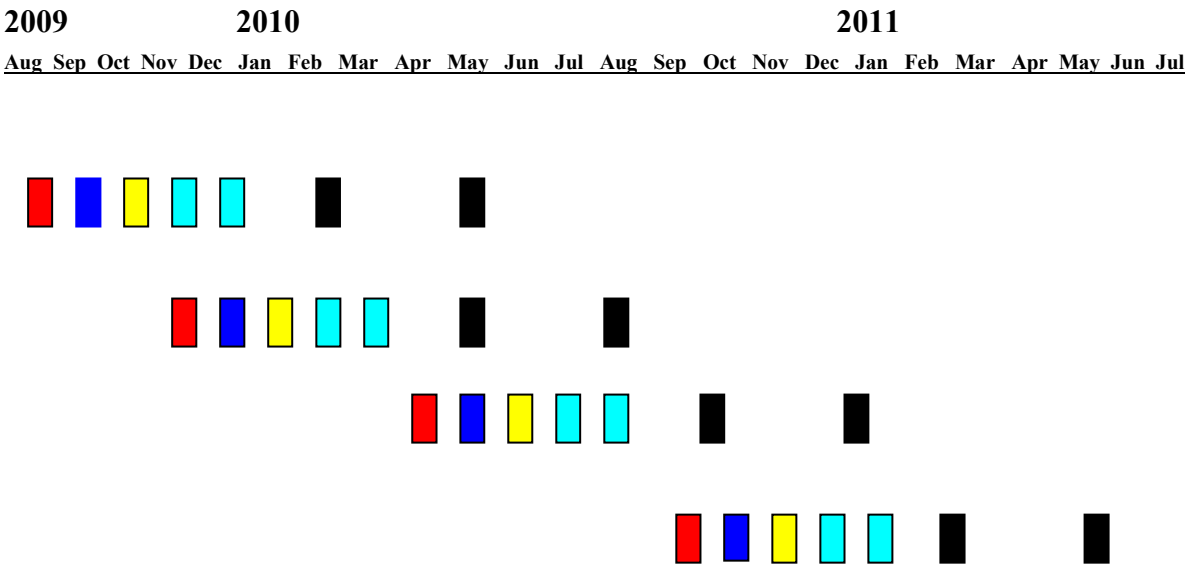
The procedure

The research programme itself was divided into several steps, each consisting of 5 substeps (boxes) in which 12-17 children were assessed each time, followed by the start of medication, baseline measurements, the start of treatment, and three and six months after baseline outcome assessment time points (Figure 5).

Figure 5: The trial procedure



The different steps sketched above are repeated four times in a staggered manner. The last outcome measurements were carried out in July 2011.



Measurements

The outcome measures were planned to be ADHD core symptoms and social skills. Furthermore, we wanted to see if the children's attachment patterns measured by the CAI and the parent's own ADHD symptoms measured by ASRS could predict the outcomes. We did not find any suitable rating scales in Danish; therefore, in cooperation with the Hogrefe Psychological Publisher, we performed a translation of the internationally often used Conners ADHD 3 Rating Scale (115 questions) and the Conners CBRS Rating Scale (204 questions). Both rating scales used the Likert 0–3 scale (not true (0), sometimes true (1), often true (2), practically true all the time (3)), indexes from these rating scales were used as primary and secondary outcome measurements. The primary outcome was the hyperactivity/impulsivity index from the Conners 3 Rating Scales (Table 6).

Table 6: Outcome measures

Primary Outcome	**Measurement Tool**
ADHD symptoms	Conners 3rd Edition 'hyperactivity-impulsivity' subscale (teacher-rated)
Secondary Outcomes	
Social skills	Conners CBRS 'social problems' subscale (teacher-rated); Conners 3rd Edition subscale 'peer relations' subscale (teacher-rated)
Aggressive behaviour	Conners CBRS 'aggressive behaviour' subscale (teacher-rated)
Emotional distress	Conners CBRS 'emotional distress' subscale (teacher-rated)
Executive functions	Conners 3rd Edition 'executive functioning' subscale (teacher-rated)
Academic performance	Conners CBRS 'academic performances' subscale (teacher-rated)
Predictor variables:	
Attachment patterns	Child Attachment Interview
Adult ADHD symptoms	Adult Self-Report Scale

Both Conners 3 and Conners CBRS are validated on large (more than 2000) representative normative samples and have high reliability (102;103). In this kind of research investigating the effects of psychosocial interventions, it is very common to use different types of rating scales as outcome measures. The rating scales are rated by parents, teachers, or the children themselves. Even if these measurement instruments have good psychometric properties and are valid and reliable, they are often scored by non-blinded raters. It is necessary that the raters know the child; otherwise, it is not possible to rate the child's behaviour. However, this introduces the problem of bias, e.g. systematic errors that influence the reliability of the treatment effect. A blinded rater can be used, but then the problem of sensitivity is introduced since they do not know the child, making it difficult for them to rate the child's behaviour. It is possible to make blinded ratings using specific methods where the raters do not know the child, but this is a complicated method. The teachers can be blinded to treatment assignment, but the problem is that they often have 20 other pupils in the class to manage. The teacher, of course, knows the child, but it can be difficult for them to see gradual changes in the child's behaviour. Nevertheless, we ended up using the teacher rating scales because they were blinded to the treatment allocation. We could also have used the parents' rating scales, but since the parents also participated in the treatment this would have introduced a very high risk of bias.

Missing data

We hoped to avoid missing data by informing each teacher of the importance of answering every question in the questionnaires. After receiving the questionnaires, the principal investigator and research secretary assessed the responses. If they found any unanswered questions, they contacted the teachers to ensure that the missing data were completed. We also planned a short one-day course about children with ADHD for the teachers whose students participated in the trial. This course was arranged in order to make the teachers more motivated to complete all the outcome forms. This course was arranged in September 2011, two months after we received the last questionnaires from the teachers.

Randomisation and sample size calculation

We also discussed the method of randomisation in the planning process of the design of the trial. It was possible to use the coin toss method, but there would still be problems with allocation concealment; therefore, we decided to use a central computer-generated randomisation procedure with two stratification variables - sex and comorbidity.

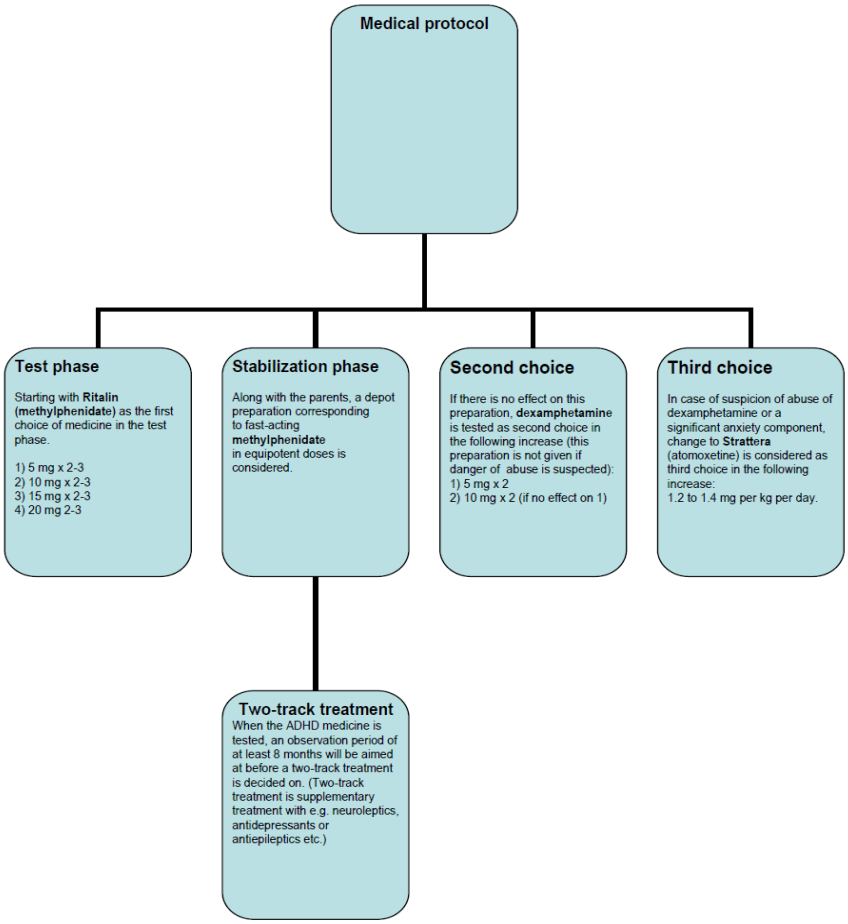
The sample size calculation was a little bit tricky since our first calculation showed the need for 120 patients, an amount that was unrealistic to include in the trial within the time limit of this research project. Therefore, we based our sample size calculation on those of earlier studies. There was not much literature guiding the achievable effect sizes or appropriate SDs for the primary outcome with the type of intervention we were investigating; however, from a meta-analysis by Bjornstad and Montgomery (50), we found an effect size on the "hyperactivity-impulsivity" index of the Connors scale of 2 and an SD of 5. The only included study Horns et al. (104) had a small sample size of 25, and the intervention was administered only to the parents. Looking at other trials using Likert scales as an assessment tool similar to the one used in our trial, we could see varying effect sizes (3; 5–8) and SDs (5; 3–9.5), but only in one of these trials the intervention was given to both the children and the parents (85;105;106).

We based our difference in the mean score of 4 on the primary outcome on index "hyperactivity-impulsivity" from the Conners scale on the existing literature and prior experience of our research department. We consider the difference in means to be of profound clinical relevance in this patient group and under the present settings. We chose an SD of 5, which can be considered a tad low; however, in the present setting, with the present population and specific intervention conditions, we foresaw limited variation. This estimate of the SD for the "hyperactivity-impulsivity" index on the Connors scale is primarily influenced by the data from Horns et al. (104). Finally, the sample size was calculated on the basis of a type I error (α) of 5% and a type II error (β) of 20%; thus, it had a power of 80% and an allocation ratio of 1:1. With a Δ of 4 and an SD of 5, a sample size of 26 participants was needed in each group.

The standard treatment

The standard treatment consisted of medication following a medication protocol (Figure 6). Before starting the medication, the child underwent physical examination and the parents were informed about the advantages and disadvantages of the medication. The family was asked to contact the unit no later than a week after the medication had begun to report how the child was doing. All the children were seen again one month after the beginning of the treatment; the positive and adverse effects were evaluated; and pedagogical counselling was given. The somatic condition of the child was examined again, and the extent of the adverse effects was evaluated. Nutrition advice was given if the child's weight had decreased. The standard treatment involves a parent group in which up to six pairs of parents meet three times over the eight-week period. The focus in this group was, in addition to general information about the disorder, different ADHD-relevant topics, e.g. the child's relationships with siblings and peers.

Figure 6: The standard treatment following a medication protocol



The experimental treatment

The group therapists participated in training courses before the start of the intervention to obtain adequate qualifications and received 24 h of supervision during the trial period. The children

were offered social skills training once a week for 1.5 h. During that time, the parents participated in parent groups. There were two therapists in each group, and they conducted four identical eight-week treatment programs. There were 6–8 patients in each group and two groups in each treatment programme. The treatment was thoroughly described in a manual, and each session with the children was recorded on video to ensure that the therapist followed the manual. The principal investigator watched the recordings through. The treatment programme was organized on the basis of several randomized trials (83;84). Different methods of teaching the children social skills were used; methods with which several other social skills programmes had obtained good results (107). Didactic instructions were used in which the children worked with symbols (e.g. dolls) and role playing. Different games, creative techniques, physical exercises, reading stories, and movies were also used. Each session had a theme, examples of which included problem solving, non-verbal communication, feelings, anger management, and conflict resolution.

In the manual, a "self/other perspective taking", which easily adapts to social skills training, was used. An aim is that the children can learn from other people's opinions about the topic that they work with. However, it is important to accept and appreciate the children's own opinions before challenging them with alternative ways of seeing things. We worked to create a safe environment in the group where the children felt safe enough to play and experiment with their own and other people's understanding of themselves and the other participants as well as of the different topics of focus. The interventions were simple and clear.

The pedagogy in the groups considered the children's special cognitive difficulties so the structure in each session was predictable, and importance was attached to learning. This method was secured by regular items on the agenda that were written on the blackboard each time.

- Round – what has happened since the last meeting?
- Revision from last time
- Homework from last time
- Presentation/education
- Participant working with the topic
- Role play/creative activities
- New homework
- Closing round

Importance was given to empathy, positive reinforcement, and a curious "non-knowing" mental attitude of the group. The aim was to create a relaxed atmosphere with room for humour.

In the parental groups, the themes from the children's groups were reviewed and discussed with the parents. Likewise, the children's homework was discussed with the parents.

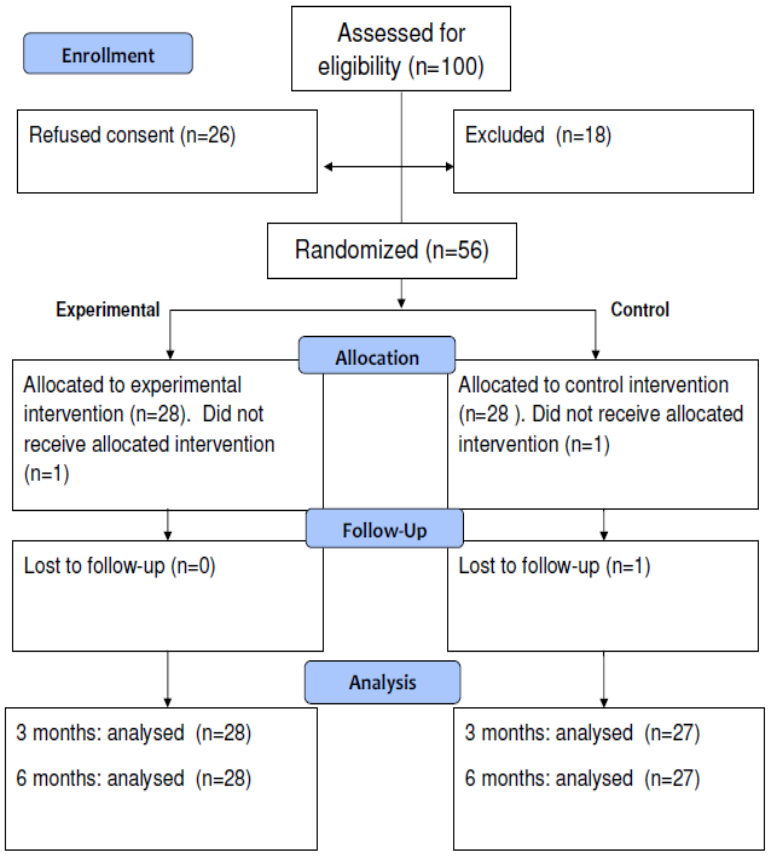
Ethical considerations

The parents received information about personal data protection, the trial purpose and methods, possible disadvantages to participating, the effect of the research project on both the individual child and children with ADHD in general: under which circumstances the trial as a whole could be interrupted and the standard treatment could be determined, and where they could obtain further information about the trial and read the attached supplement entitled "The rights of participants in a biomedical research project".

Paper 3: The SOSTRA trial results

We contacted 100 families with children referred to the clinic for an ADHD assessment to inform them about the project. A total of 26 families refused to participate in the project. Their 26 children included 25 boys and one girl. The most common reasons for not wanting to participate were not having time to participate in the groups, children already receiving medication for ADHD, and parents not wanting their children to receive medication to treat their problems. In total, 74 families agreed to participate in the project; of those, 18 were excluded (17 boys and one girl) due to not fulfilling the diagnosis of ADHD, having a diagnosis of autism or psychosis, not wanting to participate in the groups, or having a low IQ. These exclusions left a total of 56 children (39 boys and 17 girls) for randomisation. One child was excluded shortly after the randomisation because his mother decided her child should not receive medication. This child was lost to follow-up assessment. One child and his parents did not want to participate in the treatment, but all of his outcome assessments were fulfilled. All of the other children and parents fulfilled the treatment steps (Figure 7) (108). The therapist in both groups fulfilled the trial registration schedules to comply with the interventions. This measure was used to ensure that the planned material in the intervention was being sufficiently implemented.

Figure 7: CONSORT flow chart of participants in the SOSTRA trial



The demographic and clinical variables at baseline are shown in Table 7. This table shows reasonably similar demographic variables between the two groups. An interesting finding is the children's attachment patterns at baseline: 7% of these children had secure attachment competence. This value is much lower than that in a population of normal children, in which 61% were assessed to have secure attachment patterns (77).

Table 7: Sociodemographic and clinical variables (N=56)

	Experimental (N = 28)	**Standard (N = 27)**
Sociodemographic:		
Males No(%)	19 (67.8)	20 (74.1)
Age/year mean(SD)	10.6(1.29)	10.2(1.34)
ADHD problematic in the parents:		
ASRS scores ≥ 4 (father) No(%)	6(28.6)	1(5.0)
ASRS score ≥4 (mother) No(%)	6(21.4)	6(24.0)
ADHD diagnoses:		
ADHD-inattentive No(%)	10(35.7)	6(22.2)
ADHD-hyperactive/impulsive No(%)	0(0.0)	2(7.4)
ADHD-combined No(%)	16(57.1)	16(59.2)
ADHD NOS No(%)	2(7.1)	3(11.1)
Other axis 1 disorders:		
Oppositional defiant disorder No(%)	4(33.3)	4(40.0)
Anxiety disorder No(%)	4(33.3)	2(20.0)
Depressive disorder No(%)	1(8.3)	1(10.0)
Tics and Obsessive Compulsive Disorder No(%)	0(0.0)	1(10.0)
Enuresis No(%)	2(20.0)	2(20.0)
Stuttering	1(5.0)	0
Attachment competences:		
Secure No(%)	2(7.1)	2 (7.4)
Insecure/preoccupied No(%)	2(7.1)	1(3.7)
Insecure/dismissing No(%)	19(67.9)	20(74.1)
Disorganized/secure No(%)	0(0.0)	0(0.0)
Disorganized/insecure No(%)	5(17.9)	4(14.8)
Intelligence quotient:		
WISC verbal mean(SD)	93.9(15.7)	87.4(13.3)
WISC non-verbal mean(SD)	94.8(19.0)	88.9(10.5)

In Table 8, the mean values and SD are shown for all seven outcomes: hyperactivity, academic difficulties, aggresive behaviour, emotional competence, peer relations, social problems, and executive functions. There was a significant development over time in most of the outcomes, indicating that all of the children get significantly better. The time courses were not linear, i.e.

there was a highly significant effect after three months that reduced after six months (Table 8). To make this course more linear, we added a quadratic time term to the analysis. The statistical analysis of the outcomes was based on the "intention to treat" principle and was primarily performed with adjustment for the stratification variables sex and comorbidity, and was secondarily performed without this adjustment. The level of significance was 0.05. The mixed model repeated measures method was used to compare the effect of the two interventions over time on the outcome measures. A sequential hypothesis test was used, and three types of covariance matrices were examined: compound symmetric, AR (1), and unstructured. Using the Akaike and Schwartz Bayesian criteria, the best of these three covariant structures was chosen. There were 1.3–7.2% missing indices, and only two of the 165 set of questionnaires were missing. Except for the two missing questionnaires, missing data were due to inadequate questionnaire answering. We, therefore, did not conduct any imputation methods.

Table 8: Mean and standard deviation (SD) values, at entry, 3 months, and 6 months

Outcome measure	Time/month	**Experimental treatment**			**Standard treatment**		
		N	Mean	SD	N	Mean	SD
Executive s.	0	26	12.00	4.49	27	12.48	4.53
	3	27	9.30	4.58	27	8.44	4.21
	6	28	8.54	4.29	27	9.15	4.55
Academic s.	0	24	25.71	14.54	26	25.31	11.86
	3	24	20.13	15.15	26	17.88	10.11
	6	26	21.04	11.98	27	21.52	12.56
Aggressiveness s.	0	27	17.59	18.03	27	27.85	24.25
	3	27	10.00	12.58	26	11.58	11.89
	6	28	10.50	12.41	27	12.78	12.25
Emotional score	0	27	20.37	15.11	27	17.89	15.25
	3	27	17.26	11.25	26	13.04	12.31
	6	28	16.79	12.09	27	14.44	12.51
Hyperactivity score	0	27	20.70	11.38	27	24.70	14.05
	3	27	16.15	11.45	27	13.93	13.24
	6	28	15.21	9.58	27	13.37	11.86
Peer relation	0	27	8.22	6.12	27	8.63	5.41
	3	27	5.44	5.00	26	4.81	4.48
	6	28	4.86	4.58	27	5.37	5.51
Social p. score	0	27	10.33	6.34	27	11.52	7.03
	3	27	6.89	5.68	27	7.85	5.93
	6	28	8.57	6.00	27	9.56	6.76

The social skills training did not show any significant differences on any of the outcomes when the time and group variables were combined (Table 9). The mixed model analysis of each outcome measure with and without the group variable included in the model, but with the CAI and the ASRS included stepwise variables, showed that either the CAI or the ASRS predictor variables influenced the time course of an outcome measure. In some of the outcomes, it was necessary to perform a square root transformation due to the presence of skewed data prior to performance of the mixed model analysis.

Table 9: Mixed model analyses of the primary and the 6 secondary outcome measures (p values)

Outcome measure (priority)	Fixed effects of mixed model						
	Sex	Co-morbidity	t	t^2	Intervention-group (G)	G·t	$G·t^2$
SQ (hyperactivity score)*) (primary)	0.0009	0.013	<0.0001	0.051	0.40	0.33	0.40
Academic score (secondary)	0.97	0.10	0.16	0.010	0.69	0.96	0.30
SQ (aggressiveness score)*) (secondary)	0.037	0.018	0.0013	0.003	0.50	0.79	0.58
SQ (emotional score)*) (secondary)	0.42	0.0051	0.043	0.83	0.14	0.94	0.62
SQ (peer score)*) (secondary)	0.31	0.074	<0.0001	0.056	0.55	0.39	0.76
SQ(social score)*) (secondary)	0.048	0.79	0.089	0.005	0.80	0.68	0.93
Executive score (secondary)	0.55	0.028	<0.0001	0.027	0.22	0.99	0.41

*To fulfil the assumption of normally distributed values, a square root transformation (SQ) was performed prior to the mixed model analyses

The Cochrane review and the SOSTRA trial: updated meta-analyses

I updated the Cochrane review by including data from the SOSTRA trial in some of the meta-analyses. The SOSTRA trial will probably be included in the next Cochrane review update, but this decision will be made by some of the review's co-authors because I, as the primary investigator of the SOSTRA trial, may not be fully objective about that decision. I have included the ADHD symptoms and the social outcomes from the SOSTRA trial in the two meta-analyses: *teacher-rated ADHD symptoms* (Figure 8) and *teacher-rated social skills* (Figure 9). The inverse-variance method was used in the random-effects meta-analyses. I used the random-effect models analysis because the treatments are somewhat heterogenic. This method, however, gives more weight to the smaller studies and therefore I also conducted a fixed-effect-model meta-analysis as this gives more weight to the large studies. These analyses showed no significant differences. I used the SMD measures because of differences in the trial measure scales used (86).

The primary analysis: the *teacher-rated ADHD symptoms end of treatment, all eligible trials,* showed a SMD of 0.00, [95% CI 0.16 to 0.17], p = 0.96, and I^2 = 0%. The sensitivity analysis: *Teacher-rated ADHD symptoms end of treatment, excluding the trial with longest treatment duration,* shows no significant differences to the primary analysis: Test for subgroup differences: Chi^2 = 0.11, df = 1 (P = 0.74), I^2 = 0% (Figure 8).
The secondary analysis: *teacher-rated ADHD symptoms, longest follow-up,* had an SMD of -0.20 [95% CI -0.57 to 0.16], p = 0.28, and I^2 = 0% (Figure 8).

The primary analysis: *the teacher-rated social skills competences at end of treatment, all eligible trials*, showed an SMD of 0.12 [95% CI -0.06 to 0.31], p = 0.20, I^2 = 0%. The sensitivity analysis: *Teacher-rated social skills competences, excluding the trial with the longest treatment intervention*, showed no significant differences to the primary analysis: Test for subgroup differences: Chi^2 = 0.00, df = 1 (P = 0.97), I^2 = 0% (Figure 9).
The secondary analysis: *Teacher-rated social skills competences, longest follow-up*, subgroup had an SMD of 0.09 [95% CI -0.37 to 0.55], p = 0.70, and I^2 = 0% (Figure 9).

These findings show that including the ADHD and social skills outcome from the SOSTRA Trial only supports the conclusions of the Cochrane review: that there is little evidence for social skills training for children with ADHD.

Figure 8: Teacher-rated ADHD symptoms between social skills training versus control

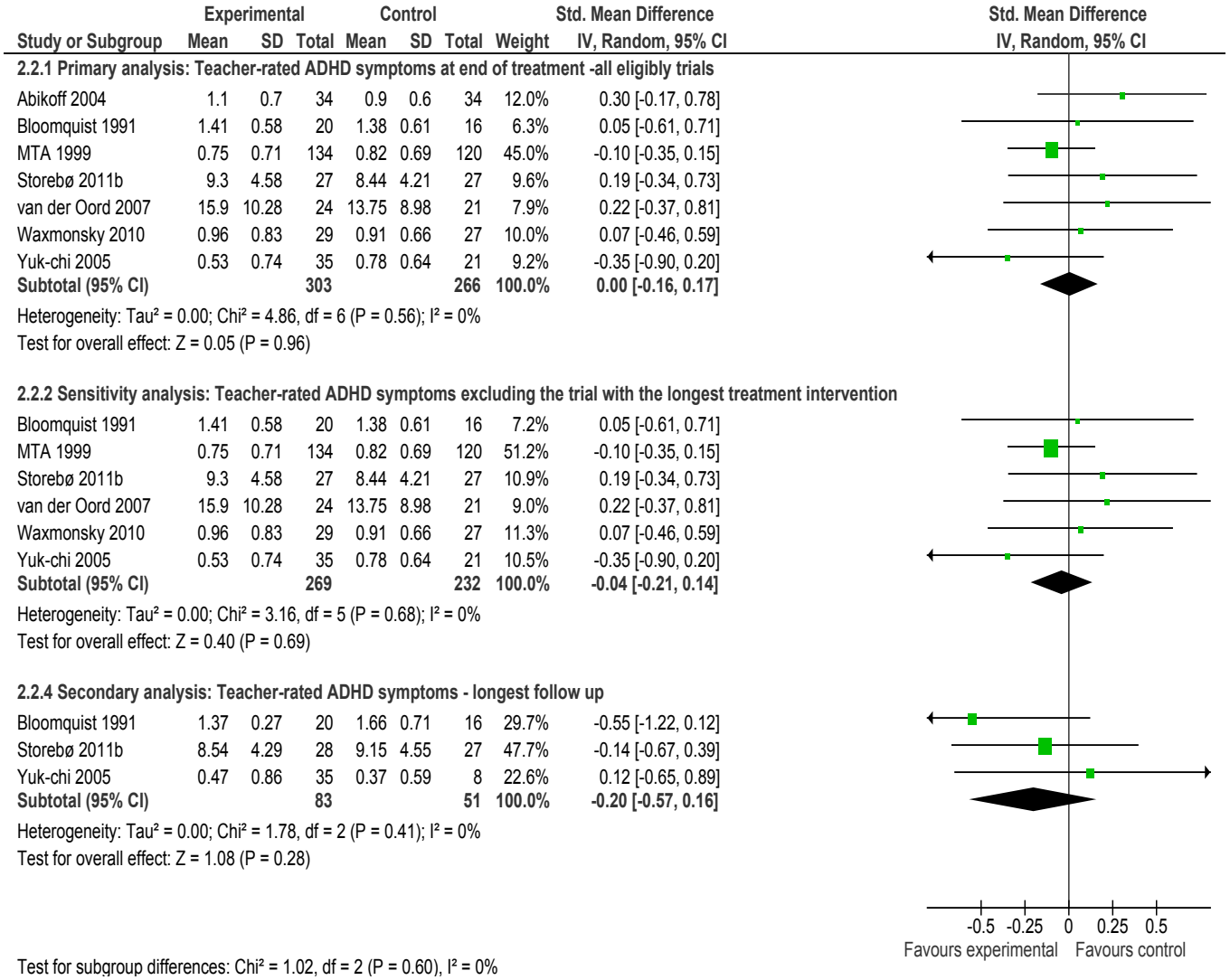
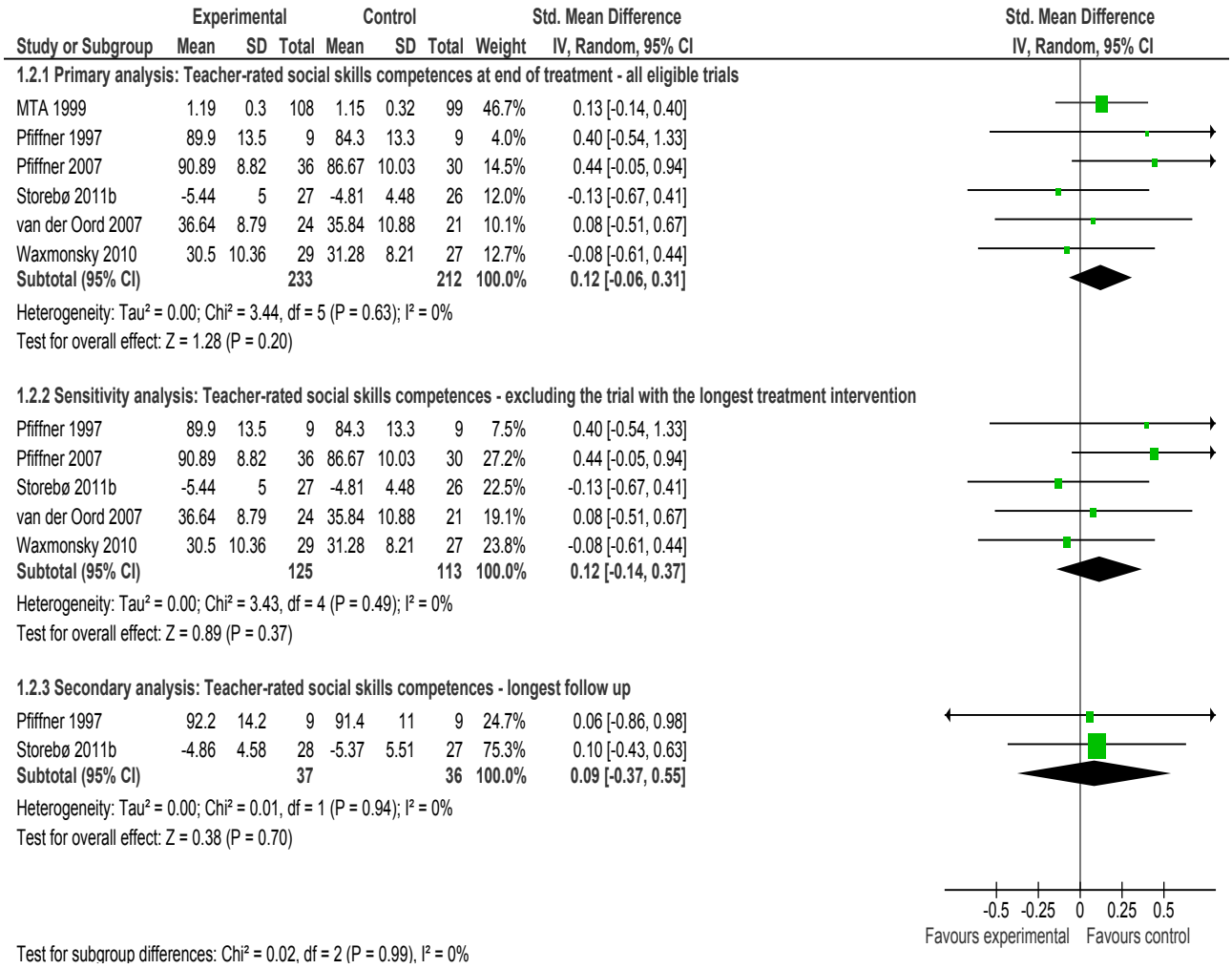


Figure 9: Teacher-rated social skills between social skills training versus control



Trial sequential analysis

I updated the trial sequential analysis, adding data from the SOSTRA Trial to the primary analysis in the Cochrane review: *teacher-rated social skills competences at end of treatment*. To calculate the *post hoc* heterogeneity-adjusted required information size (PHHRIS), I used an alpha of 5%, estimated intervention effect of 4, a standard deviation of 5, and an estimated heterogeneity of 25%. At a power of 80%, a total of 292 participants are to be included in the meta-analysis before a firm conclusion can be drawn (Figure10). As the Z-curve is reaching into the futility area this signals that the social skills intervention on teacher-rated social skills competences at end of treatment is not superior to the control intervention. Further, when

repeating the analysis using a power of 90% similar results are obtained (Figure 11). This gives reasons to conclude that there is no need of conducting more trials assessing social skills intervention.

In this analysis, we did not include the MTA trial as the data from this trial differed too much from the other trials bringing too much clinical heterogeneity into the meta-analysis. The data from the SOSTRA Trial is based on an index in the Conners CBRS rating scale: Social problems scale and differ from the full scales used in the other included trials, thus analysing these data together as mean differences in the TSA analysis can be misleading and the results over interpreted.

Figure 10: TSA based on available data - the teacher-rated social skills competences meta-analysis with power of 80%

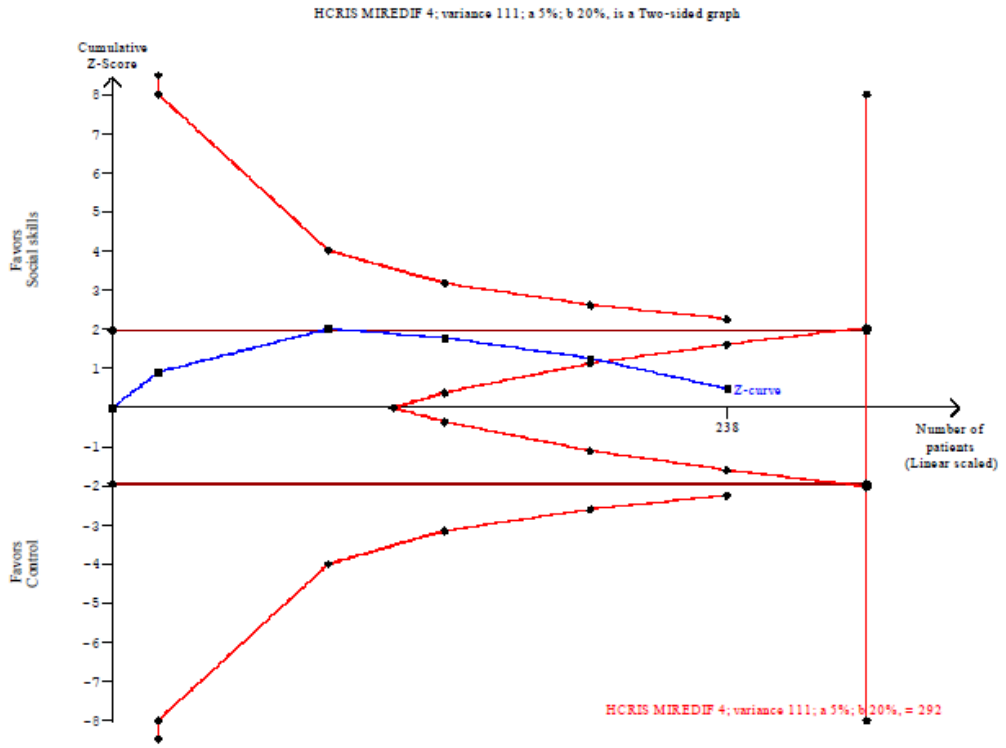
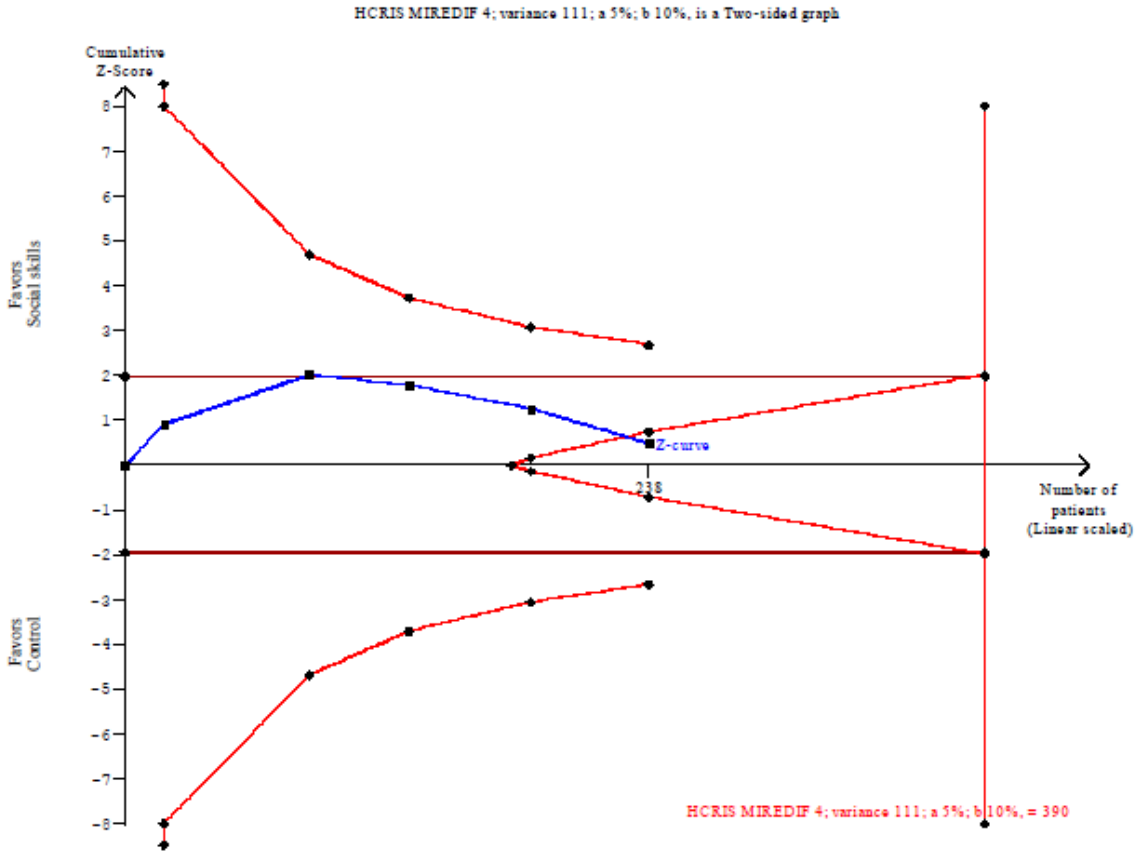


Figure 11: TSA based on available data - the teacher-rated social skills competences meta-analysis with power of 90%



Discussion

In this thesis, I investigated the evidence of social skills training for children with ADHD. This is based on the fact, that many children with ADHD have social skill problems, which cause a lot of suffering for themselves and their families, and they face the possible risk of developing serious problems such as personality disorders and psychosis. I searched for an evidence-based treatment that could alleviate these problems, firstly by conducting a Cochrane systematic review and secondly by conducting a randomised clinical trial. Unfortunately, neither the Cochrane systematic review nor the randomised trial supports the notion that social skills training can alleviate these children's social skill problems. The Cochrane review underlined that now there is little evidence of the efficacy of social skills training for children with ADHD. The SOSTRA trial results were on the same line, as it did not show efficacy in any of the outcome measures. Upon inclusion of the SOSTRA trial data in the meta-analysis of teacher-rated ADHD symptoms and teacher-rated social skills competences, the conclusions were just as strong, as this new analysis showed even less evidence of social skills training efficacy. Both of these conclusions might be questioned because of the limitations mentioned below, but the strength of the research also suggests that at the moment it might be reasonable to conclude that there is little evidence of the benefits of social skills training for children with ADHD. The updated trial sequential analysis shows that the Z-curve is reaching into the futility area and this signals that the social skills intervention on teacher-rated social skills competences at end of treatment is not superior to the control intervention; this gives reasons to conclude that there seems to be no need of conducting more trials assessing social skills intervention. There is, however, a necessity to make a reservation here because the data from the SOSTRA trial was from a single index and therefore differed from the other data.

In the SOSTRA trial we discovered, however, a large effect over time for both the groups together, e.g., the children's social problems scores, aggressiveness, and hyperactivity scores showed highly significant changes (Table 8). These changes show the natural history of these patients under the provided medical treatment. These findings are positive and should be given to the parents so that they can maintain or develop an optimistic attitude.

An interesting finding of the SOSTRA trial was that only 7% of the children had a secure attachment pattern, suggesting that these children also have serious difficulties with attachment to other people. In a normal sample of children in the same age group, 61% had a secure attachment pattern, suggesting a much larger proportion of children with good attachment competences (77). In the attachment section of this thesis, I suggested a possible association between ADHD and a type of insecure attachment pattern based on several studies (63-71;76). This finding underlines the need for a treatment that affects the deeper layers of the children's personality to improve their attachment capacities. Social skills training is a cognitive-

behavioural-based treatment that focuses on changing the children's cognitive assessment of other people and social situations**.** Even if social skills training focus on how the children can control their negative emotions, the training is grounded in cognitive understanding and emotional reflection. Earlier in this thesis, I described that children with ADHD might have difficulty dealing with disappointment since they struggle to regulate their emotions (78). It is possible that current social skills training is often too short and does not focus enough on the affective components of their social skills problems. This idea suggests that a longer and another type of social skills training affecting the more profound part of the child's personality might be relevant for these children.

Medication is currently a treatment with clear evidence of improvement. The MTA study has shown that the combination of behavioural and medical treatment has more efficacy than medication alone, but this trial has systematic errors as not all the outcome assessments are blinded (26). Reviews assessing the effect of methylphenidate have shown clear positive treatment effects. However, the increasing use of methylphenidate in children is a topic of concern. Although stimulants have a favourable risk-benefit profile, they carry the potential risks of minor and serious adverse effects in children and adolescents. The most common adverse effects associated with methylphenidate are headaches, sleeping problems, fatigue, and decreased appetite. Most of these adverse effects become muted over time. Serious adverse reactions such as psychotic symptoms and mood disorders affect 3–6% of children treated with methylphenidate (27).

Strength and limitations

The systematic searching for evidence using a Cochrane review is one of the strengths of this thesis. This review was conducted according to the instructions in The Cochrane Handbook for Systematic Reviews of Interventions (86). The protocol of the review was published before we embarked on the review itself. Extensive searches in relevant databases were performed. Trials were selected for inclusion and data extraction and evaluation of the bias risk were conducted by two independent review authors. We performed a number of meta-analyses based on data from the included trials. Many researchers conducting randomized trials have only performed selective reviews without assessing trial quality or using meta-analysis as a basis for their trials. One of the limitations of the Cochrane review is the limited numbers of participants (n = 747); thus, many of the included trials had an overall assessment of "high risk of bias". Because of the limited numbers of included trials, we cannot clearly state whether there was a publication bias. The social skills interventions comprised a mixture of different forms and content, which imposes a heterogeneity that lowers the quality of the meta-analysis. The review results are in agreement with the meta-analysis results of Kavale et al. and Van der Oord et al. (45;47). They

found little evidence of the effectiveness of social skills training for children with ADHD. The meta-analyses of De Boo & Prins and Majewicz-Hefley & Carlson (44;46) state different findings that social skills training is probably helpful for children with ADHD. However, looking at the quality of this meta-analysis, all of their findings must be questioned due to several methodological weaknesses, as these latter reviews did not evaluate systematic errors (bias) in the included trials, making them questionable.

The SOSTRA trial has a number of strengths. We published the protocol before conducting the trial, performed a sample size calculation, completed a computer-generated randomization procedure, and used a videotaped manual-based treatment. We also conducted "blind" outcome assessments, data management, and intent-to-treat analyses. We reported on all of the outcomes reported in our protocol. We included a parent group in the experimental treatment to support the children's group. The measurement of the attachment patterns is another strength of this trial.

There are also several limitations of the SOSTRA trial. Firstly, we did not find any effects of social skills training based on our sample size calculation, but there is 20% risk for type 2 errors because we used a β size of 80%. It is possible that a trial including more patients could have discovered a smaller effect that some clinicians could consider meaningful. The use of teacher-rated measurement scales can also be considered a limitation. Even if the teachers were "blind" to the treatment allocations, they might be too insensitive to see possible changes in the children's behaviour since they often have classes of up to 25 pupils, making it difficult to notice the children's possible developments. The questions used in the rating scales were long and numerous, resulting in much work for the teachers completing the questionnaires, and this could have resulted in erroneous answers. Furthermore, we used the Conners indices of social problems, peer relations, aggressiveness, and emotional competences to measure social skills. This choice can be questioned, as it is an indirect way to measure social skills. However, this can also be seen as a strength since social skills is a broad function that includes different emotions, emotional competences, and relational competences. This is why we wanted to assess social skills by assessing psychological functioning on a broader level, including peer relationship quality and emotional competency. There might be a risk of confounding because the same therapist conducted both the children's group in the experimental treatment and the parent's group in the standard treatment. Finally, some of the children moved to another school during the trial, so different teachers completed the outcome forms, resulting in unsystematic errors.

Conclusion

Further studies of efficacy of other psychosocial interventions are needed, i.e., investigations regarding a possible link between attachment style and ADHD and intervention programmes that specifically addresses these issues. There is little evidence to support or refute social skills training for children with ADHD at present. There might be an association between ADHD and attachment, suggesting that social skills treatment must also address the attachment problems to be effective. Therefore, it is possible that a treatment addressing the more profound aspects of children's personality would be more effective for the treatment of ADHD core symptoms and related social skill problems.

Clinical implications

The Danish guideline for the assessment and treatment of children with ADHD stated that social skills training could be used to improve the children's social behaviour (25). In the UK guidelines, psychosocial treatment is the first choice of treatment for school-aged children with middle impairment: *Group-based parent-training/education programmes are usually the first-line treatment for parents and caregivers of children and young people of school age with ADHD and moderate impairment. This may also include group psychological treatment (cognitive behavioural therapy [CBT] and/or social skills training) for the younger child* (22). The evidence in this thesis suggests that there is little support for this recommendation. It is not possible to refute the effect of social skills training for children with ADHD, but these recommendations must be questioned. In the Swedish guideline for the assessment and treatment of children with ADHD, social skills training is not recommended (11).

Implications for future research

This is in accordance with our Cochrane review and the meta-analyses performed by Kavale et al. and Van der Oord et al. (45;47) but differ from the results of de Boo & Prins and Majewicz-Hefley & Carlson (44;46). However, both of these latter reviews had no systematic evaluation of systematic errors (bias) in the included trials and the results are therefore questionable.

Summary

Attention-deficit hyperactivity disorder (ADHD) is characterized by impulsive actions, attention difficulties, and hyperactivity, at home and especially in the school setting and also difficulties with social interactions with parents, peers, and teachers. Children with ADHD often have comorbid diseases and have an increased risk of developing personality disorders and psychotic conditions, drug abuse or alcohol abuse, and criminal behaviour. These children often have seriously disturbed relationships with other people and struggle to develop and maintain friendships. Children with ADHD are commonly treated with medication, which often have a good effect on their core symptoms. However, this treatment does not alleviate all of these children's social problems. There exists the need for more specific treatment to address these children's social problems. It is crucial that the overall treatment also focuses on treating comorbid disorders and preventing the development of later disorders and illnesses. Some psychosocial treatments might alleviate both the ADHD symptoms and the social skills problems; behavioural/cognitive treatments, including social skills training, are the best documented. To make a qualified contribution to investigate the efficacy of social skills training for children with symptoms of ADHD and the following social problems, I performed this thesis. The aim of the thesis and the empirical research was firstly, to assess the beneficial and possible harmful effects of social skills training in children and adolescents with ADHD by performing a systematic review; secondly, to conduct a randomized trial based on the findings in the Cochrane review. The effect of the combination of standard treatment plus social skills training and parental training, versus standard treatment alone on the outcome measures of ADHD core symptoms and social and emotional skills in children with ADHD were assessed in the SOSTRA Trial. Furthermore, the trial had the aim to investigate whether the parents' own ADHD symptoms and the children's attachments patterns had any impact on influence the effect of the treatment.

The thesis also focuses on the attachment aspect, as this is associated with both ADHD and social skills competences. Several studies have shown the association between attachment and social skills. I conducted a brief narrative review of the empirical literature on attachment and ADHD and it seems that there is an association between ADHD and attachment**.**

To investigate the evidence of social skills training for children with ADHD a complete Cochrane review was conducted. We identified 3,681 records after the database search. A total of 144 full text articles were considered for inclusion. Ultimately, 11 trials, including 747 patients, published in 26 articles were included in the review, and 10 of these trials were used in meta-analyses. All of the patients in the included trials were 5–12-year-old children with an ADHD diagnosis.

All the included trials were considered as high risk of bias, as there were systematic errors (bias) in all of them. We performed meta-analyses on the teacher-rated social skills, general behaviour, and ADHD symptom outcomes. We chose the teacher rated as our primary analyses because the teachers, in some way, were more blinded than the parents, who were not blinded at all. We performed subgroup analyses, but found no statistical differences in these comparisons. We also conducted sensitivity analyses to test the robustness of the primary analysis and found no statistical differences in those. There were, however, significant differences between the three teacher-rated primary analyses; social skills competences, general behaviour, and ADHD symptoms and the three parents-rated secondary analysis; social skills competences, general behaviour, and ADHD symptoms. This difference is interesting and questions our decision of choosing the teacher-ratings as the primary analyses in this outcome. The parents might be more sensitive to the children's changes; however, they are highly subjective and therefore it is our opinion that the teacher ratings are more valid. The conclusion of the review was that there is currently no evidence to support or refute social skills training for children with ADHD.

The SOSTRA trial was constructed as a two-armed, parallel-group, randomised superiority trial with blinded assessment of outcomes. The participants were randomised to social skills training and parental training plus standard treatment or standard treatment alone. The outcomes measured were ADHD core symptoms and social skills. Furthermore, we wanted to see if the children's attachment patterns measured by the CAI and the parents' own ADHD symptoms measured by ASRS could predict the outcomes. 74 families agreed to participate in the project and after exclusions 56 children (39 boys and 17 girls) were left for randomisation.
The demographic and clinical variables at baseline were reasonably similar between the two groups. The results showed an interesting finding: the children's attachment patterns at baseline showed that 7% of these children had secure attachment competence. This value is much lower than that in a population of normal children, in which 61% were assessed to have secure attachment patterns.
There was a significant development over time in most of the outcomes, indicating that all of the children get significantly better. The time courses were not linear, i.e., there was a highly significant effect after three months that reduced after six months. To make this course more linear, we added a quadratic time term to the analysis. The statistical analysis of the outcomes was based on the "intention to treat" principle and was primarily performed with adjustment for the stratification variables sex and comorbidity, and was secondarily performed without this adjustment. The level of significance was 0.05. The mixed model repeated measures method was used to compare the effect of the two interventions over time on the outcome measures.

There were 1.3–7.2% missing indices, and only two of the 165 set of questionnaires were missing. Except for the two missing questionnaires, missing data were due to inadequate questionnaire answering. Therefore, we did not conduct any imputation methods.

The social skills training did not show any significant differences on any of the outcomes when the time and group variables were combined. The mixed model analysis of each outcome measures with and without the group variable included in the model, but with the CAI and the ASRS included stepwise variables, showed that either the CAI or the ASRS predictor variables influenced the time course of an outcome measure.

The updated meta-analysis were data from the Cochrane review and the SOSTRA trial combined - and only support the conclusions of the Cochrane review - that there is little evidence for social skills training for children with ADHD. Trial sequential analysis showed after data from the SOSTRA trial was added to the social skills competences meta-analysis that addition of new trials will not change the outcome, e.g., there is no significant effect of social skills training measured by this endpoint and the addition of new trials will not change this.

There is little evidence of the efficacy of social skills training for children with ADHD. There might be an association between ADHD and attachment, suggesting that social skills treatment must also address the attachment problems to be effective. It is, therefore, possible that a treatment addressing the more profound aspects of children's personality would be more effective for the treatment of ADHD core symptoms and related social skill problems.

Dansk resumé

Attention-Deficit Hyperactivity Disorder (ADHD) er karakteriseret ved impulsivitet, opmærksomhedsproblemer og hyperaktivitet både i hjemmet og i skolen. Ofte ses også vanskeligheder i det sociale samspil med forældre, kammerater og lærere. Børn med ADHD har ofte komorbide lidelser samt en øget risiko for at udvikle personlighedsforstyrrelser og psykotiske tilstande, stofmisbrug eller alkoholmisbrug samt kriminel adfærd. Disse børn har ofte alvorlige forstyrrede relationer til andre mennesker og har svært ved at udvikle og vedligeholde venskaber. Børn med ADHD er almindeligvis effektivt behandlet med medicin, der ofte har en god virkning på deres kernesymptomer, men ikke nødvendigvis afhjælper børnenes sociale problemer. Der eksisterer derfor et behov for en mere specifik behandling, der fokuserer mere eksplicit på børnenes udvikling af de sociale kompetencer. Det er afgørende, at den samlede behandling også fokuserer på behandling af komorbide lidelser samt forebygger udviklingen af senere lidelser og sygdomme. Nogle psykosociale behandlinger kan mindske både ADHD symptomerne og de psykosociale problemer. De adfærdsmæssige/kognitive behandlingsformer, herunder social færdighedstræning, er de bedst dokumenterede.

Jeg ønskede med denne afhandling at undersøge effekten af social færdighedstræning for børn med ADHD og deraf følgende sociale problemer. Formålet med afhandlingen var først og fremmest at vurdere gavnlige og mulige skadelige virkninger af social færdighedstræning hos børn og unge med ADHD. For det første ved at udføre et systematisk review, og for det andet ved at gennemføre et randomiseret klinisk forsøg. I det randomiserede forsøg undersøgte jeg kombinationen af standardbehandling samt social færdighedstræning og forældretræning, versus standardbehandling alene. Effekten blev målt på ADHD kernesymptomer, og sociale og følelsesmæssige kompetencer. Endvidere var formålet i det randomiserede forsøg at undersøge, om forældrenes egne ADHD symptomer og børnenes tilknytningsmønstre havde nogen indflydelse på effekten af behandlingen.
Flere undersøgelser har vist sammenhængen mellem tilknytning og sociale færdigheder. Jeg udførte et narrativt review af den empiriske litteratur om tilknytning og ADHD, og generelt ser det ud til, at der også er en sammenhæng mellem tilknytning og ADHD.

Et Cochrane review blev gennemført. Vi identificerede 3.681 artikler efter databasesøgning. 144 artikler i fuld tekst blev nøje gennemlæst, hvilket medførte, at i alt 11 forsøg blev inkluderet, indeholdende 747 patienter, disse 11 forsøg var publiceret i 26 artikler. 10 af forsøgene blev brugt i meta-analyser i Cochrane reviewet. Alle patienter i de inkluderede forsøg var 5-12-årige børn med en ADHD diagnose.
Alle de inkluderede studier blev betragtet som forsøg med høj risiko for systematiske fejl (bias). Vi udførte meta-analyser på effektmålene: sociale færdigheder, generel adfærd og ADHD symptomer. Vi valgte at bruge de skemaer, der var scoret af skolelærere frem for forældrene i

vores primære analyser, fordi lærerne var mere ”blindet” end forældrene. Vi udførte analyser af subgrupper, men fandt ingen statistiske forskelle i disse analyser. Vi gennemførte også sensitivitetsanalyser for at teste robustheden af de primære analyser og fandt ingen statistisk forskel på disse. Der var betydelige forskelle mellem de lærer-ratede primære analyser og de sekundære analyser; forældre-ratede sociale færdigheder, forældre-ratede generel adfærd, og forældre-ratede ADHD symptomer. Disse forskelle er interessante og stiller spørgsmål ved vores beslutning om at vælge de lærer-ratede skemaer som de primære analyser. Forældrene kan være mere følsomme over for børnenes ændringer, men de er meget mere subjektive. Valget af de lærer-ratede effektmål betragtes som det mest valide. Reviewets konklusion var, at det for tiden ikke er muligt at påvise eller afvise en effekt af social færdighedstræning for børn med ADHD.

SOSTRA forsøget blev lavet som et 2-armet, parallel-gruppe, effektmål blindet klinisk forsøg. Deltagerne blev randomiseret til social færdighedstræning og forældrenes træning plus standard behandling versus standardbehandling alene. Effektmålene var ADHD symptomer og sociale færdigheder. Desuden ønskede vi at se, om børnenes tilknytningsmønstre og forældrenes eventuelle egne ADHD symptomer kunne prædikere resultaterne. 74 familier indvilligede i at deltage i projektet og efter assessment blev i alt 56 børn (39 drenge og 17 piger) randomiseret.
De sociodemografiske og kliniske variabler ved baseline var rimelig ens mellem de to grupper. Baselinetallene viste et interessant fund, idet kun 7% af børnene blev vurderet til at have en sikker tilknytning. Dette er meget lavere end i en population af normale børn, hvor 61% er vurderet til at have sikker tilknytning.
Der var en signifikant udvikling over tid i de fleste af resultaterne, hvilket indikerer, at alle børnene fik det væsentligt bedre. Denne udvikling var ikke lineær, dvs. der var fx en betydelig effekt efter tre måneder, som så var reduceret efter seks måneder. For at gøre dette forløb mere lineært, lavede vi en transformation af tallene og inkluderede også kvadratroden til analysen. Den statistiske analyse blev baseret på "intention to treat"-princippet og blev primært udført med justering for variablerne køn og komorbiditet, og blev sekundært udført uden denne justering. Signifikans niveauet blev sat til 0,05. En mixed-model analysemetode blev brugt til at sammenligne effekten af de to grupper over tid.

Kun to af de 165 sæt af spørgeskemaer manglede, og der var 1,3 - 7, 2 % manglede indekser. Vi har derfor ikke foretaget nogen imputation metode.

Den sociale færdighedstræning viste ingen signifikante forskelle på nogen effektmål, når både tiden og gruppevariablerne blev kombineret. Mixed-model analysen af hvert enkelt effektmål med og uden de gruppevariable, der indgår i modellen viste også, at hverken tilknytning eller forældrenes egne ADHD symptomer prædikerede nogle af effektmålene.

I de opdaterede meta-analyser, hvor data fra Cochrane reviewet og SOSTRA forsøget blev kombineret, kunne man finde en yderligere støtte for konklusionerne i Cochrane reviewet. Sekventiel analyse af forsøgene (trial sequential analysis - TSA) viste, at tilføjelse af flere forsøg i meta-analysen af de lærer-ratede "social skills competences outcomes" sandsynligvis ikke vil ændre resultatet afgørende - dvs., at der ikke var nogen signifikant effekt af social færdighedstræning målt på dette effektmål, og at tilføjelse af nye forsøg ikke vil ændre dette resultat.

Der er derfor ikke evidens for, at social færdighedstræning til børn med ADHD kan afhjælpe deres ADHD symptomer eller manglende sociale kompetencer.

Det ser ud til, at der er en sammenhæng mellem ADHD og tilknytning, hvilket kan tyde på, at den sociale færdighedstræning også må fokusere på disse problemer for at være effektiv. Det er derfor muligt, at en form for social færdighedstræning, som også fokuserer på de mere dybtgående aspekter af børnenes personlighed, vil være mere effektiv til behandling af børnenes ADHD symptomer og relaterede problemer med sociale færdigheder.

References

(1) Sergeant JA, Geurts H, Huijbregts S, Scheres A, Oosterlaan J. The top and the bottom of ADHD: a neuropsychological perspective. Neurosci Biobehav Rev 2003 Nov;27(7):583-92.

(2) Pasini A, Paloscia C, Alessandrelli R, Porfirio MC, Curatolo P. Attention and executive functions profile in drug naive ADHD subtypes. Brain Dev 2007 Aug;29(7):400-8.

(3) Polanczyk G, Rohde LA. Epidemiology of attention-deficit/hyperactivity disorder across the lifespan. Curr Opin Psychiatry 2007 Jul;20(4):386-92.

(4) Schmidt S, Petermann F. Developmental psychopathology: Attention Deficit Hyperactivity Disorder (ADHD). BMC Psychiatry 2009;9:58.

(5) Cantwell DP. Attention deficit disorder: a review of the past 10 years. J Am Acad Child Adolesc Psychiatry 1996 Aug;35(8):978-87.

(6) Brown RT, Madan-Swain A, Baldwin K. Gender differences in a clinic-referred sample of attention-deficit-disordered children. Child Psychiatry Hum Dev 1991;22(2):111-28.

(7) Carlson CL, Tamm L, Gaub M. Gender differences in children with ADHD, ODD, and co-occurring ADHD/ODD identified in a school population. J Am Acad Child Adolesc Psychiatry 1997 Dec;36(12):1706-14.

(8) Gaub M, Carlson CL. Gender differences in ADHD: a meta-analysis and critical review. J Am Acad Child Adolesc Psychiatry 1997 Aug;36(8):1036-45.

(9) Lionel AC, Crosbie J, Barbosa N, Goodale T, Thiruvahindrapuram B, Rickaby J, et al. Rare copy number variation discovery and cross-disorder comparisons identify risk genes for ADHD. Sci Transl Med 2011 Aug 10;3(95):95ra75.

(10) Jensen PS, Hinshaw SP, Kraemer HC, Lenora N, Newcorn JH, Abikoff HB, et al. ADHD comorbidity findings from the MTA study: comparing comorbid subgroups. J Am Acad Child Adolesc Psychiatry 2001 Feb;40(2):147-58.

(11) Kadesjo B, Gillberg C. The comorbidity of ADHD in the general population of Swedish school-age children. J Child Psychol Psychiatry 2001 May;42(4):487-92.

(12) Miller CJ, Flory JD, Miller SR, Harty SC, Newcorn JH, Halperin JM. Childhood attention-deficit/hyperactivity disorder and the emergence of personality disorders in adolescence: a prospective follow-up study. J Clin Psychiatry 2008 Sep;69(9):1477-84.

(13) Dalsgaard S, Mortensen PB, Frydenberg M, Thomsen PH. Conduct problems, gender and adult psychiatric outcome of children with attention-deficit hyperactivity disorder. Br J Psychiatry 2002 Nov;181:416-21.

(14) Whalen CK, Henker B. The social worlds of hyperactive (ADDH) children. Clinical Psychology Review 1985;(5):447-78.

(15) Landau S, Moore LA. Social skill deficits in children with attention-deficit hyperactivity disorder. School Psychology Review 1991.

(16) Castellanos FX, Sonuga-Barke EJ, Milham MP, Tannock R. Characterizing cognition in ADHD: beyond executive dysfunction. Trends Cogn Sci 2006 Mar;10(3):117-23.

(17) Nigg JT, Casey BJ. An integrative theory of attention-deficit/ hyperactivity disorder based on the cognitive and affective neurosciences. Dev Psychopathol 2005;17(3):785-806.

(18) American Psychiatric Association. Diagnostic and statistical manual of mental disorders (4th ed.). 4th ed. Arlington: American Psychiatric Publishing, Inc.; 1994.

(19) American Psychiatric Association, American Psychiatric Association.Task Force on DSM-IV. Diagnostic and statistical manual of mental disorders: DSM-IV-TR. American Psychiatric Publishing, Inc.; 2000.

(20) World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. World Health Organization; 1992.

(21) Scahill L, Schwab-Stone M. Epidemiology of ADHD in school-age children. Child Adolesc Psychiatr Clin N Am 2000 Jul;9(3):541-55, vii.

(22) Atkinson M, Hollis C. NICE guideline: attention deficit hyperactivity disorder. Archives of disease in childhood-Education & practice edition 2010;95(1):24.

(23) Goldman LS, Genel M, Bezman RJ, Slanetz PJ. Diagnosis and treatment of attention-deficit/hyperactivity disorder in children and adolescents. Council on Scientific Affairs, American Medical Association. JAMA 1998 Apr 8;279(14):1100-7.

(24) Swanson JM, Lerner M, Williams L. More frequent diagnosis of attention deficit-hyperactivity disorder. N Engl J Med 1995 Oct 5;333(14):944.

(25) Thomsen PH. Referenceprogram for udredning og behandling af børn og unge med ADHD April 2008. 2008.

(26) The MTA Cooperative-Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. Multimodal Treatment Study of Children with ADHD. Archives of General Psychiatry 1999;56:1073-86.

(27) Storebø OJ, Rosendal S, Skoog M, Groth C., Bille T., Buch Rasmussen K, et al. Methylphenidate for attention deficit hyperactivity disorder(ADHD) in children and adolescents. Cochrane Database of Systematic Reviews-protocol. In press 2011.

(28) Greenhill L, Kollins S, Abikoff H, McCracken J, Riddle M, Swanson J, et al. Efficacy and safety of immediate-release methylphenidate treatment for preschoolers with ADHD. Journal of the American Academy of Child and Adolescent Psychiatry 2006;45:1284-93.

(29) Engert V, Pruessner JC. Dopaminergic and noradrenergic contributions to functionality in ADHD: the role of methylphenidate. Curr Neuropharmacol 2008 Dec;6(4):322-8.

(30) Hinshaw SP, Henker B, Whalen CK. Cognitive-behavioral and pharmacologic interventions for hyperactive boys: comparative and combined effects. J Consult Clin Psychol 1984 Oct;52(5):739-49.

(31) Hinshaw SP, Henker B, Whalen CK. Self-control in hyperactive boys in anger-inducing situations: effects of cognitive-behavioral training and of methylphenidate. Journal of Abnormal Child Psychology 1984;12:55-77.

(32) Tannock R, Martinussen R. Reconceptualizing ADHD. Educational Leadership 2001;59(3):20-5.

(33) Block SL. Attention-deficit disorder. A paradigm for psychotropic medication intervention in pediatrics. [Review] [87 refs]. Pediatric Clinics of North America 1998 Oct;45(5):1053-83.

(34) Cherland E, Fitzpatrick R. Psychotic side effects of psychostimulants: a 5-year review. Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie 1999 Oct;44(8):811-3.

(35) Pliszka SR. The use of psychostimulants in the pediatric patient. [Review] [53 refs]. Pediatric Clinics of North America 1998 Oct;45(5):1085-98.

(36) Wolraich ML, McGuinn L, Doffing M. Treatment of attention deficit hyperactivity disorder in children and adolescents: safety considerations. Drug Saf 2007;30(1):17-26.

(37) Schachar RJ, Tannock R, Cunningham C, Corkum PV. Behavioral, situational, and temporal effects of treatment of ADHD with methylphenidate. Journal of the American Academy of Child and Adolescent Psychiatry 1997;36:754-63.

(38) Swanson JM, Hinshaw SP, Arnold LE, Gibbons RD, Marcus S, Hur K, et al. Secondary evaluations of MTA 36-month outcomes: propensity score and growth mixture model analyses. J Am Acad Child Adolesc Psychiatry 2007 Aug;46(8):1003-14.

(39) US Food and Drug Administraion. Communication about an ongoing safety review of stimulant medications used in children with attention-deficit/hyperactivity disorder (ADHD). 2011.

(40) Gilmore A, Milne R. Methylphenidate in children with hyperactivity: review and cost-utility analysis (Structured abstract). Pharmacoepidemiology and Drug Safety 2001;10:85-94.

(41) Conners CK, Epstein JN, March JS, Angold A, Wells KC, Klaric J, et al. Multimodal treatment of ADHD in the MTA: an alternative outcome analysis. J Am Acad Child Adolesc Psychiatry 2001 Feb;40(2):159-67.

(42) Carr A. What works with children and adolescents?: A critical review of psychological interventions with children, adolescents and their families. 2000.

(43) Pelham WE, Jr., Wheeler T, Chronis A. Empirically supported psychosocial treatments for attention deficit hyperactivity disorder. J Clin Child Psychol 1998 Jun;27(2):190-205.

(44) de Boo GM, Prins PJM. Social incompetence in children with ADHD: Possible moderators and mediators in social-skills training. Clinical Psychology Review 2007 Jan;27(1):78-97.

(45) Kavale KA, Mathur SR, Forness SR, Rutherford RB, Quinn MM. Effectiveness of social skills training for students with behavior disorders: A meta-analysis. Advances in learning and behavioral disabilities 1997;11:1-26.

(46) Majewicz-Hefley A, Carlson JS. A meta-analysis of combined treatments for children diagnosed with ADHD. Journal of Attention Disorders 2007 Feb;10(3):239-50.

(47) Van der Oord S, Prins PJ, Oosterlaan J, Emmelkamp PM. Efficacy of methylphenidate, psychosocial treatments and their combination in school-aged children with ADHD: a meta-analysis. Clinical Psychology Review 2008 Jun;28(5):783-800.

(48) Zwi M Jones H Thorgaard C York A Dennsi JA. Parent training interventions in school aged children/adolescents with Attention Deficit Hyperactivity Disorder (ADHD). Cochrane Database of Systematic Reviews. In press 2011.

(49) Raggi VL, Chronis AM. Interventions to address the academic impairment of children and adolescents with ADHD. Clin Child Fam Psychol Rev 2006 Jun;9(2):85-111.

(50) Bjornstad G, Montgomery P. Family therapy for attention-deficit disorder or attention-deficit/hyperactivity disorder in children and adolescents. [Review] [64 refs]. Cochrane Database of Systematic Reviews (2):CD005042, 2005 2005;(2):CD005042.

(51) Heirs M DM. Homeopathy for attention deficit/hyperactivity disorder or hyperkinetic disorder. Cochrane Database of Systematic Reviews 2007 2011;(Issue 4).

(52) Krisanaprakornkit T, Ngamjarus C, Witoonchart C, Piyavhatkul N. Meditation therapies for attention-deficit/hyperactivity disorder (ADHD). [Review] [95 refs]. Cochrane Database of Systematic Reviews (6):CD006507, 2010 2010;(6):CD006507.

(53) li S, Yu B, Zhau D, He C, Kang L, Songhe W, et al. Acupuncture for Attention Deficit Hyperactivity Disorder (ADHD) in children and adolescents. Cochrane Database of Systematic Reviews 2011 2011;(4).

(54) DiTommaso E, Brannen-McNulty C, Ross L, Burgess M. Attachment styles, social skills and loneliness in young adults. Personality and Individual Differences 2003;35(2):303-12.

(55) Allen JP, Marsh P, McFarland C, McElhaney KB, Land DJ, Jodl KM, et al. Attachment and autonomy as predictors of the development of social skills and delinquency during midadolescence. Journal of Consulting and Clinical Psychology 2002;70(1):56.

(56) BOWLBY J. The nature of the child's tie to his mother. International Journal of Psycho-Analysis 1958 Sep;39(5):350-73.

(57) BOWLBY J. Separation anxiety. International Journal of Psycho-Analysis 1960 Mar;41:89-113.

(58) BOWLBY J. Grief and mourning in infancy and early childhood. Psychoanalytic study of the child 1960;15:9-52.

(59) Ainsworth MDS, Blehar MC, Waters E, Wall S. Patterns of attachment: A psychological study of the strange situation. Hillsdale, NJ 1978.

(60) Main M, Solomon J. Procedures for identifying infants as disorganized/disoriented during the Ainsworth Strange Situation. Attachment in the preschool years: Theory, research, and intervention 1990;1:121-60.

(61) BOWLBY J. Attachment and loss: Volume 1: Attachment. London: The Hogarth Press and the Institute of Psycho-Analysis; 1969.

(62) Higgins JPT, Green J. Cochrane handbook for systematic reviews of interventions version 2009;5(2).

(63) Niederhofer H. Attachment as a component of attention-deficit hyperactivity disorder. Psychol Rep 2009 Apr;104(2):645-8.

(64) Kissgen R, Krischer M, Kummetat V, Spiess R, Schleiffer R, Sevecke K. Attachment representation in mothers of children with attention deficit hyperactivity disorder. Psychopathology 2009;42(3):201-8.

(65) Clarke L, Ungerer J, Chahoud K, Johnson S, Stiefel I. Attention deficit hyperactivity disorder is associated with attachment insecurity. Clinical Child Psychology and Psychiatry 2002;7(2):179-98.

(66) Pinto C, Turton P, Hughes P, White S, Gillberg C. ADHD and infant disorganized attachment: a prospective study of children next-born after stillbirth. Journal of Attention Disorders 2006 Aug;10(1):83-91.

(67) Finzi-Dottan R, Manor I, Tyano S. ADHD, temperament, and parental style as predictors of the child's attachment patterns. Child Psychiatry and Human Development 2006 Dec;37(2):103-14.

(68) Audet K, Le ML. Mitigating effects of the adoptive caregiving environment on inattention/overactivity in children adopted from Romanian orphanages. International Journal of Behavioral Development 35 (2) (pp 107-115), 2011 Date of Publication: March 2011 2011;(2):March.

(69) Karabekiroglu K, Rodopman-Arman A. Parental attachment style and severity of emotional/behavioral problems in toddlerhood. Noropsikiyatri Arsivi 48 (2) (pp 147-154), 2011 Date of Publication: 2011 2011;(2):2011.

(70) Abdel-Hamid M, Heinrich V, Sperber S, Wiltfang J, Kis B, Uekermann J. Attachment in adult patients with attention-deficit hyperactivity disorder (ADHD). European Psychiatry Conference: 19th European Congress of Psychiatry, EPA 2011 Vienna Austria Conference Start: 20110312 Conference End: 20110315 Conference Publication: (var pagings) 26 , 2011 Date of Publication: March 2011 2011;(var.pagings):March.

(71) Bohlin G, Thorell L, Eninger L, Brocki C. Are attachment disorganization and inhibition independent predictors of symptoms of ADHD, externalizing problem behaviors and callous unemotional traits? European Child and Adolescent Psychiatry Conference: Eunethydis 1st International ADHD Conference: From Data to Best Clinical Practice Amsterdam Netherlands Conference Start: 20100526 Conference End: 20100528 Conference Publication: (var pagings) 19 (2010;(var.pagings):June.

(72) Green J, Stanley C, Peters S. Disorganized attachment representation and atypical parenting in young school age children with externalizing disorder. Attachment and Human Development 2007 Sep;9(3):207-22.

(73) Johnston C, Murray C, Hinshaw SP, Pelham WEJr, Hoza B. Responsiveness in interactions of mothers and sons with ADHD: Relations to maternal and child characteristics. [References]. Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology 2002 Feb;(1):77-88.

(74) Follan M, Anderson S, Huline-Dickens S, Lidstone E, Young D, Brown G, et al. Discrimination between attention deficit hyperactivity disorder and reactive attachment disorder in school aged children. Research in Developmental Disabilities 32 (2) (pp 520-526), 2011 Date of Publication: March-April 2011 2011;(2):March-April.

(75) Lifford KJ, Harold GT, Thapar A. Parent-child relationships and ADHD symptoms: A longitudinal analysis. [References]. Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology 2008 Feb;(2):285-96.

(76) Skovgaard AM. Mental health problems and psychopathology in infancy and early childhood. Danish medical bulletin 2010;57(10):B4193.

(77) Shmueli-Goetz Y, Target M, Fonagy P, Datta A. The Child Attachment Interview: a psychometric study of reliability and discriminant validity. Dev Psychol 2008 Jul;44(4):939-56.

(78) Walcott CM, Landau S. The relation between disinhibition and emotion regulation in boys with attention deficit hyperactivity disorder. Journal of Clinical Child and Adolescent Psychology 2004;33(4):772-82.

(79) Hoza B, Gerdes AC, Mrug S, Hinshaw SP, Bukowski WM, Gold JA, et al. Peer-assessed outcomes in the multimodal treatment study of children with attention deficit hyperactivity disorder. J Clin Child Adolesc Psychol 2005 Mar;34(1):74-86.

(80) Fohlmann AH. Social færdighedstræning. In: Kjær SK, Nordentoft M, Melau M, Iversen T, editors. Psykose hos unge. Psykiatrifondens forlag; 2009.

(81) Liberman RP, Martin T. Social skills training. Psychiatric rehabilitation of chronic mental patients 1988;147-98.

(82) Abikoff H, Hechtman L, Klein RG, Weiss G, Fleiss K, Etcovitch J, et al. Symptomatic improvement in children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. Journal of the American Academy of Child and Adolescent Psychiatry 2004;43:802-11.

(83) Antshel KM, Remer R. Social skills training in children with attention deficit hyperactivity disorder: A randomized-controlled clinical trial. [References]. Journal of Clinical Child and Adolescent Psychology 2003;32(1):153-65.

(84) Pfiffner LJ, McBurnett K. Social skills training with parent generalization: Treatment effects for children with attention deficit disorder. Journal of Consulting and Clinical Psychology 1997 Oct;65(5):749-57.

(85) Tutty S, Gephart H, Wurzbacher K. Enhancing behavioral and social skill functioning in children newly diagnosed with attention-deficit hyperactivity disorder in a pediatric setting. [References]. Journal of Developmental & Behavioral Pediatrics 2003;24(1):51-7.

(86) Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1. 0 [updated March 2011]. The Cochrane Collaboration 2011.

(87) Storebø OJ, Skoog M, Damm D, Thomsen PH, Simonsen E, Gluud C. Social skills training for children with attention deficit hyperactivity disorder (ADHD). The Cochrane Library 2010;Protocol.

(88) Brok J, Thorlund K, Gluud C, Wetterslev J. Trial sequential analysis reveals insufficient information size and potentially false positive results in many meta-analyses. Journal of clinical epidemiology 2008;61(8):763-9.

(89) Brok J, Thorlund K, Wetterslev J, Gluud C. Apparently conclusive meta-analyses may be inconclusiveùTrial sequential analysis adjustment of random error risk due to repetitive testing of accumulating data in apparently conclusive neonatal meta-analyses. International journal of epidemiology 2009;38(1):287.

(90) Thorlund K, Devereaux PJ, Wetterslev J, Guyatt G, Ioannidis J, Thabane L, et al. Can trial sequential monitoring boundaries reduce spurious inferences from meta-analyses? International journal of epidemiology 2009;38(1):276.

(91) Wetterslev J, Thorlund K, Brok J, Gluud C. Trial sequential analysis may establish when firm evidence is reached in cumulative meta-analysis. Journal of clinical epidemiology 2008;61(1):64-75.

(92) Berkey CS, Mosteller F, Lau J, Antman EM. Uncertainty of the time of first significance in random effects cumulative meta-analysis. Controlled clinical trials 1996;17(5):357-71.

(93) Lau J, Schmid CH, Chalmers TC. Cumulative meta-analysis of clinical trials builds evidence for exemplary medical care. Journal of clinical epidemiology 1995;48(1):45-57.

(94) Atkins D, Eccles M, Flottorp S, Guyatt GH, Henry D, Hill S, et al. GRADE Working Group. Systems for grading the quality of evidence and the strength of recommendations I: critical appraisal of existing approaches The GRADE Working Group. BMC Health Serv Res 2004;4(1):38.

(95) Storebø OJ, Skoog M, Damm D, Thomsen PH, Simonsen E, Gluud C. Social skills training for children with attention deficit hyperactivity disorder (ADHD). Cochrane Database of Systematic Reviews. In press 2011.

(96) Storebo OJ, Pedersen J, Skoog M, Thomsen PH, Winkel P, Gluud C, et al. Randomised social-skills training and parental training plus standard treatment versus standard treatment of children with attention deficit hyperactivity disorder - the SOSTRA trial protocol. Trials 2011;12:18.

(97) Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry 1997 Jul;36(7):980-8.

(98) Rutter M, Bailey A, Lord C, Berument SK. Social communication questionnaire. Los Angeles, CA: Western Psychological Services 2003.

(99) Adler LA, Spencer T, Faraone SV, Kessler RC, Howes MJ, Biederman J, et al. Validity of pilot Adult ADHD Self- Report Scale (ASRS) to Rate Adult ADHD symptoms. Ann Clin Psychiatry 2006 Jul;18(3):145-8.

(100) Wechsler D, Psychological Corporation. WISC-III: Wechsler intelligence scale for children. Psychological Corporation, Harcourt Brace Jovanovich; 1991.

(101) Target M, Fonagy P, Shmueli-Goetz Y. Attachment representations in school-age children: The development of the child attachment interview (CAI). [References]. Journal of Child Psychotherapy 2003 Aug;(2):171-86.

(102) Conners CK. Conners 3rd Edition(Conners 3). 2008.

(103) Conners KC. Conners Comprehensive Behavior Rating Scales (Conner's CBRS). Toronto, Canada: Multi-Health Systems Inc; 2008.

(104) Horn WF, Ialongo NS, Pascoe JM, Greenberg G, Packard T, Lopez M, et al. Additive effects of psychostimulants, parent training, and self-control therapy with ADHD children. J Am Acad Child Adolesc Psychiatry 1991 Mar;30(2):233-40.

(105) Corkum PV, McKinnon MM, Mullane JC. The effect of involving classroom teachers in a parent training program for families of children with ADHD. Child & Family Behavior Therapy 2005 Dec;27(4):29-49.

(106) Miranda A, Jarque S, Rosel J. Treatment of children with ADHD: Psychopedagogical program at school versus psychostimulant medication. Psicothema 2006;18(3):335-41.

(107) Elliott SN, Gresham FM. Social skills interventions for children. Behavior Modification 1993 Jul;(3):287-313.

(108) Storebø OJ, Simonsen E, Winkel P, Gluud C. Social-skills and Parental Training plus Standard Treatment versus Standard Treatment for Children with Attention Deficit Hyperactivity Disorder. Plos ONE. In press 2011.

Appendix

Update-search Attachment and ADHD, 20-9-2011

EMBASE
1. exp Attention Deficit Disorder/
2. adhd.mp.
3. addh.mp.
4. exp Hyperactivity/
5. Hyperkinesia/
6. (attention adj3 deficit).mp.
7. hyperactiv*.mp.
8. hyperkinesis*.mp.
9. (minimal adj brain adj3 disorder*).mp.
10. (minimal adj brain adj3 dysfunction*).mp.
11. (minimal adj brain adj3 damage*).mp.
12. 6 or 11 or 3 or 7 or 9 or 2 or 8 or 1 or 4 or 10 or 5
13. controlled study.de.
14. clinical trial.de.
15. major clinical study.de.
16. randomized controlled trial.de.
17. double blind procedure.de.
18. clinical article.de.
19. random*.mp.
20. exp comparative study/
21. control*.mp.
22. follow up.mp.
23. ((singl$ or doubl$ or tripl$ or trebl$) adj (blind$ or mask$ or dummy)).mp.
24. placebo$.mp.
25. (clinic$ adj (trial$ or study or studies$)).mp.
26. 25 or 21 or 17 or 20 or 15 or 14 or 22 or 18 or 24 or 23 or 13 or 16 or 19
27. 26 and 12
28. attachment.ti,ab.
29. *emotional attachment/ or *emotional deprivation/ or *empathy/ or *love/
30. 28 or 29
31. 27 and 30

32. Limit 31 to em=201020-201138

MEDLINE
1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized controlled trials.mp.
4. random allocation.mp.
5. double blind method.mp.
6. single blind method.mp.
7. clinical trial.pt.
8. (clin$ adj25 trial$).ti,ab.
9. ((singl$ or doubl$ or tripl$ or trebl$) adj25 (blind$ or mask$ or dummy$)).mp.
10. exp clinical trial/
11. placebos.mp.
12. placebo$.ti,ab.
13. random$.ti,ab.
14. comparative study.mp.
15. evaluation studies as topic/
16. exp clinical trials as topic/
17. follow up studies.mp.
18. prospective studies.mp.
19. (control$ or prospectiv$ or volunteer$).ti,ab.
20. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21. exp Attention Deficit Disorder with Hyperactivity/
22. adhd.mp.
23. addh.mp.
24. (attention adj3 deficit).mp.
25. hyperactiv$.mp.
26. hyperkinesis$.mp.
27. exp Hyperkinesis/
28. (minimal adj brain adj3 disorder$).mp.
29. (minimal adj brain adj3 dysfunction$).mp.
30. (minimal adj brain adj3 damage$).mp.
31. 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
32. Object Attachment/
33. exp family relations/ or interpersonal relations/
34. attachment.ti,ab.

35. 32 or 33 or 34
36. 20 and 31 and 35
37. limit 36 to ((danish or english or german or norwegian or swedish) and last 3 years)
(rekonstrueret, da den oprindelige søgestrategi ikke var gemt)

PsycINFO
1. exp attention deficit disorder/
2. adhd.mp.
3. addh.mp.
4. (attention adj3 deficit).mp.
5. hyperactiv$.mp.
6. hyperkinesis$.mp.
7. exp Hyperkinesis/
8. (minimal adj brain adj3 disorder$).mp.
9. (minimal adj brain adj3 dysfunction$).mp.
10. (minimal adj brain adj3 damage$).mp.
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. random$.mp.
13. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or dummy or mask$)).mp.
14. placebo$.mp.
15. crossover.mp.
16. assign$.mp.
17. allocat$.mp.
18. ((clin$ or control$ or compar$ or evaluat$ or prospectiv$) adj25 (trial$ or studi$ or study)).mp.
19. exp placebo/
20. exp treatment effectiveness evaluation/
21. exp mental health program evaluation/
22. exp experimental design/
23. versus.id.
24. vs.id.
25. 17 or 15 or 14 or 21 or 22 or 18 or 23 or 24 or 20 or 16 or 12 or 19 or 13
26. 11 and 25
27. exp attachment behavior/ or exp attachment disorders/ or exp attachment theory/ or exp "dependency (personality)"/ or exp emotional development/ or exp intimacy/ or exp love/ or exp

object relations/ or exp parent child relations/ or exp psychological distance/ or exp separation reactions/
28. attachment.ti,ab.
29. 27 or 28
30. 26 and 29
31. Limit 30 to up=20100520-20110920

Papers

Paper 1: Storebø OJ, Skoog M, Damm D, Thomsen PH, Simonsen E, Gluud C. Social skills training for attention deficit hyperactivity disorder (ADHD) in children aged 5 to 18 years. Cochrane Database of Systematic Reviews 2011, Issue 12.

Paper 2: Storebø OJ, Pedersen J, Skoog M, Hove Thomsen P, Winkel P, Gluud C, Simonsen E. Randomised social skills training and parental training plus standard treatment versus standard treatment of children with attention deficit hyperactivity disorder - the SOSTRA trial protocol. Trials 2011, 12:18

Paper 3: Storebø OJ, Simonsen E, Winkel P, Gluud C. Social skills training for children with ADHD - the randomised SOSTRA trial. Submitted to PLoS ONE in October 2011.

Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years (Review)

Storebø OJ, Skoog M, Damm D, Thomsen PH, Simonsen E, Gluud C

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2011, Issue 12

http://www.thecochranelibrary.com

TABLE OF CONTENTS

[Intervention Review]

Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years

Ole Jakob Storebø[1,2,6], Maria Skoog[1], Dorte Damm[3], Per Hove Thomsen[3], Erik Simonsen[4], Christian Gluud[5]

[1]Copenhagen Trial Unit, Centre for Clinical Intervention Research, Department 3344, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark. [2]Child Psychiatric Clinic, Psychiatric Department, Region Zealand, Holbaek, Denmark. [3]Psychiatric Hospital for Children and Adolescents, Risskov, Denmark. [4]Psychiatric Research Unit, Region Zealand Psychiatry, Roskilde, Denmark. [5]The Cochrane Hepato-Biliary Group, Copenhagen Trial Unit, Centre for Clinical Intervention Research, Department 3344, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark. [6]Region Sjælland, Børnepsykiatrisk Ambulatorium, Holbæk, Denmark

Contact address: Ole Jakob Storebø, ojst@regionsjaelland.dk.

Editorial group: Cochrane Developmental, Psychosocial and Learning Problems Group.
Publication status and date: New, published in Issue 12, 2011.
Review content assessed as up-to-date: 14 September 2011.

Citation: Storebø OJ, Skoog M, Damm D, Thomsen PH, Simonsen E, Gluud C. Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years. *Cochrane Database of Systematic Reviews* 2011, Issue 12. Art. No.: CD008223. DOI: 10.1002/14651858.CD008223.pub2.

ABSTRACT

Background

Attention Deficit Hyperactivity Disorder (ADHD) in children is associated with hyperactivity and impulsitivity, attention problems, and difficulties with social interactions. Pharmacological treatment may alleviate symptoms of ADHD but seldom solves difficulties with social interactions. Social skills training may benefit ADHD children in their social interactions. We examined the effects of social skills training on children's social competences, general behaviour, ADHD symptoms, and performance in school.

Objectives

To assess the effects of social skills training in children and adolescents with ADHD.

Search methods

We searched the following electronic databases: CENTRAL (2011, Issue1), MEDLINE (1948 to March 2011), EMBASE (1980 to March 2011), ERIC (1966 to March 2011), AMED (1985 to June 2011), PsycINFO (1806 to March 2011), CINAHL (1980 to March 2011), and Sociological Abstracts (1952 to March 2011). We also searched the *meta*Register of Controlled Trials on 15 October 2010. We did not apply any language or date restrictions to the searches. We searched online conference abstracts and contacted 176 experts in the field for possible information about unpublished or ongoing RCTs.

Selection criteria

Randomised trials investigating social skills training for children with ADHD as a stand alone treatment or as an adjunct to pharmacological treatment.

Data collection and analysis

We conducted the review according to the *Cochrane Handbook for Systematic Reviews of Intervention.* Two authors (OJS, MS) extracted data independently using an appropriate data collection form. We performed the analyses using Review Manager 5 software.

Main results

We included 11 randomised trials described in 26 records (all full text articles) in the review. The trials included a total of 747 participants. All participants were between five and 12 years of age. No trials assessed adolescents. In 10 of the trials the participants suffered from different comorbidities.

The duration of the interventions ranged from eight to 10 weeks (eight trials) up to two years. The types of social skills interventions were named social skills training, cognitive behavioural intervention, multimodal behavioural/psychosocial therapy, behavioural therapy/ treatment, behavioural and social skills treatment, and psychosocial treatment. The content of the social skills interventions were comparable and based on a cognitive behavioural model. Most of the trials compared child social skills training and parent training plus medication versus medication alone. Some of the experimental interventions also included teacher consultations.

More than half of the trials were at high risk of bias regarding generation of the allocation sequence and allocation concealment. No trial reported blinding of participants and personnel and most of the trials had no reports regarding differences between groups in collateral medication for comorbid disorders. Overall, the trials had high risk of bias due to systematic errors. Even so, as recommended by the *Cochrane Handbook of Systematic Reviews of Interventions*, we used all eligible trials in the meta-analysis, but the results are downgraded to low quality evidence.

There were no statistically significant treatment effects either on social skills competences (positive value = better for the intervention group) (SMD 0.16; 95% CI -0.04 to 0.36; 5 trials, n = 392), on the teacher-rated general behaviour (negative value = better for the intervention group) (SMD 0.00; 95% CI -0.21 to 0.21; 3 trials, n = 358), or on the ADHD symptoms (negative value = better for the intervention group) (SMD -0.02; 95% CI -0.19 to 0.16; 6 trials, n = 515).

No serious or non-serious adverse events were reported.

Authors' conclusions

The review suggests that there is little evidence to support or refute social skills training for adolescents with ADHD. There is need for more trials, with low risk of bias and with a sufficient number of participants, investigating the efficacy of social skills training versus no training for both children and adolescents.

PLAIN LANGUAGE SUMMARY

Social skills training for children aged between 5 and 18 with Attention Deficit Hyperactivity Disorder (ADHD)

Children with Attention Deficit Hyperactivity Disorder (ADHD) are hyperactive and impulsive, cannot maintain attention, and have difficulties with social interactions. This review looks at whether social skills training benefits children with ADHD in their social interactions. Eleven trials including a total of 747 participants met the inclusion criteria. This review suggests that there is little evidence for social skills training for children with ADHD at the moment. It is not possible to recommend or refute social skills training for children with ADHD. There is need for more randomised clinical trials, with low risk of bias and with a sufficient number of participants, investigating the efficacy of social skills training for children with ADHD.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Social skills training compared to no intervention

Patient or population: Children aged 5 to 18 years with ADHD
Settings: All
Intervention: Social skills training
Comparison: No intervention

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
		Social skills training				
Teacher-rated social skills competences at end of treatment - all eligible trials (SSRS)		The mean score for teacher-rated social skills competences at end of treatment in the intervention groups was **0.16 standard deviations higher** (0.04 lower to 0.36 higher)		392 (5 studies)	⊕⊕◯◯ **low**	
Teacher-rated general behaviour at end of treatment - all eligible trials		The difference in mean scores for teacher-rated general behaviour at end of treatment between the intervention and control groups was **0.00 standard deviations** (-0.21 lower to 0.21 higher)		358 (3 studies)	⊕⊕◯◯ **low**	

Teacher-rated ADHD symptoms - all eligible trials		The mean score for teacher-rated ADHD symptoms at end of treatment in the intervention groups was **0.02 standard deviations lower** (0.19 lower to 0.16 higher)	515 (6 studies)	⊕⊕◯◯ **low**

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% confidence interval).

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

BACKGROUND

Description of the condition

Attention Deficit Hyperactivity Disorder

Attention Deficit Hyperactivity Disorder (ADHD) affects 3% to 5% of all children (Polanczyk 2007). The main symptoms in ADHD consist of problems with attention, impulsiveness, and hyperactivity (Barkley 1998; Goldman 1998). Individuals with ADHD present difficulties in domains of attentional and cognitive functions, such as problem solving, planning, orienting, flexibility, sustained attention, response inhibition, and working memory (Sergeant 2003; Pasini 2007). Other difficulties involve affective components, such as motivation delay and mood regulation (Nigg 2005; Castellanos 2006; Schmidt 2009). This is the fundamental basis for the children's problems with social skills, and these problems are closely related to the condition (Whalen 1985; Landau 1991).

Prevalence estimates for ADHD vary across studies in the international literature. A large survey in the UK found that 3.6% of boys aged five to 15 years had ADHD; for girls of the same age, this study reported a prevalence of 0.9% (Ford 2003). In one study from Columbia, the reported prevalence was considerably higher: 19.9% for boys and 12.3% for girls (Pineda 2003). A systematic review on the prevalence of ADHD concluded that much of the variation is derived from the differences in methods used to diagnose the condition, and the investigators reported a mean proportion of 5.3% overall (Polanczyk 2007). The number of children who are referred to child psychiatrists with an ADHD diagnosis is increasing internationally (Swanson 1995; Goldman 1998; BUP 2008; NICE 2009).

The ADHD diagnosis may be split into 18 subgroups of symptoms according to the principal diagnostic classification systems, the International Classification of Diseases (ICD-10) (WHO 1992) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, DSM-IV-TR) (APA 1994; APA 2000). In the DSM-IV there are different sub-diagnoses, where particular symptoms are identified. These subtypes are 'predominantly inattentive type' or 'predominantly hyperactive-impulsive type'. The most common subtype diagnosis in children and adolescents is the combined type: 'attention-deficit hyperactivity disorder'.

Pharmacological management of ADHD

The effect of pharmacological treatment of children and adolescents with ADHD is well documented. It is reported to have a beneficial effect on major symptoms of hyperactivity, impulsivity, and inattention in about 80% of children treated, while the placebo response proportion is about 3% to 10% (Gadow 1990; Malone 1993; Spencer 1996; Barkley 1997; Gillberg 1997; Cyr 1998; Klassen 1999; MTA 1999; Gilmore 2001).The drug used most commonly for the treatment of ADHD in children and adolescents is methylphenidate, and less often atomoxetine and dexamphetamine are used (NICE 2009). There is one published Cochrane review on pharmacological treatment for children with ADHD and comorbid tic disorders (Pringsheim 2011). In this review many different types of medication were assessed, all of them showed effectiveness with the exception of deprenyl. It was not possible for the review authors to combine any of the included studies in meta-analysis. Another Cochrane review assessed the effectiveness of amphetamine for ADHD in people (including children) with intellectual disabilities (Thomson 2011). It concluded that there is very little evidence for the effectiveness of amphetamine for ADHD in people with intellectual disabilities .

The research on neurochemical basis of ADHD has primarily focused on the cathecolamine, noradrenaline, and dopamine neurotransmitters and their receptors in the central nervous system (CNS). Although the neurophysiological mechanism of the medications is not clearly known, it is presumed that the primary effects on the ADHD symptoms are explained primarily by the stimulant effects of the dopaminergic and to some extent the noradrenergic neurotransmission (Kadesjö 2002). More selective noradrenaline-acting tricyclic medications and alpha-2-adrenergic agonists have also been found to reduce symptoms in ADHD in children (Zametkin 1987).

Adverse effects are a cause for concern, the most common being headaches, sleeping problems, tiredness, and fluctuations in appetite. Most of these adverse reactions stop when the medication intake stops. Serious adverse reactions affect between 3% and 6% of children (Block 1998; Pliszka 1998; Cherland 1999; MTA 1999). Dexamphetamine seems to affect the children's sleeping, can give dry mouth, thirst and weight loss, decreased appetite, stomachache, and the risk of regressive, dependent behaviour and psychosis (NICE 2009). Atomoxetine can give pain, nausea and vomiting, decreased appetite with associated weight loss, dizziness, and slight increases in heart rate and blood pressure (Wolraich 2007). Methylphenidate also affects the children's height and weight curves (Schachar 1997; Swanson 2007). There have been some reports of sudden death in children and adults treated with this medication, but it is unclear if these are directly related to the use of methylphenidate and more research is being conducted on this topic (US FDA 2011).

Many children with ADHD have difficulties with social interaction, affecting their relationship with their parents, family, and friends, as well as other significant adults, for example, teachers (Whalen 1985; Landau 1991). These difficulties can be severe. Whilst medication can help in the management of core behavioural symptoms, it is not designed to address skills deficits. Children and adolescents with ADHD also have an increased risk of developing personality disturbance and possibly psychotic conditions, abuse of drugs or alcohol, and criminality later on in life (Hectman 1983; Mannuzza 1990; Biederman 1998; Mannuzza 1998; Biederman 2000; Barkley 2002; Dalsgaard 2002). Comor-

bid disorders often include behavioural disorders, depression, anxiety, tics, motor skill development disturbance, learning difficulties, and verbal and cognitive difficulties (MTA 1999; Kadesjö 2001). Children with ADHD have problems with severe social incompetence, and display off-task, disruptive and rule-violating behaviour (Kolko 1990; Landau 1991). More than 50% of children with ADHD have comorbid oppositional defiant disorder or conduct disorder (Pliszka 1999).

Description of the intervention

Social skills training

Social-skills training aims to improve and maintain the individual's social skills. The children are taught how to adjust their verbal and nonverbal behaviour in their social interactions. It also includes efforts to change the children's cognitive assessment of the 'social world'. The training generally focuses on teaching the children how to 'read' the subtle cues in social interaction, such as learning to wait for their turn, knowing when to shift topics during a conversation, and being able to recognise the emotional expressions of others (Fohlmann 2009a; Fohlmann 2009b (pers comm)). Social skills training also includes teaching social norms, social 'rules', and expectations of others (Liberman 1988). Social skills training is also referred to as cognitive behavioural training, and often consists of role play, exercises and games, as well as homework, and may include parents and sometimes teachers.

Emotional skills are about the child's ability to deal with, manage, express, and control his or her emotions. Emotional self-regulation is an important aspect of resilience. Children who have effective strategies for dealing with disappointment, loss, and other upsetting events are much more likely to be able to bounce back from adversity than those who do not. Managing positive emotion is also important. Success both socially and at school depends on being able to control exuberance when appropriate. An inability to regulate both positive and negative emotion has been associated with disorders such as ADHD and conduct disorder (Walcott 2004).

Social skills training is often taught in groups and is a relatively short intervention, most often consisting of a eight to 12 week programme. The duration of each group session is usually 50 to 90 minutes. Treatment frequency can be from a couple of times per month to several times a week. Programmes vary but tend to focus on problem solving, control of emotions, and verbal and non-verbal communication. The effect of the intervention may be measured by looking at social skills per se, or by looking at a more global assessment of psychological functioning, for example, the quality of peer relationships, emotional competences, and general behaviour. Often the program also includes parental groups, where the focus is on giving the parents the opportunity to support the training the children receive in the social skills groups by understanding the nature of ADHD and the content of the treatment programme.

Why it is important to do this review

Several randomised clinical trials suggest that social skills training may help children with ADHD (Pfiffner 1997; Antshel 2003; Pfiffner 2007). Like medical treatments, the effects of social skills training do not always appear to endure. Some studies indicate that not all children benefit from social skills training, potentially due to lack of parental engagement in the treatment (Kadesjö 2002). Some have argued that social skills training groups can have a negative effect on children with behavioural problems because the children's aggressive and restless behaviour can limit their ability to learn social skills and this, paradoxically, can increase negative behaviour (Mager 2005).

We have identified two meta-analyses and one review investigating the efficacy of social skills or psychosocial training for children with ADHD.Two of these meta-analyses found a significant effect with the social skills and psychosocial treatment (Boo 2007; Majewicz-Hefley 2007) and one did not find any significant effect (Van der Oord 2008). Furthermore, we found a meta-analysis where the effectiveness of social skills training for students with behaviour disorders was assessed (Kavale 1997). This meta-analysis did not find any significant benefit from the social skills training. All of these meta-analyses and reviews have serious methodological deficits, and none of them were systematic reviews. They all lacked a published protocol before they were conducted. Furthermore they had no systematic evaluation of systematic errors (bias) or systematic evaluation of random errors (play of chance) and the results are therefore questionable.

As the evidence is unclear, a systematic review is necessary to evaluate the effects of social skills training within this population.

OBJECTIVES

To assess the effects of social skills training in children and adolescents with Attention Deficit Hyperactivity Disorder (ADHD).

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials investigating social skills training alone or as an adjunct to pharmacological treatment in comparison

with no intervention or wait list control. We included trials where the children were taking concurrent medication as long as it was in both arms of the trial.

Types of participants

Children and adolescents between five and 18 years diagnosed with ADHD according to DSM-IV (APA 1994; APA 2000) or hyperkinetic disorders from ICD-10 (WHO 1992). The main term in DSM-IV is ADHD 314, which is divided into three subdiagnoses: predominantly inattentive type (314.00), predominantly hyperactive/impulsive type (314.01), and combined type (314.02). The DSM-IV diagnosis ADHD unspecified (314.9) may also be used, as well as diagnostic categories from earlier DSM systems (DSM-III and DSM-III-R) (APA 1980; APA 1987) and from hyperkinetic disorders in ICD-9 (WHO 1992).

In addition, we included participants with a diagnosis of ADHD based on a cut-off score from a validated diagnostic assessment instrument, for example, Conners' parent rating scales (Conners 1998). We also included participants with different kinds of comorbidity such as conduct or oppositional disorders, depression, attachment disorder, or anxiety disorders.

Types of interventions

We considered all forms of social skills training where training focused on behavioural and cognitive-behavioural efforts to improve social skills and emotional competence. This means behavioural and cognitive treatments focusing on teaching the children how to 'read' the subtle cues in social interaction, such as learning to wait for their turn, knowing when to shift topics during a conversation, and being able to recognise the emotional expressions of others, social 'rules', and expectations of others.

We included trials comparing social skills training versus either no intervention or wait list control. We considered these control groups equal. We therefore did not distinguish between the control groups, but analysed the trials with relevant outcomes together in the same comparison. We also included trials with concurrent medical treatment if the medication was administered equally in both groups. In further updates of the review we will also include trials with social skills training versus placebo or sham intervention as was described in our protocol.

Types of outcome measures

Primary outcomes

1. Social skills and emotional competences in school or at home, measured at post-treatment and longest follow-up, by well-established and validated instruments, for example, Social Skills Rating System (SSRS) or Conners' CBRS (Gresham 1990; Conners 2008a).
2. General behaviour in school or at home, measured at post-treatment and longest follow-up, by well-established and validated instruments, for example, the Achenbach Child Behavior Checklist (Achenbach 1991).

Secondary outcomes

1. Core ADHD symptoms of inattention, impulsivity, and hyperactivity, measured at post-treatment and longest follow-up, by well-established and validated instruments, for example, Conners' parents' rating scales (Conners 1998; Conners 2008b).
2. Performance and grades in school, measured at post-treatment and longest follow-up.
3. Participant and/or parent satisfaction with the treatment, measured as continuous outcomes by psychometrically validated instruments such as the Client Satisfaction Questionnaire (Attkinson 1982).
4. Adverse events: a) severe and b) non-severe. The severity was assessed according to the International Committee of Harmonization guidelines (ICH 1996). Serious adverse events are defined as any event that leads to death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability, and any important medical event that may have jeopardised the patient's health or requires intervention to prevent it. All other adverse events will be considered non-serious.

Search methods for identification of studies

Electronic searches

We searched the following electronic databases.

The Cochrane Central Register of Controlled Trials (CENTRAL) , 2011 (Issue 1) (searched 2 March 2011)
MEDLINE (1948 to current, searched 2 March 2011)
EMBASE (1980 to week 9 2011, searched 2 March 2011)
ERIC (1966 to current, searched 2 March 2011)
AMED (1985 to week 24 2011, searched 17 June, 2011)
PsycINFO (1806 to week 9 2011, searched 2 March, 2011)
CINAHL (1980 to current, searched 2 March 2011)
Sociological Abstracts (1952 to current, searched 2 March 2011)
*meta*Register of Controlled Trials (searched 15 October 2010)
Searches were not restricted by date or language. The search strategy for each database is in Appendix 1 .

Searching other resources

We searched the following online conference abstracts.

2nd International Congress on ADHD: from childhood to adult disease, 21 to 24 May 2009, Vienna, Austria

Eunethydis 1st international ADHD conference: from data to best clinical practice, 26 to 28 May 2010, Amsterdam, The Netherlands
Nordic ADHD-konference 19. og 20. maj 2010 i Aalborg
InternationaI Society for Research in Child and Adolescent Psychopathology (ISRCAP) conference, 17-20 June 2009, Seattle, Washington, USA
We contacted 176 experts in the field for possible information about unpublished or ongoing randomised clinical trials and . We received email answers from 15 of these experts (a list of those contacted is available from the review contact author).

Data collection and analysis

We conducted the review according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We performed the analyses using Review Manager 5 (RevMan) (RevMan 2011).

Selection of studies

Two reviewers (OJS and DD) independently evaluated and selected trials for inclusion. We assessed titles and abstracts and excluded those that clearly did not meet the inclusion criteria, for example, non-randomised trials or trials with participants outside the specified age range. Secondly, we retrieved full text articles and assessed the trials according to inclusion criteria. We discussed differing interpretations and in those cases where we did not reach an agreement, we consulted a third review author (PHT). We have listed randomised clinical trials that do not fulfil the inclusion criteria with reason for exclusion.

Dealing with duplicate publication

The Abikoff trial was reported in four publications, and the MTA in 13. In the rest of the included trials, there was only one report of the original trial. We assessed all pertinent articles together to maximize data collection (MTA 1999; Abikoff 2004).

Data extraction and management

Two authors (OJS, MS) extracted data independently using a data collection form (Appendix 2). OJS entered data into RevMan. OJS and MS resolved differences by discussion. In those cases where there were not enough data or unclear data in the published trial reports, we contacted nine of the authors, requesting them to supply the missing information. We received information back from five authors.

Assessment of risk of bias in included studies

For each included randomised clinical trial, OJS and MS independently evaluated all the bias components mentioned below. We resolved disagreements by discussion. We assigned studies to one of three categories: low risk of bias, uncertain risk of bias, and high risk of bias, according to guidelines in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011, section 8.2.1) and guidelines from the Cochrane Hepato-Biliary Group (Gluud 2009).
There is, however, no sufficiently well-designed method to combine the results of trials with high, unclear, or low risk of bias. Therefore, our main approach to incorporating risk of bias assessments in this review is to restrict meta-analysis to trials' with comparable risk of bias, and perform sensitivity analyses accordingly. In the *Cochrane Handbook for Systematic Reviews of Interventions* it is states that it is possible to perform meta-analysis when all the studies are low risk, all unclear, or all the trials are at high risk of bias. As there were no trials with low risk of bias, but only trials with high risk of bias we used them all in meta-analysis as suggested in the *Cochrane Handbook for Systematic Interventions*.
We also add an evaluation of our results following the GRADE system to ensure quality judgment about risk of bias, as well as other factors affecting the quality of evidence (Higgins 2011, section 8.8.3.1).

Generation of the allocation sequence

- Low risk of bias: the method used is either adequate (for example, computer-generated random numbers or table of random numbers) or is unlikely to introduce selection bias.
- Uncertain risk of bias: there is not enough information to assess whether the method used could cause bias.
- High risk of bias: the method used is improper and likely to introduce bias.

Allocation concealment

- Low risk of bias: the method used (for example, central allocation) will probably not cause bias on the observed intervention effect.
- Uncertain risk of bias: there is not enough information to assess whether the method used could cause bias on the estimate of effect.
- High risk of bias: the used method (for example, open random allocation schedule) will probably cause bias on the observed intervention effect.

Blinding of participants and personnel

- Low risk of bias: the method of blinding is described and blinding was made in a satisfactory way.
- Uncertain risk of bias: there is insufficient information to assess whether the type of blinding used is likely to induce bias on the estimate of effect.
- High risk of bias: no blinding or incomplete blinding.

Blinding of outcome assessors

- Low risk of bias: the method of blinding is described and blinding was made in a satisfactory way.
- Uncertain risk of bias: there is insufficient information to assess whether the type of blinding used is likely to induce bias on the estimate of effect.
- High risk of bias: no blinding or incomplete blinding.

Incomplete outcome data

- Low risk of bias: the underlying reasons for the missing data will probably not affect the outcome measurement of the effect of the trial, or valid methods have been used to handle missing data.
- Uncertain risk of bias: there is not enough information to assess whether the missing data or the method used to handle missing data will create bias on the estimate of effect.
- High risk of bias: the crude estimate of effects will definitely be biased due to the underlying reasons for the absence of data, or the methods used to handle missing data are unsatisfactory.

Selective outcome reporting

- Low risk of bias: the trial protocol is available or all prespecified outcomes that are of interest have been reported.
- Uncertain risk of bias: there is not enough information to assess whether the magnitude and direction of the observed effect is related to selective outcome reporting.
- High risk of bias: not all of the primary outcomes specified beforehand have been reported or similar.

Vested interest bias

- Low risk of bias: the trial's source(s) of funding did not come from any parties that might have conflict of interest (for example, a drug or a device manufacturer) or the authors of the trial has not conducted previous trials addressing the same interventions.
- Uncertain risk of bias: the source of funding was not clear, or it is not clear if the author has conducted previous trials addressing the same interventions.
- High risk of bias: the trial was funded by parties that might have conflict of interest (for example, a drug or a device manufacturer), or the authors of the trial has conducted previous trials addressing the same interventions. (e.g.,the pharmacological industry might induce an interest in finding no effect of other than pharmacological treatment for ADHD. Further, when you have been previously involved in a similar trial, you have a preferable interest in this treatment as well as beforehand thoughts about the results and this may induce unintentional bias.)

Other sources of bias

- Low risk of bias: the trial appears to be free of other sources of bias.
- Uncertain risk of bias: there is inadequate information and it is therefore not possible to assess other possible sources to bias.
- High risk of bias: it is likely that potential sources of bias are present, for example, that is related to the specific design used, early termination due to some data-dependent process, or lack of power calculation, or other bias risks.

We will consider trials with one or more unclear or inadequate component as trials with high risk of bias.

Measures of treatment effect

Dichotomous data

None of the included trials had relevant outcomes with dichotomous data to be used in meta-analyses. In future updates we will analyse dichotomous data as risk ratios (RR) with 95% confidence intervals (CI), and we will calculate risk difference (RD), and the number needed to treat (NNT) in case there is a significant effect with the intervention and reasonable homogeneity of trials; that is, clinical, methodological, or statistical heterogeneity is within reasonable limits (Higgins 2011, section 9.2).

Continuous data

For continuous data, we compared the mean score between the two intervention groups to give a mean difference (MD) with 95% CI. We used the overall MD where possible to compare the outcome measures from studies. We calculated the standardised MD (SMD) where there were different outcome measures used to measure the same construct in the trials.
One of the trials did not report means and standard deviations but P-values connected to F values (Cohen 1981). We tried to transform these into standard deviations, but this was not possible because we did not have the necessary between-groups values. For one trial (Pfiffner 2007) we received raw data on the SSRS parent and teacher scores and these were used for calculation.

Unit of analysis issues

Cluster-randomised trials

None of the trials used cluster randomisation. If we find cluster-randomised trials for the update of this review, we anticipate that investigators will have presented their results after appropriately check for clustering effects (robust standard errors or hierarchical linear models). If it is unclear whether a cluster-randomised trial has used appropriate checks for clustering, we will contact the investigators for further information. Where appropriate checks

were not used, we will request and re-analyse individual participant data using multilevel models that check for clustering. Following this, we will analyse effect sizes and standard errors in RevMan 5 (RevMan 2011) using the generic inverse method (Higgins 2011, section 9.3.2). If there is insufficient information to check for clustering, we will enter outcome data into RevMan 5 using individuals as the units of analysis, and then use sensitivity analysis to assess the potential biasing effects of inadequately controlled clustered trials (Donner 2002).

Dealing with missing data

Our intention was to assess impact of missing data, by applying 'intention-to-treat' and 'best-case scenario' and 'worst-case scenario' procedures, but as there were no dichotomous data this was not possible. We will do this in future updates if we have appropriate data for these analyses. On the continuous outcomes it was possible for us to do 'as reported' analyses. We made a great effort to retrieve missing data from the authors, and we evaluated the methods used to handle the missing data in the publications and to what extent it was likely that the missing data would influence the results of outcomes of interest

Assessment of heterogeneity

We considered variability in the participants, interventions, or outcomes in the trials as clinical heterogeneity. We considered methodological heterogeneity as the variability in designs of the trials and statistical heterogeneity as the difference in the intervention effects of the trials. We also quantified the heterogeneity by I^2 assessment where I^2 values between 30 to 60 per cent indicated a moderate level of heterogeneity (as suggested by Higgins 2011, section 9.5.2). We furthermore assessed potential reasons for the heterogeneity by examining individual trial characteristics and subgroups. Fixed-effect model meta-analyses are used when there is an assumption that the observed differences between the study results are just due to 'play of chance'. When there is heterogeneity that cannot be explained as 'play of chance', it is common to use a random-effects model meta-analyses. A random-effects model has the assumption that apparent differences between study effects are random, but the estimated difference follows a normal distribution. This method gives more weight to the small trials, whereas the fixed-effect model meta-analysis gives more weight to the large trials. We therefore performed both fixed- and random-effects models, and checked for differences between these methods of analyses (Higgins 2011, section 9.5.4). If both models gave the same results, then only the random-effects model is reported.

Assessment of reporting biases

We handled different forms of reporting bias, especially publication bias and outcome reporting bias, according to the recommendations of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011, section 10.1). We did not draw funnel plots to give a visual assessment about whether effects are associated with the size of the study because there were not over 10 studies in any of the meta-analyses. In further updates we will construct funnel plots when there are more than 10 studies in a comparison. There are several reasons for the asymmetry of a funnel plot, for example, true heterogeneity, poor methodological quality, or publication bias (Higgins 2011, section 10.4.1).

Data synthesis

We included and analysed trials undertaken in any configuration or setting; for instance, in groups, in the home, at a centre. We summarised data meta-analytically when they were available. We performed statistical analysis according to recommendations in the latest version of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011section 9.4.1). We synthesised data by using final values and the inverse variance method in the meta-analyses. We generally used random-effect models because we expected differences in the treatments, but we undertook both a random-effects model and a fixed-effect model meta-analysis for the trials with a moderate level of heterogeneity. These methods give different weights to the trials depending on their size, and therefore it is wise to perform both analyses. For trials with a higher level of statistical heterogeneity, and where the amount of clinical heterogeneity made it inappropriate to use these trials in meta-analyses, we provided a narrative description of the trial results. We did not combine trials where there were great differences, such as in the included participants' characteristics. For some of the outcomes it was not possible to do meta-analysis because the outcomes were only reported in one single trial. We therefore provided a narrative description of those outcomes.

Subgroup analysis and investigation of heterogeneity

We conducted subgroup analysis both where we found statistically significant differences between intervention groups, and in other cases to make hypotheses about the subgroups mentioned below. We performed three subgroup analyses according to the following categories.

- Trials with ADHD and comorbidity compared to trials with ADHD and no comorbidity.
- Trials with social skills training only compared to trials with social skills training supported by parent training.
- Trials with social skills training, parent training, and medication compared to trials with social skills training and parent training without medication.

Sensitivity analysis

- Repeated the analysis excluding the trial with longest treatment duration or the largest trial.

- Repeated the analysis testing the robustness of the results using different statistical models (fixed-effect or random-effects) (Higgins 2011).

Heterogeneity-adjusted required information size and trial sequential analysis

Trial sequential analysis (TSA) is a tool for quantifying the statistical reliability of the data in a cumulative meta-analysis and gives a valuable overview of the number of participants needed to make a firm evaluation of a possible intervention effect (Brok 2008; Wetterslev 2008; Brok 2009; Thorlund 2009).
Comparable to the a priori sample size estimation in a single RCT, a meta-analysis should include an information size (IS) at least as large as the sample size of an adequately powered single trial to reduce the risk of random error. The TSA provides the required information size (RIS) in meta-analysis to adjust the significance level for sparse data and repetitive testing on accumulating data to avoid the increased risk of random error (Wetterslev 2008).
Multiple analysis of accumulating data when new trials emerge leads to 'repeated significant testing', thus, use of conventional P-value criterion is prone to exacerbate the risk of random error (Lau 1995; Berkley 1996). Meta-analyses not reaching the RIS are analysed with trial sequential monitoring boundaries analogous to interim monitoring boundaries in a single trial (Wetterslev 2008). This approach will be crucial in coming updates of the review.
We calculated the a priori heterogeneity-adjusted required information size (APHRIS) (that is the number of participants required to detect or reject a specific intervention effect in the meta-analysis) and performed trial sequential analysis for the primary outcome, teacher-rated social skills competences at end of treatment, based on the following a priori assumptions:

1. the standard deviation of the primary outcome is 1.0;
2. an anticipated intervention effect equal to Hedge's g 0.5;
3. a maximum type I error of 5%;
4. a maximum type II error of 20% (minimum 80% power) and of 10% (minimum 90% power); and
5. a priori anticipated 50% heterogeneity (Brok 2008; Wetterslev 2008; Brok 2009; Thorlund 2009).

We also calculated a post hoc heterogeneity-adjusted required information size (PHHRIS) (i.e., number of patients required to detect or reject a specific intervention effect in the meta-analysis) and performed trial sequential analysis for the primary outcome; teacher-rated social skills competences at end of treatment, based on the following estimated assumptions:

1. the standard deviation of the primary outcome in patients in the control group of trials with lower risk of bias;
2. the estimated intervention effects in trials with lower risk of bias;
3. a maximum type 1 error of 5%;
4. a maximum type II error of 20% (minimum 80% power); and
5. the estimated heterogeneity in the trials included in the meta-analysis. The standard deviation of the primary outcome in patients in the control group of trials with lower risk of bias (Brok 2008; Wetterslev 2008; Brok 2009; Thorlund 2009).

RESULTS

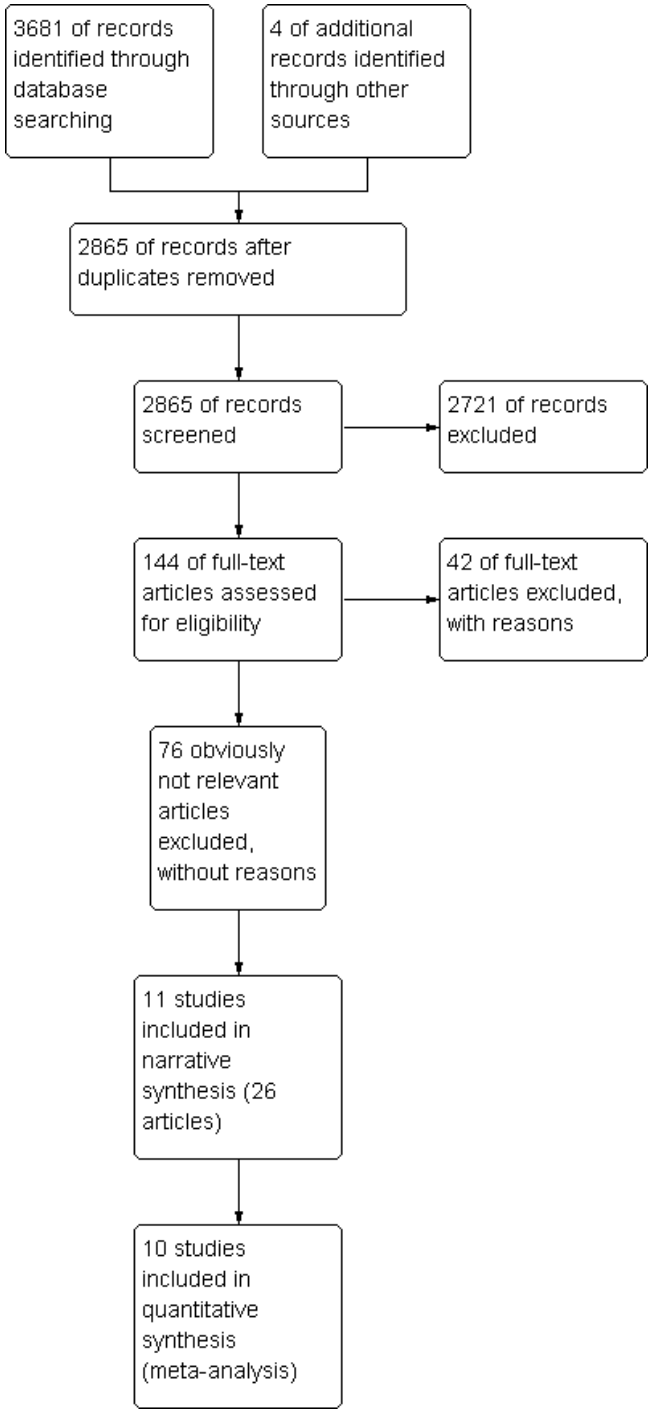
Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.

Results of the search

We carried out electronic searches over three time periods. Searches up to February 2009 produced 2500 publications after duplicates were removed (3045 initial records). Searches from February 2009 until June 2010 produced an additional 200 publications after duplicates were removed (643 initial records). Searches from June 2010 until March 2011 produced an additional 165 publications after duplicates were removed (208 initial records). We identified four publications from other sources (Figure 1).

Figure 1.



Included studies

We included 11 randomised trials described in 26 publications (all full text articles) in the review. We included trials where the social skills training was supported by parental training or supplemental efforts focused on parents and teachers.

Setting

Eight of the 11 trials were carried out in the USA (Bloomquist 1991; Pfiffner 1997; MTA 1999; Antshel 2003; Tutty 2003; Abikoff 2004; Pfiffner 2007; Waxmonsky 2010). One trial was from Canada (Cohen 1981), one from the Netherlands (van der Oord 2007), and one from Hong Kong (China) (Yuk-chi 2005).

Participants

The 11 randomised trials included a total of 747 participants. These were all children between five and 12 years old. All participants were diagnosed with ADHD using tools that had been accepted for inclusion in this review. All these diagnostic tools were based on the international DSM or ICD diagnostic systems, or a cut-off score from the Conners' Rating Scale. In 10 trials, the children had different types of comorbidities, for example, oppositional defiant disorder, conduct disorder, anxiety disorder, in addition to the ADHD diagnosis, but in Tutty 2003comorbidities were an exclusion criteria.

In four of the trials, the number of girls compared to boys was 1:3 or 1:4 (MTA 1999; Antshel 2003; Tutty 2003; Waxmonsky 2010), and in three trials, the number of girls compared to boys was nearly 1:2 (Bloomquist 1991; Pfiffner 1997; Pfiffner 2007). In three trials, the number of girls compared to boys was as low as between 1:7 and 1:10 (Cohen 1981; Yuk-chi 2005; van der Oord 2007).

In seven of the trials, the participants were between 80% and 90% Caucasians (Cohen 1981; Bloomquist 1991; Pfiffner 1997; Antshel 2003; Abikoff 2004; van der Oord 2007; Waxmonsky 2010). In two trials, the ethnicity was more mixed, with 49% to 61% Caucasians and the majority being of another ethnicity, i.e., 4% to 20% Afro-American and 5% to 16% Asian (MTA 1999; Pfiffner 2007). In one trial, the participants were all Chinese children (Yuk-chi 2005).

Sample size

Only one trial reported doing a sample size calculation before the start of the trial (MTA 1999). There was considerable variation in sample sizes between the trials. The number of participants randomised per trial ranged from 27 to 576 participants.

Interventions

The 11 trials had comparable treatment interventions. The interventions were named social skills training (Pfiffner 1997; Antshel 2003); cognitive behavioural intervention (Cohen 1981; Bloomquist 1991); multimodal behavioural/psychosocial therapy (MTA 1999; Abikoff 2004; van der Oord 2007); behavioural therapy/treatment (Pfiffner 2007; Waxmonsky 2010); behavioural and social skills treatment (Tutty 2003), and psychosocial treatment (Yuk-chi 2005). In the rest of the review, all the experimental child interventions will be referred to as 'child social skills training', which is in accordance with the description of the intervention in the background section.

Experimental

Five trials had child social skills training and parent training plus medical treatment in the experimental treatment versus medical treatment alone (Cohen 1981; Antshel 2003; Tutty 2003; Abikoff 2004; Waxmonsky 2010). Another one of these trials also administrated academic organisational skills training and individual psychotherapy (Abikoff 2004).Two trials had child social skills training, parent training, and teacher consultations in the experimental treatment (Yuk-chi 2005; van der Oord 2007). The MTA trial used child social skills training, parent training, teacher consultations, and classroom behavioural intervention in the experimental treatment (MTA 1999). Two trials used child social skills training and parent training plus teacher consultation in the experimental treatment (Bloomquist 1991; Pfiffner 2007). All of the interventions in the trials were group interventions except Cohen 1981.

Control

Eight trials used medications in both the experimental treatment and as the only treatment in the control treatment and therefore it is comparable with a no treatment control group (Cohen 1981; MTA 1999; Antshel 2003; Tutty 2003; Abikoff 2004; Yuk-chi 2005; van der Oord 2007; Waxmonsky 2010). One of these trials also included a no treatment control group (Cohen 1981). Three trials used a wait list control group, without medication in any of the groups (Bloomquist 1991; Pfiffner 1997; Pfiffner 2007).

The duration of the intervention was comparable in eight of the included trials and was between eight weeks and 10 weeks. In one trial, the intervention lasted for 24 weeks (Yuk-chi 2005); in one trial for 14 months (MTA 1999), and in one trial the intervention lasted for two years (Abikoff 2004).

Outcome measures

Social skills competences

Social Skills Rating Scale (SSRS) parent-, teacher- or child-rated versions were used in seven of the trials (Pfiffner 1997; MTA 1999; Antshel 2003; Abikoff 2004; Pfiffner 2007; van der Oord 2007; Waxmonsky 2010). SSRS is a standardised measurement instrument to assess children's social skills and provides a comprehensive picture of social behaviours. The SSRS is based on a large amount of research and was standardised on a national sample of over 4000. The forms are rated by parents, teachers and the child themselves. The SSRS used by the trials in this review consists of different versions with different numbers of items from 30 items to 55 items. The teacher, parent and child version of the SSRS are rated on a three point Likert scale ranging from zero (never) to two (often). Higher scores indicate better social skills competences and lower scores indicate social skills impairment.

Social Skills Scale (UCI) is a 10 item measurement instrument with a five point scale ranging from one (low skills) to five (high skills), and is measured by parents.The scale is showing the degree of children's social competences. This scale was used only by Pfiffner 1997.

Teacher Report - Walker - McConnell Scale of Social Competence and School Adjustment is a 43 item checklist to sample behaviour, social, and academic competence according to the scales, teacher-preferred social behaviour, peer-preferred social behaviour, and school adjustment. The instrument consisted of a five point rating scale ranging from zero (never) to five (frequently). This instrument was used in one trial (Bloomquist 1991).

Social Interaction Observation Code records spontaneously initiated positive, negative, and neutral social behaviour towards the child and their response. Observation was done by raters blinded to treatment assignment and lasted for 30 minutes. The behaviour was scored on a four point scale in one included trial (Abikoff 2004).

Test of social skill knowledge is designed to measure the children's knowledge about social skills taught during the class and was scored by blinded raters and consist of six questions each scored from one (low knowledge) to 15 (high knowledge) in one trial (Pfiffner 1997).

Observation in classrooms. This was used in one trial (Cohen 1981). The children were observed for three eight minute periods over one hour. Two categories of behaviour were observed: play behaviour and social behaviour.

Higher scores for social skills competences mean better outcomes.

General behaviour

Conners Behavior Rating Scale (CBRS). This rating scale measures behaviour, and consist of different indexes. For this outcome the conduct problem index was used in Cohen 1981.

Child Behavior Checklist. This rating scale is designed to measure the behavioural problems and social competences of children as reported by parents. It consists of 118 items related to behaviour problems and scored on a three point scale ranging from zero (not true) to two (often true) (MTA 1999).

Clinical Global Impression. This measures the child's overall level of improvement on a seven point scale ranging from one (much worse) to seven (much improved). This measure was used in Pfiffner 2007.

Conners Teacher Rating Scale (CTRS). CTRS measures hyperactivity and behavioural problems in children, and consist of different indexes. In this outcome the conduct problems index is used. There are a total of 39 items and a four point Likert scale ranging from zero (not at all true) to three (very true). This rating scale was used in Abikoff 2004.

Lower scores for the general behaviour outcomes means better outcomes, except the Clinical Global Impression where higher scores are better.

ADHD symptoms

Disruptive Behavior Disorders Rating Scale (DBDRS). This rating scale assesses DSM-IV disruptive behaviour disorders symptoms. The DBDRS consist of 42 items and contains four indexes: inattention, hyperactivity/impulsitivity, oppositional defiant disorder (ODD), and conduct disorder (CD). Both parent and teacher versions were used and the scale uses a four point Likert scale ranging from zero (not at all) to three (very much). This scale was used in van der Oord 2007; Waxmonsky 2010).

Child Symptom Inventory (inattention). The inattention items from this instrument (completed by parents and teachers) correspond to DSM-IV inattention symptoms and are rated on a four point Likert scale ranging from zero (never) to three (very often) (Pfiffner 2007).

Conners Parent Rating Scale (CPRS). This measures hyperactivity and behavioural problems in children, and consist of different indexes. For this outcome the hyperkinesis index is used. There are 39 items in total and a four point Likert scale ranging from zero (not at all true) to three (very true). This scale was used in Abikoff 2004.

Strengths and Weaknesses of ADHD Symptoms and Normal Behaviors (SWAN).This rating scale is developed to assess the indication for ADHD in children. Factor analyses have demonstrated strong measures of reliability, including test-retest reliability, inter-rater reliability, and measures of internal consistency (Lakes 2011). The SWAN consists of nine DSM-IV items for Attention Deficit (AD) and nine DSM-IV items for Hyperactivity/Impulsivity. This version of SWAN consist of 30 items rated on a seven point scale including both positive and negative scores to reflect strengths and weaknesses (one (slightly below average) to minus three (far above average)). This scale was used in Yuk-chi 2005.

The ADHD Rating Scales. This scale consist of 18 items and is linked directly to DSM-IV diagnostic criteria for ADHD. It is rated on a five point Likert scale from zero (never) to four (almost always) and was assessed by telephone interviews of parents This

scale was used in Tutty 2003.

Conner Teacher Rating Scale (CTRS). This is a scale for the assessment of ADHD and measures hyperactivity and behavioural problems in children, and consists of different indexes. The norm data comes from a large community-based sample of children and adolescents collected throughout the United States and Canada. The instrument has high validity and reliability. In this outcome the hyperactivity index is used. There are 39 items and a four point Likert scale ranging from zero (not at all true) to three (very true). This scale was used in Bloomquist 1991 and Abikoff 2004.

The SNAP-IV Teacher Rating Scale. The SNAP-IV is a revision of the Swanson, Nolan and Pelham (SNAP) scale and measures ADHD symptoms from the DSM-IV criteria. The scale has 26 items and scores is based on a zero (not at al) to three (very often) rating scale. The psychometric properties have been evaluated and the reliability was acceptable (Bussing 2008). This scale was used in MTA 1999.

The Child Attention Profile. This is a 12 items scale with a three point rating scale (not true, sometimes true, very often true), and was assessed by telephone interviews of teachers. The measurement scale measures the child's attention capacity. This scale was used in Tutty 2003.

DSM-III-R checklist. This is a checklist for ADHD symptoms used by the child psychiatrist (Abikoff 2004).

Structured behavioural observations. Observers were blind to treatment assignment and trained in the use of this instrument. Each of the children were observed in an unobtrusive manner during 10 minute observation periods. The behaviour codes were (1) on-task, (2) off-task, and (3) off-task/disruptive (Bloomquist 1991).

Sluggish Cognitive Tempo (SCT). This measures cognitive tempo and consists of 15 items rated on a four point scale from zero (never) to three (very often) (Pfiffner 2007).

Lower values of ADHD symptoms mean better outcomes, except SWAN, which measures both strengths and weaknesses.

Performance in school

Academic Performance Rating Scale (APRS). This is a 19 item scale with a five point Likert scale (Waxmonsky 2010).

Stanford Achievement Scale. This is a standardised test that measures mathematics, reading, comprehension, and spelling competences (Waxmonsky 2010).

Wechsler Individual Achievement Test (WIAT). This records the children´ s level of achievement and consists of 16 subtests (higher scores better) (MTA 1999).

Satisfaction with the treatment

Participant and/or parent satisfaction with the treatment (Pfiffner 1997; MTA 1999; Yuk-chi 2005; Pfiffner 2007; Waxmonsky 2010).

Adverse events

None of the trials reported on this outcome.

Excluded studies

17 of the 38 excluded studies described trials that were not randomised (Pelham 1980; Hinshaw 1984; Abikoff 1985; Carlson 1992; Pelham 1993; Williams 1993; Frankel 1997; Carlson 2000; Evans 2000; Frölich 2002; Fabiano 2003; Chang 2004; Ercan 2005; Pelham 2005; Fenstermacher 2006; Miranda 2006a; Waxmonsky 2008). In 12 of the excluded publications, the intervention and/or the control group were not acceptable for inclusion in this review (Wolraich 1978; Rosén 1984; Horn 1990; Klein 1997; Kolko 1999; Gonzalez 2002; Miranda 2002; Döpfner 2004; Corkum 2005; Gol 2005; Langberg 2008; Molina 2008). Three of the trials had participants below the age group for the review (Webster-Stratton 2001; Webster-Stratton 2004; Lösel 2006). Two publications were review articles (Jensen 1999; Miranda 2006b). Two trials did not include children with ADHD (Kolko 1990; Feinfield 2004). One publication was not a trial (Gadow 1985) and one was a letter to editors (MTA 2009). We have also listed in Excluded studies four publications that related to one of the included studies (MTA 1999) but did not provide data relevant to the outcomes in this review (Hinshaw 2000; Pelham 2000; Jensen 2001; Langberg 2010).

Risk of bias in included studies

Allocation

Generation of the allocation sequence

We considered the random sequence generation to be at low risk of bias in seven trials where allocation was assigned by random numbers that were computer-generated, derived from a table, or by the coin toss method (MTA 1999; Antshel 2003; Tutty 2003; Abikoff 2004; Yuk-chi 2005; Pfiffner 2007; Waxmonsky 2010). In four trials, the random sequence generation method used was not stated (Pfiffner 1997; Cohen 1981; Bloomquist 1991; van der Oord 2007) and therefore considered as unclear risk of bias.

Allocation concealment

The allocation concealment was at low risk of bias in five trials (MTA 1999; Antshel 2003; Abikoff 2004; Pfiffner 2007; Waxmonsky 2010). In five trials, there was no description of allocation concealment and therefore the trials were considered to as unclear risk of bias (Bloomquist 1991; Pfiffner 1997; Tutty 2003; Yuk-chi 2005; van der Oord 2007). In one trial we considered

the risk of bias high because four participants were moved between groups after randomisation due to adverse reactions (Cohen 1981).

Blinding

We are of the opinion that it is not possible to blind participants or personnel involved in the delivery of the social skills intervention and this means that all the included trials had high risk of bias on this aspect. However, it is very possible to employ blinded ratings and observations of the participants. None of the 11 included trials used blinded ratings and observations for all the outcomes. In five of the trials there was blinding on at least one of the outcomes, but these outcomes are not used in our meta-analysis. The outcomes from the trials used in the meta-analysis were not blinded and are therefore considered as at high risk of bias as in the other included trials (Cohen 1981; Bloomquist 1991; Pfiffner 1997; MTA 1999; Abikoff 2004).

Incomplete outcome data

Six trials were at low risk of bias, having adequately addressed incomplete outcome data (Pfiffner 1997; MTA 1999; Antshel 2003; Tutty 2003; Pfiffner 2007; van der Oord 2007). Two trials were assessed as high risk of bias: in one it was reported that 22 out of 103 children failed to complete the trial (Abikoff 2004); in the other, up to 50% missing items on indexes was allowed, and participants were dropped when there was not enough data (Waxmonsky 2010). Three trials were considered not to have adequately addressed incomplete outcome data (Cohen 1981; Bloomquist 1991; Yuk-chi 2005). Accordingly, five trials were considered high risk of bias regarding this component.

Selective reporting

None of the 11 trials had protocols published before the trial started. Most of the trials reported on all outcomes expected to be addressed, except for Pfiffner 1997 where two important outcomes - SNAP and CLAM (Conners, Loney, and Milich rating scale) used in pre- and post-treatment assessments - were not reported. In MTA 1999 it was not possible to find reports on all the prespecified outcomes, and in Waxmonsky 2010 there was an inconsistency between the published article and the description of the study on clinicaltrials.gov. In Abikoff 2004 the design article was published at the same time as the results article, thus making it difficult to assess if there had been selective reporting. These three trials were therefore rated as unclear because of lack of information.

Other potential sources of bias

In the trial of Abikoff 2004, one of the authors (Dr. Klein) was a member of an advisory board of a medical company. In two trials (Pfiffner 1997; Pfiffner 2007), the families and teachers were paid for doing the assessment at follow-up, leading to potentially selection of data from those who are prone to this incentive. Some authors have conducted previous research on the topic and there was therefore potential vested interest bias in those trials (Abikoff 2004; Yuk-chi 2005; Pfiffner 2007). In one trial, 44% of the participants were medicated with stimulant medication, but the number of medicated children in the each group was not stated (Pfiffner 1997). The distribution of stimulant medication was balanced between intervention groups in six of the trials (MTA 1999; Antshel 2003; Tutty 2003; Abikoff 2004; van der Oord 2007; Waxmonsky 2010). In two of the trials, there was no information about between-group stimulant medication balance (Cohen 1981; Yuk-chi 2005). In most of the trials there were no information about any co-medication for comorbid disorders, except the MTA 1999 trial where all kinds of medication were balanced between groups. In Antshel 2003, the selective serotonin receptor inhibitor (SSRI) medication (so called ' antidepressive medication') was balanced between groups.

All the review authors' judgements about each risk of bias item for each included study are shown in Figure 2 and Figure 3.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study

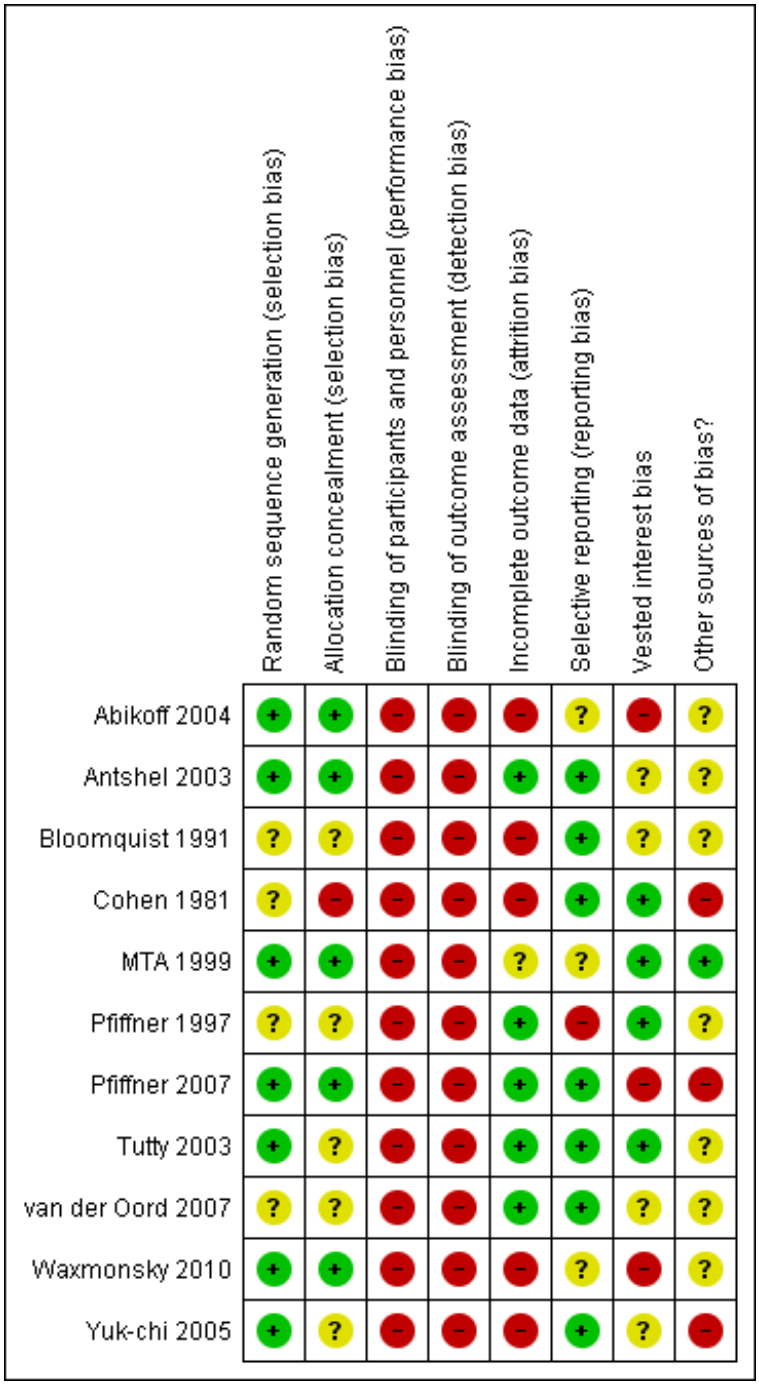
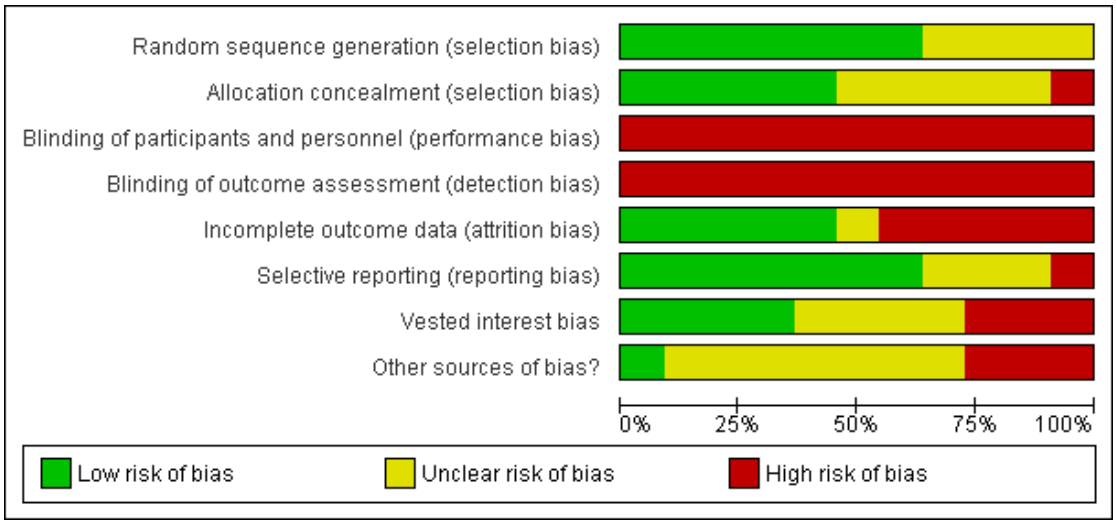


Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies



Effects of interventions

See: **Summary of findings for the main comparison** Social skills training compared to no intervention

We present the results for each of the two primary and the four secondary outcomes below. The effect sizes have been calculated as standardised mean differences (SMD) and, where possible, as mean differences (MD). A SMD effect size of 0.15 or less is considered to have no clinically meaningful effect. An SMD effect size of 0.15 to 0.40 is considered to have clinical meaningful but small effect (Thalheimer 2002). An SMD effect size of 0.40 to 0.75 is considered to have a moderate effect. An SMD effect size greater than 0.75 is considered to have a large treatment effect. In those trials where it has not been possible to obtain the necessary data to calculate an effect size, we have reported the results in the same way as they were reported in the original article. We have contacted the authors of trials with unclear or missing data and requested the necessary data. We contacted authors from nine of the trials (some of them several times) (Bloomquist 1991; Pfiffner 1997; MTA 1999; Antshel 2003; Tutty 2003; Abikoff 2004; Pfiffner 2007; van der Oord 2007; Waxmonsky 2010) and received information back from five of the authors (Pfiffner 1997; Antshel 2003; Abikoff 2004; Pfiffner 2007; Waxmonsky 2010).

For three trials (Antshel 2003; Pfiffner 2007; van der Oord 2007), all the outcomes in the trials are used in the meta-analysis. In seven of the trials, some outcomes are used in the meta analysis and some are reported separately (Bloomquist 1991; Pfiffner 1997; MTA 1999; Tutty 2003; Abikoff 2004; Yuk-chi 2005; Waxmonsky 2010). Only the data from Cohen 1981 had no outcomes included in meta-analysis and all outcomes are reported separately.

All the trials had high risk of bias due to systematic errors. We used all eligible trials in the meta-analysis, as it is recommend in the *Cochrane Handbook for Systematic Reviews of Interventions* to do so when all the studies are assigned the same risk of bias. We also added an evaluation of our results following the GRADE system to ensure quality judgment about risk of bias, as well as other factors affecting the quality of evidence (Higgins 2011, section 8.8.3.1).

The analysis is organised by outcome with the teacher-rated outcomes as our primary analyses. The 'Summary of findings' table consists of the three most important comparisons. These are the two primary and the first secondary outcomes, and the only outcomes where it was possible to perform meta-analysis.

Primary outcome: Social skills and emotional competences

Meta-analyses

The primary analysis in this outcome: *Teacher-rated social skills competences at end of treatment - all eligible trials* showed no significant effect of the treatment (SMD 0.16; 95% CI -0.04 to 0.36, I^2 = 0%, P = 0.12). This was tested with one sensitivity analysis: *Teacher-rated social skills competences - excluding the trial with the longest treatment intervention (and the largest trial)* (SMD 0.19; 95% CI -0.10 to 0.48, I^2= 0%, P = 0.20). This sensitivity analysis showed no significant differences, which showed the robustness of the primary analysis (test for subgroup differences: Chi^2 = 0.03, df = 1 (P = 0.86), I^2 = 0%). We also conducted three secondary analyses for this outcome: *Teacher-rated social skills competences - longest follow up* (SMD 0.06; 95% CI -0.86 to 0.98, P = 0.90); *Parent-rated social skills competences at end of treatment - all eligible trials* (SMD 0.22; 95% CI 0.04 to 0.40, I^2= 13%, P = 0.02), and *Participant-rated social skills competences at end of treatment - all eligible trials* (SMD 0.21; 95% CI -0.09 to 0.51, I^2=0%, P = 0.17)(Analysis 1.1). Only the *Parent-rated social skills competences at end of treatment - all eligible trials* showed significant differences. We also performed meta-analysis of four studies using comparable types of the SSRS scale (MD) and this comparison showed no significant effect on the *Teacher-rated social skills competence* (MD 1.81; 95% CI -1.02 to 4.64) *(*Analysis 1.2). The trial sequential analyses showed that there is a need for more participants in new randomised trials to make reliable statistical analysis on the comparison (Figure 4; Figure 5; Figure 6).

Figure 4. TSA 1

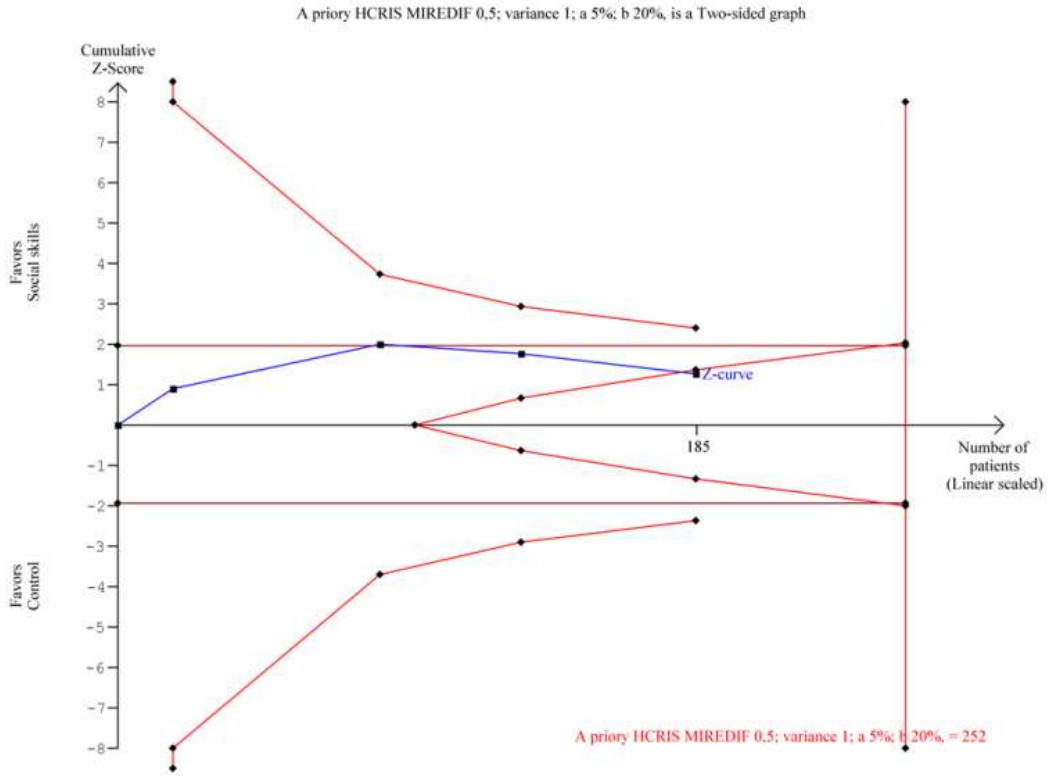


Figure 5. TSA 2

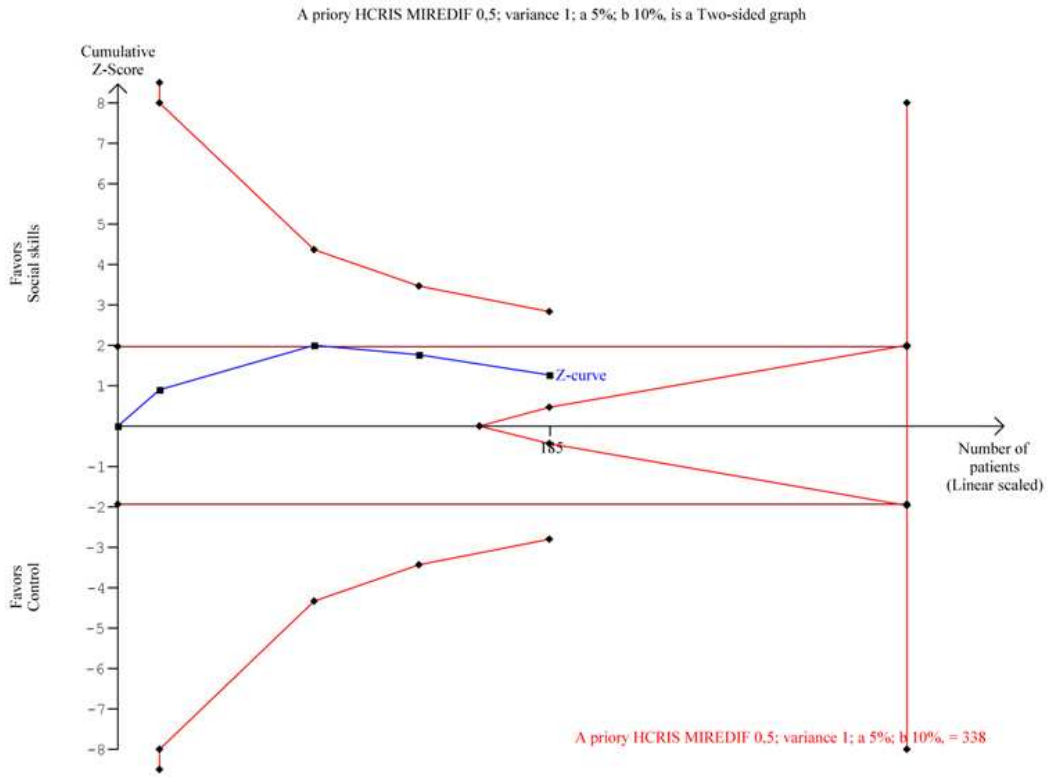
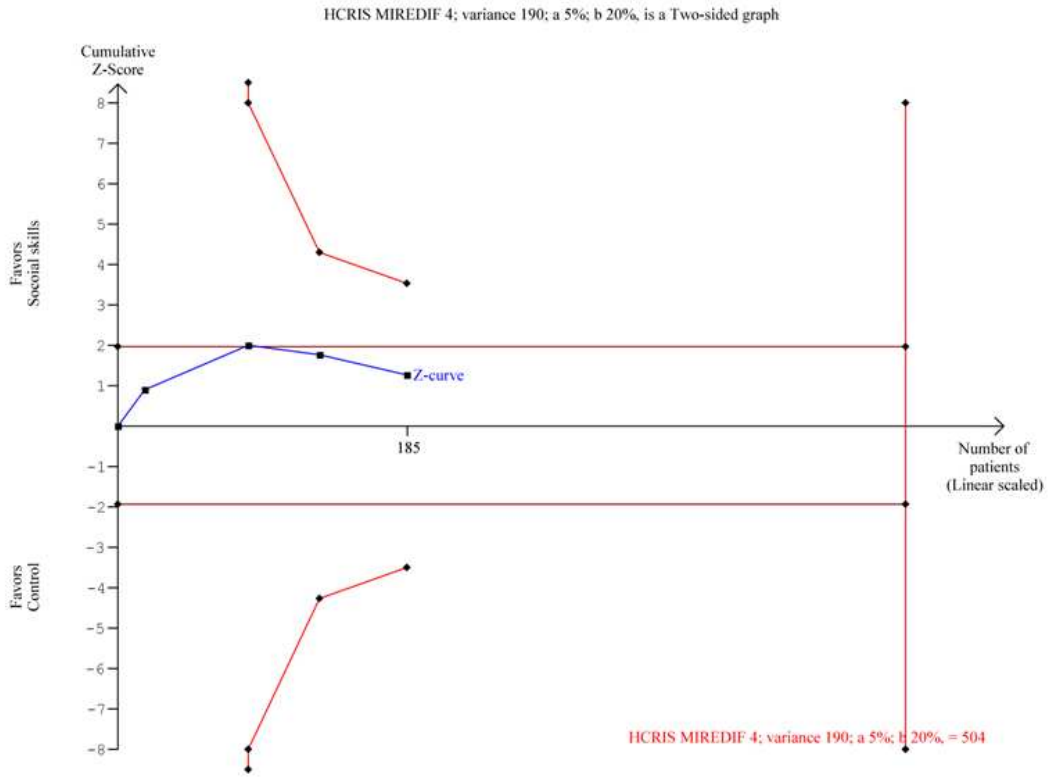


Figure 6. TSA 2



Single trial results

The *Teacher Report - Walker-McConnell Scale of Social Competence and School Adjustment* (Bloomquist 1991) showed no significant difference between groups (MD 1.06; 95% CI -0.47 to 2.59) (Analysis 1.4). The *Social Skills Scale* (UCI) used by Pfiffner 1997 showed a large treatment effect (MD 9.70; 95% CI 6.07 to 13.33) (Analysis 1.5). The single outcome measure in Abikoff 2004 - *Social Interaction Observation Code* - is reported as showing no significant difference in negative behaviour (MD 0.20; 95% CI -0.11 to 0.51) (Analysis 1.7). *The Test of Social Skill Knowledge* (scored by blinded raters) (Pfiffner 1997) showed a significant difference (MD 4.20; 95% CI 1.99 to 6.41) (Analysis 1.6). *Observation in classrooms* from Cohen 1981 is reported to have no significant group differences.

Primary outcome: General behaviour

Meta-analyses

The primary outcome and the main analysis in this outcome was *Teacher-rated general behaviour at end of treatment,* which showed no significant effect at the end of treatment (SMD 0.00; 95% CI -0.21 to 0.21, I^2=0%, P = 0.99). This outcome were tested with two sensitivity analyses: *Teacher-rated general behaviour - excluding the largest trial* (SMD 0.15; 95% CI -0.24 to 0.53, I^2=0%, P = 0.46. Test for subgroup differences: Chi² = 0.03, df = 1, P = 0.86, I² = 0%) and *Teacher-rated general behaviour - excluding the trial with the longest duration of the intervention* (SMD -0.04; 95% CI -0.27 to 0.19, I^2=0%, P = 0.73. Test for subgroup differences: Chi² = 0.07, df = 1 (P = 0.79), I² = 0%). These sensitivity analyses showed no significant subgroup differences compared to the primary outcome. We also conducted two secondary analyses: *Teacher-rated general behaviour - longest follow-up* (SMD -0.23; 95% CI -0.48 to 0.01, I^2=0%, P = 0.06); *Parent-rated general behaviour at end of treatment* (SMD -0.26; 95% CI -0.51 to -0.01, P = 0.04). *Parent-rated general behaviour at end of treatment* showed significant differences, but not the longest follow-up (Analysis 2.1; Analysis 3.1).

Single trial results

Pfiffner 2007 measured general behaviour by using clinical global impression, both by parents and teachers, and the experimental intervention group showed significantly greater improvement than in the control group (parents: F1, 51 = 28.46, P < 0.0001; teachers: F1, 51 = 11.73, P = 0.0012).

Secondary outcome: ADHD symptoms

Meta-analyses

The main analysis in this outcome: *Teacher-rated ADHD symptoms at end of treatment - all eligible trials* showed no significant effect of the treatment (SMD -0.02; 95% CI -0.19 to 0.16). This was tested with two sensitivity analyses: *Teacher-rated ADHD symptoms excluding the trial with the longest treatment intervention* (SMD -0.06; 95% CI -0.25 to 0.12. Test for subgroup differences: Chi² = 0.14, df = 1 (P = 0.71), I² = 0%), *Teacher-rated ADHD symptoms excluding the largest trial* (SMD 0.07; 95% CI -0.18 to 0.31. Test for subgroup differences: Chi² = 0.30, df = 1 (P = 0.59), I² = 0%). Neither of these sensitivity analyses showed significant subgroup differences when stepwise compared to the primary outcome. We also conducted the following secondary analyses: *Teacher-rated ADHD symptoms - longest follow up* (SMD -0.24; 95% CI -0.90 to 0.41, I^2=40%, P = 0.47), *Teacher-rated ADHD symptoms - MTA inattention* (SMD 0.01; 95% CI -0.23 to 0.26, P = 0.92), *Teacher-rated ADHD symptoms at end of treatment - sluggish cognitive tempo* (SMD -0.29; 95% CI -0.78 to 0.20, P = 0.24), *Parent-rated ADHD symptoms at end of treatment - all eligible trials* (SMD -0.49; 95% CI -0.79 to -0.19, I^2=68%, P = 0.001). Only the last secondary analysis showed a significant difference.

Single trial results

In the Abikoff 2004 and Bloomquist 1991 trials, there were no significant differences between groups in the classroom observations.

In the Pfiffner 2007 trial, the SCT parent- and teacher-rated were measured at post-treatment and follow-up. The parent-rated results at post-treatment and follow-up showed a significant treatment effect (MD -0.30; 95% CI -0.53 to -0.07), (MD -0.21; 95% CI -0.43 to 0.02), but the teacher-rated results at post-treatment and follow-up showed no significant treatment effect (MD -0.17; 95% CI -0.46 to 0.11), (MD 0.10; 95% CI -0.32 to 0.52).

MTA 1999 reported on subgroup analyses on children with ADHD only compared to children with ADHD and comorbid anxiety disorder. This analysis showed significant differences in teacher-rated hyperactivity/impulsivity (F = 1.64, P = 0.04), teacher-rated social skills (F = 1.68, P = 0.03) between the ADHD only and the ADHD/anxiety children subgroups in connection with all four active treatments used in this trial (MTA 1999).

Secondary outcome: Performance and grades in school

Three trials had measured this outcome using different tools (MTA 1999; Abikoff 2004; Waxmonsky 2010). None of these outcomes showed significant treatment effects.

Secondary outcome: Participant or parent satisfaction with the treatment

Four trials measured these outcomes, and in all of them the satisfaction with the treatment was high, but there was no significant difference between the intervention and controI in two of them (Pfiffner 1997; Waxmonsky 2010). In Pfiffner 2007 and Yuk-chi 2005 there was generally high satisfaction with the interventions, but nothing stated about differences between groups.

Secondary outcome: Adverse events

None of the included trials reported adverse events as an outcome.

Subgroup analysis

We performed three subgroup analyses. None of them showed significant differences in the intervention effects.

1. Social skills training without parent training compared to social skills training combined with parent training. Test for subgroup differences: Chi² = 0.17, df = 1 (P = 0.68), I² = 0% (Analysis 4.1).
2. Comorbidity versus no comorbidity .Test for subgroup differences: Chi² = 1.56, df = 1 (P = 0.21), I² = 35.9% (Analysis 5.1).
3. Social skills training, parent training and medication versus social skills training and parent training without medication. Test for subgroup differences: Chi² = 0.58, df = 1 (P = 0.45), I² = 0% (Analysis 6.1).

Sensitivity analysis

Repeating the analysis with the fixed-effect model for all meta-analyses gave similar results; only random-effects models are presented.

Trial sequential analysis

The primary analysis, teacher-rated social skills competences at end of treatment, was further analysed with TSA. Using an a priori assumption about the intervention effect being half of the standard deviation, the intervention effect is barely reaching into the futility area possibly signalling that there is no effect of social skills intervention on teacher-rated social skills competences at end of treatment (Figure 4). With this a priori assumption, however, there is a 20% risk of overlooking a true effect, and minimising this risk to 10% gives a required information size (APHRIS) of 338 participants (Figure 5) before a firm conclusion can be made.

Using available data from this meta-analysis (Analysis 1.2) to calculate the required information size in the TSA yields a PHHRIS of 504 participants before a firm conclusion can be drawn (Figure 6). The estimated effect size of MD 1.8 (95% CI-1.02. 4.64) is low and not considered clinically relevant, and as none of the trials was low risk of bias we chose an intervention effect of four, which is more clinically relevant for social skills rating scales, and a potential likely heterogeneity of 25% (available data: 95% CI for I^2:0.00 to 0.59, mean: 0.00).
Both the a priori and the post hoc trial sequential analyses shows that there is a need for more participants to make a firm conclusion about whether social skills training improves social skills competences.

DISCUSSION

We conducted this systematic review to examine the effects of social skills training for children and adolescents with ADHD. 144 full text articles were considered and 11 trials published in 26 articles were included in our review. Of these, results from 10 trials could be used in meta-analyses. Only children between five and 12 years were included as we were unable to identify any randomised clinical trials dealing with adolescents.

All the trials had high risk of bias due to systematic errors. We used all eligible trials in the meta-analysis as it is recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). The overall findings point towards no significant treatment effects of social skills training on the teacher-rated outcome of social skills competences (SMD 0.16; 95% CI -0.04 to 0.36), general behaviour (SMD 0.00; 95% CI -0.21 to 0.21) and ADHD symptoms (SMD -0.02; 95% CI -0.19 to 0.16). We chose to use the teacher-rated outcomes as the primary analysis and tested the robustness of this decision by including several sensitivity analyses. For social skills competences, general behaviour, and the ADHD symptoms, none of the sensitivity analyses differed significantly from the primary analysis when they were included stepwise in the analysis. All results are presented using the random-effects model of meta-analysis, thus giving more weight to smaller trials; however, the statistical significance did not change when a fixed-effect model was applied. Thus we conclude that the statistical heterogeneity is not of importance in the present review.

In the secondary analyses, both the parent-rated social skills competences, general behaviour, and ADHD symptoms showed significant improvement due to social skills training. Still we consider these findings as more questionable than our primary analyses, which are based on the teacher-rated outcomes, due to high risk of systematic errors in the parent-rated outcomes.

Most of the interventions were manual-based (Bloomquist 1991; MTA 1999; Tutty 2003; Abikoff 2004;Yuk-chi 2005; Pfiffner 2007; van der Oord 2007; Waxmonsky 2010). The social skills interventions in the trials were different in form and content, though all of them were cognitive-behaviourial based treatments, there were differences in the use of behaviour techniques. Some of the trials used reinforcement techniques (Cohen 1981; Bloomquist 1991; Abikoff 2004; Pfiffner 2007), others used more cognitive techniques, and some of the trials used themes for each session (problem solving and controlling emotions being the only ones common across trials) (Cohen 1981; Bloomquist 1991; Pfiffner 1997; Antshel 2003; van der Oord 2007; Yuk-chi 2005). Most of the trials also included parent training in the social skills intervention, and almost all of these included efforts to support the training being done with the children and included psychoeducation about ADHD. The inherent differences in the interventions are in accordance with the review inclusion criteria, but are likely to produce heterogeneity in the analysis. It would be optimal to generate a more standardised training method, clearly manualised, as this would likely reduce some of the hetereogenity between trials. The duration of the treatment also differed greatly, from 10 weeks to 14 to 24 months.However, there were no differences in results when we excluded the trial with the longest intervention from the analysis of the social skills competences outcome or ADHD symptoms outcomes. In most of the meta-analysis the statistical heterogeneity was low (0%), most likely due to inherent features of the trials leading to wide confidence intervals of the estimates, and was therefore not mirroring the clinical and methodological heterogeneity we know is present.

A serious limitation of these types of trials is the lack of blinding or inability to blind. This introduces a high risk of bias in the assessment of outcomes (Schultz 1995; Kjaergard 2002; Wood 2008). It is noteworthy that the only significant findings supporting social skills training are outcomes rated by parents, and that the same outcomes rated by teachers showed no significant treatment effect. On one hand, parents are more prone to be biased because, for most trials, they actively participated in the intervention and also they have a very close attachment to the child. On the other hand, parents also possess a greater sensibility to actual change in the child's behaviour due to the close attachment. The ratings provided by teachers are possibly less biased due to lack of this close attachment to the child; however, the teachers' assessments may be tainted by less sensitivity towards a change in a specific child's behaviour in a class of 20 to 30 pupils.

Although the measurable beneficial effects of social skills training are vague and questionable, participant, parent, and teacher satisfaction with the intervention overall was positive and most would recommend the treatment programme to others. However, half of the trials measuring this outcome did not find any significant difference between the experimental or control group in terms of satisfaction and the other half did not report on between group differences. This is a problem as participant satisfaction with the treatment is often used as an argument for this kind of treatment.

In this review we have used the measurement of conduct disorder as a measurement of general behaviour. This can be questioned. We believe, however, that this is a sensible approach as the behaviour of the children will be measured in this outcome.

In general, all of the included trials had a large number of different outcome measurements, most of them measuring important outcomes for these children, but this is problematic as the likelihood of finding a significant result just by chance increases. When there are multiple comparisons, it becomes more likely that the groups being compared will appear to differ in terms of one or more attributes. This is real problem in this field of research. The trial protocols need to be published before the trial is conducted with a clear plan for the analysis and statistical analyses. This could help with the problem with multiple outcomes where there are problems identifying the primary outcomes and the secondary outcomes.

In MTA 1999, the multimodal treatment had a superior treatment effect on the children with ADHD and comorbid anxiety disorder compared to those without that comorbidity. This is an interesting subgroup finding and suggests that future trials on this topic should investigate these findings further by planning for subgroup analyses on children with and without comorbid anxiety disorder.

Summary of main results

In the Summary of findings for the main comparison we have included the three most important comparisons. The first one, *Teacher-rated social skills competences at end of treatment - all eligible trials* (SMD 0.16; 95% CI -0.04 to 0.36) (Analysis 1.1) showed no significant treatment effect. The second analysis *Teacher-rated general behaviour at end of treatment* (SMD 0.00; 95% CI -0.21 to 0.21) (Analysis 2.1) also showed no significant treatment effect. The third analysis *Teacher-rated ADHD symptoms at end of treatment - all eligible trials* (SMD -0.02; 95% CI -0.19 to 0.16) (Analysis 3.1) did not support the efficacy of social skills training for children with ADHD. Finally, for all outcomes, we warn against the risks of systematic errors and random errors.

Overall completeness and applicability of evidence

The 11 trials included 747 participants with ADHD. Most of the data from the trials could be used in our meta-analyses, which makes a good basis for the evidence in this review, however, the interventions might be considered too heterogeneous. The multiplicity of different outcome measures might limit the external validity of this review. A small treatment effect in the parent-rated outcomes was found, but all the trials had high risk of bias.
Randomised clinical trials are generally considered to be the highest level of evidence, but most of the trials included in this systematic review were at high risk of bias and the vast majority had high risk of random errors due to their low sample sizes. Generally we rated the quality of the evidence as low (GRADE Working Group: http://www.gradeworkinggroup.org/). Overall the evidence was downgraded two grades due to the low quality. Further research should have a potential to change the estimates of no effect for the treatment, but such trials ought to be conducted without risk of systematic errors (bias), random errors (play of chance), and design errors (Keus 2010).

Quality of the evidence

The present review has many strengths. We developed a protocol for this review according to the instructions in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Our protocol was published before we embarked on the review itself. We conducted extensive searches in relevant databases. Trials for inclusion were selected by two independent authors. Data were extracted independently by two authors, and disagreements were resolved. We also independently assessed the risk of bias in all trials according to the *Cochrane Handbook on Systematic Reviews of Interventions* (Higgins 2011). We conducted trial sequential analyses to reduce the risk of type I errors and to estimate how far we are from obtaining the required information size to detect or reject a certain modest intervention effect. In all meta-analyses that achieved significant findings with conventional boundaries, the trial sequential analyses showed that the observed intervention effects could be due to type I errors. The results of the trial sequential analyses confirmed that insufficient data have been obtained. This shows the need for more clinical research on the topic.
The review has a number of limitations. Our results are based on only 11 trials with a limited number of participants (n = 747). Both the a priori and the post hoc trial sequential analyses shows that there is a need for more participants in order to make a firm conclusion in the meta-analysis. Many of the trials were prone to selection bias due to unclear or inadequate generation of the allocation sequence or allocation concealment. None of the included trials assessed outcomes with adequate blinding of assessors. Furthermore, all 11 trials had an overall assessment as 'high risk of bias', so our results might not be robust and reliable (Figure 2). Due to the limited number of included trials, we did not perform funnel plot or other analyses to explore the risk of publication bias. There is therefore insufficient evidence to draw any conclusions about any form of social skills training as having an effect on ADHD patients at the moment. Furthermore, some of the trials are very small, and only one reported on a sample size calculation. There is a need for more high quality randomised clinical trials with large numbers of participants.
The important methodological limitations, which have been elaborated on above, reduced the reliability of the results of most of the trials included in this review.

Potential biases in the review process

We did not identify any potential biases in the review process.

Agreements and disagreements with other studies or reviews

We are aware of two meta-analyses that conclude that there is no effect of social skills training for children with ADHD (Kavale 1997; Van der Oord 2008) and two meta-analyses supporting the view that social skills training has a significant treatment effect (Boo 2007; Majewicz-Hefley 2007). However, looking at the quality of these meta-analyses, all of their findings must be questioned due to several methodological weaknesses, as these latter reviews did not evaluate systematic errors (bias), and random errors (play of chance) in the included trials.

AUTHORS' CONCLUSIONS

Implications for practice

It is not possible to recommend or refute social skills training for children with ADHD at the moment. Parent and participant satisfaction with the treatment is rated as high and most teachers would recommend the treatment to others, but in two trials there was no difference in this outcome between the social skills training groups and the control group.

Implications for research

This review highlights the need for more standardised treatment interventions that can be investigated in more high quality trials, with low risk of bias and with sufficient numbers of participants, investigating the effects of social skills training versus no training for children as well as adolescents with ADHD. There is a need for prepublished protocols, which could help with the problem with multiple outcomes and the difficulty of identifying the primary outcomes and the secondary outcomes.

ACKNOWLEDGEMENTS

Kirsten Buch Rasmussen for her support in the searching process.

Connie Enevoldsen for her support in the searching process.

We would like to acknowledge the contribution from Trygfonden (Denmark) for their financial support completion of this review.

REFERENCES

References to studies included in this review

Abikoff 2004 *{published data only}*

Abikoff H, Hectman L, Klein RG, Gallagher R, Fleiss K, Etcovitch J, et al.Social functioning in children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. *Journal of the American Academy of Child and Adolescent Psychiatry* 2004;**43**(7):820–29.

* Abikoff H, Hectman L, Klein RG, Weiss G, Fleiss K, Etcovitch J, et al.Symptomatic improvement in children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. *Journal of American Academy of Child and Adolescent Psychiatry* 2004;**43**(7): 802–11.

Hechtman L, Abikoff H, Klein RG, Weiss G, Respitz C, Kouri J, et al.Academic achievement and emotional status of children with ADHD treated with long-term methylphenidate and multimodal psychosocial treatment. *Journal of American Academy of Child and Adolescent Psychiatry* 2004;**43**(7):812–19.

Klein RG, Abikoff H, Hechtman L, Weiss G. Design and rationale of controlled study of long-term methylphenidate and multimodal psychosocial treatment in children with ADHD. *Journal of American Academy of Child and Adolescent Psychiatry* 2004;**43**(7):792–801.

Antshel 2003 *{published data only}*

Antshel KM, Remer R. Social skills training in children with attention deficit hyperactivity disorder: a randomized-controlled clinical trial. *Journal of Clinical Child and Adolescent Psychology* 2003;**32**(1):153–65.

Bloomquist 1991 *{published data only}*

Bloomquist ML, August GJ, Ostrander R. Effects of a school-based cognitive-behavioral intervention for ADHD children. *Journal of Abnormal Child Psychology* 1991;**19**(5): 591–605.

Cohen 1981 *{published data only}*

Cohen NJ, Sullivan J, Minde K, Novak K, Helwig C. Evaluation of the relative effectiveness of methylphenidate and cognitive behavior modification in the treatment of kindergarten-aged hyperactive children. *Journal of Abnormal Child Psychology* 1981;**9**(1):43–54.

MTA 1999 *{published data only}*

Arnold LE, Abikoff HB, Cantwell DP, Conners CK, Elliott GR, Greenhill LL, et al.NIMH collaborative multimodal treatment study of children with ADHD (MTA): design methodology and protocol evolution. *Journal of Attention Disorder* 1997;**2**(3):141–58.

Arnold LE, Chuang S, Davies M, Abikoff HB, Conners CK, Elliot GR, et al.Nine months of multicomponent behavioral treatment for ADHD and effectiveness of MTA

fading procedures. *Journal of Abnormal Child Psychology* 2004;**32**(1):39–51.

Arnold LE, Sachs L, Kraemer HC, Abikoff HB, Conners CK, Greenhill LL, et al.Effects of ethnicity on treatment attendance, stimulant response/dose, and 14-month outcome in ADHD. *Journal of Consulting and Clinical Psychology* 2003;**71**(4):713–27.

Hinshaw SP, March JS, Abikoff H, Arnold LE, Cantwell DP, Conners CK, et al.Comprehensive assessment of childhood attention-deficit hyperactivity disorder in the context of a multisite, multimodal clinical trial. *Journal of Attention Disorder* 1997;**1**(4):217–34.

Jensen PS, Arnold LE, Swanson JM, Vitiello B, Abikoff HB, Greenhill LL, et al.3-Year follow-up of the NIMH MTA study. *Journal of American Academy of Child and Adolescent Psychiatry* 2007;**46**(8):989–1002.

Jensen PS, Hinshaw SP, Kraemer HC, Lenora N, Newcorn JH, Abikoff HB, et al.ADHD comorbidity findings from the MTA study: comparing comorbid subgroups. *Journal of American Academy of Child and Adolescent Psychiatry* 2001; **40**(2):147–58.

Molina BSG, Hinshaw SP, Swanson JM, Arnold LE, Vitiello B, Jensen PS, et al.The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. *Journal of American Academy of Child and Adolescent Psychiatry* 2009;**48**(5):484–500.

MTA Cooperative Group. A 14-month randomized clinical trial of treatment strategies for attention-deficit/ hyperactivity disorder. *Archives of General Psychiatry* 1999; **56**(12):1073–86.

MTA Cooperative Group. Moderators and mediators of treatment response for children with attention-deficit/ hyperactivity disorder. *Archives of General Psychiatry* 1999; **56**(12):1088–96.

MTA Cooperative Group. National Institute of Mental Health multimodal treatment study of ADHD follow-up: 24-month outcomes of treatment strategies for attention-deficit/hyperactivity disorder. *Pediatrics* 2004;**113**(4): 754–61.

MTA Cooperative Group. National Institute of Mental Health multimodal treatment study of ADHD follow-up: changes in effectiveness and growth after the end of treatment. *Pediatrics* 2004;**113**(4):762–9.

Swanson J. The MTA follow-up into adolescence: implications for personalized treatment.. Oral presentation at The International Society for Research in Child and Adolescent Psychopathology Conference; 2009 June 19; Seattle. Seattle: ISRCAP, 2009.

Wells KC, Pelham WE, Kotkin RA, Hoza B, Abikoff HB, Abramowitz A, et al.Psychosocial treatment strategies in the MTA study: rationale, methods, and critical issues in design and implementation. *Journal of Abnormal Child Psychology* 2000;**28**(6):483–505.

Pfiffner 1997 ***{published data only}***

Pfiffner L, McBurnett K. Social skills training with parent generalization: treatment effects for children with attention deficit disorder. *Journal of Consulting and Clinical Psychology* 1997;**65**(5):749–57.

Pfiffner 2007 ***{published data only}***

Pfiffner LJ, Mikami AY, Huang-Pollock C, Easterlin B, Zalecki C, McBurnett K. A randomized, controlled trial of integrated home-school behavioral treatment for ADHD, predominantly inattentive type. *Journal of American Academy of Child and Adolescent Psychiatry* 2007;**46**(8): 1041–50.

Tutty 2003 ***{published data only}***

Tutty S, Gephart H, Wurzbacher K. Enhancing behavioral and social skill functioning in children newly diagnosed with attention-deficit hyperactivity disorder in a pediatric setting. *Developmental and Behavioral Pediatrics* 2003;**24** (1):51–7.

van der Oord 2007 ***{published data only}***

van der Oord S, Prins PJM, Oosterlaan J, Emmelkamp PMG. Does brief, clinically based, intensive multimodal behaviour therapy enhance the effects of methylphenidate in children with ADHD?. *European Child and Adolescent Psychiatry* 2007;**16**(1):48–57.

Waxmonsky 2010 ***{published data only}***

Waxmonsky JG, Waschbusch DA, Pelham WE, Draganac-Cardona L, Rotella B, Ryan L. Effects of atomoxetine with and without behavior therapy on the school and home functioning of children with attention-deficit/hyperactivity disorder. *Journal of Clinical Psychiatry* 2010;**71**(11): 1535–51.

Yuk-chi 2005 ***{published data only}***

Yuk-chi S. *Effectiveness of Methylphenidate and Combined Treatment (Methylphenidate and Psychosocial Treatment) for Chinese Children with Attention-Deficit/Hyperactivity Disorder in a Community Mental Health Center (PhD theses)*. Hong Kong: The Chinese University of Hong Kong, 2005.

References to studies excluded from this review

Abikoff 1985 ***{published data only}***

Abikoff H, Gittelman R. Hyperactive children treated with stimulants. Is cognitive training a useful adjunct?. *Archives of General Psychiatry* 1985;**42**(10):953–61.

Carlson 2000 ***{published data only}***

Carlson CL, Tamm L. Responsiveness of children with attention-deficit/hyperactivity disorder to reward and response cost: differential impact on performance and motivation. *Journal of Consulting and Clinical Psychology* 2000;**68**(1):73–83.

Carlson 1992 ***{published data only}***

Carlson CL, Pelham WE, Milich R, Dixon J. Single and combined effects of methylphenidate and behavior therapy on the classroom performance of children with attention-deficit hyperactivity disorder. *Journal of Abnormal Child Psychology;1992* April;**20**(2):213–32.

Chang 2004 ***{published data only}***

Chang CC, Tsou KS, Shen WW, Wong CC, Chao CC. A social skills training program for preschool children with attention-deficit/hyperactivity disorder. *Chang Gung Medical Journal* 2004;**27**(12):918–23.

Corkum 2005 *{published data only}*
Corkum PV, McKinnon MM, Mullane JC. The effect of involving classroom teachers in a parent training program for families of children with ADHD. *Child & Family Behavior Therapy* 2005;**27**(4):29–49.

Döpfner 2004 *{published data only}*
Döpfner M, Breuer D, Schürmann S, Metternich TW, Rademacher C, Lehmkuhl G. Effectiveness of an adaptive multimodal treatment in children with attention-deficit/ hyperactivity disorder - global outcome. *European Child and Adolescent Psychiatry* 2004;**13**(suppl 1):117–29.

Ercan 2005 *{published data only}*
Ercan ES, Varan A, Deniz Ü. Effects of combined treatment on turkish children diagnosed with attention-deficit/hyperactivity disorder: a preliminary report. *Journal of Child and Adolescent Psychopharmacology* 2005;**15**(2): 203–19.

Evans 2000 *{published data only}*
Evans SW, Axelrod JL, Sapia JL. Effective school-based mental health interventions: advancing the social skills training paradigm. *Journal of School Health* 2000;**70**(5): 191–4.

Fabiano 2003 *{published data only}*
Fabiano GA, Pelham WE. Improving the effectiveness of behavioral classroom interventions for attention-deficit/ yyperactivity disorder: a case study. *Journal of Emotional and Behavioral Disorders* 2003;**11**(2):122–8. [DOI: 10.1177/ 106342660301100206]

Feinfield 2004 *{published data only}*
Feinfield KA, Baker BL. Empirical support for a treatment program for families of young children with externalizing problems. *Journal of Clinical Child and Adolescent Psychology* 2004;**33**(1):182–95.

Fenstermacher 2006 *{published data only}*
Fenstermacher K, Olympia D, Sheridan SM. Effectiveness of a computer-facilitated, interactive social skills training program for boys with attention deficit hyperactivity disorder. *School Psychology Quarterly* 2006;**21**(2):197–224.

Frankel 1997 *{published data only}*
Frankel F, Myatt R, Cantwell DP, Feinberg DT. Use of the child behavior checklist and DSM-III-R diagnosis in predicting outcome of children´ s social skills training. *Journal of Behavior Therapy and Experimental Psychiatry* 1997;**28**(2):149–61.

Frölich 2002 *{published data only}*
Frölich J, Döpfner M, Berner W, Lehmkuhl G. Combined cognitive behavioural treatment with parent management training in ADHD [Behandlungseffekte kombinierter kognitiver Verhaltenstherapie mit Elterntraining bei hyperkinetischen Kindern]. *Praxis der Kinderpsychologie und Kinderpsychiatrie* 2002;**51**:476–93.

Gadow 1985 *{published data only}*
Gadow KD. Relative efficacy of pharmacological, behavioral, and combination treatments for enhancing academic performance. *Clinical Psychology Review* 1985;**5** (5):513–33.

Gol 2005 *{published data only}*
Gol D, Jarsus T. Effect of a social skills training group on everyday activities of children with attention deficit-hyperactivity disorder. *Developmental Medicine and Child Neurology* 2005;**47**(8):539–45.

Gonzalez 2002 *{published data only}*
Gonzalez LO, Sellers EW. The effects of a stress-management program on self-concept, locus of control, and the acquisition of coping skills in school-age children diagnosed with attention deficit hyperactivity disorder. *Journal of Child and Adolescent Psychiatric Nursing* 2002;**15** (1):5–15.

Hinshaw 1984 *{published data only}*
Hinshaw SP, Whalen CK, Henker B. Cognitive-behavioral and pharmacological interventions for hyperactive boys: comparative and combined effects. *Journal of Consulting and Clinical Psychology* 1984;**52**(5):739–49.

Hinshaw 2000 *{published data only}*
Hinshaw SP, Owens EB, Wells KC, Kraemer HC, Abikoff HB, Arnold LE, et al.Family processes and treatment outcome in the MTA: negative/ineffective parenting practices in relation to multimodal treatment. *Journal of Abnormal Child Psychology* 2000;**28**(6):555–68.

Horn 1990 *{published data only}*
Horn WF, Ialongo N, Greenberg G, Packard T, Smith-Winberry C. Additive effects of behavioral parent training and self-control therapy with attention deficit/ hyperactivity disordered children. *Journal of Clinical Child Psychology* 1990;**19**(2):98–110.

Jensen 1999 *{published data only}*
Jensen PS. Fact versus fancy concerning the multimodal treatment study for attention-deficit/hyperactivity disorder. *Canadian Journal of Psychiatry* 1999;**44**(10):975–80.

Jensen 2001 *{published data only}*
Jensen PS, Hinshaw SP, Swanson JM, Greenhill LL, Conners CK, Arnold LE. Findings from the NIMH multimodal treatment study of ADHD (MTA): implications and applications for primary care providers. *Journal of Developmental and Behavioral Pediatrics* 2001;**22**(1):60–73.

Klein 1997 *{published data only}*
Klein RG, Abikoff H. Behavior therapy and methylphenidate in the treatment of children with ADHD. *Journal of Attention Disorders* 1997;**2**(2):89–114.

Kolko 1990 *{published data only}*
Kolko DJ, Loar LL, Sturnick D. Inpatient social-cognitive skills training groups with conduct disordered and attention deficit disordered children. *Journal of Child Psychology and Psychiatry* 1990;**31**(5):737–48.

Kolko 1999 *{published data only}*
Kolko DJ, Bukstein OG, Barron J. Methylphenidate and behavior modification in children with ADHD and comorbid ODD or CD: main and incremental effects across settings. *Journal of American Academic Child and Adolescent Psychiatry* 1999;**38**(5):578–86.

Langberg 2008 *{published data only}*
Langberg JM, Epstein JN. Efficacy of an organization skills intervention to Improve the academic functioning of students with attention-deficit/hyperactivity disorder. *School Psychology Quarterly* 2008;**23**(3):407–17.

Langberg 2010 *{published data only}*
Langberg JM, Arnold LE, Flowers AM, Epstein JN, Altaye M, Hinshaw SP, et al.Parent-reported homework problems in the MTA study: evidence for sustained improvement with behavioral treatment. *Journal of Clinical Child and Adolescent Psychology* 2010;**39**(2):220–33.

Lösel 2006 *{published data only}*
Lösel F, Beelmann A, Stemmler M, Jarusch S. Prevention of social behaviour problems at preeschool age. Evaluation of the parent and child training program package [Prävention von Problemen des Sozialverhaltens im Vorschulalter. Evaluation des Eltern– und Kindertrainings EFFEKT]. *Zeitschrift für Klinische Psychologie und Psychotherapie* 2006; **35**(2):127–39.

Miranda 2002 *{published data only}*
Miranda A, Presentación J, Soriano M. Effectiveness of a school-based multicomponent program for the treatment of children with ADHD. *Journal of Learning Disabilities* 2002; **35**(6):547–63.

Miranda 2006a *{published data only}*
Miranda A, Jarque S, Rosel J. Treatment of children with ADHD: psychopedagogical program at school versus psychostimulant medication. *Psicothema* 2006;**18**(3): 335–41.

Miranda 2006b *{published data only}*
Miranda A, Jarque S, Tarraga R. Interventions in school settings for students with ADHD. *Exceptionality* 2006;**14** (1):35–52.

Molina 2008 *{published data only}*
Molina BSG, Flory K, Bukstein OG, Greiner AR, Baker JL, Krug V, Evans SW. Feasibility and preliminary efficacy of an after-school program for middle schoolers with ADHD. *Journal of Attention Disorders* 2008;**12**(3):207–17.

MTA 2009 *{published data only}*
Breggin PR, Klein RG, Jensen PS. [Letters to editors]. Archives of General Psychiatry September 2009.

Pelham 1980 *{published data only}*
Pelham WE, Schnedler RW, Bologna NC, Contreras JA. Behavioral and stimulant treatment of hyperactive children: a therapy study with methylphenidate probes in a within-subject design. *Journal of Applied Behavior Analysis* 1980;**13** (2):221–36.

Pelham 1993 *{published data only}*
Pelham WE, Carlson C, Sams SE, Vallano G, Dixon JM, Hoza B. Separate and combined effects of methyphenidate and behavior modification on boys with attention deficit/ hyperactivity disorder in the classroom. *Journal of Consulting and Clinical Psychology* 1993;**61**(3):506–15.

Pelham 2000 *{published data only}*
Pelham WE, Gnagy EM, Greiner AR, Hoza B, Hinshaw SP, Swanson JM. Behavioral versus behavioral and pharmacological treatment of the ADHD children attending a summer treatment program. *Journal of Abnormal Child Psychology* 2000;**28**(6):507–25.

Pelham 2005 *{published data only}*
Pelham WE, Burrows-MacLean L, Gnagy EM, Fabiano GA, Coles EK, Tresco KE, et al.Transdermal methylphenidate, behavioral, and combined treatment for children with ADHD. *Experimental and Clinical Psychopharmacology* 2005;**13**(2):111–26.

Rosén 1984 *{published data only}*
Rosén LA, O′ Leary SG, Joyce AS Conway G, Pfiffner L. The importance of prudent negative consequences for maintaining the appropriate behavior of hyperactive students. *Journal of Abnormal Child Psychology* 1984;**12**(4): 581–604.

Waxmonsky 2008 *{published data only}*
Waxmonsky J, Pelham WE, Gnagy E, Cummings MR, O′ Connor B, Majumdar A, et al.The efficacy and tolerability of methylphenidate and behavior modification in children with attention-deficit/hyperactivity disorder and severe mood dysregulation. *Journal of Child and Adolescent Psychopharmacology* 2008;**18**(6):573–88.

Webster-Stratton 2001 *{published data only}*
Webster-Stratton C, Reid J, Hammond M. Social skills and problem-solving training for children with early-onset conduct problems: who benefits?. *Journal of Child Psychology and Psychiatry* 2001;**42**(7):943–52.

Webster-Stratton 2004 *{published data only}*
Webster-Stratton C. Reid J. Strengthening social and emotional competence in young children - the foundation for early school readiness and success. Incredible Years classroom social skills and problem-solving curriculum. *Infants and Young Children* 2004;**17**(2):96–113.

Williams 1993 *{published data only}*
Williams RA, Horn S, Daley SP, Nader PR. Evaluation of access to care and medical and behavioral outcomes in a school-based intervention program for attention-deficit hyperactivity disorder. *Journal of School Health* 1993;**63**(7): 294–7.

Wolraich 1978 *{published data only}*
Wolraich M, Drummond T, Salomon MK, O′ Brian ML, Sivage C. Effects of methylphenidate alone and in combination with behavior modification procedures on the behavior and academic performance of hyperactive children. *Journal of Abnormal Child Psychology* 1978;**6**(1):149–61.

References to ongoing studies

Safren 2011 *{published data only}*
Compensatory executive functioning skills training for adolescents with ADHD.. Ongoing study October 2009. Estimated study completion date: May 2012..

Storebø 2011 *{published data only}*
Randomised social-skills training and parental training plus standard treatment versus standard treatment of children

with attention deficit hyperactivity disorder - The SOSTRA trial.. Ongoing study August 2009. Finished August 2011..

Additional references

Achenbach 1991

Achenbach TM. *Integrative Guide to the 1991 CBCL/4-18, YSR, and the TRF Profiles*. Burlington, VT: University of Vermont, Department of Psychology, 1991.

APA 1980

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-III)*. 3rd Edition. Washington, DC: American Psychiatric Association, 1980.

APA 1987

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R)*. 3rd Edition. Washington, DC: American Psychiatric Association, 1987.

APA 1994

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)*. 4th Edition. Washington, DC: American Psychiatric Association, 1994.

APA 2000

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders DSM-IV-TR*. 4th Edition. Washington, DC: American Psychiatric Association, 2000.

Attkinson 1982

Attkinsson CC, Zwick R. The client satisfaction questionnaire. Psychometric properties and correlations with service utilization and psychotherapy outcome. *Evaluation and Program Planning* 1982;**5**(3):233–7.

Barkley 1997

Barkley RA. A review stimulant drug research with hyperactive children. *Journal of Child Psychology and Psychiatry* 1977;**18**(2):137–65.

Barkley 1998

Barkely RA. *Attention-Deficit/Hyperactivity Disorder: A Handbook for Diagnosis and Treatment*. 2nd Edition. New York: Guildford, 1998.

Barkley 2002

Barkely RA, Fischer M, Smallish L, Fletcher K. The persistence of attention-deficit/hyperactivity disorder into young adulthood as a function of reporting source and definition of disorder. *Journal of Abnormal Psychology* 2002; **111**(2):279–89.

Berkley 1996

Berkey CS, Mosteller F, Lau J, Antman EM. Uncertainty of the time of first significance in random effects cumulative meta-analysis. *Controlled Clinical Trials* October 1996;**17** (5):357–71.

Biederman 1998

Biederman J, Faraone SV, Taylor A, Sienna M, Williamson S, Fine C. Diagnostic continuity between child and adolescent ADHD: Findings from a longitudinal clinical sample. *Journal of American Academic Child and Adolescence Psychiatry* 1998;**37**(3):305–13.

Biederman 2000

Biederman J, Mick E, Faraone SV. Age-dependent decline of symptoms of attention deficit hyperactivity disorder: impact of remission definition and symptom type. *American Journal of Psychiatry* 2000;**157**(5):816–8.

Block 1998

Block S. Attention-deficit disorder. In: Findling R, Blumer J editor(s). *Child and Adolescent Psychopharmacology*. Vol. **45**, London: WB Saunders Company, 1998:1053–84.

Boo 2007

Boo de GM, Prins PJM. Social incompetence in children with ADHD: possible moderators and mediators in social-skills training. *Clinical Psychology Review* 2007;**27**(1): 78–97.

Brok 2008

Brok J, Thorlund K, Gluud C, Wetterslev J. Trial sequential analysis reveals insufficient information size and potentially false positive results in many meta-analyses. *Journal of Clinical Epidemiology* 2008;**61**(8):763–9.

Brok 2009

Brok J, Thorlund K, Wetterslev J, Gluud C. Apparently conclusive meta-analyses may be inconclusive - Trial sequential analysis adjustment of random error risk due to repetitive testing of accumulating data in apparently conclusive neonatal meta-analyses. *International Journal of Epidemiology* Feb 2009;**38**(1):287–98.

BUP 2008

BUP - Børne- og Ungdomspsykiatrisk Selskab. Reference programme for assessment and treatment of children and young people with ADHD [Referenceprogram for udredning og behandling af børn og unge med ADHD [Danish]]. http://www.bupnet.dk/media/ADHDReferenceprogram080508˙jsb[1].pdf (accessed March 2010).

Bussing 2008

Bussing R, Fernadez M, Harwood M, Hou W, Garvan CW, Eyberg SM, Swanson JM. Parent and teacher SNAP-IV ratings of attention deficit/hyperactivity disorder symptoms - psychometric properties and normative ratings from a school district sample. *Assessment* September 2008;**15**(3): 317–28.

Castellanos 2006

Castellanos FX, Sonuga-Barke EJ, Milham MP, Tannock R. Characterizing cognition in ADHD: beyond executive dysfunction. *Trends in Cognitive Sciences* 2006;**10**(3): 117–23.

Cherland 1999

Cherland E, Fritzpark R. Psychotic side effects of psychostimulants: a 5-year review. *Canadian Journal of Psychiatry* 1999;**44**(8):811–3.

Conners 1998

Conners KC, Sitarenios G, Parker JDA, Epstein JN. The revised Conners´ Parent Rating Scale (CPRS-R): factor structure, reliability, and criterion validity. *Journal of Abnormal Child Psychology* 1998;**26**(4):257–68.

Conners 2008a
Conners KC. *Conners Comprehensive Behavior Rating Scales (Conners CBRS)*. Toronto, Canada: Multi-Health Systems Inc, 2008.

Conners 2008b
Conners KC. *Conners 3*. Toronto, Canada: Multi-Health Systems Inc, 2008.

Cyr 1998
Cyr M, Brown C. Current drug therapy recommendations for the treatment of attention-deficit/hyperactivity disorder. *Drugs* 1998;**56**(2):215–23.

Dalsgaard 2002
Dalsgaard S, Mortensen PB, Frydenberg M, Thomsen PH. Conduct problems, gender and adult psychiatric outcome of children with attention-deficit hyperactivity disorder. *British Journal of Psychiatry.* 2002;**181**(5):416–21.

Donner 2002
Donner A, Klar N. Issues in the meta-analysis of cluster randomised trials. *Statistics in Medicine* 2002;**21**(19):2971-80.

Fohlmann 2009a
Fohlmann AH. Social skills training [Social færdighedstræning [Danish]]. *Merete Nordentoft, Marianne Melau, Tina Iversen & Sanne Kjær (editor(s): Psychosis in the young. Symptoms, treatment and the future [Psykose hos unge. Symptomer, behandling og fremtid [Danish]]*. Copenhagen: Psykiatrifondens Forlag, 2009:161–89.

Fohlmann 2009b (pers comm)
Fohlmann AH. Personal communication - email correspondence April 2009.

Ford 2003
Ford T, Goodman R, Meltzer H. The British Child and Adolescent Mental Health Survey 1999: the prevalence of DSM-IV disorders. *Journal of the American Academy of Child and Adolescent Psychiatry* 2003;**42**(10):1203-11.

Gadow 1990
Gadow KD, Nolan EE, Sverd J, Sprafkin J, Paolicelli L. Methylphenidate in aggressive-hyperactive boys: In effects on peer aggression in public school settings. *Journal of American Academy of Child and Adolesent Psychiatry* 1990; **29**(5):710–8.

Gillberg 1997
Gillberg C, Melander H, von Knorring A, Janols L, Thernlund G, Hagglof B, et al.Long-term stimulant treatment of children with attention-deficit hyperactivity disorder symptoms. A randomised, double-blind, placebo-controlled trial. *Archives of General Psychiatry* 1997;**54**(9): 857–64.

Gilmore 2001
Gilmore A, Milne R. Methylphenidate in children with hyperactivity: review and cost-utility analysis. *Pharmacoepidemology and Drug Safety* 2001;**10**(2):85–94.

Gluud 2009
Gluud C, Nikolova D, Klingenberg SL, Alexakis N, Als-Nielsen B, D'Amico G, et al.Cochrane Hepato-Biliary Group. About The Cochrane Collaboration (Cochrane Review Groups (CRGs). Available online at: http://mrw.interscience.wiley.com/cochrane/clabout/articles/LIVER/frame.html 2009.

Goldman 1998
Goldman LS, Genel M, Bezman RJ, Slanetz PJ. Diagnosis and treatment of attention-deficit disorder in children and adolescents. *JAMA* 1998;**279**(14):1100–7.

Gresham 1990
Gresham FM, Elliot SN. *Social Skills Rating System*. Circle Pines, MN: Assistance Service, 1990.

Hectman 1983
Hechtman L, Weiss G. Long-term outcome of hyperactive children. *American Journal of Orthopsychiatry* 1983;**53**(3): 532–41.

Higgins 2011
Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]*. Available from www.cochrane-handbook.org, The Cochrane Collaboration, 2011.

ICH 1996
International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. ICH Harmonised Tripartite Guideline. Guideline for good Clinical Practice E6(R1). 1996. http://www.ich.org/products/guidelines/efficacy/efficacy-single/article/good-clinical-practice.html (accessed 6 May 2011).

Kadesjö 2001
Kadesjö B, Gillberg C. The comorbidity of ADHD in the general population of Swedish school-age children. *Journal of Child Psychology and Psychiatry* 2001;**42**(4):487–92.

Kadesjö 2002
Kadesjö B. *ADHD in Children and Adults. ADHD hos barn och vuxna [Swedish]*. Stockholm: Socialstyrelsen, 2002.

Kavale 1997
Kavale KA, Mathur SR, Forness SR, Rutherford Jr RB, Quinn MM. Effectiveness of social skills training for students with behaviour disorders: A meta-analysis. *Advances in Learning and Behavioral Disabilities* 1997;**11**: 1–26.

Keus 2010
Keus F, Wetterslev J, Gluud C, van Laarhoven CJ. Evidence at a glance: error matrix approach for overviewing available evidence. *BMC Medical Research Methodology* 2010;**10**(90): http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2959031/ (accessed 10 October 2011).

Kjaergard 2002
Kjaergard LL, Gluud C. Citation bias of hepato-biliary randomised clinical trials. *Journal of Clinical Epidemiology* 2002;**55**(4):407–10.

Klassen 1999
Klassen A, Miller A, Raina P, Lee S K, Olsen L. Attention-deficit hyperactivity disorder on children and youth: a quantitative systematic review of the efficacy of different management strategies. *Canadian Journal of Psychiatry* 1999;**44**(10):1007–16.

Lakes 2011
Lakes KD, Swanson JM, Riggs M. The reliability and validity of the English and Spanish Strengths and Weaknesses of ADHD and Normal Behavior rating scales in a preschool sample: continuum measures of hyperactivity and inattention. *Journal of Attention Disorders* August 2011; **1**:1–7.

Landau 1991
Landau S, Moore LA. Social skill deficit in children with attention-deficit hyperactivity disorder. *School Psychology Review* 1991;**20**(2):235–51.

Lau 1995
Lau, J, Schmid, C. H, & Chalmers, T. C. Cumulative meta-analysis of clinical trials builds evidence for exemplary medical care. *Journal Of Clinical Epidemiology* 1995;**48**: 45–57. [DOI: doi: 10.1016/0895-4356(94)00106-Z]

Liberman 1988
Liberman RP. Social skills training. In: Liberman RP editor (s). *Psychiatric Rehabilitation of Chronic Mental Patients*. Washington, DC: American Psychiatric Press, 1988.

Mager 2005
Mager W, Milich R, Harris MJ, Howard A. Intervention group for adolescents with conduct problems: Is aggression harmful or helpful?. *Journal of Abnormal Child Psychology* 2005;**33**(3):349–62.

Majewicz-Hefley 2007
Majewicz-Hefley A, Carlson JS. A meta-analysis of combined treatments for children diagnosed with ADHD. *Journal of Attention Disorders* 2007;**10**(3):239–50.

Malone 1993
Malone MA, Swanson JM. Effects of methylphenidate on impulsive responding in children with attention deficit hyperactivity disorder. *Journal of Child Neurology* 1993;**8** (2):157–63.

Mannuzza 1990
Mannuzza S, Klein RG, Konig PH, Giampino TL . Childhood predictors of psychiatric status in the young adulthood of hyperactive boys: a study controlling for chance associations. In: Robins LN, Rutter M editor(s). *Straight and Devious Pathways from Childhood to Adulthood*. New York: Cambridge University Press, 1990:279–99.

Mannuzza 1998
Mannuzza S, Klein RG, Bessler A, Malloy P, LaPadula M. Adult psychiatric status of hyperactive boys grown up. *American Journal of Psychiatry* 1998;**155**(4):493–8.

NICE 2009
National Collaborating Centre for Mental Health commissioned by the National Institute for Health and Clinical Excellence. *Attention Deficit Hyperactivity Disorder: Diagnosis and Management of ADHD in Children, Young People and Adults. National Clinical Practice Guideline Number 72*. Leicester and London: The British Psychological Society and The Royal College of Psychiatrists, 2009.

Nigg 2005
Nigg JT, Casey BJ. An integrative theory of attention-deficit/hyperactivity disorder based on the cognitive and affective neurosciences. *Development and Psychopathology* 2005;**17**(3):785–806.

Pasini 2007
Pasini A, Paloscia C, Alessandrelli R, Porfirio MC, Curatolo P. Attention and executive functions profile in drug naive ADHD subtypes. *Brain and Development* 2007;**29**(7): 400–8.

Pineda 2003
Pineda DA, Lopera F, Palacio JD, Ramirez D, Henao GC. Prevalence estimations of attention-deficit/hyperactivity disorder: differential diagnoses and comorbidities in a Columbian sample. *International Journal of Neuroscience* 2003;**113**(1):49–71.

Pliszka 1998
Pliszka S. The use of psychostimulants in the paediatric patient. In: Findling R, Blumer J editor(s). *Child and Adolescent Psychopharmacology (The Pediatric Clinics of North America)*. Vol. **45**, London: WB Saunders Company, 1998: 1085–98.

Pliszka 1999
Pliszka SR, Carlson CL, Swansom JM. *ADHD with comorbid disorder. Clinical assessment and management*. New York: Guildford Press, 1999.

Polanczyk 2007
Polanczyk G, Rohde LA. Epidemiology of attention-deficit/ hyperactivity disorder across the lifespan. *Current Opinion in Psychiatry* 2007;**20**(4):386–92.

Pringsheim 2011
Pringsheim T Steeves T. Pharmacological treatment for Attention Deficit Hyperactivity Disorder (ADHD) in children with comorbid tic disorders. *Cochrane Database of Systematic Reviews* 2011, Issue 4. [DOI: 10.1002/ 14651858.CD007990.pub2]

RevMan 2011
The Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager (RevMan). 5.1. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011.

Schachar 1997
Schachar RJ, Tannock R, Cunningham C, Corkum PV. Behavioral, situational, and temporal effects of treatment of ADHD with methylphenidate. *Journal of the American Academy of Child and Adolescent Psychiatry* 1997;**36**(6): 754–63.

Schmidt 2009
Schmidt S, Peterman F. Developmental psychopathology: attention deficit hyperactivity disorder(ADHD). *BMC Psychiatry* 2009;**9**(58):(http://www.ncbi.nlm.nih.gov/pmc/ articles/PMC2751746/ - accessed online 25 September 2011). [DOI: 10.1186/1471-244X-9-58]

Schultz 1995
Schultz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality

associated with estimates of treatment effects in controlled trials. *JAMA* 1995;**273**(5):408–12.

Sergeant 2003
Sergeant JA, Geurts H, Huijbregts S, Scheres A, Oosterlaan J. The top and the bottom of ADHD: a neuropsychological perspective. *Neuroscience and Biobehavioural Reviews* 2003; **27**(7):583–92.

Spencer 1996
Spencer T, Biederman J, Wilens T, Harding M, O´ Donnel D, Griffin S. Pharmacotherapy of attention-deficit hyperactivity disorder across the life cycle. *Journal of the American Academy of Child and Adolescent Psychiatry* 1996; **35**(4):409–32.

Swanson 1995
Swanson JM, Lerner M, Williams L. More frequent diagnosis of attention deficit-hyperactivity disorder. *New England Journal of Medicine* 1995;**333**(14):944.

Swanson 2007
Swanson JM, Hinshaw SP, Arnold LE, Gibbons RD, Marcus S, Hur K, et al.Secondary evaluations of MTA 36-month outcomes: propensity score and growth mixture model analysis. *Journal of American Academy of Child and Adolescent Psychiatry* 2007;**46**(8):1003–14.

Thalheimer 2002
Thalheimer W, Cook S. How to calculate effect sizes from published research articles: a simplified methodology. from http://work-learning.com/effect˙sizes.htm. (acessed 28 May 2011).

Thomson 2011
Thomson A, Maltezos S, Paliokosta E, Xenitidis K. Amfetamine for attention deficit hyperactivity disorder inpeople with intellectual disabilities. *Cochrane Database of Systematic Reviews* 2009, Issue 1. [DOI: 10.1002/14651858.CD007009.pub2]

Thorlund 2009
Thorlund K, Devereaux PJ, Wetterslev J, Guyatt G, Ioannidis JP, Thabane L, et al.Can trial sequential monitoring boundaries reduce spurious inferences from meta-analyses?. *International Journal of Epidemiology* 2009; **38**(1):276–86.

US FDA 2011
US Food, Drug Administration. Communication about an ongoing safety review of stimulant medications used in children with attention-deficit/hyperactivity disorder (ADHD). http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm165858.htm (accessed 6 May 2011).

Van der Oord 2008
Van der Oord S, Prins PJM, Oosterlaan J, Emmelkamp PMG. Efficacy of methylphenidate, psychosocial treatments and their combination in school-aged children with ADHD: a meta-analysis. *Clinical Psychology Review* 2008; **28**(5):783–800.

Walcott 2004
Walcott CM, Landau S. The relation between disinhibition and emotion regulation in boys with attention deficit hyperactivity disorder. *Journal of Clinical Child and Adolescent Psychology* 2004;**33**(4):772–82.

Wetterslev 2008
Wetterslev J, Thorlund K, Brok J, Gluud C. Trial sequential analysis may establish when firm evidence is reached in cumulative meta-analysis. *Journal of Clinical Epidemiology* 2008;**61**(1):64–75.

Whalen 1985
Whalen CK, Henker B. The social world of the hyperactive (ADHD) children. *Clinical Psychology Review* 1985;**5**: 447–78.

WHO 1992
World Health Organisation. *The ICD-10 Classification of Mental and Behavioural Disorders. Clinical Descriptions and Diagnostic Guidelines*. Geneva: World Health Organisation, 1992.

Wolraich 2007
Wolraich ML, McGuinn L, Doffing M. Treatment of attention deficit hyperactivity disorder in children and adolescents: safety considerations. *Drug Safety* 2007;**30**(1): 17–26.

Wood 2008
Wood L, Egger M, Gluud LL, Schultz K, Jüni P, Altman DG, et al.Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *BMJ* 2008;**336** (7644):601–5.

Zametkin 1987
Zametkin AJ, Rapoport JL. Neurobiology of attention deficit disorder with hyperactivity: where have we come in 50 years?. *Journal of American Academy of Child and Adolescent Psychiatry* 1987;**26**(5):676–86.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Abikoff 2004

Methods	Randomised Clinical Trial
Participants	103 children(age 7.0 - 9.9 years) participated in the study Sex: 93% boys, 7% girls Ethnicity: 84% white, 13% African American, 2% Hispanic, and 1% other Sample size calculation is not reported. Comorbidity: 53.4% had oppositional defiant disorder, 30% had conduct disorder, 16.5% anxiety disorder All the participants in the study received psychostimulant medication 84 of the children (81.2%) lived with both parents, 13 (12.6%) with one parent and 6 (5.8%) with their mother and stepfather Setting: Outpatient clinic in two large medicals Centre in New York and Montreal Baseline between group differences: No differences except on socioeconomic status, where there were differences between the M alone and M + ACT Medications for comorbid disorders: no information Inclusion criteria: 1) A diagnosis of ADHD based on the DISC-P2 conducted by a clinical psychologist. The diagnosis had to be confirmed by a child psychiatrist based on a comprehensive clinical interview with the child, and parent and teacher reports. The children had to, on two different occasions, receive a mean teacher rating of at least 1.5 on the hyperactivity factor or the hyperactivity index of the Conners Teachers Rating Scale 2) Children had to be medication free for at last 2 weeks before evaluation 3) Normal IQ (i.e.,WISC-R $\geq$ 85). 4) Living with at least one parent, and have telephone access 5) Positive response to methylphenidate. Exclusion criteria: 1) Children with diagnosable neurological disorders. 2) Psychosis. 3) Significant medical illness. 4) Current physical or sexual abuse. 5) Chronic tic disorder or Tourette´ s disorder. 6) DSM-III-R based developmental reading or arithmetic disorder, defined as a standard score in reading or mathematics on the Kaufmann Test of Educational Achievement of 85 or less 7) Children with a diagnosis of conduct disorder.
Interventions	Number of participants allocated per group: 34 children were randomised to methylphenidate (M), 34 to M+ MultiModal Psychosocial Treatment (MPT), and 35 to M+ Attention Control Treatment (ACT) Number of patients lost to follow up per group: 22 children failed to complete the study, 10 from the M alone group, 6 from the combined M+MPT group, and 6 from the M+ ACT group Format and duration of the intervention: Duration of the trial: 2 years.

	M+MPT= Methylphenidate + Parent training/family therapy, academic organizational skills training, individualized academic assistance, academic remediation (when necessary), social skills training, and individual psychotherapy. All the treatment modules were fully manual-based and the manual was developed before the start of the study. Each component was delivered once a week in the first year and once monthly during the second year M+MPT= Methylphenidate + attention control program (delivered once a week in the first year and once monthly during the second year.) A 75% of attendance was required. Content of the intervention: The Multimodal Psychosocial Treatment (MPT) was manual-based and integrated several treatment components. Children received individualized academic assistance, organizational skills training, individual psychotherapy, social skills training and, when necessary, reading remediation. Parents received parent management training and counselling. Daily report cards were completed by teachers and formed the basis for a home-based reinforcement program for targeted school behaviour and academic performance The Attention Control Psychosocial Treatment consisted of components parallel to those in the MPT but excluded the therapeutic content Medication: The medical treatment consisted of a medical manual and efforts was made to give each child a maximal dose of methylphenidate. There was a five week open methylphenidate titration trial before randomisation. No between groups difference were found in the methylphenidate medication
Outcomes	Parent rated: Hyperkinesis Index from Conners Parent Rating Scale. Home situations questionnaire (parents). SSRS - Social Skills Rating Scale(parents). Teacher rated: Hyperactivity and Conduct Problems Factors from the Conners Teacher Rating Scale School Situations Questionnaire (teachers). Children rated: SSRS - Social Skills Rating Scale (children). Clinician rated: Child Psychiatrists completed a DSM-III R checklist for ADHD, ODD, conduct disorder symptoms, and a C-GAS Observations: School Observations: The Classroom Observation Code. CTRS Hyperkinesis Index(rated by observers). IOWA CTRS(rated by observers). Children were evaluated at baseline, 6, 12, 18, and 24 months after baseline School observation: Social Interaction Observation Code.
Notes	Authors conclusions: There is no support for adding ambitious long-term psychosocial interventions to methylphendidate to improve ADHD and ODD symptoms

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Abikoff 2004 (*Continued*)

Random sequence generation (selection bias)	Low risk	Clarification has been requested from the one of the trial investigators and Hovard Abikoff informed us in an email on 28 January 2011 that they had used a block randomisation scheme with blocks of 4 children. The groups were balanced for age, sex, ODD and ethnicity
Allocation concealment (selection bias)	Low risk	Clarification has been requested from the one of the trial investigators and Howard Abikoff informed in an email that they had used sealed envelops
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	There were blinding on at least one of this reviews primary outcomes, in the rest of the outcomes there were no blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	22 out of 103 children failed to complete the study.
Selective reporting (reporting bias)	Unclear risk	No prior statement of assessment tools. Design article published at the same time as trial article
Vested interest bias	High risk	The trial was based in two large medical centres and the centres have extensive previous experience with research focused on ADHD and behavioural treatment
Other sources of bias?	Unclear risk	Dr. Klein is a member of a pharmaceutical board.

Antshel 2003

Methods	Randomised Clinical Trial
Participants	120 children from 8-12 years with ADHD, Inattentive type (n = 59) or ADHD, Combined type (n = 61) Sex: 90 boys, 30 girls. Ethnicity: 112 children were Caucasian, 6 African American, 2 Asian American Participants were recruited from newspaper advertisement and from consecutive referrals to a university based behavioural paediatric clinic specialized in ADHD and related disorders Comorbidity: 53 children had comorbid ODD, 29 had mood disorders, 11 had anxiety disorders, and 5 tic disorders Al 120 participants were taking stimulant medication (n = 110) or selective Serotonin reuptake inhibitor medications Sample size calculation not reported. Pre randomisation: 142 Post randomisation:120

	No statistical significant between-groups differences in age, sex, or classroom placement, duration and severity of ADHD symptoms, or comorbid conditions Setting:Out patient clinic, Kentucky, USA. Co-medications for comorbid-disorders: SSRI balanced between groups Inclusion criteria: 1) A diagnosis ADHD based on DSM-IV (DICA-R-P). Only the children which scored >1.0 SD above the mean on the CBCL Attention subscale were included Exclusion criteria: 1) Not having an ADHD diagnosis. 2) Ages 8-12, children with significant cognitive delays (IQ < 70) 3) Children with English as a second language. (Information received in an email from Kevin Antshel, 16 December 2010)
Interventions	Format and duration of the intervention: The treatment groups consisted of 8 weeks treatment and there were 90 minutes group sessions for the children during consecutive weeks. The parents met in 3 parent sessions Content of the interventions: All sessions were conducted by the same two therapists, a male doctoral student i psychology and a female master´ s student in social work. The treatment were videotaped to ensure treatment consistency. The therapist followed a treatment manual. The child groups consisted of different methods to promote generalization of social skills.There were 6 themes which consisted of: Cooperation with peers, learning how to take others perspective, problem solving, recognizing and controlling anger, assertiveness, conversations (giving and receiving complements). The parent sessions consisted of information about the themes and content in the Childrens group and discussion of how to assess and monitor homework completion Mean attendance at the 8 treatment session was 94% for the diagnostically homogeneous and 92% for the diagnostically heterogenous treatment groups The control group was a wait list group. Medication: No statistically significant between groups differences on medication type and dosage
Outcomes	Parent rated: SSRS - Social Skills Rating Scale. (38 items) Higher scores indicate more social skills competences. The scale has indexes which are used as outcomes in this study; cooperation, assertion, self-control, empathy (child version only) and responsibility (parents version only). Both the child and parent version of the SSRS, social skill domain scores range from 0 (less skilled) to 20 (high level of skills) Child rated: The SSRS - Social Skills Rating Scale (34 items). The outcome assessment were 8 weeks after the pretest and follow up were 3 months after the posttest. There were 100% completion rate at all tree assessment intervals(pre-, post-treatment and follow-up)
Notes	Authors conclusion: The results of this trial do not support the efficacy of social skills training for children with ADHD
Risk of bias	

Antshel 2003 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	They used a computer generated randomisation process. Information received from Kevin Antshel in an email 13 July 2011
Allocation concealment (selection bias)	Low risk	Allocation was concealed. Information received from Kevin Antshel in an email 13 July 2011
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinded outcome assessors. High risk of bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	There is stated that there was 100% completion rate.
Selective reporting (reporting bias)	Low risk	All of interest reported.
Vested interest bias	Unclear risk	No funding source reported.
Other sources of bias?	Unclear risk	Referal of patients, selection of ADHD-I effort due to low prevalence can skew the data

Bloomquist 1991

Methods	Randomised Clinical Trial.
Participants	A multistage identification process based on cut of scores in the CBCL: Child Behaviour Checklist teacher/parent resulted in a group of 64 children who were assessed by the Diagnostic Interview for Children and Adolescents- DICA-R. Finally 52 children with ADHD were randomised to either the multi component CBT condition, a teacher intervention, and a wait list control group Sex: 36 boys and 16 girls in the age 8-9 years. Ethnicity: 95% was Caucasian students. Comorbidity: 18 (35%) had also ODD. Sample size calculation not reported. The groups were highly comparable on the descriptive and subjective identification measures; age, IQ, Academic achievement, hyperactivity and self-control behaviour, externalising, internalising behaviour on baseline Setting: Three suburban elementary schools in the same school district Co-medications for comorbid disorders: no information Inclusion criteria: 1) T≥60 on the CBCL-Teacher. 2) Signed consent form.

Bloomquist 1991 (*Continued*)

	3) TT≥60 on the CBCL-Parent. 4) An ADHD diagnosis on the basis of DIACA-R. Exclusion criteria: 1) Mental retardation. 2) Epilepsy. 3) Severe emotional disorder. 4) Pervasive development disorder.
Interventions	Format and duration of the intervention: The intervention consisted of Multicomponent Cognitive-Behavioral Therapy Intervention(MLB): The intervention included coordinated child, parent, and teacher training components. The child component consisted of two one hour group sessions each week over a 10 week period (20 sessions). The teacher component consisted of one 2 hour in service and six 45-60 minutes consultation over a 10 week- period. The parent intervention component consisted of seven 90 minutes group sessions Teacher-only Intervention: This component consisted as the same teacher component as above but without the child only and the parent component Waiting-list control: No intervention. Content of the intervention: The intervention based on Braswell and Bloomquist(1991) and Bloomquist and Braswell´ s cognitive-behavioural therapy program for ADHD children. A variety of cognitive- behavioural techniques were utilized in the child component such as: didactic instructions, modelling, role-play exercises and so on.The teacher intervention was focused on, for example, problem solving in the classroom and on reinforcing appropriate behaviour and consequating disruptive behaviour. The parent intervention targeted to teach the parents about ADHD, to establish a positive trusting atmosphere among the parents, and to teach them cognitive/behavioural principles identical to those adressed in the teacher training component The child group was led by school psychologist, the parents' groups by therapist and the teacher intervention by a consultant The child and teacher interventions had almost 100% attendance
Outcomes	Observations: Structured behavioural observations(blinded to treatment assignment) Children rated: Self-Control Rating Scale (SCRS) (33 item questionnaire, 7 point scale. The higher the score, the more the child lacked self-control) Teacher rated: Conners Teacher Rating Scale (CTRS) (39 items questionnaire, 4 point Likert scale: from not at all (0) to very much (3)) Teacher Report-Walker-McConnell Scale of Social Competance and School Adjustment (43 items) There was a comprehensive treatment manual for the MLB and for the teacher only intervention
Notes	Key conclusions of the study authors: No difference between groups Authors refer to another paper by Bloomquist 1991. We cannot find this paper. We do not know if it was ever published

Bloomquist 1991 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No description of the randomisation method used.
Allocation concealment (selection bias)	Unclear risk	No description of the allocation method used.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	The observers were blinded to treatment assignment but the teachers were not. No blinding on primary outcomes
Incomplete outcome data (attrition bias) All outcomes	High risk	16 excluded data sets with much likelihood to bias results.
Selective reporting (reporting bias)	Low risk	All of interest reported
Vested interest bias	Unclear risk	No funding stated.
Other sources of bias?	Unclear risk	No test for compliance of the intervention groups.

Cohen 1981

Methods	Randomised Clinical Trial
Participants	24 children were randomised to four different groups. Six received cognitive behaviour modification, eight received methylphenidate only, six received both treatments, and four were untreated Sex: 21 boys and three girls. Age: 5-6 years. Comorbidity: No information. Co-medications for comorbid-disorders: no information Inclusion criteria: 1)Scores ≥1,5 on Conners abbreviated Teacher Rating Scale(CTRS) 2) IQ≥80 on WPPSI. 3)No neurological damage or psychosis. Ethnicity: Canadian. No sample size calculation.
Interventions	Format and duration of the intervention: Cognitive Behaviour Treatment: Individual training 1 hour twice weekly sessions for a total of 20 sessions (10 weeks) Content of the intervention:

Cohen 1981 (*Continued*)

	The aim of the treatment was to teach the children to slow down, developing better problem solving ability, and to evaluate his/hers own performance Medication: Drug dosage was individually titrated. Dosages ranged from 10 to 30 mg methylphenidate pr. day. No information about medication balance between groups
Outcomes	Teacher rated: Conners Behaviour Rating Scale(teacher version) PMFFT/MFFT(measuring cognitive impulsivity) Parents rated: Conners Behaviour Rating Scale. Observation: Observations in classrooms. Motor impulsivity. What Happens Next and Preschool Interpersonal Problem Solving Test measured social problem-solving skills Nowick- Strickland Scale(Locus of control). Richman-Graham(emotional and social adjustment).
Notes	Key conclusion of the study authors: No difference in treatment effect

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Unclear.
Allocation concealment (selection bias)	High risk	No description of the allocation concealment, but four patients were moved between groups
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	There were blinding on at least one of this reviews primary outcomes, in the rest of the outcomes there were no blinding
Incomplete outcome data (attrition bias) All outcomes	High risk	Many tables different from text. No explanation. Lack of teacher responses
Selective reporting (reporting bias)	Low risk	All apparent assessments are made.
Vested interest bias	Low risk	Funding ok, no previous research on the topic.
Other sources of bias?	High risk	The selection procedure of patients not stated in article.

MTA 1999

Methods	Randomised Clinical Trial
Participants	576 children with ADHD (DSM-IV) aged to 9.9 years were randomised to either 14 month of medical treatment, intensive behavioural treatment, the two combined and standard community care Setting: Six multi site outpatient clinics in USA. Sex: 465 boys and 111 girls. Ethnicity: 61% white, 20% African American, and 8% Hispanic. Comorbidity: 33.5% anxiety disorder, 14.3% conduct disorder, 39.9% oppositional-defiant disorder, 3.8 % affective disorder, 10.9% tic disorder, 2.2%, other (bulimia, enuresis) Co-medications for comorbid disorders: balanced between groups Inclusion criteria: 1) Boys and girls, aged 7.0 - 9.9 years (1 st-4th grades), residing with primary caretakers for at least 6 months, who meet dimensional criteria for hyperactivity on the basis of parent end teacher rating scales and full diagnostic criteria for ADHD, Combined type Exclusion criteria: 1) Currently in hospital (inability to obtain school assessments) 2) Currently in another treatment study (confounding of assessments and treatments) 3) Below 80 on WISC-III Verbal IQ, Performance IQ, or Full Scale IQ scores and on Scales of Independent Behavior (insufficient ability to participate in psychosocial interventions) 4) Bipolar disorder, psychosis, pervasive developmental disorder, severe obsessive-compulsive disorder (treatment may be incompatible with MTA treatments) 5) Chronic, serious tics or Tourette´ s Disorder (possible contraindication for stimulant treatment) 6) Neuroleptic treatment in previous 6 months (may need resumption, which is incompatible with MTA treatments) 7) Major neurological or medical illness that would interfere with study participation or require medications incompatible with MTA medications (inability to participate in MTA treatment) 8) History of intolerance to MTA medications (dangerous if participants assigned to arm involving medications) 9) Suicidal of homicidal (needs more intensive treatment than MTA provides) 10) Ongoing or previously undisclosed child abuse (risk of removal from home precludes parent intervention and consistent parent data) 11) Missed more than 25% of school days in previous 2 months (interference with teacher assessments and school intervention) 12) Another child in household already participating in MTA (cross-arm contamination if two children in same household randomised to different arms) 13)Same classroom as child already participating in MTA (cross-arm contamination if two pupils in same classroom are randomised to different arms) 14) Parental stimulant/cocaine abuse in past 2 years (possible co-opting of child´ s medications) 15) Inability of parent to speak English (inability to participate in parent training) 16) No telephone (inability to participate in telephone calls with therapists)
Interventions	There were four treatment conditions; Medication Treatment Group, Psychosocial Treatment Group, Combined Treatment (M+PS), and Community Care Group Format and duration of the treatment:

MTA 1999 (*Continued*)

	Medication Treatment Group: 1 month of blind titration. Monthly visits after the titration period, doses adjusted as indicated by monthly monitors Behavioural Treatment Group: Intense, Multi-Component, including 27 group & 8 individual sessions of parent training, 16-20 sessions teacher consultations, 8 week full time Summer Treatment Program, and 12 week of half-time classroom behavioural specialist. No medication Combined Treatment Group: Integration of all treatment components in Medication Treatment Group and Behavioral Treatment Group Community Care Group: Treatment of own choosing in the community. No treatment provided by MTA Content of the Treatment: Medical Treatment Group: 1 month of blind titration with methylphenidate for best dose, if unsatisfactory, then open titration with d-amphetamine, pemoline, imipramine, others. Supplementary general advice and selected readings without systematic behavioural intervention Behavioural Treatment Group: Consisted of three major components: parent training, a two part school intervention component, and a child treatment component anchored in an intensive summer treatment program
Outcomes	Parent rated: Homework Problems Checklist Social Skills Rating System DISC 3.0 Conners Rating Scale Child Behavior Checklist SNAP-IV DSM-IV Conduct Disorder Checklist Consumer Satisfaction Teacher rated: Social Skills Rating System Conners Rating Scale Child Behavior Checklist SNAP-IV Child rated: WIAT Social Skills Rating System DISC 3.0 Self Report of Antisocial Behaviour Observator rated: Classroom Observations
Notes	The authors states that medication and combined treatment do not differ on teacher and parent rated social skills

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

MTA 1999 (*Continued*)

Random sequence generation (selection bias)	Low risk	Adequate method used.
Allocation concealment (selection bias)	Low risk	Adequate method used.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Blinded and unblinded raters.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Imputation method?
Selective reporting (reporting bias)	Unclear risk	Where is the consumer satisfaction and the CBCL data reported? Clarification has been requested from one of the trial investigators, but we had received no answer when this review was finished
Vested interest bias	Low risk	Funding okay.
Other sources of bias?	Low risk	Low risk.

Pfiffner 1997

Methods	Design: Randomised Clinical Trial.
Participants	Participants were recruited from newspaper advertisement and from consecutive referrals to a university-based behavioural paediatric clinic specialized in ADHD and related disorders Children 8-10 years with an ADHD diagnosis made on the basis of DSM-III-R criteria Sex: 19 boys, 8 girls. Ethnicity: Patients were Caucasian except from 1 boy, who was African American Socioeconomic status were from middle to upper middle class. Two children were from single-parent families Comorbidity: 25 children met criteria for ADHD and 2 met criteria for UADD. 19 children met criteria for comorbid oppositional defiant disorder, 3 for conduct disorder, 4 for separation anxiety disorder, 5 for overanxious disorder, and 2 for dysthymic disorder Only 12 of the children (44%) were receiving stimulant medication Sample size calculation not reported. Pre randomisation: 27. Post randomisation: 18. Setting: University based paediatric clinic, USA. Co-medications for comorbid disorders: no information Inclusion criteria:

	1) Diagnosis of ADHD (DSM-III-R), a mean score at or above 1,5 on at least one of the parent-completed sub scales assessing ADHD. behaviour from the CLAM rating scale or the SNAP-R, a T score of at least 60 on the Attention Problem subscale of the CBCL Exclusion criteria: Not reported. We have attempted to get information about this from the study investigators but have not succeeded in this attempt
Interventions	Three conditions: Social skills training for the children (SST), Social skills training for the children with parent mediated generalisation (SST-PG) and a wait list control group Format and duration of the intervention: The two treatment groups attended 8 group sessions. There were assessment at pre and post treatment and follow-up 3-4 months post treatment. Children in the treatment groups received 90 min group sessions during consecutive weeks Content of the intervention: The same two therapists were teaching in all the children groups. Six themes/modules were covered during the 8 weeks. 1) good sportsmanship, 2) accepting consequences, 3) assertiveness, 4) ignoring provocations, 5) problem solving, 6) recognising and dealing with feelings. Children were assigned homework to practice at home. The children received points for following the rules of the groups, participate and attend the sessions.The points could be exchanged for child-selected games and activities during the last 10 minute for each group In the SST-PG parent were used as a primary vehicle to program generalisation of the social skills learned in the SST groups to home and school settings. The parents group were led by a licensed psychologist. The parents went through the same group themes or agendas as the children did. The parents met with their childrens teacher and gave the teacher a template for the scorecard, also called the daily report card.The teacher scored the child on a 4 point scale and parents rewarded the child when the child scored high on the scale. There were a protocol for both the SST and the SST-PG intervention The intervention groups were led by psychologist.
Outcomes	Parent rated: Social Skils Rating System (SSRS) The Social Skills scale consists of 30 items on a Likert scale (0-3) Social Skills Scale (UCI) 10 items (5 point scale: 1-5) (parent) Consumer Satisfaction Questionnaire (12 items, 7 point scale (scores above 4 reflecting satisfaction and scores below 4 reflecting dissatisfaction) Teacher rated: Social Skils Rating System (SSRS). The Social Skills scale consists of 30 items on a Likert scale (0-3) Interviewers: Test of social skill knowledge (six questions each scored from 1-15)(scored by blinded raters)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Pfiffner 1997 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	No information given in the article. Clarification requested from the trial investigators and they reported in an email 26 May 2011 that it is not possible to find this data now
Allocation concealment (selection bias)	Unclear risk	No information given in the article. Clarification requested from the trial investigators and they reported in an email 26 May 2011 that it was not possible to find this data now
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	There was blinding on at least one of this study's primary outcomes; in the rest of the outcomes there was no blinding
Incomplete outcome data (attrition bias) All outcomes	Low risk	Imputation method used. F.u. scores for 3 participants replaced by m
Selective reporting (reporting bias)	High risk	The author informed in an email that the CLAM and SNAP were used post treatment, but not reported in the article. It was not possible to get the data because they had been lost over time
Vested interest bias	Low risk	Funding okay. No previous publication on the topic.
Other sources of bias?	Unclear risk	$12 (f.u.) paid to families. $10, $25 for teachers. 44% of the participant were medicated with stimulant medication, but the number of medicated children in the different groups is not stated

Pfiffner 2007

Methods	Design: Randomised Clinical Trial.
Participants	There were 69 children in the age 7- 11 years randomised to Child Life and Attention Skills Program (CLAS) or a control group who did not receive the intervention Setting: Outpatient clinic. Sex: 46 boys, 23 girls. Ethnicity: White 51%, Asian 16%, Hispanic 10%, Afro American 6%, and mixed 17% There were not any significant difference between group in the form of child age, sex, race, symptoms of hyperactivity/impulsivity, comorbid oppositional defiant disorder, anxiety or depression, IQ or academic achievement Comorbidity: ODD (23%), depressive (1%), anxiety (12%)

	Co-medications for comorbid disorders: no information Inclusion criteria: 1) DSM-IV diagnosis of ADHD-I. 2) IQ > 80 (based on Wechsler Abbreviated Scale of Intelligence) 3) Living with at least one parent for the past year. 4) Attending school full time. 5) The school consenting to participate in school-based treatment Exclusion criteria: 1) Families expecting to change medication status for their child during the study 2) Children with visual or hearing impairment. 3) Severe language delay. 4) Major neurological illness. 5) Psychosis, or pervasive development disorder. 6) A child being in the same classroom as another participant or having a sibling who was already enrolled In the intervention group 7 children were lost to follow-up and in the control group 8 children were lost to follow-up
Interventions	The treatment included three components administrated concurrently over 12 weeks: teacher consultation, parent training, and child skills training Format and duration of the treatment: Child skills training: 8 (cohort:1-4) and 10 (cohort 5) 1 ½ hours a week groups with child skills training in the 12 week period Parent Training: 8 (cohort:1-4) or 10 (cohort 5) 1½ hour group sessions and 4 to 5 family sessions (cohort 2-5) Teacher Consultations: 1/2 hour overview of behavioural interventions and classroom-based accommodations for ADHD followed by 4-5 1/2 hour meetings of teacher, child, and therapist over the 12 week period Content of the intervention: Child Skills Training: The training were divided into modules focused on skills for independence and skills for social competance. There were both behavioural interventions (for example, a reward based contingency management program) and cognitive-behavioural interventions (for example, problem-solving, the use of cues/verbal mediation strategies to stay on task and focused) Parent Training: The modules in the child group were reviewed each week and the parents were taught methods to promote end reinforce the childs use of skills at home. The parents were also taught methods to managing ADHD Teacher consultations: A school-home daily report card was designed and used (Classroom Challenge-CC). Also a special notebook was created for each child containing copies of CC All the interventions were manual-based. There were made some changes to the manuals to refine the interventions based on feedback from clinicians, participants, teachers, and parents Attendance: Parents in all cohorts participated in more than 95% of the group meetings
Outcomes	Parent rated: Child Symptom Inventory (parents and teachers) corresponds to DSM-IV inattention symptoms and are rated on a 4 point scale (0 = never to 3 = very often) The SCT scale (parents and teachers) consists of 15 SCT items rated on a 4-point scale

	(0 = never to 3 = very often) SSRS - Social Skills Rating Scale. 30 items rated on a 3 point scale (never, sometimes, very often) Organisational Skills (parents: 58 items, 4 point scale, 1 = never to 4 = just about all time) Clinical Global Impression - Improvement. Teacher rated: Child Symptom Inventory (parents and teachers) corresponds to DSM-IV inattention symptoms and are rated on a 4 point scale (0 = never to 3 = very often) The SCT scale (parents and teachers) consists of 15 SCT items rated on a 4-point scale (0 = never to 3 = very often) SSRS - Social Skills Rating Scale. 30 items rated on a 3 point scale (never, sometimes, very often) Organisational Skills (teacher: 38 items, 4 point scale, 1 = never to 4 = just about all time) Clinical Global Impression-Improvement. Children rated: Test of Life Skill Knowledge Consumer satisfaction: Parents: 100% very satisfied 35% improved or much improved 90% useful or very useful Teachers: 32 of 36 rated the programme as appropriate 73% rated improved attentional difficulties Children: 32 of 36 liked the group. 83% found the programme helped at home. 78% found the programme helped in school.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random table. Information received from Pfiffner in an email 25 May 2011
Allocation concealment (selection bias)	Low risk	Sealed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Imputation method used.

Pfiffner 2007 (*Continued*)

Selective reporting (reporting bias)	Low risk	All apparent assessment are made.
Vested interest bias	High risk	Has done previous trials
Other sources of bias?	High risk	Changes in treatment protocol. Timing for follow up differ; same school year vs next school year (both approximately 3 months after treatment but summer break between). Families and teachers were paid for each of the post treatment and follow-up assessment

Tutty 2003

Methods	Design: Randomised Clinical Trial.
Participants	Children 5-12 with an ADHD diagnosis made on the basis of DSM-IV criteria Sex: 75 boys and 25 girls Ethnicity: White (49% intervention group, 38% control group), Afro-American (4% IG, 2% CG), Asian (5% IG, 1% CG), Hispanic 1% IG, 0% CG) Sample size calculation not reported. Setting:Outpatient clinic, Washington, USA Pre randomisation: 100 Post randomisation: Blinded follow-up measures were completed by 97% and 98% of parent or guardian participants at 3 and 6 months after enrolment, respectively. Follow-up completion rates for teacher participants yielded 92% and 75% for 3 and 6 months after enrolment, respectively. Participants with missing data did not differ from participants with complete data sets across time or any clinical, functional, and demographic variables according to the authors of the study article. For the ADHD Rating Scale outcome 2 children where lost to follow up. For the Child Attention Profile outcome totally 24 children where lost to follow-up (16 in the IG and 8 in the CG) Co-medications for comorbid disorders: it was allowed but not stated if it were balanced between groups Inclusion criteria: Diagnosis of ADHD (DSM-IV) Exclusion criteria: 1) Conduct disorder 2) Oppositional defiant disorder 3) Tourette syndrome 4) Affective disorder 5) Active alcohol or other substance abuse during previously 90 days 6) Chronic mental ilness 7) Patients enrolled in BSS class at GHC in the past. Baseline characteristics: Mean baseline parented attention-deficit hyperactivity disorder symptom scores were more symptomatic for the IG than for the CG, as well as the use of parent discipline practice. These between groups differences were adjusted before follow-up analysis

Tutty 2003 (*Continued*)

Interventions	Two conditions: Behavioural and social skills class versus control group (waiting list). Both groups received psychostimulant treatment Format and duration of the intervention: The BSS intervention consisted of 8 once a week, 50 minute group sessions. The children were divided into one of three child groups according to age; 5-7, 8-10 and 11-12 years. There was a parent only group at the same time as the child only group Content of the intervention: The BSS intervention was based on an existing ADHD program previously developed by the CADD clinical team. The intervention are designed to enhance the children's overall understanding of ADHD and how to cope and manage with many of the physical and psychosocial problems connected to this condition. Each BSS session was based on a structured session by session agenda. The intervention was delivered by master levels therapist with at least two years experience. The child and parents were divided into a child only and a parent only group There was no significant between-groups difference in psychostimulant use found at 3 (49.01% vs 53,6%; X^2= 0.196, P = 0.658) months and 6 months (52,94% vs 39.02% x^2 = 1.768, P = 0.184) for both IG and CG participants. Co-medication: allowed, but not stated if equal in groups.
Outcomes	Outcome assessment were conducted at 3 and 6 months. Clinican rated: The ADHD Rating Scale (18 items, Likert scale) assessed by a blinded research assistant at baseline, 3 months and 6 months. Assessment by telephone interviews of parents The Child Attention Profile (12 items. Likert scale) assessed by a blinded research assistant at baseline, 3 months and 6 months. Assessment by telephone interviews of teachers
Notes	There was a third outcome used in this study, but it is not relevant for this review, because it measured the parents' discipline practice

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	The study used coin toss method performed by the research assistant and this is an adequate method according to the Cochrane Handbook
Allocation concealment (selection bias)	Unclear risk	Information on this is not reported. Clarification about method of allocation concealment has been requested form the trial investigators, but no information on this topic was available at the time the review was prepared
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding.

Tutty 2003 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessment by telephone interviews of parents and teacher performed by a blinded research assistant. The parents not blinded, and therefore not an adequate method
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were used an ITT method.
Selective reporting (reporting bias)	Low risk	All of interest reported.
Vested interest bias	Low risk	Funding okay, and no previous trials on the topic.
Other sources of bias?	Unclear risk	The co-medication not specified.

van der Oord 2007

Methods	Design: Randomised Clinical Trial.
Participants	Children aged 8-12 years with ADHD diagnosed according to DSM-IV Ethnicity: 40 children(89%) children from Caucasian parents, 1 child(2%) was from Caribbean parents, and 4(9%) from mixed origin Comorbidity: ODD/CD 61,9% in one group and 41,7% in the other Sample size calculation not reported. Setting: Five different outpatient clinics in Netherland. Co-medications for comorbid disorders: no information Inclusion criteria: 1) ADHD diagnosis based on DSM-IV established with the parent version of DISC-IV 2) Total IQ of 75 or above based on the short version of WISC-R 3) Parents must give informed consent for their child to participate in the trial Baseline characteristic: One-way ANOVAs and Chi^2 analyses showed not significant differences between the two conditions in terms of baseline demographic characteristics. Furthermore one-way ANOVAs showed no significant group differences Exclusion criteria: 1) Inadequate mastering of the Dutch language by the child or both parents 2) A history of methylphenidate use. Of the 50 randomised children one declined the methylphenidate only group and two of the children in the methylphenidate plus BT discontinued the intervention. Furthermore, one child was lost to posttest and follow up in the methylphenidate only intervention, one was omitted from analysis in the combined intervention group Medication:There were used a four-week, pseudo-randomised, multiple-blind placebo-controlled, crossover medication design, as described in the MTA study. The treatment groups did not differ on dose of methylphenidate either at baseline or posttreatment
Interventions	Format and duration of the intervention. 50 children were randomised to either methylphenidate (n = 23) or methylphenidate plus multimodal behaviour therapy (n = 27) The multimodal treatment consisted of child cognitive-behaviour therapy, parent behaviour therapy and teacher behavioural training. The child cognitive-behaviour ther-

	apy consisted of 10 weekly, 75 minutes group sessions, provided by two therapists. The parent behaviour therapy onsite of 10 weekly sessions of 90 minutes group therapy, provided by two therapists Content of the intervention. There were used a treatment program and there were manuals in all the groups. In the child group there were used cognitive- behaviour techniques and the program for this group was adapted from Kendall and Braswell. It consisted of problem solving techniques, relaxation techniques, contingency management techniques, role playing, and guided practice. The parent group was based on Barkley´ s training's manual "Defiant children: A clinicians manual for parent training." Components included, for example, psychoeducation on ADHD, structuring the environments, practicing positive attending skills and contingency management skills. The teacher training was based on the teacher training manual by Pelham and consisted of a two hour workshop, which consisted of, for example, psycho-education on ADHD, structuring the classroom environment, and a daily report card Mean treatment attendance in the combined condition was 88.6% To ensure treatment compliance all therapist completed a treatment integrity checklist
Outcomes	Parent rated: DBDRS consist of 42 items and contains four sub scales: Inattention (9 items), Hyperactivity/Impulsivity (9 items), ODD (8 items), and CD (16 items). Has a 4-point Likert scale (0-3). The Inattention and the Hyperactivity/Impulsitivity sub scale were combined into one ADHD score. Higher scores indicate more increased symptoms SSRS - Social Skills Rating Scale. (The parent version consist of 38 items. Has a 3-point Likert scale rating from 0-2.) Parenting Stress Index(PSI) Teacher rated: DBDRS consist of 42 items and contains four sub scales: Inattention(9 items), Hyperactivity/Impulsivity (9 items), ODD (8 items), and CD (16 items).Has a 4-point Likert scale (0-3). The Inattention and the Hyperactivity/Impulsitivity sub scale were combined into one ADHD score. Higher scores indicate more increased symptoms SSRS - Social Skills Rating Scale. The teacher version consist of 30 items. Has a 3-point Likert scale rating from 0-2 Child rated: Self-Perception Profile for Children (SPPC). State Trait Anxiety Inventory for Children (STAIC).
Notes	Authors conclusion is that there are no additive effect of multi modal treatment compared to medical treatment alone

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Information on this is not reported. Clarification about method of allocation concealment has been requested form the trial investigators, but no information on this topic was available at the time the review was prepared

van der Oord 2007 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Information on this is not reported. Clarification about method of allocation concealment has been requested form the trial investigators, but no information on this topic was available at the time the review was prepared
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All the participants lost to follow up were stated and lost to follow up not believed to influence results
Selective reporting (reporting bias)	Low risk	No.
Vested interest bias	Unclear risk	Funding not stated.
Other sources of bias?	Unclear risk	Co-medication not specified.

Waxmonsky 2010

Methods	Design: Randomised Clinical Trial.
Participants	Children aged 6-12 years with ADHD diagnosed according to DSM-IV-TR Ethnicity: 80,4% white, 10.7% African American, and 8,9% mixed. 7 children (12.5%) discontinued the study, 5 in the IG and 2 in the CG Sample size calculation not reported. Of the 56 children 48 were diagnosed with ADHD-combined type, 7 were diagnosed with ADHD-inattentive type, and 1 was diagnosed with ADHD-hyperactive/impulsive type. 22 children met criteria for comorbid conduct disorder and 24 for oppositional defiant disorder, leaving only 10 children with non comorbid ADHD Setting: Outpatient (attending school), Buffalo, USA Co-medications for comorbid disorders: no information Inclusion criteria: ADHD based on DSM-IV Exclusion criteria: 1) Current or past history of seizures (not including benign febrile seizures) 2) Other physical conditions that precluded administration of atomoxetine (for example, marked cardiac conduction delay) 3) Documented failed trial of atomoxetine, defined as 3 weeks or more on treatment with at least 0.8 mg/kg/d, or a documented inability to tolerate this dose 4) Serious forms of psychopathology other than ADHD, such as autism, bi-polar disorder, schizophrenia, or any other psychopathology requiring urgent treatment with psychotropic medication

	5) Any history of major depression requiring treatment, or any past history of self-harm or serious suicidal ideation 6) An intelligence quotient of less than 75 (based on Wechsler Intelligence Scale for Children, 3rd edition) 7) No evidence of ADHD-related impairment at school. Baseline characteristics: 56 children randomised. 45 boys and 11 girls Medication: All patients received psychostimulant medications. No significant between group differences in mean doses of atomoxetine
Interventions	8 week intervention + Medication versus Medication alone. Number of participants allocated per group: 27 (Med); 29 (Med + BT) Number of patents lost to follow up per group: 2 (Med); 5 (BT + Med) Format and duration of the intervention: The 8 week intervention consisted of: Parent group: 8 week group, 2 hours session;1 session/week. Child group - SST: 8 week. 2 hours session;1 session/week. Teacher: Daily report card. Content of the intervention: Parent group: Based on the COPE program and consisted of social learning's principals targeting at the Childrens behaviour and lack of impulse control. Group leaders were advanced graduate students or doctoral level clinicians Child group: Social skills training program. Group leaders were graduate students in clinical psychology Treatment compliance: The parent intervention was based on a manual (COPE). It is unclear whether the child group intervention also was based on a manual 62% of the parents attended 8 sessions, 62% attended 6 or more sessions. The children's attendance in the SST group is not reported
Outcomes	Parent rated: DBD (45 items, Likert scale 0 (not very much) to 3 (very much)) SSRS (Social Skills Rating Scale) (55 items on the parent version, rated from 0 (not at all) to 2 (very often)) Treatment satisfaction (Likert scale from 1 (strongly disagree) to 7 (strongly agree)) Teacher rated: DBD (45 items, Likert scale 0 (not very much) to 3 (very much)) SSRS (Social Skills Rating Scale) (57 items on the teacher version, rated from 0 (not at all) to 2 (very often) and from 0(lowest 10%) to 5 (highest 10%) APRS (Academic Performance Rating Scale) (19 items scale, 1-5 Likert scale) DRC (Daily Report Card). Observations: Observations of violence to classroom rules using Student Behaviour Teacher Response Observation Code Clinician ratings: CGI(Clinical Global Impressions scale). Classroom behaviour. ADHD symptoms and functioning at home and at school.

Notes	Key conclusion of the author: Behavioural therapy improved ADHD symptoms at the home but not at school	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Clarification requested from the one of the trial investigators and Dan Wascbusch informed in an email 22 June 2011 that they had used a computer generated randomisation process
Allocation concealment (selection bias)	Low risk	Clarification requested from the one of the trial investigators and Dan Wascbusch informed in an email 22 June 2011 that the clinicians did not know the treatment assignment before it was assigned
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding.
Incomplete outcome data (attrition bias) All outcomes	High risk	Clarification requested from the one of the trial investigators and Dan Wascbusch informed in an email that subjects were dropped if there was not sufficient information. Scores in indexes were computed if there were at least 50% of the items in the index answered and counted them missing if they were not. Dan Wascbusch also informed that they had essentially complete data pre-treatment and nearly complete at post-treatment. For teachers they had a lower response. They included whatever they had in the analyses and dropped subjects when there was not sufficient information, repeating this for each analysis
Selective reporting (reporting bias)	Unclear risk	Protocol published in Clinicaltrials.gov after trial conduct. Publication and report in Clinicaltrials gov. is not consistent
Vested interest bias	High risk	Fundings from and collaboration with Eli-Lilly Company.
Other sources of bias?	Unclear risk	Co-medication not specified.

Yuk-chi 2005

Methods	Design: Randomised Clinical Trial
Participants	90 children with ADHD were randomised to psychosocial treatment plus methylphenidate versus methylphenidate treatment alone Children aged 7 - 9.9 years. Ethnicity: Chinese children. Sample size calculation was made. Sex: 77 boys, 9 girls. Comorbidity: Anxiety 29%, Depression 6%, ODD 50%, Conduct Disorder 6% Setting: Community mental health center: Out patient clinic in Hong Kong Socio demographic: No significant differences between the two treatment groups in demographic and social economic status, comorbid conditions, and additional intervention received in the first six months of the treatment Medication: All participants received methylphenidate treatment. No information about between group differences in the medical treatment Co-medications for comorbid disorders: no information Inclusion criteria: 1) ADHD-Combined Type based on DSM-IV criteria 2) Children in the age 7-9.9 years. 3) Studying first to fourth grade. 4) Living with a parent, who is the major caretaker. 5) IQ>80. 6) No significant physical disability. 7) No stimulant medication (methylphenidate) use for more than 2 weeks previously 8) Their parents willingness to accept stimulant medication and psychosocial intervention of this study 9) The parents willingness to accept random allocation. 10) No parent suffering from intellectual impairment or current psychosis
Interventions	There were three components in the psychosocial treatment; child training, cognitive-behavioural parent training, and school consultations Pre randomisation: 146 Post randomisation: 90 Form and duration of the treatment: Child training: 24 weekly sessions. Each group session lasted for 1 hour and 30 minutes to 2 hours Cognitive-Behavioral Parent Training: 18 weekly sessions in total. Each session lasted for 1 hour and 30 minutes to 2 hours School Consultations: There were two telephone consultations, Content of the intervention: The child training:The training provided a rich direct contingency management environment, in which the training of problem solving's skills and anger control management was provided. All sessions were videotaped to check treatment integrity. Themes were, for example, feelings, games, problem solving, stop & think, role play school and home Parent training: The child training and the parent training were developed to implement concommitantly.Themes in the group were for instance: know yourself, attention rules, stress management, child mood management, homework coaching School consultations: The therapist in the child groups talked to the teachers about implementations of classroom management strategies and review of the child's progress

Yuk-chi 2005 (*Continued*)

	in school No protocol violations to both child and parent training treatment program were detected
Outcomes	Parent rated: SWAN rating scale, (30 items, 7 point scale, 1(slightly below average) to -3 (far above average) Teacher rated: SWAN rating scale.(30 items, 7 point scale, 1(slightly below average) to -3 (far above average) Clinician rated: MFFT(computer programme to measure impulsivity. Scores time taken to make the response, and total numbers of errors.) Consumer satisfaction: At post treatment: 40% very useful, 60% useful
Notes	Combined Medication + PST yielded benefits on primary ADHD symptoms and on conduct problems

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Table of random numbers, with block size of two.
Allocation concealment (selection bias)	Unclear risk	Unclear.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding.
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding on this reviews primary outcome.
Incomplete outcome data (attrition bias) All outcomes	High risk	Type of imputation method used is unclear.
Selective reporting (reporting bias)	Low risk	Low risk.
Vested interest bias	Unclear risk	Yuk-Chi So has done previous research on the topic.
Other sources of bias?	High risk	Have done previous research and no statement of funding.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abikoff 1985	Not a randomised clinical trial.
Carlson 2000	Not a randomised clinical trial.
Carlson 1992	Not a randomised clinical trial.
Chang 2004	Not a randomised clinical trial.
Corkum 2005	Only parent training programme.
Döpfner 2004	Intervention not eligible.
Ercan 2005	Not a randomised clinical trial.
Evans 2000	Not a randomised clinical trial.
Fabiano 2003	Not a randomised clinical trial.
Feinfield 2004	Not children with ADHD.
Fenstermacher 2006	Not a randomised clinical trial.
Frankel 1997	Not a randomised clinical trial.
Frölich 2002	Not a randomised clinical trial.
Gadow 1985	Article - not a trial.
Gol 2005	Control group without ADHD.
Gonzalez 2002	Not social skills training.
Hinshaw 1984	Not a randomised clinical trial.
Hinshaw 2000	Not a suitable outcome.
Horn 1990	Not a control as specified in the review protocol.
Jensen 1999	A review.
Jensen 2001	Not adding relevant data to the review.
Klein 1997	Not social skills training.
Kolko 1990	Not all of the children was diagnosed with ADHD.

(*Continued*)

Kolko 1999	Not social skills training.
Langberg 2008	Not social skills training.
Langberg 2010	Not a suitable outcome for this review.
Lösel 2006	Participants under five years of age.
Miranda 2002	Intervention for the teachers, not a clinical ADHD diagnosis
Miranda 2006a	Not a randomised clinical trial.
Miranda 2006b	Review.
Molina 2008	The control group is not suitable.
MTA 2009	Not adding necessary data to the review.
Pelham 1980	Not a randomised clinical trial.
Pelham 1993	Not a randomised clinical trial.
Pelham 2000	No relevant data for the review.
Pelham 2005	Not a randomised clinical trial.
Rosén 1984	Not social skills training.
Waxmonsky 2008	Not a randomised clinical trial.
Webster-Stratton 2001	Participants under five years of age.
Webster-Stratton 2004	Participants under five years of age.
Williams 1993	Not a randomised clinical trial.
Wolraich 1978	Not social skills training.

Characteristics of ongoing studies *[ordered by study ID]*

Safren 2011

Trial name or title	Compensatory executive functioning skills training for adolescents with ADHD
Methods	Randomised efficacy study, single blind crossover assignment
Participants	Adolescents from 14 to 18 years diagnosed with ADHD. Both genders
Interventions	Twelve weekly treatment sessions either immediately upon enrolling in the study or after a four month-waiting period. Cognitive behavioural therapy versus wait list control. This study, adapted from a similar research study for adults with ADHD, will examine whether cognitive behavioural therapy (CBT) plus medication is more effective at treating ADHD than medication therapy alone in adolescents with ADHD
Outcomes	Primary outcome measures: Changes in ADHD symptoms, measured before randomisation, and at 4 months and 8 months follow up. Secondary outcomes measures: Changes in secondary symptoms af ADHD (for example, mood)
Starting date	October 2009. Estimated study completion date: May 2012.
Contact information	Principal Investigators: Steven A. Safren, Ph.D., Massachusetts General Hospital. Susan E. Sprich, Ph.D., Massachusetts General Hospital
Notes	Clincaltrials.gov Identifier: NCT0109252

Storebø 2011

Trial name or title	Randomised social-skills training and parental training plus standard treatment versus standard treatment of children with attention deficit hyperactivity disorder - The SOSTRA trial
Methods	The design is randomised two-armed, parallel group, assessor-blinded trial
Participants	Children aged 8-12 years with a diagnosis of ADHD are randomised to social-skills training and parental training plus standard treatment versus standard treatment alone. A sample size calculation estimated that at least 52 children must be included to show a 4-point difference in the primary outcome on the Conners 3rd Edition subscale for 'hyperactivity-impulsivity' between the intervention group and the control group
Interventions	Social skills training will consist of 8 weeks of group treatment with weekly sessions of one and a half hours and includes role play, exercises and games as well as home work which will include the parents. At the same time the parents are participating in parental training groups, that will focus on supporting the children's social training. Both the children and the parental groups are lead by two group therapists. The intervention will be additional to the received standard treatment The standard treatment consists of medical treatment, briefing, consulting and supporting conversations with a focus on securing compliance to the treatments and on aiding children and their families with the difficulties arising with the children's illness. Furthermore the parents participate in parental groups three times during the 8 weeks in which the experiment takes place. This group lasts 2 hours and is managed by two nurses who are attached to the ADHD- treatment group
Outcomes	The outcomes will be assessed 3 and 6 months after randomisation. The primary outcome measure is ADHD symptoms. The secondary outcome is social skills. Tertiary outcomes include the relationship between social

Storebø 2011 (*Continued*)

	skills and symptoms of ADHD, the ability to form attachment, and parents' ADHD symptoms
Starting date	August 2009. Finished August 2011.
Contact information	Contact: Ole J. Storebø, psychol., MS ojst@regionsjaelland.dk Contact: Jesper Pedersen, MD, Phd. jpee@regionsjaelland.dk
Notes	Clincal Trials.gov Identifier:NCT00937469

DATA AND ANALYSES

Comparison 1. Social skills (SSRS)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Primary analysis: Social skills competences	7		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Primary analysis: Teacher-rated social skills competences at end of treatment - all eligible trials	5	392	Std. Mean Difference (IV, Random, 95% CI)	0.16 [-0.04, 0.36]
1.2 Sensitivity analysis:Teacher-rated social skills competences - excluding the trial with longest intervention duration (also largest trial)	4	185	Std. Mean Difference (IV, Random, 95% CI)	0.19 [-0.10, 0.48]
1.3 Teacher-rated social skills competences - longest follow-up	1	18	Std. Mean Difference (IV, Random, 95% CI)	0.06 [-0.86, 0.98]
1.4 Secondary analysis: Parent-rated social skills competences at end of treatment - all eligible trials	7	628	Std. Mean Difference (IV, Random, 95% CI)	0.22 [0.04, 0.40]
1.5 Secondary analysis: Participant-rated social skills competences at end of treatment - all eligible trials	2	188	Std. Mean Difference (IV, Random, 95% CI)	0.21 [-0.09, 0.51]
2 Teacher-rated social skills (Mean Difference)	4	185	Mean Difference (IV, Random, 95% CI)	1.81 [-1.02, 4.64]
3 Parent-rated social skills competences (Mean Difference)	5	313	Mean Difference (IV, Random, 95% CI)	2.82 [-0.92, 6.56]
4 Walker-McConnel Social skills	1	46	Mean Difference (IV, Fixed, 95% CI)	1.06 [-0.47, 2.59]
5 Social skills scale (UCI) parent-rated	1	18	Mean Difference (IV, Fixed, 95% CI)	9.70 [6.07, 13.33]
6 Child social skills knowledge scale	1	18	Mean Difference (IV, Fixed, 95% CI)	4.20 [1.99, 6.41]
7 Social interaction observation - negative behaviour	1	68	Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.11, 0.51]

Comparison 2. General behaviour

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Primary analysis: Teacher-rated general behaviour	3		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 Primary analysis: Teacher-rated general behaviour at end of treatment - all eligible trials	3	358	Std. Mean Difference (IV, Fixed, 95% CI)	7.10 [-0.21, 0.21]
1.2 Sensitivity analysis: Teacher-rated general behaviour excluding the trial with longest intervention duration	2	290	Std. Mean Difference (IV, Fixed, 95% CI)	-0.04 [-0.27, 0.19]
1.3 Sensitivity analysis: Teacher-rated general behaviour excluding the largest trial	2	104	Std. Mean Difference (IV, Fixed, 95% CI)	0.15 [-0.24, 0.53]
1.4 Teacher-rated general behaviour - longest follow-up	2	256	Std. Mean Difference (IV, Fixed, 95% CI)	-0.23 [-0.48, 0.01]
1.5 Secondary analysis: Parent-rated general behaviour at end of treatment	1	254	Std. Mean Difference (IV, Fixed, 95% CI)	-0.26 [-0.51, -0.01]

Comparison 3. ADHD symptoms

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Teacher-rated ADHD symptoms	8		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Primary analysis: Teacher-rated ADHD symptoms at end of treatment -all eligible trials	6	515	Std. Mean Difference (IV, Random, 95% CI)	-0.02 [-0.19, 0.16]
1.2 Sensitivity analysis:Teacher-rated ADHD symptoms excluding the trial with the longest treatment intervention	5	447	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.25, 0.12]
1.3 Sensitivity analysis: Teacher-rated ADHD symptoms at end of treatment excluding the largest trial	5	261	Std. Mean Difference (IV, Random, 95% CI)	0.07 [-0.18, 0.31]
1.4 Teacher-rated ADHD symptoms - longest follow-up	2	79	Std. Mean Difference (IV, Random, 95% CI)	-0.24 [-0.90, 0.41]

1.5 Teacher-rated ADHD symptoms - MTA inattention outcome	1	254	Std. Mean Difference (IV, Random, 95% CI)	0.01 [-0.23, 0.26]
1.6 Teacher-rated Sluggish cognitive tempo end of treatment	1	66	Std. Mean Difference (IV, Random, 95% CI)	-0.29 [-0.78, 0.20]
1.7 Secondary analysis: Parent-rated ADHD symptoms at end of treatment - all eligible trials	7	654	Std. Mean Difference (IV, Random, 95% CI)	-0.49 [-0.79, -0.19]

Comparison 4. Subgroup analysis 1: trials with social skills training without parental training compared to social skills training combined with parental training

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Teacher-rated	1	36	Mean Difference (IV, Fixed, 95% CI)	7.42 [-1.42, 16.25]
1.1 Teacher-rated social skills training with parent training	1	18	Mean Difference (IV, Fixed, 95% CI)	5.60 [-6.78, 17.98]
1.2 Teacher-rated social skills training without parent training	1	18	Mean Difference (IV, Fixed, 95% CI)	9.30 [-3.31, 21.91]

Comparison 5. Subgroup analysis 2: trials with ADHD including comorbidity compared to trials with ADHD and no comorbidity

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Parent-rated ADHD symptoms at end of treatment	7		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Parent-rated ADHD symptoms at end of treatment without comorbidity	1	97	Std. Mean Difference (IV, Random, 95% CI)	-0.78 [-1.19, -0.36]
1.2 Parent-rated ADHD symptoms at end of treatment - with comorbidity	6	557	Std. Mean Difference (IV, Random, 95% CI)	-0.44 [-0.76, -0.11]

Comparison 6. Subgroup analysis 3: trials with social skills training, parental training and medication compared to trials with social skills training and parental training without medication

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Social skills training, parent training, teacher consultations with and without medication	5	331	Std. Mean Difference (IV, Random, 95% CI)	0.26 [-0.04, 0.56]
1.1 Social skills training and parent training with medication	3	244	Std. Mean Difference (IV, Random, 95% CI)	0.19 [-0.10, 0.48]
1.2 Social skills training, parent training without medication	2	87	Std. Mean Difference (IV, Random, 95% CI)	0.64 [-0.48, 1.76]

Analysis 1.1. Comparison 1 Social skills (SSRS), Outcome 1 Primary analysis: Social skills competences.

Review: Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years

Comparison: 1 Social skills (SSRS)

Outcome: 1 Primary analysis: Social skills competences

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 Primary analysis: Teacher-rated social skills competences at end of treatment - all eligible trials							
Pfiffner 1997	9	89.9 (13.5)	9	84.3 (13.3)		4.5 %	0.40 [-0.54, 1.33]
van der Oord 2007	24	36.64 (8.79)	21	35.84 (10.68)		11.5 %	0.08 [-0.51, 0.67]
Waxmonsky 2010	29	30.5 (10.36)	27	31.28 (8.21)		14.4 %	-0.08 [-0.61, 0.44]
Pfiffner 2007	36	90.89 (8.82)	30	86.67 (10.03)		16.4 %	0.44 [-0.05, 0.94]
MTA 1999	108	1.19 (0.3)	99	1.15 (0.32)		53.1 %	0.13 [-0.14, 0.40]
Subtotal (95% CI)	**206**		**186**			**100.0 %**	**0.16 [-0.04, 0.36]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.47$, df = 4 (P = 0.65); $I^2 = 0.0\%$							
Test for overall effect: Z = 1.55 (P = 0.12)							
2 Sensitivity analysis:Teacher-rated social skills competences - excluding the trial with longest intervention duration (also largest trial)							
Pfiffner 1997	9	89.9 (13.5)	9	84.3 (13.3)		9.6 %	0.40 [-0.54, 1.33]
van der Oord 2007	24	36.64 (8.79)	21	35.84 (10.88)		24.6 %	0.08 [-0.51, 0.67]
Waxmonsky 2010	29	30.5 (10.36)	27	31.28 (8.21)		30.7 %	-0.08 [-0.61, 0.44]
Pfiffner 2007	36	90.89 (8.82)	30	86.67 (10.03)		35.1 %	0.44 [-0.05, 0.94]

(*Continued* . . .)

(. . . *Continued*)

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Subtotal (95% CI)	**98**		**87**			**100.0 %**	**0.19 [-0.10, 0.48]**
Heterogeneity: Tau² = 0.0; Chi² = 2.39, df = 3 (P = 0.50); I² =0.0%							
Test for overall effect: Z = 1.27 (P = 0.20)							
3 Teacher-rated social skills competences - longest follow-up							
Pfiffner 1997	9	92.2 (14.2)	9	91.4 (11)		100.0 %	0.06 [-0.86, 0.98]
Subtotal (95% CI)	**9**		**9**			**100.0 %**	**0.06 [-0.86, 0.98]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.13 (P = 0.90)							
4 Secondary analysis: Parent-rated social skills competences at end of treatment - all eligible trials							
Pfiffner 1997	9	86.4 (12.8)	9	72.4 (6.4)		2.8 %	1.32 [0.27, 2.36]
van der Oord 2007	27	48.79 (9.2)	23	46.9 (10.72)		9.3 %	0.19 [-0.37, 0.74]
Waxmonsky 2010	29	43.57 (11.79)	27	45 (8.56)		10.4 %	-0.14 [-0.66, 0.39]
Abikoff 2004	34	88.3 (14.8)	34	80.8 (19.5)		12.1 %	0.43 [-0.05, 0.91]
Pfiffner 2007	36	99.56 (13.91)	33	97.18 (15.72)		12.5 %	0.16 [-0.31, 0.63]
Antshel 2003	80	81.9 (11.8)	40	79.3 (10.6)		18.2 %	0.23 [-0.15, 0.61]
MTA 1999	127	1.22 (0.27)	120	1.17 (0.26)		34.6 %	0.19 [-0.06, 0.44]
Subtotal (95% CI)	**342**		**286**			**100.0 %**	**0.22 [0.04, 0.40]**
Heterogeneity: Tau² = 0.01; Chi² = 6.87, df = 6 (P = 0.33); I² =13%							
Test for overall effect: Z = 2.41 (P = 0.016)							
5 Secondary analysis: Participant-rated social skills competences at end of treatment - all eligible trials							
Abikoff 2004	34	112.6 (19.9)	34	106.3 (23.9)		38.8 %	0.28 [-0.19, 0.76]
Antshel 2003	80	98.5 (9.1)	40	96.95 (10.2)		61.2 %	0.16 [-0.22, 0.54]
Subtotal (95% CI)	**114**		**74**			**100.0 %**	**0.21 [-0.09, 0.51]**
Heterogeneity: Tau² = 0.0; Chi² = 0.15, df = 1 (P = 0.70); I² =0.0%							
Test for overall effect: Z = 1.38 (P = 0.17)							
Test for subgroup differences: Chi² = 0.30, df = 4 (P = 0.99), I² =0.0%							

Analysis 1.2. Comparison 1 Social skills (SSRS), Outcome 2 Teacher-rated social skills (Mean Difference).

Review: Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years

Comparison: 1 Social skills (SSRS)

Outcome: 2 Teacher-rated social skills (Mean Difference)

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Pfiffner 1997	9	89.9 (13.5)	9	84.3 (13.3)		5.2 %	5.60 [-6.78, 17.98]
van der Oord 2007	24	36.64 (8.79)	21	35.84 (10.88)		23.5 %	0.80 [-5.03, 6.63]
Waxmonsky 2010	29	30.5 (10.36)	27	31.28 (8.21)		33.6 %	-0.78 [-5.66, 4.10]
Pfiffner 2007	36	90.89 (8.82)	30	86.67 (10.03)		37.7 %	4.22 [-0.38, 8.82]
Total (95% CI)	**98**		**87**			**100.0 %**	**1.81 [-1.02, 4.64]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 2.61$, df = 3 (P = 0.46); $I^2 = 0.0\%$

Test for overall effect: Z = 1.25 (P = 0.21)

Test for subgroup differences: Not applicable

Analysis 1.3. Comparison 1 Social skills (SSRS), Outcome 3 Parent-rated social skills competences (Mean Difference).

Review: Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years

Comparison: 1 Social skills (SSRS)

Outcome: 3 Parent-rated social skills competences (Mean Difference)

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Antshel 2003	80	81.9 (11.8)	40	79.3 (10.6)		27.5 %	2.60 [-1.58, 6.78]
Pfiffner 1997	9	86.4 (12.8)	9	72.4 (6.4)		11.6 %	14.00 [4.65, 23.35]
Pfiffner 2007	36	99.56 (13.91)	33	97.18 (15.72)		16.9 %	2.38 [-4.65, 9.41]
van der Oord 2007	27	48.79 (9.2)	23	46.9 (10.72)		21.6 %	1.89 [-3.70, 7.48]
Waxmonsky 2010	29	43.57 (11.79)	27	45 (8.56)		22.5 %	-1.43 [-6.80, 3.94]
Total (95% CI)	**181**		**132**			**100.0 %**	**2.82 [-0.92, 6.56]**

Heterogeneity: $Tau^2 = 8.71$; $Chi^2 = 7.91$, df = 4 (P = 0.10); $I^2 = 49\%$

Test for overall effect: Z = 1.48 (P = 0.14)

Test for subgroup differences: Not applicable

Analysis 1.4. Comparison 1 Social skills (SSRS), Outcome 4 Walker-McConnel Social skills.

Review: Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years

Comparison: 1 Social skills (SSRS)

Outcome: 4 Walker-McConnel Social skills

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Bloomquist 1991	20	7.6 (3.06)	26	6.54 (1.94)		100.0 %	1.06 [-0.47, 2.59]
Total (95% CI)	**20**		**26**			**100.0 %**	**1.06 [-0.47, 2.59]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.35 (P = 0.18)

Test for subgroup differences: Not applicable

Analysis 1.5. Comparison 1 Social skills (SSRS), Outcome 5 Social skills scale (UCI) parent-rated.

Review: Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years

Comparison: 1 Social skills (SSRS)

Outcome: 5 Social skills scale (UCI) parent-rated

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Pfiffner 1997	9	32.3 (4.4)	9	22.6 (3.4)		100.0 %	9.70 [6.07, 13.33]
Total (95% CI)	**9**		**9**			**100.0 %**	**9.70 [6.07, 13.33]**

Heterogeneity: not applicable

Test for overall effect: Z = 5.23 (P < 0.00001)

Test for subgroup differences: Not applicable

Analysis 1.6. Comparison 1 Social skills (SSRS), Outcome 6 Child social skills knowledge scale.

Review: Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years

Comparison: 1 Social skills (SSRS)

Outcome: 6 Child social skills knowledge scale

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Pfiffner 1997	9	11.2 (2.8)	9	7 (1.9)		100.0 %	4.20 [1.99, 6.41]
Total (95% CI)	**9**		**9**			**100.0 %**	**4.20 [1.99, 6.41]**

Heterogeneity: not applicable

Test for overall effect: Z = 3.72 (P = 0.00020)

Test for subgroup differences: Not applicable

Analysis 1.7. Comparison 1 Social skills (SSRS), Outcome 7 Social interaction observation - negative behaviour.

Review: Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years

Comparison: 1 Social skills (SSRS)

Outcome: 7 Social interaction observation - negative behaviour

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Abikoff 2004	34	0.6 (0.7)	34	0.4 (0.6)		100.0 %	0.20 [-0.11, 0.51]
Total (95% CI)	**34**		**34**			**100.0 %**	**0.20 [-0.11, 0.51]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.26 (P = 0.21)

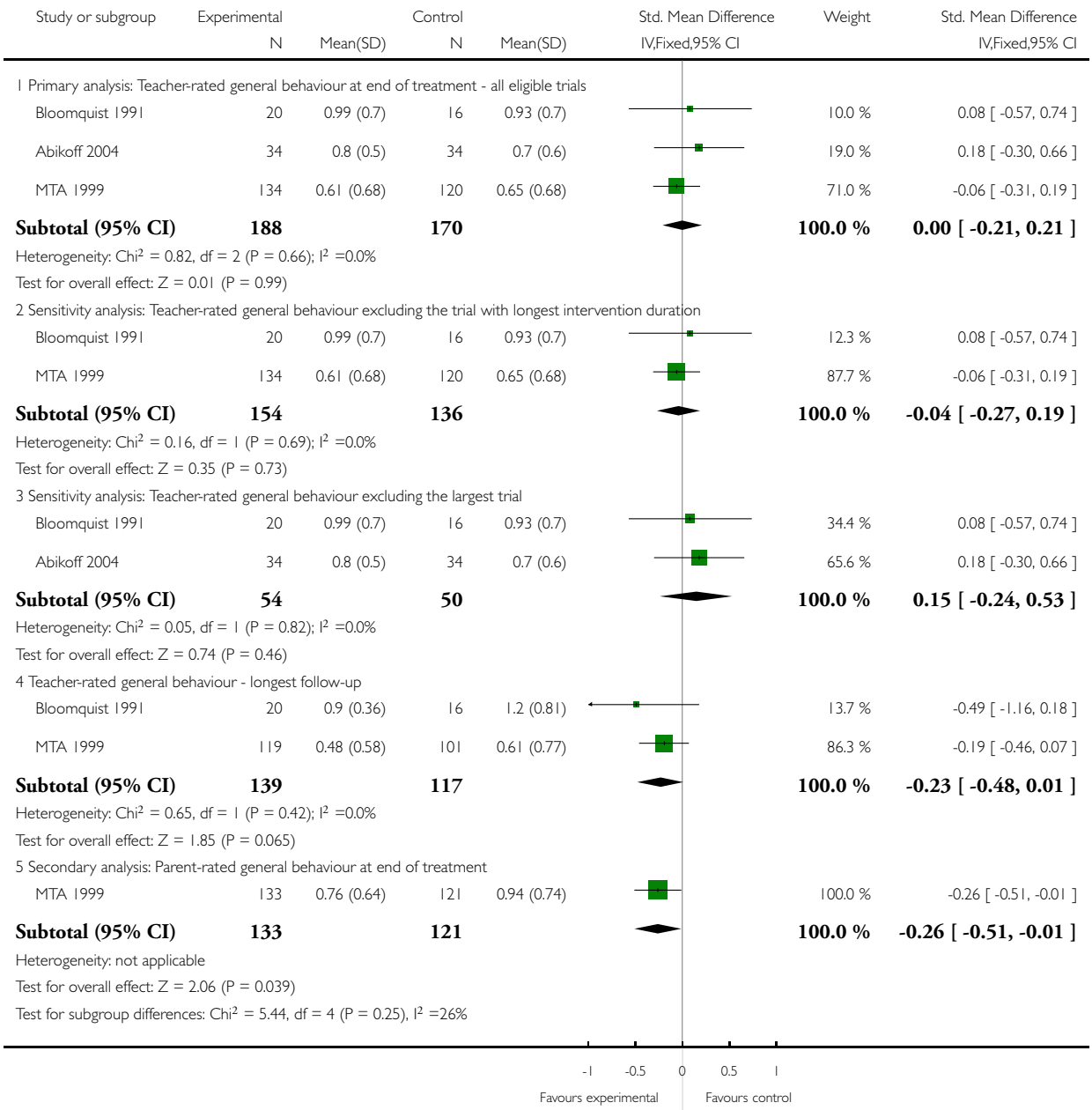
Test for subgroup differences: Not applicable

Analysis 2.1. Comparison 2 General behaviour, Outcome 1 Primary analysis: Teacher-rated general behaviour.

Review: Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years

Comparison: 2 General behaviour

Outcome: 1 Primary analysis: Teacher-rated general behaviour

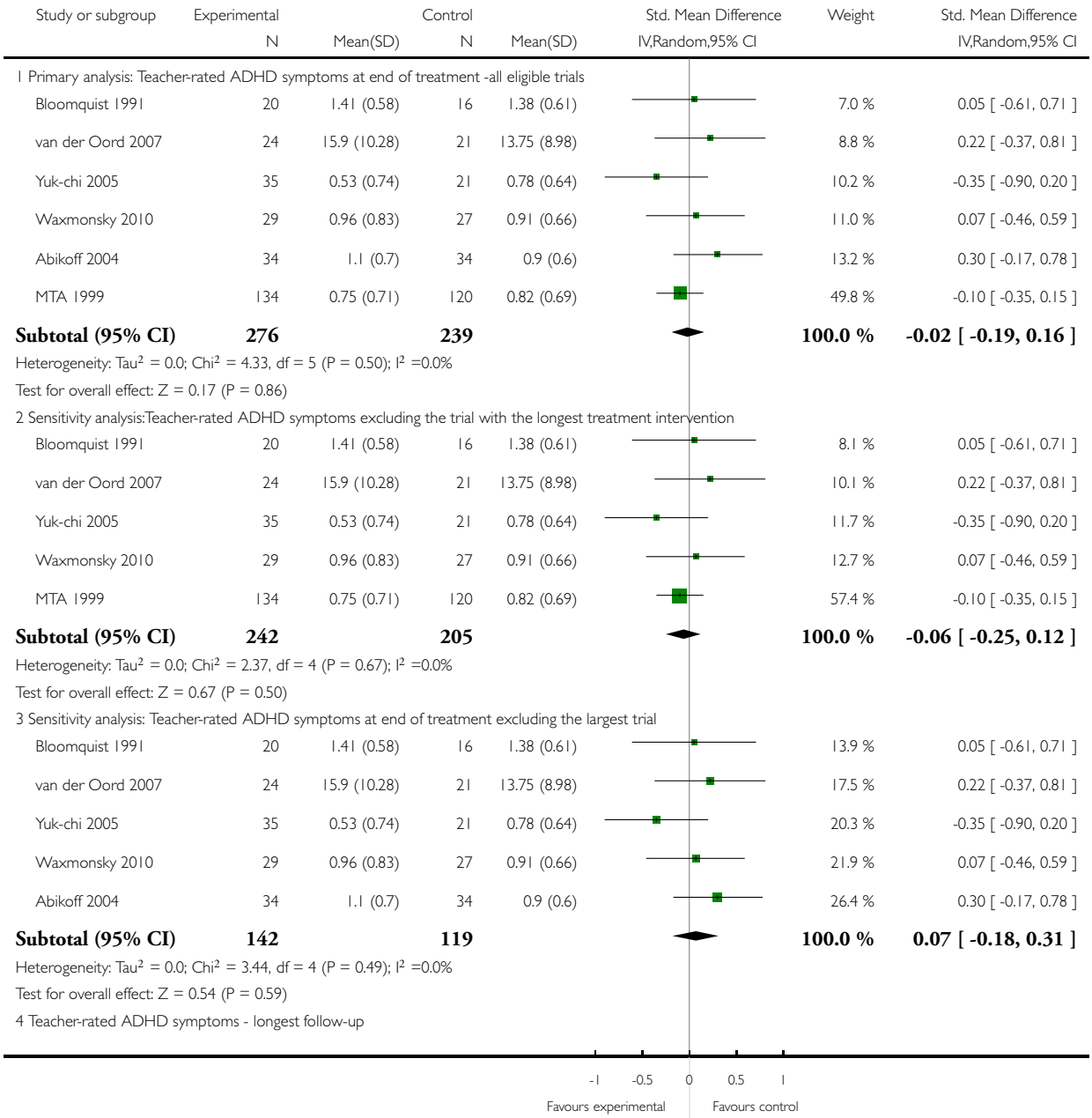


Analysis 3.1. Comparison 3 ADHD symptoms, Outcome 1 Teacher-rated ADHD symptoms.

Review: Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years

Comparison: 3 ADHD symptoms

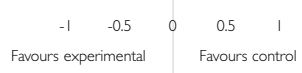
Outcome: 1 Teacher-rated ADHD symptoms



(*Continued . . .*)

(. . . *Continued*)

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Yuk-chi 2005	35	0.47 (0.86)	8	0.37 (0.59)		46.0 %	0.12 [-0.65, 0.89]
Bloomquist 1991	20	1.37 (0.27)	16	1.66 (0.71)		54.0 %	-0.55 [-1.22, 0.12]
Subtotal (95% CI)	**55**		**24**			**100.0 %**	**-0.24 [-0.90, 0.41]**
Heterogeneity: Tau^2 = 0.09; Chi^2 = 1.67, df = 1 (P = 0.20); I^2 =40%							
Test for overall effect: Z = 0.73 (P = 0.47)							
5 Teacher-rated ADHD symptoms - MTA inattention outcome							
MTA 1999	134	1.12 (0.75)	120	1.11 (0.77)		100.0 %	0.01 [-0.23, 0.26]
Subtotal (95% CI)	**134**		**120**			**100.0 %**	**0.01 [-0.23, 0.26]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.10 (P = 0.92)							
6 Teacher-rated Sluggish cognitive tempo end of treatment							
Pfiffner 2007	36	1.2764 (0.5907)	30	1.45 (0.5819)		100.0 %	-0.29 [-0.78, 0.20]
Subtotal (95% CI)	**36**		**30**			**100.0 %**	**-0.29 [-0.78, 0.20]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.16 (P = 0.24)							
7 Secondary analysis: Parent-rated ADHD symptoms at end of treatment - all eligible trials							
van der Oord 2007	24	12.86 (8.08)	21	16.9 (10.77)		11.8 %	-0.42 [-1.01, 0.17]
Waxmonsky 2010	29	0.95 (0.61)	27	1.28 (0.66)		13.0 %	-0.51 [-1.05, 0.02]
Yuk-chi 2005	44	0.56 (0.86)	24	1.32 (0.86)		13.2 %	-0.87 [-1.39, -0.35]
Pfiffner 2007	36	3 (2.1)	30	5.1 (2.5)		13.4 %	-0.91 [-1.42, -0.40]
Abikoff 2004	34	1.2 (0.6)	34	1.2 (0.5)		14.1 %	0.0 [-0.48, 0.48]
Tutty 2003	57	21.15 (8.37)	40	28.3 (10.16)		15.3 %	-0.78 [-1.19, -0.36]
MTA 1999	133	0.85 (0.63)	121	0.91 (0.65)		19.1 %	-0.09 [-0.34, 0.15]
Subtotal (95% CI)	**357**		**297**			**100.0 %**	**-0.49 [-0.79, -0.19]**
Heterogeneity: Tau^2 = 0.11; Chi^2 = 18.87, df = 6 (P = 0.004); I^2 =68%							
Test for overall effect: Z = 3.20 (P = 0.0014)							
Test for subgroup differences: Chi^2 = 10.61, df = 6 (P = 0.10), I^2 =43%							

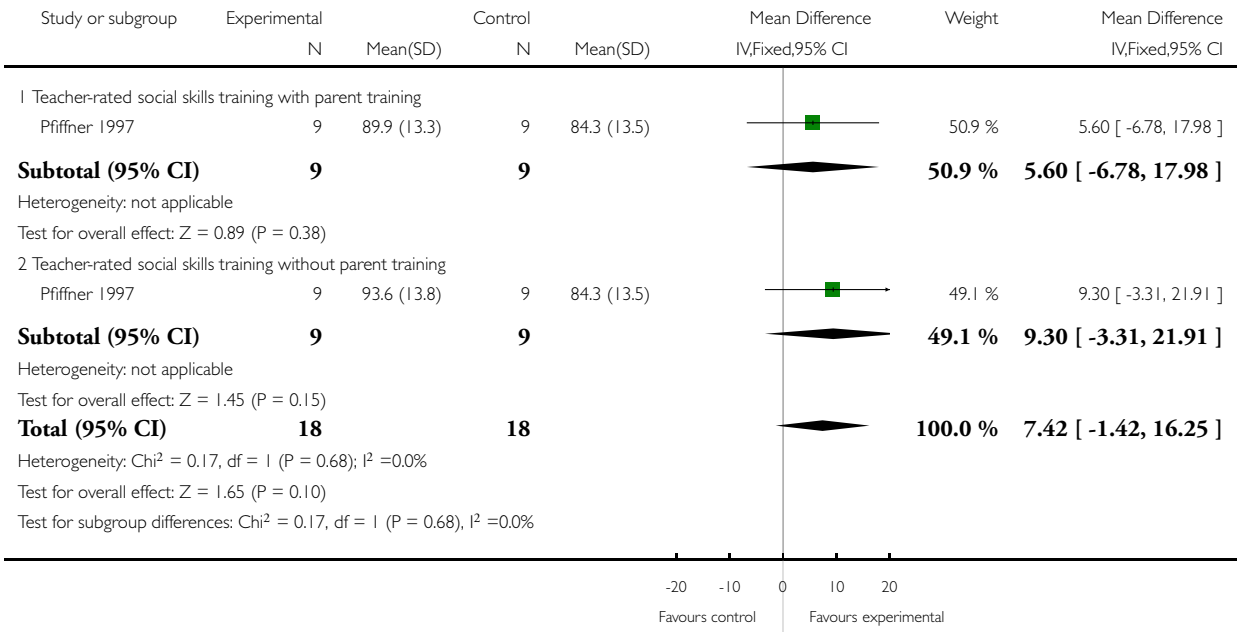


Analysis 4.1. Comparison 4 Subgroup analysis 1: trials with social skills training without parental training compared to social skills training combined with parental training, Outcome 1 Teacher-rated.

Review: Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years

Comparison: 4 Subgroup analysis 1: trials with social skills training without parental training compared to social skills training combined with parental training

Outcome: 1 Teacher-rated

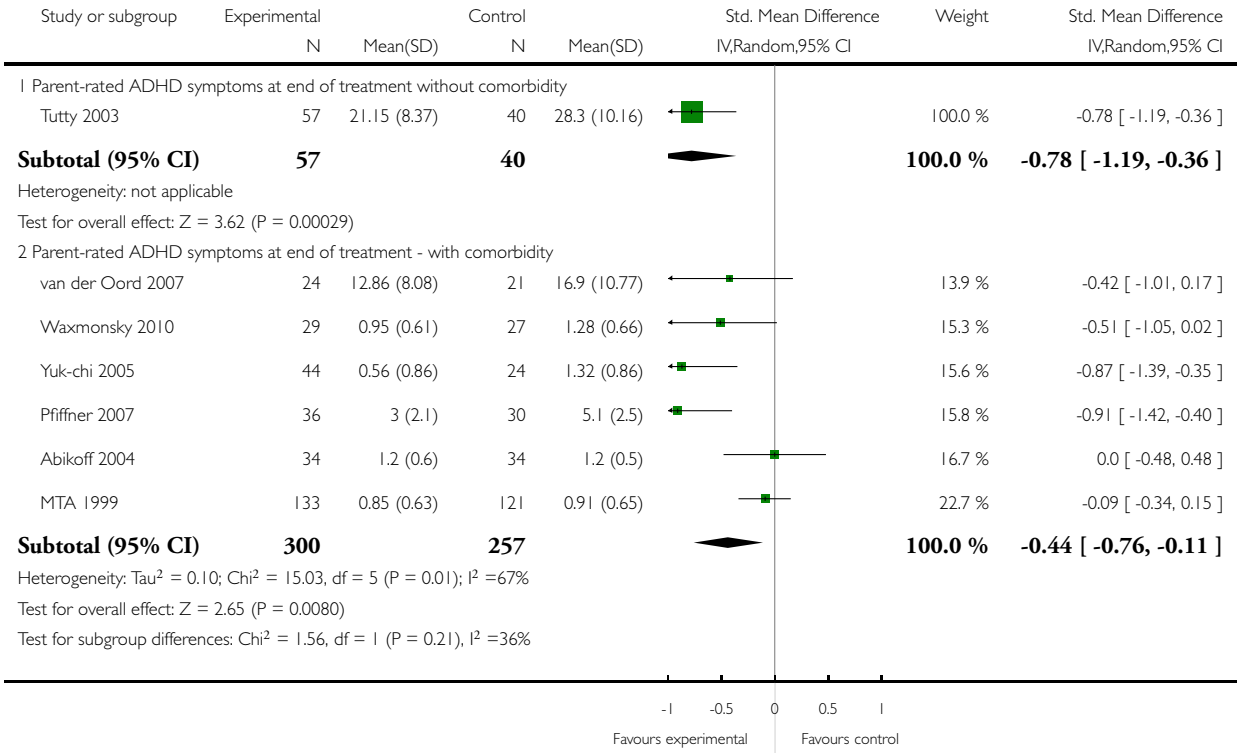


Analysis 5.1. Comparison 5 Subgroup analysis 2: trials with ADHD including comorbidity compared to trials with ADHD and no comorbidity, Outcome 1 Parent-rated ADHD symptoms at end of treatment.

Review: Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years

Comparison: 5 Subgroup analysis 2: trials with ADHD including comorbidity compared to trials with ADHD and no comorbidity

Outcome: 1 Parent-rated ADHD symptoms at end of treatment

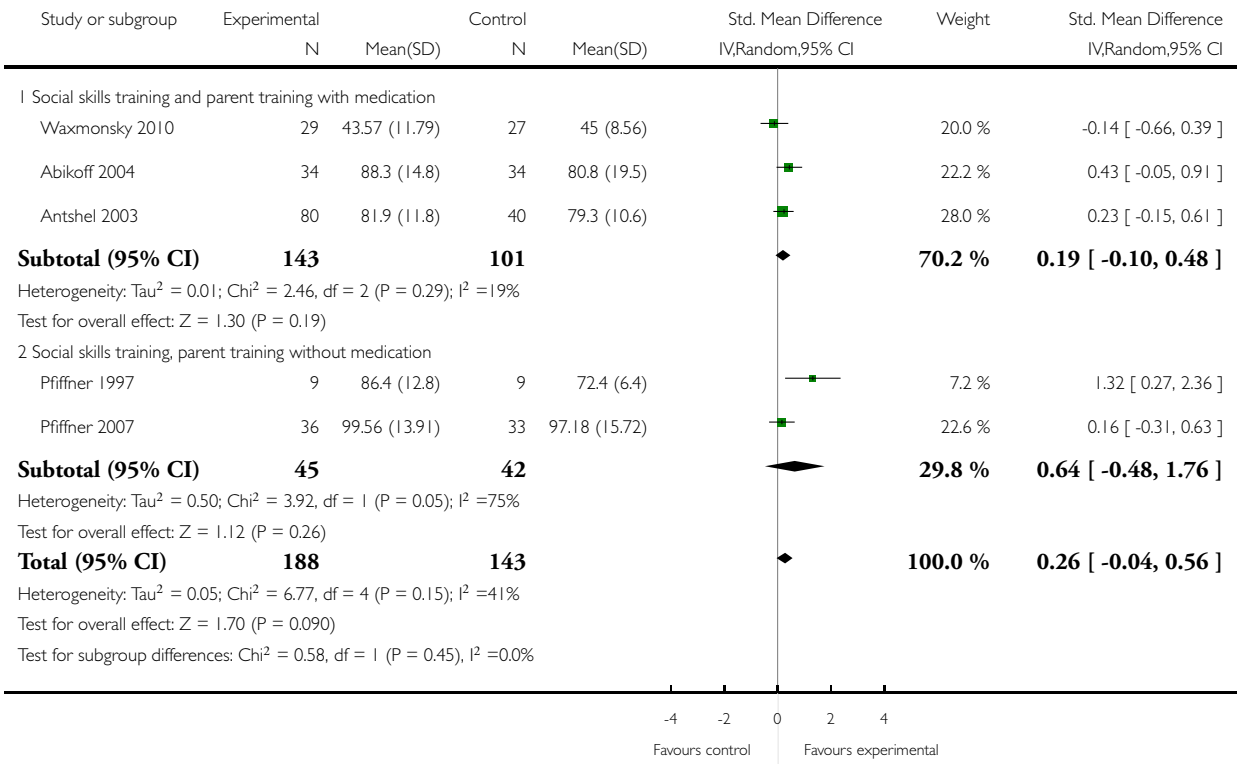


Analysis 6.1. Comparison 6 Subgroup analysis 3: trials with social skills training, parental training and medication compared to trials with social skills training and parental training without medication, Outcome 1 Social skills training, parent training, teacher consultations with and without medication.

Review: Social skills training for Attention Deficit Hyperactivity Disorder (ADHD) in children aged 5 to 18 years

Comparison: 6 Subgroup analysis 3: trials with social skills training, parental training and medication compared to trials with social skills training and parental training without medication

Outcome: 1 Social skills training, parent training, teacher consultations with and without medication



ADDITIONAL TABLES

Table 1. Differences between protocol and review

Protocol	Review
Outcomes: In the protocol we stated that we would measure the two primary and the first two of secondary outcomes at short term (up to six months), medium term (six to 12 months), and long term (more than 12 months) In the protocol we did not prespecify the most important comparisons for the 'Summary of findings' table	In the review this has been changed to at the end of treatment and at the longest follow-up. We have added definition of adverse outcomes according to the International Committee of Harmonization guidelines (ICH 1996). In the review we used our two primary outcomes (teacher-rated social-skills and general behaviour) and the first secondary outcome (ADHD symptoms) in the 'Summary of findings' table

Table 1. Differences between protocol and review (*Continued*)

Subgroup analysis: In the protocol we planned to perform subgroup analysis according to the following categories: 1. Children aged five to 11 years compared to children aged 12 to 18 years. 2. Social skills training in a group setting compared to individual social skills training. 3. Trials with social skills training only compared to trials with social skills training supported by parental training or supporting efforts focused on parents/teachers. 4. Children with ADHD compared to children with ADHD and comorbid behavioural disorders (conduct disorder, oppositional disorder). 5. Children with ADHD plus depression, attachment disorder, or anxiety disorders compared to children with ADHD without these comorbidities. 6. Trials with low risk of bias compared to trials with high risk	In the review it was not possible to perform subgroup analysis 1, 2, 5, and 6 due to lack of sufficient data in the included trials
Risk of bias: In the protocol we had not planned to evaluate blinding of participants and personnel In the protocol we stated that we would only use trials with low risk (or lower risk) of bias in the meta-analysis	In the review we also assessed the blinding of participants and personnel In the review we changed this decision to restrict meta-analysis to trials with comparable risk of bias (for example, all low risk, all unclear, or all the trials are at high risk of bias), and perform sensitivity analyses accordingly
Sensitivity analysis: In the protocol we stated that we would repeat the analysis taking different methods used to handle the missing data into consideration	In the review we did not perform this due to lack of necessary data. We have analysed the data 'as reported'

APPENDICES

Appendix 1. Search strategy

AMED

S37 S20 and S36
S36 S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34 or S35
S35 (DE "PSYCHOTHERAPY GROUP")
S34 TX behaviour modification
S33 TX behavior modification
S32 TX educat* N3 parent*
S31 TX parent education
S30 TX parent training
S29 TX psychosocial treatment
S28 TX role play*
S27 TX social N5 skills
S26 TX learning N5 social

S25 TX behaviour regulation
S24 TX behavior regulation
S23 TX social competence*
S22 TX social skills education
S21 TX social skills training
S20 S9 and S19
S19 S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18
S18 random*
S17 TX (singl* OR doubl* OR tripl* OR trebl*) and TX (blind* OR dummy OR mask*)
S16 TX placebo*
S15 TX crossover
S14 TX allocat*
S13 TX (clin* or control* or compar* or evaluat* or prospectiv*) and TX (trial* or studi* or study)
S12 (DE "RESEARCH DESIGN")
S11 (DE "PLACEBOS")
S10 (DE "TREATMENT OUTCOME")
S9 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8
S8 TX minimal N1 brain N3 damage*
S7 TX minimal N1 brain N3 dysfunction*
S6 TX minimal N1 brain N3 disorder*
S5 TX hyperkinesis*
S4 TX hyperactiv*
S3 TX attention N3 deficit
S2 TX adhd OR addh
S1 (DE "ATTENTION DEFICIT DISORDER WITH HYPERACTIVITY") OR (DE "ATTENTION DEFICIT DISORDER WITHHYPERACTIVITY")

CINAHL

S42 S20 and S41
S41 S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30
or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40
S40 TI behaviour modification or AB behaviour modification
S39 TI behavior modification or AB behavior modification
S38 TI learning N3 social or AB learning N3 social
S37 TI social N3 skills or AB social N3 skills
S36 TI educat* N2 parent* or AB educat* N2 parent*
S35 (MH "Psychotherapy, Group")
S34 (MH "Role Playing")
S33 TX parent education
S32 TX parent training
S31 TX psychosocial treatment
S30 TX behaviour regulation
S29 TX behavior regulation
S28 TX social competence*
S27 TX social skills education
S26 TX social skills training
S25 (MH "Social Skills")
S24 (MH "Social Behavior+/ED")
S23 (MH "Interpersonal Relations+/ED")
S22 (MH "Social Skills Training")
S21 S9 and S19
S20 S9 and S19
S19 S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18

S18 TX (singl* OR doubl* OR tripl* OR trebl*) and TX (blind* OR mask* OR dummy*)
S17 TX clin* N25 trial*
S16 (MH "Placebos")
S15 TX placebo* OR random*
S14 TX control* OR prospectiv* OR volunteer*
S13 (MH "Evaluation Research+")
S12 (MH "Prospective Studies+")
S11 PT clinical trial
S10 (MH "Clinical Trials+")
S9 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8
S8 TX minimal N1 brain N3 damage*
S7 TX minimal N1 brain N3 dysfunction*
S6 TX minimal N1 brain N3 disorder*
S5 TX hyperkinesis*
S4 TX hyperactiv*
S3 TX attention N3 deficit
S2 TX adhd or addh
S1 (MH "Attention Deficit Hyperactivity Disorder")

Cochrane Library (CR and CENTRAL)
#1 (intellect* disabl*):ti,ab,kw
#2 MeSH descriptor Attention Deficit Disorder with Hyperactivity explode all trees
#3 (adhd or addh):ti,ab,kw
#4 (attention near/3 deficit):ti,ab,kw
#5 (hyperactiv*):ti,ab,kw
#6 (hyperkinesis*):ti,ab,kw
#7 MeSH descriptor Hyperkinesis explode all trees
#8 (minimal brain near/3 disorder*):ti,ab,kw
#9 ((minimal brain near/3 dysfunction*) or (minimal brain near/3 damage*)):ti,ab,kw
#10 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9)
#11 (social skill training):ti,ab,kw
#12 (social skills education):ti,ab,kw
#13 (social competen*):ti,ab,kw
#14 ((behavior regulation) or (behaviour regulation)):ti,ab,kw
#15 (social near/10 skills):ti,ab,kw
#16 (learning near/25 social):ti,ab,kw
#17 (role play*):ti,ab,kw
#18 (psychosocial treatment):ti,ab,kw
#19 (parent education):ti,ab,kw
#20 (educat* near/10 parent*):ti,ab,kw
#21 MeSH descriptor Psychotherapy, Group explode all trees
#22 (behavior modification):ti,ab,kw
#23 (behaviour modification):ti,ab,kw
#24 (parent training):ti,ab,kw
#25 (#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19
OR #20 OR #21 OR #22 OR #23 OR #24)
#26 (#10 AND #25)
EMBASE
1 exp Attention Deficit Disorder/
2 adhd.mp.
3 addh.mp.
4 exp Hyperactivity/
5 Hyperkinesia/

6 (attention adj3 deficit).mp.
7 hyperactiv*.mp.
8 hyperkinesis*.mp.
9 (minimal adj brain adj3 disorder*).mp.
10 (minimal adj brain adj3 dysfunction*).mp.
11 (minimal adj brain adj3 damage*).mp. 79
12 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13 social skills training.mp.
14 social skills education.mp.
15 social competence*.mp.
16 behavior regulation.mp.
17 behaviour regulation.mp.
18 (learning adj25 social).mp.
19 (social adj10 skills).mp.
20 role play*.mp.
21 psychosocial treatment.mp.
22 parent training.mp.
23 parent education.mp.
24 (educat* adj10 parent*).mp.
25 exp behavior modification/
26 exp group therapy/
27 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26
28 controlled study.de.
29 clinical trial.de.
30 major clinical study.de.
31 randomized controlled trial.de.
32 double blind procedure.de.
33 clinical article.de.
34 random$.mp.
35 control$.mp.
36 follow up.mp.
37 ((singl$ or doubl$ or tripl$ or trebl$) adj (blind$ or mask$ or dummy)).mp.
38 placebo$.mp.
39 (clinic$ adj (trial$ or study or studies$)).mp.
40 exp comparative study/
41 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40
42 12 and 27 and 41

ERIC

Block A

DE=Attention deficit disorders
DE=Attention deficit hyperactivity disorder
DE=Hyperactivity
adhd or addh
attention within 3 deficit
hyperkines*
(minimal within 1 brain within 3 disorder*)
(minimal within 1 brain within 3 dysfunction*)
(minimal within 1 brain within 3 damage*)

Block B

kw=randomi*
kw=(random* NEAR (allocat* OR allot* OR assign* OR basis OR divid* OR order))
kw=(random* NEAR (trial* OR study OR studies))
kw=((control* OR clinic* OR prospectiv*) WITHIN 5 (trial* OR study OR studies))

kw=(allocat* OR allot* OR assign* OR divid* OR order*)) NEAR
(kw=((compar* OR control* OR experiment* OR internvent* OR therap* OR treatment) NEAR (group* OR class*))
kw=((singl* OR doubl* OR trebl* OR tripl*) NEAR (blind* OR mask*))
kw=crossover OR (cross WITHIN 1 over)
kw=latin WITHIN 1 square
kw=placebo*
kw=(compar* WITHIN 5 (trial* OR study OR studies))
kw=((clinic* OR control*) NEAR (trial* OR study* OR studies*))

Block C

DE=("interpersonal competence" or "daily living skills" or "emotional intelligence" or "extraversion introversion" or "interpersonal communication" or "prosocial behavior" or "sharing behavior" or "sensitivity training" or "interpersonal relationship" or "board administrator relationship" or "caregiver child relationship" or "collegiality" or "counselor client relationship" or "dating social" or "employer employee relationship" or "family relationship" or "parent child relationship" or "parent student relationship" or "sibling relationship" or "friendship" or "group unity" or "helping relationship" or "interpersonal attraction" or "interprofessional relationship" or "supervisor supervisee relationship" or "teacher administrator relationship" or "marriage" or "teacher student relationship" or "parent caregiver relationship" or "peer relationship" or "physician patient relationship")
DE=behavior modification
DE=("group therapy" or "group counseling" or "sensitivity training")
DE=("role playing" or "dramatic play")
DE=parent education
kw=social skills training
kw=social skills education
kw=social competenc*
kw=behavior regulation
kw=behaviour regulation
kw=(learning WITHIN 5 social)
kw=(social WITHIN 5 skills)
kw=psychosocial treatment
kw=parent training
kw=educat* WITHIN 3 parent*

A and B and C

Medline

1 exp Attention Deficit Disorder with Hyperactivity/
2 adhd.mp.
3 addh.mp.
4 (attention adj3 deficit).mp.
5 hyperactiv$.mp.
6 hyperkinesis$.mp.
7 exp Hyperkinesis/
8 (minimal adj brain adj3 disorder$).mp.
9 (minimal adj brain adj3 dysfunction$).mp.
10 (minimal adj brain adj3 damage$).mp.
11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12 social skills training.mp.
13 social skills education.mp.
14 social competenc$.mp.
15 behavior regulation.mp.
16 behaviour regulation.mp.
17 (social adj10 skills).mp.
18 (learning adj25 social).mp.
19 role play$.mp.

20 psychosocial treatment.mp.
21 parent education.mp.
22 (educat$ adj10 parent$).mp.
23 exp psychotherapy, group/
24 behavior modification.mp.
25 behaviour modification.mp.
26 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25
27 randomized controlled trial.pt.
28 controlled clinical trial.pt.
29 randomized controlled trials.mp.
30 random allocation.mp.
31 double blind method.mp.
32 single blind method.mp.
33 clinical trial.pt.
34 (clin$ adj25 trial$).ti,ab.
35 ((singl$ or doubl$ or tripl$ or trebl$) adj25 (blind$ or mask$ or dummy$)).mp.
36 exp clinical trial/
37 placebos.mp.
38 placebo$.ti,ab.
39 random$.ti,ab.
40 comparative study.mp.
41 evaluation studies as topic/
42 exp clinical trials as topic/
43 follow up studies.mp.
44 prospective studies.mp.
45 (control$ or prospectiv$ or volunteer$).ti,ab.
46 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45
47 11 and 26 and 46

PsycINFO

1 exp attention deficit disorder/
2 adhd.mp.
3 addh.mp.
4 (attention adj3 deficit).mp.
5 hyperactiv$.mp.
6 hyperkinesis$.mp.
7 exp Hyperkinesis/
8 (minimal adj brain adj3 disorder$).mp.
9 (minimal adj brain adj3 dysfunction$).mp.
10 (minimal adj brain adj3 damage$).mp.
11 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12 exp Social Skills Training/
13 exp Social Skills/
14 Skill Learning/
15 exp Human Relations Training/
16 exp Parent Training/
17 social skills training.mp.
18 social skills education.mp.
19 social competence$.mp.
20 behavior regulation.mp.
21 (social adj10 skills).mp.
22 (learning adj25 social).mp.
23 role play$.mp.
24 exp Communication skills training/

25 psychosocial treatment.mp.
26 exp Assertiveness training/
27 exp Behavior modification/
28 behaviour regulation.mp.
29 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28
30 random$.mp.
31 ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or dummy or mask$)).mp.
32 placebo$.mp.
33 crossover.mp.
34 assign$.mp.
35 allocat$.mp.
36 ((clin$ or control$ or compar$ or evaluat$ or prospectiv$) adj25
(trial$ or studi$ or study)).mp.
37 exp placebo/
38 exp treatment effectiveness evaluation/
39 exp mental health program evaluation/
40 exp experimental design/
41 versus.id.
42 vs.id.
43 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42
44 11 and 29 and 43

Sociological Abstracts

((DE="attention deficit disorder") or(adhd or addh) or(hyperactiv* OR hyperkines*) or(minimal within 1 brain within 3 disorder*) or(minimal within 1 brain within 3 dysfunction*) or(minimal within 1 brain within 3 damage$) or(attention within 3 deficit)) and(((kw=randomi*) or(kw=(random* NEAR (allocat* OR assign* OR divid*))) or(kw=(random* NEAR (trial* OR study OR studies))) or(kw=((control* OR clinic* OR prospectiv*) WITHIN 5 (trial* OR study OR studies))) or(kw=((allocat* OR assign* OR divid*) WITHIN 5 (condition* OR experiment* OR treatment* OR control* OR group*))) or(kw=((singl* OR doubl*) NEAR (blind* OR mask*))) or(kw=placebo*) or(kw=(crossover OR cross over)) or(kw=(compar* WITHIN 5 (trial* OR study OR studies)))) and(DE=(health OR medicine OR illness)))

***meta* Register of Controlled Trials**

((Attention Deficit Disorder Hyperactivity) OR adhd OR addh OR hyperactive% OR hyperkines% OR (minimal brain disorder%) OR (minimal brain dysfunction) OR (minimal brain damage%)) AND ((social skills training) OR (social skills education) or (social competenc%) OR (behavior regulation) or (behaviour regulation) OR (social skill%) or (role play%) OR (psychosocial treatment) or (parent education) OR (group therapy) or (group psychotherapy) OR (behavior modification))

Appendix 2. Data extraction sheet

Version nr.: 1:1-MS 08 10 2010

Til notater:

Source

Study ID	
Report ID	
Year of publication Year of trial conduct	
Review author	
Citation source Authors (2-3)	

Eligibility

Confirm eligibility	
Reasons for exclusion	

Study

Design (eg, randomized, blinded, placebo, etc.)		
Location (eg, hospital, out clinic)		
Duration of trial		
Inclusion criteria		
Exclusion criteria		
Outcomes listing	Primary	
	Secondary	

Risk of bias

Item	Judgement (low/ uncertain/ high)	Adequacy (yes/ unclear/no)	Descriptions
Sequence generation			Quote: Comment:
Randomization			Quote: Comment:
Allocation concealment			Quote: Comment:
Blinding of participants, personnel and outcome assessors			Quote: Comment:
Incomplete outcome data			Quote: Comment:
Selective outcome reporting			Quote: Comment:
Baseline imbalance			Quote: comment:
Early stopping			Quote: Comment:
Invested interest bias			Quote: Comment:
Other sources of bias			Quote: Comment:

Participants

Sample size or power calculation (yes/no)	Quote: Comment:
Total number (sample size)	Pre-randomisation
	Post -randomisation
Diagnostic criteria (for example, ICD-10 nr., DSM IV nr. or by a cut of score from	

(*Continued*)

report)	
Age	
Sex	
Comorbidity	
Socio-demographics (for example, double or single parent families, low, middle or upper class)	
Country/Ethnicity	
Co-medication	

Interventions

Intervention groups
Number of participants allocated per group
Number of patients lost to follow up per group
Format and duration of the intervention (eg, group base, individual, and setting)
Specific intervention (eg, type of programe) and by whom (eg, nurse, psychologist, teacher)
Content of the intervention
Treatment compliance (treatment to manual and participant to treatment)

Outcomes

Outcomes specified	Reported (yes/no)	Definition and unit of measurement	Type of scale	Summary statistic for each intervention group Short medium or long term

Miscellaneous

Funding source
Key conclusions of the study authors
References to other relevant studies
Correspondence required
Miscellaneous comments from the study authors
Miscellaneous comments from the review authors

FEEDBACK

Comments on protocol by Peter Gøtzche, 16 February 2010

Summary

1. The Background notes that drugs have a beneficial effect on major symptoms in about 80% of the patients treated. Such a statement is meaningless when we don't know what the effect was in groups treated with placebo. The authors need to rectify this so that the readers can understand what the effect is.

2. Social skills training is the focus of the review and the authors state that "We have been unable to identify meta-analyses or systematic reviews on the topic". This statement is a bit surprising. A quick and simple search on PubMed on "(attention deficit hyperactivity disorder children) AND training", limited to meta-analysis, yielded 7 hits, of which one appears to be highly relevant for the authors' review, as they also want to review combination therapy: Majewicz-Hefley A, Carlson JS. A meta-analysis of combined treatments for children diagnosed with ADHD. J Atten Disord. 2007 Feb;10(3):239-50.

3. The following reference may also be relevant, particularly as the authors of the Cochrane protocol mention that training may increase negative behaviour, with reference to a single study. In contrast, based on its abstract, this reference seems to be to a meta-analysis, and had different findings: Weiss B, Caron A, Ball S, Tapp J, Johnson M, Weisz JR. Latrogenic effects of group treatment for antisocial youths. J Consult Clin Psychol. 2005 Dec;73(6):1036-44

Reply

We thank Peter Gøtzsche for his interest in our review and for raising the comments.

Point 1

Peter Gøtzsche is correct that only giving the proportion of patients who respond to the active intervention and leaving out the response proportion among placebo-treated patients does not inform the reader with regard to the relative risk reduction between the two. We will amend the protocol accordingly to make it explicit that the response proportion of response from 'stimulant' drugs is about 80% while the placebo response proportion is about 3% to 10%, leading to a relative risk reduction of at least 77%. We thus acknowledge Peter Gøtzsche's vigilance, and have now taken steps to correct the mistake.

Point 2

We would argue, regarding this point, that the truth may be more complex than the statement above. Six of the meta-analyses identified by Dr Gøtzsche are not relevant to our review. The seventh, to which he makes particular reference, is potentially relevant. This is the meta-analysis by Majewicz-Hefley and Carlson (2007). The meta-analysis includes a total of eight studies. The article divides the outcomes into five different categories of outcome variables. The Social Skills variable was based on four studies. Two of the four studies are not relevant for our review. One concerns behaviour therapy (and not social skills training); the other one is not a randomised trial. That leaves two studies in the meta-analysis of the social skills outcome variable, which we could have mentioned in the protocol, but chose not to. Both studies will of course be considered for the review, and be cited there.

Point 3

Our point in the protocol here was simply to show that we are aware of the possibility that group training can have adverse effects. We could have found articles (or meta-analyses) that suggested the opposite, viz., that group training of children with attention deficit hyperactivity disorder (ADHD) or conduct disorder has positive effects, as this finding is more common, but this also would have not been pertinent. Furthermore, the article Peter Gøtzsche refers to concerns antisocial youths, and this population is not the same as that diagnosed with ADHD or conduct disorder.

Contributors

This feedback was prepared by Jane Dennis, feedback editor for CDPLPG, in consultation with the submitter, the authors, the CDPLPG Co-ordinating Editor Geraldine Macdonald and the former CDPLPG Managing Editor Chris Champion.

HISTORY

Protocol first published: Issue 1, 2010

Review first published: Issue 12, 2011

Date	Event	Description
14 April 2010	Amended	US FDA reference corrected
16 March 2010	Feedback has been incorporated	Feedback comments from Peter Gøtzsche incorporated

CONTRIBUTIONS OF AUTHORS

Ole Jakob Storebø: development of protocol, selection of trials, data extraction, risk of bias assessment of studies, data analysis, contact person, development of the final review.

Maria Skoog: development of protocol, data extraction, risk of bias assessment of trials, development of the final review.

Dorte Damm: development of protocol, selection of trials.

Per Hove Thomsen: selection of trials, development of the final review.

Erik Simonsen: risk of bias assessment of trials, development of the final review.

Christian Gluud: development of protocol, advising on statistical methods and analysis, development of the final review.

DECLARATIONS OF INTEREST

Christian Gluud, Maria Skoog, Erik Simonsen, and Per Hove Thomsen have been involved in the design of a trial that is potentially eligible for inclusion in this review. Ole Jakob Storebø is lead investigator on the trial and Erik Simonsen is the sub-investigator. Details of the trial can be found at ClinicalTrials.gov (identifier: NCT 00937469).

Per Hove Thomsen has received fees for lecturing on behalf of the pharmacological companies: NOVARTIS and UCB and lecturing and consulting on behalf of Eli-Lilly. He also serves on the advisory board of Eli-Lilly.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- CopenhagenTrial Unit, Denmark.
- Research Library, Unit for Psychiatric Research, Region Zealand, Roskilde, Denmark.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

See Table 1.

NOTES

An administrative error was made in the first published version of the protocol and important information about the declaration of interest of the authors was not included in the publication. This has now been rectified.

TRIALS

STUDY PROTOCOL Open Access

Randomised social-skills training and parental training plus standard treatment versus standard treatment of children with attention deficit hyperactivity disorder - The SOSTRA trial protocol

Ole Jakob Storebø[1,2,3,6*], Jesper Pedersen[1], Maria Skoog[3], Per Hove Thomsen[4,8], Per Winkel[3], Christian Gluud[3,5], Erik Simonsen[2,6,7]

Abstract

Background: Children with attention deficit hyperactivity disorder (ADHD) are hyperactive and impulsive, cannot maintain attention, and have difficulties with social interactions. Medical treatment may alleviate symptoms of ADHD, but seldom solves difficulties with social interactions. Social-skills training may benefit ADHD children in their social interactions. We want to examine the effects of social-skills training on difficulties related to the children's ADHD symptoms and social interactions.

Methods/Design: The design is randomised two-armed, parallel group, assessor-blinded trial. Children aged 8-12 years with a diagnosis of ADHD are randomised to social-skills training and parental training plus standard treatment versus standard treatment alone. A sample size calculation estimated that at least 52 children must be included to show a 4-point difference in the primary outcome on the Conners 3rd Edition subscale for 'hyperactivity-impulsivity' between the intervention group and the control group. The outcomes will be assessed 3 and 6 months after randomisation. The primary outcome measure is ADHD symptoms. The secondary outcome is social skills. Tertiary outcomes include the relationship between social skills and symptoms of ADHD, the ability to form attachment, and parents' ADHD symptoms.

Discussion: We hope that the results from this trial will show that the social-skills training together with medication may have a greater general effect on ADHD symptoms and social and emotional competencies than medication alone.

Trial registration: ClinicalTrials (NCT): NCT00937469

Background

Attention deficit hyperactivity disorder (ADHD) affects 3% to 5% of all children [1]. The main ADHD symptoms consist of problems with attention, impulsiveness, and hyperactivity [2,3]. Pharmacological treatment of children and adolescents with ADHD has beneficial effects on these symptoms in about 80% of the patients [4-12]. However, many children and adolescents with ADHD also frequently have difficulties regarding language, learning, anxiety, and interaction with parents and teachers. These difficulties can be severe, and there is little evidence that medication has an effect on these outcome measures [13-17]. Children with ADHD also have an increased risk of developing personality disturbance and possibly psychotic conditions, abuse of drugs or alcohol, and criminality [18-24]. Comorbid disorders in children with ADHD often include behavioural disorders, depression, anxiety, tics, motor skill development disturbance, learning difficulties, and verbal and cognitive difficulties [25,26].

* Correspondence: ojst@regionsjaelland.dk
[1]Child Psychiatric Daytime Clinic, Child and Adolescent Psychiatric Centre, Region Zealand, Holbaek, Denmark
Full list of author information is available at the end of the article

Social-skills training

Social-skills training aims to develop, improve, and maintain the individual's social skills. This is achieved by teaching how to regulate verbal and nonverbal behaviours involved in social interactions and in compliance with social norms [27,28]. The main elements in social-skills training include training of social skills and efforts to change the individual's cognitive assessment of the 'social world' and to develop these cognitive skills (Fohlmann AH: E-mail correspondence in April 2009). Concretely, the training focuses on teaching the children to read the subtle cues in social interactions, such as learning to wait for their turn or knowing when to shift topics during a conversation and being able to recognise the emotional expressions of others. A few randomised clinical trials suggest that social-skills training may help children with ADHD [29-31]. Other studies indicate that only some children benefit from social-skills training, possibly due to lack of parental engagement in the training [32]. Like with medical treatment, the effects of social-skills training do not always appear to endure over time. It is even argued that social-skills training groups can have a negative effect on children with behavioural problems because the aggressive and restless behaviour in itself can limit the ability to learn social skills [33]. We have been unable to identify any meta-analyses or systematic reviews on the topic.

Abilities in forming attachments

A child's ability to form attachments is developed in early childhood through interaction with primary caregivers. Different forms of attachment are secure, insecure dismissing, insecure preoccupied, and disorganised. It is assumed that these different forms of attachment will influence the outcome of social-skills training. A connection between early disorganised attachment and later ADHD has been demonstrated by Punto et al. [34], who followed children from birth to 7 years of age.

The primary aim of the SOSTRA trial is to examine the effect of the combination of social-skills training and parental training plus standard treatment versus standard treatment alone in children with ADHD and their families on the outcome measures of ADHD core symptoms, social skills, and the attachment between the child and the parents.

Methods/Design

Children aged 8-12 years with a diagnosis of ADHD and their parents are randomised to the combination of social-skills training and parental training plus standard treatment versus standard treatment alone. The trial flowchart is shown in Figure 1. The trial is a randomised two-armed, parallel group, assessor-blinded trial. The children will be examined at entry, 3 months, and 6 months after randomisation.

Experimental intervention

Children and parents randomised to the experimental intervention are included in 1 of 4 identical 8-week social-skills treatment programs with 12 to 16 participants per program. Here, the children are offered weekly social-skills training sessions of 90 minutes in duration. During that time, the parents attend parental training. Each group has two therapists who have been trained in management of social-skills training at Langager School in Aarhus [35]. The experimental interventions are thoroughly described in a manual, and each session with the children will be video recorded. The group sessions are planned to be on the same day and at the same time every week, just as the structure and the agenda of the sessions will be the same. The experimental intervention program is organized similarly to other randomised trials [29-31] and with supervision from the Langager School. Different methods of teaching the children social skills are used, all of which have proved successful in other social-skills programs [36]. These include didactic instructions, work with symbols (e.g. dolls), role-play, creative techniques, physical exercises, music, story reading, games, and movies. Each session has a theme, such as self worth, nonverbal communication, feelings, impulse control, aggression management, conflict resolution, and problem solving. The themes are connected to the trials outcome measures of ADHD core symptoms, social skills, and the attachment between the child and the parents.

Social skills are based on the broad area of cognition and emotions. The iceberg model (Division TEACCH, North Carolina, USA) emphasizes the importance of considering each child's problems and resources distinctly and incorporating these in the training programme. For instance, some children may need more sessions with visualization techniques to better learn the management of aggression. When they get better at managing their aggression, they will also be able to improve their social skills. The social-skills experimental intervention will focus on strengthening the ability of the children to control themselves and start a self-help process. For the parents, efforts will be directed at helping them develop strategies to assist their children in controlling their impulses. It is important that this training equips the children and parents with the skill to cope better and to reverse the bad circles. The efficacy of the experimental intervention will be assessed by improvements in ADHD symptoms and social skills per se or by assessing psychological functioning on a broader aspect, including the quality of peer relationships and emotional competencies.

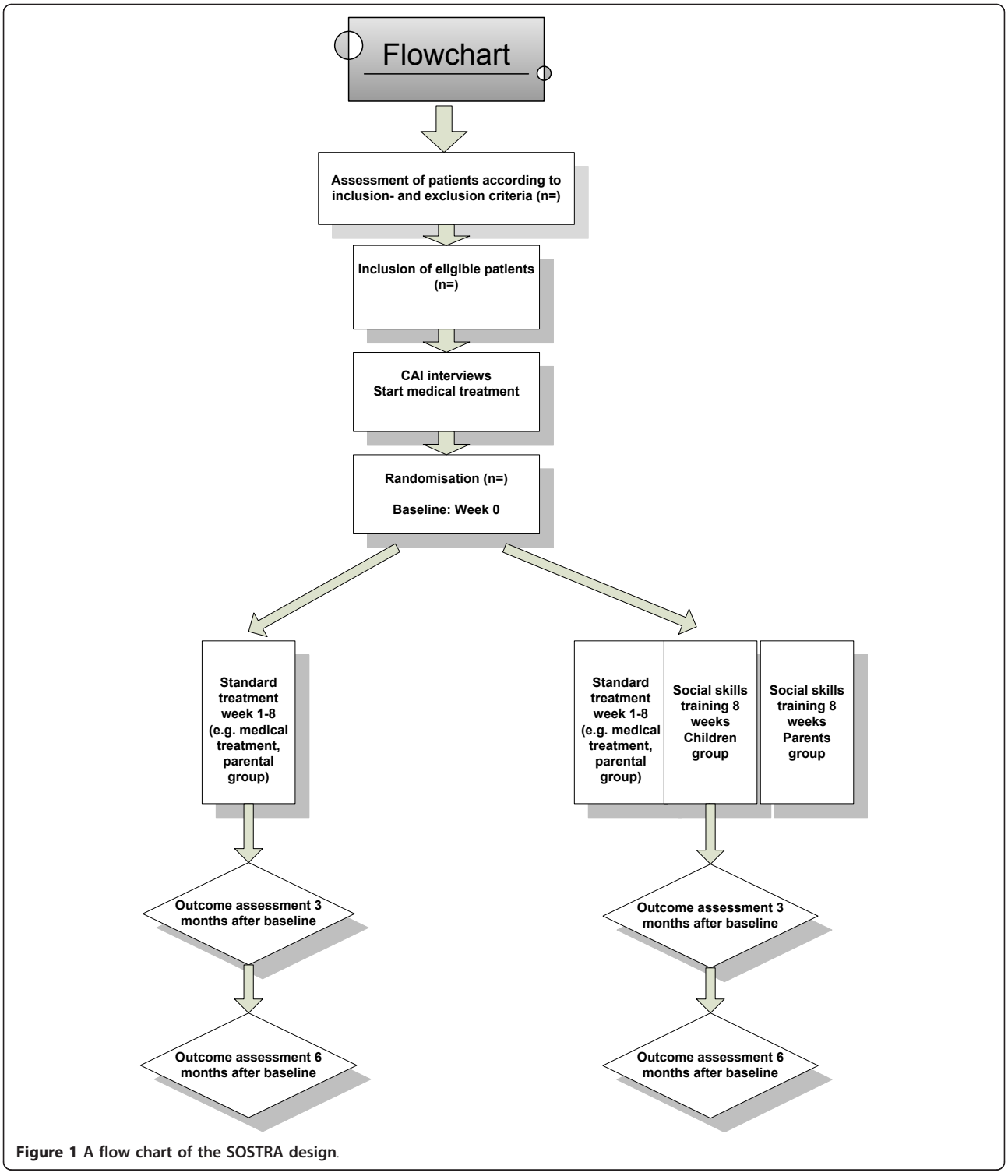


Figure 1 A flow chart of the SOSTRA design.

Efforts must be made to create a safe environment in the group. The children should feel safe enough to play and experiment with exploring their own and other people's understanding of them along with understanding the other participants and the different topics in focus. The assignments must be clear and simple. The educational style in the groups will take into account the children's special cognitive difficulties; accordingly, the structure in each session will be predictable. This is secured by regular items on the agenda, which are

written on the blackboard every time: Opening round–what has happened since the last time? — revision of the previous session; homework from previous session; presentation/education; role play/creative activities; new homework; closing round.

The therapists must be clear and direct but not confrontational or critical. Weight is attached to empathy, positive reinforcement, and a curious 'non-knowing' mentalizing attitude. A relaxed atmosphere with room for humour is the aim.

The therapists who are responsible for the children's group in the experimental intervention arm are also responsible for the parents' group in the standard treatment arm. This risk of bias will be limited by writing the detailed manual that will describe the content in each group. Content forms are to be completed by the therapists after each group sessions and will function as a control of the content of the sessions given.

In the parental groups, the themes from the children's groups will be presented and discussed. Likewise, the children's homework will be discussed and parents are encouraged to discuss their specific problems with their children and there will be an exchange of experiences among the participants.

Standard treatment

The standard treatment offered to both the experimental group and the control group encompasses the normal practice regarding ADHD patients at the Child Psychiatric Daytime Clinic in Holbaek. The overall objective is to secure compliance with the treatment, which means that the team attaches importance to building an alliance with the family, creating safety, and ensuring that the family receives sufficient counselling, psychological education, and support to enable them to be more confident and autonomous regarding the problems and challenges of having a child with an ADHD. After assessment and confirmation of the ADHD diagnosis, the family is offered medical treatment for the child. The medical protocol is shown in Figure 2. Medical treatment is always preceded by a physical examination; the somatic condition of the child is examined and an individually adapted neurological examination is performed. The physician informs the parents of the advantages and disadvantages of medical treatment. The family is asked to contact the clinic within a week of medical treatment initiation to report on the child's progress. From this meeting, it is decided whether the dosage regimen is satisfactory. All children are examined again after 1 month of treatment; positive and adverse effects are evaluated and educational counselling is given. If the child has gained weight, nutrition advice is given; if the child has developed sleeping problems, a special duvet can be borrowed or medication can be prescribed. The standard treatment involves a parent group where the parents meet three times during the 8-week trial period. In addition to general information about ADHD, focus is placed on different aspects related to the disorder, such as the child's relationship with siblings and peers. Talks will be given by visiting adults who have been diagnosed with ADHD. They talk to the group about their experiences of living with ADHD, having children, and making everyday life function.

Screening and recruitment of participants

The children are those referred to the Child Psychiatric Clinics in Holbaek and Roskilde with an ADHD diagnosis. They are screened according to the inclusion and exclusion criteria (Table 1). The parents will sign a written informed consent in the first meeting in the clinic. The Schedule for Affective Disorders and Schizophrenia for School-aged Children (K-SADS) will be used in the baseline assessment. This semi-structured interview includes algorithms from the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) in children and adolescents [37]. The child will also be screened for autism with the two Social Communication Questionnaires (SCQ) completed by the parents. The child will be excluded from the trial if there is a cut-off score above 15 on both the SCQ questionnaires [38]. The parents also complete the Adult Self-Report Scale (ASRS), which is a screening for adult ADHD symptoms [39]. The child's teachers will be asked to complete the Strength and Difficulties Questionnaire (SDQ) [40]. The child will be tested with the Children Attachment Interview (CAI) [41] before any medical treatment is initiated. The children who have not been assessed by the Wechsler Intelligence Scale for Children (Wisc-3 test) during the last 3 years will be tested with the Wisc-3 test by psychologists from the Clinic [42].

We estimate that 20 children will be assessed per treatment program (four identical programs are scheduled). This is the number that we believe is needed to produce approximately 12 to 16 participants for randomisation.

Outcome measures

All outcomes will be assessed before the interventions starts and at 3 months and 6 months after randomisation. The primary outcome measure is an assessment of ADHD core symptoms. The secondary outcome measures are an assessment of the children's social skills. The tertiary outcomes are an assessment of the attachment between the child and the parents and an assessment of the parents own ADHD symptoms (Table 2).

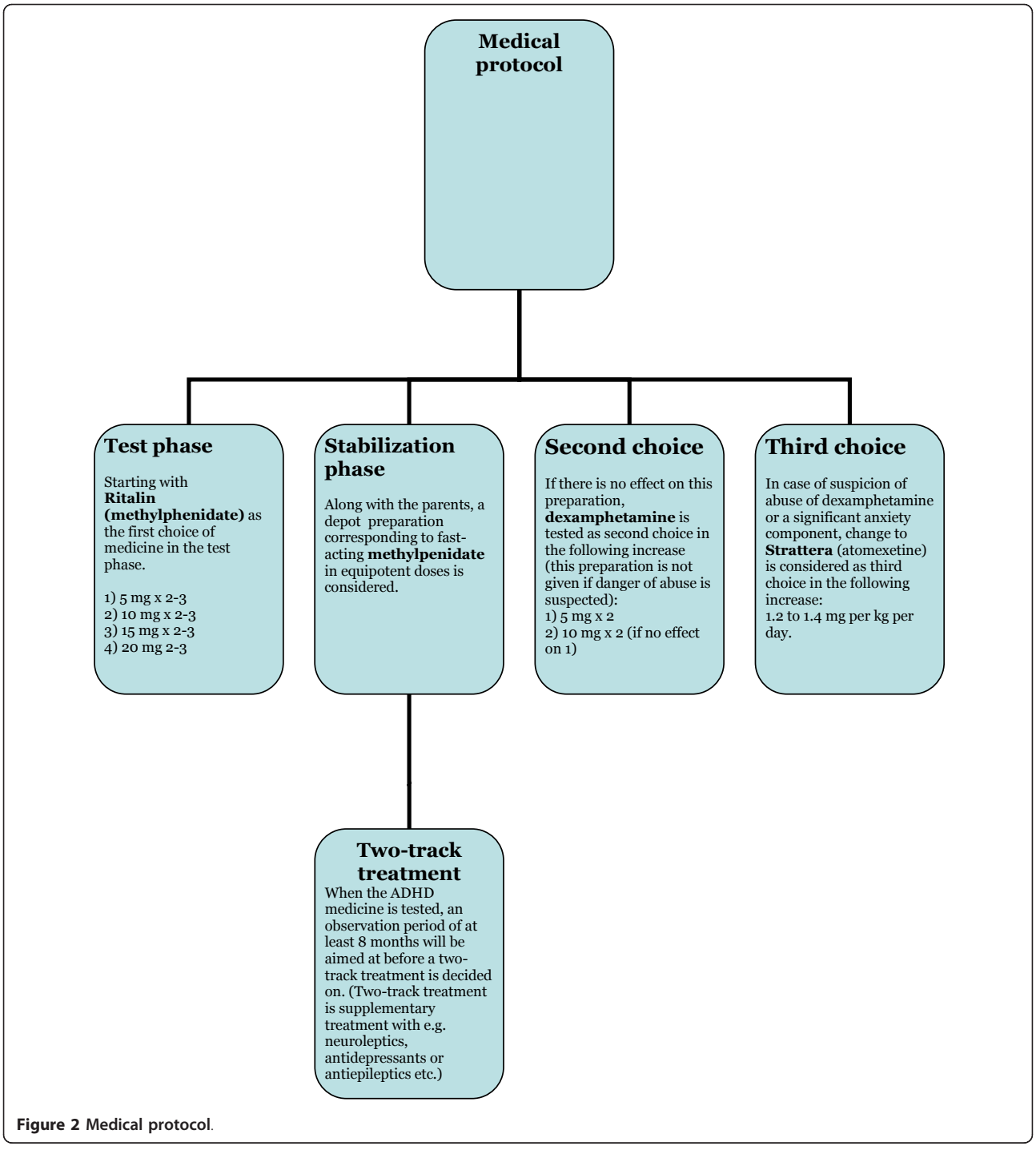


Figure 2 Medical protocol.

Assessment instruments

• **CAI** [41]. The CAI focuses on the child's experiences of his/her own present relevant relations and measures the child's view of his/her attachment figures' accessibility and sensitivity through the exploration of the inner object representations. The test consists of 19 questions that ask the child to recall experiences with his/her important attachment figures, especially at times where the child has been sad, anxious, or ill. The interview will be video recorded, and a scoring weight will be attached both to verbal and nonverbal statements. The test can assign the children to 1 of 6 possible attachment

Table 1 Criteria for inclusion and exclusion in the SOSTRA trial

Inclusion:	Exclusion:
1) The parents should be interested in taking part in parental groups in Child Psychiatric Clinic in Holbaek.	Patients with the following diagnoses according to DSM IV: 1) Schizophrenia: 295.30 (Paranoid type); 295.10 (Disorganized type); 295.20 (Catatonic type); 295.90 (Undifferentiated type); 295.60 (Residual type); 295.70 (Schizoaffective Disorder); 297.1 (Delusional Disorder); 298.8 (Brief Psychotic Disorder); 297.3 (Shared Psychotic Disorder); 298.9 (Psychotic Disorder Not Otherwise Specified).
2) The patients (and the parents) must understand and speak Danish language to an extent where a translator is not needed in order to be able to complete the assessment and the treatment.	2) Children with autism according to DSM IV: 299.00 (Autistic Disorder); 299.10 (Childhood Disintegrative Disorder); 299.80 (Asperger's Disorder), *or a cut of score on both the SCQ questionnaires above 15.*
3) The patients' parents must give informed consent to participate in the trial.	3) Violent and criminal youngsters.
4) The child must be between 8 to 12 years old by the time of the start of the assessment.	4) Children with a total verbal and nonverbal intelligence quotient below 80 according to WISC III
5) Both boys and girls can participate.	5) Strong resistance from the child against participating.
6) Children with a total verbal or nonverbal intelligence quotient over 80 according to the WISC III.	6) Previous started medical treatment for ADHD.
7) The children must fulfil research criteria for the diagnosis ADHD according to DSM IV (1994): 314.00, 314.01, 314.02. or 314.9.	7) Lacking informed consent.
8) The parents must consent in medical treatment for their child and there must be clinical indication for medical treatment.	

categories. In this study, the children are given 1 of the following four attachment categories: *secure attachment*, *insecure*, *disorganized/secure, or disorganized/insecure attachment*. This test can be used for children aged 6 to 14 years. (Danish version).

• **K-SADS clinical diagnostic interview** [37]. This test has been translated into Danish by Dorthe Janne Petersen and Niels Bilenberg. It is an internationally known diagnostic interview system, referred as Schedule for Affective Disorders and Schizophrenia for School-aged Children, Present and Lifetime Version (K-SADS-PL). The interview is used to diagnose children aged 6 to 18 years. Using the interview makes it possible to classify child and youth psychiatric diagnoses according to the DSM-III-R and DSM-IV-systems.

• **Conners CBRS Teacher** [43]. This questionnaire has been translated into Danish by psychologist Ole Jakob Storebø and psychologist Kirsten Bach in collaboration with Dorte Damm, Per Hove Thomsen, and the Dansk Psykologisk Forlag. This is an internationally approved instrument, which is used on children aged 6 to 18 years. The instrument has strong psychometrically qualities and measures behaviour, school performance, and emotional and social abilities.

Table 2 Outcome measures in the SOSTRA trial

Primary outcome:	*Measured by:*
ADHD symptoms.	Conners' 3rd Edition subscale 'hyperactivity-impulsivity' (teacher rated).
Secondary outcomes:	
Social skills.	Conners' CBRS subscale 'social problems' (teacher rated) and by Conners' 3rd Edition subscale: 'peer relations' (teacher rated).
Aggressive behaviour.	Conners' CBRS subscale: 'aggressive behavior' (teacher rated).
Emotional distress.	Conners' CBRS subscale: 'emotional distress' (teacher rated).
Executive functions.	Conners' 3rd Edition subscale: 'executive functioning' (teacher rated).
Academic performance.	Conners' CBRS: subscale: 'academic performances' (teacher rated).
Tertiary outcomes:	
Social skills and symptoms of ADHD measured in relation to attachment.	Children Attachment Interview.
Improvements in the ability to form attachments.	Children Attachment Interview.
Social skills and symptoms of ADHD measured in relation to parental ADHD symptoms.	Adult Self Report Scale Symptom Checklist.

• **Conners 3rd Edition Teacher** [44]. This questionnaire has been translated into Danish by psychologist Ole Jakob Storebø and psychologist Kirsten Bach in collaboration with Dorte Damm, Per Hove Thomsen, and Dansk Psykologisk Forlag. This is an internationally approved instrument, which is used on children aged 6 to 18 years. The instrument has strong psychometrically qualities and measures ADHD core symptoms, behaviour, and emotional and social abilities.
• **ASRS Symptom Checklist** [39]. This questionnaire covers the 18 DSM-IV-TR criteria for ADHD. It is used on adults. According to the American background material, 6 of the 18 questions have been identified as the most predicative of symptoms in relation to ADHD. These 6 questions form the basis of the ASRS v1.1 screening instrument and represents section A of the symptom checklist. Section B of the symptom checklist contains the remaining 12 questions. (Danish version).
• **SCQ** [38]. This is a screening instrument for autism and autism-spectrum disturbance among children aged four years and older, and is filled out by the parents.
• **SDQ** [40]. This is a brief behavioural questionnaire for children aged 3 to 16 years, and is filled out by the teacher.
• **Wisc 3** [42]. This is a test used to evaluate intelligence and cognitive functions among children aged 6-16 years.

Randomisation

Central randomisation is performed by the Copenhagen Trial Unit (CTU) with computer generated, permuted randomisation sequence with unknown block size for the investigators. A research secretary will call the CTU and providing a personal pin code, patient number, and the stratification variables of sex (female/male) and comorbidity (yes/no). Then the randomisation will be announced.

Blinding

The interventions are not blinded to participants, parents, treating physicians, or personnel in the clinic. However, the outcome assessor of the primary and secondary outcomes is the teacher, who is kept blinded of the child's allocated intervention. The involved parties (the parents and children) are instructed not to inform the teacher of the allocation. To secure integrity of trial data, the principal investigator will collect the questionnaires blind to the intervention. Blinded data will be handed over to the CTU, which will be in charge of data entry and statistical analyses blinded to intervention. Standardised procedures will be assured.

Sample size

The sample size is calculated on the basis of a type I error (α) of 5% and a type II error (β) of 20%, thus a power of 80%, and an allocation ratio of 1:1. With a clinically relevant difference of a score of 4 between the experimental intervention group and the control group on the Conners 3rd Edition Rating Scale 'hyperactivity-impulsivity' sub index (primary outcome) and an assumed standard deviation of 5 on the same scale [45,46], a sample size of 26 participants in each group is needed. This corresponds to a total of 52 participants to be randomised. In case of missing follow-up data (>5%), multiple imputations will be conducted (see below).

Statistical analysis

Intention-to-treat and per-protocol analyses

The statistical analysis of the outcomes will be based on the 'intention-to-treat' principle, i.e. all randomised participants will be included in the analysis in the intervention group to which they were randomized, irrespective of how much of the intervention they have received. Per-protocol analyses will be conducted secondarily for the participants who have completed 50% or more of their randomised intervention.

According to the ICH Harmonised Tripartite Guideline, Statistical Principles for Clinical Trials E9 Analysis of Drug Trials [47], the analyses will primarily be conducted with adjustment for stratification variables and will secondarily be conducted without adjustment for stratification variables.

Statistical analysis plan

The analysis of each outcome measure investigates if the outcome measure changes (increases or decreases) significantly over time in one intervention group as compared with the other one. The group coding is concealed for the statistician. Provided the outcome measure is a primary or secondary one, it will be investigated to determine if the effect depends on each of the tertiary outcome measures as measured at entry. If this is the case, *post hoc* explorative subgroup analyses prompted by the result may be conducted.

To deal with the multiplicity problem, the hypotheses will be ordered into families of hypotheses, and these families will in turn be ordered into a hierarchy of families. The general multistage gate keeping procedure of Dmitrienko et al. (2008) will then be applied [48]. The two-sided significance level will be 0.05. The gate keeping will be parallel, and the hypotheses will be organised into the following families:

1. Hypotheses related to the effect on the primary outcome measure.
2. Hypotheses related to the effect on the secondary outcome measures.

3. Hypotheses related to the effect on the tertiary outcome measures.

Once none of the null hypotheses in a family are rejected, the procedure stops and the rest of the null hypotheses are accepted. However, the raw P-values of the remaining tests will be calculated and presented as the results of *post hoc* analyses for hypothesis generating purposes.

The complete analysis of each outcome measure is the same for the primary and secondary outcome measures. The outcome measures is set to be M (continuous variable), the indicator of intervention to be I (binary categorical variable), time to be t (a continuous variable (0, 3, or 6 months)), and the tertiary outcome at baseline to be O3-baseline (it will be dealt with as a nominal variable in this context). The possibility that the value of M increases between month 3 and 6 is a real one. Therefore, the full model may not necessarily be a linear model in t. Consequently, we will include the quadratic component t2 in the full model. However, the final choice of model may be tempered by the impression obtained from the inspection of the marginal mean values.

The mixed model repeated measures method will be used. The model statement without the O3-baseline included will be specified as follows:

$$M = \text{intercept} + aI + bt + ct^2 + dIt + eIt^2$$

where a thru e are coefficients in the model. This model will test if the mean level as well as the linear and the quadratic effect of time differ significantly between the two interventions. A sequential hypothesis testing is used, which is appropriate for polynomial models. Initially, four types of covariance matrices will be tested: compound symmetric, AR(1), AR(1) with heterogeneous variances, and unstructured. Using the Akaike and the Schwartz Bayesian criteria, the best covariance structure will be chosen. In the analysis of the continuous tertiary outcome measures (measurements at entry and after 6 months), compound symmetric and unstructured covariance structures will be compared. When the O3-baseline is included, the full model will be augmented by the main effect of O3-baseline and interactions between O3-baseline and previously included components containing I, the intervention indicator.

Each analysis will be repeated twice for comparison (see sensitivity analyses). Missing observations imputed by the multiple imputations (MI) method will be included the first time, and only 'complete cases' will be included the second time. However, the main analysis will be a mixed model analysis including all original values (without any imputed ones included).

The second tertiary outcome measure is an ordinal variable with four possible categories. The proportional odds model with the same type of model statement as explained above will be used. If the assumption of this model is not fulfilled, various types of ordinal regression (SPSS version 17) will be attempted and, if this fails, a multinomial model will be used. If more than 5% of the values are missing, two analyses will be made, one only including 'complete cases' and the other including MI values.

Prevention of missing values

The teachers will be personally informed of the questionnaires by the therapist, who will assess the behaviour of the children in school. This therapist will inform the teacher of the importance that every question is answered in the questionnaires. The teachers will receive the questionnaire, along with a letter, at entry and at 3 and 6 months after treatment. In this letter, the necessity to answer all of the questions will be emphasized, and the teachers will be encouraged to call the principal investigator in case of any queries. The principal investigator and research secretary will play active roles in contacting the teachers of the children with ADHD and ensuring data collection in case the teachers fail to return the questionnaires. After receiving the questionnaires, the principal investigator and research secretary will assess all of the responses. If they find any questions unanswered, they will contact the teachers within 1 week of receiving the questionnaires, ensure that the missing data is completed, and find out why those questions were left unanswered. A short 1-day course will be arranged after the final follow-up and after receiving the final questionnaires for all of the teachers whose students participated in the trial. The teachers will be informed about this course once they receive the questionnaires at the baseline. All children and their parents will be contacted by the ADHD team for a long period of time after the end of this treatment, often as long as several years; therefore, all children and their parents will be bound to ambulatory settings and this study.

Types of missing values

Table 2 shows the outcome measures. From the forms (Connor 3rd Edition or Connor CBRS), the results of questions are combined algebraically to produce a number that is treated as the result of a continuous variable (the outcome measure). In the forms, the answers to the questions pertaining to the child's behaviour during the previous month are ordinal values (not true (0), sometimes true (1), often true (2), practically true all the time (3)). It is presumed that whether an outcome measure is reported or not reported due to at least one question remaining unanswered within a completed form does not depend on the unobserved value of the outcome

measure. This type of missing outcome measure result is referred to as a type 1 missing value.

Outcome measure results may also be missing because the corresponding form was not completed due to drop out or other causes (type 2 missing value). In this case, it is not safe to presume that the pattern of missing values is not related to the unobserved data. The potential impact of type 2 missing values is explored using a worst-case analysis (see below).

Statistical analysis of missing values

One approach for dealing with missing values is to use a mixed model for repeated measures (MMRM) in the statistical analysis (see statistical analysis). This model prevents bias only if the missing at random (MAR) assumption is fulfilled (the pattern of missing values is related to the observed data only). The results of the study are those obtained by this method when it is applicable for the analysis of the data (the outcome result of the patients follow a normal distribution with reasonable approximation in each of the 6 groups formed by the possible treatment by time combinations).

For comparison, the method of MMRM is supplemented by that of MI using the model variables and additional variables significantly related to the variables with missing values and/or the absence of these variables. The method used is the fully conditional specification method of SPSS (version 17.0). This is an iterative Markov chain Monte Carlo method that can be used when the pattern of missing data is arbitrary (monotone or non-monotone). The default number of iterations is used initially and then increased if the Markov chain has not converged. Prior to the MI, the distributions of the continuous variables are inspected to see if serious deviations from the normal distribution that need transformations are present. Constraints are set to restrict the range of imputed values of continuous variables so that they are plausible. In total, 10 imputed data sets are produced.

Sensitivity analyses

Two sensitivity analyses will be performed.

1. Parameter estimates obtained by complete case analysis, MMRM, and MI followed by MMCM on the imputed data sets will be compared [49].
2. A worst-case analysis of the effect of type 2 missing values will be conducted as follows. The group coded Effect group will be designated the group with a significant and beneficial effect on the outcome measure (say it decreases over time) as compared to the group coded No Effect group. Missing values will now be imputed as follows: A). Value(s) missing in the Effect Group: A single value missing is imputed with an average of the 2 observed values. Two values missing are both imputed by the third observed value. Three values missing are all imputed by the grand mean of the No Effect group. B). Value (s) missing in the No Effect-group: A missing 6-month value is imputed by the smallest observed 6-month value in the data. A missing baseline value is imputed by the largest observed baseline value in the data. A missing 3-month value is imputed by the average of 0 and 6-month values whether observed or imputed as explained above. This should minimize the response to intervention based on imputed values in patients from the Effect group and give a maximal negative linear response based on imputed values in patients from the No Effect group given the constraint that values more extreme than those observed must never be used.

MI will only be used if the missing values exceed 5%.

Group comparison at entry

To establish if participant characteristics at trial entry are relatively similar in the 2 intervention groups (thereby a low risk of selection bias and confounding), demographic data (sex and age) and other factors that can be expected to influence the primary outcomes will be presented in a table of the entry characteristics.

Ethical considerations and regulatory approval

Participants will be informed of the trial in writing and orally; written informed consent will be obtained from the participant's principal caregivers. There are no apparent ethical problems since all participants are offered standard medical treatment, and standard control treatment in this population, further, there are no known disadvantages of social-skills training. Nevertheless, any adverse events of the intervention will be reported. The trial has obtained approval by the Regional Ethics Committee of Zealand (SJ-85) and is registered with the Danish Data Protection Agency (J. nr.2008-41-2613) and at ClinicalTrials.gov (NCT00937469).

Discussion

This trial compares the effects of social-skills training groups supported by parental training plus standard treatment versus standard treatment alone on the outcome of core ADHD symptoms of hyperactivity and impulsivity. A secondary objective is to examine differences in the effect of the treatment in relation to the children's different abilities in forming attachments: secure, insecure, disorganized/secure, or disorganized/insecure attachment. The last objective is to examine differences in the effect of the treatment in relation to the degree of parents' symptoms of ADHD.

The results from this trial can greatly benefit children with ADHD because social-skills training may have a greater general effect on social and emotional competencies than medication alone. Additionally, the

connection between the ability to form different attachments and the effect of the social-skills training can influence both the understanding and the treatment of the disease. One of the trial's strengths is that it is related to very important matters in the development of comprehensive treatment programs for ADHD children. Many children with ADHD have serious problems with peers because of their lack of emotional and social abilities. ADHD children are often lonely, and their social problems often lead to a vicious circle, which is difficult to break [16,17].

Other strengths of this trial are the measurement of attachment styles in children with ADHD and the comparison between the effect of the social-skills training and the attachment competencies. We do not know of other studies in which children with an ADHD diagnosis are tested with the CAI test. Punto et al. stated that there is a significant connection between disorganised attachment in early childhood and ADHD symptoms in the school-age period [34]. This shows the necessity for more research on the topic. The possible connection between attachment problems and ADHD is an interesting topic in the ethological discussion. It must also be assumed that these children need a form of treatment that focuses on their inability to form relationships and their social problems. With the SOSTRA trial, we aim for improved the treatment of children with ADHD. There is a greater tendency towards pure medical treatment for children with ADHD, which is reprehensible because children need a more comprehensive treatment.

The experimental intervention in this trial is relatively short (8 weeks) and is therefore not very costly. This will allow other child psychiatric units to incorporate social-skills training for children with ADHD. A limitation of this trial is the relatively small sample size, which could make it difficult to draw firm conclusions about the research questions. However, if successful, it will be indicative of further directions for research on this topic.

Abbreviations

ADHD: Attention Deficit Hyperactivity Disorder; **ASRS**: Adult Self-Report Scale; **CAI**: Children Attachment Interview; **DSM-IV**: Diagnostic and Statistical Manual of Mental Disorders; **ICD-10**: International Classification of Diseases; **IQ**: Intelligence quotient; **K-SADS-PL**: Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version; **MTA**: Multimodal Treatment Study of ADHD; **SCQ**: Social Communication Questionnaire; **SDQ**: Strength and Difficulties Questionnaire; **SOSTRA**: Social Skills Training and Attachment; **WISC-III**: Wechsler Intelligence Scale for Children; **Conners CBRS**: Conners Comprehensive Behaviour Rating Scales.

Acknowledgements

The study was financially supported by Region's Zealand University Hospital (RESUS), Region Zealand Research Foundation, and Psychiatric Research Unit, Region Zealand. Funding was also received from the Fru C. Hermansens Foundation, Slagtermester Max Wørzner and Inger Wørzners Foundation, and TrygFonden.

Author details

[1]Child Psychiatric Daytime Clinic, Child and Adolescent Psychiatric Centre, Region Zealand, Holbaek, Denmark. [2]Psychiatric Research Unit, Region Zealand, Roskilde, Denmark. [3]Copenhagen Trial Unit, Centre for Clinical Intervention Research, Department 3344, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark. [4]Psychiatric Hospital for Children and Adolescents, Risskov, Denmark. [5]Cochrane Hepato-Biliary Group, Copenhagen Trial Unit, Centre for Clinical Intervention Research, Department 3344, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark. [6]Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark. [7]Institute of Psychology and Education, Roskilde University, Denmark. [8]Aarhus University, Clinical Institute, Child and Adolescent Hospital, Centre for Research and Development, 8000 Aarhus, Denmark.

Authors' contributions

All authors contributed to the design of the trial. OJS drafted the manuscript. All authors contributed to the further review of the manuscript. All authors read and approved the final manuscript.

Competing interests

Per Hove Thomsen has received a fee for lecturing on behalf of NOVARTIS and UCB as well as lecturing and consulting on behalf of Eli-Lilly. He also serves on the advisory board of Eli-Lilly.
All the other authors declare that they have no competing interests.

Received: 9 November 2010 Accepted: 21 January 2011
Published: 21 January 2011

References

1. Polanczyk G, Rohde LA: **Epidemiology of attention-deficit/hyperactivity disorder across lifespan.** *Curr Opin Psychiatry* 2007, **20**:386-92.
2. Goldman LS, Genel M, Bezman RJ, Slanetz PJ: **Diagnosis and treatment of attention-deficit disorder in children and adolescents.** *J Am Med Assoc* 1998, **279**:1100-07.
3. Barkley RA: *Attention Deficit Hyperactivity Disorder: A Handbook for Diagnoses and Treatment* New York: Guildford; 1998.
4. Gadow KD, Nolan EE, Sverd J, Sprafkin J, Paolicelli LL: **Methylphenidate in aggressive-hyperactive boys: I. Effects on peer aggression in public school settings.** *J Am Acad Child Adolesc Psychiatry* 1990, **29**:710-8.
5. Malone MA, Swanson JM: **Effects of methylphenidate on impulsive responding in children with attention deficit hyperactivity disorder.** *J Child Neurol* 1993, **8**:157-63.
6. Spencer T, Biederman J, Wilens T, Harding M, O'Donnell D, Griffin S: **Pharmacotherapy of attention-deficit hyperactivity disorder across the life cycle.** *J Am Acad Child Adolesc Psychiatry* 1996, **35**:409-32.
7. Barkley RA: **A review of stimulant drug research with hyperactive children.** *J Child Psychol Psychiatry* 1997, **18**:137-65.
8. Gilberg C, Melander H, von Knorring A, Janols L, Thernlund G, Hagglof B, Eidevall-Walin L, Gustafsson P, Kopp S: **Long-term stimulant treatment of children with attention-deficit hyperactivity disorder symptoms. A randomized, double blind, placebo-controlled trial.** *Arch Gen Psychiatry* 1997, **54**:857-864.
9. Cyr M, Brown C: **Current drug therapy recommendations for the treatment of attention deficit hyperactivity disorder.** *Drug* 1998, **56**:215-223.
10. Klassen A, Miller A, Raina P, Lee SK, Olsen L: **Attention-deficit hyperactivity disorder on children and youth: a quantitative systematic review of the efficacy of different management strategies.** *Can J Psychiatry* 1999, **44**:1007-1016.
11. MTA Cooperation Group: **A 14-month randomized clinical trial of treatment strategies for attention deficit hyperactivity disorder.** *Arch Gen Psychiatry* 1999, **56**:1073-1086.
12. Gilmore A, Milne R: **Methylphenidate in children with hyperactivity: review and cost-utility analysis.** *Pharmacoepidemiol Drug Safety* 2001, **10**:85-94.
13. Hinshaw S, Henker B, Whalen C: **Cognitive-behavioural interventions for hyperactive boys: comparative and combined effects.** *J Clin Psychol* 1984, **52**:739-749.

14. Hinshaw S, Henker B, Whalen C: **Self-control in hyperactive boys in anger inducing situations: effects on cognitive behavioral training and of methylphenidate.** *J Abnormal Child Psychol* 1984, **12**:55-77.
15. Tannock R, Martinussen R: **Reconceptualizing ADHD.** *Educational Leadership* 2001, **59**:20-25.
16. Whalen CK, Henker B: **The social worlds of hyperactive (ADHD) children.** *Clin Psychol Rev* 1985, **5**:447-478.
17. Landau S, Moore LA: **Social skill deficit in children with attention-deficit hyperactivity disorder.** *School Psychol Rev* 1991, **20**:235-251.
18. Hectman L, Weiss G: **Long-term outcome of hyperactive children.** *Am J Orthopsychiatry* 1983, **53**:532-41.
19. Manuzza S, Klein RG, Konig PH, Giampino TL: **Childhood predicators of psychiatric status in the young adulthood of hyperactive boys: a study controlling for chance associations.** In *Straight and Devious Pathways from Childhood to Adulthood.* Edited by: Robins LN, Rutter M. New York: Cambridge University Press; 1990:279-299.
20. Manuzza S, Klein RG, Bessler A, Malloy P, LaPadula M: **Adult psychiatric status of hyperactive boys grown up.** *A J Psychiatry* 1998, **155**:493-8.
21. Biederman J, Faraone SV, Taylor A, Sienna M, Williamson S, Fine C: **Diagnostic continuity between child and adolescent ADHD: findings from a longitudinal clinical sample.** *J Am Acad Child Adolesc Psychiatry* 1998, **37**:305-13.
22. Biederman J, Mick E, Faraone SV: **Age-dependent decline of symptoms of attention deficit hyperactivity disorder: impact of remission definition and symptom type.** *Am J Psychiatry* 2000, **157**:816-8.
23. Barkley RA, Fischer M, Smallish L, Fletcher K: **The persistence of attention-deficit/hyperactivity disorder into young adulthood as a function of reporting source and definition of disorder.** *J Abnormal Psychol* 2002, **111**:279-89.
24. Dalsgaard S, Mortensen PB, Frydenberg M, Thomsen PH: **Conduct problems, gender and adult psychiatric outcome of children with attention-deficit hyperactivity disorder.** *Br J Psychiatry* 2002, **181**:416-21.
25. Jensen PS, Hinshaw SP, Kraemer HC, Lenora N, Newcorn JH, Abikoff HB, March JS, Arnold LE, Cantwell DP, Conners CK, Elliott GR, Greenhill LL, Hechtman L, Hoza B, Pelham WE, Severe JB, Swanson JM, Wells KC, Wigal T, Vitiello B: **ADHD comorbidity findings from the MTA study: comparing comorbid subgroups.** *J Am Acad Child Adolesc Psychiatry* 2001, **40**:147-58.
26. Kadesjö B, Gillberg C: **The comorbidity of ADHD in the general population of Swedish school-age children.** *J Child Psychol Psychiatry* 2001, **42**:487-92.
27. Fohlmann AH: **Social færdighedstræning.** In *Psykose hos unge. Symptomer, behandling og fremtid.* Edited by: Nordentoft M, Melau M, Iversen T, Kjær S. København: Psykiatrifondens Forlag; 2009:161-189.
28. Liberman RP: **Social skills training.** In *Psychiatric Rehabilitation of Chronic Mental Patients.* Edited by: Liberman RP. Washington, D.C: American Psychiatric Press; 1998:.
29. Pfiffner LJ, McBurnet K: **Social skills training with parent generalization: treatment effects for children with attention deficit disorder.** *J Consulting Clin Psychol* 1997, **65**:749-757.
30. Antshel KM, Remer R: **Social skills training in children with attention deficit hyperactivity disorder: a randomized-controlled clinical trial.** *J Clin Child Adolescent Psychol* 2003, **32**:153-165.
31. Tutty S, Gephart H, Wurzbacher K: **Enhancing behavioural and social skill functioning in children newly diagnosed with hyperactivity disorder in a pediatric setting.** *Develop Behav Pediatr* 2003, **24**:1.
32. Socialstyrelsen, Sverige: **ADHD hos barn och vuxna.** Stockholm, maj; 2002.
33. Mager W, Millich R, Harris MJ, Howard A: **Interventions group for adolescents with conduct problems: is aggression harmful or helpful?** *J Abnormal Child Psychol* 2005, **33**:349-62.
34. Punto C, Turton P, Hughes P, White S, Gillberg C: **ADHD and infant disorganized attachment: a prospective study of children next-born after stillbirth.** *J Atten Disord* 2006, **10**:83-91.
35. **Langager skole intra.** [http://www.langager.skoleintra.dk/Infoweb/Designskabelon9/Rammeside.asp?Action=&Side=&Klasse=&Id=&Startside=&ForumID].
36. Elliot SN, Gresham FM: **Social Skills interventions for children.** *Behav Modif* 1993, **17**:287-313.
37. Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, Williamson D, Ryan N: **Schedule for Affective Disorders and Schizophrenia from School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data.** *J Am Acad Child Adolesc Psychiatry* 1997, **36**:980-8.
38. Rutter M, Bailey A, Lord C: *Social Communication Questionnaire (SCQ)* Los Angeles: Western Psychological Services; 2003.
39. Adler LA, Spencer T, Faraone SV, Kessler RC, Howens MJ, Biedermann J, Secnik K: **Validity of pilot Adult ADHD Self-Report Scale (ASRS) to rate adult ADHD symptoms.** *Ann Clin Psychiatry* 2006, **18**:145-8.
40. Fletcher J, Tannock R, Bishop DVM: **Utility of brief teacher rating scales to identify children with educational problems.** *Aust J Psychol* 2001, **53**:63-71.
41. Target M, Fonagy P, Shmueli-Goetz Y: **Attachment representations in school-age children: the development of the child attachment interview (CAI).** *J Child Psychother* 2003, **29**:171-186.
42. Wechsler D: *Wechsler Intelligence Scale for Children–3rd Edition (WISC-III®). Swedish edition* Stockholm: Psykologiförlaget AB; 1998.
43. Conners KC: *Conners Comprehensive Behavior Rating Scales (Conner's CBRS)* Toronto, Canada: Multi-Health Systems Inc; 2008.
44. Conners KC: *Conners 3* Toronto, Canada: Multi-Health Systems Inc; 2008.
45. Horns WF, Ialongo NS, Pascoe JM, Greenberg G, Packard T, Lopez M, Wagner A, Puttler L: **Additive effects of psychostimulants, parent training, and self-control therapy with ADHD children.** *J Am Acad Child and Adolesc Psychiatry* 1991, **30**:233-240.
46. Corkum PV, McKinnon MM, Mullane JC: **The effect of involving classroom teachers in a parent training program for families of children with ADHD.** *Child Fam Behav Ther* 2005, **27(4)**:29-49.
47. **International Conference on Harmonisation Guideline for International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.** Guideline for Good Clinical Practice E6 (R1). ICH Harmonised Tripartite Guideline; 1996.
48. Guideline on missing data in confirmatory clinical trials: **Draft. Doc. Ref. CPMP/EWP/1776/99 Rev. 1 Coor.** *Committee for medicinal products for human use* European Medicines Agency, London; 2009.
49. Dmitrienko A, Tamhane AC, Wiens BL: **General multistage gatekeeping procedures.** *Biometric J* 2008, **50(5)**:667-677.

doi:10.1186/1745-6215-12-18
Cite this article as: Storebø *et al.*: Randomised social-skills training and parental training plus standard treatment versus standard treatment of children with attention deficit hyperactivity disorder - The SOSTRA trial protocol. *Trials* 2011 **12**:18.

Social-skills and Parental Training plus Standard Treatment versus Standard Treatment for Children with Attention Deficit Hyperactivity Disorder- The Randomised SOSTRA Trial

Ole Jakob Storebø MA, Erik Simonsen MD., PhD, Dr.h.c., Per Winkel MD., Christian Gluud MD, Dr. Med. Sci.

Mr. Storebø is a psychologist and PhD student in Child Psychiatric Clinic, Child and Adolescent Psychiatric Department, Region Zealand**,** Denmark, phone nr. +45 59484735, **OJS**: ojst@regionsjaelland.dk **(**Corresponding author).
Dr. Simonsen is Professor and Director of Psychiatric Research Unit, Region Zealand, Roskilde, Denmark, **ES**: es@regionsjaelland.dk
Dr Winkel works with the Copenhagen Trial Unit, Center for Clinical Intervention Research, Department 3344, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, **PW**: winkelper9@gmail.com
Dr. Gluud is Head of the Copenhagen Trial Unit, Center for Clinical Intervention Research, Department 3344, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark, **CG**: cgluud@ctu.rh.dk

Abstract
Objective: To investigate the effect of social-skills training and parental training programme for children with attention deficit hyperactivity disorder (ADHD). **Method:** We conducted a randomized two-armed, parallel group, assessor-blinded superiority trial consisting of standard treatment and social-skills training plus parental training versus standard treatment alone. A prior calculation of sample size showed at least 52 children should be included for the trial with follow up three and six months after randomization. The primary outcome measure was ADHD symptoms and secondary outcomes were social skills and emotional competences. **Results**: 56 children (39 boys, 17 girls, mean age 10.4 years, SD 1.31) with ADHD were randomized for the treatment. A mixed model analysis with repeated measures showed that the time course ($y = a + bt + ct^2$) was not significantly ($p > 0.05$) influenced by the intervention. **Conclusion:** Social skills training did not show any significant benefit for children with attention deficit hyperactivity disorder.

Trial registration: Clinical Trials.gov Identifier: NCT00937469

Introduction

Attention-deficit hyperactivity disorder (ADHD) affects 3% to 5% of all children [1]. The core ADHD symptoms include lack of attention, impulsiveness, and hyperactivity [2,3].
Pharmacological treatment of children with ADHD shows beneficial effects on core symptoms in about 80% of patients [4]. However, many children and adolescents with ADHD also frequently suffer from lack of social competence and have language difficulties, learning problems, and difficulties in interacting with parents and teachers. There is a question as to whether pharmacological treatment alone has any effect on these outcome measures [5-10]. We have looked for other possible predictors. Some studies demonstrate that there is a possible connection between unsecured attachment patterns and ADHD, and the specific attachment style has a prognostic influence [11-14]. ADHD is an inherited disease, and parent's own ADHD symptoms might also predict the outcome [15].

Other possible predictors are comorbid disorders [16,17]. Children with ADHD have an increased risk of developing personality disorders and psychotic conditions, drug abuse or alcohol abuse, and criminal behaviour [18,19]. It is crucial that the overall treatment also focuses on treating comorbid disorders and preventing the development of later disorders and illnesses. There are different types of psychosocial treatments, which might alleviate core symptoms, and the different psychological and social aspects of ADHD.

In three Cochrane reviews the effects of family therapy, parent training, and meditation for children with attention deficit hyperactivity disorder were assessed, and these showed no evidence of either treatment [20-22].

The best-documented psychosocial treatments are behavioural/cognitive forms. These consist of behavioural training, social skills training, cognitive training, and different forms of expedient adjustment of the child's difficulties in relation to the environment at home and at school [7]. We have identified four meta-analyses of social skills training for children with ADHD. Two of them state that social skills training for children with ADHD has no effect [23,24], and two of them state that social skills training for children with ADHD has a significant treatment effect [25,26].

Recently, we conducted a Cochrane review to investigate the effect of social skills training for children with ADHD. This review shows no significant treatment effect—except for an occasional small effect on the parent rated measurement of social skills competence (standard mean difference (SMD) 0.22; 95% CI 0.04 to 0.40; 7 trials, 628 participants) and ADHD symptoms (SMD -0.49; 95% CI -0.79 to -0.19; 7 trials, 654 participants). Because of the high risk of bias (systematic errors) in all the included trials and insufficient power (few participants in the trials), these findings are inconclusive [27]. Subsequently, we designed the social skills training attachment (SOSTRA) trial on the basis of this review and efforts were made to avoid systematic errors in its design [28].
The primary aim of the SOSTRA trial is to examine the effect of the combination of social-skills training and parental training, plus standard treatment versus standard treatment alone in children with ADHD and their families on the outcome measures of ADHD core symptoms, social skills and emotional competence.

Method

Design

We have previously described the design and plan for the analysis of the trial [28]. Briefly, children aged 8 to 12 years who had been diagnosed with ADHD and their parents were given randomized treatment: this was a combination of standard treatment and social-skills training, plus parental training versus standard treatment alone. It was a randomized, two-armed, parallel group, assessor-blinded superiority trial. The children were examined at baseline, three months, and six months after randomization. In this trial we included a baseline assessment of the children's attachment competence and the parent's ADHD symptoms, and analysed the prognostic influence of these factors.

Subjects

The children were those suspected to have an attention deficit hyperactivity disorder, who had been referred to the Child Psychiatric Units in Holbaek and Roskilde. They were screened according to the following inclusion criteria: ADHD diagnosis according to DSM-IV (1994), 8–12 years at the time of the start of assessment, and parents willing to take part in the trial and give consent for medication treatment. Exclusion criteria were: schizophrenia or the autism diagnosis according to DSM IV, violent and criminal children, both verbal and nonverbal intelligence quotient (IQ) <80, previously medicated for ADHD, and strong resistance against participating.

Measure and Reliability

The children were screened at entry by the K-SADS. This semi-structured interview includes algorithms from the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) in children and adolescents [29]. The Schedule for Affective Disorders and Schizophrenia for School-aged Children (K-SADS) was administered by the first author who was trained to administer the K-SADS at a training course (OJS). The child was screened for autism and the parents completed Social Communication Questionnaires (SCQ). Children with scores above 15 on two SCQ questionnaires were excluded [30]. The parents also completed the Adult Self-Report Scale (ASRS) to screen for adult ADHD symptoms [31]. The children who had not been subjected to the Wechsler Intelligence Scale for Children (Wisc-3 test) during the last three years were tested with the Wisc-3 test by psychologists from the Unit [32].
All of the children were tested using the Children Attachment Interview (CAI) [14]. This interview was scored by a certified rater who was 'blinded' to the treatment assignment. The children's teachers completed the Conners 3 and the Conners Comprehensive Behaviour Rating Scales (CBRS) rating scales [33,34].
Outcome Measures:

The outcomes measured at three months and six months after randomization included indexes from the Conners 3 and the Conners Comprehensive Behaviour Rating Scale (CBRS) rating scales. The Primary outcome were: 'hyperactivity/impulsitivity', the secondary outcomes: 'social problems', 'peer relations', 'aggressive behaviour', 'emotional distress', 'executive functioning', and 'academic performances' respectively [33,34].

Randomization and Blinding

The Copenhagen Trial Unit (CTU) conducted central randomization with computer generated, permuted randomization sequences in blocks of four with an allocation ratio of 1:1 stratified for sex and comorbidity. The block size was unknown to the investigators. A research secretary randomized the patient by calling the CTU providing a personal pin code, patient number, and values of the stratification variables.

The interventions given were not 'blind' to participants, parents, treating physicians, or personnel in the Unit. However, the outcome assessor of the primary and secondary outcomes (the teachers) were kept blinded of the allocated intervention. The involved parties were also instructed not to inform the teacher of the intervention allocated. To secure integrity, the principal investigator 'blinded' the collected questionnaires, i.e., hid all data that can be used to identify the patient's allocation before data entry. 'Blinded' data were handled over to the CTU, which was in charge of data entry and statistical analyses. Standardized procedures including double data entry were assured.

Ethical Considerations and Regulatory Approval

Participants were informed of the trial in writing and orally; written informed consent was obtained from the participant's principal caregiver. There were no apparent ethical problems since all participants were offered medical treatment, and there were no known disadvantages of social-skills training; nevertheless, any adverse events of the intervention were reported. The trial obtained approval from the Regional Ethics Committee of Zealand (SJ-85), was registered at the Danish Data Protection Agency DO50892, and registered at www.clincal trials.gov NCT00937469.

Treatment Samples

Standard Treatment

The standard treatment offered to both the experimental group and the control group encompasses the normal practice regarding ADHD patients at the Child Psychiatric Clinic in Holbaek. After assessment and confirmation of the ADHD diagnosis, the family was offered medical treatment for the child following a medication protocol. The children had never previously received medication treatment for ADHD. There were defined treatment algorithms for the medication of ADHD. The treatment started with first choice: methylphenidate; the second choice: dexamphetamine; and atomoxetine was considered in those cases where there was a suspicion of abuse of dexamphetamine or a significant anxiety component change. During the eight months following randomization, the children were not offered any supplementary treatment, such as anti-psychotics or antidepressants. All children were examined one week and again one month after the start of medical treatment; positive and adverse effects were evaluated. The standard treatment involved an educational parent group, where the parents met three times during the eight week trial and received general information about ADHD.

The Experimental Treatment

Social-skills training aimed to improve and maintain the individual's social skills. The children were taught how to adjust their verbal and nonverbal behaviour in their social interaction. It also included efforts to change the children's cognitive assessment of the 'social world' [35]. The training generally focused on teaching the children to 'read' the subtle cues in social interaction, such as learning to wait for their turn [36]. The children in SOSTRA were offered eight weekly 90 minute social-skills training sessions. Each group included two therapists trained in social-skills training before the trial, and therapists from the Langager School in Aarhus giving continuous supervision throughout the trial. Each session was video recorded, and the therapist completed forms confirming that he/she had followed the manual. The intervention manual, which may be obtained from the corresponding author conforms to the programme of several randomized trials [37,38]. Different methods of teaching the children social skills were used, all of which have proved successful in other social-skills programmes [39]. Didactic instructions were used, including work with symbols, games, creative techniques, music, story reading and movies. Each session had a theme, such as self-worth, nonverbal communication, feelings, impulse control, aggression management, conflict resolution, and problem solving. The treatment focused on strengthening the ability of the children to control themselves to start a self-help process.

During the process the children received social skills training and the parents attended parental training. The themes from the children's groups were discussed in the parental groups. The children's homework was also discussed. The efficacy of the intervention was assessed by studying the amount of improvement in ADHD symptoms and social skills per se, or by assessing psychological functioning on a broader aspect, including the quality of peer relationships and emotional competency.

Data Analysis

The sample size was calculated on the basis of a type I error (α) of 5% and a type II error (β) of 20%, thus a power of 80% and an allocation ratio of 1:1. With a clinically relevant difference of 4 between the intervention group and the control group on the Conners 3rd Edition Rating Scale 'hyperactivity-impulsivity' sub index (primary outcome) and an assumed standard deviation of 5 on the same scale [40,41], a sample size of 26 participants in each group was needed.
The statistical analysis of the outcomes was based on the 'intention-to-treat' principle and primarily conducted with adjustment for the protocol specified stratification variables (sex and presence of co-morbidity) and secondarily conducted without this adjustment [28]. The group coding was concealed for the statistician. The level of significance was 0.05.
The mixed-model repeated measures method (SAS version 9.1) was used to compare the effect of the two interventions over time on the outcome measures.
The model is the following: Outcome measure = a · sex + b · co-morbidity + c · intervention-group + d · t + e · t^2 + f · intervention-group · t + g · intervention-group · t^2 where co-morbidity, sex and intervention-group are binary indicator variables and t is treated as a continuous variable; a through g are coefficients to be estimated during the analysis. The basic model is Outcome measure = a · sex + b · co-morbidity + d · t + e · t^2 where the outcome measure is modelled as a linear function of time (t) and time squared (t^2). The latter term is included to model a time course that may be almost linear initially and then blunted as time goes by. If sex and/or co-morbidity is having an impact on the outcome measure this effect is compensated for by including the terms sex and co-morbidity in the model to improve the precision.
To model a possible impact of the intervention on the mean level, the slope of the linear function (t) and/or the slope of t^2 the terms intervention-group + intervention-group · t + intervention-group · t^2 respectively are added to the model.
A sequential hypothesis testing was used, which is appropriate for polynomial models. Since the measurements within a given patient are probably dependent, this dependency is modelled by a co-variance matrix, common to all patients. Initially, three types of covariance matrices were examined: compound symmetric, AR(1), and unstructured. Using the Akaike and the Schwartz Bayesian criteria, the best of these three covariance structures was chosen.
Prior to each analysis the six distributions of the outcome measure defined by time and intervention-group were examined to see if the assumption of normality was fulfilled (tests of kurtosis and skewness as well as Shapiro Wilks test ($p < 0.01$) plus inspection of histograms and probability distributions). Prognostic factors measured were: assessment of the attachment between the child and the parents and an assessment of the parent's own ADHD symptoms [14,31]. Of the 165 planned measurements per outcome measure, the percentage missing ranged from 1.3 to 7.2. Two out of the 165 sets of questionnaires were missing. The rest of the missing data were due to inadequate answering of the questionnaires and resulted in a few missed indexes on some of the participants.
For the purpose of this trial the baseline values of the variables CAI group, ASRS score (father), and ASRS score (mother) were recoded into binary variables (CAI-binary, ASRS (father)-binary, and ASRS (mother)-binary respectively). (ASRS: 0= scores 1-3, 1= 4-6, CAI: 0=secure, unsecured/preoccupied, unsecure/dismissing, 1=disorganized/secure and disorganized/not secure).

Results

100 families were eligible and 26 refused to participate in the project (see figure 1). 21 of these 26 children were boys and 5 were girls. The most common reasons for not wanting to participate were: not having time to participate in the groups; already received medical treatment for ADHD, or not wanting to the children to receive medication for their problems. 74 children were assessed, 18 children were excluded (17 boys and 1 girl) and this left 56 children (39 boys, 17 girls) to be randomized in total, and they were all of Danish ethnicity. The 18 children were excluded because of not fulfilling the diagnosis of ADHD, or had autism, psychosis, low IQ, or the child/parents not wanting to participate in the groups. Table 1 shows the distribution of demographic data, DSM diagnoses and clinical variables in the two

intervention groups. The two groups appear to be reasonably similar. Only 7.3% of the children were assessed with secure attachment patterns as compared to 61% in a normal population [42]. The children and parents were included in one of four identical eight-week treatment programmes with 12–17 participants per programme. Two children were excluded a few days after the randomization, one of them because his mother did not want her child to receive central stimulating medication, and we were not allowed to obtain outcome assessment from this child. The other child and his parents did not want to participate in the treatment, but all his outcome assessments were obtained and this child is included in the analysis.

Table 2 shows the mean and SD values at baseline, three month, and six month by treatment group.

It appears that the time course is often not linear justifying the quadratic time term in the statistical model.

Prior to the mixed-model analysis it was necessary to square root transform the outcome measure in five out of the seven analyses to normalize the data (see table 3). Table 3 presents the p values of the tests of the fixed effects conducted in each of the seven mixed-model analyses. It appears from the three right hand columns on the table, which show the p values of the main effect of the intervention and its interaction with t and with t^2 that on no occasion did the time course of an outcome measure differ significantly between the two intervention groups. This was not altered if insignificant effects including the intervention indicator were removed from the model one at a time and the analysis each time repeated using the reduced model. An analysis not including the two protocol specified stratification variables (sex and co-morbidity) gave similar insignificant results.

A mixed-model analysis of each outcome measure without the intervention indicator included in the model but with the latter augmented by CAI-binary, CAI-binary•t, and CAI-binary•t^2 showed that on no occasion did CAI-binary significantly influence the time course of an outcome measure. The same was found when the analysis was repeated but this time with all fixed effects involving the intervention indicator (see table 3) retained in the model. Corresponding analyses of ASRS (father)-binary and of ASRS (mother)-binary gave similar insignificant results.

We did not find any adverse event following the social skills training.

Discussion

The outcome measure changed significantly over time for most outcome measures. The time course did not differ significantly for any of them (between the two intervention groups).

This is in accordance with our Cochrane review and the meta-analyses performed by Kavale et al. and Van der Oord et al. [23.24,27] but differ from the results of de Boo and Prins and Majewicz-Hefley [25,26]. However, both of these latter reviews had no systematic evaluation of systematic errors (bias) in the included trials and the results are therefore questionable.

The SOSTRA trial shows that this kind of treatment does not add any positive changes either to the children's ADHD core symptoms or the social and emotional problems that these children have. One of the baseline findings in SOSTRA is especially interesting, as only 7.3% of the children had a secure attachment competence, as opposed to 61% in a normal population. This has also been found in other studies [11-13] and supports the contention that there is a association between attachment problems and ADHD. It may therefore be speculated that these children need a form of treatment that focuses on their inability to form relationships and their social problems. There is a tendency towards more medication for children with ADHD and even if this treatment has a short-term effect, it is not addressed to alleviate social skills problems. Furthermore, there is no evidence for the long-term effect of ADHD medication, and the adverse effects of this medication are not fully investigated [4]. Therefore there is a need for another type of training/therapy, which can help the children to deal with their attachment problems as well. This means a longer treatment programme, and a treatment that can change more profound aspects of the children's personality. This treatment needs to focus on the cognitive aspect and also the affective. One treatment that might make the necessary profound changes in the children's difficulties, and then possibly avoid the development of personality disorders, abuse, and later criminality, is child and/or parent psychotherapy. This therapy is an intensive treatment with sessions several times a week and lasting for more than one year, and is combined with parent therapy. There is, however, at present, no evidence of the efficacy of this treatment for children with ADHD, So more research is needed.

In the SOSTRA trial we discovered a large effect over time for both the groups together, e.g. the children's social problems scores, aggressiveness, and hyperactivity scores showed highly significant changes (table 3). We cannot state anything about the reason for this.

This trial has several limitations. The most important one is the small number of subjects. Based on our sample size calculation and our decision on a clinical relevance, we did not find any effects of social skills training. If more patients had been included we might have been able to discover smaller clinical significant effects. We used a beta size on 80% that give a 20% change for a type 2 mistake. Another limitation is the use of teacher-rated measurement scales. The teachers might not be able to track potential small changes in the children's symptoms in classes with 25 other children. Furthermore, the therapists who were responsible for the children during the experimental intervention were also (but not on the same day) responsible for the parent group in the control arm. It is possible that these therapists have transferred elements from the experimental treatment to the parent group in the standard treatment. Finally, some of the children moved to another school during the trial, so different teachers completed the outcome forms, resulting in unsystematic errors.

The strength of the trial is that we published the design protocol before we embarked on the trial. We performed sample size calculation based on the primary outcome measure, conducted a computer generated randomization procedure, and conducted a proper allocation concealment to reduce selection bias. Finally, to strengthen reliability, we videotaped our manual based interventions. Furthermore, we conducted 'blind' outcome assessments, data management, and intention-to-treat analyses, and reported on all outcomes as stipulated in our protocol. Hereby we tried to minimize bias [43-45]. We also included a parent group that was designed to support the children's group, giving parents information about the topic that their children were working with, and also assuring parents that the children could manage their homework in social skills training. Another strength was the measurement of attachment styles in children with ADHD.

Conclusion

In accordance with our Cochrane review on social skills training for children with ADHD, we found no significant benefit or harm in any of the outcome measures of the SOSTRA trial. This suggests that on the basis of our sample size calculation and our consideration of a necessary relevant effect size, currently, there is no evidence to recommend social-skills training with or without parental training for ADHD children. This result and the fact that 93% of the children who were assessed by the Child Attachment Interview at baseline had a type unsecure attachment disorder, leads us to believe that there may be a need for a more profound, longer lasting type of treatment that might result in a change in children's ADHD symptoms, to improve their social and relational competence, and thereby avoid serious further development of the disease.

Competing interests

None of the authors have any competing interests

Authors' contribution

All authors contributed to the design of the study. OJS drafted the manuscript. PW drafted the data analyses and statistical section. All authors contributed to the further review of the manuscript. All authors read and approved the final manuscript.

Abbreviations

ADHD: Attention Deficit Hyperactivity Disorder
IQ: Intelligence quotient
MTA: Multimodal Treatment Study of ADHD
K-SADS: The Schedule for Affective Disorders and Schizophrenia for School-aged Children
SOSTRA: Social Skills Training and Attachment
WISC-III: Wechsler Intelligence Scale for Children
Conners CBRS: Conners Comprehensive Behaviour Rating Scales

Acknowledgements

We would like to thank medical director, Jesper Pedersen, PhD., in the Child and Adolescent Psychiatric Department in Region Zealand, for his support making it possible to complete this trial. Without his help, it would have not been possible. We also thank professor Per Hove Thomsen, M.D., Dr. Med. Sci., Aarhus University Hospital for his advice and support in the process to fulfil this trial. Finally, we are grateful to research associate Maria Skoog, PhD, Copenhagen Trial Unit, for her advice in the design process.
The SOSTRA trial was financially supported by Region's Zealand University Hospital (RESUS), Region Zealand Research Foundation, and Psychiatric Research Unit, Region Zealand. Funding was also received from the Fru C. Hermansens Foundation, Slagtermester Max Wørzner and Inger Wørzners Foundation, and TrygFonden.

References

1. Polanczyk G, Rohde LA (2007) Epidemiology of attention-deficit/hyperactivity disorder across lifespan. Curr Opin in Psychiatry 20: 386-92.

2. Goldman LS, Genel M, Bezman RJ, Slanetz PJ (1998) Diagnosis and treatment of attention-deficit disorder in children and adolescents. J Am Med Association 279: 1100-07.

3. Barkley RA (1998) Attention Deficit Hyperactivity Disorder: A Handbook for Diagnoses and Treatment. New York: Guildford.

4. Storebø OJ, Rosendal S, Skoog M, Groth C, Bille T et al. Methylphenidate for attention deficit hyperactivity disorder (ADHD) in children and adolescents. Cochrane Development Psychosocial and Learning Problems Group. The Cochrane Library. 2012.In press.

5. Gadow KD, Nolan EE, Sverd J, Sprafkin J, Paolicelli L (1990) Methylphenidate in aggressive-hyperactive boys: I. Effects on peer aggression in public school settings. J Am Acad Child and Adoles Psychiatry 29(5): 710-8.

6. Swanson J, McBurnett K, Wigal T, Pfiffner LJ (1993) Effect of stimulant medication on children with attention deficit disorder: a 'review of reviews'. Exceptional Children 60(2): 154-61.

7. MTA Cooperation Group (1999a) A 14-month randomized clinical trial of treatment strategies for attention deficit hyperactivity disorder. Arch Gen Psychiatry 56: 1073-1086.

8. Gilberg C, Melander H, von Knorring A, Janols L, Thernlund G et al. (1997) Long-term stimulant treatment of children with attention-deficit hyperactivity disorder symptoms. A randomized, double blind, placebo-controlled trial. Arch Gen Psychiatry 54: 857-864.

9. Cyr M, Brown C (1998) Current drug therapy recommendations for the treatment of attention deficit hyperactivity disorder. Drug 56: 215-223.

10. Malone MA, Swanson JM (1993) Effects of methylphenidate on impulsive responding in children with attention deficit hyperactivity disorder. J of Child Neurology 8: 157-63.

11. Niderhofer H (2009) Attachment as a component of attention-deficit hyperactivity disorder. Psychological Reports 104: 645-648.

12. Clarke L, Ungerer J, Chahoud K (2002) Attention deficit hyperactivity disorder is associated with attachment insecurity. Clin Child Psych and Psychiatry 7(2): 179-198.

13. Punto C, Turton P, Hughes P, White S, Gillberg C (2006) ADHD and infant disorganized attachment: a prospective study of children next-born after stillbirth. J Atten Disorder 10: 83-91.

14. Target M, Fonagy P, Shmueli-Goetz Y (2003) Attachment representations in school-age children: the development of the child attachment interview (CAI). J of Child Psychotherapy 29: 171-186.

15. Lionel AC, Crosbie J, Barbosa N, Goodale T, Thiruvahindrapuram B. et al., (2011) Rare Copy Number Variation Discovery and Cross-Disorder Comparisons Identify Risk Genes for ADHD. Science Translational Medicine 3(95): 95ra75.

16. Jensen PS, Hinshaw SP, Kraemer HC, Lenora N, Newcorn JH. et al., (2001) ADHD comorbidity findings from the MTA study: comparing comorbid subgroups. J Am Acad Child and Adolesc Psychiatry 40: 147-58.

17. Kadesjö B, Gillberg C (2001) The comorbidity of ADHD in the general population of Swedish school-age children. J Child Psychol Psychiatry 42: 487-92.

18. Miller CJ, Flory JD, Miller SR, Harty SC, Newcorn JH et al. (2008) Childhood ADHD and the Emergence of Personality Disorders in Adolescence: A Prospective Follow-up Study. J Clin Psychiatry 69(9): 1477-1484.

19. Dalsgaard S, Mortensen PB, Frydenberg M, Thomsen PH (2002) Conduct problems, gender and adult psychiatric outcome of children with attention-deficit hyperactivity disorder. British J of Psychiatry 181: 416-21.

20. Bjornstad GJ, Montgomery P (2005) Family therapy for attention-deficit disorder or attention deficit/hyperactivity disorder in children and adolescents. Cochrane Database of Systematic Reviews Issue 2. Art. No.: CD005042. DOI: 10.1002/14651858.CD005042.pub2.

21. Krisanaprakornkit T, Ngamjarus C, Witoonchart C, Piyavhatkul N (2010) Meditation therapies for attention-deficit/hyperactivity disorder (ADHD). Cochrane Database of Systematic Reviews Issue 6. Art. No.: CD006507. DOI: 10.1002/14651858.CD006507.pub2.

22. Zwi M, Jones H, Thorgaard C, York A, Dennis JA. Parent training interventions in school aged children/adolescents with Attention Deficit Hyperactivity Disorder (ADHD). Cochrane Database of Systematic Reviews. In press.

23. Kavale KA, Mathur SR, Forness SR, Rutherford Jr RB, Quinn MM (1997) Effectiveness of social skills training for students with behaviour disorders: A meta-analysis. Advances in Learning and behavioural Disabilities 11: 1-26.

24. Van der oord S, Prins PJM. Oosterlaan J, Emmelkamp PMG (2008) Efficacy of methylphenidate, psychosocial treatment and their combination in school-aged children with ADHD: a meta-analysis. Clin Psychol Review 28(5): 783-800.

25. de Boo GM Prins PJM (2007) Social incompetence in children with ADHD: Possible moderators and mediators in social-skills training. Clin Psychol Review 27: 78-97.

26. Majewicz-Hefley A, Carlson JS (2007) A meta-analysis of combined treatment for children diagnosed with ADHD. J of Attention Disorders 10(3): 239-50.

27. Storebø OJ, Skoog M, Damm D, Thomsen PH, Simonsen E et al. Social skills training for children with attention deficit hyperactivity disorder (ADHD). A Cochrane systematic review. The Cochrane Development Psychosocial and Learning Problems Group. The Cochrane Library. Accepted.

28. Storebø OJ, Pedersen J, Skoog M, Hove Thomsen P, Winkel P et al. (2011) Randomized social-skills training and parental training plus standard treatment versus standard treatment of children with attention deficit hyperactivity disorder—The SOSTRA trial protocol. Trials 12:18.

29. Kaufman J, Birmaher B, Brent D, Rao U, Flynn C et al. (1997) Schedule for Affective Disorders and Schizophrenia from School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. J Am Acad Child and Adolesc Psychiatry 36: 980-8.

30. Rutter M, Bailey A, Lord C (2003) Social Communication Questionnaire (SCQ). Los Angeles: Western Psychological Services.

31. Adler LA, Spencer T, Faraone SV, Kessler RC, Howens MJ et al. (2006) Validity of pilot Adult ADHD Self-Report Scale (ASRS) to rate adult ADHD symptoms. Annual Clinical Psychiatry 18: 145-8.

32. Wechsler D. Wechsler (1998) Intelligence Scale for Children—3rd Edition (WISC-III®). Swedish edition. Stockholm: Psykologiförlaget AB.

33. Conners KC (2008) Conners Comprehensive Behaviour Rating Scales (Conner's CBRS). Toronto, Canada: Multi-Health Systems Inc..

34. Conners KC (2008) Conners 3. Toronto, Canada: Multi-Health Systems Inc..

35. Fohlmann AH (2009) Social færdighedstræning. In: Nordentoft M, Melau M, Iversen T, Kjær S København, editors. Psykose hos unge. Symptomer, behandling og fremtid: Psykiatrifondens Forlag. pp.161-189.

36. Liberman RP (1998) Social skills training. In: Liberman RP, editor. Psychiatric Rehabilitation of Chronic Mental Patients. Washington, D.C: American Psychiatric Press.

37. Pfiffner LJ, McBurnet K (1997) Social skills training with parent generalization: treatment effects for children with attention deficit disorder. J of Consult Clin Psychology 65: 749-757.

38. Antshel KM, Remer R (2003) Social skills training in children with attention deficit hyperactivity disorder: a randomized-controlled clinical trial. J of Clin Child Adolesc Psychology 32: 153-165.

39. Elliot SN, Gresham FM (1993) Social skills interventions for children. Behaviour Modification 17: 287-313.

40. Horns WF, Ialongo NS, Pascoe JM, Greenberg G, Packard T et al. (1991) Additive effects of psychostimulants, parent training, and self-control therapy with ADHD children. J Am Acad of Child and Adolesc Psychiatry 30: 233-240.

41. Corkum PV, McKinnon MM, Mullane JC (2005) The effect of involving classroom teachers in a parent training programme for families of children with ADHD. Child and Family Behaviour Therapy 27: 4, 29-49.

42. Shmueli-Goetz, Target M, Fonagy P, Datta A (2008) The Child Attachment Interview: A psychometric Study of Reliability and Discriminant Validity. Developmental Psychology 44(4): 939-956.

43. Wood L, Egger M, Gluud LL, Schulz KF, Jüni P et al. (2008) Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. BMJ 336(7644): 601-5. Epub 2008 Mar 3.

44. Keus F, Wetterslev J, Gluud C, van Laarhoven CJ (2010) Evidence at a glance: error matrix approach for overviewing available evidence. BMC Med Res Methodol 10: 90.

45. Higgins JPT, Green S, editors (2011) Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration. Available: http://www.cochrane-handbook.org.

Table 1

Sociodemographic and clinical variables (N=56)

	Experimental (N = 28)	Standard (N = 27)
Sociodemographic:		
Males No(%)	19 (67.8)	20 (74.1)
Age/year mean(SD)	10.6(1.29)	10.2(1.34)
ASRS scores ≥ 4 (father) No(%)	6(28.6)	1(5.0)
ASRS score ≥4 (mother) No(%)	6(21.4)	6(24.0)
ADHD diagnoses:		
ADHD-inattentive No(%)	10(35.7)	6(22.2)
ADHD-hyperactive/impulsive No(%)	0(0.0)	2(7.4)
ADHD-combined No(%)	16(57.1)	16(59.2)
ADHD NOS No(%)	2(7.1)	3(11.1)
Other axis 1 disorders:		
Oppositional defiant disorder No(%)	4(33.3)	4(40.0)
Anxiety disorder No(%)	4(33.3)	2(20.0)
Depressive disorder No(%)	1(8.3)	1(10.0)
Tics and Obsessive Compulsive Disorder No(%)	0(0.0)	1(10.0)
Enuresis No(%)	2(20.0)	2(20.0)
Stuttering	1(5.0)	0
Attachment competences:		
Secure No(%)	2(7.1)	2 (7.4)
Insecure/preoccupied No(%)	2(7.1)	1(3.7)
Insecure/dismissing No(%)	19(67.9)	20(74.1)
Disorganized/secure No(%)	0(0.0)	0(0.0)
Disorganized/insecure No(%)	5(17.9)	4(14.8)
Intelligence quotient:		
WISC verbal mean(SD)	93.9(15.7)	87.4(13.3)
WISC non-verbal mean(SD)	94.8(19.0)	88.9(10.5)

Tabel 2 Mean and standard deviation (SD) values, at entry, 3 month, and 6 month

Outcome measure	Time/month	Experimental treatment			Standard treatment		
		N	Mean	SD	N	Mean	SD
Executive s.	0	26	12.00	4.49	27	12.48	4.53
	3	27	9.30	4.58	27	8.44	4.21
	6	28	8.54	4.29	27	9.15	4.55
Academic s.	0	24	25.71	14.54	26	25.31	11.86
	3	24	20.13	15.15	26	17.88	10.11
	6	26	21.04	11.98	27	21.52	12.56
Aggressiveness s.	0	27	17.59	18.03	27	27.85	24.25
	3	27	10.00	12.58	26	11.58	11.89
	6	28	10.50	12.41	27	12.78	12.25
Emotional score	0	27	20.37	15.11	27	17.89	15.25
	3	27	17.26	11.25	26	13.04	12.31
	6	28	16.79	12.09	27	14.44	12.51
Hyperactivity score	0	27	20.70	11.38	27	24.70	14.05
	3	27	16.15	11.45	27	13.93	13.24
	6	28	15.21	9.58	27	13.37	11.86
Peer relation	0	27	8.22	6.12	27	8.63	5.41
	3	27	5.44	5.00	26	4.81	4.48
	6	28	4.86	4.58	27	5.37	5.51
Social p. score	0	27	10.33	6.34	27	11.52	7.03
	3	27	6.89	5.68	27	7.85	5.93
	6	28	8.57	6.00	27	9.56	6.76

Table 3
A mixed model analyses of the primary and the six secondary outcome measures (p-values)

Outcome measure (priority)	Fixed effects of mixed model						
	Sex	Co-morbidity	t	t^2	Intervention-group (G)	G • t	G • t^2
SQ (hyperactivity score)*) (primary)	0.0009	0.013	<0.0001	0.051	0.40	0.33	0.40
Academic score (secondary)	0.97	0.10	0.16	0.010	0.69	0.96	0.30
SQ (aggressiveness score)a) (secondary)	0.037	0.018	0.0013	0.003	0.50	0.79	0.58
SQ (emotional score)*) (secondary)	0.42	0.0051	0.043	0.83	0.14	0.94	0.62
SQ (peer score)*) (secondary)	0.31	0.074	<0.0001	0.056	0.55	0.39	0.76
SQ(social score)*) (secondary)	0.048	0.79	0.089	0.005	0.80	0.68	0.93
Executive score (secondary)	0.55	0.028	<0.0001	0.027	0.22	0.99	0.41

*)To fulfil the assumption of normally distributed values a square root transformation (SQ) was done prior to the mixed model analyses.

Supporting information legends

Figure 1