*Scandinavian Journal of Child and Adolescent Psychiatry and Psychology*
Vol. 2(1):2-10 (2014)

SJCAPP

**Research Article** **Open Access**

# A multicenter, randomized, controlled study of Training Executive, Attention, and Motor Skills (TEAMS) in Danish preschool children with attention-deficit/hyperactivity disorder: Rationale and description of the intervention and study protocol

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**Abstract**

**Background:** Attention-deficit/hyperactivity disorder (ADHD) is a highly prevalent neurodevelopmental disorder that is often detected during the preschool years. Neuroimaging data indicate that children with ADHD have brains that are characterized by growth and functional anomalies. Data suggest that the diminution of ADHD symptoms is correlated with improved neural functioning and growth. On the basis of these findings, interventions that target neural growth, which indicates neural development, can possibly lead to a more enduring treatment for ADHD. Training Executive, Attention, and Motor Skills (TEAMS) is a non-pharmacological neurocognitive intervention program that targets preschool children with ADHD. The program is designed to stimulate neurocognitive growth through physical activity and play in combination with psychoeducation and guidance for the parents.
**Population:** Children between the ages of three and six years from Region Zealand in Denmark who have been diagnosed with ADHD are offered participation in the trial. According to a calculation of the strength needed to result in a statistically significant outcome, the estimated group size should be, at minimum, 87 children. On the basis of Region Zealand's visitation history records, the cohort is expected to include approximately 100 to 120 children.
**Method:** The intervention groups participate in eight weekly group sessions that consist of separate parent and children's groups. The control groups receive the standard treatment program as outlined by the clinical guidelines of Region Zealand. The ADHD Rating Scale-IV and the Danish version of the Strengths and Difficulties Questionnaire are used to assess ADHD symptom severity before and after the intervention and to monitor the duration of the outcome. A comparative analysis of data from the intervention and control groups will illustrate the study's results.
**Study aim:** This is a multicenter, randomized, controlled, single-blind, parallel-group study with the primary aims of testing the TEAMS concept and investigating whether the intervention significantly lowers ADHD symptoms and increases the functionality level after the intervention as compared with the control group. A secondary aim is to monitor the duration and endurance of the outcome for six months after the intervention. This study is currently in progress. Full results and conclusions will be reported after the study's completion in 2015.

**Key words:** Attention-deficit/hyperactivity disorder, preschool, group interventions, TEAMS intervention, randomized controlled trial

**Trial registration**
This trial is registered with ClinicalTrial.Gov: registration no. NCT01918436. It is also registered with Region's Zealand Committee on Health Research Ethics: project registration number 34758, project number SJ-331. The project involves the use of the OPEN Randomize tool (Odense Patient data Explorative Network), and it is registered with the number OP_38.

**Background**

Attention-deficit/hyperactivity disorder (ADHD) is a highly prevalent neurodevelopmental disorder that is typically detected during the preschool years. ADHD is recognized as a chronic disorder, with some associated difficulties persisting into adulthood (1-4).

There are several evidence-based psychopharmacologic (5-7) and behavioral interventions for school-aged children with ADHD that provide short-term symptomatic relief (8-11). Unfortunately, such gains are rarely documented as being maintained after the termination of treatment (12-20).

In addition, studies have shown that few individuals with ADHD receive effective treatment throughout the full course of their disorder (21). Therefore, the development of novel treatments that provide enduring therapeutic benefits by altering the chronic and often incapacitating course of the disorder could have a huge impact on the individual as well as on society, in terms of both cost and human suffering.

Recent research has begun to clarify the underlying neural and neurocognitive determinants of ADHD and may thus provide guidance for the development of interventions that have more lasting effects. Neuroimaging data indicate that children with ADHD have brains that are characterized by delayed, if not permanently stunted, growth as well as by functional anomalies. These are apparent throughout much of the neocortex as well as other parts of the brain (22-27). Emerging neuroimaging and neuropsychological data suggest that the diminution of ADHD symptoms is linked to the development of improved neural functioning (28;29). These findings suggest that interventions that target neural growth and development may provide more sustainable ADHD treatment. The scientific literature demonstrates that neurodevelopmental processes are highly responsive to environmental influences, particularly environmental enrichment and physical exercise (30;31).

Because early childhood is a critical period for brain development, it has been argued that early intervention can be extremely vital (32-35). This has been supported by Halperin and colleagues who studied an intervention that had the aim of addressing the array of neurodevelopmental disorders that are consistent with ADHD (32-36).

**Intervention hypotheses**

The program used in this study - Training Executive, Attention, and Motor Skills (TEAMS) - was designed by Professor Jeffrey Halperin and his team at New York University to enhance brain development and to precipitate enduring changes that could modify the developmental course of ADHD. Halperin's preliminary results were quite promising (37;38).

The main theory behind the TEAMS program is that the way children live their lives has an impact on brain development, which in turn can alter the severity and trajectory of ADHD, and potentially other neurodevelopmental disabilities. TEAMS consists of a menu of game-like activities that place demands on an array of neurocognitive and motor skills; these are interspersed with periods of physical exercise and relaxation exercises. Most data suggest that ADHD is the result of deficient neural networks that affect a wide array of neurocognitive and behavioral processes, including - but not limited to - inhibitory control, working memory, planning, and a range of other executive and non-executive functions. TEAMS' games and activities are designed to improve such neurocognitive domains. Specifically, they are designed to enhance working memory, inhibitory control, visual and spatial planning, and motor skills. Most activities also involve multiple cognitive and behavioral functions, including self-regulation as well as sustained attention and concentration. In addition, TEAMS actively incorporates aerobic physical exercise and relaxation techniques into the program. Aerobic physical exercise has consistently been shown to stimulate brain growth and development, and relaxation is another approach to facilitating attention and inhibitory control while teaching children purposeful winding down (31;36;39).

TEAMS is based on the following hypotheses:

1. The behavioral manifestations of ADHD are the result of deficient neural networks that affect a wide array of neurocognitive and behavioral processes, which are not necessarily identical in all children with the disorder
2. Neurodevelopment is sensitive to and can be positively affected by appropriate environmental influences (39)
3. Effective environmental stimulation will be best achieved within a social context
4. The engagement of the child in the core activities of the treatment must be intrinsically rewarding (i.e., fun) rather than only extrinsically reinforced (i.e., with rewards or tokens) to facilitate the self-imposed continuation of the intervention, which will lead to generalization over time and across settings

**Study aim**

This is a multicenter, randomized, and controlled, single-blind, and parallel group study.

The aims of this study are to test the TEAMS concept and to investigate whether the intervention significantly lowers ADHD symptoms and increases the functionality level after the intervention as compared with the control group. Furthermore, we wish to examine whether the effects are still present six months after the intervention. If the intervention is proved to have a significant effect, the ambition is to implement the TEAMS method as an addition to the existing treatment program in Region Zealand's child psychiatry department. By improving the child's cognitive and social competence, this intervention may possibly ease the difficulties and suffering that are often related to starting school.

**Sample and recruitment**

Children from Region Zealand are diagnosed with ADHD after thorough examination and on the basis of the clinical guidelines as well as 10th revision of the International Statistical Classification of Diseases and Related Health Problems and *Diagnostic and Statistical Manual of Mental Disorders* criteria (1). The clinical guidelines prescribe a minimum examination that consists of the following:

1. Patient anamnesis, information from the child's kindergarten or preschool, and, if necessary, information from social services and municipal files
2. Clinical assessment, including play observation, kindergarten and preschool observation, and a home visit; neurological evaluation; blood pressure, pulse, height, and weight measurement; and heart and lung stethoscope evaluation
3. Paraclinical examination that includes blood testing, electrocardiography, and electroencephalography if anamnesis or clinical assessment arouses the suspicion of a somatic condition
4. Specialized testing, including cognitive testing, projective testing, neuropsychological testing, and ADHD Rating Scale—IV (ADHD-RS-IV) evaluation from the child's parents and preschool or kindergarten teacher (40)

Children who are between the ages of three and six years, who are diagnosed with ADHD as their primary diagnosis, and who fit the established inclusion criteria are referred to further treatment in the ADHD clinic in Holbaek, Denmark.

The families are invited to an individual meeting at the clinic, where they are informed about existing treatment options in Region Zealand, including the possibility of participating in the TEAMS project. During the first meeting, it is determined whether or not the child and his or her family can comply with the criteria of the project and if they wish to participate. After agreeing to participate in the project, the parents sign a declaration of agreement. The child is then randomized to either the intervention group or the control group with the use of the OPEN Randomize tool.

After the families are randomized, they receive an informational letter in the mail in which they are informed of which group they will be following. In this letter is also included a meeting schedule, Region Zealand's rules for mileage allowance, an inquiry forms for the ADHD-RS-IV and for the Danish version of the Strengths and Difficulties Questionnaire (SDQ-DAN) (41;42). Both forms must be completed by the child's parents as well as his or her primary preschool or kindergarten teacher and then returned to the group leader at the first meeting. The members of the intervention group receive an additional form including the rules of the child's group; this form must also be signed and returned to the group leader at the first group session. For a quick overview, see flowchart, Figure 1.

The inclusion criteria are as follows:

- Children between the ages of three and six years who have ADHD as their primary diagnosis

The exclusion criteria are as follows:

- Children of parents who are not capable of cooperating to implement the program
- Children who are living in a residential institution or in an unstable environment outside of the home
- Children or parents who do not speak or understand the Danish language
- Children who are taking medication for ADHD
- Children with significant disabilities as a result of comorbidity such as autism, attachment disorder, or mental retardation

The project design and method have been approved by Region Zealand University Hospital, Region's Zealand Committee on Health Research Ethics, and the Danish Data Protection Agency.

Recruitment from the ADHD clinics in Region Zealand will be ongoing until June 2015.

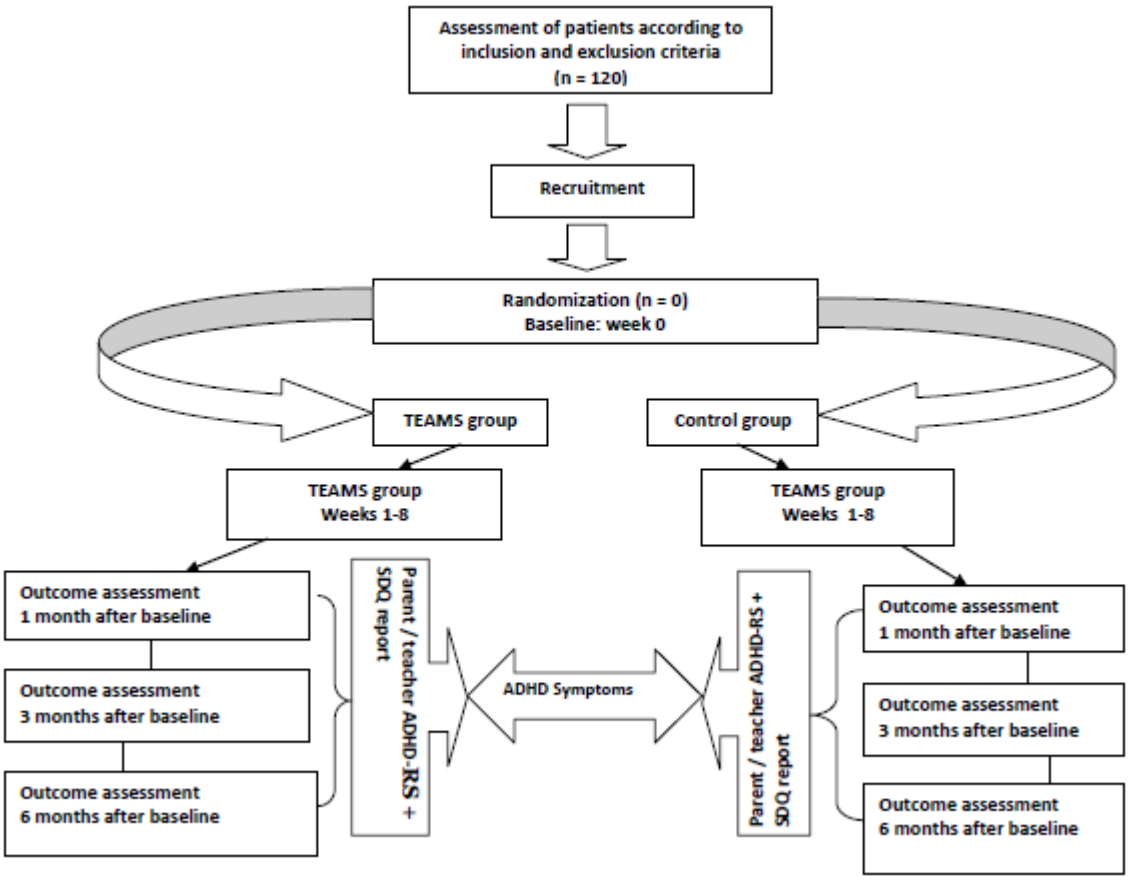


**FIGURE 1. Flowchart showing project outline**

## TEAMS

TEAMS is administered within the context of a small-group setting (i.e., two to five families) and consists of eight weekly separate parent and child group sessions in the clinic.

The notion of "keeping it fun" plays a central role in both the child and parent groups. Parents and children must find TEAMS sessions enjoyable to support their compliance with the treatment. The more enjoyable the games, the more likely it is that they will be played and that neurocognitive growth will thus be stimulated. The importance of having fun together as a family is emphasized by the program, both to facilitate treatment compliance and generalization and to benefit parent–child relationships. The intervention does not include pharmacological treatment during the time period of the intervention.

## Staffing

Two group leaders and one student assistant are present in the playgroup. The group leaders have extensive training in the management of such groups and in the implementation of behavioral procedures. The primary group leader manages the parent sessions while the other staff members attend the children in a coexisting play area, where they are offered a healthy snack and a cold beverage. After the parent's group session is completed, it is the children's turn to participate in the children's group. While the children are active, the parents can relax in a coexisting waiting room, where they also have an opportunity to get acquainted and to discuss their experiences in a more informal atmosphere.

**Parent group**

A main component of the parent intervention involves psychoeducation, collaborative problem solving, and facilitating the child's consistent engagement in TEAMS-related activities outside of the clinical setting.

Specific topics about which the parents receive instruction include the following:

1. The etiology of ADHD, the manifestations of ADHD symptoms across the lifespan, and the framework and philosophy behind TEAMS
2. Symptoms and developmental trends in ADHD; comorbidity
3. Evidence-based treatments: medication
4. Evidence-based treatments: psychosocial treatment of ADHD
5. ADHD and sleep disorders
6. ADHD and nutrition
7. Sibling and family relationships and ADHD
8. Resources for children and families with ADHD

Each topic is accompanied by a handout that provides a brief synopsis of key discussion points; this handout can be accessed for later reference.

Each parent session starts with an outline of the current session and is followed by an evaluation of the past week's experiences. Here the clinician and the families can assess any progress or setbacks that families may have experienced during the week and provide encouragement to each other with regard to the continued engagement of their children in the program's games and goals. This also allows families to clarify issues that they have encountered during the previous week.

The parents are then informed of and instructed in the coming week's activities by the group leader, who provides a brief description of each task and links each activity to its underlying skill sets. Each week there are new games and activities. During the meetings, it is stressed that these activities are to be carried out for 30 to 45 minutes every day and that the children should engage in at least 20 minutes of exercise for a minimum of three days per week. Parents are also asked to complete a relaxation module each day (31;36;38).

Parents are encouraged to adapt TEAMS games, activities, and exercises to fit their children's skill levels and to continually create new and more age-appropriate activities for their children as they grow older; this is known as *scaffolding*. Scaffolding is a central part of the conceptual basis of TEAMS, and it refers to gradual systematic increases in task demands. The process of scaffolding slowly increases the cognitive and motor demands of games and activities with the aim of gradually increasing the level of mastery (31;36;38;43).

Parents are told to allow children some degree of choice in selecting the games that they wish to play. At the same time, parents must ensure that all TEAMS domains are covered during the course of a given week.

Parents are asked to complete daily diaries with the use of a preprinted "Treatment Compliance Assessment" form, which is used to monitor compliance with the program within the home setting. Each week, the parents hand in the completed diaries and receive a new one that is specific to the coming week's activities.

**Children's group**

After the parent group meeting has ended, it is time for the children to play. The activities that the group leader has described to the parent group are now introduced to the children. An average of four new games and activities are introduced each week.

Each session consists of two units, both of which include a five-minute warm-up (e.g., jumping jacks, dancing) and 15 minutes of games and activities. Between the two units, the children are offered a short break and a drink of water.

To ensure behavior management within the group setting, children are reminded of the rules of the children's group and praised for their participation and good fellowship. Enjoyment of the games is emphasized so that children play for the fun of it rather than for prizes or rewards. Because most games involve some form of skill development, the group leader matches the level of difficulty to the child's actual abilities. Games are introduced with enthusiasm, played in a mutually supportive atmosphere, and terminated before moving on to other activities by reinforcing the children's success in the games and encouraging them to play the games with their parents (31;36;38).

**Visualizing the games and activities**

A description of each game or activity is printed on small illustrated card that includes instructions and tips for scaffolding. Each card is color coded, with each color corresponding to a particular cognitive domain:

- **Red** games: motor control (e.g., hopscotch)
- **Green** games: memory (e.g., memory matching games)
- **Yellow** games: visual–spatial skills and planning (e.g., tic-tac-toe)
- **Blue** games: inhibitory control (e.g., freeze dancing)
- **Black** games: exercise (e.g., biking)

- **Purple** games: relaxation (e.g., deep-breathing exercises)

Each child in the group is given a small cardboard suitcase in which they can store the activity cards. New games and activities are added to the suitcase every week.

**Control group intervention**

The families that are randomized to the control group are offered the conventional treatment regime from Region Zealand. The conventional treatment mainly takes place in one of the region's four outpatient clinics. For the sake of this study, all controlgroup patients are also followed by the group leader in the Holbaek clinic, for the whole intervention period. The treatment regime for ADHD consists of a combination of specialized education, psychoeducation targeted at both the child and the parents, and network contact and cooperation. Families are also given guidance regarding positive social training, nutrition, sleep, and exercise as well as they prevention of antisocial behavior and conduct problems. Pharmacological treatment can be supplementary, but it is not offered during the intervention period. The control groups receive three 1-hour individual counseling sessions that are focused on each child's specific needs.

If, for some reason, the child does start receiving medication, he or she is excluded from the study.

**Measuring results and analysis**

For the primary impact measurements, the ADHD-RS-IV and the SDQ-DAN are used. The ADHD-RS-IV is a validated 18-item scale that rates the severity of ADHD symptoms. Each item corresponds to one of the 18 items on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, symptom checklist that is used to diagnose ADHD (44). The SDQ-DAN instrument has been validated, and it corresponds to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems *and Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,* criteria for the diagnosis of ADHD. It consists of 25 statements that focus on the child's strengths and weaknesses involving activity, attention, emotional problems, behavioral difficulties, and so on (34). Both the ADHD-RS-IV and the SDQ-DAN exist in parent/teacher versions as well as versions that have been modified to fit various age groups (42).

A secondary impact measurement is also used. The Treatment Compliance Assessment is a journal-like log that was developed by Halperin and colleagues to induce compliance with the TEAMS treatment program. It is used to record the time spent on TEAMS-related and non-TEAMS-related activities on a weekly basis (31;38).

The intervention group receives ADHD-RS-IV and SDQ-DAN questionnaires by mail. The questionnaires are completed by the parents and the children's primary teachers before the first group meeting, directly after the last week of the program, and then again one, three, and six months after the termination of the intervention. After six months, an individual evaluation meeting is held in the clinic, where the child's current status and future treatment plan are discussed.

The same principles also apply for the control groups.

**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 teachers, who are kept blinded with regard to the child's allocated intervention. The involved parties (i.e., the parents and the children) are instructed not to inform the teacher of the allocation. To secure the integrity of trial data, the principal investigator who will be collecting the questionnaires will be blind to the intervention. Blinded data will be handed over to the South Danish University via the OPEN database; the university will be blinded to the interventions and will be in charge of data entry and statistical analyses. Standardized procedures will be ensured.

**Statistical and outcome analysis**

The questionnaires are all continuously catalogued in the SurveyXact database at Odense University, Denmark. SurveyXact is a web-based application developed by Ramboll, Copenhagen Denmark for the management of questionnaires. This database will be used for data entry, data storage, and data extraction.

The sample size is calculated on the basis of a type I error (α) of 5% and a type II error (β) of 20% (thereby resulting in a power of 80%), with an allocation ratio of 1:1. With a clinically relevant difference of a score of three between the experimental intervention group and the control group on the ADHD-RS-IV (primary outcome) and an assumed standard deviation of five on the same scale, a sample size of 45 participants in each group is needed. With an estimated withdrawal of approximately 30 patients, this corresponds to a total of 120 random-

ized participants. For missing follow-up data (>5%), multiple imputations will be conducted.

To statistically evaluate the effect size of the TEAMS intervention, we will use the same approach that was used in the preliminary research by Halperin and his team (31;38). Halperin describes the data analysis as follows:

**Plan for the analyses**

The statistical analysis of the outcomes will be based on the "intention-to-treat" principle: all randomized 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 randomized intervention. According to the International Conference on Harmonization Tripartite Guideline, Statistical Principles for Clinical Trials E9 Analysis of Drug Trials (45), the analyses will primarily be conducted with adjustment for stratification variables and will secondarily be conducted without adjustment for stratification variables. Descriptive statistics for the two groups will be generated. To investigate the statistical analyses of a possible effect, the mixed model repeated measures method will be used to test the effect of the intervention and the effect of time. The significance level will be set at $P< 0.05$. All effect measures will be inspected for normality and transformed as appropriate. Missing values will be handled via the multiple imputation method.

**Discussion**

The TEAMS program manual is still being improved by Professor Halperin and his team. The manual that this project is based on is an unedited edition that was kindly released to us by Professor Halperin so that we could test the program in a randomized, controlled study outside of the United States.

In response to cultural, linguistic, and demographic differences, it was necessary to translate the manual into Danish and to adjust some of the guidelines to fit Danish society, clinical resources, logistic possibilities, and Danish legislation.

Examples of such modifications include not paying the participants to attend and not giving the children prizes or rewards for participating in the playgroup.

It was also necessary to translate the TEAMS game cards. The games themselves are cross-culturally identifiable, so relevant Danish titles were used rather than directly translating the game names.

Most children in Denmark attend kindergarten, and the majority of primary caretakers in Denmark work outside of the home. To accommodate this, it has been necessary to schedule the group sessions late in the afternoon so that they do not interfere too much with the families' domestic lives. We expect that this may involve the children being tired when they arrive after a long day, which could make their cooperation more challenging.

Initially the TEAMS program was designed to be an eight-week course, but it was later modified to consist of only five weekly sessions. A new outline was created that concurred with the original eight-week outline. This project will thus follow the initial outline based on the assumption that the reduced program, in our clinical setting, would not provide the time necessary to establish the positive connection with the families that is needed for positive collaboration in the group sessions. This assumption is based on the late appointment schedule and the recruitment design. Most families are new to the surroundings and to the clinical staff, because we are recruiting from four different geographic areas of Region Zealand. We anticipate that this might result in the families and children needing time to adjust before they can be confident and relaxed enough in the new environment to optimally participate in the intervention.

It is well documented that psychostimulant medication has a positive effect on ADHD symptoms. In Denmark, psychostimulant medication is generally not an acceptable treatment for children who are less than six years old. Therefore, it is not considered unethical to prolong the participants' inability to obtain this type of treatment by engaging them in the study. In addition, the intervention period is short, and, during the intervention period, the families and their networks are offered a high level of psychoeducation, which is considered the first choice from among the available treatment strategies for this condition. It is also well known that psychostimulant medication is no longer potent for these individuals after treatment is terminated. Thus, it has been contemplated that the intervention presented by this study could possibly result in more durable symptom relief (on the basis of the hypothesis of TEAMS) and that the targeted activities may create neurocognitive growth, thereby possibly diminishing ADHD symptoms on a more permanent basis.

An apparent limitation of this study is the resources available for the group work. It is only possible to have one group at a time, which prolongs the study and causes waiting lists to be necessary, thereby forcing families to wait until the next group starts up. Because we recruit from four different locations, the families must relate to many different professionals; this can have an effect on the family's

relationships with the professionals, which in this case may obstruct learning and inhibit the family's response to the group leaders. In addition, in some instances, participants have a long way to travel late in the afternoon, which can also have a negative impact on the general outcome.

This study has a very simple design and is considered to be low-tech according to instruments and accessories that are needed for the groups, both of which can be considered as strengths. The concept of the program is also very positive: the children and their families have fun together; they learn and evolve while building bonds and having positive relations. It is a safe, ethically strong study that is instructive, educational, and fun.

## Trial status

This project is still recruiting and is currently in progress. The first three trial groups have successfully been completed. Data will be evaluated in October 2015, at which time results will be published in acknowledged national and international journals.

## Competing interests

The authors declare that they have no competing interests.

## Acknowledgements

This study was financially supported by Region Zealand University Hospital (RESUS), Region Zealand Research Foundation. The funding bodies have no role in the design of this study; in the collection, analysis, and interpretation of data; or in the writing of this manuscript.

Odense Patient data Explorative Network (OPEN) has supported this study by providing access to the OPEN Randomize and SurveyXact database facilities at Odense University.

Jeffrey M. Halperin, PhD, of the Department of Psychology at Queens College (New York, NY) and The Graduate Centre at the City University of New York (New York, NY) has given the authors of this study permission to cite his work and to conduct a randomized, controlled study to further the ongoing development of the TEAMS program.

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