The PhD plan

The PhD plan is prepared jointly by the applicant/PhD student and the supervisors. The document is provisional at the time of application but a final complete version must be provided within 3 months after enrolment. Subsequent adjustments to the plan may be made in connection with the half year evaluation and when relevant.

1. The plan relates to
   Name: Maria Søgaard Nielsen

2. Status
   Provisional PhD plan in connection with the application for admission
   Final PhD plan – 3 months after admission
   Adjusted PhD plan
   If this is a final or adjusted PhD plan, please provide a brief description of the changes you have made.

3. Planned PhD education
   Name and number of department: Department of Human Nutrition
   Research group: Pediatric and International Nutrition
   Research School affiliation: FOOD
   Affiliated institution (if any): VIA University College, Department of Nutrition and Health
   Principal supervisor (name/title/departm./phone/e-mail): Lotte Lauritzen/Associate professor/Dept. of Human Nutr./35332508/l1@life.ku.dk
   Supplementary supervisor (name/title/depart./phone/E-mail): Kim Fleischer Michaelsen/Professor/Dept. of Human Nutr./35332495/kfm@life.ku.dk
   PhD project (working title): Dietary habits and nutritional status of Danish children with ADHD and the effect of n-3 LCPUFA on ADHD symptoms
   Is your project related to developing countries? No

4. Objective and hypotheses for the project

   The main purposes of the present project are as follows:

   1) **To examine the dietary habits and nutritional status of Danish children diagnosed with ADHD (attention deficit/hyperactivity disorder)**

   Hypothesizing that children diagnosed with ADHD have altered dietary patterns and a lower nutritional status compared with children not showing any symptoms of ADHD, the specific research objectives of the first part of the project are as follows:

   - To examine the dietary habits of 6- to 15-year-old children diagnosed with ADHD and compare the results with those of the general population of Danish children of the same age. The purpose of this study is to investigate if the dietary habits of children diagnosed with ADHD differ from the general population of children of the same age and, if so, to consider if the difference is due to the disorder of the children or other factors of relevance (e.g., medical treatment and socioeconomic class).
   - To examine the nutritional status and overall health status of 6- to 15-year-old children diagnosed with ADHD using parameters such as height, weight, lean body mass, fat mass, and blood biomarkers (e.g., blood fatty acid composition). In addition to this, there will be a questionnaire examining psychological/social factors (e.g., loneliness) as well as an assessment of physical activity. The qualitative part of the study will also investigate if families of ADHD children have been following specific dietary pieces of advice due to the disorder (e.g., elimination diets also referred to as “few-food diets,” avoidance of specific food or food groups, and intake of fish-oil supplementation or other type
4. Objective and hypotheses for the project

- To examine the effect of fish-oil supplementation on ADHD symptoms in children
  Hypothesizing that intake of long-chain n-3 fatty acids (n-3 LCPUFA), from fish and fish oil, have an effect on symptoms of ADHD in children due to their role on brain function (monoaminergic neurotransmission), the specific research objectives of the second part of the project are as follows:
  - To examine the effect of early supplementation with n-3 LCPUFA on ADHD related symptoms in 12- to 13-year-old children and intake of n-3 LCPUFA in 9- to 11-year-old children on ADHD-like function (especially activity level and social behavior). This study will utilize data from children that have been breast-fed by mothers receiving fish-oil supplementation during the first four months of lactation and data from children in the OPUS (Øptimal trivsel, Udvikling & Sundhed for danske børn gennem en sund ny nordisk kost) school meal intervention. The purpose of this is to examine whether early intake of n-3 LCPUFA has an effect on development of ADHD related symptoms during childhood in children not diagnosed with ADHD.
  - To examine the effect of fish-oil supplementation on ADHD symptoms in children diagnosed with ADHD in a randomized trial. The purpose of this is to see if supplementation with a high dose of fish oil (2–3 g/d of n-3 LCPUFA) can improve the ADHD symptoms in children diagnosed with ADHD.

5. Background, state-of-the-art and relevance

**What is ADHD?**

Attention deficit/hyperactivity disorder (ADHD) is a behavioral disorder characterized by inattention, hyperactivity, and impulsivity (1). Symptoms appear during early childhood and are known to persist through adulthood, where it may cause serious impairments on social, academic, and occupational functioning (2). ADHD is one of the most frequent psychiatric childhood conditions; 3–5% of school-aged children are estimated to meet the criteria for the diagnosis of ADHD, and according to data from the National Health Interview Survey 1998–2009, rates are increasing in the United States and other countries (3). The symptoms vary in different patients and change throughout life; the disorder has huge social, emotional, and behavioral consequences for children as well as adults. At present, the cause of ADHD is unknown, but it is thought to be multifactorial, involving genetic factors as well as neurotransmitter imbalances. Food sensitivities and nutritional problems have also been suggested to affect behavior in children diagnosed with ADHD.

The recommended medical treatment for children with ADHD is central nervous system (CNS)-stimulating drugs such as Ritalin, and over a 10-year period the use of medical treatment for children with ADHD has increased (4;5). Positive effect of medical treatment is observed in 70–80% of the children, but some of the children experience negative side effects such as decrease in appetite, headache, stomachache, and decreased growth probably due to decrease in appetite.

**Why a research project on the relationship between diet and ADHD symptoms in children?**

Because of the fact that 20–30% of the children with ADHD do not benefit from medical treatment, the negative side effects as well as a general concern of treating children with CNS-stimulating medications for a longer period; parents of ADHD children, dieticians, and other health-care professionals have been showing interest in the importance of the diet in treatment of ADHD symptoms in children.

Many studies examining the role of the diet in ADHD treatment have been published. There are studies examining the effects of diets that avoid dietary colorants, addition of fish oils, and other dietary factors as well as using strict elimination diets in the ADHD treatment. None of these have at present reached the status of consensus in treatment of ADHD. In April 2012, a systematic literature review describing the role of the diet in treatment of ADHD in children was published (6). The review was financed by the Ministry of Social Affairs and Integration due to the rising interest among dieticians, other health-care professionals, and parents in using dietary intervention in the daily treatment of ADHD symptoms in children. The literature review was based on 69 scientific articles and suggested that diet may play a role in the treatment of ADHD in children. The review concluded that fish-oil supplementation seems to be one of the most promising dietary interventions to reduce the symptoms of ADHD in children. Moreover, the review highlighted that a comprehensive examination of dietary habits and nutritional status of children with ADHD have never been conducted. Thus, research on the relationship between ADHD and diet is an area that is more relevant than ever.
5. Background, state-of-the-art and relevance

Why examine dietary habits and nutritional status of children with ADHD?

While diet and dietary supplementation in ADHD continue to remain a popular explanation of the disorder that has generated a lot of research (6), there have been only few studies examining the dietary habits and nutritional status of children with ADHD. If a change in dietary intake can cause a change in ADHD symptoms, it may imply that dietary factors play a role in the development of ADHD or that children with ADHD have other nutritional needs than healthy children.

Few studies have investigated the dietary habits and nutritional status of children diagnosed with ADHD. A Canadian study showed that ADHD children had a lower intake of meat compared with healthy children in the same age group, but this study did not find a difference in total energy intake or intake of the macronutrients (e.g., protein, carbohydrate, and fat) (7). However, the study found that the children diagnosed with ADHD had an intake of zinc and copper below the recommended daily intake. An Australian study showed that a "Western dietary pattern" characterized by a high intake of fat, refined sugars, and salt and a low intake of dietary fibers, folic acid, and essential fatty acids was associated with a higher prevalence of ADHD compared with a more healthy dietary pattern in adolescents (8). In addition to this, a Norwegian study concluded that high consumption of sugar-sweetened soft drinks was associated with hyperactivity among adolescents (9). These findings were, however, not supported by a study conducted in Taiwan, where the researchers found no difference in the dietary intake of children diagnosed with ADHD and healthy children of the same age (10).

As indicated above, only few studies have examined the dietary habits and nutritional status of children diagnosed with ADHD, and no such studies have ever been conducted in a Danish population. Dietary patterns are present in the local culture in a specific country or region, and based on this, the results of foreign research might not reflect the actual situation in Denmark. In addition, the medical treatment has side effects that cause decrease in appetite, stomachache, and decreased growth in some children with ADHD; thus, a change in dietary habits could cause an impairment in nutritional status. Taken together, a detailed dietary examination is needed to determine if ADHD children actually do have other dietary habits and a different nutritional status compared with children not diagnosed with ADHD.

Why examine the effect of fish-oil supplementation on ADHD symptoms in children?

It is well known that metabolism of essential fatty acids, the n-3 and n-6 fatty acids, may affect brain function (11). The essential fatty acids cannot be synthesized by the human body; therefore, they must be provided in the diet. n-3 LCPUFA from fish and fish oil are believed to play a central role in brain function by their effect on transmitters in the brain. The n-3 LCPUFA docosahexaenoic acid (DHA) is of special interest in this context, as animal studies have shown that a low intake of DHA can cause an imbalance in signals in the brain, which is hypothesized to influence the degree of inattention in children diagnosed with ADHD (12). Other studies have shown a relationship between blood levels of DHA and the degree of ADHD symptoms in children (13).

According to the newly published review on diet and ADHD (6), 15 studies have been published within this field, and the results on whether fish-oil supplementation may reduce ADHD symptoms are conflicting. A meta-analysis published in 2011 had a special focus on the effect of n-3 fatty acid supplementation in the treatment of children with symptoms of ADHD (14). This meta-analysis concluded that fish-oil supplementation probably has an effect on ADHD symptoms in children, but the authors called for a large intervention study including a sufficient number of children with a high dose of fish-oil supplementation. The meta-analysis estimated that a minimum of 330 subjects are needed to prove the effect.

In what way is this research project relevant for dieticians and other health-care professionals?

Clinical dieticians and other health-care professionals have shown an interest in the importance of the diet in treatment of ADHD symptoms in children for a longer period. But because only few studies have examined the dietary habits and nutritional status of children with ADHD, and none of these studies have been conducted in a Danish population, it is difficult to draw conclusions on the general nutritional status of ADHD children and also to target a nutritional status, in order to plan a dietary treatment of ADHD.

Because 20–30 % of the children with ADHD do not benefit from a medical treatment, parents are searching for pieces of advice among dieticians and other nutrition and health counselors. However, the conflicting results on the nutritional status and the effect of fish-oil supplementation on ADHD symptoms make it difficult to give professional and evidence-based advice to parents of children diagnosed with ADHD. Thus, the proposed research project would facilitate the work of dieticians and nutrition counselors involved in dietary treatment of ADHD children as well as other health-care professionals working with the same group of children.

References
5. Background, state-of-the-art and relevance

(5) Lægemiddelstyrelsen. MEDSTAT.DK. 15-7-2011. 27-2-2012

6. Research plan and methods

Research Plan
This research project has two focus areas: the first focus area (part 1) is an examination of the dietary habits and nutritional status of Danish children diagnosed with ADHD, and this part of the project also includes a study of correlations between intake of specific food items and activity level of healthy children not diagnosed with ADHD.

The second focus area (part 2) is on the effect of early fish-oil supplementation on the later development of ADHD related symptoms in children, and this part will also include a randomized controlled intervention study on the effect of fish-oil supplementation on ADHD symptoms in children diagnosed with ADHD.

Part 1: Examination of dietary habits and nutritional status of Danish children diagnosed with ADHD

1a. A record of intake of food and drinks will be collected from a sample of approximately 330 children aged 6–15 years and diagnosed with ADHD. The children will be recruited from clinics in Copenhagen, Odense, and Esbjerg, where the ADHD children are following established treatment programs.

The children will keep a weighed food record for four consecutive days. The children and their parents will also be interviewed about their experiences following specific dietary pieces of advice (qualitative interview).

The dietary assessment and qualitative interview will be followed by an anthropometric assessment of the ADHD children and biochemical analysis of blood samples from the children.

1b. In addition to the dietary survey of children diagnosed with ADHD, dietary data and data on activity level from 1,600 healthy children included in the OPUS project (OPimal trivsel, Undvikling & Sundhed for danske
5. Background, state-of-the-art and relevance

børn gennem en sund ny nordisk kost) will be analyzed to search for correlations between intake of specific food items/nutrients and the activity level of the children, to investigate if intake of specific food items in any way can be related to symptoms of ADHD (e.g., hyperactivity).

Part 2: The effect of fish-oil supplementation on development of ADHD related symptoms in children

2a. The first part of this study will include a follow-up on 122 children aged 12–13 years. While these children were breast-fed, their mothers received fish-oil supplementation during the four months of lactation. Dietary data from the children will be connected to activity level and social behaviour in search for an effect of early supplementation of fish oil (intake of n-3 LCPUFA) on ADHD related symptoms in children not diagnosed with ADHD.

This part of the study will also utilize data from children participating in the OPUS (OPtimal trivsel, Udvikling & Sundhed for danske børn gennem en sund ny nordisk kost) school meal intervention. The purpose of this is to examine whether early intake of n-3 LCPUFA from the diet has an effect on development of ADHD related symptoms (e.g. activity level and social behavior) during childhood in children not diagnosed with ADHD.

2b. The second part of the examination of the effect of fish-oil supplementation on ADHD symptoms will include an intervention study in approximately 330 children diagnosed with ADHD (the same cohort used for the dietary survey described above). The ADHD children will be randomized to receive either fish-oil supplementation (2–3 g n-3 LCPUFA /day) or placebo for 5 months, and the main focus of the study will be on the effect of the fish-oil supplementation on ADHD symptoms in the children.

7. Planned PhD Courses

PhD students must send documentation for passed external PhD courses to Study and Students’ Affairs (Generic PhD courses may constitute no more than 10 ECTS credits. To be approved, each ad hoc courses must provide at least 2 ECTS credits)

<table>
<thead>
<tr>
<th>Ordinary LIFE PhD courses</th>
<th>Institution</th>
<th>ECTS-credits</th>
<th>Has the course been passed?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction course for PhD students at LIFE</td>
<td>KU LIFE</td>
<td>2</td>
<td>Not yet</td>
</tr>
<tr>
<td>Scientific Writing (A)</td>
<td>KU LIFE</td>
<td>3</td>
<td>Not yet</td>
</tr>
<tr>
<td>Current Trends in Human Nutrition</td>
<td>KU LIFE</td>
<td>6</td>
<td>Not yet</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other PhD courses (ad hoc courses, courses outside of LIFE)</th>
<th>Institution</th>
<th>ECTS-credits</th>
<th>Has the course been passed?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Research</td>
<td>AU</td>
<td>4</td>
<td>Not yet</td>
</tr>
<tr>
<td>Clinical Trials – An Introduction</td>
<td>AU</td>
<td>2,4</td>
<td>Not yet</td>
</tr>
<tr>
<td>Basic Biostatistics</td>
<td>AU</td>
<td>7</td>
<td>Not yet</td>
</tr>
<tr>
<td>STATA &amp; data documentation</td>
<td>AU</td>
<td>1,4</td>
<td>Not yet</td>
</tr>
<tr>
<td>Epidemiology II</td>
<td>AU</td>
<td>4,9</td>
<td>Not yet</td>
</tr>
</tbody>
</table>

*Ad hoc PhD courses outside of LIFE must be pre-approved. Include course description and work load.

Please remember to sign up for each course via the course responsible. Approval of the course portfolio does NOT ensure access to the relevant courses.

8. Allocation of work, percentages.

<table>
<thead>
<tr>
<th>LIFE (min. 15 %)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Affiliated institution (if any)</td>
<td>VIA University College</td>
</tr>
<tr>
<td>Reason for applying for external principal place of work:</td>
<td></td>
</tr>
</tbody>
</table>

9. Agreement regarding patents. Specify any patent agreement appended to the plan here.

No relevant.
10. **Planned stays in other research environments in Denmark and abroad.** Specify period, institution and country. If the plan does not include a stay abroad, provide brief justification.

At this time, an agreement of a stay abroad has not been settled but it is planned that the PhD period will include shorter stays at research environments abroad.

11. **Planned teaching and dissemination activities.** Specify institution and time (min. 70 hours a year).

Will be specified according to the official agreement between LIFE KU and VIA UC.

12. **Budget** (specify whether special financing over and above the standard terms is required as per the financing plan prepared by the department (form F5 – section 3))

Not prepared yet, but no special financing over and above the standard terms of a PhD project will be required to conduct the research project.

13. **Description of research for which a credit transfer is requested**

Not relevant.

14. **Timetable** (indicate the most important milestones)

<table>
<thead>
<tr>
<th>Total time</th>
<th>Activities (courses, research, teaching, dissemination, stays at other research institutions, publications/thesis etc.)</th>
</tr>
</thead>
</table>
| **Phase 1**<br>**Autumn 2012** | Literature study and brainstorming meetings with supervisors  
Collect data from children receiving fish oil-supplementation during lactation (part 2a)  
Planned PhD courses:  
- Introduction course for PhD students at LIFE (KU LIFE) |
| **Phase 2**<br>**Spring 2013** | Final design of part 1 of the project: Dietary habits and nutritional status of children with ADHD  
Recruiting subjects for the dietary survey (part 1a)  
Analyse data from children receiving fish oil-supplementation during lactation (part 2a)  
Analyse data from OPUS: correlations between intake of specific food items/nutrients and activity level of the children (part 1b)  
Planned PhD courses:  
- STATA & data documentation (AU)  
- Basic Biostatistics (AU) |
| **Phase 3**<br>**Autumn 2013** | Collect data on dietary habits and nutritional status of children with ADHD (part 1a)  
 *(BA students from VIA are expected to take part in the practical part of the field work)*  
Write paper on the basis of results from the data collection on children receiving fish-oil supplementation during lactation (part 2a)  
Planned PhD courses:  
- Clinical Research (AU)  
- Clinical Trials – An Introduction (AU) |
| **Phase 4**<br>**Spring 2014** | Analyse results from the dietary survey (part 1a)  
Final design of the intervention study: dietary intervention with fish oil-supplementation in ADHD children (part 2b)  
Start the dietary intervention (part 2b)  
 *(BA students from VIA are expected to take part in the data collection during the intervention study)*  
Planned PhD courses: |
14. **Timetable** (indicate the most important milestones)

<table>
<thead>
<tr>
<th>Phase 5</th>
<th>Autumn 2014</th>
<th>Write 1-2 paper on the basis of results from the investigation of dietary habits and nutritional status of children with ADHD as well as the results from the OPUS study (part 1a + 1b)</th>
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<tbody>
<tr>
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<td></td>
<td>Dietary intervention with fish oil supplementation continued (part 2b) (BA students from VIA are expected to take part in the collection during the intervention study)</td>
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<td>Planned PhD courses:</td>
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<td></td>
<td></td>
<td>- Current Trends in Human Nutrition (KU LIFE)</td>
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</table>

<table>
<thead>
<tr>
<th>Phase 6</th>
<th>Spring 2015</th>
<th>Dietary intervention with fish oil-supplementation continued (part 2b) (BA students from VIA are expected to take part in the data collection during the intervention study)</th>
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<tr>
<td></td>
<td></td>
<td>End of dietary intervention with fish oil-supplementation (part 2b)</td>
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<tr>
<td></td>
<td></td>
<td>Analyse results of the dietary intervention with fish oil-supplementation (part 2b)</td>
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<tr>
<td></td>
<td></td>
<td>Planned PhD courses:</td>
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<td></td>
<td></td>
<td>- Epidemiology II (AU)</td>
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</table>

| Phase 7 | Autumn 2015          | Write paper on the basis of results from the dietary intervention with fish oil-supplementation (part 2b)                                                                                          |

<table>
<thead>
<tr>
<th>Phase 8</th>
<th>Spring 2016</th>
<th>Writing articles (continued)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Finalizing the PhD thesis</td>
</tr>
</tbody>
</table>

Note: Teaching will take place continuously during the four year PhD period.

15. **Agreement on the form of supervision and frequency of meetings**

Get inspiration from the [PhD website](https://www.example.com), see “Good PhD Practice”

An agreement is currently in preparation.

16. **Date and signatures**

<table>
<thead>
<tr>
<th>Principal supervisor</th>
<th>Date</th>
<th>Name</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supplementary supervisors, if any</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>PhD student</td>
<td></td>
<td></td>
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</table>

Revised February 2010