# Functional somatic symptoms in 5-7-year-old children.

## Assessment, prevalence and co-occurrence

*Charlotte Ulrikka Rask*

This review has been accepted as a thesis together with four original papers previously published papers by Aarhus University 26th January 2009 and defended on 13th March 2009

Tutors: Per Hove Thomsen, Per Fink & Anne Mette Skovgaard

Official opponents: Raben Rosenberg, Elena Gerralda & Steffen Husby

Correspondence: The Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital, Nørrebrogade 44, 8000 Aarhus C, Denmark

E-mail: charrask@rm.dk

Dan Med J 2012;59(11): B4537

**THE FOUR ORIGINAL PAPERS ARE**

1. Rask CU, Elberling H, Skovgaard AM, Thomsen PH, Fink P. Parental-reported health anxiety symptoms in 5- to 7-year-old children: the Copenhagen Child Cohort CCC 2000. Psychosomatics. 2012;53(1):58-67.
2. Rask CU, Borg C, Søndergaard C, Schulz-Pedersen S, Thomsen PH, Fink P. A medical record review for functional somatic symptoms in children. J Psychosom Res. 2010;68(4):345-52.
3. Rask CU, Olsen EM, Elberling H, Christensen MF, Ornbøl E, Fink P, Thomsen PH, Skovgaard AM. Functional somatic symptoms and associated impairment in 5-7-year-old children: the Copenhagen Child Cohort 2000. Eur J Epidemiol. 2009;24(10):625-34.
4. Rask CU, Christensen MF, Borg C, Søndergaard C, Thomsen PH, Fink P. The Soma Assessment Interview: new parent interview on functional somatic symptoms in children. J Psychosom Res. 2009;66(5):455-64.

**SETTING**

This thesis is based on two studies. Originally, we set out to conduct a population-based study on functional somatic symptoms in 5-7-year-old children but lacked a standardised comprehensive measure to assess these symptoms in young children.

In study one, we developed such a measure, and in study two we applied it in an epidemiological study on the Copenhagen Child Cohort 2000. This birth cohort was established with the main intention to investigate early predictors of child psychiatric disorders and possibilities of intervention from infancy and onward. The data presented in this thesis stem from a 5-7-year follow-up in which the prevalence of mental disorders, eating problems and functional somatic symptoms were measured by questionnaires and interviews. The children in the cohort have previously been described based on diverse register data and standardised, longitudinal data from the first year of living obtained by public health nurses. This comprehensive data set offers a unique opportunity to perform exploratory and descriptive studies on functional somatic symptoms in young children and to investigate early risk factors for developing these symptoms.

**INTRODUCTION**

**Terminology and definition**

Many terms, diagnoses and clinical labels have been used to refer to conditions characterised by subjective report of physical symptoms in the absence of clear physical pathology (Table 1). Presently, only little agreement exists on which label is the most appropriate. In the paediatric literature, terms like 'somatisation', 'functional' or 'psychosomatic' have been commonly employed, whereas 'medically unexplained symptoms' (MUS) has only been introduced recently [2]. The term psychosomatic can be criticised for implying unproven psychological mechanisms for the symptoms in question, whereas MUS implies that an explanation for the symptoms cannot be found. This is clearly against findings suggesting that e.g. autonomic arousal and physiological deconditioning may play a causal role as may theoretical models in which the symptoms are explained in terms of interacting biological, psychological and/or social processes [3-7].

The term 'functional somatic symptoms' (FSS) is primarily used in this thesis as it is regarded as more acceptable than many others terms [8]. I will refer to the descriptive definition by Fink P et al: 'FSS are complaints or symptoms defying the clinical picture of known, verifiable, conventionally defined diseases and unbacked by clinical or paraclinical findings' [9]. At times, the term 'somatisation' will be used according to Lipowski's definition from 1988: ' A tendency to experience and communicate somatic distress and symptoms unaccounted for by pathological findings, to attribute them to physical illness and to seek medical help for them' [10].

**Classification**

Within psychiatry, FSS are the central feature for a number of International Statistical Classification of Diseases and Related Health problems, tenth revision (ICD-10) and Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) diagnoses, mainly classified under somatoform disorders (Table 2).

**Table 1. Examples of terms used for FSS and conditions dominated by FSS**

| |
|---|
| Medically unexplained (physical/somatic/bodily) symptoms/complaints |
| Non-organic physical/somatic/bodily symptoms/complaints |
| Functional somatic/bodily symptoms/complaints |
| Psychosomatic symptoms/complaints |
| Somatoform symptoms/complaints |
| Idiopathic physical/somatic/bodily symptoms/complaints |
| Conversion symptoms |
| Subjective health complaints |
| Psychogenic somatic/bodily symptoms/complaints |
| Somatization/somatisation |
| Unexplained medical condition |
| Somatoform disorders/somatization disorders |
| Conversion disorders |
| Dissociative disorders (DS) |
| Functional disorders |
| Functional somatic/physical syndrome |
| Chronic fatigue syndrome/neurasthenia/myalgic encephalomyelitis |
| Growing pains |
| Recurrent abdominal pain (RAP)* |
| Functional abdominal pain |
| Functional gastrointestinal/intestinal disorders |
| Functional intestinal disorders |
| Functional headache |
| Tension headache |
| Fibromyalgia |
| 'Psychiatric syndromes with somatic presentation' |
| Medically unexplained chronic pain |
| Non-specific musculoskeletal pain |
| Idiopathic musculoskeletal pain |
| Pseudo seizures |
| Cyclic vomiting syndrome |
| Noncardiac chest pain |
| Chronic benign pain |
| Hypochondriasis** |
| Health anxiety** |
| Illness worry** |

**Table 2. DSM-IV and ICD-10 somatoform and related disorders with FSS as central feature**

| DSM-IV (300.X) | ICD-10 (F45.X) |
|---|---|
| Somatization disorder | Somatisation disorder |
| Undifferentiated somatoform disorder (SD) | Undifferentiated SD |
| Hypochondriasis | Hypochondriacal disorder |
| Pain disorder | Persistent somatoform pain disorder |
| SD not otherwise specified | SD unspecified |
| Conversion disorder | Dissociative disorder (DS) (F44.4-7) |
| -- / -- | Other DS |
| -- / -- | Somatoform autonomic dysfunction |
| Body dysmorphic disorder | Persistent delusional disorders (F22.8) |
| -- / -- | Neurasthenia (F48.0) |

It is generally accepted that the diagnostic criteria for these conditions are poorly applicable to children [11,12], and at present the diagnoses are inconsistently used by professionals in children's settings including child and adolescent psychiatry [13]. Some progress has been made with a recent classification of a child and adolescent mental diagnosis in primary care, which takes into account developmentally appropriate considerations adding two new categories: Somatic Complaint Variation and Somatic Complaint Problem [14].

While the psychiatric system primarily may represent a lumping perspective (looking at similarities), the paediatric system may represent a splitting perspective (looking for differences) [15]. Thus, within paediatrics, different functional somatic syndromes, symptom diagnoses and clinical labels are used, e.g. functional (recurrent) abdominal pain, growing pains, chronic fatigue syndrome (CFS), irritable bowel syndrome and fibromyalgia. In many cases, however, the paediatric and psychiatric classifications refer to the same children and symptoms, which have resulted in largely separate research lines in literatures on FSS [2,16,17].

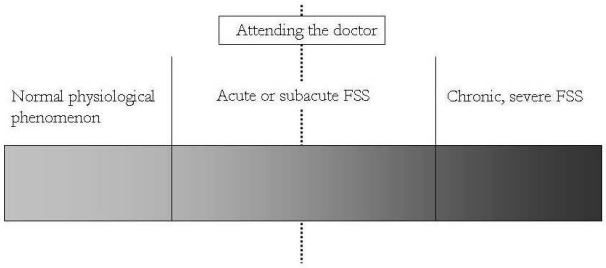
**Clinical presentations**

FSS have long been recognised as a common and challenging phenomenon in paediatric practice with description of 'pain-prone' children with recurrent complaints [18,19]. Clinical presentations vary greatly. FSS may be seen on a continuum of severity [2] ranging from children with transient and relatively mild symptoms that may be difficult to separate from a normal physiological phenomenon to an 'adjustment reaction' with acute or subacute FSS and to conditions with severe, chronic and disabling FSS (Figure 1). FSS can be related to any bodily system, and the types of symptoms encountered may vary according to the subspecialty in question, e.g. functional abdominal pain in paediatric gastroenterology [20], gait disturbances or sensory loss or non-epileptic seizures in neurological settings [21] and chronic fatigue in paediatric infectious disease clinics [22]. The symptoms may be monosymptomatic, oligo- and multisymptomatic. Co-occurrence between or clustering of different types of FSS, especially between different functional pain complaints, have been shown in several studies [23-28]. However, particularly in prepubertal children, the symptoms are seldom sufficiently varied, severe or disabling to qualify for the somatoform disorders in ICD-10 or DSM-IV [11,29].

There is considerable evidence for links between psychopathology and FSS. In a population-based study, psychiatric disorders were reported in nearly half the children/adolescents with high somatic scores in contrast to one in ten for the rest [30], and associations are generally found between different types of recurrent somatic and psychological symptoms [24,31-33]. While emotional symptoms seem to be the most common problem among older children, behavioural difficulties may be more common in children aged 6 years and younger [34,35]. The same findings of a frequent association with especially emotional symptoms or disorders have been reported amongst children and adolescents with FSS and FSS-related disorders in clinic settings [36-40].

In addition to psychological problems, recurrent FSS have been shown to be associated with impairment in important areas of functioning (e.g. prolonged daycare and school absences, fewer hobbies, impact on daily life and leisure activities) and health care utilisation [36,41-48]. Levels of distress, functional disability, health resource utilisation and associated psychopathology are likely to increase from one end of the FSS continuum to the other (Figure 1).

**Figure 1. Functional somatic symptoms on a continuum**




A controversial issue is whether several different conditions dominated by FSS exist or if it is just one underlying trait of somatisation that receives different labels [49-53]. On balance, the evidence based on e.g. explorative factor analysis of symptom patterns [54] seems to be consistent with the intermediate view that somatisation can be expressed in many bodily systems (e.g., nervous, musculoskeletal, circulatory, gastrointestinal). That is, there may be different subgroups of patients with FSS, some of whom experience symptoms that are specific to a particular body system [37,55,56], and others who have fluctuating and several types of FSS.

Hypochondriasis, now often designated health anxiety, refers in DSM-IV and ICD-10 to the persistent, preoccupying fear that one has a serious disease and is classified as a subtype of the somatoform disorders. Studies on adults [57] and also adolescents [58] show that there is considerable overlap between health concerns and somatic symptoms but very little is known and less reported in the literature about the occurrence of health anxiety in children [59,60].

**Risk factors**

The exact etiology of FSS is unknown, but it is probably multifactorial. Child characteristics such as age, gender, personality features, health problems, stress reactivity and coping as well as environmental domains have been shown to affect the prevalence and course of FSS and FSS related disorders in children and adolescents.

***Child characteristics***

Age may be an important factor in the type of symptoms experienced and reported. Certain symptoms seem to be more prevalent at different developmental stages, e.g. abdominal pain in preschoolers and headache in older children. Second, the overall prevalence, especially multi-symptomatic presentation, increases with age [16]. Epidemiological research presents conflicting results on gender and FSS. Some studies report no prepuberty gender difference in the prevalence of FSS [43,61,62], others report a higher frequency in girls than boys before puberty [24,27] as also seen in adolescence and adulthood. Proposed hypotheses of this gender difference include a gender-specific socialisation of females to express symptom experiences to a higher degree [63-66], whereas physiological and neurobiological changes associated with puberty may play a role later on [67]. Clinical experience and some studies suggest that personal experience of illness in childhood may be a precursor or predictor for FSS or FSS related disorders, e.g. chronic fatigue syndrome [68-70]. However, in a large British birth cohort, childhood experience of illness in parents and unexplained symptoms, but not severe physical disease in the child itself, were shown to predict FSS later in life [71].

Although there is a lack of strong empirical evidence identifying particular psychological profiles in children with FSS, clinicians' accounts and a study on adolescents with CFS have noted certain common characteristics with particular strong traits of vulnerability, conscientiousness and anxiousness [72-74]. FSS may reflect an anxious child's increased focus on bodily sensations and rumination of physical symptoms as opposed to adaptively coping with the pain or sensation. Empirical evidence, from e.g. studies on children with headache and abdominal pain, offers support for the idea that children with high levels of FSS have fewer adaptive coping strategies and to some extent a heightened emotional response to stress compared with children with organic illness and community samples of children [1,41,42,75-79]. Especially blood pressure (marker of autonomic nervous system) and cortisol (a marker of the limbic hypothalamic-pituitary-adrenocortical system) have been measured as physiological markers of stress reactivity in children with FSS [75,80-82], but the findings are inconsistent. It is also important to emphasise that the mentioned personality traits may not be specific for children with FSS but a shared vulnerability in children with FSS and children with emotional disorders.

***Environmental factors***

FSS and FSS related disorders, including somatoform disorders, are highly familial, and children and other family members often share similar symptoms. Genetic predisposition and different factors such as high rates of health problems and long-term illnesses, psychological distress and preoccupation with illness in the family are thought to contribute [83-87]. These factors are likely to serve as a model for the child's symptoms. Furthermore, empirical evidence support that negative, adverse events or stressors in the home, including socioeconomic factors, or at school increase FSS in community and clinic samples of children [70,88-93]. Physical or sexual abuse may be present in a minority of cases [94-96].

Many of the mentioned factors are also described as risk factors for overall mental distress. It has been suggested that a combination of psychological distress and health problems in the family with a tendency of somatic attribution and prominent illness-focused behavior and impairment may be specific for the development of FSS [97]. Thus, familiar somatic attribution or disease conviction, a belief in a biological medical cause or disease even after multiple negative medical opinions and investigations, may be a phenomenon specific to FSS across the severity range [58,98].

**Prognosis**

Relatively few long-term prospective studies have been performed, and they have primarily been on adolescents, highly selected clinical populations and population-based samples. Results from a large population-based birth cohort study in UK suggest that FSS in childhood may continue over time with the risk of persistent FSS, unnecessary treatment and hospitalisation as well as the risk of future psychiatric disorders[99-101]. Two other general population-based studies have also shown continuity of FSS from adolescence to early adulthood [102,103]. Furthermore, in 'highly somatising' adolescents, an increased risk of major depression and panic attacks was shown at 4-year follow-up [104].

Follow-up studies on children with recurrent abdominal pain (RAP) have shown persistence of pain in adulthood for one third to a half [105,106], and these children also display other FSS and

more functional disability compared with healthy controls when they become adolescents and young adults [107,108]. However, one study showed that former RAP patients were more likely to display psychiatric morbidity (anxiety symptoms and disorders, hypochondriacal beliefs) and functional disability, but not abdominal pain or other somatic symptoms [109]. In children with severe handicapping CFS, it was shown that two thirds had recovered at 45.5 months (mean) follow-up [110]. Poor prognostic indicators were parental somatic attribution style and an insidious onset.

*In summary*, the interpretation of the results on prognosis is complicated by the different populations and varying impairment levels. The studies provide some evidence of the continuity of a general component of FSS from childhood through adolescence and young adulthood. However, at this point the data are few, especially as to whether or not a chronic course of FSS is a risk factor for later psychopathology, specifically clinical depression.

**Treatment**

Many children with transient symptoms clearly related to obvious precipitant/stress factors can be managed effectively in primary care or by paediatric clinicians by the exclusion of organic disease, explanation of FSS and reassurance. In more complicated cases, a rehabilitative approach with an active, problem-focused approach to coping as well as engagement of the family, taking into account their fears and beliefs about physical causation of the symptoms, are all emphasised as being important in the management [111-117]. Many children with transient symptoms clearly related to obvious precipitant/stress factors can be managed effectively in primary care or by paediatric clinicians by the exclusion of organic disease, explanation of FSS and reassurance. In more complicated cases, a rehabilitative approach with an active, problem-focused approach to coping as well as engagement of the family, taking into account their fears and beliefs about physical causation of the symptoms, are all emphasised as being important in the management [111-117]. These strategies are not evidence-based but rely on clinical experience. Specifically for headache, RAP, fibromyalgia and chronic fatigue syndrome, the use of family cognitive behavioural techniques have shown to be effective [118-125]. A balanced management between biomedical, organ-oriented and family cognitive behavioural techniques may therefore be preferable in the most complicated cases. For a number of cases, this will call for a joint paediatric/mental health approach [97]. In this context, a stepped care model, as recommended in the management of adult patients, that differentiates between uncomplicated and complicated FSS, may be relevant [126].

*In summary*, even though there is now some evidence from controlled trials that cognitive behavioural therapy can be more effective for FSS than standard treatment alone, there is still a lack of methodological rigorous studies to provide guidelines for evidence-based treatment in this area. Key clinical issues may be additional psychopharmacological treatment and management of family disease beliefs and parental coping of the child's FSS.

**Prevalence estimates and methodological issues in epidemiological studies**

Counting cases is an important first step toward measuring the social burden caused by FSS and the effectiveness of prevention. 'Psychosomatic problems' have been shown to account for 8-10% of visits in primary care facilities [127], and among children attending their family doctors, 'psychosomatic-type symptoms' were the presenting problem in 17% [128]. However, population-based studies are needed to measure the extent of need and unmet need for prevention or treatment. A major task facing the area of FSS in children is to develop assessment measures that accurately identify true cases, i.e. children with clinically significant FSS. Recurrent FSS are often reported to affect 10-30% of children and adolescents [3,16,129,130]. Still, the present prevalence estimates in various epidemiological studies vary not only due to differences between design and study populations, but also because different methods and case definitions have been used (Table 3). Each of these methodological issues will be briefly presented below.

***Design***

Many studies have addressed specific types of symptoms (e.g. limb pain/growing pain, recurrent abdominal pain or headache), rather than providing a comprehensive analysis of FSS in childhood [34,131,132], which might produce an underestimation of the overall prevalence. Such a design also hampers the examination of co-occurrence or clustering of FSS in children; an examination that could provide important information for the development of age-appropriate criteria for functional disorders in children if appropriately designed. Several studies have now shown a high co-occurrence between different pain complaints even in young children [24-26,133,134].

***Source populations***

Sample representativeness is another issue which must be critically apprised. Some studies have examined subjects of a narrow age range, others a very broad age range. The children can be derived from schools, hospital catchment areas, primarily urban areas, large birth cohorts or the sampling frame is not specified (Table 3). Moreover, the majority of studies address prevalence of FSS in children in a single country, whereas one large study was performed in five Nordic countries [88]. These issues are important to consider when judging if a generalisation of the results to the whole population or across countries is valid.

**Table 3. Selected population-based studies on somatic complaints/FSS (including children <10 years)**

| Reference/Country | Symptoms | N/age | Design | Prevalence/time frame |
|---|---|---|---|---|
| Naish and Apley [135]<br>UK | Growing pain | N=721<br>'school-aged' | School sample<br>Clinical assessment plus parental and child report - unspecified questions | 4.2%/not stated<br>♂: 4.0%, ♀: 4.7% |
| Brenning [136]<br>Sweden | Growing pain | N=257<br>6-7 yrs<br>N=419<br>10-11 yrs | School sample<br>Clinical assessment plus parental reportunspecified questions | 6-7 yrs: 13.6 %/not stated<br>♂: 9.1%, ♀: 18.4%<br>10-11 yrs: 19.8%/not stated<br>♂: 19.9%, ♀: 19.7% |
| Abu-Arafeh and Russell [131]<br>UK | Recurrent limb pain (unknown etiology) | N=1,754<br>5-15 yrs | School sample<br>Two-step: Screening questionnaire followed by a physical examination and clinical interview with symptomatic children and parents using specific diagnostic criteria | 2.6 %/past year<br>♂: 2.3%, ♀: 2.9% |
| Oberklaid [23]<br>Australia | Growing pain | N=1,605<br>8 yrs | Well-defined cohort (ATP)<br>Two-step: Screening item followed by detailed questionnaire on growing pains. Parental report | 11.4%/past year<br>Gender estimates not given<br>Associated with headaches and stomach aches and chronic illness |
| Evans and Scutter [137]<br>Australia | Growing pain | N=1,445<br>4-6 yrs | Sample from schools and child care centers<br>Questionnaire on growing pains with specific case criteria. Parental report | 36.9%/not stated<br>Gender estimates not given |
| Apley and Naish [138]<br>UK | Recurrent abdominal pain | N=1,000<br>'school-aged' | School sample<br>Clinical assessment plus parental and child report. Apley's criteria for RAP | 10.8%/past year<br>♂: 9.5%, ♀: 12.3% |
| Faull and Nicol [34]<br>UK | Recurrent abdominal pain | N=494<br>5-6 yrs | School sample<br>Two-step: Screening questionnaire followed by parental interview using Apley's criteria for RAP | 24.5-26.9%/past year<br>No gender difference |
| Ramchandani et al [24]<br>UK | Recurrent abdominal pain | N=10,205<br>2 yrs<br>N=9,845<br>3 yrs<br>N= 8,272<br>6 yrs | Well-defined birth cohort (ALSPAC)<br>Same questionnaire on 3 occasions: when the child was 30, 42 and 81 months. Maternal report<br>Case definition: ≥ 5 episodes of pain in the past year | 2 yrs: 3.8%/past year<br>3 yrs: 6.9%/past year<br>6 yrs:11.8%/past year<br>♀ > ♂, Odds Ratio (OR): 1.59<br>Associated with headache and limb pain |
| Dahl-Larsen et al [139] Denmark | Recurrent abdominal pain | N=849<br>9-13 yrs | School sample<br>Apley's criteria slightly modified (past 3 months) | 12%/past three months<br>♂: 9.7%, ♀: 14.7%<br>Associated with upper dyspepsia, constipation and asthma/allergy |
| Silanpaa and Kero [132]<br>Finland | Headache | N=4,405<br>5 yrs | Well-defined birth cohort<br>Prestructured questionnaire and data collection from public health nurses and parents<br>Case definitions not specified | Total: 19.5%/lifetime<br>Highly or fairly frequent: 0.7%<br>Less frequent or infrequent: 18.8%<br>Gender estimates not given<br>Associated with stomach ache, diurnal enuresis |
| Zuckerman et al [35]<br>UK | Recurrent abdominal pain and headaches | N= 308<br>3 yrs | Recruited from postnatal mothers' groups in three general practices in outer London<br>Semi-structured maternal interview<br>Case definition: pain occurred during the preceding 4 weeks and any time prior to this | Headache: 3%/past 4 weeks<br>Abdominal pain: 9%/past 4 weeks<br>Gender estimates not given |
| Stevenson et al [140]<br>UK | Recurrent abdominal pain and headaches | N=189<br>3 yrs | Children identified by health visitors<br>Replication of study by Zuckerman et al | Headache: 3%/past 4 weeks<br>Abdominal pain: 5%/past 4 weeks<br>Gender estimates not given |
| Borge et al [133]<br>Norway | Abdominal pain and headache | N=140<br>4 yrs<br>N=136<br>10 yrs | Well-defined cohort<br>4 yrs: semi-structured interviews with mothers by public health nurses<br>Frequent pain: pain three times per week or more<br>10 yrs: parent and teacher questionnaires<br>Frequent pain: at least one episode once a week | 4 yrs/frequent pain/past 4 weeks:<br>abdominal pain: 6.6%; headache: 0%<br>Co-occurrence: 4.4%<br>10 yrs/frequent pain/last year:<br>abdominal pain: 5.1%, headache: 5.9%<br>Co-occurrence: 20.6%<br>Gender estimates not given |
| Oster [25]<br>Denmark | Growing pain, abdominal pain, headache | N=2,178<br>6-19 yrs | School sample<br>Clinical assessment and child report on presence of symptoms | Growing pain 15.5%/not stated<br>♂: 12.5%, ♀: 18.4%<br>Abdominal pain 12.3 %/not stated<br>♂: 9.6%, ♀: 14.8%<br>Headache 20.6%/not stated<br>♂: 18.3%, ♀: 22.8 %<br>Multiple pain: 9.2% |

| | | | | |
|---|---|---|---|---|
| Egger et al [32]<br>USA | Abdominal pain, headache and musculoskeletal pain | N=1,013<br>9-15 yrs | Well-defined cohort (GSMS)<br>Interview (CAPA) with child and parent<br>Case definition: headache or abdominal pain lasting for at least 1 hour and at least once a week. Musculoskeletal pain at least 3 times a week and not due to sport. | Abdominal pain: 2.8%/past 3 months<br>♂: 1.9%, ♀: 3.8%<br>Headache: 10.3%/past 3 months<br>no gender difference<br>Musculoskeletal pain: 2.2%/past 3 months<br>no gender difference<br>Multiple pain: 1.4% |
| Petersen et al [26],[141] Sweden | Abdominal pain, headache, back-ache and tiredness | N=1,121<br>6-13 yrs | School sample<br>Questionnaire (HBSC), grade 0-4 self-report plus assistance from parents, grade 5 & 6 only self-report<br>Case definition by frequency of the different symptoms | Experience > 1 per week/past 6 months:<br>Abdominal pain: 7.9%, ♂: 7.0%, ♀: 8.9%<br>Headache: 9.0%, ♂: 8.3%, ♀: 9.9%<br>Backache: 3.3%, ♂: 2.7%, ♀: 3.9%<br>All three pain types: 9%<br>Tiredness: 16% (almost every day), ♂: 17.7%, ♀: 14.3% |
| Christensen et al [134]<br>Denmark | Abdominal pain, headache, pain in arms/legs, consti-pation, diarrhoea, enuresis, encopre-sis | N=2,530<br>5-16 yrs | School sample<br>Questionnaire using Apley's criteria for RAP, parental report | Symptom present/past year<br>RAP: 11.4%, ♂: 9,2%, ♀: 13,7%<br>Headache: 20.3%, ♂: 17.8%, ♀: 22.9%<br>Pain in arms/legs: 17.2%, ♂: 16.0%, ♀: 18.5%<br>Constipation: 2.3%, ♂: 2.2%, ♀: 2.5%<br>Diarrhoea: 3.8%, ♂: 4.4%, ♀: 3.2%<br>Enuresis: 7.0%, ♂: 7.7%, ♀: 6.2%<br>Encopresis: 1.3%, ♂: 1.5%, ♀: 1.0%<br>Association between RAP and other symptoms |
| Tamminen [62]<br>Finland | Abdominal pain, headache, other pain or aches, nausea or vomit-ing | N=1,103<br>8 yrs | Sample from the University Hospital Region of Tampere<br>Questionnaires to parents and teachers (Rutters Scale) and child (CDI plus 4 items on somatic complaints). Case definition by frequency | Child reports (almost every day)/not stated<br>Headache: ♂: 3.8%, ♀: 3.8 %<br>Abdominal pain: ♂: 2.6%, ♀: 3.5%<br>Pain or aches: ♂: 2.4%, ♀: 2.4%<br>Nausea or vomiting: ♂: 3.1%, ♀ 3.4% |
| Berntsson et al [142]<br>Nordic Countries (Denmark, Finland, Iceland, Norway and Sweden) | Stomach com-plaints, headache, sleeplessness, dizziness, back-ache, loss of appetite | N=3,812<br>7-12 yrs | Five random samples drawn from population registers of each country<br><br>Questionnaire. Combined child and parent report.<br>Case definition: one or more symptoms occurring every or every other week | Any symptom: 25.0 %/not stated (mild: 16.7%, moderate: 7.5%, severe: 0.8%), ♂: 22.7%, ♀: 27.2%<br>Stomach complaints: 10.9%<br>Headache: 13.0%<br>Backache: 2.3 %<br>Sleeplessness: 2.0%<br>Dizziness: 1.0%<br>Loss of appetite: 4.7% |
| Perquin et al [27]<br>Holland | Pain<br>(loactions: head, abdomen, limb, ear, throat, back, or elsewhere) | N=5,423<br>0-18 yrs | 0-3 yrs random sample from the register of popu-lation in Rotterdam, 4-18 yrs school sample<br><br>Structured pain questionnaire, 0-7 yrs parental report, 8-18 yrs child report.<br>Case definition: chronic pain if recurrent or con-tinuous pain for more than 3 months | Chronic pain/past 3 months<br>Total: 25.0%, ♂: 19.5%, ♀ : 30.4%<br>0-3 yrs: 11.8%, ♂: 13.6%, ♀ : 9.9%<br>4-7 yrs: 19.3%, ♂: 15.8%, ♀ : 22.7%<br>8-11 yrs: 23.7%, ♂: 19.7%, ♀ : 27.7%<br>12-15 yrs: 35.7%, ♂: 25.6%,♀ : 44.0%,,<br>16-18 yrs: 31.2%, ♂: 19.7%,♀ : 43.2%,<br>Headache, abdominal pain and limb pain most frequent. Multiple chronic pain: 12.9% |
| Domenech-Llaberia et al [43]<br>Spain | Abdominal pain, leg pain, head-aches, tiredness, dizziness | N=807<br>3-5 yrs | Children attending preschool public and private nurseries in two Catalan populations (urban and rural)<br>Questionnaire including request about paediatric help-seeking and preschool absence. Parental report. Children with a chronic physical disorder excluded<br>Case definition by frequency | ≥ 4 times complaints/past 2 weeks:<br>20.4% Abdominal pain: 7.9%<br>Tiredness: 5.7%<br>Leg pains: 3.8 %<br>Headaches: 2.0 %<br>Dizziness: 0.4%<br>Frequent complaints associated with more paediatric consultations and absence from preschool. No gender difference |

| | | | | |
|---|---|---|---|---|
| Garber et al [28]<br>USA | 35 symptoms | N=540<br>'school-aged' | School sample<br>Questionnaire (CSI), child report for all, parent report for a subset<br>Case definition: calculation of CSI score plus number of reported symptoms | Child report/past 2 weeks<br>≥ 4 symptoms: 15.2%<br>≥ 13 symptoms: 1.1%<br>♀ > ♂ in high school students. No gender difference in younger age groups |
| Offord et al [29]<br>Canada | Combination of possible unexplained symptoms, loss of function and health concerns | N=2,674<br>4-16 yrs | Well-defined population (OCHS) drawn from household dwellings<br>Questionnaire. Combinations of parental, child and teacher report.<br>Case definition: distressing recurrent somatic symptoms with no known organic cause and perception of oneself as sickly. Binary rating using scores that best discriminated independently made clinical diagnoses of somatisation | Somatisation/past 6 months<br>4-11 yrs: not measurable<br>12-16 yrs: ♀: 10.7%, ♂: 4.5% |
| ALSPAC: the Avon Longitudinal Study of Parents And Children, ATP: Australian Temperament Project, CAPA: Child and Adolescent Psychiatric Assessment, CDI: Children Depression Inventory, CSI: Childrens' Somatisation Inventory, RAP: Recurrent Abdominal Pain: at least 3 bouts of abdominal pain, severe enough to affect the child's activities, over a period of not less than 3 months, with attacks continuing in the year preceding the examination, GSMS: the Great Smoky Mountains Study, HBSC: Health Behavior in School-aged Children, OCHS: Ontario Child Health Study | | | | |

***Instrumentation***

FSS are most often studied solely by measures of subjective or perceived symptoms as medical assessments are too resource demanding in large epidemiological studies. Scales and symptom check lists are commonly used measurement formats (Table 4). These are considered easy to understand and to yield satisfactory face validity, but few have studied other types of validity. One of the most used and validated check lists, the Children's Somatization Inventory (CSI), is like most of the other check lists derived from adult symptom lists [28]. This is problematic given the pattern and number of symptoms experienced, and the language used in reporting symptoms is obviously different for children [143,144]. Thus, the authors have recently refined the original CSI by removing statistically weak items [54].

Check lists primarily provide figures on symptom prevalence (occurrence or non-occurrence [58,145]) rather than qualitative aspects such as impairment and well-being. Some of the check lists obtain additional information of frequency, intensity and sometimes duration, which may partly correct this problem [28,146,147]. Furthermore, possible organic causes for the symptoms are usually not assessed. Therefore, these measures present methodological problems in determining whether the symptoms are functional or not and whether the severity is clinically significant.

At present, a few standardised interviews comprise sections on somatisation/FSS [148-151]. However, these have not been specifically validated, which makes it difficult to know whether the intended construct is actually measured. Besides, the sections either use diagnostic criteria for somatoform disorders, which as previously mentioned is problematic when dealing with especially young children, or only address few symptoms.

***Informants***

Parents are frequently asked to assess and report on the health of their child, particularly for children younger than 9-10 years of age, who may have difficulties in recalling and describing their symptoms. In assessing a child's symptoms, parents necessarily have to rely either on what is observable or what the child says about his/her symptoms. Parents may only be aware of the symptoms when they are severe [152] and hence underestimate their children's somatic symptoms and impact [30,153]. However, it seems likely that parental health and gender may influence the parents' reports. In consequence, in a population-based study on 5-18-year-old children, the mothers' self-reported health was strongly associated with their reporting of their child's health; this was not observed for fathers [154]. In preschool children, a significant association between parental mental distress and parental reports of frequent symptoms in the children was shown [43], and in a clinical sample, high levels of maternal distress was associated with great mother-child discordance in the direction of mothers reporting more child symptoms than did their children [155].

**Table 4. Selected measures of somatic/physical complaints/FSS and/or health anxiety symptoms (HAS)**

| Measure [Ages] | Symptoms examed/versions | Time frame/scale | Psychometric properties | Critical comments |
|---|---|---|---|---|
| Children's Somatization Inventory (CSI)* [8-18 yrs] [28,54,156-158] | 35 symptoms (CSI-35)<br>Derived from DSM-III-R criteria for SD and HSCL<br><br>Child, parent version<br>Short version (CSI-18)<br>Revised version (CSI-24) | Past 2 weeks<br><br>5 point scale: bothered *not at all* to *a whole lot*<br>(score 0-140) | IC: 0.9 (clinical and healthy samples)<br>TR: 2 wk-1yr: 0.81-0.34 (clinical sample), 1 yr: 0.61 (healthy sample)<br>CONV: correlates with measures of personality, psychopathology, and functional disability (e.g. ABVK neuroticism, neuroticism-somatic complaints, STAIC trait anxiety, CDI, DQC, internalizing scores of CBCL, FDI)<br>DIFF: discriminates well between healthy and paediatric patients<br>FACTORS: pseudo neurological symptoms, cardiovascular symptoms, gastrointestinal symptoms, and pain & weakness<br><br>Concordance between parent and child version: 0.38-0.46 (C-CSI score > P-CSI score)<br>CSI-18 correlates 0.97 with CSI-35<br>CSI-24 correlates 0.99 with CSI-35 | Derived from a symptom list for adults. Heterogeneous set of symptoms that are relatively rare in healthy children and adolescents.<br>In the new revised version, statistically weak items have been removed and it is more appropriate for children/adolescents<br><br>Associated impairment, duration and possible organic basis not examined<br><br>Advantage: has been used in numerous studies of paediatric patients and also in some community samples |
| The Somatic Complaint List (SCL) [Not specified, applied for children aged 8-12 yrs] [146,159] | 9 symptoms plus 2 items on well and healthy<br>Based on observations of school teachers and commonly reported symptoms in children<br><br>Child version | Past 4 weeks<br><br>5 point scale: never to quite often | IC: 0.83 (school sample)<br>TR: 6 months: 0.55<br>CONV: correlates with CSI and negative moods | Associated impairment, duration and possible organic basis not examined |
| Children's Psychosomatic Symptom Checklist (C-PSC) [Not specified, applied for children/adolescents aged 11-14 yrs] [147] | 12 symptoms derived from the PSC for adults<br><br>Child version | Not stated<br><br>5 point scale: 'How often': not a problem to every day, and 'How bad': not a problem to very, very bad.<br>(score 0-272) | IC: 0.83<br>TR: 1-5 wk:0.9-0.87<br>CONV: correlates with RCMAS and CDI | Derived from a symptom list for adults<br><br>Associated impairment, duration and possible organic basis not examined |
| Somatic Symptom Checklist (SSC) [Not specified, applied for children/adolescents aged 11-16 yrs][58] | 31 symptoms and 1 item on general health<br><br>Primarily derived from DSM-III-R criteria for SD<br>Wording based on that used in the CIDI<br><br>Child version | Lifetime<br><br>2 point scale: present: yes or no<br>(score 0-31) | TR: 2 wk: 0.95<br>CONV: correlates with IAS | Derived from a symptom list for adults<br><br>Frequency, intensity, associated impairment, duration and possible organic basis not examined |

| | | | | |
|---|---|---|---|---|
| Recent Symptoms [Not specified, applied for children/adolescents aged 11, 13, 15 yrs][145] | 7 physical: headaches, asthma or wheeze, sickness or stomach aches, fainting, aches, cold or flu, skin problems<br>4 malaise: nervousness, sadness, irritability and sleeping difficulty<br><br>Child version | Past month<br><br>2 point scale: present: *yes* or *no* | Face validity examined in pilot studies, no specific psychometric properties reported | Mixture of possible 'explained' and 'unexplained' symptoms<br><br>Frequency, intensity, associated impairment, duration and possible organic basis not examined |
| Somatic Complaint Subscale of the Child Behaviour Check List (CBCL) [4-18 yrs.][160-162] | 9 items: dizzy, overtired and 7 physical problems without medical explanation: aches or pains, headaches, nausea, eye problems, rashes/skin problems, stomach-ache, vomiting<br><br>Parent version<br>Similar versions for youths and teachers | Past 6 months<br><br>3 point scale: applies: *not true, somewhat true* or *often true or very true*<br>(score 0-18) | IC: 0.78 (non-referred children)<br>TR: 8 days: 0.92<br>DIFF: Non-clinic and general clinic samples<br>Predictive of somatic disorders: Sens: 0.1, Spec 1.0, PPV: 1.0, NPV:0.95 | Little evidence of good discrimination between clinical diagnoses. Shown to predict anxiety, mood disorder and ADHD.<br><br>Intensity, associated impairment, and duration not examined |
| Somatisation Subscale** in Survey Diagnostic Instrument<br>[Applied in children aged 4-16 yrs][30,163,164] | 7 physical symptoms without medical explanation (derived from CBCL)<br>3 on health concerns<br>7 on losses of function<br><br>Parent version(4-16 yrs)<br>Youth version (12-16 yrs)<br>Teacher version (4-11 yrs) | Past 6 months<br><br>3 point scale: applies: never or not, sometimes or often or very true<br>(score 0-34)<br><br>Binary rating based on best discriminating score of an independently made psychiatric diagnosis | TR: 88% agreement 6-9 months interval<br>Agreement with psychiatrists diagnosis: Sens: 0.36, Spec: 0.96 | The used score for somatisation occurred too rarely in children < 12 yrs to set a threshold for measurement |

| | | | | |
|---|---|---|---|---|
| Childhood Illness Attitude Scales (CIAS)*** [8-15 yrs][60,165] | 35 items covering fears, beliefs and attitudes associated with hypocondriasis and abnormal illness behaviour and parents'/guardians' role in facilitating medical attention or treatment<br><br>Derived from the IAS for adults<br><br>Child version | Not stated<br><br>3 point scale: applies: none, some or a lot<br>(score 33-99) | IC: 0.88 (school sample)<br>TR: 10-14 days: 0.86<br>CONV: correlates with CASI, FSSC-R and CDI.<br><br>FACTORS: fears, help seeking, treatment experience, and symptom effects | Questions regarding recent medical treatment less reliable and probably needs revision. |
| **INTERVIEW MODULES** | | | | |
| **Interview [Ages]** | **Symptoms examined/administration** | **Time frame/diagnoses** | **Psychometric properties** | **Critical comments** |
| Munich-Composite International Diagnostic Interview (M-CIDI)<br>[ Adult interview applied in children and adolescents with age as low as 12 yrs][150,166] [167] | Highly structured interview including 46 symptoms according to DSM-IV or ICD-10<br><br>Trained lay interviewers | Lifetime prevalence<br><br>Somatoform and dissociative disorders including subtypes | TR: mean 38 days: 0.62 (60 community persons 14-28 yrs)<br>Comparing 68 M-CIDI diagnoses to clinical diagnoses: kappa: 0.5, Sens: 93.8%, Spec: 71.2% | Probably not applicable to younger children (use of DSM-IV criteria), no parent version |
| The Child and Adolescent Psychiatric Assessment (CAPA)<br>[9-17 yrs] & The Preschool Age Psychiatric Assessment (PAPA) [3-6 yrs][32,148,149,168,169] | Interviewer-and glossary-based interview including 3 symptoms: headache, stomach ache and musculoskeletal pain<br><br>CAPA: child and parent version,<br>PAPA: parent version<br><br>Highly trained lay interviewers or clinicians | Past 3 months<br><br>Symptom diagnosis based on information on onset date, duration, frequency and impact | Specific psychometric data not reported | Only few symptoms |
| Diagnostic Interview for Children and Adolescents-Revised (DICA-R) [6-17 yrs][151,153] | Moved form highly structured to more flexible, semi structured including symptoms derived from DSM-III-R<br><br>Highly trained lay interviewers<br><br>Parent, child and adolescent versions | Lifetime and current diagnoses. Latest version compatible with DSM-IV diagnoses | Specific psychometric data not reported | Modelled after the adult interview, DIS, and diagnostic criteria used are according to DSM-IV |

IC: consistency reliability, TR: test-retest reliability, CONV: convergent validity, DIFF: discrimination between groups, PPV: Positive Predictive Value, Spec: specificity, Sens: sensitivity, NPV: Negative Predictive Value.

ABVK: The Amsterdamse Biografische Vragenlijst voor Kinderen [Amsterdam Biographical Questionnaire for Children], ADHD: Attention Deficit Hyperactivity Disorder, CASI: Children's Attributional Style Interview, CBCL: Children Behaviour Check List, CDI: Children Depression Inventory, CIDI: Composite International Diagnostic Interview, DQC: Depression Questionnaire for Children, DIS: Diagnostic Interview Schedule, DSM-III-R/IV: Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised/ Fourth Edition, FDI: Functional Disability Inventory, FSSC-R: Fear Survey Schedule for Children-Revised, HSCL: Hopkins Symptom Check List, IAS: Illness Attitude Scale, ICD-10: International Classification of Diseases and Related Health Problems, PSC: Psychosomatic Check List, RCMAS: Revised Children's Manifest Anxiety Scale, SD: Somatization Disorder, STAIC: State-Trait Anxiety Inventory for Children.

*: the parent version has been used for children as young as 56 months [1], **: includes both items on FSS and HAS, ***: measure HAS

***Case definition***
In the absence of agreement on classification, numerous case definitions have been used to decide when a symptom is a 'problem' or an 'illness' (Table 3). Temporal features such as frequency and episode duration are often used as threshold definition. Another threshold is severity quantified by modifying terms such as 'bothered a lot' by the symptom or the symptom is 'a major problem' intended to clinically distinguish bothersome symptoms from the universe symptoms that affect everyone at one time or another. Very few have included symptom-related impairment: the effect that a particular symptom has on the child's functioning, e.g. in terms of distress, social activities, school performance etc. Clearly, the inclusion of impairment criteria decreases prevalence estimates [170].

***Time frame***
Most epidemiological studies are retrospective. Informants are asked to recall their child's somatic complaints within a certain time frame in the past, and the use of different time frames obviously leads to different prevalence estimates. Extremely long time frames are likely to be unreliable, and data on life time prevalence have shown to be problematic in adults due to recall problems [171]. Too short a time frame (e.g. one day) may yield less meaningful information because children with fluctuating or recurrent symptoms may not be captured or inclusion of children with acute and short-lived symptoms may lead to an overestimated prevalence. For many children, FSS are troublesome in certain phases of life, and most epidemiologic studies therefore address a limited life span such as one year or six months, or three months or two weeks. The figures obtained by using these time frames indicate the proportion of children having an active problem, which may be considered more relevant for health economic calculation than lifetime prevalence.

*In summary*, detecting FSS in children in epidemiological studies is influenced by many factors: the sample of children selected for the study, the informants providing data, case criteria and methods used for data collection. These factors need to be taken into account when evaluating the validity of the data in the current studies and may also explain why the reported prevalence estimates often differ. Also, at present no data regarding the symptom epidemiology of hypochondriasis or health anxiety in younger children exist [60].

**AIMS**
Clinical experience and the present literature suggest that FSS: 1) are common in childhood and may present as many different types of complaints, 2) appear to cluster also in young children, 3) may in some cases cause functional impairment and distress and thus constitute a functional syndrome or disorder, even though the criteria for a SD as defined in DSM-IV and ICD-10 are seldom fulfilled, and 4) may, as in adults, coexist with significant health concerns.

Especially in young children, there is currently little epidemiological data on the prevalence, process, clinical impact and potential clustering of FSS in distinct syndromes and diagnostic enitities. Studies of single symptoms are of limited value in this context because they fail to identify those children with a tendency to develop multiple symptoms, either simultaneously or episodically. However, an exploration of the literature and personal contacts with researchers in the field revealed the lack of a standardised measure to simultaneously assess many types of FSS and associated impairment in this age group. The aims of this PhD project therefore were:
First to:
- develop and validate a comprehensive measure to assess FSS in young children (paper 1)
- develop and test a procedure for a systematic medical record review for FSS in children to be used as part of the validation of this new measure (paper 2)

Next to:
- investigate the prevalence, types and co-occurrence of parent-reported FSS and the consequences of these with regard to perceived well-being, functional impairment and number of doctors visits in a population-based sample of Danish 5-7-year-old children (paper 3)
- investigate, in the same children, parent-reported health anxiety symptoms (HAS) and their association with different health problems, including FSS (paper 4).

**DEVELOPMENT OF MEASURES (STUDY I, PAPER I & II)**
**Material and Methods**
Study one comprised two steps. First, we developed two measures to identify FSS in children: the Soma Assessment Interview (SAI) and the Medical Record Review for Functional Somatic Symptoms in Children (MRFC). Second, a preliminary validation of the SAI and testing of the usability of the MRFC were performed.

**Step one: Development of measures**
***The Soma Assessment Interview***
In order to assess FSS in preschool children in a population-based study, the measure should:
- be feasible in a large epidemiological study
- permit a comprehensive analysis of FSS
- assess the associated impairment of the symptoms to identify 'clinically relevant' cases
- include a clinical evaluation to increase the validity of the FSS diagnosis

The SAI was derived from the Section on Physical Health and Somatoform Disorders, a supplementary section to the Development and Well-Being Assessment (DAWBA) [172]. This section has not yet been published or formally validated, but the authors reported the face validity to be satisfactory in a population study in Bangladeshi children (personal communication with Professor R. Goodman and associate Professor M. Mullick) [173]. We found that this measure best complied with the demands listed above. Furthermore, it was advantageous to keep the DAWBA design as our measure on FSS was planned to be administered together with the DAWBA in the population study (study two).

**Major modifications compared with the original interview**
Many of the SAI items are close to the original section, but major modifications were undertaken in order to adapt the interview for a population of young children. The modifications were based on a literature review on FSS in children, consultant assistance from professor L. Walker and one of the authors of the original version, associate Professor M. Mullick as well as our pilot testing results. In the latter, a panel of researchers consisting of a paediatrician, a psychiatrist, a child and adolescent psychiatrist and a senior resident in child and adolescent psychiatry examined the interview's face validity by means of data from interviews of parents to 58 5-6-year-old children with diverse physical, func-

tional and psychiatric disorders. The parents were also asked to express their immediate impression of the interview. The results led to a number of corrections. The final version was tested in a sample of 10 new parents. The main modifications were:

- adaption of a predefined list of well-defined physical diseases:
  - e.g. inclusion of heart disease, exclusion of sickle cell disease or thalassaemia
  - questions on the impact adaption of a predefined list of physical complaints
  - e.g. inclusion of constipation and diarrhoea
  - questions on whether positive complaints are attributable to a physical disease or not
- new items on
  - the child's general health
  - cleanliness
  - HAS
  - associated impairment/impact due to possible FSS (i.e. use of pain medication, absence from daycare/school, doctors' visits/hospitalisation and parental worries about the symptoms)
  - alternation of the case definition to 'impairing FSS' instead of somatoform disorders

The SAI is a respondent-based measure combined with a clinical rating to assess the 1-year-prevalence of FSS in 5-10-year-old children. It intends to use parents as proxy informants.
It consists of 5 sections covering the child's physical health and cleanliness, physical complaints, duration and impairment of possible unexplained physical complaints, HAS and dissociative symptoms and finally open-ended questions to get the parents to describe possible unexplained physical complaints in their own words. A skip rule is incorporated so that items on impairment and open-ended questions are skipped if no unexplained complaints during the past year are reported (Figure 2).

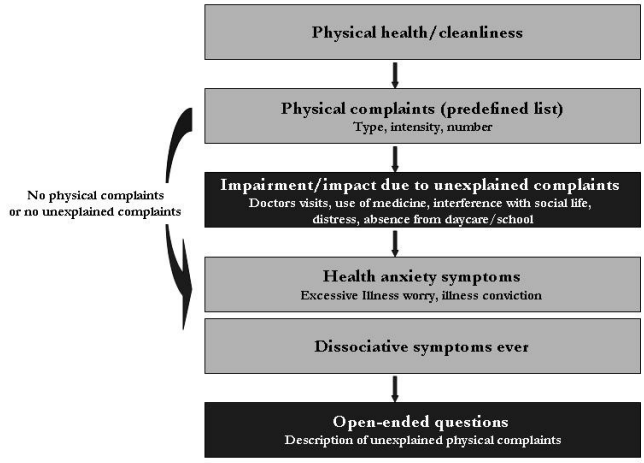
The interview can be administered by a lay interviewer with a subsequent review of all the obtained data by a clinical assessor (i.e. a physician) who makes the final assessment of FSS.
For the Danish version of the SAI and the instruction for the lay interviewer and the corresponding English version, which is attached to paper I, see appendices, chapter 10.

**The Medical Record Review for Functional Somatic Symptoms in Children**

As part of a preliminary validation of the SAI, an evaluation of paediatric patients' medical records was used as a 'gold standard' for diagnosing FSS. A systematic procedure, the MRFC, was derived from described review procedures for FSS in adult patients [174,175]. A pilot testing of a first draft on five records was performed by experienced paediatricians. Based on their comments, we did a subsequent refinement.

In the final procedure, the reviewers (i.e. paediatricians) were asked to systematically rate the presence/absence of a well-defined physical disease, all presenting symptoms during a specified time period and to determine if any of the symptoms could be categorised as functional. If relevant, duration and associated impairment of the child's FSS were also assessed. In conclusion, the reviewers summarised all information supporting their judgement of presence/no presence of FSS. For the Danish version and instruction for the reviewers and the corresponding English version, which is attached to paper II, see appendices, chapter 10.

**Figure 2. Structure and dimensions in the Soma Assessment Interview**




**Step two: Preliminary validation of the SAI and testing of the MRFC**

***Study population***

Samples of children, aged 5-10 years, were drawn from four paediatric outpatient clinics (two university hospitals and two general hospitals) and from the community. The clinical samples were intended to fall in two groups: a sample of children with a well-defined disease and a sample of children with a likely functional disorder. The flowchart is shown in figure 1 in paper I (see appendices, chapter 10).

*Clinical samples*: Children with any of the selected primary discharge ICD-10 diagnoses (described below) were identified from patient lists and were eligible if they had been clinically assessed during the year prior to the study period. For a sample of children with a well-defined disease (clinical sample I), we selected diagnoses for diabetes type I and asthma because these diseases may present with diverse symptomatology. For a sample of children with a likely functional disorder (clinical sample II), we selected various diagnoses according to: 1) a review of the literature on the most common functional disorders and symptoms in children and 2) consultations with experienced paediatricians on the discharge diagnoses they used for these disorders. Besides the diagnoses for somatoform and dissociative disorders and neurasthenia, these were ICD-10 'symptom diagnoses' likely to represent diverse disorders dominated by functional gastrointestinal, neurological or musculoskeletal symptoms (Table 5. Random samples of 84 children with asthma and/or diabetes and 96 children with 'symptom diagnoses' were drawn. In total, 113 patients joined the study corresponding to a participation rate in clinical sample I of 64% and 61% in clinical sample II.

*Community sample*: A random sample of 178 children was drawn from the Danish Central Population Register. The geographical area was restricted to the catchment area from which the clinical samples were also drawn, i.e. of the four paediatric outpatient clinics. Children who occurred both on the patient lists and in the register sample were only included in the latter (N=2). One hundred and five children participated, representing 59% of those approached.

**Data**

Data for the validation of the SAI were obtained from the following sources:

- The SAI itself (SAI diagnoses of FSS)
- External validating measures
- Medical record reviews (MRFC diagnoses of FSS)
- Data for testing the usability of MRFC only concerned the last source.

**SAI diagnoses of FSS**

Five experienced lay interviewers from the Danish National Institute of Social Research received a one-day training course in administration of the SAI by the project leader. The interview was administered by phone to the parents who were also asked to evaluate the interview. Subsequently, FSS was assessed by an experienced paediatrician and a senior resident in child and adolescent psychiatry (i.e. the project leader). After independent assessments, all possible cases were jointly discussed to reach consensus. Both interviewers and clinical assessors were blinded towards the child's clinical status.

**Table 5. Selected ICD-10 diagnoses to identify children for the two clinical samples.**

| ICD-10 diagnosis | Clinic I | Clinic II | Clinic III | Clinic IV | Total |
|---|---|---|---|---|---|
| E10.9 Diabetes | 22 | 14 | 32 | 30 | 98 |
| J45.0, 45.1, 45.8 Asthma | 45 | 70 | 180 | 77 | 372 |
| F45.0-F45.9 Somatoform disorders | 0 | 0 | 0 | 0 | 0 |
| F44.0-F44.9 Dissociative disorders | 0 | 0 | 0 | 0 | 0 |
| F48.0 Neurasthenia | 0 | 0 | 0 | 0 | 0 |
| R.53 Fatigue | 0 | 0 | 0 | 0 | 0 |
| R.51 Headache | 12 | 4 | 0 | 13 | 29 |
| R.55 Syncope and collapse | 5 | 3 | 2 | 13 | 23 |
| M62.6 Muscle strain | 0 | 0 | 1 | 1 | 2 |
| R.42.9 Dizziness and giddiness | 1 | 1 | 0 | 1 | 3 |
| G44.2 Tension-type headache | 0 | 11 | 13 | 1 | 25 |
| M79.6 Pain in limb | 0 | 1 | 0 | 3 | 4 |
| R.10.8 Abdominal pain NOS | 17 | 22 | 45 | 25 | 109 |
| K59.0 Constipation | 22 | 11 | 15 | 17 | 65 |
| K59.1 Functional diarrhoea | 0 | 1 | 1 | 2 | 4 |
| R.15 Encopresis NOS | 31 | 5 | 43 | 8 | 87 |
| **All diagnoses** | **155** | **143** | **332** | **191** | **821** |

Number of 5-10-year-old children during year 2006 with the listed primary discharge diagnoses, identified from patient lists from four paediatric outclinics. The psychiatric diagnoses in ICD-10 in which FSS are the central feature are marked in grey.

**External validating measures**

Parents to participating children completed a questionnaire before the administration of the SAI, which contained various independent measures of the child's physical complaints. These served as external validators of the SAI:

The Childrens Somatization Inventory (CSI) is a symptom checklist assessing a variety of non-specific physcial symptoms. It has been used in both children with RAP, non-clinical populations and children with organic disases, and the validity and reliability are well examined [28,156-158]. We used the short parent-report, P-CSI-18, in which items shown to be rarely endorsed in children from a normal population have been omitted [157].

Apley's criteria are often used to define RAP in population-based studies [138]. We applied these, slightly modified corresponding to the version used by Dahl-Larsen in a recent Danish study [139], to assess this specific complaint, which is often functional [176].

The Strengths and Difficulties Questionnaire (SDQ) is a questionnaire used worldwide. The psychometric properties are well established [177-181]. It is a brief questionnaire covering common areas of emotional and behavioural difficulties with 25 core items. The time frame is the past six months. Scores for emotional symptoms, conduct problems, hyperactivity-inattention, peer relationship problems, prosocial behaviour and total difficulties can be generated. The emotional score contains one item concerning somatic complaints, which was used in the present analyses.

**MRFC diagnosis of FSS**

In the two clinical samples, three experienced paediatrians (one senior resident and two consultants), who were blind to the SAI results, reviewed the medical records from hospitals and the children's general practitioners (GPs). They used the MRFC to determine whether or not the children met the diagnosis of FSS within the same time frame (i.e. the last year) as measured by the SAI. The reviewers received a short introduction in the procedure and performed consensus review on five records before they made independent reviews.

**Data processing and error checking**

The SAI data were obtained in an electronic format. Programming was performed using Delphi 2005 (writing in Pascal) with data transfer to databases in Microsoft Access 2003 using Borland Database Engine. The parent questionnaire with external validating measures and the MRFC were both designed and processed using the TELEform computer programme, which allows for optical reading of data. This method has been shown to have an error rate as low as double manual data entry by research secretaries [182].

All data were checked in the SAI and the parent questionnaires at receipt, and the parents were contacted to obtain information on missing data. We succeeded to obtain full data sets on all participants except for the SAI evaluation data in which missing data occurred in 18 instances.

**Preliminary validation of the SAI**

- The following were examined to determine feasibility and psychometric properties of the SAI:
- The parents' evaluation of the interview
- The duration of the interview
- The inter-rater reliability on detection of FSS at clinical assessor level
  - The validity by three approaches:
  - Approach one examined the discriminative validity by a comparison of the clinical and community samples of children on FSS rates
  - Approach two examined the convergent validity by the extent to which the SAI results correlated with results on independent measures of physical complaints in the community sample of children
  - Approach three examined the overlap between the SAI and MRFC diagnoses of FSS in the two clinical samples. Complete agreement between the SAI and the review results was defined as no FSS in either the SAI or the MRFC or FSS in the SAI and FSS definitely present in the MRFC.

**Testing of the usability of the MRFC**

The following were examined in the clinical samples to test the usability of the MRFC:

- The time used for the review
- The correlation between MFRC results and clinical diagnoses
- The inter-rater agreement on the recognition of FSS and other main items in the review, i.e. impairment and duration of FSS and presence of comorbid physical disease.

**STATISTICAL ANALYSES**

Correlations between SAI results and results on independent measures of physical complaints were examined by using non–parametric tests (two-tailed Fisher's exact test for categorised data and Kruskal Walli's test for continuous data).

Logistic regression analyses were used to examine the chance of being detected with FSS by means of the SAI in the two clinical samples using the community sample as reference.

$\chi 2$ test for trend and calculations of sensitivity, specificity and predictive values were used to examine the agreement between the SAI and MFRC diagnoses of FSS.

Kappa coefficients were calculated to determine inter-rater reliability of FSS detection in the SAI and in the MFRC. In the latter, we reported a combined kappa as well as weighted kappas for each pair of reviewers with weights for discrepancies of 0, 1 and 2 set as 1, 0.5 and 0, respectively.

The statistical significance was set at $p<.05$ in all analyses. The analyses were conducted in STATA 9.0 (www.stata.com).

**RESULTS (PAPER I & II)**

**Preliminary validation of the SAI**

Our results suggest that the SAI is a feasible, reliable and valid measure.

Feasibility was documented by:

- A median duration of the interview of 18 minutes (range 6-126)
- A positive evaluation of the interview by the majority of parents (Table 6)
- Reliability was documented by:
- A good agreement on detection of FSS between two clinical assessors (kappa=0.86)
- Validity was documented by:
- A good discrimination between paediatric outpatients with a likely functional disorder (clinical sample II), outpatients with diabetes or asthma (clinical sample I) and children from the community by the rates of FSS. Thus, children from clinical sample II, but not children from clinical sample I, had a significantly higher chance of being detected with FSS than children from the community (age-adjusted OR: 7.90, 95% confidence interval (CI): 3.44-18.13)
- A good correlation between the SAI and independent measures (i.e. questionnaires) on physical complaints. Thus, children from the community sample and with different FSS case status in the SAI differed predictably on the total CSI score, the somatic item of the SDQ and the RAP questions
- A substantial agreement between the SAI and MFRC diagnoses of FSS in the two clinical samples (sensitivity=89%, 95% CI: 80-98%)

**Table 6. Parents' evaluation of the SAI**

| | No | Yes | Don't know | |
|---|---|---|---|---|
| Do the questions cover your child's physical complaints sufficiently? | 8 (4%) | 190 (95%) | 2 (1%) | |
| Do you find any of the questions inappropriate or irrelevant? | 190 (95%) | 7 (3.5%) | 3 (1.5%) | |
| Do you find any of the questions difficult? | 180 (90%) | 20 (10%) | 0 (0%) | |
| Do you find any of the questions unpleasant? | 198 (99%) | 2 (2%) | 0 (0%) | |
| | Too long | Adequate | Too short | Don't know |
| How do you find the length of the interview? | 2 (1%) | 192 (96%) | 3 (1.5%) | 3 (1.5%) |

Participation rate: 200/218. In 18 instances (8 community children and 10 clinical children) the parent declined or the interviewer forgot to ask the questions.

**Testing of the usability of the medical record review (MRFC)**

Our results suggest that the MFRC is a usable method to identify FSS in paediatric outpatients:

- The median duration of the review was 20 minutes (range 7-60)
- A primary discharge diagnosis of a well-defined disease was confirmed in 93%
- The rate of a review diagnosis of FSS was highest in clinical sample II (children with symptom diagnoses) (88.1% in clinical sample II vs. 16.7% in clinical sample I, $p<.0001$).
- Subgroups of children with multisymptomatic FSS, long-term and/or impairing FSS were identified.
- The inter-rater agreement on detection of FSS and presence of a physical disease was good (combined kappa=0.69 and 0.93 respectively) and fair for associated impairment and duration of FSS (combined kappa=0.29 and 0.57 respectively).

**METHODOLOGICAL DISCUSSION (PAPER I & II)**

**Representativeness of samples**

The participation rate in the three samples varied from 59-64%. No significant differences were found with regard to age and gender between non-participants and participants in any of the samples. However, selective attrition on other sociodemograhpic variables (e.g. maternal education, family size and economy) known to be associated with FSS [70,183-185] cannot be ruled out.

Outpatients were chosen to ensure that children with a wide range of severity and clinical presentions of FSS were included in the clinical samples. This was indeed achieved as the MRFC detected children with different prominent types of FSS (i.e. primarily gastrointestinal, musculoskeletal or neurological symptoms) as well as children with both non-impairing and impairing FSS.

The community sample was drawn in the catchment area of the paediatric departments to ensure that it resembled the clinical samples on the sociodemographic variables. This was warranted by the similarities in the baseline characteristics between the participants in the three samples except from age; the children in the clinical samples were significantly older than the community children. We adjusted accordingly for age in the relevant analyses.

**Development and validation of the SAI**

The DSM and ICD systems have never attempted to encompass the range of functional disorders in children, and at present there is no consensus on how FSS in children should be considered within a diagnostic framework [2]. To ensure inclusion of appropriate items for children, the development of the SAI was based

on multiple sources: 1) an existing interview reported to have good face validity in a population study on children, 2) a review on the existing literature of FSS and functional disorders in children and 3) symptom checklist measures used in studies on children.

The median interview duration was acceptable for both interviewers and parents. The validity of the SAI was examined by discriminative and convergent validity. The discriminative validity, sometimes termed known-groups validity, compares the SAI results for a group known to have the problem with a group that is known not to have the problem (or to a lesser degree) [186]. This examination could be hampered if the rates of FSS were too similar in the three groups leading to a spuriously low validity. The opposite could be the case, i.e. a spuriously high validity, if it was possible for the clinical assessors of the SAI to guess the sample affiliation of the children [187]. The sampling procedure did not ensure that all children in clinical sample II had a functional disorder, which could introduce the first problem. On the other hand, the presence of all FSS categories in all three samples could minimise the latter problem. The results of the medical record reviews confirmed that FSS cases were present in both clinical samples but, as expected, with the highest rate in clinical sample II. We had anticipated to find the FSS rate in clinical sample I (children with a well-defined disease) in between the FSS rates of the community sample and clinical sample II as physical problems and medical treatment have been described as possible risk factors of FSS [69]. However, clinical sample I represented a rather selected group of children with a primary diagnosis of diabetes and asthma attending a paediatric outpatient clinic. Frequent medical specialist visits and repeated enquiries about the symptoms attributable to these diseases may have influenced the subsequent parental reporting on the child's symptoms in the SAI, i.e. an underreporting of possible unexplained complaints.

The convergent validity, i.e. the extent to which the SAI correlates with some theoretically relevant variables, was examined by three independent well-known measures of physical complaints (i.e. the CSI, RAP questions and the somatic item in the SDQ). They were administered within 3 months prior to the SAI. The time lag and also the different time frames used in the measures could have minimised the correlation due to a fluctuating/recurrent nature of the physical symptoms involved. Thus, self-limited or transient symptoms may be assessed to a lesser degree in the SAI than in the CSI in which the assessment period is much shorter. Still, we found a statistically significant correlation between the two measures. A significant correlation was also shown with the somatic item in the SDQ in which the time frame is the past six months. The comprehensive assessment of FSS in the SAI as opposed to the assessment of a specific physical complaint may explain the lack of a statistically significant correlation between the SAI result and RAP.

It was not possible to perform a medical assessment of all children due to ethical reasons and limited resources. Review of medical records has been suggested to be a more reliable method of establishing whether particular symptoms are medically unexplained than self reports of symptoms [188] and was used in the present study to serve as a gold standard for comparison of the SAI results. It is, however, debatable whether a medical record review should be considered a gold standard as it tends to underestimate overall symptom experience because the physicians are inclined to describe the most problematic symptoms [189,190]. This may explain why more non-impairing FSS were assessed in the SAI.

The reliability of the SAI was examined with regard to the inter-rater agreement of two assessors' detection of FSS. This was high for two physicians even though they had different degree of clinical experience and subspecialisation (i.e. a very experienced consultant in paediatrics and a senior resident in child and adolescent psychiatry with half a year of paediatric training).

**Development and testing of the MRFC**

To our knowledge, a systematic medical record review for FSS in paediatric patients has not previously been described, and the MRFC was derived from record rating methods proven to be usable and reliable in identifying adult FSS patients [174,175]. The usability of the MRFC was examined on paediatric patients' medical records from the hospitals, but records from the children's GPs were also used in most cases. However, according to feedback from the reviewers, it was often difficult to use the GPs' records due to the structure and short descriptions.

The mean duration of a review was acceptable with a tendency to be shorter as the reviewers became more familiar with the procedure. Despite minimal training and supervision of the three reviewers, their agreement on FSS was good. Disagreement mainly existed among patients with an inconclusive diagnostic work-up or with a concurrent physical disease. The two reviewers, who agreed to the highest extent, worked at the same paediatric department which could suggest that local 'culture-specific aspects' influenced the reviewers' conceptual definition of FSS. A higher inter-rater agreement may therefore have been achieved if more time was spent on training and supervision.

The agreement on associated impairment was only fair. The reviewers reported impairment items difficult to rate as they were quite unspecific, and often the information about impairment in the medical records was very sparse. This may well suggest that the review should be supplemented with other sources of information, e.g. questionnaires such as the Functional Disability Inventory [191] in order to assess impairment more reliably for e.g. clinical research purposes.

## GENERAL POPULATION STUDY ON 5-7-YEAR-OLD CHILDREN (STUDY II, PAPER III & IV)

### Material and methods

#### *Study design*

The study was a cross sectional general population study.

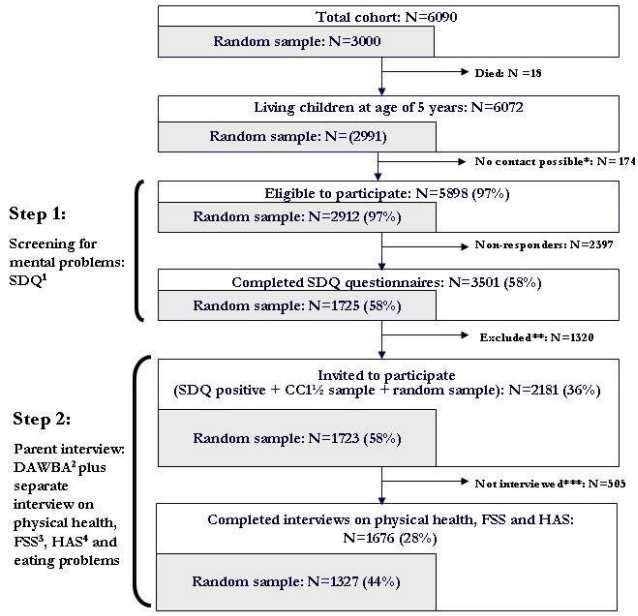
#### *Study population*

The basic study population was 'The Copenhagen Child Cohort' (CCC 2000) [192]. This is a birth cohort consisting of all 6,090 (3,127 boys, 2,963 girls) children born in 16 municipalities during the calendar year 2000 in the former Copenhagen County in Denmark. The birth cohort was defined as children living in the catchment area at time of birth and was selected by means of the Danish Central Civil Registration System using the unique civil ID number allocated to each individual in Denmark for identification.

The present study was part of The Copenhagen Child Cohort 5-7-year follow-up (CC 5-7), carried out between August 2005 and December 2007. The overall aim was to investigate mental health and psychiatric illness in a two-step design with a general mental health screening at step one (Figure 3). At step two, parents of screening-positive children, a subsample of children who had previously participated in a case-control study at the age of 1½ years [193] and 3,000 random sample children drawn at baseline were invited to be interviewed at home by lay interviewers from the Danish National Institute of Social Research. The parent inter-

view included measures on mental disorders (DAWBA), on physical health, FSS and HAS (see below) and on eating behaviour problems (Child Eating Behaviour Questionnaire (CEBQ)). The analyses in the present study were restricted to the 3,000 randomly selected children.

**Figure 3. Flowchart of the 5-7 year follow-up, CC5-7**




**Data**

Data for the present study were obtained from three sources:

- Screening questionnaire for mental problems in step one
- Parent interview on physical health, FSS and HAS in step two
- Danish national registers

**Screening questionnaire**

The parent version of the SDQ was applied in step one in the follow-up to screen for mental problems in the children. As previously described in chapter 3, it is a brief questionnaire in which scores for emotional, conduct problems, hyperactivity-inattention, peer problems and prosocial behaviour can be generated. The assessment period is the past 6 months. The emotional score, including the specific item on somatic complaints, was used in the analyses in the present study.

**Parent interview**

The separate parent interview on physical health, FSS and HAS, applied in step two, included three different measures: 1) the SAI assessing the one-year prevalence and associated impairment of FSS as well as the prevalence of HAS, 2) the short parent form of the CSI in which the parent rates the extent to which the child has experienced 18 different physical symptoms within the past two weeks, and 3) questions on RAP. A detailed description of these measures is given in chapter 3.

**Danish national registers**

Data on sociodemographic details and perinatal adversities and physical and mental morbidity were obtained from different Danish national registers, which cover the whole Danish population.

The variable 'Social level of living area' relates to the municipality in which the child was born and was constructed on the basis of information from the Danish Central Civil Registration System using the categorisation described by Klebak and Osler [194].

Perinatal data including birth weight and information on gestational age, apgar score, maternal parity, parental age, ethnicity and whether parents lived together at time of birth were obtained from the Medical Birth Register.

Information concerning ICD-10 diagnoses for birth complications and congenital disorders was obtained from the Danish National Patient Registry.

The Psychiatric Central Register contains information about all admissions to psychiatric hospitals in Denmark, including outpatient and casualty department contacts. Information was obtained concerning all ICD-10 diagnoses on mental disorders given within the first four years of living.

Information pertaining to the mother's education and annual household income at time of the child's birth was obtained from the Integrated Database for Labour Market Research.

**Data processing and error checking**

The SDQ was a hard copy questionnaire which was photoscanned and turned into explicit variables in a research database. A photo file of each questionnaire was kept for error checking. Specific error checking involved verification of the child's master data. SDQ scores were generated using standardised algorithms (www.SDQinfo.com). Missing values for the emotional score were present in 54 subjects, and these were excluded in the relevant analyses.

The parent interview on physical health, FSS and HAS was administered in an electronic format. Programming was performed using Delphi 2005 (writing in Pascal) with data transfer to databases in Microsoft Access 2003 using Borland Database Engine. Interview data were forwarded to the project leader during the study period to be checked for missing information. Ninty-nine (7.5%) interviews were judged as incomplete due to many missings values on cleanliness, physical complaints, associated impairment and/or open-ended descriptions of possible FSS. In 85 of these interviews, the missing information was completed by a phone call to the families by one of the lay interviewers with a median latency from first data collection of 1.15 years. All available data were used in the final analyses. Specific error checking was performed by comparison between master data of the collected data and the baseline cohort data (i.e. verification of serial number, name, birth date, gender). Other error checking involved answers on presence of physical disease/disabilities, cleanliness, unexplained physical complaints and open-ended descriptions on possible unexplained symptoms. Questionable answers that could not be confirmed or corrected were considered missing. In the final data set, there were few missing values with a maximum of 45 on the item about the child's general health.

**Assessment of general health and concurrent physical disease**

Assessment of the child's general health and the presence of a physical disease during the past year were based on items in the SAI. In the analyses, general health was classified in two groups:

'Bad/Poor', 'Good/Very good/Excellent', and concurrent chronic physical disease was defined as presence of at least one of nine different diseases on a predefined list, i.e. asthma, heart disease, epilepsy, rheumatic disease, kidney disease, diabetes, severe vision/hearing problem, disorders affecting the function of nerves and muscles, and other serious physical disease or handicap (to be specified).

**Assessment of FSS and definition of impairing FSS**

The assessment of FSS in the SAI was performed by the same two clinical assessors as in study I. After independent rating, all possible cases were jointly discussed to reach consensus on case status.

A priori definition of impairing FSS was based on the definition for a functional disorder previously presented by Fink et al, in which the symptoms should cause excessive worry or discomfort or lead the person to seek treatment [9]. Thus, children where only assigned a diagnosis of impairing FSS if their symptoms caused significant distress, social impairment, high use of health resources and/or substantial absence from daycare or school based on answers to structured questions in the SAI. In the present study, the threshold for impairing FSS was set at 1) 'A medium amount' of distress and/or social impairment corresponding to the threshold in the DAWBA measures [195], and/or 2) hospitalisation and/or at least three doctor's visits and/or 3) at least 1 week of absence from daycare or school during the past year due to FSS.

Other SAI variables regarding FSS used in the present analyses were 1) duration of FSS classified in two groups: < 6 months, ≥ 6 months, 2) parent worries and 3) family burden due to the child's FSS classified in two groups: 'Not at all/A little', 'A medium amount/A great deal', 4) use of pain medication due to FSS on a 2-point scale: 'Yes', 'No', and finally 5) stress as a possible contributing factor to FSS classified in two groups: 'No', 'Maybe/Yes, definitely'.

**Assessment of HAS and definition of severe HAS**

Health anxiety symptoms (HAS) were defined by parental reports on three items in the SAI concerning the child having excessive worries about its health, displaying a tendency to complain about physical symptoms when nothing serious seemed to be wrong, and/or being difficult to reassure when having these worries / physical symptoms. The possible response categories were: 'No', 'Yes, a little' or 'Yes, a lot'. A positive score for mild HAS was given if the response was 'Yes, a little' to at least one of the items. Correspondingly, a positive score for severe HAS was given if the response was 'Yes, a lot' to at least one of the items.

**STATISTICAL ANALYSES**

Attrition analyses were performed using the SAS statistical software package version 9.1 (http://support.sas.com/documentation/onlinedoc/91pdf/index.html). Other management and analyses of data were performed using the STATA statistical software package, version 9.0 (www.stata.com).

Prevalence estimates were given with 95% CIs.

The inter-rater reliability of FSS detection in the SAI was determined by the kappa coefficient. Univariate logistic regression analyses were conducted to evaluate the association between different SAI variables, CSI score, the presence of RAP and impairing FSS. Adjustment for concurrent physical disease was carried out by multiple logistic regression analyses. The associations were presented as OR with 95% CIs.

Associations between the level of HAS and different physical health problems, emotional symptoms, impact due to FSS and parental worries about the child's FSS were assessed by $\chi 2$ tests.

**RESULTS (PAPER III & IV)**

**Attrition analyses**

Among the 3,000 randomly sampled children, data were obtained for 1,327 (667 girls, 660 boys, median age: 6.1 years) (Figure 1). Additionally, 4 subjects had at least one missing item on HAS, and these were excluded from the HAS analyses.

The attrition analyses were based on register data. Compared with the remaining children in the cohort, alive at the age of five (N=4,575), the participating group included more children with high socioeconomic status, e.g. a highly educated mother, living in an area of high social level and in a household with a high annual income at the time of the childs birth, and more children of Danish origin. Detailed attrition analyses are shown in supplemental data, paper IV (see appendices, chapter 10).

**General health and concurrent physical disease**

Less than 2 percent (N=25, 1.9%) were reported by the parents as having a bad or poor general health during the past year.

Ten percent (N=133) were reported to have at least one of the chronic physical diseases according to a predefined list in the SAI (Table 7). Thirteen of the children had more than one type of disease.

**Table 7. Parent-reported physical diseases among 1,327 5-7-year-old children**

| Physical disease during the past year | No. | % | Missing values |
|---|---|---|---|
| Asthma | 65 | 4.90 | 0 |
| Heart disease | 8 | 0.60 | 1 |
| Epilepsy | 6 | 0.45 | 6 |
| Rheumatic disease | 1 | 0.08 | 4 |
| Kidney disease | 2 | 0.15 | 2 |
| Diabetes | 1 | 0.08 | 5 |
| Severe vision/hearing problem | 35 | 2.64 | 4 |
| Disorders affecting the function of nerves and muscles | 4 | 0.30 | 19 |
| Other serious physical disease or handicap* | 24 | 1.81 | 29 |

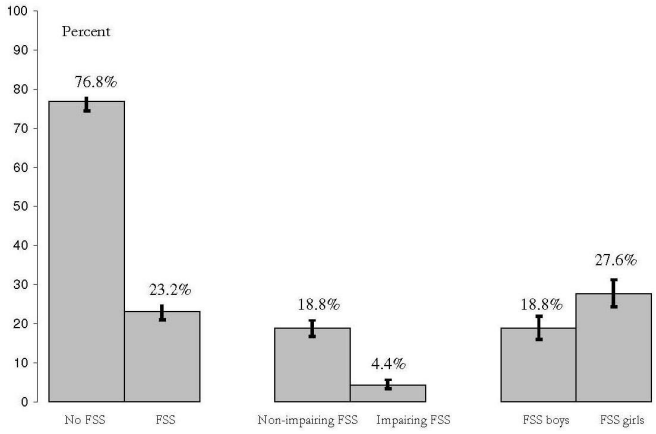
* E.g.: cancer, metabolic disorders, genetic syndromes, celiac disease, eczema and allergy

**FSS results**

- The 1-year prevalence of any FSS in 5-7-year-old children was 23.2% (95% CI: 21.0-25.6% (N=308), see Figure 4), with a duration of 6 months or more in 58.2%. This means that the 1-year prevalence of FSS with ≥ 6 months duration was 13.4% (N=178)
- FSS were more prevalent in girls than in boys (27.6% (N=184/667) vs. 18.8% (N=124/660), p< 0.0001)
- In 27% (N=83) of the FSS cases, the symptoms were reported as 'Maybe/Definitely' attributable to stress

- Forty percent of the children with FSS had more than one type of FSS (i.e. multisymptomatic FSS) (N=124). This corresponds to the presence of multisymptomatic FSS in 9.3% of all the children in the study
- Pain complaints, i.e. limb pain, headache and/or stomach ache were the most prevalent types of FSS occurring in 280 of the 308 FSS cases. In 21.4% (N=66) of the FSS cases, at least two of the three pain symptoms co-occurred, and all three co-occurred in 4.9% (N=15). This corresponds to the presence of multiple pain in 5% of all the children in the study
- Pain complaints were also reported to be the most prominent type of FSS in the majority of cases. This pattern was similar among children with non-impairing and impairing FSS (data not shown). Except from constipation and diarrhoea, other prominent types of FSS were rare
- Impairing FSS were found in 4.4% (95% CI: 3.3-5.6% (N=58)).
- Compared with children with no or non-impairing FSS, children with impairing FSS were statistically significantly more likely to:
    - be reported to have a concurrent physical disease and a bad general health during the past year
    - have a higher CSI score and rate of RAP
- Compared with children with non-impairing FSS, children with impairing FSS were statistically significantly more likely to:
    - receive pain medication due to FSS
    - have parents reporting worries and family bur den due to FSS
        - present multisymptomatic FSS

**Figure 4. One-year prevalence of FSS**




Total percent with 95% CI is shown for different subgroups

**HAS results**

- Among 5-7-year-old children, 17.6% (95% CI: 15.6-19.8%), fulfilled the criteria of having HAS
- No statistically significant gender difference was demonstrated
- Severe HAS was reported by the parents in 2.4% (95% CI: 1.7-3.4% (N=32))
- The level of HAS was associated with parental-reported health problems in the child, i.e. a general poor health, concurrent physical disease and physical complaints including FSS. Stratifying for the presence of a physical disease did not change the results
- In children with FSS, we found strong associations between the level of HAS and the impact of FSS in terms of number of doctor's visits and missed school and/or daycare due to the child's FSS and degree of parental worries about the child's FSS
- Emotional symptoms rated by the SDQ were positively associated with the presence of HAS

**METHODOLOGICAL DISCUSSION (PAPER III & IV)**

**Representativeness of sample**

Denmark is a small country with a homogeneous population of about five and a half million people. The representativeness of the cohort compared with the general population of Danish children in this age group is fair to good. The CCC 2000 includes 9% of all children born in Denmark during the year 2000. It is representative of Danish children born in 2000 as far as gender, birth weight, gestational and apgar score is concerned (Table 8) [192] but includes more children with non-Danish origin (14.7% vs. 9.2% in the general population). Furthermore, the catchment area is primarily urban. Higher levels of FSS in children in immigrant families and in urban populations have been reported [43,90]. Thus, we would expect a higher prevalence of FSS and maybe also HAS in this cohort than for Danish children in general. However, the selective attrition of families with parents of non-Danish origin may have equalised the skewness with regard to ethnicity. Furthermore, selective attrition in general of children with a putative risk of FSS, such as low socioeconomic status [70], may also have biased the prevalence estimates in the other direction.

Physical health problems have been described to precipitate or co-exist with FSS [69] and also to play a contributory role for HAS [196]. A high or low occurrence of physical health problems in our study sample may therefore influence the prevalence estimates of FSS and HAS. However, our study sample can be seen as comparable with the general Danish population on this aspect based on the following: 1) the attrition with regard to biological variables, i.e. gender, birth weight, gestational and apgar score was not clinically significantly skewed in the study. With reference to representativeness of the cohort in general (Table 8), the study sample could be regarded as representative for the general population on these parameters, 2) the prevalence (10%) of chronic physical diseases in the present study corresponds to the reported prevalence of long-term illness (covering diabetes, visual impairment, hearing problems, speech problems, nervous disorder, epilepsia, gastric disorder, asthma, allergy, eczema, physical disablement, overweight and hyperactivity) of 12.8% in a representative sample of Danish children, aged 2-12 years [197]. Even though the included diseases disabilities between the mentioned study and our study are not quite the same, the comparable numbers suggest that our study sample is representative with regard to serious physical health problems.

**Data quality**

Data collection involved about 30 lay interviewers without medical training and only two clinical assessors (i.e. physicians), which made it economically feasible. The lay interviewers asked prescribed questions verbatim in a preset order, and the informants' responses were recorded with a minimum of interpretation or clarification on the interviewers' part. This approach should decrease variability in content due to differing interviewing styles [198]. However, a variation in case frequency among the lay

interviewers was observed. This may partly be explained by the assignment to the individual interviewers of different geographical areas with varying sociodemographic profiles and thereby basic rates of FSS/HAS in the children examined. Optimally, we would have liked to examine the inter-rater reliability between the lay interviewers, but this was not possible due to the number of interviewers, limited resources and because we did not wish to overburden families whom we wanted to engage in a longitudinal study. We did perform quality control monitoring of the collected data throughout the study with feedback to the interviewers to try to prevent them from drifting into idiosyncratic techniques.

There was a long latency of performing the reinterviews due to practical reasons (median latency from first data collection: 1.15 years). In order to minimise recall bias, the already collected information was summarised for the informants before the missing information was obtained.

**Specific points concerning assessment of FSS**

To measure FSS, the SAI combines the advantages of a highly structured interview with the advantages of a clinical review. This could potentially increase the diagnostic consistency and validity of FSS compared with assessment of FSS based on symptom checklists [28,146,147]. However, the SAI's categorisation of symptoms into functional and not functional must still be interpreted with some caution. Like the majority of epidemiological studies in this area (see Table 3), we did not have objective data (e.g. laboratory evaluations) or a physical examination which could provide more hard indicators to decide the physical basis of the symptoms classified as functional. The assessments relied on the parental reports and clinical evaluation of this information, and therefore we cannot be completely certain that none of the symptoms rated as functional had a medical explanation. To minimise this potential problem of misclassification, the interviewers were instructed to perform the full SAI interview, i.e. including detailed symptom description, in case of the slightest doubt about the origin of the reported symptoms in order to allow for clinical evaluation. Furthermore, the two clinical assessors discussed all cases to reach consensus. The symptoms could be rated as not, probably or certainly functional, but in the final analyses, only children with certain functional symptoms were classified as cases.

**Table 8. Representativeness of the Copenhagen Child Cohort 2000**

| Variables | CCCC 2000 (N=6090) % | Remaining Danish children born in year 2000 (N=60994) % | Statistics |
|---|---|---|---|
| Gender | | | |
| Boys | 51.35 | 51.32 | X2=0.001, d.f.(1), |
| Girls | 48.65 | 48.68 | p=0.974 |
| Birth weight (g) | | | |
| 500-999 | 0.26 | 0.29 | X2=74.047, |
| 1000-1499 | 0.49 | 0.54 | d.f.(9), p<0.0001 |
| 1500-1999 | 0.89 | 1.13 | |
| 2000-2499 | 3.02 | 2.93 | No clinical |
| 2500-2999 | 11.10 | 10.64 | significance |
| 3000-3499 | 29.70 | 29.57 | |
| 3500-3999 | 32.40 | 33.47 | |
| 4000-4499 | 16.52 | 16.30 | |
| 4500 + | 3.63 | 4.22 | |
| | *Missing 1.99* | *Missing 0.91* | |
| Gestational age (weeks) | | | |
| 22-27 | 0.23 | 0.24 | X2=56.875, |
| 28-31 | 0.59 | 0.74 | d.f.(5), p<0.0001 |
| 32-34 | 1.77 | 1.73 | |
| 35-36 | 3.73 | 3.61 | No clinical |
| 37+ | 92.63 | 93.29 | significance |
| | *Missing 1.05* | *Missing 0.39* | |
| Abgar score | | | |
| 1 | 0.02 | 0.05 | X2=23.291, |
| 2 | 0.02 | 0.04 | d.f.(10), p=0.0097 |
| 3 | 0.03 | 0.06 | |
| 4 | 0.05 | 0.13 | No clinical |
| 5 | 0.25 | 0.18 | significance |
| 6 | 0.25 | 0.26 | |
| 7 | 0.74 | 0.62 | |
| 8 | 1.66 | 1.78 | |
| 9 | 4.29 | 4.48 | |
| 10 | 90.97 | 91.19 | |
| | *Missing 1.74* | *Missing 1.19* | |

The data were obtained from the National Health Service of Denmark

**Specific points concerning assessment of HAS**

The measurement of HAS relied on three items that were constructed to reflect cognitive symptoms believed to be characteristic for health anxiety in adults. We demonstrated a good face validity in a pilot study, but the items were not further validated. To our knowledge, the only specific instrument to measure health anxiety in children (aged 8-15 years) is the Childhood Illness Attitude Scales (CIAS) [60]. We chose not to use this as it only exits in a self-report version and probably would not be age-appropriate for children younger than 8 years. It is also quite long consisting of 35 items, which was judged by us to be too many in a study in which the main aim was to assess FSS. However, according to a recently reported factor analysis on the CIAS items [165] and new empirically established diagnostic criteria for health anxiety in adults [199], other items may have been relevant to include, e.g. items intended to assess behaviour motivated by concerns regarding illness (help seeking) or items concerning suggestibility or obsessive rumination about illness. Still, especially internalising symptoms may be difficult to reveal when using parental reports [153], but, as emphasised previously, in young children, parent's reports are inevitable sources of information.

**Specific points concerning assessment of emotional symptoms**

The SDQ measures the child's symptoms and positive attributes in 5 domains: emotional symptoms, conduct problems, hyperactivity-inattention, peer relationship problems, and prosocial

behaviour. The present analysis concentrates on the first four domains, especially on the first domain, whereas the impact supplement was not included. Thus, report of emotional symptoms can indicate but does not necessarily mean that the child has clinically significant emotional problems. Furthermore, as with assessment of FSS and HAS, parents' reports may also underestimate the child's emotional symptoms.

The associations of HAS and emotional symptoms were examined with a time lag in data collection as the SDQ was performed in step one and information on HAS was obtained in step two in the follow-up. The time lag varied to a considerable degree (median lag time: 228 days). However, as the assessment period in the SAI refers to the last year, whereas the SDQ refers to the past 6 months, a cautious conclusion is that contemporary emotional symptoms and HAS were examined.

## GENERAL DISCUSSION

### Study I. Development of measures

#### *Overall strengths and comparison with other measures*

Before a detailed discussion on the epidemiological findings, a more critical issue will be raised, namely, if it was really necessary to develop a new measure of FSS considering the problems associated with undertaking such a task.

With respect to the resources available for training and supervisions of interviewers in the present epidemiological study, we found it advantageous to conduct a structured interview (administered by lay interviewers) rather than a semistructured interview (administered by clinical or highly trained interviewers) [200]. However, when using structured diagnostic interview data in community surveys to assess conditions without detectable pathophysiology, it has been suggested to include an element of clinical re-appraisal to increase the validity and clinical relevance [201]. With these considerations and study conditions and a review of existing measures in mind, it was clear to us that we needed a new measure to pursue our main research question, namely to assess the full range of FSS and associated impairment in young children in a large population-based study.

Compared with existing measures, the SAI has some potential strengths. First, it is derived from an existing but unpublished DAWBA section on somatoform disorders. The original structure has been preserved, so it can still easily be administered together with the DAWBA interview. Thus, as the DAWBA, it uses a best-estimate approach by combining highly structured questions with additional material, if necessary, to allow for a final judgment of the presence and severity of symptoms by qualified clinical assessors. Second, significant revisions of content made the SAI more appropriate for young children and offered the possibility to assess symptoms instead of diagnoses. Symptom assessment is highly relevant as one of the great challenges in this area is the development of a coherent and clinically meaningful nosology for functional disorders in children [11,12]. Assessing the range of possible presentations of FSS in young children gives the opportunity to empirically test the usefulness and meaningfulness of various case criteria. Third, in contrast to existing interview sections on somatisation for younger children [149,153,169], we examined the psychometric properties in terms of an external validation and the inter-rater reliability of the clinical assessors on their assessment of FSS. Fourth, we also examined the userfriendliness which is rarely reported in a systematic way in papers on new measures. This aspect is highly relevant as respondent acceptance is important with regard to obtain good response rates [202].

The development of the MRFC was a spin-off of the preliminary validation of the SAI. In order to compare the SAI results with information from clinical assessments, it was necessary to perform a medical record review as different unspecific diagnoses were used for children with FSS. Relatively high rates of disagreement between general paediatricians' opinions about the presumed cause of pain and the optimal diagnostic approach for children with unexplained chronic pain have been shown [203]. We therefore needed a systematic procedure to reduce the variability in the way FSS diagnoses were made by the reviewers.

Record review methodology to identify paediatric FSS patients is very sparse [204], and very few methods have been described for adults [174,175]. Especially, it may be difficult to address the fundamental issue, namely how to identify clinical patterns in the record information that indicates FSS. We adapted the approach by Smith et al. They developed a method for record reviews on adult patients by which reviewers made FSS diagnoses based on identification of individual symptoms and determination of the degree and results of medical work-up for the symptoms. The procedure proved to succesfully identify and classify subjects with FSS for a clinical trial [174].

#### Limitations

Some limitations need to be addressed. Ideally, we would have wanted to measure the SAI's test-retest reliability as it can be argued that this is the first critical step in establishing the validity [186]. However, one may expect a low stability over longer intervals simply due to the natural history, i.e. fluctuating patterns, of FSS. We would also have liked to compare the SAI with other interview sections on somatisation such as the PAPA/CAPA [148,149,169,198], but designs that involve administration of two quite lengthy interviews in fairly rapid succession could be problematic due to attenuation problems, i.e. the tendency that informants admit to fewer problems on the second interview [205]. We did though compare the results of the SAI with the results of one of the most used and validated check lists, the CSI, and found a good correlation. We did not examine the reliability at lay interviewer level. This could be relevant as interviewers' capabilities/interviewing styles have been reported to also matter to a high degree, even with respondent-based interviews [189,198].

Regarding the MRFC, this method is limited by the potential lack of sufficient details in the material to make a 'definite rating'. Thus, comparisons of record review studies with clinic surveys suggest that symptoms often go unrecorded [189]. Furthermore, our study did not involve examination of the validity of the record review diagnoses, e.g. stability over time; neither did we examine the MRFC's usability in different settings. The reviewer training and demonstration of the reviewers' skills before performing individual record review was very sparse compared with the procedure described by Smith et al [174]. This may have resulted in a higher review variability. Finally, as the current version of the MFRC requires the knowledge and the diagnostic skills of experienced paediatricians and is quite time consuming, it is primarily for research purposes at this point.

### Study II. General population study

#### *Overall strengths*

Part of the novelty of this study lies in the examination of a wide range of reported symptoms in a non-clinical sample of young children providing a perspective in which clinical presentations may be evaluated in this age group. The cross-sectional design gave a unique opportunity to perform explorative analysis of co-

occurrence between the different symptoms, i.e. FSS, HAS and emotional symptoms, in this specific age group.

Ideally, epidemiological prevalence studies should be based on large and representative populations. The present study is quite large-scaled, and the prevalence estimates of both FSS and HAS were determined with rather narrow confidence intervals. Based on parental reports on children in a well- defined birth cohort, we performed a comprehensive assessment of FSS in young children. This is in contrast to the majority of studies on this age group, which mainly have concentrated on a single or few symptoms (see Table 3). We also used criteria for impairment to detect the number of children with FSS with a potential need for clinical intervention. This is furthermore in contrast to most studies, which have not included items on how the symptoms influenced the child. We examined a narrow age range to provide specific data for young children, whereas some studies have reported a general prevalence estimate for a much broader age range. Compared with other studies, we used a quite long time frame, a year, with the intention to assess recurrent symptoms and at the same time minimise the assessment of self-limited or transient symptoms without clinical significance. Finally, the collected information was rated clinically to judge whether the reported symptoms could be explained by a physical disease. We believe that this approach increases the diagnostic validity of FSS compared with most other studies in which symptoms have been assumed to be functional based on the low rate of chronic physical disease among normal children or in which children with a reported concurrent chronic physical disease have been excluded.

Also based on parental reports, the prevalence of HAS and their association with physical health and emotional symptoms were examined. To our knowledge, this is the first study to provide standardised assessment of HAS symptoms in such young children.

**Comparison with other studies**

As mentioned in the introduction, the wide variation in sampling, measures, case definitions and use of informants in addition to differences in age range and type of and number of FSS studied complicates comparison of results.

In the present study, the data are based on parental reports of children's FSS and HAS with the obvious restriction that the effect of parents' own health beliefs on the obtained information could not be taken into account. However, the one-year FSS prevalence of 23.2% corroborates the findings in other studies examining several symptoms in young children using parents' and/or children's reports [27,43,142]. In a Nordic survey from 1996 on health and well-being of 10,317 representative children aged 2-17 years, the parents were instructed to fill in a questionnaire, including items on 'psychosomatic complaints', together with the child, if possible [88,142]. In the subsample of children aged 7-12 years (N=3,816), 25% complained of at least one symptom occurring weekly or every other week. The corresponding prevalence among children aged 2-6 years (N=3,351) was 17.6%. Our sample included children aged 5-7 years, and in Denmark school entry is often at the age of six. Starting school increases symptom reports [2,206], and this may partly explain why our prevalence estimate is closer to the one reported in school children than in preschool children. Our overall prevalence estimate is also comparable to another large population-based study on 3-5-year-old Spanish children. Parental reports were used to examine the presence and frequency of five somatic complaints (stomach aches, headaches, leg pain, tiredness and dizziness) [43]. Frequent somatic complaints (four or more times during past two weeks) occurred in 20%. Finally, in a large population sample of Dutch children aged 0 to 18 years, questionnaires regarding chronic pain (defined as recurrent or continuous pain for more than 3 months) were filled in by parents to the young children, i.e. ages of 0-7 years, and by the children themselves from 8 years and up. Chronic pain (various locations) occurred in 19.3% of the children aged 4-7 years [27].

Several studies have demonstrated that the inclusion of impact criteria decreases prevalence estimates [170,200]. Berntsson et al reported that among Nordic 7-12-years-old children, the symptoms were mild in 16.7%, moderate in 7.5% and severe in 0.8% [142]. Among the Spanish preschool children, 'frequent symptoms complainers' (20%) were more likely than children with no complaints to have absence from preschool, to attend paediatric clinics and to present emotional and behavioural symptoms. The latter study suggests a somewhat higher number of children with impairing FSS compared to the result of 4.4% of impairing FSS in our study. However, in the study on Spanish preschoolers, the symptom reporting period was short (2 weeks), which may have implied inclusion of more children with short-lived or transient symptoms.

No gender difference was reported in the before mentioned study, which is in contrast to our findings showing that girls had a higher prevalence of FSS than boys. Methodological and/or cultural differences may account for these differences, and in general the epidemiological research presents conflicting results on gender and FSS in prepubertal children [3].

We found that 9.3% presented more than one type of FSS, i.e. multisymptomatic symptoms, which is corroborant with the findings in another Danish study by Oster 25. He assessed the prevalence of headache, abdominal pain and limb pain in children aged 6-19 years and found a prevalence rate of 9.2% for multiple pains (combination of two or three sorts of pain); however the period for recall was unspecified. In a large population sample of Dutch children aged 0 to 18 years, Perquin et al reported chronic pain with more than one location in 12.9%.

The present findings confirm pain complaints, i.e. headache, stomach aches and pain in limbs to be the most frequent and dominating types of FSS in this age group [27,43,134,197]. Moreover, we found considerable co-occurrence between these symptoms in accordance with several other studies [24-26,134].

FSS was statistically significantly associated with the presence of a chronic physical disease. Physical illness or ailment have been described to precipitate a somatising disorder or co-exist with it in many cases, which may suggest a physical vulnerability [69]. Specifically in a comparative study on childhood CFS and emotional disorders, physical illness precipitants and a prior history of recurrent infections as reported by parents were more prominent in children with CFS [68].

In the present study, the childrens' physical symptoms were also assessed by the presence of RAP and the score on the short version of the CSI. In total, 9.3% were reported to have experienced at least three bouts of stomach aches during the past three months, but only 3.5% had pain severe enough to affect their activities, i.e. stopped playing, went to bed, were seen by a doctor or stayed home from school or daycare. This is in contrast to the majority of studies on RAP in young children reporting a prevalence of ≥10 %[24] [34,134]. However, different definitions of RAP, among these different versions of Apley's criteria, have been used [207], which could to some extent explain the variation in results. Thus, we applied the rather strict and specified definition used in a recent Danish population-based study on children

aged 9-13 years [139]. In this study, they reported a RAP prevalence of 12%, but the different age groups plus the use of self-reports and not parental reports make a direct comparison with our result difficult.

The mean score on the short parental version of CSI was 1.37 (range 0-23). This is a lower score compared to the mean CSI score of 5.20 (range 0-29) reported in well patients [157]. However, the latter children had been treated for an acute minor illness or injury at a paediatric clinic or emergency room and may therefore represent a selected group. Moreover, the mean age of these children was considerably higher (11.5 years) compared to mean age of 6.1 years in the present study. In a study on pain reactivity and somatisation in preschool children, the mean score on the full parent version of CSI (35 items) was also quite low: 3.48 [1].

In the present study, HAS according to specified criteria and by the use of parental reports were found in 17.6% of 5-7-year-old children, and 2.4% had 'severe' HAS. To our knowledge, no previous studies have aimed at estimating the prevalence of HAS in young children, but our findings corroborate results from studies of regular health anxiety in adults in population-based samples in which prevalence figures of 0.02-7.7% have been reported. Our findings also support results from studies on older children and adolescents. Eminson et al examined adolescent attitudes surrounding illness by the use of the Illness Attitude Scales (IAS) as well as the lifetime prevalence of physical symptoms in a school population of 805 students (ages 11-16 years) [58]. Participants who endorsed an elevated number of symptoms scored significantly higher on 7 IAS subscales than lower symptom scorers indicating more distress about illness and more treatment experience. Taylor et al described everyday bodily experiences and health concerns in a general population study of adolescents, 12 to 16 years of age, in which subjects with a chronic medical condition were excluded. 'Worry a lot about health' was endorsed by 50% [30]. Wright et al developed and examined the psychometric properties of the Childhood Illness Attitude Scales (CIAS), which evaluates health anxiety in school-age children (ages 8-15 years) [60,165]. In 201 school children with a mean age of 10.9 years, the average CIAS total score was 59 (range 38-87) out of a possible range of 33 to 99. Thus, these studies provide an indication that school aged children and adolescents do experience significant health anxiety. As in studies on adults [199,208], Wright et al found no significant gender difference which corresponds to our findings; neither did they find a significant correlation with age and the total CIAS score. They described significant associations between CIAS total score and measures of childhood anxiety sensitivity, fear and depression, and in the present study we found a significant association between emotional symptoms and HAS. These findings are consistent with adult studies reporting co-occurrence between illness worry, numerous physical symptoms, anxiety and depression[57].

**Limitations**

Beyond the specific considerations in chapter 4 regarding the representativeness of the study sample and the assessment of FSS, HAS and emotional symptoms, there are some main, overall limitations to be addressed. First, the measures of FSS and HAS were based on a single informant, i.e. parental report. Parents have been shown in general to underreport childrens' physical symptoms and illness worries[30,153]. However, parents' perception of, and willingness to tolerate, physical symptoms in the child, and the parents' own attendance history, health anxiety and perception of physical symptoms have been shown to be important factors for childhood attendance in general practice [209] and may also influence the presence and reporting of both FSS and HAS in children [83,84,210-212]. In the present study, we did not obtain data on these factors and consequently could not control for them in the analyses. Second, the assessment period was the past year, which is quite long compared to other studies, and problems with recall bias cannot be ruled out. Thus, adults have been shown to be able to accurately recall and rate the severity of their own pain or discomfort for a period of 3 months [213], whereas lifetime symptom reporting is unreliable [171]. Third, the selective attrition, described in detail in chapter 4, of families with children with a putative risk of FSS may have biased the prevalence estimates, i.e. led to an underestimation. Moreover, the parents were informed that the aim of the study was to investigate the development and well-being of children in order to obtain knowledge about prevention of mental problems. This may have demotivated parents to children with somatic/physical problems to participate, which may further have led to an underrepresentation of children with FSS in the investigated sample. Fourth, because our data are cross–sectional, we cannot infer causality between FSS, HAS and emotional symptoms and limitations in every day functioning. Fifth, the relatively small number of cases with severe HAS and impairing FSS reduces the power of associations and hampers the possibilities for performing multiple logistic regression analysis or stratified analyses to adjust for other potential important confounding variables than comorbid chronic physical disease, e.g. sociodemographic characteristics.

**CONCLUSION**

**Main conclusions in relation to aims**

***I. Development and validation of a comprehensive measure to assess FSS in young children***

The Soma Assessment Interview (SAI) developed in this study offers comprehensive assessment of FSS and their associated impairment in young children in population-based studies. It is readily accepted, relatively quick to complete and it demonstrated good validity in terms of discriminative and convergent validity. Currently there is no satisfactory 'gold standard' for FSS measurement. Further refinement and ascertainment of the SAI's construct validity is an ongoing task, which should be supported by additional measurements of concurrent and predictive validity, e.g. by head-to-head comparison with the SAI and other standard assessments.

***II. Development and testing of a systematic medical record review for FSS in children***

The Medical Record Review for Functional Somatic Symptoms in Children (MRFC) developed in this study allows identification of subgroups of paediatric patients with multisymptomatic FSS, long-term and/or impairing FSS based on already collected data. Paediatricians identifying FSS directly from this systematic examination of paediatric medical records were in good agreement. A medical record review may not be regarded as a 'gold standard' for FSS, but still the MRFC can serve as a tool to perform external validation of new measures of FSS in children. It may also prove useful for validation of case findings in both clinical and epidemiological research.

***III. Functional somatic symptoms (FSS) and their impairment in 5-7-year-old children***

The present study shows that FSS are common in 5-7-year-old children from the general population with a 1-year prevalence of 23.2%. Girls have a higher overall FSS prevalence than boys and pain complaints, i.e. limb pain, abdominal pain and headache, are the most prevalent types of FSS with considerable co-occurrence. A subgroup of 4.4% of the children present impairing FSS defined as FSS causing substantial discomfort, impairment of everyday life, absence from daycare or school and/or help-seeking in the health care system. These children may have a likely need for clinical intervention. Thus, the findings suggest an early onset of impairing FSS and point to the need for clinical and preventive intervention in a substantial proportion of young children.

***IV. Health anxiety symptoms (HAS) and their associations with health problems in 5-7-year-old children.***

The present study shows that among 5-7-year-old children, 17.6% present HAS and 2.4% prominent HAS. The level of HAS is associated with parent-reported health problems in the child, i.e. a general poor health, concurrent physical disease and physical complaints including FSS. In the subgroup of children with FSS, we found strong associations between the level of HAS and number of doctor's visits and missed school and/or day care due to the child's FSS as well as the degree of parental worries about the child's FSS. Emotional symptoms measured by the SDQ were positively associated with the presence of HAS at this age. The findings suggest that HAS are prevalent at 5-7 years of age and associated with impairing child health problems in the area of FSS and emotional symptoms.

**CLINICAL PERSPECTIVES**

Study II provides standardised information on FSS and HAS on a large sample of 5-7-year-old children in a little explored area. Although principally an epidemiological study, the findings emphasize that in a substantial proportion of young children, FSS are associated with impairment. The findings also suggest a close link between FSS, HAS and possibly also emotional problems. Therefore, it seems important that clinicians pay attention to children, in whom FSS tend to cluster and are associated to school absence, doctor's visits, distress, social impairment and illness worries. In this context, the two standardised/systematic measures of FSS types described in study I may prove useful. Though at this point primarily intended for research, both measures may have potential in the clinical service evaluation of children as young as 5 years old. The synthesisation of information from multiple sources may be helpful to identify children with clinically significant FSS as early as possible in a clinical setting. The MRFC along with information obtained directly from patients and their proxies and an objective medical examination could be a useful approach for classifying children with physical complaints. An important task in this respect would be to further refine the procedure to make it more cost-effective, e.g. by further testing and feedback by clinicians in different settings. Also examination by use of the SAI, subject to further validation, could be very useful as part of a systematic clinical assessment of paediatric patients referred with possible FSS.

Early identification of 'at risk' children could lead to intervention to prevent development of regular functional disorders in later childhood. The use of psychoeducation and cognitive behavioural techniques to alter the parents' and/or the child's symptom interpretation may be useful approaches in this respect.

**RESEARCH PERSPECTIVES**

**Future research on new measures**

In research, standardised assessment measures are essential if the results are to be meaningful across studies. An important step would therefore be to further investigate the psychometric properties of the SAI. Especially examinations of inter-rater reliability at lay interviewer level, test-retest reliability and internal consistency may be important tasks in future studies.

Further research could also engage in a refinement of the interview by supplementary qualitative analyses. This could yield more detailed knowledge on e.g. which physical complaints children in different age groups spontaneously report as well as the informants' interpretation of the physical complaints in the present list. For example 'heart beating' may be related to normal activities and positive experiences in life (excitement) rather than being perceived as a complaint.

**Future research on FSS in children from CCC 2000**

Existing data on the children in CCC 2000 on infant health and family background collected prospectively by community health nurses between first week of the child's life and 10 months of age and data obtained from national registers [193,214] provide a unique opportunity for examination of potential risk factors/predictors of FSS in young children, e.g.:

- Birth complications
- Non-organic failure to thrive (FTT) 0-10 months
- Markers for abnormal neuro-cognitive development 0-10 months such as deviant language development
- Regulation problems 0-10 months such as sleeping, feeding/eating and/or emotional regulation problems
- Sickliness during the first five years of living

Based on data from the present follow-up, it could also be interesting to examine psychiatric comorbidity (DAWBA data) and the co-occurrence between FSS and eating problems (CEBQ data). Future follow-up studies of the cohort, the next is planned for when the children are 10-12 years of age, could provide information on the developmental changes, continuity and course of FSS in childhood.

Finally, register-based data on parental physical and mental illness and use of health resources could be used in studies on familiar risk factors for the development of FSS in children.

**Suggestions for future research in general**

Design and validation of standardised assessment tools of FSS is an ongoing task. Also, there is a need for more epidemiological studies comparing the numbers, prevalence and severity of FSS in community and paediatric samples to provide empirical basis for age-appropriate diagnostic criteria for functional disorders in children. A relatively low concordance between parents and older children's reports is generally consistent with the literature. Therefore, a critical issue will be to determine which informant in children, especially in older children, is the better to provide information, or how different information should be combined to obtain the most valid results.

Our findings suggest that FSS and HAS are closely linked, which may imply a high comorbidity, a diagnostic overlap due to similarity between the symptomatology asked for (displaying a tendency to complain about physical symptoms) or reflect a general factor of somatisation rather than the existence of specific subtypes. It is also unclear whether HAS are a consequence of having FSS (uncertainty-inducing symptoms) or whether it is a primary factor leading to FSS. Future research should through

longitudinal studies examine whether specific pictures of somatisation are chronic or if it is rather a remarkable degree of fluctuation or mobility between different types of somatisation suggesting an overall phenomenon with variations in the clinical picture over time.

Finally, elucidation of the close links between FSS, HAS and emotional disorders are also called for. In this context, possible hypotheses could be: 1) there is a common genetic vulnerability for the development of FSS, HAS and emotional disturbances, 2) FSS cause mental distress, 3) FSS are an early expression of emotional disorders and/or 4) FSS present a certain subgroup of emotional disorders in children.

**LIST OF ABBREVIATIONS**

| | |
|---|---|
| CCC 2000 | The Copenhagen Child Cohort 2000 |
| CC 5-7 | The Copenhagen Child Cohort 5-7-year follow-up |
| CC 1½ | Substudy of children in CCC 2000 at the age of 1½ years |
| CEBQ | Child Eating Behaviour Questionnaire |
| CFS | Chronic Fatigue Syndrome |
| CIAS | Childrens Illness Attitude Scales |
| CI | Confidence Interval |
| CSI | Children's Somatization Inventory |
| DAWBA | Development and Well-Being Assessment |
| DS | Dissociative Disorder |
| DSM-IV | Diagnostic and Statistical Manual of Mental Disorders, 4th edition |
| FSS | Functional Somatic Symptoms |
| GP | General Practitioner |
| HAS | Health Anxiety Symptoms |
| IAS | Illness Attitude Scales |
| ICD-10 | International Classification Diseases and Health Related Problems, 10th revision |
| MRFC | Medical Record Review for Functional Somatic Symptoms in Children |
| MUS | Medically Unexplained Symptoms |
| OR | Odds Ratio |
| SAI | Soma Assessment Interview |
| SDQ | Strengths and Difficulties Questionnaire |
| SD | Somatoform Disorder |
| RAP | Recurrent Abdominal Pain |

**SUMMARY**

Medically unexplained or functional somatic symptoms (FSS) in children constitute a major clinical problem. However, research data on FSS in young children are few, and epidemiological studies are hampered by lack of good standardised measures.
The present thesis consists of two studies:

In study one, we developed two measures to assess FSS in young children. The first measure is a parent interview, the Soma Assessment Interview (SAI), to assess the 1-year prevalence and associated impairment caused by FSS. The interview can be performed by lay interviewers and subsequently rated clinically by physicians. A preliminary validation showed a good agreement on FSS recognition between two clinical raters (kappa=0.86), a good concurrent validity with independent measures of physical complaints and a good discrimination on the prevalence of FSS between a community sample and clinical samples.

The second measure is a systematic medical record review of FSS in paediatric patients: the Medical Record Review for Functional Somatic Symptoms in Children (MRFC). Our findings suggest that the MRFC allows identification of subgroups of paediatric patients with multisymptomatic FSS and long-term and/or impairing FSS and it may prove useful for case finding in clinical and epidemiological research.

In study two, we investigated the parent-reported FSS and their impairment in a population-based sample of Danish 5-7-year-old children. We used the SAI as the main measure. Data from 1,327 children from The Copenhagen Child Cohort 2000 were analysed. Impairing symptoms were defined as FSS causing substantial discomfort, impairment of everyday life, absence from daycare or school and/or health care seeking. We found that FSS are common in this age group with a 1-year prevalence of 23.2%. Different pain complaints, i.e. limb pain, abdominal pain and headache, were the most prevalent types of FSS. A subgroup of children with impairing FSS (4.4%) was identified. These children were more likely to present multisymptomatic FSS than children with non-impairing FSS.

Health anxiety symptoms (HAS) and their associations with different physical health variables, including FSS, were investigated in the same population of 5-7-year-old children. In total, 2.4% presented prominent HAS, and the level of HAS was correlated with general poor health, chronic physical disease and physical complaints including FSS. In children with FSS, we found significant associations between the level of HAS and the impact of the childrens' FSS in terms of number of doctor's visits and missed school and/or daycare due to FSS as well as the degree of parental worries about the childrens' FSS. Furthermore, HAS were significantly associated with emotional symptoms. The findings suggest an early onset of somatisation and point to the need for clinical and preventive intervention in a substantial proportion of children. The findings also suggest a close link between HAS, FSS and emotional symptoms.

Medically unexplained or functional somatic symptoms (FSS) in children constitute a major clinical problem. However, research data on FSS in young children are few, and epidemiological studies are hampered by lack of good standardised measures.

**REFERENCES**

1. Rocha EM,Prkachin KM,Beaumont SL,Hardy CL,Zumbo BD. Pain reactivity and somatization in kindergarten-age children. J Pediatr Psychol 2003;28(1):47-57.
2. Eminson DM. Medically unexplained symptoms in children and adolescents. Clin Psychol Rev 2007;27(7):855-71.
3. Beck JE. A developmental perspective on functional somatic symptoms. J Pediatr Psychol 2008;33(5):547-62.
4. Walker LS,Jones DS. Psychosocial factors: impact on symptom severity and outcomes of pediatric functional gastrointestinal disorders. J Pediatr Gastroenterol Nutr 2005;41 Suppl 1:S51-S52.
5. Anthony KK,Schanberg LE. Pediatric pain syndromes and management of pain in children and adolescents with rheumatic disease. Pediatr Clin North Am 2005;52(2):611-39, vii.
6. Hyams JS,Hyman PE. Recurrent abdominal pain and the biopsychosocial model of medical practice. J Pediatr 1998;133(4):473-8.
7. Crushell E,Rowland M. Biopsychosocial approach to functional abdominal pain. Arch Dis Child 2005;90(11):1202.
8. Stone J,Wojcik W,Durrance D, et al. What should we say to patients with symptoms unexplained by disease? The

"number needed to offend". BMJ 21-12-2002;325(7378):1449-50.
9. Fink P,Rosendal M,Toft T. Assessment and treatment of functional disorders in general practice: the extended reattribution and management model--an advanced educational program for nonpsychiatric doctors. Psychosomatics 2002;43(2):93-131.
10. Lipowski ZJ. Somatization: the concept and its clinical application. Am J Psychiatry 1988;145(11):1358-68.
11. Silber TJ,Pao M. Somatization disorders in children and adolescents. Pediatr Rev 2003;24(8):255-64.
12. Nunn K.,Nicholls D.,Lask B. A New Taxonomy: The Uluru Personal Experiential Profile. Clinical Child Psychology and Psychiatry 2000;5(3):313-27.
13. Moller LR,Sorensen MJ,Thomsen PH. ICD-10 classification in Danish child and adolescent psychiatry--have diagnoses changed after the introduction of ICD-10? Nord J Psychiatry 2007;61(1):71-8.
14. Drotar D. The diagnostic and statistical manual for primary care (DSM-PC), child and adolescent version: what pediatric psychologists need to know. J Pediatr Psychol 1999;24(5):369-80.
15. Hyams JS. Functional gastrointestinal disorders. Curr Opin Pediatr 1999;11(5):375-8.
16. Campo JV,Fritsch SL. Somatization in children and adolescents. J Am Acad Child Adolesc Psychiatry 1994;33(9):1223-35.
17. Di Lorenzo C,Colletti RB,Lehmann HP, et al. Chronic abdominal pain in children: a clinical report of the American Academy of Pediatrics and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Pediatr Gastroenterol Nutr 2005;40(3):245-8.
18. Wyllie WG, Schlesinger B. The periodic group of disorders in childhood. British Journal of Childhood Diseases 30, 1. 1933.
19. Bennie PB. Growing pains. Archives of Pediatrics 11, 337-347. 1894.
20. Chronic abdominal pain in children. Pediatrics 2005;115(3):e370-e381.
21. Lancman ME,Asconape JJ,Graves S,Gibson PA. Psychogenic seizures in children: long-term analysis of 43 cases. J Child Neurol 1994;9(4):404-7.
22. Carter BD,Edwards JF,Kronenberger WG,Michalczyk L,Marshall GS. Case control study of chronic fatigue in pediatric patients. Pediatrics 1995;95(2):179-86.
23. Oberklaid F,Amos D,Liu C, et al. "Growing pains": clinical and behavioral correlates in a community sample. J Dev Behav Pediatr 1997;18(2):102-6.
24. Ramchandani PG,Hotopf M,Sandhu B,Stein A. The epidemiology of recurrent abdominal pain from 2 to 6 years of age: results of a large, population-based study. Pediatrics 2005;116(1):46-50.
25. Oster J. Recurrent abdominal pain, headache and limb pains in children and adolescents. Pediatrics 1972;50(3):429-36.
26. Petersen S,Brulin C,Bergstrom E. Recurrent pain symptoms in young schoolchildren are often multiple. Pain 2006;121(1-2):145-50.
27. Perquin CW,Hazebroek-Kampschreur AA,Hunfeld JA, et al. Pain in children and adolescents: a common experience. Pain 2000;87(1):51-8.
28. Garber J, Walker LS, Zeman J. Somatization symptoms in a community sample of children and adolescents: further validation of The Childrens Somatization Inventory. Psychological Assessment 3, 588-595. 1991.
29. Offord DR,Boyle MH,Szatmari P, et al. Ontario Child Health Study. II. Six-month prevalence of disorder and rates of service utilization. Arch Gen Psychiatry 1987;44(9):832-6.
30. Taylor DC,Szatmari P,Boyle MH,Offord DR. Somatization and the vocabulary of everyday bodily experiences and concerns: a community study of adolescents. J Am Acad Child Adolesc Psychiatry 1996;35(4):491-9.
31. Strine TW,Okoro CA,McGuire LC,Balluz LS. The associations among childhood headaches, emotional and behavioral difficulties, and health care use. Pediatrics 2006;117(5):1728-35.
32. Egger HL,Costello EJ,Erkanli A,Angold A. Somatic complaints and psychopathology in children and adolescents: stomach aches, musculoskeletal pains, and headaches. J Am Acad Child Adolesc Psychiatry 1999;38(7):852-60.
33. Mikkelsson M,Sourander A,Piha J,Salminen JJ. Psychiatric symptoms in preadolescents with musculoskeletal pain and fibromyalgia. Pediatrics 1997;100(2 Pt 1):220-7.
34. Faull C,Nicol AR. Abdominal pain in six-year-olds: an epidemiological study in a new town. J Child Psychol Psychiatry 1986;27(2):251-60.
35. Zuckerman B,Stevenson J,Bailey V. Stomachaches and headaches in a community sample of preschool children. Pediatrics 1987;79(5):677-82.
36. Campo JV,Jansen-Mcwilliams L,Comer DM,Kelleher KJ. Somatization in pediatric primary care: association with psychopathology, functional impairment, and use of services. J Am Acad Child Adolesc Psychiatry 1999;38(9):1093-101.
37. Garralda ME,Rangel L. Annotation: Chronic Fatigue Syndrome in children and adolescents. J Child Psychol Psychiatry 2002;43(2):169-76.
38. Just U,Oelkers R,Bender S, et al. Emotional and behavioural problems in children and adolescents with primary headache. Cephalalgia 2003;23(3):206-13.
39. Walker LS,Greene JW. Children with recurrent abdominal pain and their parents: more somatic complaints, anxiety, and depression than other patient families? J Pediatr Psychol 1989;14(2):231-43.
40. Lipsitz JD,Masia C,Apfel H, et al. Noncardiac chest pain and psychopathology in children and adolescents. J Psychosom Res 2005;59(3):185-8.
41. Aromaa M,Sillanpaa M,Rautava P,Helenius H. Pain experience of children with headache and their families: A controlled study. Pediatrics 2000;106(2 Pt 1):270-5.
42. Bandell-Hoekstra IE,Abu-Saad HH,Passchier J, et al. Coping and Quality of Life in relation to headache in Dutch schoolchildren. Eur J Pain 2002;6(4):315-21.
43. Domenech-Llaberia E,Jane C,Canals J, et al. Parental reports of somatic symptoms in preschool children: prevalence and associations in a Spanish sample. J Am Acad Child Adolesc Psychiatry 2004;43(5):598-604.
44. Hunfeld JA,Perquin CW,Duivenvoorden HJ, et al. Chronic pain and its impact on quality of life in adolescents and their families. J Pediatr Psychol 2001;26(3):145-53.

45. Perquin CW,Hazebroek-Kampschreur AA,Hunfeld JA, et al. Chronic pain among children and adolescents: physician consultation and medication use. Clin J Pain 2000;16(3):229-35.
46. Konijnenberg AY,Uiterwaal CS,Kimpen JL, et al. Children with unexplained chronic pain: substantial impairment in everyday life. Arch Dis Child 2005;90(7):680-6.
47. Lindley KJ,Glaser D,Milla PJ. Consumerism in healthcare can be detrimental to child health: lessons from children with functional abdominal pain. Arch Dis Child 2005;90(4):335-7.
48. Huang RC,Palmer LJ,Forbes DA. Prevalence and pattern of childhood abdominal pain in an Australian general practice. J Paediatr Child Health 2000;36(4):349-53.
49. Wessely S,White PD. There is only one functional somatic syndrome. Br J Psychiatry 2004;185:95-6.
50. Wessely S,Nimnuan C,Sharpe M. Functional somatic syndromes: one or many? Lancet 11-9-1999;354(9182):936-9.
51. Fink P,Toft T,Hansen MS,Ornbol E,Olesen F. Symptoms and syndromes of bodily distress: an exploratory study of 978 internal medical, neurological, and primary care patients. Psychosom Med 2007;69(1):30-9.
52. Barsky AJ,Borus JF. Functional somatic syndromes. Ann Intern Med 1-7-1999;130(11):910-21.
53. Olde Hartman TC,Lucassen PL,van de Lisdonk EH,Bor HH,van Weel C. Chronic functional somatic symptoms: a single syndrome? Br J Gen Pract 2004;54(509):922-7.
54. Walker LS,Beck JE,Garber J,Lambert W. Children's Somatization Inventory: Psychometric Properties of the Revised Form (CSI-24). J Pediatr Psychol 9-9-2008.
55. Walker LS,Lipani TA,Greene JW, et al. Recurrent abdominal pain: symptom subtypes based on the Rome II Criteria for pediatric functional gastrointestinal disorders. J Pediatr Gastroenterol Nutr 2004;38(2):187-91.
56. Uziel Y,Hashkes PJ. Growing pains in children. Pediatr Rheumatol Online J 2007;5:5.
57. Creed F,Barsky A. A systematic review of the epidemiology of somatisation disorder and hypochondriasis. J Psychosom Res 2004;56(4):391-408.
58. Eminson M,Benjamin S,Shortall A,Woods T,Faragher B. Physical symptoms and illness attitudes in adolescents: an epidemiological study. J Child Psychol Psychiatry 1996;37(5):519-28.
59. Fritz GK,Fritsch S,Hagino O. Somatoform disorders in children and adolescents: a review of the past 10 years. J Am Acad Child Adolesc Psychiatry 1997;36(10):1329-38.
60. Wright KD,Asmundson GJ. Health anxiety in children: development and psychometric properties of the Childhood Illness Attitude Scales. Cogn Behav Ther 2003;32(4):194-202.
61. Santalahti P,Aromaa M,Sourander A,Helenius H,Piha J. Have there been changes in children's psychosomatic symptoms? A 10-year comparison from Finland. Pediatrics 2005;115(4):e434-e442.
62. Tamminen TM,Bredenberg P,Escartin T, et al. Psychosomatic symptoms in preadolescent children. Psychother Psychosom 1991;56(1-2):70-7.
63. Unruh AM,Ritchie J,Merskey H. Does gender affect appraisal of pain and pain coping strategies? Clin J Pain 1999;15(1):31-40.
64. Malatesta CZ,Haviland JM. Learning display rules: the socialization of emotion expression in infancy. Child Dev 1982;53(4):991-1003.
65. Walker LS,Zeman JL. Parental response to child illness behavior. J Pediatr Psychol 1992;17(1):49-71.
66. van Wijk CM,Kolk AM. Sex differences in physical symptoms: the contribution of symptom perception theory. Soc Sci Med 1997;45(2):231-46.
67. Rhee H. Relationships between physical symptoms and pubertal development. J Pediatr Health Care 2005;19(2):95-103.
68. Garralda ME,Rangel L. Chronic fatigue syndrome of childhood. Comparative study with emotional disorders. Eur Child Adolesc Psychiatry 2005;14(8):424-30.
69. Garralda ME. A selective review of child psychiatric syndromes with a somatic presentation. Br J Psychiatry 1992;161:759-73.
70. Berntsson LT,Gustafsson JE. Determinants of psychosomatic complaints in Swedish schoolchildren aged seven to twelve years. Scand J Public Health 2000;28(4):283-93.
71. Hotopf M. Childhood experience of illness as a risk factor for medically unexplained symptoms. Scand J Psychol 2002;43(2):139-46.
72. Rangel L,Garralda E,Levin M,Roberts H. Personality in adolescents with chronic fatigue syndrome. Eur Child Adolesc Psychiatry 2000;9(1):39-45.
73. Rangel L,Garralda ME,Hall A,Woodham S. Psychiatric adjustment in chronic fatigue syndrome of childhood and in juvenile idiopathic arthritis. Psychol Med 2003;33(2):289-97.
74. Garralda ME. Somatisation in children. J Child Psychol Psychiatry 1996;37(1):13-33.
75. Rauste-von Wright M,von Wright J. A longitudinal study of psychosomatic symptoms in healthy 11-18 year old girls and boys. J Psychosom Res 1981;25(6):525-34.
76. Thomsen AH,Compas BE,Colletti RB, et al. Parent reports of coping and stress responses in children with recurrent abdominal pain. J Pediatr Psychol 2002;27(3):215-26.
77. Walker LS. Development and validation of the Pain Response Inventory for children. Smith CA, Garber J, Van Slyke DA, editors. Psychological Assessment 9, 392-405. 1997.
78. Ruchkin VV,Eisemann M,Hagglof B. Coping styles and psychosomatic problems: are they related? Psychopathology 2000;33(5):235-9.
79. Walker LS,Smith CA,Garber J,Claar RL. Appraisal and coping with daily stressors by pediatric patients with chronic abdominal pain. J Pediatr Psychol 2007;32(2):206-16.
80. Alfven G,de la TB,Uvnas-Moberg K. Depressed concentrations of oxytocin and cortisol in children with recurrent abdominal pain of non-organic origin. Acta Paediatr 1994;83(10):1076-80.
81. Dorn LD,Campo JC,Thato S, et al. Psychological comorbidity and stress reactivity in children and adolescents with recurrent abdominal pain and anxiety disorders. J Am Acad Child Adolesc Psychiatry 2003;42(1):66-75.
82. Borres MP,Tanaka H,Thulesius O. Psychosomatic and psychosocial symptoms are associated with low blood pressure in Swedish schoolchildren. Psychother Psychosom 1998;67(2):88-93.

83. Craig TK,Cox AD,Klein K. Intergenerational transmission of somatization behaviour: a study of chronic somatizers and their children. Psychol Med 2002;32(5):805-16.
84. Marshall T,Jones DP,Ramchandani PG,Stein A,Bass C. Intergenerational transmission of health beliefs in somatoform disorders: exploratory study. Br J Psychiatry 2007;191:449-50.
85. Rangel L,Garralda ME,Jeffs J,Rose G. Family health and characteristics in chronic fatigue syndrome, juvenile rheumatoid arthritis, and emotional disorders of childhood. J Am Acad Child Adolesc Psychiatry 2005;44(2):150-8.
86. Jamison RN,Walker LS. Illness behavior in children of chronic pain patients. Int J Psychiatry Med 1992;22(4):329-42.
87. Levy RL,Whitehead WE,Walker LS, et al. Increased Somatic Complaints and Health-Care Utilization in Children: Effects of Parent IBS Status and Parent Response to Gastrointestinal Symptoms. Am J Gastroenterol 2004;99(12):2442-51.
88. Berntsson LT,Kohler L. Long-term illness and psychosomatic complaints in children aged 2-17 years in the five Nordic countries. Comparison between 1984 and 1996. Eur J Public Health 2001;11(1):35-42.
89. Due P,Holstein BE,Lynch J, et al. Bullying and symptoms among school-aged children: international comparative cross sectional study in 28 countries. Eur J Public Health 2005;15(2):128-32.
90. Alfven G. The covariation of common psychosomatic symptoms among children from socio-economically differing residential areas. An epidemiological study. Acta Paediatr 1993;82(5):484-7.
91. Aro H. Life stress and psychosomatic symptoms among 14 to 16-year old Finnish adolescents. Psychol Med 1987;17(1):191-201.
92. Boey CC,Goh KL. The significance of life-events as contributing factors in childhood recurrent abdominal pain in an urban community in Malaysia. J Psychosom Res 2001;51(4):559-62.
93. Walker LS,Garber J,Smith CA,Van Slyke DA,Claar RL. The relation of daily stressors to somatic and emotional symptoms in children with and without recurrent abdominal pain. J Consult Clin Psychol 2001;69(1):85-91.
94. Friedrich WN,Schafer LC. Somatic symptoms in sexually abused children. J Pediatr Psychol 1995;20(5):661-70.
95. Kinzl JF,Traweger C,Biebl W. Family background and sexual abuse associated with somatization. Psychother Psychosom 1995;64(2):82-7.
96. Reilly J,Baker GA,Rhodes J,Salmon P. The association of sexual and physical abuse with somatization: characteristics of patients presenting with irritable bowel syndrome and non-epileptic attack disorder. Psychol Med 1999;29(2):399-406.
97. Garralda ME. The Interface Between Physical and Mental Health Problems and Medical Help Seeking in Children and Adolescents: A Research Perspective. Child and Adolescent Mental Health 9, 146-155. 2004.
98. Garralda ME,Rangel L. Childhood chronic fatigue syndrome. Am J Psychiatry 2001;158(7):1161.
99. Fearon P,Hotopf M. Relation between headache in childhood and physical and psychiatric symptoms in adulthood: national birth cohort study. BMJ 12-5-2001;322(7295):1145.
100. Hotopf M,Carr S,Mayou R,Wadsworth M,Wessely S. Why do children have chronic abdominal pain, and what happens to them when they grow up? Population based cohort study. BMJ 18-4-1998;316(7139):1196-200.
101. Hotopf M,Wilson-Jones C,Mayou R,Wadsworth M,Wessely S. Childhood predictors of adult medically unexplained hospitalisations. Results from a national birth cohort study. Br J Psychiatry 2000;176:273-80.
102. Dhossche D,Ferdinand R,van der EJ,Verhulst F. Outcome of self-reported functional-somatic symptoms in a community sample of adolescents. Ann Clin Psychiatry 2001;13(4):191-9.
103. Steinhausen HC,Winkler MC. Continuity of functional-somatic symptoms from late childhood to young adulthood in a community sample. J Child Psychol Psychiatry 2007;48(5):508-13.
104. Zwaigenbaum L,Szatmari P,Boyle MH,Offord DR. Highly somatizing young adolescents and the risk of depression. Pediatrics 1999;103(6 Pt 1):1203-9.
105. Christensen MF,Mortensen O. Long-term prognosis in children with recurrent abdominal pain. Arch Dis Child 1975;50(2):110-4.
106. Apley J,Hale B. Children with recurrent abdominal pain: how do they grow up? Br Med J 7-7-1973;3(5870):7-9.
107. Mulvaney S,Lambert EW,Garber J,Walker LS. Trajectories of symptoms and impairment for pediatric patients with functional abdominal pain: a 5-year longitudinal study. J Am Acad Child Adolesc Psychiatry 2006;45(6):737-44.
108. Walker LS,Garber J,Van Slyke DA,Greene JW. Long-term health outcomes in patients with recurrent abdominal pain. J Pediatr Psychol 1995;20(2):233-45.
109. Campo JV,Di Lorenzo C,Chiappetta L, et al. Adult outcomes of pediatric recurrent abdominal pain: do they just grow out of it? Pediatrics 2001;108(1):E1.
110. Rangel L,Garralda ME,Levin M,Roberts H. The course of severe chronic fatigue syndrome in childhood. J R Soc Med 2000;93(3):129-34.
111. Hardwick PJ. Engaging Families Who Hold Strong Medical Beliefs in a Psychosomatic Approach. Clinical Child Psychology and Psychiatry 10[4], 601-616. 2005.
112. Elena GM,Chalder T. Practitioner review: chronic fatigue syndrome in childhood. J Child Psychol Psychiatry 2005;46(11):1143-51.
113. Garralda ME. Practitioner review: Assessment and management of somatisation in childhood and adolescence: a practical perspective. J Child Psychol Psychiatry 1999;40(8):1159-67.
114. Campo JV,Fritz G. A management model for pediatric somatization. Psychosomatics 2001;42(6):467-76.
115. Griffin A,Christie D. Taking the Psycho out of Psychosomatic: Using Systemic Approaches in a Paediatric Setting for the Treatment of Adolescents with Unexplained Physical Symptoms. Clin Child Psychol Psychiatry 2008;13(4):531-42.
116. Eminson DM. Somatising in children and adolescents. 2. Management and outcomes. Advances in Psychiatric Treatment 7, 388-398. 2001.
117. Rickert VI,Jay MS. Psychosomatic disorders: the approach. Pediatr Rev 1994;15(11):448-54.
118. Eccleston C,Yorke L,Morley S,Williams AC,Mastroyannopoulou K. Psychological therapies for

the management of chronic and recurrent pain in children and adolescents. Cochrane Database Syst Rev 2003;(1):CD003968.
119. Sanders MR,Shepherd RW,Cleghorn G,Woolford H. The treatment of recurrent abdominal pain in children: a controlled comparison of cognitive-behavioral family intervention and standard pediatric care. J Consult Clin Psychol 1994;62(2):306-14.
120. Huertas-Ceballos A,Logan S,Bennett C,Macarthur C. Psychosocial interventions for recurrent abdominal pain (RAP) and irritable bowel syndrome (IBS) in childhood. Cochrane Database Syst Rev 2008;(1):CD003014.
121. Husain K, Browne T, Chalder T. A review of psychological models and interventions for medically unexplained somatic symptoms in children. Child and Adolescent Mental Health 12, 2-7. 2008.
122. Brown GT,Delisle R,Gagnon N,Sauve AE. Juvenile fibromyalgia syndrome: proposed management using a cognitive-behavioral approach. Phys Occup Ther Pediatr 2001;21(1):19-36.
123. Degotardi PJ,Klass ES,Rosenberg BS, et al. Development and Evaluation of a Cognitive-Behavioral Intervention for Juvenile Fibromyalgia. J Pediatr Psychol 24-8-2005.
124. Chalder T,Tong J,Deary V. Family cognitive behaviour therapy for chronic fatigue syndrome: an uncontrolled study. Arch Dis Child 2002;86(2):95-7.
125. Stulemeijer M,de Jong LW,Fiselier TJ,Hoogveld SW,Bleijenberg G. Cognitive behaviour therapy for adolescents with chronic fatigue syndrome: randomised controlled trial. BMJ 14-12-2004.
126. Henningsen P,Zipfel S,Herzog W. Management of functional somatic syndromes. Lancet 17-3-2007;369(9565):946-55.
127. Starfield B,Gross E,Wood M, et al. Psychosocial and psychosomatic diagnoses in primary care of children. Pediatrics 1980;66(2):159-67.
128. Garralda ME,Bailey D. Psychosomatic aspects of children's consultations in primary care. Eur Arch Psychiatry Neurol Sci 1987;236(5):319-22.
129. Goodman JE,McGrath PJ. The epidemiology of pain in children and adolescents: a review. Pain 1991;46(3):247-64.
130. Royal College of Psychiatrists. Medically unexplained physical symptoms. Factsheet for parents and teahcers. Mental Health and Growing Up Factsheet 28, 1-2. 2004.
131. Abu-Arafeh I,Russell G. Recurrent limb pain in schoolchildren. Arch Dis Child 1996;74(4):336-9.
132. Sillanpaa M,Piekkala P,Kero P. Prevalence of headache at preschool age in an unselected child population. Cephalalgia 1991;11(5):239-42.
133. Borge AI,Nordhagen R,Moe B,Botten G,Bakketeig LS. Prevalence and persistence of stomach ache and headache among children. Follow-up of a cohort of Norwegian children from 4 to 10 years of age. Acta Paediatr 1994;83(4):433-7.
134. Christensen MF,Holm E,Sahlholdt I. [Recurrent abdominal pain in Danish school children. A cross-sectional study]. Ugeskr Laeger 3-9-1984;146(36):2690-5.
135. NAISH JM,Apley J. "Growing pains": a clinical study of non-arthritic limb pains in children. Arch Dis Child 1951;26(126):134-40.
136. BRENNING R. ["Growing pains".]. Sven Lakartidn 8-1-1960;57:85-103.
137. Evans AM,Scutter SD. Prevalence of "growing pains" in young children. J Pediatr 2004;145(2):255-8.
138. Apley J. Recurrent abdominal pains: a field survey of 1000 school children. Naish N, editor. Arch Dis Child 33, 165-170. 1958.
139. Dahl-Larsen R,Buhl SB,Husby S,Qvist N. [Recurrent abdominal pain, dyspepsia and constipation in children aged 9-13. A questionnaire investigation]. Ugeskr Laeger 25-4-2005;167(17):1848-51.
140. Stevenson J,Simpson J,Bailey V. Research note: recurrent headaches and stomachaches in preschool children. J Child Psychol Psychiatry 1988;29(6):897-900.
141. Petersen S,Bergstrom E,Brulin C. High prevalence of tiredness and pain in young schoolchildren. Scand J Public Health 2003;31(5):367-74.
142. Berntsson LT,Kohler L,Gustafsson JE. Psychosomatic complaints in schoolchildren: a Nordic comparison. Scand J Public Health 2001;29(1):44-54.
143. Gaffney A,Dunne EA. Developmental aspects of children's definitions of pain. Pain 1986;26(1):105-17.
144. McGrath PJ. Annotation: aspects of pain in children and adolescents. J Child Psychol Psychiatry 1995;36(5):717-30.
145. Sweeting H,West P. Sex differences in health at ages 11, 13 and 15. Soc Sci Med 2003;56(1):31-9.
146. Jellesma FC,Rieffe C,Terwogt MM. The Somatic Complaint List: Validation of a self-report questionnaire assessing somatic complaints in children. J Psychosom Res 2007;63(4):399-401.
147. Wisniewski JJ,Naglieri JA,Mulick JA. Psychometric properties of a Children's Psychosomatic Symptom Checklist. J Behav Med 1988;11(5):497-507.
148. Egger HL,Erkanli A,Keeler G, et al. Test-Retest Reliability of the Preschool Age Psychiatric Assessment (PAPA). J Am Acad Child Adolesc Psychiatry 2006;45(5):538-49.
149. Angold A,Costello EJ. The Child and Adolescent Psychiatric Assessment (CAPA). J Am Acad Child Adolesc Psychiatry 2000;39(1):39-48.
150. Wittchen HU,Lachner G,Wunderlich U,Pfister H. Test-retest reliability of the computerized DSM-IV version of the Munich-Composite International Diagnostic Interview (M-CIDI). Soc Psychiatry Psychiatr Epidemiol 1998;33(11):568-78.
151. Reich W. Diagnostic interview for children and adolescents (DICA). J Am Acad Child Adolesc Psychiatry 2000;39(1):59-66.
152. Laurell K,Larsson B,Eeg-Olofsson O. Headache in schoolchildren: agreement between different sources of information. Cephalalgia 2003;23(6):420-8.
153. Herjanic B,Reich W. Development of a structured psychiatric interview for children: agreement between child and parent on individual symptoms. J Abnorm Child Psychol 1997;25(1):21-31.
154. Waters E,Doyle J,Wolfe R, et al. Influence of parental gender and self-reported health and illness on parent-reported child health. Pediatrics 2000;106(6):1422-8.
155. Garber J,Van Slyke DA,Walker LS. Concordance between mothers' and children's reports of somatic and emotional symptoms in patients with recurrent abdominal pain or emotional disorders. J Abnorm Child Psychol 1998;26(5):381-91.
156. Litcher L,Bromet E,Carlson G, et al. Ukrainian application of the Children's Somatization Inventory: psycho-

metric properties and associations with internalizing symptoms. J Abnorm Child Psychol 2001;29(2):165-75.
157. Walker LS, Garber J. Manual for the Children's Somatization Inventory. 2003. Divsion of Adolescent Medicine and Behavioral Science, Department of Pediatrics, Vanderbilt Unverisity School of Medicine, Nashville.
158. Meesters C,Muris P,Ghys A,Reumerman T,Rooijmans M. The Children's Somatization Inventory: further evidence for its reliability and validity in a pediatric and a community sample of Dutch children and adolescents. J Pediatr Psychol 2003;28(6):413-22.
159. Jellesma FC,Rieffe C,Terwogt MM,Kneepkens CM. Somatic complaints and health care use in children: Mood, emotion awareness and sense of coherence. Soc Sci Med 2006;63(10):2640-8.
160. Achenbach TM. Manual for the Child Behavior Checklist/4-18 and 1991 Profile. 1991. Burlington: University of Vermont, Department of Psychiatry.
161. Achenbach TM,Dumenci L. Advances in empirically based assessment: revised cross-informant syndromes and new DSM-oriented scales for the CBCL, YSR, and TRF: comment on Lengua, Sadowksi, Friedrich, and Fischer (2001). J Consult Clin Psychol 2001;69(4):699-702.
162. Lengua LJ,Sadowski CA,Friedrich WN,Fisher J. Rationally and empirically derived dimensions of children's symptomatology: expert ratings and confirmatory factor analyses of the CBCL. J Consult Clin Psychol 2001;69(4):683-98.
163. Boyle MH,Offord DR,Hofmann HG, et al. Ontario Child Health Study. I. Methodology. Arch Gen Psychiatry 1987;44(9):826-31.
164. Offord DR,Boyle MH,Racine Y. Ontario Child Health Study: correlates of disorder. J Am Acad Child Adolesc Psychiatry 1989;28(6):856-60.
165. Wright KD,Asmundson GJ. Brief report: factor structure of the Childhood Illness Attitude Scales (CIAS). J Pediatr Psychol 2005;30(2):213-8.
166. Lieb R,Pfister H,Mastaler M,Wittchen HU. Somatoform syndromes and disorders in a representative population sample of adolescents and young adults: prevalence, comorbidity and impairments. Acta Psychiatr Scand 2000;101(3):194-208.
167. Essau CA, Conradt J, Petermann F. Prevalence, comorbidity and psychosocial impairment of somatoform disorders in adolescents. Psychology, Health & Medicine 4, 169-180. 1999.
168. Egger HL,Angold A,Costello EJ. Headaches and psychopathology in children and adolescents. J Am Acad Child Adolesc Psychiatry 1998;37(9):951-8.
169. Egger HL, Angold A. The Preschool Age Psychiatric Assessment (PAPA): a structured parent interview for diagnosing psychiatric disorders in preschool children. In: Handbook of Infant, Toddler, and Preschool Mental Assessment , 223-243. 2004. DelCarmen-Wiggins R, Carter A, eds. New York, Oxford University Press.
170. Stovner LJ,Zwart JA,Hagen K,Terwindt GM,Pascual J. Epidemiology of headache in Europe. Eur J Neurol 2006;13(4):333-45.
171. Leiknes KA,Finset A,Moum T,Sandanger I. Methodological issues concerning lifetime medically unexplained and medically explained symptoms of the Composite International Diagnostic Interview: a prospective 11-year follow-up study. J Psychosom Res 2006;61(2):169-79.
172. Goodman R,Ford T,Richards H,Gatward R,Meltzer H. The Development and Well-Being Assessment: description and initial validation of an integrated assessment of child and adolescent psychopathology. J Child Psychol Psychiatry 2000;41(5):645-55.
173. Mullick MS,Goodman R. The prevalence of psychiatric disorders among 5-10 year olds in rural, urban and slum areas in Bangladesh: an exploratory study. Soc Psychiatry Psychiatr Epidemiol 2005;40(8):663-71.
174. Smith RC,Korban E,Kanj M, et al. A method for rating charts to identify and classify patients with medically unexplained symptoms. Psychother Psychosom 2004;73(1):36-42.
175. Reid S,Crayford T,Richards S,Nimnuan C,Hotopf M. Recognition of medically unexplained symptoms--do doctors agree? J Psychosom Res 1999;47(5):483-5.
176. Chitkara DK,Rawat DJ,Talley NJ. The epidemiology of childhood recurrent abdominal pain in Western countries: a systematic review. Am J Gastroenterol 2005;100(8):1868-75.
177. Goodman R,Ford T,Simmons H,Gatward R,Meltzer H. Using the Strengths and Difficulties Questionnaire (SDQ) to screen for child psychiatric disorders in a community sample. Br J Psychiatry 2000;177:534-9.
178. Goodman R,Scott S. Comparing the Strengths and Difficulties Questionnaire and the Child Behavior Checklist: is small beautiful? J Abnorm Child Psychol 1999;27(1):17-24.
179. Goodman R. Psychometric properties of the strengths and difficulties questionnaire. J Am Acad Child Adolesc Psychiatry 2001;40(11):1337-45.
180. Obel C,Heiervang E,Rodriguez A, et al. The Strengths and Difficulties Questionnaire in the Nordic countries. Eur Child Adolesc Psychiatry 2004;13 Suppl 2:II32-II39.
181. Obel C,Dalsgaard S,Stax HP,Bilenberg N. [Strengths and Difficulties Questionnaire (SDQ-Dan). A new instrument for psychopathologic screening of children aged 4-16 years]. Ugeskr Laeger 27-2-2003;165(5):462-5.
182. Jorgensen CK,Karlsmose B. Validation of automated forms processing. A comparison of Teleform with manual data entry. Comput Biol Med 1998;28(6):659-67.
183. Ostberg V,Alfven G,Hjern A. Living conditions and psychosomatic complaints in Swedish schoolchildren. Acta Paediatr 2006;95(8):929-34.
184. Groholt EK,Stigum H,Nordhagen R,Kohler L. Recurrent pain in children, socio-economic factors and accumulation in families. Eur J Epidemiol 2003;18(10):965-75.
185. Halldorsson M,Cavelaars AE,Kunst AE,Mackenbach JP. Socioeconomic differences in health and well-being of children and adolescents in Iceland. Scand J Public Health 1999;27(1):43-7.
186. Myers K,Winters NC. Ten-year review of rating scales. I: overview of scale functioning, psychometric properties, and selection. J Am Acad Child Adolesc Psychiatry 2002;41(2):114-22.
187. Petho B,Tusnady G,Vargha A, et al. Validity of reliability: comparison of interrater reliabilities of psychopathological symptoms. J Nerv Ment Dis 2007;195(7):606-13.
188. Brown RJ. Introduction to the special issue on medically unexplained symptoms: Background and future directions. Clin Psychol Rev 2007;27(7):769-80.

189. Kroenke K. Studying symptoms: sampling and measurement issues. Ann Intern Med 1-5-2001;134(9 Pt 2):844-53.
190. Aaronson LS,Burman ME. Use of health records in research: reliability and validity issues. Res Nurs Health 1994;17(1):67-73.
191. Walker LS,Greene JW. The functional disability inventory: measuring a neglected dimension of child health status. J Pediatr Psychol 1991;16(1):39-58.
192. Skovgaard AM,Olsen EM,Houmann T, et al. The Copenhagen County child cohort: design of a longitudinal study of child mental health. Scand J Public Health 2005;33(3):197-202.
193. Skovgaard AM,Olsen EM,Christiansen E, et al. Predictors (0-10 months) of psychopathology at age 11/2 years - a general population study in The Copenhagen Child Cohort CCC 2000. J Child Psychol Psychiatry 2008;49(5):553-62.
194. Osler M,Klebak S. Social differences in health in an affluent Danish county. Scand J Soc Med 1998;26(4):289-92.
195. Ford T,Goodman R,Meltzer H. The British Child and Adolescent Mental Health Survey 1999: the prevalence of DSM-IV disorders. J Am Acad Child Adolesc Psychiatry 2003;42(10):1203-11.
196. Noyes R, Jr.,Stuart S,Langbehn DR, et al. Childhood antecedents of hypochondriasis. Psychosomatics 2002;43(4):282-9.
197. Nielsen A, Reinhardt PC, Madsen M. Children and childfamilies health and wellbeing in Denmark - and the development since 1984. 2001. Statens Institut for Folkesundhed.
198. Angold A,Prendergast M,Cox A, et al. The Child and Adolescent Psychiatric Assessment (CAPA). Psychol Med 1995;25(4):739-53.
199. Fink P,Ornbol E,Toft T, et al. A new, empirically established hypochondriasis diagnosis. Am J Psychiatry 2004;161(9):1680-91.
200. Costello EJ,Egger H,Angold A. 10-year research update review: the epidemiology of child and adolescent psychiatric disorders: I. Methods and public health burden. J Am Acad Child Adolesc Psychiatry 2005;44(10):972-86.
201. Brugha TS,Jenkins R,Taub N,Meltzer H,Bebbington PE. A general population comparison of the Composite International Diagnostic Interview (CIDI) and the Schedules for Clinical Assessment in Neuropsychiatry (SCAN). Psychol Med 2001;31(6):1001-13.
202. Edwards P,Roberts I,Clarke M, et al. Methods to increase response rates to postal questionnaires. Cochrane Database Syst Rev 2007;(2):MR000008.
203. Konijnenberg AY,Graeff-Meeder ER,Kimpen JL, et al. Children with unexplained chronic pain: do pediatricians agree regarding the diagnostic approach and presumed primary cause? Pediatrics 2004;114(5):1220-6.
204. Postilnik I,Eisman HD,Price R,Fogel J. An algorithm for defining somatization in children. J Can Acad Child Adolesc Psychiatry 2006;15(2):64-74.
205. Jensen P,Roper M,Fisher P, et al. Test-retest reliability of the Diagnostic Interview Schedule for Children (DISC 2.1). Parent, child, and combined algorithms. Arch Gen Psychiatry 1995;52(1):61-71.
206. Anttila P,Metsahonkala L,Sillanpaa M. School start and occurrence of headache. Pediatrics 1999;103(6):e80.
207. von Baeyer CL,Walker LS. Children with recurrent abdominal pain: issues in the selection and description of research participants. J Dev Behav Pediatr 1999;20(5):307-13.
208. Gureje O,Ustun TB,Simon GE. The syndrome of hypochondriasis: a cross-national study in primary care. Psychol Med 1997;27(5):1001-10.
209. Little P,Somerville J,Williamson I, et al. Family influences in a cross-sectional survey of higher child attendance. Br J Gen Pract 2001;51(473):977-81, 984.
210. Crane C,Martin M. Illness-related parenting in mothers with functional gastrointestinal symptoms. Am J Gastroenterol 2004;99(4):694-702.
211. Barnes J, Stein A. Effects of parental physical and psychiatric illness on child development. [In New Oxford Textbook of Psychiatry (eds M. Gelder, J. Lopes-Ibor & N. Andreasen)], 1848-1855. 2003. Oxford University Press.
212. Garralda ME. The links between somatisation in children and adults. In: Family Matters (eds. P. Reder, M. McClure & A. Jolley). Routlegde, 122-134. 2000.
213. Brauer C,Thomsen JF,Loft IP,Mikkelsen S. Can we rely on retrospective pain assessments? Am J Epidemiol 15-3-2003;157(6):552-7.
214. Olsen EM,Petersen J,Skovgaard AM, et al. The growth pattern of 0-1-year-old Danish children, when screened by public health nurses--the Copenhagen County Child Cohort 2000. Ann Hum Biol 2005;32(3):297-315.