Recurrent Pain and Health Related Quality of Life in Young Schoolchildren

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To Erling
Søren and Stine
Abstract

The objectives in of this thesis were 1) to describe the occurrence and co-occurrence of recurrent pain (headache, stomach-ache, and backache) in young schoolchildren; 2) to describe Health Related Quality of Life (HRQoL) in these children, from the perspective of the child, 3) to examine the psychometric properties of the PedsQL 4.0, Generic Core Scale, an instrument for measuring HRQoL in children.

Three data collections were performed, two in Umeå, a university city in northern Sweden and one in a nearby smaller municipality, Lycksele. In Umeå, the first survey included schoolchildren from grades 0-6 and three years later all schoolchildren attending grade three and six were approached. In Lycksele all schoolchildren attending grades three through six and grade nine were invited to participate. Pain and quality of life were measured by questionnaires.

The main findings of the thesis were that 2/3 of the children experienced pain from the head, stomach or back recurrently (at least monthly) and 1/3 experienced weekly pain. Weekly headache was reported by 23% of the children, 19% reported weekly stomach-ache and 7% weekly backache. Half of the children with recurrent pain conditions reported pain from several body sites, and, in children with weekly pain, 2/3 reported multi-site pain. HRQoL in children with recurrent pain problems was markedly impaired, especially in children with multi-site pain and in children with weekly pain. Impairment was found across all studied domains of HRQoL (physical, emotional, social and school function and well-being) and was seen in both girls and boys as well as among both third grades and six graders. Finally, The Swedish PedsQL self-report forms showed acceptable psychometric properties.

In conclusion, also in young schoolchildren, headache, stomach-ache and backache are common conditions which are associated with a clearly reduced HRQoL. The results show an urgent need for early preventive and curative programs targeting HRQoL domains such as physical, emotional, social and school areas. The results also indicate that recurrent pain should be regarded a potential general pain disorder rather than merely a local disorder. Finally, the PedsQL was found to be a reliable and valid measure of HRQoL in young Swedish school-aged children.

Keywords abdominal pain, back pain, child, headache, pain, psychometrics, quality of life, schools, validation studies.
Original Papers


III. Petersen S, Hägglöf B, Stenlund H, Bergström E. Psychometric properties of the Pediatric Quality of Life Inventory 4.0 Generic Core Scale. (Submitted)

IV. Petersen S, Hägglöf B & Bergström E. Low health related quality of life in young schoolchildren with recurrent pain. (Manuscript)

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# Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AD</td>
<td>Anno Domini (after Christ)</td>
</tr>
<tr>
<td>ADHD</td>
<td>Attention-Deficit Hyperactivity Disorder</td>
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<td>ADF</td>
<td>Asymptotically Distribution</td>
</tr>
<tr>
<td>BC</td>
<td>Before Christ</td>
</tr>
<tr>
<td>CBCL</td>
<td>Child Behavior Checklist</td>
</tr>
<tr>
<td>CFA</td>
<td>Confirmative Factor Analysis</td>
</tr>
<tr>
<td>CFI</td>
<td>Comparative Fit Index</td>
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<tr>
<td>CNS</td>
<td>Central Nervous System</td>
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<tr>
<td>EFA</td>
<td>Explorative Factor Analysis</td>
</tr>
<tr>
<td>FAP</td>
<td>Functional Abdominal Pain</td>
</tr>
<tr>
<td>FAPS</td>
<td>Functional Abdominal Pain Syndrome</td>
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<tr>
<td>FGID</td>
<td>Functional Gastrointestinal Disorder</td>
</tr>
<tr>
<td>GH</td>
<td>Gamma Hat</td>
</tr>
<tr>
<td>HBSC</td>
<td>Health Behavior of School-aged Children</td>
</tr>
<tr>
<td>HRQoL</td>
<td>Health Related Quality of Life</td>
</tr>
<tr>
<td>IASP</td>
<td>International Association for the Study of Pain</td>
</tr>
<tr>
<td>IBS</td>
<td>Irritable Bowel Syndrome</td>
</tr>
<tr>
<td>ICC I</td>
<td>Intra-class Correlation Coefficient</td>
</tr>
<tr>
<td>ICHD</td>
<td>International Classification of Headache Disorders</td>
</tr>
<tr>
<td>IHS</td>
<td>International Headache Society</td>
</tr>
<tr>
<td>Mc</td>
<td>McDonald's centrality index</td>
</tr>
<tr>
<td>ML</td>
<td>Maximum Likelihood</td>
</tr>
<tr>
<td>NNFI</td>
<td>Non-Normed Fit Index</td>
</tr>
<tr>
<td>QLA-CP</td>
<td>Quality of Life Questionnaire for Adolescents with Chronic Pain</td>
</tr>
<tr>
<td>QLH-Y</td>
<td>Quality of Life Headache-Youth</td>
</tr>
<tr>
<td>QLP-Y</td>
<td>Quality of Life Pain-Youth</td>
</tr>
<tr>
<td>OR</td>
<td>Odds Ratio</td>
</tr>
<tr>
<td>PedsQL</td>
<td>Pediatric Quality Of Life Inventory 4.0 Generic Core Scales</td>
</tr>
<tr>
<td>PedsQL-15</td>
<td>Short form Pediatric Quality Of Life Inventory</td>
</tr>
<tr>
<td>PedsQL-23</td>
<td>Full form Pediatric Quality Of Life Inventory</td>
</tr>
<tr>
<td>QoL</td>
<td>Quality of Life</td>
</tr>
<tr>
<td>RAP</td>
<td>Recurrent Abdominal Pain</td>
</tr>
<tr>
<td>RMSEA</td>
<td>Root Mean Square Error of Approximation</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
<tr>
<td>SRMR</td>
<td>Standardized root mean square residual</td>
</tr>
<tr>
<td>SPSS</td>
<td>Statistical Package for the Social Science</td>
</tr>
<tr>
<td>TLI</td>
<td>Tucker Lewis Index</td>
</tr>
<tr>
<td>TTH</td>
<td>Tension Type Headache</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>US</td>
<td>United States of America</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>YSR</td>
<td>Youth Self Report</td>
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</tbody>
</table>
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Introduction

It is often said that children are the future of a society. It is a great, and challenging, societal responsibility to help children navigate between the landmines of childhood in a way that enable them to take over expected future responsibilities.

But children are not only human “becomings”. They are also human “beings”, with limited influential power, but all the same with their own rights of a good life - here and now.

Glancing over a group of children, the pains and quality of life - or lack of that – will often be invisible for the eye of the spectator. The work on which this thesis is based may be seen as an attempt to give young children a possibility to express their present every day experiences of life and health. It is now up to the ones possessing influential power to handle their information with wisdom.
Background

A shift in child health

Until the first half of the 20th century, the most common child health problems were different types of infectious diseases, e.g. pneumonia, tuberculosis, diphtheria, measles, smallpox, diarrhea etc. [1-3]. Although these diseases still prevail in poor countries of the world, growing wealth, as well as major progress in medical science and health technology, has changed the panorama of childhood ill-health markedly in many countries. Shifting into the 21st century, the earlier main problem of infectious diseases has been partly replaced by non communicable diseases, e.g. asthma and juvenile diabetes, along with life style related conditions, e.g. overweight and mental health problems [1,2,4-6]. In several western countries, including Sweden, recurrent pain conditions have become among the most common ill-health conditions influencing the lives of children [7-10].

Definitions and classifications of pain

The most widely accepted definition of pain was stated 1975 by the International Association for the Study of Pain (IASP) and claims that

“Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” [11].

There is no generally accepted definition of recurrent or chronic pain, but it has been suggested to be pain persisting beyond what is expected (usually taken to be 3 months) or what can be considered a useful function [12,13]. It should be noticed that there are some confusion in the literature regarding the terms recurrent and chronic. Although they may be seen as separate concepts [14], they are commonly over-
lapping and used interchangeably [15,16]. For simplicity the term recurrent will be used in this thesis.

In children, recurrent pain is most commonly located in the head, stomach or musculoskeletal system, e.g. the back [17-19].

**Headache**

Headache classifications have changed considerably over time. In studies of migraine headache by Vahlquist [20] and Bille [21] and later Pretsky and Sommer [22], migraine was proposed to be characterized by pain attacks separated by pain free periods. Attacks should include several additional features, e.g. visual aura, nausea, unilateral pain, family history of pain. This definition of migraine influenced the field of headache for years from 1955 and onward. In the 1960s a special interest group of the US National Institutes of Health, as well as the World Federation of Neurology, proposed criteria also for a number of other headache types. For instance, tension headache was described as situated predominately in the sub occipital area and characterized by a long-lasting tightness and pressure or constriction of changing frequency, intensity and duration [23,24].

The first comprehensive classification of headache types, the International Classification of Headache Disorders (ICHD-I), was put forward year 1988 by the International Headache Society (IHS) [25]. The ICHD-I had a hierarchical structure organizing headaches into either primary headache types, e.g. migraine headache, Tension Type Headache (TTH) etc. or headache secondary to another ill-health condition, e.g. head trauma, brain tumors etc. For each subtype explicit criteria’s were given, see Table 1a and 1b for description of the two most common recurrent headache types, migraine headache and TTH.

The ICHD-I has been widely used, but the criteria’s were primarily formulated for adults and as such offered a solid basis for adult conditions, while their sensitivity for childhood headache has been criticized [26-28]. A revision, IHCD-II published 2004, included some modifications for children, but also this classification’s appropriateness in child populations has been questioned [29,30].
Table 1a. IHS criteria’s for pediatric migraine headache without aura.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>≥ 5 headache attacks</td>
<td>≥ 5 headache attacks</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>2-72 hours (no or unsuccessful treatment)</td>
<td>1-72 hours (no or unsuccessful treatment)</td>
</tr>
<tr>
<td><strong>Characteristics (at least two)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Location: unilateral</td>
<td>• Location: unilateral (or bilateral)</td>
<td></td>
</tr>
<tr>
<td>• Quality: pulsating</td>
<td>• Quality: pulsating</td>
<td></td>
</tr>
<tr>
<td>• Intensity: moderate or severe</td>
<td>• Intensity: moderate or severe</td>
<td></td>
</tr>
<tr>
<td>• Aggravation by physical activity</td>
<td>• Aggravation by physical activity</td>
<td></td>
</tr>
<tr>
<td><strong>Characteristics (at least one)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Nausea and/or vomiting</td>
<td>• Nausea and/or vomiting</td>
<td></td>
</tr>
<tr>
<td>• Photophobia and phonophobia</td>
<td>• Photophobia and phonophobia</td>
<td></td>
</tr>
<tr>
<td><strong>Characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Not attributed to other disorder</td>
<td>• Not attributed to other disorder</td>
<td></td>
</tr>
</tbody>
</table>

*No medication overuse

Table 1b. IHS criteria’s for Tension Type Headache.

<table>
<thead>
<tr>
<th>Tension Type Headache (TTH)</th>
<th>ICHD-I (1988) and ICHD-II (2004)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>Infrequent episodic: ≥ 10 attacks</td>
</tr>
<tr>
<td></td>
<td>Frequent episodic: ≥ 10 attacks</td>
</tr>
<tr>
<td></td>
<td>Chronic: ≥ 10 attacks</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>30 minutes to 7 days (chronic: 1 hour to continuously)</td>
</tr>
<tr>
<td><strong>Characteristics (at least two)</strong></td>
<td></td>
</tr>
<tr>
<td>• Location: bilateral</td>
<td></td>
</tr>
<tr>
<td>• Quality: pressing/tightening (non-pulsating)</td>
<td></td>
</tr>
<tr>
<td>• Intensity: mild or moderate</td>
<td></td>
</tr>
<tr>
<td>• No aggravation by physical activity</td>
<td></td>
</tr>
<tr>
<td><strong>Characteristics (all three)</strong></td>
<td></td>
</tr>
<tr>
<td>• No nausea or vomiting (anorexia may occur)</td>
<td></td>
</tr>
<tr>
<td>• Photophobia or phonophobia present</td>
<td></td>
</tr>
<tr>
<td>• Not attributed to other disorder</td>
<td></td>
</tr>
</tbody>
</table>

Stomach-ache

Also stomach-ache classifications have changed over time. The first to recognize the importance of recurrently occurring stomach-ache were Apley and Naish, who in the late 1950s introduced the term “Recurrent Abdominal Pain” (RAP) [31]. RAP was described as stomach-ache severe enough to cause some impairment of function and occurring at least three times over a period of at least three months. This definition became the gold standard in research and was frequently used in clinical practice for the following 40 years.
The RAP definition was all-embracing, including stomach-ache of any origin, for which it was criticized [32]. In the late 1990s, an expert group of pediatricians introduced a classification of gastrointestinal disorders also including pain conditions, the International Classification of Functional Gastrointestinal Disorders, so called Rome-II criteria [33]. Functional Gastrointestinal Disorders (FGID) were described as an inconsistent combination of “chronic, or recurrent symptoms not explained by structural or biochemical abnormalities” and diagnostic criteria for four abdominal pain conditions was provided, functional dyspepsia, Irritable Bowel Syndrome (IBS), Functional Abdominal Pain (FAP) and abdominal migraine, see Table 2 for description.

<table>
<thead>
<tr>
<th>Table 2. Criteria’s for abdominal pain in children.</th>
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<tbody>
<tr>
<td><strong>Apley and Naish, 1958</strong></td>
</tr>
<tr>
<td><em>Recurrent abdominal pain</em></td>
</tr>
<tr>
<td>≥ 3 episodes/3 months of abdominal pain affecting daily activities</td>
</tr>
<tr>
<td><strong>Rome II criteria, 1999</strong></td>
</tr>
<tr>
<td><em>≥ 12 weeks/12 months</em></td>
</tr>
<tr>
<td>No evidence of pathological disease likely to explain the symptoms</td>
</tr>
<tr>
<td><em>Irritable bowel syndrome</em></td>
</tr>
<tr>
<td>Abdominal discomfort or pain associated with bowel function</td>
</tr>
<tr>
<td><em>Functional dyspepsia</em></td>
</tr>
<tr>
<td>Persistent/recurrent pain or discomfort in upper abdomen</td>
</tr>
<tr>
<td>Not associated with bowel function</td>
</tr>
<tr>
<td><em>Abdominal migraine</em></td>
</tr>
<tr>
<td>≥ 3 Paroxysmal episodes/12 months of intense, acute midline abdominal pain</td>
</tr>
<tr>
<td>Duration: 2 hours to several days</td>
</tr>
<tr>
<td>Symptom-free intervals lasting weeks to months</td>
</tr>
<tr>
<td>Additional features of migraine (headache -unilateral, photophobia, heredity, Aura)</td>
</tr>
<tr>
<td><em>Functional abdominal pain</em></td>
</tr>
<tr>
<td>Continuous/nearly continuous periumbilical not feigned pain</td>
</tr>
<tr>
<td>Minimal relation to physiological events</td>
</tr>
<tr>
<td>Some loss of daily functioning</td>
</tr>
<tr>
<td>Insufficient criteria for other functional gastrointestinal disorders</td>
</tr>
<tr>
<td><strong>Rome III criteria, 2006</strong></td>
</tr>
<tr>
<td>At least once per week for at least 2 month</td>
</tr>
<tr>
<td>No evidence of pathological disease likely to explain the symptoms</td>
</tr>
<tr>
<td><em>Irritable bowel syndrome</em></td>
</tr>
<tr>
<td>Se Rome II</td>
</tr>
<tr>
<td><em>Functional dyspepsia</em></td>
</tr>
<tr>
<td>Se Rome II</td>
</tr>
<tr>
<td><em>Abdominal migraine</em></td>
</tr>
<tr>
<td>≥ 3 Paroxysmal episodes/12 months of intense, acute periumbilical pain interfering with normal activities</td>
</tr>
<tr>
<td>Duration: 1 hours or more</td>
</tr>
<tr>
<td>Symptom free intervals lasting weeks to months</td>
</tr>
<tr>
<td>Additional features if migraine (anorexia, nausea, vomiting, headache, photophobia, pallor)</td>
</tr>
<tr>
<td><em>Functional abdominal pain</em></td>
</tr>
<tr>
<td>Episodic/continuous abdominal pain</td>
</tr>
<tr>
<td>Insufficient criteria for other functional gastrointestinal disorders</td>
</tr>
<tr>
<td><em>Functional abdominal pain syndrome</em></td>
</tr>
<tr>
<td>Functional abdominal pain (see above)</td>
</tr>
<tr>
<td>Some loss of daily functioning and/or additional somatic symptoms</td>
</tr>
</tbody>
</table>
In a revision of the Rome II criteria’s published year 2006 (Rome III) functional abdominal pain was further split into two diagnoses, functional abdominal pain (FAP) and Functional Abdominal Pain Syndrome (FAPS) which included pain at additional sites [34].

The Rome classifications were expected to replace the wider definition of recurrent abdominal pain earlier put forward by Apley and Naish [33]. However, the new classification proved not to be able to capture all types of abdominal pain disorders experienced by children and therefore the RAP definition is still utilized to describe recurrent abdominal pain conditions in children [35].

Backache

At present there is no generally accepted classification of backache and the literature holds a plethora of definitions.

Backache may apply to pain anywhere in the back, but may also refer to pain located only in the lower, mid or upper back or in the neck region [36-39]. These regions may not be further defined or they may be more precisely described, e.g. the low back may be referred to as the lumbopelvic spine with corresponding posterior parts of the body or as the region between the gluteal folds and the scapula respectively the first lumbar vertebra. Likewise pain in the middle back and neck may be described as pain in the thoracic respective cervical spine area with corresponding posterior parts of the body [37,38,40-42].

Also pain frequency and timeframe of the back pain experience vary greatly from pain occurring once in a lifetime or during the last year, half a year, month, week, day, to pain occurring constantly or repeatedly during weeks or months [37-41,43,44]. The quality of pain may be unspecified but may also be limited to include only severe or non occasional pain [41,45].

Finally, back pain has been classified as specific or non-specific. Specific back pain being classified as pain secondary to a known diagnosis, e.g. “a systemic disease, infection, injury, trauma, cauda equina, or structural deformity”. Non-specific back pain is less well defined but includes conditions of which the cause of pain is unclear [46].

Present definition

In the studies of the present thesis, recurrent headache, stomachache and backache is considered to be present whenever the child state
Background

that she/he has experienced the pain at least monthly during the past six months.

Prevalence and natural history of pain

Recurrent pain in children is most commonly located in the head, stomach or musculoskeletal system, e.g. the back [17-19]. Prevalence of these conditions seems to vary greatly between countries as shown by the World Health Organization (WHO) in the multinational survey Health Behavior of School-aged Children (HBSC). Among the 28 countries studied year 1998, headache prevalence in, e.g. 15 year old girls differed between 25% in Belgium and 64% in Israel [7]. Although Swedish children internationally appear to be among the healthiest, reports of recurrent pain seem more common in schoolchildren from Sweden than in children from most other western countries [7].

Before describing and discussing prevalence of headache, stomachache and backache in children, it should be noted that the epidemiological data is hampered by considerable methodological differences which gives rise to some variance in prevalence. One reason for differences in prevalence figures is the above described inconsistency of case definition. Also, the available data is based on studies which vary greatly in research design (cross-sectional or longitudinal), way of data collection (self or proxy report questionnaires, interviews or physical examinations) and population size, geographic location, as well as socio-demographic profile of group approached.

Headache

A recent extensive global review by Stovner et al. revealed an adult lifetime prevalence of headache above 80% in most countries and above 90% in several European countries, e.g. Denmark (96%) and Finland (91%) [47]. It was moreover concluded that half of the global population currently may be bothered by an active headache condition. Notably, headache seemed to be more prevalent in children than in
adults and elderly, and headache was postulated to rank among the top five health problems in childhood.

The first experience of headache may occur before one year of age [48,49], and 85%-97% of children above the age of nine have experienced headache sometimes during their life [50-53]. Thus, headache is well-known to most school-aged children.

Headache has not always been acknowledged as common in children. The pioneer epidemiological works of e.g. Vahlquist et al. and Bille from the mid 1900s, established, however, that headache was a common childhood condition, experienced (infrequently) by approximately half of the 9000 Swedish schoolchildren studied. Furthermore the surveys revealed that headache in children also might occur frequently [20,21,54]. Later worldwide studies have confirmed that recurrent headache definitely is present in childhood [47,55,56].

**Prognosis**

Population based surveys studying the natural history of headache, reveal that childhood headache conditions most commonly follow the child for years. In a three year follow up study of 7-15 years old schoolchildren, 80% of the children with TTH still suffered a headache condition after three years [57]. Likewise, in a six year follow-up study, TTH persisted in 73% and migraine in 85% of six year old schoolchildren, while only 13% of the initially headache-free controls reported headache at 13 years of age [58]. The long term outcome of TTH has not been reported, but Bille followed schoolchildren with migraine over a course of 40 years [59]. In these children, 60% were headache free after six years, but after 30 and 40 years, more than half of the group experienced migraine headache. Another long-term study (26 years) found that children with non specified headache were at increased risk of not only headache, but also other physical and psychiatric adversity during adulthood [60].

The prognosis for children who has pertained medical care for headache are somewhat discouraging as well. Although there is evidence of short as well as long term improvement, between 61% and 84% still suffer from headache at follow up points varying between one year and 20 years [61-63].
Stomach-ache

The epidemiology of recurrent stomach-ache has attracted much less attention than headache, but still, information about this condition has been part of the medical literature for centuries [18,64]. Pain in the stomach may occur already in the first months of life [65] and can be found at any age after that [35].

Stomach-ache has affected most people some time during childhood [35] and back in 1958 Apley and Naish showed that abdominal pain often occurred repetitively in school-aged children [66]; a finding later confirmed by others [35].

Prognosis

Abdominal pain may persist over a considerable time. In population based samples, one year persistence in young schoolchildren has been found to be 85% [67]; three year persistence: 65 – 80% [68]; six year persistence: 54% [69,70], and 10-14 year persistence: 40% [71], while the study with the longest follow up time, 20 years, found no association between abdominal pain in childhood and abdominal in adulthood [72]. Notably, pain persistence seems to increase with increasing age [68] and pain frequency [69,70].

In clinical populations, five year persistence of stomach-ache has been shown to be 40-45% [73,74], while in between one third and one forth of pediatric patients, stomach-ache persist for more than five years [71,75,76]. Thus, studies of both clinical and non-clinical samples indicate a trend of successive lifetime pain remission. However, a convincing amount of literature also reveal that children with stomach-ache, has a propensity to develop other physical and psychiatric ailments over time, e.g. headache and anxiety, and up to half of the children who recover from stomach-ache develop other physical and psychiatric conditions [67,71,72,74-77].

Backache

In adults, backache has achieved great attention as a common disabling condition, experienced sometimes during the course of life by 51- 84% of the population [78]. In contrast to that, backache in children has been considered rather uncommon and the literature on this subject is quite meager [18,79-82]. However, during the past two decades interest of childhood backache has expanded [80].
Epidemiological studies of backache in children primarily have reported point prevalence or period prevalence of varying timeframes, i.e. life time, last month etc. Although the first childhood surveys including reports of back pain frequency were conducted in the mid and late 1980s, reports including pain frequency are few [18,45,78,83,84]. Furthermore, the epidemiological literature of backache mostly focused on older schoolchildren [78]. The reports have often addressed rather small convenience samples and their ability to represent the general population have been questioned [83].

The existing literature reveals that backache may occur already in infancy, but very seldom does the first episode take place before eight years of age [45,83,85,86]. Lifetime prevalence seems to increase markedly after the age of 11 years and up to 74% of adolescents report having experienced backache some times during their life [87], indicating that backache may be well known at least in older schoolchildren.

**Prognosis**

The natural course of backache has been reported to fluctuate over time. El Metvally and colleges found a one year remission in 46% of 10 and 12 year old children with recurrent musculoskeletal pains [88]. However, half of these children had relapsed at a four year follow up. Two other studies following children with backache for one and five years respective three and eight years, showed similar fluctuations over time with lower prevalence of pain persistence at short term than long term follow up points [45,89].

In general, it seems that one third to one half of backache suffering children experience pain persistence for at least 8-12 years, and backache in childhood has also been proved to increase the risk of back pain in adulthood [89-92]. Also the consistency of musculoskeletal pain seems to increase with older age [68,88,92]. For instance, a recent study of Swedish children found a three year persistence of musculoskeletal pain in 46% of children from grade three and in 70% of children from grade six and nine. Likewise, higher frequency of musculoskeletal pain appears to increase persistence [68,92,93].
Pain theory

The historical legacy

Understanding the nature of pain has been a challenge throughout history. In antiquity pain was often thought of as intrusions of foreign objects into the body, a punishment for sins regulated by higher powers, e.g. Homer (8th century BC) described pain as "arrows shot by gods" [94,95].

Centuries later the ancient Greek philosophical founders of western cultures, Plato (~427 – 347 BC) and his student Aristotle (384–322 BC), introduced the idea that pain was an emotional experience. They agreed that pain was not a sensation by itself but rather a "passions of the soul", which according to Aristotle was ascribed to excessively aggressive types of wave motions localized in the blood vessels to the heart and possibly initiated by sensations. Plato advanced these ideas by suggesting pain to be violent reactions in the atoms of the body due to the impact of the four elements: earth, air, fire and water. Plato further postulated that the mortal soul associated with pain was situated in the liver or the heart [94-96].

Following Aristotle, centuries of anatomy and physiology studies resulted in a counteracting pain theory. Galen (~AD 130-201), an ancient Greek physician whose theories dominated western medical science for over a millennium, forwarded the nerve and brain studies by the ancient Greek physicians Herophilus and Erasistratus (~300 BC) and concluded that pain was a sensation perceived in the brain [95-97]. Galen argued pain to be the lowest form of sensation and a result of severe nerve disturbances, but he did not find proof for nerves specialized in pain. However, half a millennium later the observations of Avicenna (AD 980–1037), a Persian Muslim philosopher and physician, led to the conclusion that pain indeed was an independent sensation [96].

As information on the nature of sensory and motor systems advanced, theories of pain being an emotion gradually weakened while the hypothesis of pain as a sensation successively rooted [97]. The brain became widely accepted as the centre of sensations and in the 17th century Descartes, a French philosopher, summed the available evidence in theories suggesting that pain was due to tissue damage starting a non-impressionable direct transmission of a pain signal to the brain via a specific nerve channel [97-99]. According to Descartes, this signal
would be passively perceived after the concept; the more damage the greater the pain. Furthermore, Descartes clearly distinguished between the body and the mind, and pain was considered either strictly mental or strictly physical.

**Gate Control and Neuromatrix**

The theories of Descartes dominated the field of pain until the second half of the 20th century, when Melzack, a Canadian psychologist and Wall, a British physiologist put forward the “Gate Control” theory and later also the “Neuromatrix” theory [100,101]. Melzack and Wall rejected the idea of pain as either “all in the mind” or “all in the body”, and prompted pain to be the result of integrated processes between the two. According to the gate control theory published 1965 [100], pain signals are transmitted through not one, but several ascending pathways, which are modulated by inhibitory as well as excitatory descending interneurons. A neural gating mechanism located in the spinal dorsal horns is suggested to inhibit or facilitate pain signal transmission, depending on activity level in different afferent pain fibers (thinly myelinated Aδ and Aβ fibers along with unmyelinated C-fibers), but also influenced by the activity in descending neural inhibitory pathways from the brainstem and cortex. Furthermore, the descending control is presumed to be influenced by the ascending activity to the brain, completing a spinal cord–brain–spinal cord loop.

Eventually the gate theory which mainly focused peripheral and spinal processes was incorporated into the wider “Neuromatrix Theory”, adding emphasis on activity in widespread areas of the brain [101]. The neuromatrix, an extensive, widespread network of neurons in the brain, is suggested to generate characteristic nerve-impulse patterns “neurosignatures”, which convert into awareness and action. The synaptic construction of the neuromatrix is described to be determined by genetic as well as sensory influences, modulated by cognitive factors and by stressors disrupting the homeostatic regulation system in the brain (Fig. 1). Thus, according to Melzack and Walls theories, pain is the result of interplay of several transmitter systems at several levels of the Central Nervous System (CNS), a multidimensional experience produced by multiple influences, and the theories create a conceptual framework integrating the sensory, affective and cognitive dimensions of pain. These theories are the basis for the earlier described definition of pain, stated by the IASP.
One implication of Melzack and Wall’s theories is that insults, which under normal circumstances initiate a process resulting in unbearable pain experiences, in special occasions, can be totally or partly neglected due to neural inhibition or modulation of pain signals. On the contrary, in special situations may pain signals, which under most circumstances are blocked in the CNS, be postponed and eventually result in significant pain experiences.

The scientific basis for Melzack and Walls theories has been questioned, but overall the theories have been broadly accepted and still guide the understanding of pain [96]. The massive quantity of neuroscientific research following these theories have during the past 40-50 years confirmed that it is reasonable to consider pain a sensation as well as an emotion [96]. Current technology has also made it possible to demonstrate complex associations between pain perception and activity in cerebral neural networks [96,102-104]. The neuromatrix, or pain matrix as it is also called, has furthermore been shown to actually be modulated by emotional, social and cognitive factors and the mechanism of pain has been confirmed to include plastic interactive ascending as well as descending processing in peripheral, spinal and brain systems such as described in the theories by Melzack and Wall. Also physical performance seem to be involved in pain modulation with physical activity.
increasing pain thresholds and tolerance, presumably by activation of the endogenous opioid system [105,106]. However, most of the research testing current pain theories have been performed in animal or adult humans models while the validity of these theories in child populations still are relatively untested.

Recurrent pain

Pain theories primarily presume that pain is initiated by noxious stimuli from peripheral nociceptors. Headache, stomach-ache as well as backache in childhood may be caused by many serious and even life threatening conditions. Examples of such conditions count trauma, inflammation, infection, and malignancy or anomalies related to the head, abdomen or back, e.g. tumors, functional constipation, diseases in the liver, gallbladder, esophagitis, gastritis, helicobacter pylori infection, nephrolithiasis, food intolerance, scoliosis, spondylolysis, spondylolisthesis, Scheuermann's disease ect.

However, when Apley back in 1958 thoroughly examined children with recurrent abdominal pain problems, an associated pathological damage or disorder explaining the pain was found only in 8% of the children [31]. Studies following Apley's investigation supported these findings and even by use of modern diagnostics, an associated explanatory condition are established only in around 20% of children with recurrent stomach-ache and in 26%-30% of children referred for specialist care [107-110]. Secondary headache rarely last for more than three months, and less than 10% of children referred to specialist clinics due to headache reveal a related explanatory disorder [111-114]. Back pain in children were until recently believed to be a condition mainly caused by serious diseases [115]. However, it has now been reported that six to seven children out of 10 referred to a specialist for backache, reveal no obviously explanatory disorder [85,91].

Thus, with the current scientific knowledge and diagnostic tools it is, in the majority of cases, not possible to find a related disorder or damage which can be held responsible for causing pediatric recurrent headache, stomach-ache and backache.

The lack of a clearly established etiology of recurrent pain problems in children has caused speculations. In general, it is poorly understood why pain turn into being recurrent, but it may be explained by a dysfunctional pain inhibitory and/or facilitatory system. For instance, the descending pain modulatory system has been shown to be altered in
persistent pain conditions [116]. Repetitive nociceptive stimulation has been shown to induce pathological alterations which increase the responsiveness and lower threshold to coming pain stimuli; also inflammatory environments have been shown to increase pain responsiveness and stress induced failing homeostasis-regulation may result in recurrent pain due to a destructive effect of cortisol on muscle, bone and neural tissue [96,101,117-119]. Thus, peripheral nociceptors as well as central neurons may be sensitized in case of persistent pain and in some cases the pain may be a reaction secondary to inflammatory processes or to stress.

In the conventional sense, nociception gives rise to pain, but recent research has proved that cerebral activity related to pain perception can occur without a primary nociceptive input, showing that pain may be experienced in the absence of such stimuli [120-123]. As mentioned above, emotional and social factors may be involved in the modulation of pain transmission and pain perception. These factors may also be involved in the initiation of non-nociceptive persistent pain. Indicators of emotional and social function and wellbeing (e.g. feelings of anxiety, depression and loneliness) are associated with activity in brain areas, which are also involved in pain perception. It has been speculated that brain activity related to, e.g. emotions, may result in a cortical reorganization of the pain-related structures, eventually leading to non-nociceptive persistent pain [124].

Pain in children

Through history there has been a concern about pain in children and it has been argued that pain differ between adults and children [64]. Until the 20th century children were believed experience greater pain than adults. In ancient time, previous experience of pain was thought to result in reduced pain sensitivity. For instance, the Greek physician Hippocrates (~460 – 370 BC) expressed that “Those who are used to bearing an accustomed pain, even if they be weak and old, bear it more easily than the young and strong who are unaccustomed”. Plato (~427–347 BC) was also interested in the issue of pain at different ages and postulated that the interactions between the four elements thought to create pain (earth, air, fire and water) was particularly vicious in the beginning of life and thus children’s pain was especially troublesome.

In the 20th century the view changed and it now became common knowledge that children due to physiological reasons experienced less
pain than adults and infants were thought to be unable to feel pain at all [64,125]. This view was dominant until recently and only a few decades ago, pain was not mentioned in standard pediatric textbooks. Recent research has not confirmed that children feel less pain than adults. On the contrary, the immature nervous system of the infant seem to give rise to pain, even in very young children [126,127], and it has been suggested that children’s pain, compared with pain in adults, is more plastic and more easily modulated by external factors [128]. Today pain management is included in pediatric textbooks and also subject to scientific interest. However, there are still great lacks in the understanding of pain in children, and children’s pain continues to be underestimated by parents as well as health care personal [18,125,129].

Significance and impact of recurrent pain

Pain is generally a valuable bodily function which is helpful when navigating through life. It is often the signal making it possible to take proper action and stop or treat an upcoming injury or disease. Headache signaling an intracranial malignancy may, for instance, give rise to action and thereby facilitate cure. Pain may also prevent aggravation of an injury and promote the process of healing by inducing inactivity and rest. Furthermore, pain experiences may help to avoid later lesions and injuries. Memories of pain after having touched a hot object, for instance, make people avoid touching hot objects in the future and thereby prevent damage due to burns. But in most cases of recurrent pain, the value or meaning of the pain is obscure; it seems to have no obvious cause, is hard to treat, and may induce a diversity of problems [101].

Recurrent pain in children may influence the family as well as society at large. Having a child suffering from recurrent pain is known to cause parental feelings of anxiety, helplessness and frustration, and it may also deprive the social life of the family and decrease attention and time devoted other family members [130-133]. Furthermore, recurrent pain in a child may force parents to take time off from work to care for
the child and thereby trouble the family as well as the working site [130,134]. Increased use of medication, ambulatory medical appointments, and hospital admissions poses further strain on the families of children with recurrent pain and on society as well [86,130,134-136]. The total direct as well as indirect yearly economical costs of pain for a children receiving help at an outpatient pain management clinic has been estimated to be approximately £14000 (£2000–£40500)(in US currency this will equal ~$28000 and in Euro it equals €19000 per child and year in 2004 prices) [134].

A most important question is how the pain impacts the life of the child. From at least five years of age children clearly describe pain as something that hurts and makes them feel bad [14,137]. School-aged children, of all ages, rate pain intensity to be medium and pain affect to be considerable for, e.g. headache, stomach-ache, and musculoskeletal pain, and greater impairment is found in girls than boys [14,19]. Notably, recurrent pain is rated as both stronger and more unpleasant than occasional pain. McGrath and colleagues reported that 5-16 years old children generally rated headache intensity to be between 4.7 and 5.8 on a 0-10 point scale, while the mean intensity rating was 7.2 in children suffering from recurrent pain; likewise pain affect on a 0-1 point scale was rated 0.67-0.76 by children in general and at 0.83 in children experiencing recurrent pain [14].

Besides the discomfort of the pain itself, recurrent pain may influence the life of the child in a number of other ways. In interviews, children describes that pain causes physical difficulties such as sleeping problems, lack of energy and problems performing physical activities [138,139]. Pain has also been held responsible for impaired social as well as emotional well-being and function, e.g. social withdrawal, absence from school and unstable or irritable feeling [139-141]. Furthermore, it has been suggested that quality of life in general may be impaired in children with recurrent pain problems [142].
Health Related Quality of life

History and theory

The term Quality of Life (QoL) was introduced in the middle of the last century, and gained common attention in the 1960s when included in a speech by the late American president Lyndon B Johnson [143-145]. Originally QoL was most commonly used as a political slogan aimed to describe levels of material standards [145,146], but eventually the term expanded to incorporate a more general view of the quality of people’s lives. Thus, the term quality of life only goes back slightly more than half a century.

The concept of a qualitative or good life has, however, a much longer history [144]. Already in ancient time philosophers like Plato and Aristotle debated what constituted a good life, and over the years, three main theories have crystallized from the philosophical tradition: a) the hedonic theory, b) the preference theory, and c) the theory of objectivistic pluralism or perfectionism [147,148].

The hedonic theory state that QoL wholly and fully depend on the presence of pleasant mental states and the absence of unpleasant experiences, i.e. feeling good is synonymous with a high QoL and feeling bad with a low QoL. In the classic formulation of hedonism, absence of pain is paired with pleasure to determine the goodness of life [148]. Also preferentialism is a monistic theory, pointing out fulfillment of a person’s intrinsic desires to be the only thing of importance for his/her QoL, i.e. if a person gets what she/he wants, QoL will be high, if the person gets what he/she does not want, QoL will be low. The third fundamental theory, objectivistic pluralism, state that QoL is determined by a number of substantial objective values, which are not necessarily desired by the affected person. Thus, by definition certain things, often related to what is supposed to be the nature of man, make life good, whether they are wanted or not. This last theory has also been named “the objective list theory” and several normative ideals have been suggested for the list, e.g. close relationships, meaningful occupation, and personal development. These three main theories has furthermore been combined in several ways and thus, theories about what constitutes a good or qualitative life are numerous and partly overlapping [147].
The term QoL has through the years been accepted not only in politics but also in many other disciplines. Searching the term in the general scientific database Web of Science shows that QoL research has increased drastically over the last two decades (Fig. 2), and QoL research is now well established in fields such as economy, geography, sociology, psychology and medicine. However, the study of QoL has been complicated by a diversity of theoretical frames and definitions between and within disciplines. For instance, in politics and economy an objectivistic pluralistic approach has been dominating, focusing basic preconditions of QoL in the community or individual possessions of “good things in life” (e.g. economic output, education, number of birds in the countryside, etc.). Sociology has emphasized subjectivity, centering individual satisfaction or happiness related to social and environmental circumstances, and in psychology a purely subjective approach focusing presence/absence of individual pleasant mental states has been put forward [144,146,149-151].

Figure 2. Number of "quality of life" related publications in the Web of Science database
Quality of life in Medicine

The main task in medicine has traditionally been to help people survive diseases and a strict biological focus has been dominant. However, to support and improve health care, the ordinary biological objectivistic judgments successively have been supplemented with a focus on QoL [143,152,153]. Along with substantially improved life expectancy due to, e.g. a decreased incidence of infectious diseases and higher survival rates in conditions such as cancer [154] and cystic fibrosis [155], incident rates of chronic or long lasting diseases have increased [156], in many cases paralleled by lifelong and/or disabling treatments. Societal changes have further raised the number of individuals experiencing long lasting illnesses, e.g. diseases secondary to stress or overweight. In addition the significance of the patient’s opinion and autonomy eventually has gained greater attention [157]. With these changes a need to focus not only the quantity, but also the quality of people’s lives has emerged and QoL measures are now considered important as a guide for decision making in clinical practice, e.g. on medical treatment. It is also regarded an important fundament for health care policy making [158].

Quality of life research appeared in medicine in the 1960s and was categorized in index medicus 1966. Searching the term in the medical database PubMed shows that only a few QoL related articles was published in the 1960s, but the number of publications increased rapidly in the beginning of the 1970th and has gone up markedly ever since, resulting in more than 10 000 publications year 2007 (Fig. 3). The first and leading attempts to perform systematic QoL research was put forward in North America and in the United Kingdom while in many other European countries, including Sweden, methodological QoL research was initiated at the end of the 1980s [159].

Quality of life research in children has achieved less attention. In medicine hardly any childhood QoL research was practiced until the 1980s [150,151] and as seen in Fig. 3, only a minor proportion of the total number of QoL related publications in PubMed addressed children. An extensive mapping of publication measuring QoL between 1980 and 1994 showed that only 13% of the total body of publications concerned children, and in schoolchildren, least attention was put on young school-aged children (6-12 years) [160].
Defining Health Related Quality of Life

Initially QoL in medicine was regarded an objective concept focusing independence and functioning, e.g. activities of daily living, but at the beginning of the 1980s influences from social science resulted in a greater focus on the subjective perspective [152]. The medical field has over the years shown great interest in a theoretical development of the QoL concept and a large number of different conceptual models are available [161]. To begin with, the standards of these models were relatively poor, but there has been a marked development toward more sophisticated theoretical approaches [161]. However, the lack of a general theory to guide research has created problems, also in medicine, and definitions of QoL are numerous [158,161]. In two reviews of QoL measures, one study identified 44 and another over 100 definitions of QoL [158].

In medicine, QoL has primarily been regarded a multidimensional construct including at least the individual’s subjective perception [143,151,161,162]. However, there are disparities concerning the dimen-
sions included in the constructs, which vary greatly by number as well as content. Some authors aim to include “all domains of a person’s life” while others have a more modest approach [153]. The breadth of the construct has been mentioned as an obstacle to achieve consensus on what constitute QoL and it has been suggested to abandon the idea of QoL as an universal entity and rather consider QoL a working or organizing concept [158].

As an attempt to narrowing the QoL construct in medicine, “Health Related Quality of Life” (HRQoL) was introduced, a construct mainly focusing health specific aspects of well-being and function [158]. It has not been easy to reach consensus of the meaning of this construct either, but qualitative and quantitative empirical data from children as well as adults support conceptualizing HRQoL into dimensions of physical, emotional and social function and wellbeing [143,163,164]. For instance, a large WHO research project involving adult individuals from fifteen nations revealed that physical fitness, social integration and support, psychological stability and ability to fulfill daily tasks seemed to contribute to HRQoL across ages, sex and nations [159,165]. Likewise, a cross-national survey of 8-18 years old children from six countries found that physical, emotional and especially social wellbeing and function was of relevance for HRQoL in both girls and boys from all participating countries [163].

Present definition

In the studies of the present thesis, HRQoL will be regarded a multidimensional construct incorporating primarily the individuals evaluation of his/her life with respect to domains related to health such as physical, emotional and social function and wellbeing.

Health Related Quality of Life assessment in children

To measure HRQoL is a challenge, especially in children. Often the multidimensionality of the concept has been ignored and HRQoL in
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Children has been assessed through measures originally meant for detecting other constructs such as emotions or psychopathology [151]. There is no generally accepted framework for HRQoL assessments, but the minimal demand of a HRQoL instrument is that it reflects the individuals perception of the core HRQoL domains of physical, emotional and social function and wellbeing in a valid and reliable way [151].

Instruments assessing HRQoL can largely be distinguished into two groups, disease specific and generic instruments, both primarily based upon the assumption that HRQoL is a multidimensional construct [151,159]. Disease specific instruments are tailored toward areas of particular interest for children experiencing a specific illness, e.g. diabetes or asthma, and are expected to have a good sensitivity for HRQoL in children with the target disease. However, a disease specific instrument is not applicable in other patient groups or in children without a diagnosis and is only of limited use in patient with multiple diagnoses. Generic instruments measure HRQoL in general and are useable across different conditions as well as in children not carrying a diagnosis. However, generic instruments may due to deficient sensitivity miss changes of clinically relevant aspects of HRQoL which are related to a specific disease.

Developmental aspects

Although the core domains influencing HRQoL are alike in adults and children, specific aspects underlying these domains are age dependent and therefore it is not appropriate to apply HRQoL instruments developed for adults on children. Children’s daily activities and experiences differ from adults and even between children of different ages. For instance, young children’s life will be influenced by the activities and social environment in kindergarten, while older children’s life is influenced by the school context and for adults the working environment will be of importance. The social context including the family, peer groups and school environment seems to be of particular importance for how children experience their life [162,163,166].

Age appropriate terminology and set of administration are other developmental issues which are of importance when assessing children HRQoL [151,162]. The instrument should be brief and reading ability may set borders for when it is appropriate to assess self reported HRQoL by pen and paper questionnaires. With regard to terminology, a study of children’s verbal understanding showed that children above
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eight years of age had a comprehensive understanding of health related terms [167]. In school-aged children below eight years, some words like “pain” and “worried” were well understood, but many children that age had poor understanding of more complicated terms like “on a dare” and “healthy enough”.

Informant

The gold standard of HRQoL assessment is self reports and there is evidence that school-aged children are capable to fully understand and report on basic health concepts [162,167,168]. However, very sick children and children with low linguistic or cognitive skills may not be capable of communicating their HRQoL verbally or through questionnaires. In such cases, ratings given by parents, teachers or caregivers may be the best proxies for evaluation of the child’s HRQoL [153].

The Pediatric Quality of Life Inventory

Until recently there has been a lack of standardized pediatric HRQoL instruments, which is one reason for the dearth of literature in this field. During the last decade a large number of HRQoL instruments have been developed especially for children. A recent review found more than 50 different HRQoL instruments used in pediatric research, most of them being disease specific [169]. For adolescents with recurrent pain, there are some specific HRQoL measures targeting, i.e. the Dutch Quality of Life Headache-Youth (QLH-Y) and its follow-ups Quality of Life Pain-Youth (QLP-Y) respective Quality of Life Questionnaire for Adolescents with Chronic Pain (QLA-CP)[132,170,171], but no recurrent pain specific HRQoL instrument are available for younger children. However, in the review, five instruments with acceptable psychometric quality were identified, which could assess self reported HRQoL in both ill and healthy schoolchildren down to at least eight years of age and; one of these being the Pediatric Quality of Life Inventory 4.0 Generic Core Scales.

The Pediatric Quality of Life Inventory is the result of 15 years of systematic research, started by Dr. James Varni in the late 1980s in the US [172,173]. The instrument was especially developed to emphasize the child’s perception of his/her HRQoL and the initial developmental efforts included repeated interviews with children, parents and medical experts [173]. Eventually, a modular model emerged comprising a ge-
neric module, the Pediatric Quality of Life Inventory 4.0 Generic Core Scales (PedsQL), as well as several disease specific modules targeting, e.g. cancer, asthma and diabetes. The PedsQL is a brief questionnaire comprising 23 or 15 items, which provides age adjusted self and parent-report forms for children ages 2-4 years (proxy version only), 5-7 years, 8-12 years and 13-18 years. Forms are available for use in more than 30 countries [174] and the PedsQL has recently been converted into Swedish by the Mapi Research Institute in collaboration with Dr. Varni. The translation procedure followed recognized standard methodology of translation including validation of the translations procedure [175,176].

The essential HRQoL domains are covered by the PedsQL forms measuring physical, emotional and social sub domains along with school functioning [172]. In studies from around the world, e.g. the US, Holland, England, Germany, Norway, Japan and China, but not yet in Sweden, the PedsQL has proved to be a reliable and valid measure with discriminating power within a number of pediatric illness samples, including samples of children with recurrent pain conditions [172,177-185].

Psychometrics

A basic requirement for any instrument measuring a complex psychological construct, e.g. HRQoL, is proper psychometric qualities in the context in which it is to be used. As pointed out by the World Health Organization [186], cultural context is of great importance for HRQoL assessment and HRQoL instruments may show diverse psychometric quality in different cultures. Thus, when transferring a HRQoL measure into a cultural context apart from the one for which it was originally developed, measurement properties of the instrument should be carefully studied in the new context.

Reliability

A measure should be reliable, i.e. stable and consistent [187]. A reliable HRQoL instrument should reveal similar result when the HRQoL
is rated by the same person at different occasions (intra-rater reliability) or by different raters measuring the same person (inter-rater reliability), provided HRQoL has not changed between measurements points and ability to measure the construct is alike in the different raters. A reliable instrument also has internal consistency, i.e. ability to provide replicable measures by itself [187,188].

Validity

Validity, i.e. that the instrument actually measures what is intended, is also of great importance [188]. Evidence for validity can be collected in numerous ways, the three major addressing content, construct and criterion (predictive and concurrent) validity [189,190]. All relevant aspects of the concept measured should be comprehensively included in the instrument (content validity), e.g. a measure of HRQoL should include questions about all aspect important for this concept [191]. The construct of the instrument should adequately reflect the specific theoretical phenomena measured (construct validity) [188]. Questions (or items) of relevance should be specified into theoretically appropriate domains and different items defining the same construct or domain should inter-correlate highly, while items not supposed to measure the exact same construct should not correlate too strongly. Empirical properties of the measure should be consistent with the theory. In addition, the instrument should obtain adequate criterion validity, i.e. it should be highly associated with other concurrent or future valid characteristics which are theoretically related with the concept measured (concurrent and predictive validity). Ideally criterion validity can be assessed by comparing the measure to a “gold stand” i.e. a valid and reliable criterion of the construct tested [190].

Measurement invariance

HRQoL has been proved conceptually consistent through ages and sex which allows for comparisons between different ages and between girls and boys [159,163,165]. However, if the measurement and structure of the underlying construct in an instrument are not equivalent across the groups being compared, it is not possible to know whether discrepancies mirror a difference in HRQoL or a different understanding of the measure between groups. To secure meaningful comparisons, the latent levels compared should be at least configural, metric and sca-
lar invariant across groups, i.e. the items should represent the same latent variable across groups, e.g. sex (configural invariance), have equal factor loadings across groups for alike items (metric invariance) and there should be no systematic response bias between groups (scalar invariance) [192,193].

Pain in relation to socio-demographics

Sex, gender and age

From birth and onward there are obvious biological differences between females and males. Furthermore, major physiological as well as cognitive changes occur through the years of childhood and these changes follow different tracks for girls and boys. For instance hormonal changes associated with puberty proceed differently and at different ages in girls and boys. Social attributes and opportunities also differ between girls and boys. From early age and through childhood girls and boys are met with different expectations and taught to act differently leading them to be exposed to different risk factors for ill-health [194].

The developmental changes along with the differences between males and females in biology (sex differences) and socialization process (gender differences) suggest that studying pain patterns through the life span in both males and females may be essential, as factors influencing pain may vary with these variables. Knowledge about the patterns of pain in males and females at different ages may provide important clues about how to understand the etiology and management of pain conditions. For simplicity the term sex will represent both sex and gender analyses in the framework of this thesis.

Other socio-demographics

Socio-economy, family structure and ethnicity are other important socio-demographic determinants of health in children [10,195]. These
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factors have been suggested of importance, also regarding children with recurrent pain, but the literature is conflicting [196-198]. It should be noted that, besides age and sex, socio-demographic factors are not in focus in the present thesis.

Rationale for the present thesis

As mentioned above, the prevalence of recurrent headache, stomach-ache and backache in adolescent schoolchildren has been studied repeatedly in many countries since 1982 [7]. When the work of the present thesis was initiated there was no current detailed information available on the magnitude of these health problems in younger schoolchildren in Sweden.

Furthermore, different recurrent pain conditions had mainly been investigated one by one, while data on the total burden of recurrent pain were limited [18]. It had also been suggested that investigations of potential inter-relationships between pain conditions might improve the deficient understanding of recurrent pain in children, but comprehensive studies, including the three most common recurrent pain symptoms simultaneously were greatly lacking [18].

The severity and significance of recurrent pain in children had been questioned [80,199]. It was argued that recurrent pain in children might be a problem mostly representing “transient turmoil” or “everyday complaints” related to “normal growth and development” [199]. The facts that parent-reports in general revealed lower pain prevalence than child reports, and also the fact that children with recurrent pain conditions rarely asked for medical attention, was further causing speculations about the significance of the problem [80]. Therefore, it seemed important to investigate the meaning of pain and aches from the child’s perspective.

HRQoL had progressively been acknowledged as a useful and comprehensive measure of illness related impairment and the PedsQL had been forwarded as an appropriate measure for HRQoL assessment in children with pain [183-185]. However, the psychometric properties of the Swedish PedsQL forms had not been established and the appropriateness of the recommended four-factor structure of the PedsQL

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had not been generally confirmed empirically. Furthermore, measurement equivalent across sexes had not been tested, making interpretation of results comparing boys and girls uncertain.

Finally, studies of relationship between HRQoL and recurrent pain in children were limited and mostly based upon data from clinical settings, not representative of the child population in general. Moreover, research reports had indicated that pain conditions might co-exist in children [70, 196, 200, 201] and number of pain locations had been shown to be associated with increased problems related to HRQoL, e.g. emotional difficulties [202, 203]. These findings stressed the importance of assessing common recurrent pain symptoms concurrently and to consider the importance of number of pain sites on HRQoL. However, when this thesis was processed, no truly population based study had reported on HRQoL in children with recurrent pain, including the three most common pain conditions. Furthermore, the influence of number of pain sites on HRQoL had not been investigated in children.
Objectives

The overall objective of the present study was

- to increase knowledge and understanding of recurrent pain conditions in children

The specific objectives were

- to describe the occurrence and co-occurrence of recurrent pain (headache, stomach-ache, and backache) in young schoolchildren, with respect to frequency of pain experiences and in relation to age and sex (Paper I and II)

- to present the psychometric performance of the Pediatric Quality of Life Inventory 4.0 Generic Core Scales, Swedish version (Paper III)

- to investigate Health Related Quality of Life in young schoolchildren with recurrent pain from the perspective of the child, and under consideration of number of pain sites, pain frequency, and socio-demographics (Paper IV)
Methods

Study population and procedure

The main study addressed children in Umeå, a university municipality in northern Sweden counting around 110 000 inhabitants. Part of the psychometric testing, i.e. the test-retest investigation, was carried out in Lycksele a nearby smaller municipality of around 13 000 inhabitants.

Three data collections were performed; two in Umeå and one in Lycksele (Table 3). Prior to each collection, the pupils, parents and all school staff members involved received thorough information about the investigation. Children enrolled in special schools for children with intellectual disability were not included in any part of the investigation.

First data collection (Paper I, II)

The first investigation was performed year 2000-01 and enrolled a randomly selected cluster sample of the 6367 pupils attending preschool class or elementary school, grades 0-6, in the city of Umeå (Table 3). The schools were stratified into three groups according to the number of pupils in the school. Three to four schools were randomly selected from each group. From these schools, one randomly selected class per grade was invited to participate in the study. All invited schools accepted the invitation and of the 1155 children selected for the study, 1121 (97%) participated, 539 girls and 582 boys aged 6-13 years.

Children from grades 0 through four were requested to complete a questionnaire at home, assisted by their parents. Children from grades five and six answered a questionnaire in the classroom. The investigator (SP) instructed the children and, with the teacher present, the pupils filled in the form anonymously. To enable all children equal opportunities to participate, questions were read aloud in class - one by one - for the older children. The children/parents who had not responded at the first contact received a new invitation after three weeks. Children from grades five and six who were absent from school at the days of investi-
gation were followed up when back in school. The follow-up was performed in the same way as the ordinary data collection.

Table 3. Methodological outline of studies in the thesis.

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>Study design</th>
<th>Population</th>
<th>Measures</th>
<th>Paper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Umeå</td>
<td>2000-2001</td>
<td>Cross sectional</td>
<td>1155 children (6–13 y)</td>
<td>Pain, Socio-demographics</td>
<td>I, II</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Randomized cluster sample Grade 0–6</td>
<td>Participation 97%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total sample Grade 3 and 6</td>
<td>1655 parents</td>
<td>Participation Child: 97% Parents: 85%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lycksele</td>
<td>2006</td>
<td>Cross sectional</td>
<td>748 children (9-17 y)</td>
<td>HRQoL, Socio-demographics</td>
<td>III</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total sample Grade 3–6 and 9</td>
<td>116 parents</td>
<td>Participation Child: 98% Parents: 92%</td>
<td></td>
</tr>
</tbody>
</table>

Second data collection (Paper III, IV)

The second investigation was conducted year 2003-04 and addressed all 1655 pupils attending grade three and grade six (aged 8-14 years) in the city of Umeå and their parents (Table 3). Again all schools accepted partaking and 1605 (97%) of the invited children, along with 1403 (85%) of the parents participated in the investigation. Pain questionnaires were available from 1495 of the children, 1570 had filled in the HRQoL questionnaire (six HRQoL forms were later excluded due to five or more missing items and 1455 of the children had filled in both questionnaires adequately. Parents of the 772 children attending
grade three were invited to take part in the psychometric analyses (Paper III) and 639 (83%) participated but five reports were excluded due to an extensive amount (> 50%) of missing items.

Instructed by one of the investigators (SP) and with the teacher present, but not partaking, all children filled in questionnaires confidentially in the classroom and parents completed a questionnaire at home. For children with reading difficulties, the questions were available from a minidisk and in grade three the investigator read all questions aloud one by one. Children from grade three completed the pain questionnaires at home assisted by a parent. In grade six the forms were filled in at two to three occasions.

Third data collection (Paper III)

The third investigation was performed year 2006 in the municipality of Lycksele and addressed all 748 schoolchildren attending grade three through six and grade nine (ages 9-17 years) along with parents of the 166 children attending grade three (Table 3). Again all schools participated and participation rates were 98% among children and 92% among parents; 81% respective 89% took part at both test and retest procedures. Excluding reports stating a major change in the child’s health or life situation between tests, left 505 child-reports and 92 proxy-reports for analysis (68% respective 79% of all).

A special trained research nurse conducted the investigation using the same procedure as described in data collection two. The retest was performed approximately two weeks after the first data collection (Children: mean difference 14.3 days [SD 1.0], range 14-18 days; Parents, mean difference 18.5 days [SD 2.5], range 7-20 days).
**Measures**

The measures of this thesis were pain, HRQoL, behavioral/ emotional problems and socio-demographics (Table 4).

<table>
<thead>
<tr>
<th>Measures</th>
<th>Assessment tools</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>WHO-HBSC</td>
</tr>
<tr>
<td>HRQoL</td>
<td>PedsQL</td>
</tr>
<tr>
<td>Behavioral/emotional problems</td>
<td>YSR/CBCL</td>
</tr>
<tr>
<td>Socio-demographics</td>
<td>Background form</td>
</tr>
</tbody>
</table>

**Table 4. Detailed outline of measures in the thesis.**

The occurrence of headache, stomach-ache and backache were assessed in a questionnaire based on questions from the WHO study of Health Behavior in School-aged Children, HBSC [39]. These questions have proved adequate face validity and test-retest reliability [204].

Pain was measured on a five-graded scale, based on the question: “In the last six months, how often have you had a headache?”. The question was repeated for stomach-ache and backache. Response categories and scores were 1 = about every day, 2 = more than once a
Methods

week, 3 = about every week, 4 = about every month (referred to as “monthly”), 5 = rarely or never.” Categories 1–3 merged were referred to as “weekly” or “frequent” pain. Categories 1–4 merged were referred to as “recurrent” pain. Categories 1–2 merged were referred to as pain more than once a week.

Health Related Quality of Life

HRQoL was assessed by the PedsQL [172,205]. For psychometric tests the 23 items as well as the 15 items self- and proxy report forms were employed and in the test-retest study an item was added measuring perceived change of health or life situation between tests (Paper III). The 23 items self report forms were used for analyses of pain–HRQoL associations (Paper IV).

The 23 item PedsQL (PedsQL-23) generates scores for four lower order scales or factors and three higher order scales (Fig. 4) [172]. To constitute the short 15-items PedsQL forms (PedsQL-15), eight items from the PedsQL-23 were excluded [205].

![Figure 4. Original factor structure of the PedsQL 4.0 Generic Core Scale. * Items excluded in short form.](image)

The physical domain measures the degree of problems doing different kinds of physical activities as well as occurrence of pain and lack of energy [172]. The emotional domain covers feeling of anxiety, fear, sadness, depression, anger, worries about the future and sleeping problems. The social domain measures the extent of problems in relation with...
other children, i.e. troubles getting along, teasing and not wanted as a friend, and the school domain encompass questions about problems with school performance, attention, remembrance, but also ability to be in school. Items expelled in the short form cover problems with bathing/showering (item 5), pain (item 7), lack of energy (item 8), sleep (item 12), ability to do like peers (item 17), ability to keep up in play (item 18) and missing school due to illness (item 22) or medical care (item 23) (Fig. 4).

With a recall time of one month, respondents rated problems on a 5-point scale from 0 (never a problem); 1 (almost never a problem), 2 (sometimes a problem), 3 (often a problem), 4 (almost always a problem) [172]. Scores were reversed and transformed into a 100-point scale, making higher scores indicate better HRQoL [172]. Furthermore, categories 0 and 1 merged were referred to as “almost never” problems, category 2 referred to as “sometimes” problems and categories 3–4 merged were referred to as “frequent” or “often/always” problems. A HRQoL problem was considered present within a scale when at least one item within the scale was scored ≥ 2 and the problem was considered to be frequent when at least one item within the scale was scored ≥ 3.

**Behavioral & emotional problems**

Children in grade six and parents of children in grade three reported behavioral and emotional problems through the standardized measures Youth Self Report (YSR) and the parallel parent-report, Child Behavior Check List (CBCL) [206] (Paper II). Reliability and validity of these forms are well established also in Sweden [206-208].

A total of 112 respective 113 statements, scored on a three-point scale (not true, sometimes true, or very true) generate eight narrow band syndrome domains and a domain of other problems. Three narrow band domains (withdrawn/depressed, somatic complaints and anxious/depressed) form a broad-band dimension of internalizing problems and two narrow band domains (rule breaking and aggressive behavior) constitute a broad-band dimension of externalizing problems.

It was hypothesized that the PedsQL psychosocial and HRQoL scales would show high and negative correlation with the CBCL/YSR scales overall problematic functioning, externalizing- and internalizing problems. Furthermore, the PedsQL physical functioning scale was ex-
Methods

expected to show a comparable weaker correlation with these CBCL/YSR dimensions.

**Socio-demographics**

Children reported sex and school grade (Paper I, II, III, IV) and in grade six also family ethnicity and structure (Paper IV). Parents reported child ill health and child healthcare contacts during the preceding six month along with parental employment and education (Paper IV). Parents of children in grade three also reported family ethnicity and family structure (Paper IV).

Ethnicity measured country of birth of the mother and father. Family structure measured whether the child lived with 1) the mother and father, 2) the mother, 3) the father, 4) alternately the father and mother, 5) others (open question). Ill-health and health care contacts measured 1) occurrence of chronic or recurrent ill-health with an expected length of at least six months and health care contacts the preceding six months due to this ill health, 2) other health care contact the preceding six months and the reason for that. Education (mother and father) was measured by the response alternatives: 1) nine-year compulsory school, 2) upper secondary school (gymnasium), 3) college or university, 4) other. Employment (mother and father) was measured by the response alternatives: 1) fulltime job, 2) part-time job, 3) unemployed, 4) student, 5) pension, 6) sick leave more than 3 month and 7) other. Variables were dichotomized to discriminate whether both parents was from North America/Europe, or not (ethnicity); lived together, or not (family structure); had more than 9 year of schooling, or not (education); had full/part-time employment, or not; and whether the child had a non-pain condition, or not.

**Data analysis**

Descriptive statistics were computed for age and sex specific pain and for age and sex specific HRQoL in children with and without recurrent pain. Group differences were tested by use of Pearson’s chi-square alternatively Fisher’s exact test (Paper I, II, III, IV) and Mann
Methods

Whitney U-test for two independent samples (Paper IV). Odds ratio (OR) were calculated to estimate the strength of associations between pain groups (Paper II) and between HRQoL in groups with and without pain (Paper IV). Cohen’s d estimated magnitude of differences between HRQoL mean scale scores (Paper IV). Furthermore pain and HRQoL associations was analyzed by use of multivariate logistic regression with “occurrence of at least one HRQoL problem” as dependent variable, pain variables as independent variables and background factors as covariates (Paper IV).

Construct validity: confirmatory factor analyses (CFA) examined the premeditated four-factor structure of the PedsQL and multiple groups CFA examined configural, metric invariance, and scalar invariance across boys and girls [192]. Guided by an earlier Exploratory Factor Analysis (EFA) [172] additionally models were tested which allowed items 7, 8, 22 and 23 – and in the proxy form also items 17 and 18 – to share variance apart from that accounted for by the theoretically applied factors.

Standardized regression weights (factor loadings, $\lambda$) were studied in the models and model adequacy was evaluated and compared by 1) Chi$^2$ tests 2) Tucker Lewis Index (TLI), 3) Comparative Fit Index (CFI), 4) Gamma Hat (GH), 5) McDonald’s centrality index (Mc), 6) Standardized root mean square residual (SRMR) and, 7) Root Mean Square Error of Approximation (RMSEA) [209-211]. Estimations were based on a Maximum Likelihood algorithm (ML) and in case of model fit rejection, an Asymptotically Distribution Free (ADF) algorithm was applied as well. Furthermore, bootstrapping technique with 2000 samples was applied in all analyses.

Criterion validity: Spearman’s rho statistics estimated correlations between PedsQL scales and YSR/CBCL scales.

Reliability: internal consistency reliability was estimated by use of Cronbach’s coefficient $\alpha$ [212]. Inter-rater and intra-rater reliability was tested at item level by weighted kappa statistics and at scale level by Spearman’s rho statistics as well as Intra-class Correlations (ICC) [213].

Software and level of significance

Data processing and statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 10.0–11.5 [214]. Weighted kappa analysis was conducted by use of the KAPPA-Agreement between categorical ratings, version 4.0. AMOS, version 5.0,
performed the analysis of factor structures. Gamma Hat and McDonald's centrality index was calculated by use of Microsoft Excel 2003.

Significance was set at the 95% level (p < 0.05) with one exception. Testing socio-demographic factors potential as confounders (Paper IV), significance was set at p < 0.10. Magnitude of differences (Paper IV) were regarded meaningful but small at Cohen’s d 0.20, medium at 0.50, and large at 0.80 [215]. Testing correlations (Paper III), values below 0.40 was suggested to indicate poor agreement; between 0.40 and 0.75 moderate agreement; and above 0.75 excellent agreement [216]. Internal consistency coefficients of at least 0.7 were considered acceptable for group comparisons and coefficients of at least 0.9 for individual comparison [187]. Finally, indicators of model fit in CFA analyses (Paper III) were considered acceptable at values above 0.05 in Chi2 tests; values above 0.90 for indexes 2 to 5 and values of 0.08 or less for indexes 6 and 7 [217-219]. Comparing models in the multiple group CFA, the null hypothesis of invariance was not rejected at ΔCFI, GH, and Mc values close to or smaller than 0.01, 0.01 and 0.02, respectively [209].
**Ethics**

In accordance with current ethical recommendations for research, children and parents were informed about the project and about their rights to reject participation at any time. Participation may also be seen as a right; therefore efforts were put into securing that all children/parents had the opportunity to participate.

At least one week prior to investigations, the children and parents obtained oral as well as written information about the studies. Families of foreign ethnicity had access to written and/or oral information in their home language and help by home language teachers during assessment. Children and parents were assured confidentiality in data processing/reporting.

When the children filled in the questionnaires, confidentiality was accomplished by securing that it was not possible for any child to overlook the response of another child. At the second and third data collection the questionnaires were coded. Codes were only accessible for the research leader and not present along with data.

The rights of participation was assures by giving children not present in school at assessment, a chance to participate at a later occasion and by offering suitable support to children with reading difficulties. Also parents who did not react on the first contact were re-contacted. Furthermore, both children and parents had the opportunity to discuss unclear points with the research leaders, in person or by telephone, before assessment.

Unfortunately, the research design was not appropriate for children with greater developmental delays, and therefore these children were not included in the study.

The studies was approved by the Ethics Committee of the Medical Faculty, Umeå University, Sweden, Um dnr 01-017 and 03-352 respectively 05-152.
Results

Prevalence (Paper I, II, IV)

In the first as well as in the second study population, approximately two thirds of the children had experienced recurrent pain during the preceding six months, i.e. pain from at least one of the three locations surveyed, the head, stomach and back (Fig. 5), and three percent of all children with recurrent pain had during the preceding six months been in contact with health care due to headache, stomach-ache or backache, (paper IV). Half of the children with recurrent pain had experienced the actual pain about once a month and the other half at least once a week (Paper II, I V). In the first investigation, daily pain was reported by 6% of the children (Paper I).

Figure 5. Prevalence of recurrent pain from the head, stomach and/or back in young schoolchildren (2000-01: grades 0 through six; 2003-04: grades three and six).
More girls than boys reported recurrent pain, but this difference was only evident among children experiencing weekly pain combined with pain from one or more additional locations (Paper I, IV). Pain prevalence also differed by age with higher prevalence of recurrent pain by higher grade (Paper II, IV) (Fig. 6). Approximately half of the youngest children from preschool class experienced pain recurrently, and 1/5 experienced weekly pain, while in grade six, nine out of ten reported recurrent pain conditions and half of the six-graders experienced pain at least once a week (Paper II). Notably, the prevalence of weekly pain increased by grade in both boys and girls, while the prevalence of monthly pain increased in boys only.

![Figure 6. Prevalence of recurrent pain conditions by grade in young schoolchildren. Pain at “any site” represent prevalence of pain from one or more of the three above pain conditions, i.e. the head, stomach and/or the back.](image)

**Headache (Paper I)**

In general, headache was the most commonly reported recurrent pain, found in 48% of the children. At least weekly episodes of headache were reported by 23% of the children and 9% experienced head-
ache more than once a week. The prevalence varied by sex, with more girls than boys reporting recurrent headache. The prevalence also varied by grade with higher prevalence by higher grade (Fig. 6); this was found in boys as well as girls, and 70% of the sixth graders reported recurrent headaches while 38% experienced headache at least once a week. Headache was also common among the youngest schoolchildren. In grades 0 to two, recurrent headache was reported by 23%-49% and weekly headache by 5%-22%.

Stomach-ache (Paper I)

The first years of school, stomach-ache was the most prevalent recurrent pain, experienced by one third of the children in grade 0 and one. Weekly pain was reported by 15%-22% of the youngest children (Fig. 6). Overall 39% of the children reported recurrent pain in the stomach. Half of these (19%) experienced weekly pain and 8% pain more than once a week. More girls than boys reported recurrent stomach-ache. Furthermore, the prevalence was higher in the older than in the younger children and showed a peak in grade one (Fig. 6), among both boys and girls. However, more frequent (weekly or more often) complaints showed no significant difference by grades.

Backache (Paper I)

The lowest pain prevalence was found for recurrent backache, reported by 18% of the children, and experienced weekly by 7%. However, the prevalence showed a large variation by grade with higher prevalence among older than younger children (Fig. 6). In preschool class (grade 0) and grade one 4%-8% of the children experienced backache recurrently, while 16% of third graders and 32% respective 43% of fifth and sixth graders reported recurrent pain in the back. In all grades about half of the children reporting recurrent backache experienced the pain every week and in grade five and six, 14% respective 17% experienced weekly backache. No significant sex difference was present.

Socio-demographics

Comparing children with and without a recurrent pain condition, children with a pain condition more often had non-cohabiting parents
(35% vs. 28%), and less often both of their parents were born in either North American or Europe (12% vs. 8%). Parental education and employment did not differ significantly between children with and without a recurrent pain condition and neither did non-pain ill-health conditions in the child.

Co-occurring pain (Paper II, IV)

Most children (77%) with weekly headache reported at least one additional recurrent pain condition (Fig. 7) (Paper II). Likewise, 72% of the children experiencing weekly stomach-ache, and 85% of the children with weekly backache, reported a co-occurring recurrent pain condition. The odds of experiencing weekly pain from additional body parts were 3–5 times as high as the odds of headache, stomach-ache or backache occurring as a single weekly pain symptom. Among children with weekly backache, one-fourth (27%) also experienced both headache and stomach-ache every week.

Figure 7. Proportions of schoolchildren (grades 0–6) with weekly headache, stomach-ache respective backache who experience co-occurring pain symptoms from other parts of the body (Reproduced from Paper II).
Overall, half of the 0 through sixth graders with recurrent pain conditions, experienced pain from more than one body site and the most prevalent combinations were headache – stomach-ache (27% of all children) followed by combinations of backache and headache (13%) or stomach-ache (11%).

As earlier mentioned, recurrent pain was found more common in older than younger schoolchildren (Paper II, IV). However, only the proportion of girls and boys with multi-site pain increased by grade, not the proportion of children reporting pain from only one part of the body.

Pain frequency and co-occurrence

Figure 8. Co-occurrence of recurrent pain by frequency of pain in young schoolchildren (2000-01: grades 0 through six; 2003-04: grades three and six)(Reproduced from Paper II, IV).

In both girls and boys monthly pain was primarily related to a single body part and weekly pain to multiple body parts. Also in all grades, although not statistically significant in grades five and six, children with monthly pain events primarily experienced single-site pain. However, regarding children with weekly pain, a gradual change was observed through grades, from a majority of children reporting single-site weekly
pain in grade 0 to a majority reporting multi-site pain in grades three through six (Fig. 9).

![Graph showing prevalence of weekly pain by number of pain sites and grade in young school-children. * p < 0.05, *** p < 0.001.]

**Psychometrics of the PedsQL (Paper III)**

**Reliability**

In both girls and boys, analysis of internal consistency revealed Chronbach’s $\alpha$ values approaching or exceeding 0.70 for all scales but the PedsQL-15 social functioning scale, and Chronbach’s $\alpha$ values $\geq 0.90$ for the full form HRQoL scales.

Intra-rater agreement between the test and retest in children as well as parents demonstrated moderate test-retest reliability at items level and high to excellent agreement at scale level for all scales.

Inter-rater agreement between girls as well as boys and their parents was poor at item and scalar level with weighted kappa and Spearman
rho values below 0.4 for almost all items respective scales. However, ICC values between 0.40 and 0.60 demonstrated moderate agreement for most scales.

**Criterion-related validity**

The scales of the PedsQL forms assumed to measure HRQoL and psychosocial health showed convincing negative correlation with the YSR/CBCL scales measuring problematic behavioral and emotional health. Moreover, the PedsQL physical functioning scales, especially in the short forms, showed weaker correlations with the YSR/CBCL scales. These patterns were replicated in subgroups of boys and girls.

**Construct validity**

Chi-2 statistics rejected model fit for most scales (Table 5), also when bootstrapping was tested (note that non-significance indicate good model fits). However, at large the self-report PedsQL scales and the proxy report PedsQL-15 scales met most pre-established fit-index criteria, while the proxy PedsQL-23 showed model fit indices suggesting improvement of all but the emotional and social functioning scales. Permitting error correlation of items 7-8 and 22-23 (and items 17-18 in the proxy form), further improved model fit, but still the physical functioning scale and the HRQoL in the proxy PedsQL-23 only met three of six index criteria’s. All items loaded adequately on the hypothesized factor and first order factors loaded adequately on the assumed higher order factors.

**Measurement invariance across boys and girls**

In multiple-group CFA, fit index criteria’s indicated viability of the suggested four-factor structure for both boys and girls, when using the self-report full-form and the two short-forms. The proxy full-form scales missed almost all fit index criteria’s.

Constraining factor loadings to be equal across boys and girls (metric invariance) generally did not result in noteworthy model fit changes and neither did further constrain of intercept equality across sex groups (scalar invariance). However, the emotional functioning scale of the child full-form showed some variance of intercepts. Removing inter.
Results

cepts constrain on item 10 (feeling sad and blue) resulted in acceptable model change also for the emotional factor, suggesting partly invariance for this scale.

Table 5. Confirmatory factor analyses of the PedsQL 4.0 Generic Core Scale factor structure.

<table>
<thead>
<tr>
<th></th>
<th>p-value</th>
<th>TLI ML</th>
<th>CFI ML</th>
<th>GH ML</th>
<th>Mc ML</th>
<th>SRMR ML</th>
<th>RMSEA ML</th>
<th>RMSEA ADF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PedsQL-23 Self report</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Physical Function</td>
<td>***</td>
<td>.88</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>.10</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Emotional Function</td>
<td>***</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>.09</td>
<td>+</td>
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</tr>
<tr>
<td>School Function</td>
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<td>+</td>
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<tr>
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<td>+</td>
<td>+</td>
<td>.87</td>
<td>+</td>
<td>+</td>
<td>+</td>
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</tr>
<tr>
<td>HRQoL</td>
<td>***</td>
<td>.86</td>
<td>.87</td>
<td>.65</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

| **PedsQL-23 Proxy report** |         |        |        |       |       |         |          |           |
| Physical Function    | ***     | .80    | .86    | +     | .83   | +       | .14      | +         |
| Emotional Function   | ***     | .89    | +      | +     | +     | +       | .12      | .09       |
| Social Function      | ***     | .80    | +      | +     | +     | +       | .21      | .09       |
| School Function      | ***     | .74    | .87    | +     | +     | .08     | .18      | +         |
| Psychosocial Health  | ***     | .85    | .88    | +     | .71   | +       | .09      | +         |
| HRQoL                | ***     | .80    | .82    | .88   | .46   | +       | +        | +         |

| **PedsQL-15 Self report** |         |        |        |       |       |         |          |           |
| Physical Function    | ***     | +      | +      | +     | +     | +       | +        | +         |
| Emotional Function   | ***     | +      | +      | +     | +     | +       | +        | +         |
| Psychosocial Health  | ***     | +      | +      | +     | +     | +       | +        | +         |
| HRQoL                | ***     | +      | +      | .87   | +     | +       | +        | +         |

| **PedsQL-15 Proxy report** |         |        |        |       |       |         |          |           |
| Physical Function    | ***     | +      | +      | +     | +     | +       | +        | +         |
| Emotional Function   | ***     | .81    | +      | +     | +     | +       | .19      | .14       |
| Psychosocial Health  | ***     | +      | +      | +     | +     | +       | +        | +         |
| HRQoL                | ***     | +      | +      | .84   | +     | +       | +        | +         |

Estimation algorithm: Maximum likelihood (ML). Asymptotically Distribution Free (ADF). ** p < 0.01; *** p < 0.001. Fit indexes: TLI: Tucker Lewis Index; CFI: Comparative Fit Index; GH: Gamma Hat; Mc: McDonald’s centrality index; SRMR: Standardized Root Mean Square Residual; RMSEA: Root Mean Square Error of Approximation; + : Estimates meeting the pre-established cut-off scores, i.e. TLI, CFI, GH, Mc ≥ 0.90, SRMR; RMSEA ≤ 0.08.
Pain and Health Related Quality of Life (Paper IV)

Children with recurrent pain conditions most commonly (81%) experienced some HRQoL problems. Comparing children with and without recurrent pain conditions, HRQoL problems were more than twice as common in children experiencing recurrent pain and four times as common in children with weekly or multi-site pain. Furthermore, HRQoL decreased by number of pain sites as well as frequency of pain episodes (Fig. 10), revealing a small to medium size impairment of HRQoL in children with single-site or monthly pain and a medium to large impairment in children with multi-site or weekly pain. Adjusting
for the potential confounders age, sex, ethnicity and family structure, did not change these results significantly.

All HRQoL domains were impaired in children with single-site as well as multi-site pain and in children with monthly as well as weekly pain (Fig. 11). However, the physical, emotional and school domains were more impaired than the social domain. Furthermore, children with multi-site or weekly pain reported greater HRQoL impairment than children with single-site or monthly pain.

![Figure 11. Impairment of HRQoL domains in young schoolchildren with recurrent pain. Cohen’s d specifies magnitude of difference between children with no pain and children with single or multi-site pain respective monthly or weekly pain- Values of 0.20 nominated as small; 0.5 as medium and 0.8 as large.](image)

Interestingly, independent of number of pain sites, physical impairment was greater in children with weekly pain than in children with monthly pain (Fig 12). On the contrary, independent of pain frequency, psychosocial impairment seemed to be greater in children with multi-site pain than single-site pain. However, in the current sample, the
greater impairment in children with multi-site monthly pain compared to children with single-site weekly pain did not reach significance.

![Figure 12. Health Related Quality of Life (HRQoL) domain scores by different number of pain sites and different pain frequency (8-14 year old schoolchildren) (Reprint Paper IV).](image)

Among children with recurrent pain, HRQoL was impaired in boys as well as girls and in both third and six graders, but the school domain was more impaired in girls than in boys. For children with multi-site or weekly pain also physical impairment was more pronounced in girls than boys, and in grade six girls showed greater emotional impairment than boys (Fig. 13).

In general, HRQoL impairment was more pronounced in pain suffering children from grade six than grade three, primarily due to a markedly greater emotional impairment in grade six. Among children with multi-site or weekly pain, boys from grade six also revealed greater school impairment than boys from grade three, and older boys with weekly pain also showed greater social impairment than their younger peers. The greatest impairment was seen in girls from grade six with multi-site or weekly pain.
HRQoL in relation to pain location (Paper IV)

Each of the specific pain conditions, headache, stomach-ache respective backache revealed a medium to large impairment of HRQoL. However, but among the minority of children experiencing the specific condition as a single-site pain, HRQoL impairment was small to medium, i.e. impairment was higher in the total sample with a pain condition, e.g. headache, than in the sub-sample experiencing the condition as a single-site pain. Noticeable, the condition reporting the lowest prevalence of co-occurring pain, i.e. headache, was also the condition showing the lowest degree of impairment.
Discussion

The present thesis demonstrates that, recurrent headache, stomachache and backache are common conditions, also in young school-aged children. Furthermore, these conditions are experienced frequently, and they often co-occur.

The results presented also support the Pediatric Quality of Life inventory 4.0 Generic Core Scales as a reliable and valid instrument for HRQoL assessment in Swedish school-aged children. By use of this instrument it was shown that HRQoL in children with recurrent pain conditions is markedly impaired in both girls and boys, at the ages studied, and especially in children with frequent or multi-site pain. Pain suffering children had a higher prevalence of HRQoL problems, a higher frequency of HRQoL problem episodes and a higher number of impaired HRQoL aspects; thus HRQoL problems were more common, occurred more often and were more widespread among children with recurrent pain conditions, than among children who rarely or never experienced pain.

Methodological issues

The rather large sample sizes, the study design including randomized alternative total samples of children, and the high participation rates ensure that the results in this thesis may be regarded representative of young schoolchildren in Umeå. The homogeneity of the Swedish society might motivate that the result also can be generalized to schoolchildren in Sweden. For instance, Umeå is comparable to Sweden at large regarding family income standard, a measure taking into account both family income and expected family expenses. Also family structures in Umeå are similar to that of Sweden in general [220].

Self-report is the gold standard for obtaining information about subjective phenomena such as pain and HRQoL and there is evidence that children from at least eight years respective 11 years of age, are able to understand and fill in HRQoL and pain forms, in a reliable way.
However, for younger children, it is more difficult to recall pain episodes over a six months’ timeframe. Therefore, the younger children were helped by their parents to fill in the pain form. The influence of parent-participation on results is unknown, but remarkable lower pain prevalence was noticed in the child/parent-reports compared with self reports. These findings may on the one side reflect true differences related to age or a changing propensity to report by age. Several studies have, however, shown that parents are less likely to report subjective complaints in children compared to the children themselves, especially regarding young schoolchildren [221-223]. Studies of six and eight year old children have shown that even frequent pain may be unrecognized by parents [223,224]. Therefore, a certain degree of underreporting among the younger children cannot be excluded.

Another strength of the study is, that three of the most common pediatric pain conditions were included in the same investigation. Furthermore, there were no restrictions of severity or disability. This made it possible to obtain a full picture of recurrent pain in young school-aged children. Asking for reports of monthly or weekly pain over half a year furthermore facilitated exclusion of minor pain due to everyday bump and scrapes as well as sporadic events like colds.

To evaluate the facture structure of the PedsQL we used multiple indexes, which taken together should provide a comprehensive evaluation of the fit of our models [210,225]. However, it should be mentioned that there has been some controversy about the cut offs for these indexes. We followed the recommendations of Marsh et al. and stayed with the conventional cutoff, which should minimize type 1 errors and meet normative criterions of appropriateness[226].

Two drawbacks of the PedsQL should be mentioned. The social scale reflects relationship with peers, but ignores family function, which may give an incomplete picture of the child’s HRQoL. Secondly, HRQoL is a construct covering the span from very poor HRQoL to excellent HRQoL. Measuring the presence or absence of ill-health, as done in the PedsQL, may reflect only one half of the scale, i.e. from very poor to indifferent HRQoL, which is also expressed by relative high ceiling effects repeatedly shown for the PedsQL [172,180,182,227].

Efforts were made to optimize reports. No information was given about expected results to any part involved, as such information may influence reporting [228]. Also the pain questions were part of a larger amount of health related questions and not focused in a separate way, which should counteract the so called “Hawthorne” effect. To avoid
answers being influenced by peer or by reluctance to expose answers for others in the school setting, children filled in forms in silence and confidentially. Furthermore, efforts were made to diminish problems related with ability to read and understand the questionnaires. However, it is important to bear in mind that results based on retrospective self-reports and proxy reports of subjective symptoms (e.g. pain and quality of life) always must be regarded as approximate values which should be interpreted with caution.

Epidemiology of recurrent pain in young schoolchildren

The results of the present thesis demonstrate high prevalence of recurrent headache and stomach-ache as well as backache, and overall a large proportion of young schoolchildren report recurrent pain (Paper I, IV). When comparing these findings with the results from other studies, it should be kept in mind that methodological differences between studies may influence the outcomes in different ways, and therefore comparisons are to be considered with caution.

The overall high prevalence of recurrent pain conditions found in the Umeå studies has been verified by four other investigations, which also studied all the most common childhood recurrent pain conditions simultaneously. A later national Swedish study reported that every other 9-15 years old child experienced at least one of the following pain conditions: recurrent headache, stomach-ache or musculoskeletal pain [229]. Furthermore, three studies of children from Iceland, Holland, and Germany has recently confirmed the Umeå results by demonstrating similar high prevalence of recurrent pain, primarily from the head, stomach, back or limbs [17,19,201]. Thus, it can be concluded that recurrent pediatric pain in general is a common problem in Sweden and in several other western countries as well.

Time trends

As mentioned before, earlier studies targeting pain from multiple body sites simultaneously are scarce. However, in the 1960s, Øster stu-
died headache, stomach-ache and growing pain concurrently in Danish children aged 6-19 years [230]. Compared with the recent results from Umeå, Øster reported a much lower prevalence of pain; 37% of the Danish children experienced at least at one of these pain conditions. Although differences in study design make this comparison uncertain, the results may suggest that recurrent pain have become more common in school-aged children over the last half a century. The reason for this increase is unclear, but a more stressful life situation for children could be one explanation. On the other hand, social acceptance of subjective health symptoms may have increased over the years, leading to an increased propensity to report pain. Also subjective symptoms of ill-health in general have been reported to increase in children from the Nordic countries [231].

**Headache**

**Time trends**

Among young schoolchildren in Sweden, the prevalence of headache has changed from 7% of “frequent” headache in the mid 1950th to 23% of monthly headache some decades later (1982), proceeding to 26% another decade later (1993) and to 32% after three more years (1996) [21,196,232,233]. In year 2001 the present project found an even higher monthly prevalence (48%) in young schoolchildren (Paper I). Thus, our results suggest an upward trend for recurrent headache in young school-aged children in Sweden.

Increasing prevalence of recurrent headache has also been shown in Swedish adolescents and in school-aged children from Finland and Holland [39,53,84,234].

**Current state in Sweden**

According to our findings, starting the 21st century, almost half of the young schoolchildren in Sweden experience headache recurrently and at least every fifth child experience weekly headache. These results have been paralleled by three recent Swedish reports (Table 6). One found a lower weekly prevalence in nine and 12 year old schoolchildren from a nationwide sample. Two other reports found weekly headache in 24% of 7-15 years old schoolchildren from Uppsala (7-12 years: 16%)

- 57 -
and in 28% of 10-18 years old children participating in a nationwide household survey [198,229,235].

Unfortunately, the studies mentioned above were hampered by high non-response rates making results somewhat uncertain. Compared with a non-participation rate of 3% in the Umeå study, the Uppsala study had a drop-out rate of 26%. In the nationwide school survey of 9 and 12 year old children, 17% of the schools declined partaking and among the rest, an additional 15% of the children rejected partaking. Finally, the household survey carried a total non-participation rate of 38%. Frequent experiences of headache can be expected to hinder participation for some children. Therefore these studies may be subject to underestimation of headache prevalence, explaining the comparatively lower headache prevalence among the young children from the two school surveys.

Current state internationally

The Umeå results have also been paralleled by several recent reports on recurrent headache in young school-aged children from other countries (Table 6). A Norwegian study [221] showed a relatively higher monthly prevalence of headache (58%), but data was obtained through diaries, which are known to give a higher prevalence, presumably due to a higher propensity to pick up clinically irrelevant pain and headache secondary to e.g. infections [236]. Also in Finland, weekly headache prevalence among 10 and 12 year old schoolchildren were somewhat higher than what was found in the present thesis (31% vs. 23%) [200]. However, the Finnish study utilized a shorter recall frame (three month) and did not include as young children as in the Umeå study.

Studies from Holland, Turkey, and Brazil have reported headache prevalence quite similar to our findings [51,53,237]. On the contrary only 8% of 7-14 year old German children were found to experience weekly headache, a low prevalence compared to earlier studies from Germany and most likely explained by the fact that data was obtained from parents and not the child [238]. The most outstanding finding has been reported from Hong Kong, where only 3% of 6-13 year old children experienced “recurrent” (not defined) headache [239], a prevalence which were argued to be well in line with earlier studies from the region.

In older schoolchildren headache prevalence has been shown to differ greatly between western countries [7], but taking into account the methodological differences, it appears that in younger school-aged
children from western countries, headache prevalence differs only little from what was found in the Umeå study.

Table 7. Reports after 1995 describing prevalence of recurrent headache.

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Age</th>
<th>Prevalence</th>
<th>Informant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweden [235]</td>
<td>1997</td>
<td>7-12y</td>
<td>Week 16%</td>
<td>Self/parent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7-15y</td>
<td>Week 24%</td>
<td>Self/parent</td>
</tr>
<tr>
<td>Sweden [229]</td>
<td>2002</td>
<td>9y+6y</td>
<td>Week 11%</td>
<td>Self</td>
</tr>
<tr>
<td>Sweden [198]</td>
<td>2000-03</td>
<td>10-18y</td>
<td>Week 28%</td>
<td>Self</td>
</tr>
<tr>
<td>Umeå [Paper I]</td>
<td>2000-01</td>
<td>6-13y</td>
<td>Month 48%</td>
<td>Self/parent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Week 23%</td>
<td>Self/parent</td>
</tr>
<tr>
<td>Hong Kong [239]</td>
<td></td>
<td>6-13 y</td>
<td>Recurrent 3%</td>
<td>Not known</td>
</tr>
<tr>
<td>Germany [238]</td>
<td>2003-04</td>
<td>7-14y</td>
<td>Month 25%</td>
<td>Parent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Week 8%</td>
<td>Parent</td>
</tr>
<tr>
<td>Turkey [237]</td>
<td></td>
<td>8-16y</td>
<td>Month 49%</td>
<td>Self/parents</td>
</tr>
<tr>
<td>Brazil [51]</td>
<td>1997</td>
<td>11-14y</td>
<td>Month 45%</td>
<td>Self</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Week 18%</td>
<td>Self</td>
</tr>
<tr>
<td>Holland [53]</td>
<td>1995</td>
<td>9-12y</td>
<td>Month 51%</td>
<td>Self</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Week 22%</td>
<td>Self</td>
</tr>
<tr>
<td>Finland [200]</td>
<td>1995</td>
<td>10y+12y</td>
<td>Week 31%</td>
<td>Self</td>
</tr>
<tr>
<td>Norway [221]</td>
<td>2004</td>
<td>7-14y</td>
<td>Month 58%</td>
<td>Self (Diary)</td>
</tr>
</tbody>
</table>

Stomach-ache

Time trends

The high prevalence of stomach-ache found in the present thesis, indicates that also stomach-ache has become more common over the last years. In the Umeå study, 39% experienced recurrent stomach-ache year 2000-01 (Paper I), while in the beginning of the 1990s Alfvén reported monthly stomach-ache in 19% of 7-15 year old children. A simi-
lar tendency of increasing stomach-ache prevalence has been found in adolescents from Sweden and in young schoolchildren from Finland [39,224].

**Current state in Sweden**

We found that close to every fifth young school-aged child experienced stomach-ache on a weekly basis. Two other recent Swedish school studies found weekly stomach-ache to be less common than reported by us, while the earlier mentioned household survey found similar prevalence in 10-18 year old children (Table 7) [198,229,240]. The HBSC survey (2000/01) reported an even higher weekly prevalence (28%) in 12 year old children and an overall prevalence of 27% in older schoolchildren [39].

Again, these results may be biased due to relative high non-participation rates. Furthermore, the studies with the lowest prevalence rates required participation in series of further tests, e.g. blood tests, other medical tests, physiological and applied motor ability tests [229,240]. Such a study design may have caused children with recurrent pain problems to decline partaking, in particular as children with pain problems may experience these medical procedures particularly demanding [241]. Thus, the rates in these current studies may have underestimated the actual occurrence of stomach-ache.

**Current state internationally**

The present thesis measured stomach-ache without any kind of restrictions. No similar recent reports have been found from other countries. However, several reports measured RAP, i.e. stomach-ache including only pain affecting daily activities. As seen in Table 7, the monthly prevalence of stomach-ache found in the Umeå study exceeded most reports of RAP from other countries.

The very low prevalence in Germany is not easy to explain. There are, however, other data from Germany showing much higher figures with a three month period prevalence of 41% in 10-12 year old children [17].

In the Danish study, schools with representation of varying ethnicities was excluded, which may have tuned down the prevalence somewhat. On the contrary, selecting schools primarily from low income areas, as done in the US study, may have tuned the prevalence upward.
Thus, currently it seems that 15-20% of parents in western countries have the opinion that their young school-aged children have RAP.

Table 7. Reports after 1995 describing prevalence of recurrent stomach-ache.

<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>Age</th>
<th>Prevalence</th>
<th>Informant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweden [229]</td>
<td>2001</td>
<td>9y+12y</td>
<td>Week 7%</td>
<td>Self</td>
</tr>
<tr>
<td>Sweden [240]</td>
<td>1998</td>
<td>9-13y</td>
<td>Week 11%</td>
<td>Parent/self</td>
</tr>
<tr>
<td>Sweden [198]</td>
<td>2000-03</td>
<td>10-18y</td>
<td>Week 19%</td>
<td>Self</td>
</tr>
<tr>
<td>Umeå [Paper I]</td>
<td>2000-01</td>
<td>6-13y</td>
<td>Month 40%</td>
<td>Self/parent</td>
</tr>
<tr>
<td>Germany [242]</td>
<td>1997-98</td>
<td>5-8y</td>
<td>RAP 3%</td>
<td>Parent</td>
</tr>
<tr>
<td>Denmark [243]</td>
<td>2003</td>
<td>9-13</td>
<td>RAP 12%</td>
<td>Parent</td>
</tr>
<tr>
<td>UK [244]</td>
<td>Published 1996</td>
<td>4-13</td>
<td>RAP 14%</td>
<td>Parent</td>
</tr>
<tr>
<td>Finland [109]</td>
<td>Published 2004</td>
<td>10-11y</td>
<td>RAP 16%</td>
<td>Parent</td>
</tr>
<tr>
<td>USA [245]</td>
<td>Published 2007</td>
<td>7-15y</td>
<td>RAP 24%</td>
<td>Parent/self</td>
</tr>
<tr>
<td>Malaysia [246]</td>
<td>Published 1999</td>
<td>11-12y</td>
<td>RAP 41%</td>
<td>Parent/teachers</td>
</tr>
<tr>
<td>Malaysia [247]</td>
<td>Published 2001</td>
<td>9-15y</td>
<td>RAP 10%</td>
<td>Self</td>
</tr>
</tbody>
</table>

The higher monthly stomach-ache prevalence found in the current Umeå study may indicate a higher rate of stomach-ache in this population, but may also be explained by methodological differences. Almost all studies used parent-reports, which may underestimate pain in the child [222,248]. Furthermore, pain reported by children in the Umeå study probably also included some pain, which were not severe enough to affect daily activity. Thus, it is not possible from the available evidence to decide on the total prevalence of stomach-ache internationally, and it is unclear whether young Swedish schoolchildren experience recurrent stomach-ache more often than children in other countries.
Backache

Time trend

The literature on recurrent backache does not allow for time trend analyses regarding young school-aged children in Sweden. However, in Swedish adolescents backache seem to have increased over the past 15 years [39,84]. Also in Finland, recurrent backache has been reported to increase in adolescents [37,40].

Current state in Sweden

The present thesis found a surprisingly high prevalence of recurrent backache. One previous study from Sweden has reported prevalence figures on recurrent backache in young school-aged children. This study from 1996, reported a much lower weekly prevalence (1% vs. 7%) in a national sample of 7-12 year old year [249]. The result was primarily based upon parental reports, which may partly explain the differences. More Swedish studies are needed to validate the reliability of the relative high level of recurrent backache found in young schoolchildren in the Umeå Study.

Current state internationally

Two studies from outside Sweden have focused recurrent backache in young schoolchildren, none of them including children below the age of 10 years. Both reports equal the results presented in the Umeå Study (Paper I). One reported that 10% of 10-12 year old Finnish children, experienced weekly backache year 1996 and the other found weekly backache in approximately 8% of 10-14 year old children in the UK year 1998 [200,250]. These results indicate only minor differences between countries regarding backache prevalence in young schoolchildren. However, studies from more countries and studies including also the youngest schoolchildren are needed to verify this assumption.

Comparing prevalence of headache, stomach-ache and backache

The present thesis reports that headache is the most common pain followed by stomach-ache and backache. This result is supported by several studies [7,17,198,229,251,252]. However, in schoolchildren
younger than eight to ten years of age, stomach-ache has been found more common than headache [14,19,229,253]. This is paralleled by a higher prevalence of stomach-ache in grades 0 and 1 (aged six and seven years) in the Umeå study.

**Age variations**

In the young schoolchildren studied, recurrent headache as well as backache increased by age. The same has repeatedly been shown in the literature [21,141,197,200,230,232,233,235,238,250].

Notable the Umeå study contradict earlier findings which suggest that episodes of backache should be extremely uncommon before the age of eight years [86], by showing that 4%-8% of the six and seven years old children, experience back pain recurrently. The discrepancy might be explained by the fact that earlier results were based upon 11-17 year old children’s lifetime recall of single backache episodes, which has been proved difficult to accomplish accurately for children this age [45,254]. The continuing lack of studies focusing recurrent backache in young schoolchildren may reflect a view that it is not a major health problem in young school-ages children. However, the results from the present thesis indicate that recurrent backache are common at all ages between six and 13 years, and after the second grade at a surprisingly high degree.

As for recurrent stomach-ache, we found a high prevalence in grades five and six (11-13 years), but also a peak prevalence in grade one (seven years) (Paper I). These results both verify and contrast previous findings, which show a variety of patterns with peak prevalence: at seven years [255]; nine years [230]; seven to nine years [245]; boys six years and girls nine years [31] and 10-13 years [196]. Thus our findings add on to the evidence for a peak prevalence of stomach-ache at school start [31,245,255]. Also headache has been shown to peak at school start [256], indicating that starting elementary school may be a stressful experience for the child and especially for girls, who show the most marked peak prevalence in this grade.

**Sex variations**

In the present thesis, recurrent headache was reported by more girls than boys (Paper I). This finding confirms what most other studies have reported for younger as well as older school-aged children.
Discussion

[51,53,141,229,235,238,257-259]. However, the literature is conflicting. Some studies of young schoolchildren have shown no difference between sexes [21,232,233], and in the first years of school, recurrent headache may be more common among young schoolboys than among young girls [223].

We also found more girls than boys suffering from recurrent stomach-ache (Paper I). However, this is not in line with the conventional view. Only a few recent studies have shown a similar result [240,243], while several others report no sex difference [17,245,260-262]. Concerning recurrent backache, the thesis found no differences between girls and boys. This is also what is found in the few reports found on this subject, at least regarding children younger than 13 years of age, while in adolescents there is evidence of a slightly higher prevalence in girls compared with boys [41,45,141,200,250,259].

HRQoL assessment by the PedsQL

HRQoL in children with pain has so far been assessed by use of four instruments. A few studies have utilized the generic Child Health Questionnaire [263,264], but most commonly HRQoL has been measured by the Dutch instruments for adolescent, i.e. the QLH- Y, QLP-Y and QLA-CP [132,170,265-267] or by the PedsQL [180,183-185,268,269].

Testing the psychometric qualities of the PedsQL in Swedish children we found that all PedsQL forms (self and proxy PedsQL-23 and PedsQL-15) showed acceptable internal consistency and intra-rater (test-retest) reliability. Also criterion validity was supported for all forms and construct validity was supported for the self-report PedsQL-23 and both PedsQL-15 forms, but questioned for the proxy-report PedsQL-23.

Validity

Comparing PedsQL scales and scales from the CBCL/YSR forms, we found that the psychosocial PedsQL scales somewhat mirrored aspects of mental ill-health and that the physical scale measured some-
thing different from this. Our findings are in line with the results reported by Bastiaansen who studied associations between PedsQL scales and CBCL/YSR scales in a Dutch child group mainly comprising mental health outpatients [178]. However, more studies are needed to fully confirm criterion validity of the PedsQL.

The structural problems showed in the Swedish proxy PedsQL-23 are in concordance with the findings from EFA of PedsQL forms filled in by two US samples [172,270]. Our findings are further supported in the Dutch study by Bastiaansen who also performed a CFA and found results suggesting that the PedsQL-23 parent proxy scales might be contaminated measures of the conceptualized scales (RMSEA 0.115; CFI: 0.888) [178]. Thus, across populations several PedsQL-23 proxy scales seem in need of improvement. The initial selection of PedsQL items was exclusively guided by measurement properties of the self report scales and the proxy scales were then constructed to parallel the self report items as closely as possible [172]. This may explain the superiority of the self report form.

Allowing error correlation suggested by EFA, based on studies of a US population [172], improved model fit for the PedsQL forms filled in by Swedish children. In addition, our Swedish study found that omitting the items suggested to be problematic in the US population, as done in the PedsQL-15 forms [205], seemed to improve model fit for the forms completed by the Swedish population, suggesting that children in the US and Sweden respond in similar ways to the questions presented in the American and Swedish PedsQL forms.

Reliability

The internal consistency of the Swedish forms supported utilizing the PedsQL forms for group level analysis of HRQoL and sub domains of HRQoL, but also for individual level ratings of overall HRQoL. Similar findings, i.e. Chronbach α-coefficients above 0.70 for most PedsQL scales and close to 0.90 for the higher order scale HRQoL, have been presented for PedsQL forms when used in school settings around the world, e.g. in the US, Norway, Finland, the UK, Greece and Japan [180-182,227,271,272]. Likewise, the PedsQL forms have shown acceptable test-retest reproducibility when applied to general populations of schoolchildren in other countries [181,272].
Child-parent agreement

The relatively low inter-rater reliability found in the current study, replicate findings reported from several comparable population based studies of the PedsQL in other countries [180-182,227,272]. In general, concordance between HRQoL reports from school-aged children and their proxies are rather low [153,273,274].

The low child-parent agreement may be attributed to the subjective nature of the HRQoL construct. In general, inter-rater agreement has been found to be greater for external constructs compared with internal or non-observable constructs [151,153,206,273]. There also seems to be a higher, although limited, agreement of child-parent HRQoL ratings in cases where an elevated level of communication about health may be assumed between rater, i.e. when the child has a chronic health condition [180], or when inter-rater communication are possible during data collection [275]. This theory is further supported by another study showing that parents commonly feel uncertain about several aspects related to their 6-14 year old children’s HRQoL [276], stressing the importance of assessing children’s HRQoL from self reports whenever possible.

Another explanation for the low agreement between child and parent responses could be the structural diversities revealed by the CFA in the present study. However, agreement did not increase by expelling the problematic items as done in the PedsQL-15, which decline this explanation. Still, when comparing child and parent-reports of the child’s HRQoL, measurement invariance across informants is an important issue. The earlier mentioned EFA of the American PedsQL forms [172], has been followed by EFAs performed in Norway and Greece, all of which suggest divergent factor structures in child and proxy measures [182,272]. Consequently it may be questioned whether it is appropriate to use a construct based on almost identical items when assessing HRQoL in children from the child and parent perspective; a topic which need to be further addressed in future research.

Assessment through sex and age subgroups

Recommended requirements for comparisons across sex subgroups were only missed by one self reported item (Paper III), and according to Byrne et al., a minor part of invariant item parameters is not likely to affect cross group comparisons significantly [277]. Based upon a
five-factor model, Limbers also provided evidence for measurement invariance across age subgroup (five to 16 years) for the self-report forms [278]. Hence, the PedsQL self-report forms may generate sex specific measures of HRQoL that are meaningful to compare and most likely also comparable age specific HRQoL measures; however, measurement invariance across age subgroups should be confirmed for the four-factor model as well.

HRQoL in children with recurrent pain

A main finding of the present thesis is the high level of HRQoL impairment in children with recurrent pain. It has previously been shown that school-aged children, who are registered at specialist clinics due to recurrent abdominal pain respective headache have a medium to large impairment of their HRQoL (Cohen’s d 0.5- 0.7), as measured by the PedsQL [185,269,279]. Only 3% of the present population based sample of children with recurrent pain conditions had attended healthcare for a pain condition. All the same, HRQoL impairment in these primarily “non-clinical” children was similar to that of these clinical samples with specific pain conditions, findings underscoring the significance of the impairment associated with recurrent pain in general populations of school-aged children.

Notably, HRQoL impairment was reflected in impairment of all studied aspects of HRQoL; also this in line with results from several clinical studies of younger and older school-aged children suffering specific pain conditions. Furthermore, also similar to results from a population based study of adolescent with recurrent pain [170,184,185,267,269,279]. These results indicate a general impairment of all the core elements of HRQoL in school-aged children with recurrent pain.

Considering the high level of impairment associated with recurrent pain, health care contact due to a pain condition was remarkably low (3%). It should be noticed that only health care obtained within the past six months was asked for, and earlier contacts due to pain was not reg-
istered. The findings should be seen in light of results from qualitative interviews of children with recurrent pain conditions. In these interviews children explain that they most commonly are misunderstood and disbelieved when they express their pain to parents and health care personal, they feel abandoned when asking for help [138,280,281].

Age and sex variations in recurrent pain and associated HRQoL

Another important finding of this thesis is that recurrent pain is common in both boys and girls and among children at all ages from six through 13 years (Paper II). Furthermore, recurrent pain is associated with HRQoL impairment in girls as well as boys and in children from grade three as well as grade six (Paper IV).

However, the prevalence of pain and magnitude of impairment differed somewhat by age and sex. Pain prevalence was higher, and associated HRQoL partly more impaired, in girls than boys. Pain prevalence as well as related HRQoL impairment was also higher in older compared with younger children (Paper II,IV).

Interestingly, in younger girls and boys, pain seems most closely associated with physical impairment, while in older boys and girls the emotional domain seemed of greatest importance (Paper IV). Furthermore, pain showed only a minor relationship with school impairment in young boys, while in girls from both grades the school functioning was one of the domains most closely related with pain. Previous reports have exposed age and/or sex specific HRQoL differences among children with pain, but they did not report how HRQoL in age and sex subgroups differed from HRQoL in healthy children within the same subgroup, i.e. did not show pain related impairment in the subgroups [132,264,265,268,282].
Multi-site pain increases by age

The present thesis reports that only the prevalence of multi-site pain increase with age, while the share of children with single-site pain are the same through ages (Paper IV). Two longitudinal studies parallel this finding. One study followed children from ages four to 10 years and found almost identical prevalence of single-site pain over the years, while the number of children with multi-site pain increased; 33% of children with no pain at baseline had single-site pain and 13% had multi-site pain at follow-up, while 32% of the primary mono-symptomatic children had turned multi-symptomatic [69]. Another study following young school-aged children for four years also reported that children with multi-site pain most often continue reporting multi-site over time, while 35% of mono-symptomatic children with persistent pain had developed multi-site pain after one year and 51% after four years [88]. The reason for these age related changes are obscure, but the above mentioned results may indicate a gradual shift over the early child years from no symptoms to single symptoms followed by multiple symptoms, suggesting a possible element of pain sensitization, which may be more pronounced in girls than boys. Longitudinal studies following large populations are needed to further investigate the higher prevalence of recurrent pain in older children.

Differences between boys and girls

It is also notable, that although pain prevalence was higher in young girls compared with boys, this was only true among children reporting a combination of multiple and weekly pain symptoms (Paper II,IV). Again, others have described multiple as well as frequent pain to be more common in girls than boys, but they did not report whether the higher prevalence was restricted to children with multiple or frequent symptoms [17,19,140].

A general female predominance of recurrent pain has for long been recognized in adults and adolescents [7,283]. Recently, our findings in young school-aged children were confirmed in two other studies of young children aged six year and 9-12 years respectively [229,253]. In the Nordic countries, a high sickliness in schoolgirls has been debated for many years. Going back to the last part of the 1800s, schoolgirls in Norway and Sweden were, also then, found to be more inclined to ill-health such as headache [284,285], and as expressed by a school doc-
tor attending a school meeting in Stockholm year 1886, it had for long been common knowledge that “flickorna äro sjuka, klena och öfverransträngda” (the girls are sick, feeble, and overstrained)[284].

The fact that girls report or perceive more ill health than boys has over the years been given several explanations. In 1878 one of the first school surveys in Sweden found that girls had no health problems during summer vacation, but some weeks after school start, an increasing share of the girls complained of headache [284]. This study generated the conclusion, that girls above the age of nine were badly influenced by attending school. At the time, girls compared to boys, were argued to have a biologically lower resistance to ill-health. Girls were thought to have a general poorer physical as well as intellectual capacity, which was extra apparent during puberty. Therefore girls’ health would be jeopardized considerably if they were exposed to the same high study demands as boys. Eventually, differences in social demands in girls and boys, e.g. a higher degree of indoor and sedentary activities associated with female gender, were considered a reason for pain differences between boys and girls as well [284].

Also today, the differences in pain prevalence between females and males are discussed in terms of biological and/or psychosocial differences [283], with sex hormones or menstruation still given a key role in explanatory models [19,201]. The results of the present thesis, showing a female dominance in recurrent pain also among young children, suggest a consistent female dominance in recurrent pain through ages. This speaks against puberty related explanations, and so does the fact that, after age adjustments, recurrent pain seems to be equally common in girls who have and have not passed menarche [286]. The stable rate of monthly pain in girls also dispute puberty related explanations in the Umeå sample; however, other explanatory sex specific biological differences cannot be out ruled. It has, for instance, been suggested that pain signal transmission or modulation may differ between males and females [287,288].

Sex differences in pain may also be due to males being socialized to suppress pain experiences, leading to underreporting of pain by males [283]. From an early age boys have been shown to meet negative responses when expressing pain whereas girls are rewarded [289]. Furthermore, girls may face higher social demands and responsibilities than boys, and girls with a low degree of social orientation have been shown to have a higher risk of headache, stomach-ache, and backache [290]. These circumstances may also influence HRQoL impairment in girls
and boys with pain differently, e.g. a female propensity to feel high demands of success in school together with a feeling of having less access to help from the teacher [291], may contribute to a greater impairment within the school domain for girls in pain compared with boys. Thus, societal structural differences between females and males or differences in gender roles may serve as essential explanatory models for the observed differences in pain prevalence and associated HRQoL between girls and boys.

General discussion on pain

Recurrent pain – a symptom or a disease entity?

Another important result from the present thesis is that children who experience a recurrent pain condition, regardless of pain location, most commonly experience recurrent pain also from other body parts, and overall, co-occurrence of pain from different sites are very common. Later these results have been partly confirmed in a study of 7-14 year old German children, showing that the majority of children with headache also suffered from backache and/or stomach-ache [238]. A Dutch study, including preadolescent as well as adolescent children, further supported the findings from Umeå by showing multi-site pain in approximately half of the afflicted children [19]. In adolescents similar high co-occurrence of recurrent pain conditions has been shown in studies from Iceland, Sweden and the US [201,292,293]. Thus, across school-ages and countries it seems that recurrent pain conditions most commonly co-occur.

The reason for clustering of pain conditions can only be speculated on, but one apparent explanation may be a general malfunction of pain processing in the CNS. Thus, when it comes to recurrent pain conditions in school-aged children, the high level of co-occurring pain may question the conventionally view of pain being a symptom of an underlying disorder. It seems more reasonable to suggest that often, recurrent headache, stomach-ache and backache may signal a universal pain disorder, i.e. a neurological problem of pain processing.
It has been described that persistent pain has its own specific pathology, signs and symptoms and therefore should be regarded a specific disease entity rather than a symptom [119,294]. This suggestion is supported by the findings of the present thesis.

Comparing our results with the earlier findings by Øster [230], we found a higher prevalence of multi-site pain in the recent Umeå study, 50% vs. 25% of the afflicted children, suggesting that, recurrent pain conditions more often are multi-site now, compared with 40 years ago.

Single-site and multi-site pain – different phenomena?

Another interesting result from this thesis is that children with single-site and multi-site pain differed in several ways. For one thing, children with multi-site pain most commonly reported weekly pain, while monthly pain was most common in children experiencing single-site pain. Similar results were presented in the above mentioned German study of 7-14 year old children and also in an earlier study of Icelandic adolescents [201,238]. It seems that in children, a propensity to recurrent pain may be expressed as both frequent and multiple symptoms.

The present thesis also shows that multi-site pain is associated with greater HRQoL impairment than single-site pain. Relationship between frequency of recurrent pain and HRQoL has been reported in several former studies of children [132,282,295] and our results are in the expected direction, i.e. the greater the frequency of pain the lower the HRQoL. However, there has been little focus on the implication of number of pain sites on HRQoL. Bergman et al. [296] showed that in adults, a higher number of pain sites was associated with a more problematic HRQoL, and psychosocial - but not physical - aspects of HRQoL could be tied to the process from single to multiple pains. A recent large worldwide study of mental health in adults partly supported these findings by showing a higher prevalence of mood and anxiety disorders by higher number of pain sites [297]. Also in children, a higher level of mental distress has been shown by increasing number of pain sites, and there are evidence that behavioral or emotional problems predict later multi-site, but not single-site pain [69]. Furthermore, young children with multi-site pain have more absence from school and experience more functional disability than children with single-site pain [200]. The present study parallel the meager previous literature by show-
ing that the higher number of pain sites associated with greater HRQoL impairment is due to both higher physical and psychosocial impairment. However, in children with multiple-site pain, psychosocial aspects are markedly more impaired than physical aspects, especially emotional and school aspects; a difference not found among children with single pain sites. These findings suggest that emotional aspects of HRQoL, and in children also school related aspects, might be more important than physical aspects to the understanding, treatment and prevention of multi-site pain conditions.

In addition to differences regarding pain frequency and pain associated HRQoL, we also found difference between children with multi-site and single-site pain regarding sex and age. Adding up the evidence, it may be speculated whether recurrent multi-site and single-site pain constitute separate phenomena.

What degree of HRQoL are directly related to a particularly pain condition?

The present thesis reports that each of the specific pain conditions, headache, stomach-ache and backache are associated with impairment of HRQoL, a finding supported by others [170,184,185,269,279]. However, our study also find that in children with headache, as well as in children with stomach-ache respective backache, HRQoL impairment vary greatly with the presence or absence of a co-occurring pain condition. For all pain conditions studied, impairment is markedly lower for a specific pain condition, if children with co-occurring pain are excluded from the group. Actually, the degree of impairment seems closer associated with the extent of co-occurring pain than with pain location. A Dutch study of adolescents with recurrent pain problems also showed pain location to be of minor importance for HRQoL [132]. Thus, studying a specific pain without taking into consideration co-occurring pain conditions may give an incorrect impression of the degree of impairment directly related to the specific condition.

A theoretical model relating recurrent pain and HRQoL

The results presented in this thesis give empirical evidence of associations between recurrent pain and all the core elements of HRQoL
(Paper IV). As mentioned before, current pain theories propose that deprived physical, social and emotional state are apt to promote pain experiences by influencing pain processing in the central nervous system [100,101,105,106]. At the same time, there is evidence that recurrent pain can give rise to a diversity of physical as well as social and emotional difficulties [138-141]. Thus, theoretically, there may be an interactive loop between recurrent pain and all the core elements covered by the HRQoL concept, i.e. physical, emotional, social (including school) functioning and wellbeing as modeled in accordance with our present findings (Fig. 14).

One implication of such a theoretical model is that improvement of the core aspects of HRQoL in young children might reduce recurrent pain problems. Furthermore, systematic attempts to secure high HRQoL might prevent the emergence of recurrent pain problems in the first place.

Figure 14. Theoretical model for the association between Health Related Quality of Life and recurrent pain.
Summary and concluding remarks

- In boys and girls, and at all ages from six to 13 years, recurrent headache, stomach-ache and backache are common. These results are confirmed in other current studies from Sweden and other Western countries. Data suggest an upward trend in prevalence. The high prevalence is troublesome as recurrent pain has been associated with discomfort for the child as well as long-term physical and psychiatric problems in adulthood.

- HRQoL in young schoolgirls and schoolboys with recurrent pain is markedly impaired. Degree of impairment in this general population of young children is comparable to that of children receiving health care at specialist clinics. This further points out the significance of recurrent pain in children, and the importance of early prevention and treatment.

- Recurrent pain conditions in young schoolchildren often occur frequently (weekly) and most commonly at multiple body sites. Multisite pain increase by age and multi-site/weekly pain is more common among girls than boys. This result gives reason for further worry as high frequency, and co-occurrence of pain conditions, increase HRQoL impairment as well as the risk of long-term pain persistence. The result also suggests that recurrent pain in children often may be regarded a general pain entity, rather than a symptom of a local organic disorder.

- The Swedish PedsQL self-report forms have acceptable psychometric properties. Psychometric properties of the Swedish PedsQL are comparable to what has been found in other countries. The PedsQL can be recommended for HRQoL assessment in Swedish children.
Challenges and future research

It is suggested that future research within the focus of this thesis should address the following issues:

- The etiology of recurrent pain and reason for pain related sex differences in children are still obscure. More knowledge is needed to design proper treatment and prevention programs. Qualitative research may give further and deeper information.

- Additional Swedish and international studies are needed to validate the relative high level of recurrent backache found in young schoolchildren in the Umeå study.

- Further validation of the PedsQL is needed, also including age groups not covered by this thesis.

- The suggested model for recurrent pain - HRQoL interaction should be further refined and empirically tested in longitudinal and intervention studies.

- Longitudinal studies exploring the development and shift in pain prevalence and co-occurring pain with growing age.

- Investigations forwarding understanding of the importance and etiology of pain clustering, e.g. studies focusing the pathophysiology of single-site pain contra multi-site pain.
Acknowledgement

The work presented at this dissertation is the result of a joint venture including at least 6000 persons. A true team work where every single person has contributed in important ways. I am grateful for all I learned, for the confidence you have shown me, for the challenging, inspiring and enjoyable moment we shared during the past years. Hope for many more to come.

Special thanks goes to all the children and parents for their kind contributions. Your answers on numerous questions, comments before and after the surveys, drawings, poems etc. have increased knowledge and understanding in so many ways.

I also extend sincere gratitude
to Erik Bergström, my principal supervisor, and head of the Pediatric Clinic, for sharing your great knowledge and experience with me. Also for guiding me with engagement, endurance, and for immediate, never failing response and support, whenever needed.

to Bruno Hägglöf, my supervisor, and head of Child & Adolescent Psychiatry, for enlightening me in the field of child psychiatry. Thank you also for your support and thoughtfulness and for creating such a stimulating and friendly multidisciplinary as well as international environment for exchange of ideas, inspiration and learning.

to Christine Brulin, for encouragement to enter the world of sciences, and for skilled supervision in the first part of the investigations included in this thesis. Also to Hans Stenlund for guiding me in the interesting world of statistics and for scientific contributions, especially in Paper three. Furthermore, to Olle Hernell, head of Pediatrics, for support and sharing of scientific knowledge and to Gisela Dalquist, Ann Öhman and Mikael Sandlund for constructive comments at the halfway defense of this thesis.

to Viveca Nordström, Carola Mohlin-Westerberg and Catharina Hedlund-Österman for great work proceeding the Lycksele study and
the most recent data collection in Umeå. Also thanks for many interesting and stimulating discussions.

to former colleagues in the school health services, for stimulating collaboration, never lacking support and for sharing your experience of child health care. Also to the schools principals for supporting the project and to all teachers for great engagement, flexibility, patience and continuous support to the children as well as everyone else. It has been a great pleasure to do this work together with your. You all deserve to be mentioned by individual names, but for the matter of space, I have to limit myself and assure you that my devoted thanks go to each and every one of you as individuals.

to Birgitta Bäklund, secretary at the CAP unit, for always being so helpful and for your great contributing to the pleasant working environment at the unit. Also to Ulla Norman, Karin Moström and Helena Brännström, administrators at Pediatric Sciences and Clinics, for all your valuable assistance.

to Mats Karling for many interesting and valuable discussions and for sharing your profound knowledge regarding pain in children. Also for being a great and supportive friend.

to the CAP research group, Karin Nilsson, Mats Karling, Krister Fredin, Jeanette Sigurdh, Stephen Goldín, Menelik Desta, Daniel Fecadu, Aijaz farooqi, Spyridoula Lekkou, Anna Zashihina, and Jenny Karlsson for valuable comments on my scientific work and for sharing your knowledge and understanding.

to the NUS Pain Team, Caroline Tellhammar, Kerstin Ahlman, Mats Karling, Maggie Wendelius, Marie Wilck, Kristina Hedenäs, Anders Westerlund, Marie Johansson, Jenny Thyssel, and Magnus Ohlsson for inspiration, fruitful discussions and enjoyable cooperation.

to the AGÅS special interest group of the Swedish association for Pain in Childhood, Göste Alfvén, Sara Holm, Mats Karling, Eva Kokinsky, Karin Berg, Stefan Nilsson, and many more, for inspiration and enriching discussions.

to fellows at Pediatric Sciences for generously sharing your clinical and scientific knowledge and experience, to Christina West, also for being a considerate roommate and for many enjoyable chats.
to Anneli Iversson, Vivica Lindh, Maria Forsner, Hans K:son Blomquist, Anneli Schmach, Anneli Lindahl, Roger Lindahl and many more co-workers and friends for interest in my work, collaboration, practical help and inspiration.

to Sören Petersen and Stine Petersen, for helpful expert comments on the study design and for doing acute contributions when practical matters got overwhelming.

to Erling Petersen for standing by my side, also in this phase of our life companionship. For encouraging me, listening, “kicking” at times, for commenting on, discussing “how to do”, and for a lot of practical support as well.

to the Vårdal Foundation, AFA insurances, the County Council of Västerbotten, Queen Silvia's Jubilee Fund, Oscar Foundation, the National Institute of Public Health, and the Swedish Society of Nursing for financial support and to Megra Media for graphical support.

I have learned so much, and have really enjoyed it!
Epilogue

Det är jobbigt att ha ont.

När man ligger i sängen och drömmer sig bort till landet ”Ingen har ont”.

När man sitter i klassrummet och tittar ut genom fönstret och ser barnen leka utan att känna ett dugg.

Om man ändå var som dom.

En dag man inte har ont njuter man som bara den.

Man glömmer vad man sagt och man gör det man inte kunnat.

Man klättrar och hoppar, hänger och klänger, och glömmer att

det är jobbigt att ha ONT

J.H., Umeå
Varför kan man ha ont i huvudet?
Varför? Varför ser ingen det?
Varför får jag inte gå hem?
Varför Varför Varför

A.E., Umeå
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