Pain and health related quality of life in adolescents with chronic fatigue syndrome

A mixed method study

Anette Winger
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Abstract

Background: Chronic fatigue syndrome (CFS) is a disabling disease that occurs among individuals across cultures and ages. Despite ample research, chronic fatigue syndrome is still poorly understood, and the ongoing debate on CFS reflects the intensive controversies linked to the disease. Patients often experience misconceptions and prejudices which constitute an extra burden. Research on adolescents with CFS is limited, especially from the patients’ perspective. Adolescents with CFS have reduced school attendance, spend less time with friends, and research indicates that living with CFS affects the adolescents quality of life negatively. Despite this, there is still limited research on HRQOL in this group. Pain is a significant additional burden in patients with CFS, however, also still insufficiently studied.

Aim: The overall aim of this study was to get a broader insight into, and more knowledge about being an adolescent living with CFS as the adolescents themselves experienced and narrated it. Additional aims were to explore pain and health related quality of life in adolescents with CFS and healthy adolescents, and finally to compare the two groups.

Methods: One hundred and twenty adolescents with CFS and 39 healthy adolescents (12-18 years) participated in this cross-sectional, mixed method study. The participants answered self-administrated, generic questionnaires to investigate HRQOL, depressive symptoms and pain. Algometry was used to measure pressure pain thresholds. A sub-sample of 18 adolescents with CFS were interviewed in depth about their experiences of living with CFS.

Results: The interviews revealed that the adolescents with CFS felt different from and forgotten by peers. They felt lonely and as outsiders, not being able to attend school and follow their peers as they moved on with their lives. Further, they felt alienated from their own bodies and different from who they used to be before they got ill. The quantitative work showed that the adolescents were severely impaired by pain compared to the control group of healthy adolescents. They also had significantly lower pressure pain thresholds compared to the healthy adolescents. One surprising discovery, however, was that despite the severity of pain, mapped by the questionnaires, physical pain was not a subject the adolescents focused during the interviews. Health related quality of life was low on all domains in the adolescents with CFS, even lower than we anticipated and far lower than in the healthy controls.

Conclusions: The integration of the qualitative and quantitative work in this study has provided more knowledge and a broader insight into the life of adolescents with CFS. Their self-understanding and development of identity are challenged when the illness make their body unfamiliar and narrows their ability to participate in “real” life. Experience of belonging might prevent mental health problems and possibly improve their health related quality of life. Despite the serious impact of the self-reported physical pain, the pain focus was different from what we expected. For adolescents with CFS, difficult feelings and existential thoughts might be equally, or even more painful than the physically measured pain. To verbalize difficulties related to their illness might be challenging and words might as well be insufficient. Awareness towards body language and other modes of expressions should be prioritized even though it might be challenging for health care professionals to prioritize time to become familiar with the individual patient’s way of expressing him or herself. Storytelling could be used as a strength and resource in assessment and treatment of adolescents with CFS.
Forord

Først og fremst vil jeg formidle en stor takk til hver og en av de flotte ungdommene som har deltatt i denne studien. Takk for alt dere har delt og at dere har vært så åpne og fortrolige til tross for at det har kostet dere både tid og krefter. Deres deltagelse har vært uvurderlig og bidrar til ny kunnskap som når pasienter, forskningsmiljøer og fagfolk over hele verden.

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List of abbreviations

BMI   Body Mass Index
BPI   Brief Pain Inventory
CATS  Cognitive Activation Theory of Stress
CDC   Centers for Disease Control and Prevention
CFS   Chronic Fatigue Syndrome
HC    Healthy Controls
HRQOL Health Related Quality of Life
IASP  International Association for the Study of Pain
ME    Myalgic Encephalomyelitis
MFQ   Mood and Feelings Questionnaire
MUS   Medically Unexplained Symptoms
NICU  Neonatal Intensive Care Unit
NorCAPITAL Norwegian Study of Chronic Fatigue Syndrome in Adolescents: Pathophysiology and Intervention Trial
PedsQL Pediatric quality of Life Inventory
PPT   Pressure Pain Threshold
QOL   Quality of Life
SEID  Systemic Exertion Intolerance Disease
WHO   World Health Organization

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1 Introduction

Starting as a nurse in a neonatal intensive care unit (NICU) brought me close to the vulnerability of life. Medical and technical development, as well as skillful health professionals, have made it possible to save children with serious congenital disorders; and to save babies as young as 22 weeks of gestational age. Pushing boundaries has given many children the possibility of life. However, surviving the first critical hours, days and weeks implies painful procedures and suffering. The children did not always get optimal pain relief, and this engaged me in working with pain and sufficient pain relief for these children. In my master’s degree, I interviewed nurses working in the NICU about their experiences with pain relief. My interest in pain brought me to a pain clinic working with post-operative and chronic pain in children, adolescents and adult patients. In 2008, I was given the opportunity to work in a project with children and adolescents with Chronic Fatigue Syndrome (CFS), who also had challenges related to pain. When the study group (NorCAPITAL) was established, I wrote the proposal for my PhD study on pain and quality of life in children.

1.1 An overall presentation of the field

CFS is a disabling disease that occurs among individuals across all cultures and ages (Cho, Menezes, Bhugra, & Wessely, 2008; Davies & Crawley, 2008; Wyller, 2007). Based upon estimates, between 10,000–20,000 adults and 600 young people under the age of 18 suffer from CFS in Norway (Helsedirektoratet, 2014). There has been a growing awareness of this syndrome in recent years, both internationally and nationally (Helsedirektoratet, 2014). Different groups of people form their opinion about the disease from their own perspectives, and health professionals, patients and patient organizations as well as journalists and politicians are engaged in this issue. Novels have been written, and documentaries from patients’ perspectives have been shown on TV and are available on social media on the internet. People have strong opinions, based frequently on assumptions, but limited knowledge in the field. The uncertainties of CFS create misconceptions and prejudices, functioning as an extra burden on patients with CFS (Fisher & Crawley, 2013). There is no doubt that this is a serious condition and that those affected are seriously impaired. Disagreements about the
disease are related to etiology, how the condition should be addressed, which criteria should be used for diagnosis and which treatment that should be recommended (Helsedirektoratet, 2014). The Centers for Disease Controls and Prevention (CDC-criteria) (Fukuda 1994) and the Pediatric CFS criteria (Carruthers et al., 2011; Fukuda et al., 1994; L.A. Jason et al., 2006; National Institute of Health and Care Excelence, 2007; Royal College of Paediatrics and Child Health, 2004) are the most commonly used; but in research, the CDC-criteria are preferred. The CDC-criteria are often referred to as the Fukuda-criteria. There are disagreements about the number of additional symptoms that are necessary to diagnose CFS (Sullivan, Pedersen, Jacks, & Evengard, 2005; Wyller & Helland, 2013). The existing case definitions do not seem to distinguish between the different subgroups of CFS patients (Brurberg, Fonhus, Larun, Flottorp, & Malterud, 2014). The disagreements raise fundamental issues regarding how we conceptualize the human and the human body, and surely cause high temperatures in the public debate.

1.2 CFS in children and adolescents
CFS is a well-known condition among adolescents, with an estimated prevalence between 0.1% and 1.0% (E. M. Crawley, Emond, & Sterne, 2011; S. L. Nijhof et al., 2011), and is more common in girls than in boys (S. L. Nijhof et al., 2011; ter Wolbeek, van Doornen, Kavelaars, & Heijnen, 2006). In Norway, an increasing number of children and adolescents are referred for evaluation of CFS (Elgen, Hikmat, Aspevik, & Hagen, 2013). Specific pediatric criteria (L.A. Jason et al., 2006) are usually applied for children and adolescents, deriving from the United States (US) Centers for Disease Control and Prevention (CDC)-criteria for the adult population (Fukuda et al., 1994). They require three months of disabling fatigue instead of six months as in the CDC criteria (National Institute of Health and Care Excelence, 2007; Royal College of Paediatrics and Child Health, 2004).

Even though the functional level varies, most patients are absent from school and are unable to maintain a normal level of social relations, which has educational and developmental consequences (Bell, Robinson, & Jordan, 2001; E. Crawley & Sterne, 2009; L. Jason et al., 2009; Rangel, Garralda, Levin, & Roberts, 2000). One study found that more than 50% of children are
bedridden at some stage (Rangel et al., 2000), and underpins how seriously affected these persons might be. Clinical experience shows that adolescents with CFS have high expectations of themselves, and one study found that their parents overestimated their children’s IQ, which might indicate equally high expectations from the parents (Godfrey et al., 2009). In one study on an adult CFS population, self-critical perfectionism predicted both fatigue and pain (Kempke, Luyten, Claes, Goossens, et al., 2013); this may also be the case in the pediatric CFS population. Research indicates that CFS has a more negative impact on adolescents’ quality of life compared with that of children and adolescents who have other chronic illnesses (Kennedy, Underwood, & Belch, 2010), but only a few studies have performed a systematic QOL assessment. A patient’s focus on symptoms is associated with poor physical functioning (Gray & Rutter, 2007), whereas accommodation to the illness has shown to have a positive influence on QOL.

Several symptoms are associated with CFS. Depression for instance is more common in CFS pediatric patients than in a general pediatric population. Despite this, one has not been able to find a causal relationship in either direction for depression or anxiety (Bould, Collin, Lewis, Rimes, & Crawley, 2013). Even though pain is a common symptom in CFS, little progress has been made in understanding the pain component (Meeus, Nijs, & Meirleir, 2007). Adolescents with CFS are sensitive to stimuli like light and sound (Wyller, 2007), and recent studies show that they are also sensitive to pressure, detected by lower pressure pain thresholds (Sanne L. Nijhof, Priesterbach, Bleijenberg, Engelbert, & van de Putte, 2013). Some researchers have hypothesized that the chronic and generalized pain in CFS is caused by increased responsiveness of the nervous system (Meeus & Nijs, 2007; Meeus, Roussel, Truijen, & Nijs, 2010; Nijs et al., 2012), possibly by reduced descendent pain inhibition in the central nervous system (Yarnitsky, 2010).

The prognosis of CFS in young people has shown to be good compared to the adult CFS population (Rimes et al., 2007). The most effective treatment strategy for this group is based on cognitive behavior therapy (CBT) (Knight, Scheinberg, & Harvey, 2013; Lloyd, Chalder, & Rimes, 2012;
S. L. Nijhof, Bleijenberg, Uiterwaal, Kimpen, & van de Putte, 2012; Stulemeijer, De Jong, Fiselier, Hoogveld, & Bleijenberg, 2005), and a multidisciplinary approach has been recommended in adolescents with problems in physical and psychosocial functioning, including CFS (Klineberg et al., 2014).

A few qualitative studies emphasize patients’ own perspective, and several authors underpin the importance of listening to adolescents’ own stories (Jelbert, Stedmon, & Stephens, 2010; Jo Richards, Chaplin, Starkey, & Turk, 2006). When asked about what they believe causes the illness, a majority of the participants emphasize infection as the cause of CFS while some also believe that psychological and psychosocial factors are important contributors (Hareide, Finset, & Wyller, 2011; Jo Richards et al., 2006). Qualitative studies also present stories of loss related to school and friends, difficult emotions and existential thoughts (Jelbert et al., 2010).

In the literature there are different terms used for adolescents under the age of 18. Some use ‘children’ for everyone between zero and 18 years; others use ‘young people’ or ‘adolescents’. In this study, the term ‘adolescent’ is the term of choice, hence the study population is between 12 and 18 years of age. In Chapter 3.9, “Ethical consideration”, the term ‘children’ is used for all children between zero and 18. This is because the literature concerns all children and is not restricted to adolescents. When referring to other studies, the population is labeled according to the terms used in these studies.

1.3 Aim of the study
The overall aim of this study was to gain a broader insight into, and more knowledge about, adolescent CFS as it is experienced and narrated by the adolescents themselves. An additional aim was to explore pain and HRQOL in adolescents with CFS and healthy controls (HC), and to compare the two groups. Different kinds of tools were included to illuminate several aspects about the illness, because it was considered important to provide new knowledge.

More specifically, the aim of the study was:
• To explore the experience of being an adolescent with CFS.

• To evaluate pain in adolescents with CFS compared to healthy adolescents, and more specifically explore: (1) the prevalence and location of pain symptoms, (2) pain severity and its functional interference in everyday life and (3) baseline pressure pain thresholds (PPTs).

• To describe self-reported health related quality of life (HRQOL) and depressive symptoms in adolescents with CFS, and to investigate in which areas of HRQOL and depressive symptoms adolescents with chronic fatigue syndrome differ from healthy adolescents.
2 Background and theoretical framework

The review of the literature builds on frequent and systematic searches in Medline, CINAHL and PsycINFO from the period when writing the research proposal (spring 2008), throughout the research period, and to the end of this project in March 2015. Searches have also been performed through Google and Google Scholar, revealing scientific work that did not show up on the web despite systematic searches in ordinary scientific databases. Some relevant papers have been found by reading the lists of references in scientific papers. Academic books, novels, newspapers and social media have been sources of knowledge and inspiration. Following discussions by different stakeholders (journalists, politicians, patient organizations etc.) has kept me updated within the field.

The key words that have been used in different combinations include: CFS, ME, chronic fatigue, adolescent, child, pain, HRQOL, QOL.

To understand the illness and some of the related controversies, a brief look at the history of fatigue is needed.

2.1 Historical perspective of fatigue
Long-lasting fatigue has been described, and in medical literature since 1600–1750 (Straus, 1991; Stubhaug, 2008). The founder of modern nursing, Florence Nightingale (1820–1910), who served as a nurse during the Crimean War (Nightingale, 1997), was in fact suffering from an exhaustion with symptoms like those described in CFS/ME (Fukuda, 1994). The condition of exhaustion was given the eponym Florence Nightingale Disease\(^1\) (L. A. Jason, Taylor, Plioplys, Stepanek, & Shlaes, 2002). By the time of the First World War, chronic fatigue was a common complaint in Europe and North America. Complaints of fatigue were diagnosed as neurasthenia (Shorter, 1993).

\(^1\) An eponym is a name given to an illness on the background of a well-known person who either had the illness or discovered it (L. A. Jason, Taylor, Plioplys, Stepanek & Shlaes, 2002).
Throughout history, overlapping and different terms for fatigue and muscle pain have been applied, and this is still the case. One example is the overlap with neurasthenia/melancholia (Deale & Wessely, 2000).

The name of a disease might be important for how people look upon the disease and how serious they consider it (L. A. Jason et al., 2002). In a historical overview of fatigued women, Lian & Bondevik (2013) show that different names have been used for conditions characterized by severe and long-lasting fatigue. At the end of the 1800, neurasthenia was established as a diagnosis and regarded as a somatic illness. From 1928, however, neurasthenia was classified as a psychiatric diagnosis. With this shift, neurasthenia changed from a highly recognized, upper class, male-associated diagnosis to a low status diagnosis affecting undereducated women from the lower social class (Lian & Bondevik, 2013). Seen in a sociological perspective, explanation for CFS has shifted from environmental explanations to individually oriented ones (Lian & Bondevik, 2013).

Shorter claims that the increase in chronic fatigue might reflect cultural factors like increased media publicity (Shorter, 1992), or be caused by infective microorganisms or environmental toxins, as well as psychological aspects (Shorter, 1993). Shorter points to three different precursors for today’s CFS. First, fatigue and muscle pain were reported as epidemic incidents in the United States in 1934, in the 1950s, and in the 1960s. The illness incidence was of unclear etiology and labeled neuromyasthenia. Second, chronic fatigue with muscle pain was demonstrated in 1968 after Epstein-Barr virus infections, but the condition was not named CFS until 1988 (Holmes 1988 in Shorter 1993). Third, the name myalgic encephalomyelitis (ME) was introduced in 1955, and stems from an epidemic-like outbreak at the Royal Free Hospital in London (Wessley, 1991 in Shorter 1993).

Fatigue is a common experience among people in general. This makes it difficult for people to understand that there is a difference between common tiredness and severe and long-lasting fatigue. Patients believe that the name CFS doesn’t reflect the severity of their illness, and that it tend to minimize the problem (L. A. Jason et al., 2002). Taking all this into account, one might
understand why patients and patients’ organizations prefer the name myalgic encephalomyelitis (ME). ME indicates a more defined disease and a condition linked to a biomedical explanation. This concept reflects the favorable ring of a biomedical diagnosis and the stigma of a psychiatric diagnosis (Album & Westin, 2008).

2.2 Chronic fatigue syndrome
In the literature, the terms CFS and ME are often used as synonyms. The combinations ME/CFS or CFS/ME are also used (Helsedirektoratet, 2014). The term CFS is the abbreviation for chronic fatigue syndrome, while ME stands for myalgic encephalomyelitis. The old Greek *myalgia* means pain in the muscles, *encefalon* is ‘brain’, *myelon* is the spinal cord; while the suffix *itis* indicates infection. The different names of CFS also reflect the strong disagreement in the research field. In this thesis, the term CFS is used, because it describes the essence of the symptoms, and does not indicate any cause of the disease which we do not know. Thus, there is no evidence to support the term ME.

CFS is a long-lasting disease with physiological as well as cognitive symptoms. The cardinal symptoms are physical and mental exhaustion, not relieved by rest (L. A. Jason et al., 2011). This may explain why CFS patients have a lower functional capacity than those with other chronic conditions like cancer, depression or rheumatoid arthritis (Komaroff et al., 1996; Nacul et al., 2011). The additional symptoms include pain, cognitive impairment, orthostatic intolerance, sleep disturbances, and hypersensitivity toward light and sound.

Infections and stressful events are considered potential initiating and perpetuating factors, respectively (Afari & Buchwald, 2003; Clements, Sharpe, Simkin, Borril, & Hawton, 1997; Theorell, Blomkvist, Lindh, & Evengård, 1999). Personal traits like perfectionism, conscientiousness and lower self-esteem have also shown to be risk factors as well as perpetuating factors of the illness (Fukuda et al., 1994; Kempke, Luyten, Claes, Goossens, et al., 2013; Poeschla, Strachan, Dansie, Buchwald, & Afari, 2013). Comorbid conditions like depression and anxiety are highly prevalent, although anxiety is not as prevalent as depression (Afari & Buchwald, 2003; Wessely, Chalder, Hirsch, Wallace, & Wright, 1997). Pain and passive coping styles like negative thoughts, rest as a response to pain and
guarding of painful body parts seem to have a negative impact on functioning and mental health (Heijmans, 1998; Ray, Jefferies, & Weir, 1997).

Different factors might contribute to both pain and QOL, and Meeus et al. (2012) found that catastrophizing and depression were correlated with pain intensity and further, that pain catastrophizing and depression contribute to reduced functioning in daily activity (Meeus, Nijs, Van Mol, Truijen, & De Meirleir, 2012). Reduced activity is a relevant factor regarding QOL (Brazier et al., 1992; Hardt et al., 2001; Lam & Lauder, 2000). A study investigating HRQOL showed that patients with CFS were significantly affected, with depressive symptoms as the strongest predictor (Rakib et al., 2005), but the authors underlined that the causal relationship is unclear. Also HRQOL has in different countries been shown to be poor in patients with CFS (Hardt et al., 2001).

Due to all the uncertainties related to CFS, a broad perspective on the disease seems reasonable. Based upon the cognitive activation theory of stress (CATS), the NorCAPITAL study suggested that a sustained arousal could serve as a potential mechanism for CFS (Wyller, Eriksen, & Malterud, 2009). ‘Sustained arousal’ is conceptualized as a chronic stress response causing alterations of cognitive, endocrine, and autonomic functions; the two latter may in turn alter the immune function. These alterations fuel the arousal, setting up a vicious circle. This model is in accordance with other CFS theories (Maloney, Boneva, Nater, & Reeves, 2009; Nijs et al., 2012), and is supported by recent findings suggesting that fatigue can be precipitated by different microorganisms, such as the Epstein Barr virus (Hickie et al., 2006), but also be related to hypervigilance, which is a feature of sustained arousal (Kadota et al., 2010). The sustained arousal-model offers a platform for integrated, translational research projects, as demanded by the scientific community (Van Houdenhove & Luyten, 2011). However, a randomized controlled intervention study (hypothesizing that low-dose clonidine would improve the sympathetic activity), which was based on this model (Sulheim et al., 2014), did not improve symptoms or function, indicating that patients’ disability might be more complexly related to the underlying pathophysiology than anticipated.
There are indeed similarities between adults and children/adolescents with CFS, but there are also differences and specific factors to take into account in adolescent CFS. A clinical difference is stomach aches, which are common in the pediatric CFS population but not in adults with CFS (L. Jason et al., 2010). One important issue is the diagnostic requirement for duration of fatigue and the number of additional symptoms. The CDC criteria require a six month duration and four additional symptoms, while the pediatric criteria require three months of unexplained fatigue and only one additional criterion (Fukuda et al., 1994; L.A. Jason et al., 2006). Due to adolescents in a vulnerable developmental stage being (forced) apart from peers, school and social (areas), this might have developmental consequences (M. E. Garralda, Rangel, L., 2002), and early diagnosis and intervention seem reasonable. CBT has shown to be effective in adolescents, and several studies with slightly different approaches demonstrate the importance of including family, school, local community and friends in the treatment (Chalder, 2002; Christie & Wilson, 2005; H. Knoop, Stulemeijer, de Jong, Fiselier, & Bleijenberg, 2008; Hans Knoop, Stulemeijer, Prins, van der Meer, & Bleijenberg, 2007; Lloyd et al., 2012; S. L. Nijhof et al., 2012). Another interesting difference found in a study by Gray and Rutter (2007), is that the pediatric CFS population understood their symptoms and pattern of the illness to be more cyclical than chronic, which is the opposite to the pattern in the adult CFS population (Gray & Rutter, 2007).

The prognosis differs between adult and children and young people, and young people, in contrast to adults, more frequently recover from the disease (Joyce, Hotopf, & Wessely, 1997; Rangel et al., 2000; Tiersky et al., 2001).

2.3 Pain
The International Association for the Study of Pain (IASP) defines pain as “An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (Merskey & Bogduk, 1994). Another well-known definition of pain recognizes the person’s own experience and the person’s own right to define what pain is: “Pain is whatever the experiencing person says it is, existing whenever he says it does” (McCaffery & Beebe, 1994). These
two definitions are often cited together and cover physical and emotional factors in addition to the individual experience of pain. Another important key issue is that the definitions call upon others (healthcare professionals) to take all kinds of pain seriously. Several researchers have called for pain control to be recognized as a major health issue and a human right (IASP Clinical updates 2004).

In a survey of chronic pain in Europe, Breivik et al. (2006) found that pain is often overlooked by doctors, and the authors stress that it is equally important to handle the chronic pain resulting from a disease as it is to treat the underlying condition (H. Breivik, Collett, Ventafridda, Cohen, & Gallacher, 2006). Few respondents in the survey reported being exposed to a multidisciplinary and cognitive treatment, despite the documented effect of such an approach. The lack of such a treatment is built upon an outdated view on and treatment of pain:

“....if one assumes that functional pain disorders emerge from a composite of biological vulnerability and psychosocial factors which jointly create abnormalities of pain processing or the misperception of those signals, then the notion that pain can be categorized as strictly physical or psychological is highly outdated and in fact destructive” (Patrick J McGrath, Stevens, Walker, & Zempsky, 2014).

This notion underpins multiple factors involved in the perception of pain and may indicate why pain frequently cannot necessarily be measured or localized to well-defined body sites. A recent published study found that chronic pain patients without clear signs and medically explained reasons for their pain, experienced distrust from health care professionals (Ojala et al., 2015). The lack of understanding from health care professionals might explain why pain is not met with a multidisciplinary approach.

Persistent and recurrent pain, lasting for more than three months, is defined as chronic (IASP, 1994), either due to a chronic disease, or of unknown origin. It is relatively common and a major health problem in children and adolescents (King et al., 2011). The prevalence of pain increases with
age and is more common in girls than in boys (Haraldstad, Sorum, Eide, Natvig, & Helseth, 2011; Hoftun, Romundstad, Zwart, & Rygg, 2011; Perquin et al., 2000).

A great deal of research has focused on single pain sites. In an epidemiological study, King et al. (2011) found that headache is the most commonly studied single pain in children and adolescents, with a median prevalence of 23%, but that the variation was huge, ranging from 8% to 83%. In an Scandinavian sample of children with chronic pain, Fichtel and Larsson (2002) found that 15% suffered from four or more pain sites (Fichtel & Larsson, 2002); and among Norwegian adolescents with chronic idiopathic pain, Hoftun et al. (2011) 25% reported pain in at least two locations, and that multisite pain was more prevalent than single site pain. The most common pain was musculoskeletal followed by headache and migraine. Generalized pain as well as headache and musculoskeletal pain are common in this group of patients (S. L. Nijhof et al., 2011; Wyller, 2007).

Cognitive processes are an important factor for the perception of pain. Hood et al. (2012) found that there is a protective link between optimism and pain perception. People with a trait of optimism have lower catastrophizing thoughts related to pain, and experience less pain (Hood, Pulvers, Carrillo, Merchant, & Thomas, 2012). Catastrophizing about pain, in contrast, leads to more intense pain and higher disability, and might further lead to avoidance behavior and physical inactivity (Leeuw et al., 2007). Also in CFS patients, the perception of pain has been shown to be influenced by negative and maladaptive thoughts, emotions, cognitions, and behaviors such as catastrophizing, hypervigilance, and avoidance behavior (Meeus & Nijs, 2007). Sometimes pain might be experienced as so intense, stealing focus in such a way, that nothing else than pain matters (Vetlese, 2004).

Existential thoughts and worries might also emerge in adolescents with CFS (Jelbert et al., 2010). When suffering an illness, the body becomes different, is experienced as alienated or broken, which contributes experiences like helplessness, resistance and lack of control (Svenaeus, 2000), which might be painful.
Pain is a complex phenomenon with both physical and mental components that can hardly be seen as either physical or mental (Vetlesen, 2004). The “origin” of pain might stem from a physical trauma or injury, or from mental stresses like experiences of loss, grief or “heartbreak”. The expression, however, regardless of origin, might be somatic (headache, stomach pain) (Vetlesen, 2004). Studying an adult CFS population, emotional trauma in early childhood was found to predict increasing levels of bodily symptoms, and may also be important in patients with CFS (Kempke, Luyten, Claes, Van Wambeke, et al., 2013). Within the frame of caring science, suffering is seen as a natural part of life (Eriksson, 1995). Suffering might be described as the suffering of illness, the suffering of life and the suffering of care given (Eriksson, 1995). According to Eriksson the suffering of illness is the suffering experienced in relation to illness and treatment, while the suffering of life is suffering experienced in relation to one’s own life (to live or not to live), and is also about loneliness. Seen in such a perspective, adolescents suffering from CFS have the components of suffering of illness as well as the suffering of life; that is being unable to participate in normal activities, absence from school, and loss of friends (Fisher & Crawley, 2013; Jelbert et al., 2010). Pain that is chronic and unexplained has in adolescents been associated with poor HRQOL for both the adolescents and for their families (Hunfeld et al., 2001).

The relation between fatigue and pain is still unclear; for instance, one study found that CBT for CFS was also effective for pain (in both adult and adolescents) without aiming at pain as the problem (Hans Knoop et al., 2007). For the adult patients, pain severity at baseline was associated with a negative treatment effect. Other researchers have hypothesized that pain is caused by an increased sensitivity in the nervous system (Meeus & Nijs, 2007; Meeus et al., 2010; Nijs et al., 2012), or that altered pain inhibition might be a potential factor in patients with generalized pain (Yarnitsky, 2010). In patients with CFS, pain is an essential symptom. This is also reflected through the diagnostic criteria for the disease (Fukuda et al., 1994).
2.4 Health related quality of life

The concept of Quality of Life (QOL) has been linked to the concept of health and can be described as “the individual’s perception of their position in life in the context of culture and value systems in which they live and in relation to their goals, expectations, standards and concerns” (Eiser & Morse, 2001).

Several terms have been used to describe QOL such as health status, well-being, life satisfaction and happiness (Ferrans et al., 2005). Due to the wide perspective of the term, including many aspects of life and not merely health related issues, the term Health Related Quality of life (HRQOL) is used when addressing health, illness, and medical treatment (Guyatt, Feeny, & Patrick, 1993). There is a consensus that HRQOL should include at least a physical, an emotional, and a social component of well-being and functioning, and be seen as a multidimensional construct (Bullinger, Schmidt, & Petersen, 2002). Taking all these aspects into account, HRQOL can be viewed as “a psychological construct which describes the physical, mental, social, psychological, and functional aspects of well-being and function from the patient perspective.” (Ravens-Sieberer & Bullinger, 1998).

Research on HRQOL is a relatively new field of research (Ravens-Sieberer et al., 2007), and even though a general definition of HRQOL for adults also might be applicable to children and adolescents (Matza, Swensen, Flood, Secnik, & Leidy, 2004), measures appropriate for the adult population do not necessarily cover child-specific issues (Ravens-Sieberer, Karow, Barthel, & Klasen, 2014). The child’s and parent’s perceptions of the child’s health are found to differ and have low to moderate correlation (Jozefiak, Larsson, Wichstrom, Mattejat, & Ravens-Sieberer, 2008; Upton, Lawford, & Eiser, 2008). Proxy reports should thus only be used as an additional source of information, since the disease is solely perceived and experienced by the children themselves (Ravens-Sieberer, Devine, et al., 2014). In order to develop HRQOL measures for children, WHO (1994), demand that “such measures should be age-appropriate and child centered, preferably take into account self-reporting, be usable independently of the health status and cross-culturally, and should include both positive and negative aspects of the relevant domains” (WHO, 1994). Among the
relevant domains/dimensions that should be considered are their self-perception, self-esteem, parent-relation, and aspects related to school (Ravens-Sieberer, Karow, et al., 2014). Supporting the relevance of these domains, a Norwegian study found that good family relations, good friends and a positive self-image were important factors in adolescents’ HRQOL (Helseth & Misvaer, 2010).

Taking into account that HRQOL can be seen as a multidimensional and subjective construct, the following definition is preferred as an overall definition for the present work “HRQOL is a multidimensional construct covering physical, emotional, mental, social and behavioral components of well-being and functioning as perceived by patients and/or other observers” (Bullinger et al., 2002).

Although peers are found to be important to adolescents, the quality of a peer relationship and HRQOL has hardly been studied (Frisen, 2007). This might be an important issue because quality of a peer relation might cover up for loss of friends when being ill. Chronically ill adolescents like those with CFS have limited contact with peers, and reduced quality of peer relations may possibly affect their HRQOL.

Perspectives of development are important to take into account when studying adolescent HRQOL; they are no longer children nor are they adults. Issues important to adolescents include intimate relations, sexuality, independence and striving for autonomy (Frisen, 2007), but also good relations with peers and parents (Helseth & Misvaer, 2010). Adolescents’ mental health is negatively affected if they are feeling lonely or if they lack a close, confidant friend (Hartberg & Hegna, 2014). Self-related health is relatively stable during adolescence, but deteriorates with lack of well-being or when afflicted with disabilities (Breidablik, Meland, & Lydersen, 2008).

Regarding a possible relationship between pain and HRQOL, Wahl et al. (2009) found no causal effect between pain and HRQOL in the adult population that they studied. What they found was that the relationship is confounded and/or mediated by socio-demographic variables, chronic illness, stress-related symptoms, fatigue and subjective health perceptions (Wahl et al., 2009). Factors that correlated most with HRQOL were negative emotions. In young schoolchildren (8–14), recurrent pain
conditions are common, and are associated with considerably impaired HRQOL (Petersen, Hagglof, & Bergstrom, 2009). In another study on children and adolescents (8–18), adolescents were more impaired in emotional functioning (measured by PedsQL) than were the group of children, which might be due to developmental issues in adolescence (Gold, Yetwin, et al., 2009). Another study found that fatigue functioned as a mediator between pain and overall HRQOL (Gold, Mahrer, Yee, & Palermo, 2009).

2.5 Health related quality of life in adolescents with CFS
Both pain and fatigue have shown to have great impact on physical activity in adolescents with CFS (E. Crawley & Sterne, 2009; Kennedy et al., 2010). Emotional disturbances like anxiety and depression are common in adolescents with CFS (Bould et al., 2013; Fisher & Crawley, 2013), and might well be intensified by social isolation (Fisher & Crawley, 2013). School absence because of the disabilities of CFS are common (S. L. Nijhof et al., 2011), and qualitative studies show that adolescents with CFS experience personal, social and academic losses as well as loss of hope for the future and confusion about identity (Fisher & Crawley, 2013; Jelbert et al., 2010); which means that living with CFS also affects the psychosocial aspects of life as well as physical aspects (Torres-Harding, Jordan, Jason, & Arias, 2006).

Physical activity, emotional well-being, friends and school attendance are areas that are affected in adolescents with CFS, and these are factors important to adolescents’ HRQOL (Varni, Seid, & Kurtin, 2001). Despite this, there are few studies on HRQOL in adolescents with CFS. These few studies have found that the HRQOL in adolescents with CFS is severely impaired, compared to that of healthy adolescents as well as adolescents with other chronic diseases such as type 1 diabetes and asthma (Kennedy et al., 2010).

2.6 Health and health models
The theoretical perspective chosen for this thesis is based upon both a biopsychosocial perspective and a life world perspective. The perspectives are best seen as complementary rather than contradictory. Different perspectives are necessary to understand the complex wholeness of both
the subjective experience of living with CFS, and pain and CFS as long-lasting conditions. Even though this is part of a larger project (NorCAPITAL), that bases the theoretical perspective on the theory of sustained arousal, this different perspective was considered appropriate. In the following, pain and CFS are discussed from the perspectives of illness and disease (2.8), which are rooted in the biomedical perspective and further, as well as from biopsychosocial perspective. The life world perspective is presented through narratives (2.9) and bodily expression (2.10).

CFS is among those diseases that are poorly understood (Natelson, 2001), with no clear etiology and no pharmacological cure. The large number of associated symptoms make it a challenge to understand this group of patients. It is likely that both pain and fatigue affect the HRQOL. Thus, CFS needs to be studied in a broader and integrated perspective beyond the biomedical perspective. Biomedical research has contributed to an enormous development of medicine that makes it possible to save lives, and the medical model of health has kept a focus on the absence of disease or disabilities, which has driven forward an advanced medical technology and knowledge (Larson, 1999). This focus has been criticized for neither taking into account emotional and psychiatric disorders, nor prevention of disease and its social causes (Culyer, 1983 | Larson 1999).

The fundamental philosophical question: What is a disease? is highly relevant (Hofmann, 2014), especially when studying CFS. WHO set a new and idealistic perspective on health. Health was first defined as “a state of complete physical, mental and social well-being and not merely absence of disease or infirmity” (WHO, 1948). Mental health was later defined as an integral part of health: “A state of well-being in which the individual realizes his or her abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community.”(WHO, 2001). WHO’s first health definition might be seen as impossible to accomplish, while the latter one emerges as more dynamic and achievable.

In 1977, Engel introduced a model adding psychological and social factors to the biomedical dimension, which was named the biopsychosocial model (Engel, 1977). The biopsychosocial
perspective on illness and disease was well-intentioned, aiming to add dimensions to the biomedical perspective on health, recognizing that issues related to health encompass more than what we are able to measure and to prove objectively. In the context of disease or illnesses, biological factors, psychological and social factors are essential in human functioning, and the model aimed to bridge the dualism of body and mind. The model has been criticized for the absence of a theory that seeks to understand how the different domains interact with each other (Quintner, Cohen, Buchanan, Katz, & Williamson, 2008). Further, Quintner et al. state that despite the effort to create an integrated model of pain, such models still perpetuate and remain inside the dualism of body and mind. Exploring the invisibility of pain in chronic pain patients, Ojala et al. (2015) found that pain without a clear pathology was considered to be imaginary pain (Ojala et al., 2015). The authors argue that dualism is still vivid in the understanding and treatment of pain, and that the biopsychosocial approach seems to be rhetorical. However, the biopsychosocial framework has been useful in broadening the perspective of the clinician, both on illnesses in general, and especially regarding pain (Quintner et al., 2008). Although it sheds light on the different components involved in a health problem, the important subjective experience of the patient is lacking. An integrated perspective on health, recognizing the subjective experience from a within perspective (taking into account the patient’s lived experience) might challenge our way of thinking, broaden our horizon and help us to achieve new perspectives. In such effort, it might be necessary to push aside what we intuitively think, while concentrating on what the patients convey to us.

2.7 Dualism and disease hierarchy
Unfortunately, the body and mind dualism is still alive, and our healthcare system is organized into psychiatric and somatic departments, functioning as separate disciplines, in which the dualistic view of the human is perpetuated. When we address CFS as an illness or disease, we focus on the etiology, namely whether the disease is caused by a “virus” (something from the outside world), or if it is caused by an internal, mental disturbance. Such a concept strongly influences how patients are treated. Another challenge is the terms we use. They are dependent on our knowledge, our view, or
whether we are a patient or a health care professional. The terms do not necessarily mean the same thing to doctor and patient, and health care professionals’ understanding of a phenomenon may differ from the patients’. A health problem with an unclear or unknown etiology might be categorized with the term “medically unexplained symptoms” (MUS) (Nimnuan, Hotopf, & Wessely, 2001), which describes illnesses with bodily complaints, but without a clear etiology, implying that the complaints cannot be fully explained by structurally based pathology (Creed et al., 2010). Even though the term MUS does not say anything about the etiology of the condition, the term is claimed to foster an underlying dualism, which points to a psychological cause rather than a biological one, although this might not be the intention of those using the term. Both for medical specialties and for diseases, a prestige rank exists, leading to stigma towards conditions that are ranked at the lower end (Album & Westin, 2008). Conditions that are associated with sophisticated technology and with a clear etiology tend to have higher prestige than chronic conditions without specific bodily location and with no technical treatment procedures available (Album & Westin, 2008). CFS is an illness that will fit under the MUS term. Despite the unexplained conditions that are based on subjective experiences (the MUS conditions), it is important that the illness does not get a second rank position, as though a person with this kind of condition is worth less than people with well-defined and more highly ranked diseases.

The terms and language we are using are not without significance and will probably affect the way we think about diseases and people affected. If we challenge ourselves to develop and to use words that could keep us aware of the complicated mechanism of the interplay within the human body, we might overcome some of the stigma attached to conditions that we cannot explain or prove (like diagnoses labeled MUS). Quintner (2008) proposes that we “move forward to explore the engagement of self-referential beings through the creative frame of language, in which the narrative of neither clinician nor patient is dominant, but the way they touch and grow in understanding, empathy, and shared outcomes is paramount” (Quintner et al., 2008). We might not get to the point where we can capture “life itself” by words alone, nevertheless; efforts are made to
introduce alternative terms containing a broader perspective. One such term is “the language of
wholeness”, which is “the expression and perception of expression in words, symbols, movement,
body language, touch and shaped sound associated with human activity in the broadest sense”
(Johannesen and Gulbrandsen, 2010). In a doctoral thesis, Melheim (2014) uses the term “the
language of wholeness” to emphasize the importance of using words that highlight diversity in
nuances, dimensions, contexts and modifications (Melheim, 2014). Also from other research
communities, questions concerning an integrated vocabulary are requested (Getz, Kirkengen, &
Ulvestad, 2011). Ulvestad, Kirkengen and Getz stress that there is a need for professional language
that enables conceptualizing of the body and mind as undivided and interacting. When such a need is
highlighted, it makes the division in the health care systems visible, as it is reflected in the general
population, which strikes back with questions about the body–mind dualism through critical
questions about causes and treatment. More specifically, disagreements regarding classifications of a
disease, the ranking of diseases, and language used among health care professionals will affect the
public. Patients have a subjective experience of being ill while the health care professionals have
theoretical and experienced-based knowledge about ill and diseased people. Acknowledging the
subjective experience and using a language that is consistent with a patient’s self-perception might
create a basis for mutual understanding. Such as: there is no pill or a medical cure for every
condition; suffering because of an incident or a difficult life condition might be solved by the patient
him- or herself with the help of an interlocutor rather than a pill.

Patients with pain might also experience that health care providers don’t understand them
(having “invisible pain”) and that communication with them is difficult (perceived illegitimacy) (Ojala
et al., 2015). This experience is equal to the experience some patients with CFS have (Fisher &
Crawley, 2013).

In science, it might be difficult or even impossible to understand a phenomenon of interest
without having knowledge of, or studying, different parts of it. By viewing the phenomenon from
different angles and then putting together the information acquired, new insight and knowledge might arise. Even if we highlight the importance of a holistic view, the danger might always be reductionism, which we might prevent by paying attention to this type of challenge.

2.8 Pain and CFS in an illness and disease perspective
Even though there are different ways of labeling the state of being unhealthy, the terms illness and disease, as Hofmann (2014) theorizes, are the terms used in this thesis. In the case of CFS, the terms are considered appropriate to illuminate the different challenges and views concerning CFS as it is noted in Chapter 2.6. In Norwegian, we have the word sykdom to describe an unhealthy body, but the word does not distinguish between being ill, having a disease or being in a role of a sick person. Sykdom is equal to the English word malady, which is an overarching term for the three different perspectives: disease, illness and sickness. These terms reflect malady from different angles and they might also correspond to the three approaches in the biopsychosocial model, as described below.

Disease refers to a diagnosis which is based on the objective and medical classification of health, and in which there is a treatment or a medical cure. Illness refers to a subjective bodily or mental experience of feeling unhealthy, while sickness refers to a public or social context (Hofmann, 2014). Toombs (1992) says that illness is grounded in lived experience while disease is an abstraction from lived experience (Toombs, 1993). Toombs further stresses that in the relation between the physician and the patient, a shared recognition between the fundamental difference between illness and disease is highly important in the relation between the physician and the patient. In this thesis, I will use both the terms illness and disease, and they will reflect the subjective experience and the objective medical view, respectively.

Both the perspectives of illness and disease, and the biopsychosocial perspective underpin the challenges of CFS and pain. The condition exists in the field of tension between the subjective experience and the objective diagnostic criteria, in which biological, psychological and social approaches are necessary to understand and treat these patients.
2.9 Reaching the life world through narratives.
Even though the perspective of illness is a subjective experience, health care professionals do not necessarily gain insight into the diverse aspects of how to live with an illness. This means that the terms lifeworld perspective and the illness perspective provide different information and knowledge, and are complementary, which enables a broader perspective. The phenomenological term lifeworld originates from Edmund Husserl’s texts (Helenius, 1990). Lifeworld is an expression for the world as it appears to us, the unspoken which constitutes both our background and our horizon (Hellesnes, 2002). A lifeworld perspective implies that the unspoken within the horizon of culture and subjectivity is the focus for interpretation of the qualitative data of this study. Despite thorough examinations within the health care system, adolescents with CFS’s own lifeworld perspective is seldom brought to our knowledge. One way to get insight and to gain such knowledge is to let the adolescents come to words through their narrated stories.

A narrative can be understood as a story, and the narrating person as the character in the story. The story told is always linked to others, and is always dependent on both desired and undesired behavior of others' (Ricoeur, 1992). As it is constituted in a dialectic movement between the past, the present and the future (Ricoeur in Lindseth and Nordberg, 2004), the listener (or the reader) may see the world from another view (Ricoeur, 1992). I understand this in the way that by being present, interviewing the adolescent, and responding to what he or she is telling; the interviewer contributes to the creation of the story, and the interviewer and the adolescent are creating the story together. This means that the adolescent also might discover new dimensions of themselves and their life through the narrative. Ezzy (1998) argues that self-identity is formed in a narrative, and that self-narrative through complex interactions between events, imagination, significant others, routines and habits form narrative identities (Ezzy, 1998). Ricoeur (1992) argues that creation of identity takes place in a dialectic process between identity as selfhood (ipse identity) and identity as sameness (idem identity). This is a dialectic process between stability and
changeability and is bound together in a meaningful whole through stories we create and tell about ourselves (Ricoeur, 1992).

This study rests upon a biomedical approach as well as a hermeneutic-phenomenological approach. Studying the subjective experience of phenomena like pain and fatigue through lifeworld narratives places this study in a phenomenological tradition. The use of interviews as a method to acquire information is hermeneutic, hence the text is analyzed through interpretation of meaning. This implies a dialectic movement back and forth in the material, using different theories to create a comprehensive picture of the phenomena. Hermeneutic and phenomenological approaches are grounded in two different traditions. Hermeneutics might be used as an approach and not a method per se, or as an ontological view. In the methodological sense, hermeneutics is a relationship between the reader and a text in which the reader sees the text in dialectic movements between own prejudices, pre-understanding, and the text, in an effort to provide new insight and understanding (Gadamer, 2010). Philosophical phenomenology, grounded by Edmund Husserl and further developed by Heidegger, is the study of phenomena experienced from the first-person point of view (Krogh, 2009). The philosopher Paul Ricoeur introduced critical hermeneutics, which questioned the old German distinction between physical science and spiritual science. Ricoeur emphasizes that hermeneutics is about the interpretation of a written text, and that interpretation of text can provide understanding of actions (Krogh, 2009). He asks what the text “talks about”, and that this must be interpreted to obtain comprehension rather than explanations. His effort to reconcile different scientific traditions has given him the name “bridge builder of hermeneutics” (Lægreid & Skorgen, 2006). From a medical perspective, phenomenology has relevance in three different areas: (1) experiences about living with a disease or the experience in the encounter with the diseased; (2) a method of empirical study through interviews that are transformed into a text, and (3) philosophical theory (ontology) working with questions like: what is health? or what is suffering? (Svenaeus, 2002). In this study, the first area concerns the stories of patients in a clinical
setting, the second persons’ experiences living with CFS, providing a text fixed through transcription. The third area is the theory of illness vs. disease as it is described in the section above (2.7).

Adolescence or early adulthood is suggested to be the broadest period of memory telling (Thorne, 2000). Because of this, the period of adolescence might be an excellent time for telling stories, and together with another person, making efforts to understand different events. According to Thorne (2000), meanings of events are characterized by emotions developed over time through reflection, where events are shared and compared with other experiences. Telling stories might be a unique opportunity for understanding personality and self-development. Storytelling through narratives is also suggested as a method to cope with serious conditions like grief (Bugge, Haugstvedt, Rokholt, Darbyshire, & Helseth, 2012), and it is common that while speaking, adolescents realize that they have learned something during their reflections (McCabe et al, 1991).

2.10 Bodily expression
Already from early childhood, bodily expressions, like crying, have a lower status than expressions through words (Rossholt, 2010). Rossholt wants us to rethink by putting the body first and to emphasize moving bodies, glances being exchanged and the energy that children and adults create together when they are placed together in a room. For the smallest children, crying is “allowed”, but for older children, efforts are made to stop the crying. There is no difference between children and adults regarding crying; the relief goes beyond age (Rossholt, 2010).

When Rossholt wants us to rethink, she is in line with the philosophy of Merleau-Ponty (1992), who argues that as humans we communicate with each other through the body. Our bodies are pre-reflexive, which means that phenomena affect the body as perceptions ahead of consciousness of mind; it follows that reflections are secondary to bodily sensation. “The lived body” is a central term in the philosophy of Merleau-Ponty. Further, the body is our appearance in the world, and the body is the means for our communication with the world (Merleau-Ponty, 2002). Communication with other people has succeeded when we confirm each other intersubjectively (Merleau-Ponty, 2002). As I understand Merleau-Ponty, he does not believe in a dualistic bodily view,
either the objective body as in a diseased body, or the subjective body as in illness. The body can only be understood and perceived as one unit, and not as consisting of several parts. Multiple factors might influence the way we communicate with other people. When one observes children play, their bodies are interwoven in the play; but teenagers move differently from small children, and interact with people in a different way. In the development from child to adolescence, different factors have changed how they communicate. The development of expressions might be illustrated by this quote from Braatøy (1952); «before words and sentences there was singing. Before singing there was movement, dance. Ahead of intentional movement, there was rocking and hovering” (Braatøy 1952, in Sviland, 2010).

Bodily language will be discussed later, both how it might influence adolescents in different situations, and how the interaction between the respondents and the researcher might have influenced interviews and the material provided.

2.11 Comments
A historical perspective was presented at the beginning of this chapter, which I believe is a fruitful piece to understand some of the controversies linked to CFS. The report on CFS in adults as well as in children and adolescents has clarified some of the differences between the groups. Pain as well as disabling fatigue are essential symptoms, which contribute to the disabilities in the group of patients and which affect the health related quality of life. From Chapter 2.5, different perspectives and traditions related to health are presented. Different ways of verbal expressions through narratives, expressions through emotions and movements are presented at the end of the chapter. The different perspectives presented are all necessary in an effort to make a comprehensive understanding of CFS, and hopefully it will give the necessary background and bring insight to the field. I have not succeeded in finding a framework that is suitable to embrace these different (but interdependent) perspectives (illness and disease, biopsychosocial and lifeworld). In the contrary, fitting the perspectives into one specific frame would reduce the plurality.
3 Materials and methods

The present study “Pain and Quality of Life in Adolescents with Chronic Fatigue Syndrome” is funded by Oslo and Akershus University College of Applied Sciences (HIOA) and represents an independent part of the project named: “The Norwegian Study of Chronic Fatigue Syndrome in Adolescents: Pathophysiology and Intervention Trial” (NorCAPITAL) which also includes a randomized, double-blinded, placebo-controlled intervention trial. The NorCAPITAL project is based on the hypothesis that “sustained arousal” may explain CFS (Wyller et al., 2009), and aims to explore possible mechanisms of the disease (NorCAPITAL protocol, 2010). The project consists of a research group of six persons cooperating on planning the study, recruiting participants, collecting and storing data.

The present study includes the same patients as the NorCAPITAL study, (see the next sections), but has a mixed method design. Some baseline data from the interventional part of the NorCAPITAL are used. Figure 1 provides an illustration of the NorCAPITAL project. Figure 2 illustrates the project of this thesis. The dotted line squares in Figure 1 illustrate the baseline data, which have been used in the present study.
All pediatric departments in Norwegian hospitals (n=20), primary care pediatricians and general practitioners were invited in Norwegian to refer adolescents with CFS, aged 12 to 18 years, to a central pediatric department. The referring units were required to confirm that the patients did not have any medical or psychiatric disorder that might explain the fatigue. In agreement with clinical
guidelines (National Institute of Health and Care Excelence, 2007; Royal College of Paediatrics and Child Health, 2004) a “broad” case definition with three months of unexplained, disabling fatigue of new onset was required. Criteria for inclusion are outlined in Table 1. In the adult CFS population and for research purposes, the CDC criteria for CFS are often used as diagnostic criteria for CFS and sub-analysis subsequently showed that 84 per cent of our adolescent study population satisfied these criteria.

Table 1: Criteria for inclusion and exclusion

<table>
<thead>
<tr>
<th>Inclusion criteria:</th>
<th>Healthy control subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFS patients</td>
<td>Age ≥ 12 years and &lt; 18 years</td>
</tr>
<tr>
<td>Persisting or constantly relapsing fatigue lasting 3 months or more.</td>
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<tr>
<td>Functional disability resulting from fatigue to a degree that prevents normal school attendance</td>
<td></td>
</tr>
<tr>
<td>Age ≥ 12 and &lt; 18 years</td>
<td></td>
</tr>
<tr>
<td>Exclusion criteria:</td>
<td>Another chronic disease</td>
</tr>
<tr>
<td>CFS patients</td>
<td>Permanent use of pharmaceuticals (including hormones)</td>
</tr>
<tr>
<td>Another current process or chronic disease or demanding life event that might explain the fatigue</td>
<td></td>
</tr>
<tr>
<td>Permanent use of pharmaceuticals (including hormones) possibly interfering with the measurements</td>
<td></td>
</tr>
<tr>
<td>Permanently bed-ridden</td>
<td></td>
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<tr>
<td>Positive pregnancy test</td>
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<tr>
<td>Pheochromocytoma</td>
<td></td>
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<tr>
<td>Evidence of reduced cerebral and/or peripheral circulation due to vessel disease</td>
<td></td>
</tr>
<tr>
<td>Polyneuropathy</td>
<td></td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td></td>
</tr>
<tr>
<td>Known hypersensitivity towards clonidine or inert substances (lactose, saccharose) in capsule</td>
<td></td>
</tr>
<tr>
<td>Abnormal ECG (apart from ectopic beats)</td>
<td></td>
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<tr>
<td>Supine heart rate &lt; 50 beats/min</td>
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<tr>
<td>Supine systolic blood pressure &lt; 85 mmHg</td>
<td></td>
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<tr>
<td>Upright systolic blood pressure fall &gt; 30 mmHg</td>
<td></td>
</tr>
<tr>
<td>Healthy control subjects</td>
<td></td>
</tr>
</tbody>
</table>

The criteria are designed for the randomized control trial in the NorCAPITAL-project (The Norwegian Study of Chronic Fatigue Syndrome in Adolescents: Pathophysiology and Intervention Trial; Clinical Trials ID: NCT01040429), which explores possible mechanisms of CFS, the effect of low-dose clonidine treatment, and patients’ experiences as adolescents with CFS.

Based upon a computer based routine, and operated by a study nurse, patients were consecutively randomized to either clonidine (Catapresan® 25μ) or placebo, ratio 1:1. All patients were recruited to either a regular or an extended research program. Patients went through the same investigational program both at baseline, 9 weeks and 30 weeks after inclusion. Patients were either given clonidine or placebo for 9 weeks and both patients and the researchers were blinded to treatment allocation at all stages. A thorough description of the investigational program in the overall project is described elsewhere (Sulheim et al., 2014), while procedures and measures relevant for the present study are described in more detail (Chapter 3).
3.1 Participants
Between March 2010 and March 2012, 120 adolescents (12–18) with CFS were included in the NorCAPITAL project. Data collection ended in October 2012. In total, 176 adolescents with CFS were referred to the project and assessed for eligibility. Patients were recruited from all over Norway, but the majority of the patients came from eastern Norway. Approximately two thirds were girls (86) and one third were boys (34). Mean age for the whole sample of patients was 15.4 years. In the same period, a control group of 39 adolescents equally distributed by age and gender were recruited from local schools. Additionally, 29 healthy adolescents were recruited for blood analyses in the RCT (Figure 1), but these data are not used in this thesis. Of the CFS patients, 39 were randomized to a more extensive research program. Twenty-five were interviewed; 18 by the researcher regarding experiences of living with CFS, and included in pain and quality of life in adolescents with CFS, and seven by an occupational therapist for her master’s degree (Njølstad, 2012). Gender distribution was the same as for the total number of patients (n: 120) and mean age was 14.8 years.

We also analyzed data from two other Norwegian studies on health related quality of life (Diseth, Tangeraas, Reinfjell, & Bjerre, 2011; Reinfjell, Diseth, Veenstra, & Vikan, 2006) to check if our control group could be considered reliable. Comparing the standard deviation and confidence intervals in all three studies, it is likely that our group of healthy adolescents is large enough to function as a control group in our study (Paper 3).

In the following, I will discuss the different approaches used in this mixed methods study.

3.2 This study - a mixed method approach
From my point of view, we need a multi-angle and multi-method approach to explore and understand the disease and phenomenon CFS. The present study has both qualitative lifeworld interviews to explore adolescents’ own experiences living with CFS, questionnaires to investigate the extent of pain, depressive symptoms and quality of life as it is reported and expressed by the adolescents themselves, and algometry to study the pain sensitivity and pressure pain thresholds. It is important to emphasize that all methods measure subjectively experienced phenomena. The
approaches represent different scientific approaches, but might provide a more complete picture of the phenomenon being studied (Johnson, 2007). Mixed method research has been considered the “third way” and a logical or practical alternative to either quantitative or qualitative research, with the aim of using the best from different paradigms (Johnson & Onwuegbuzie, 2004), acknowledging that both qualitative and quantitative paradigms have strengths and weaknesses. Several terms have been used for the mixed method approach. Johnson and Onwuegbuzie (2004) define mixed method research as: “the class of research where the researcher mixes or combines quantitative and qualitative research techniques, methods, approaches, concepts or language into a single study” (Johnson & Onwuegbuzie, 2004). Creswell et al. define mixed method study as; “A mixed method study involves the collection of analysis of both quantitative and qualitative data in a single study in which the data are collected concurrently or sequentially, are given a priority, and involve the integration of the data at one or more stages in the process of research.” (Creswell, 2014). In the present study, data are provided concurrently and the study has been carried out attempting to give different kinds of data equal priority; but the results made it necessary to give the qualitative data slightly more attention. A crucial question concerning the definition of a mixed-method design, is whether the findings are mixed or integrated at some point (Johnson & Onwuegbuzie, 2004). I define this PhD work as one study, consisting of three papers with different kinds of data. Findings from the three papers are integrated in the discussion, ensuring the requirement of mixing.
3.3 Qualitative work (Paper I)

The goal in qualitative interviewing is to gain empirical information from the person’s own perspective, including descriptions of herself/himself and the lifeworld that he or she has to deal with (Fog, 2004). In the interviews for the study, 18 adolescents emphasize their own experiences of living with CFS. One interview was excluded due to doubt about the diagnosis. All interviews were audio-recorded and lasted from 15 to 50 minutes, with an average length of half an hour. Due to difficulties regarding room facilities, the interviews were carried out in different surroundings; some took place in an office, and others in a room protected from noise and other people, and with comfortable chairs. Other interviews were interrupted because people inadvertently entered the room. In a couple of cases, this interrupted the respondent in such a way that it was not possible to regain the same optimal atmosphere and conversation.

*Questionnaires used in paper 2. **Questionnaires and assessments used in paper 3.
3.3.1 Preparing the interviews
A semi-structured interview guide was developed on the basis of the experience gained by working with adolescents, theory and research on CFS, HRQOL, pain and adolescents (Appendix 2). A psychiatrist and my supervisors were consulted during the work with the guide. To test the guide and to develop skills in interviewing adolescents, four pilot interviews were performed. The quality of the interview improved with increasing skills of the interviewer (Kvale & Brinkmann, 2009). The pilot patients were not included in the material of the main project, nor included in the present study; this because the number of tests was lower, and the clinical conditions different from those in the main project. There were no substantial differences between questions used for the pilots or for those included in the study. The main difference was the way questions were asked, and how they were followed up. Some of the questions were changed from the first to last participant. For example, the question about friends changed from a direct question about how they got along with friends, to a question that encouraged them to describe what a good friend would be like.

3.3.2 Interviewing children/adolescents
In the interviews I aimed to focus on “how to live” rather than the illness itself. The participants were encouraged to speak as freely as they could, yet in the framework of being an adolescent living with CFS. Further, I started telling a bit about what I worked with and what I liked to do in my spare time. The opening question was the same for all, but the follow up questions were different depending on what the adolescent focused on and what was revealed as important to them.

At the beginning, doing the first interviews, I was nervous and probably too bound to the guide in an effort to ensure myself that I asked all the questions. In addition, I was afraid that the adolescents might feel uncomfortable in the situation talking with me with so much focus on them. Engelsrud (2005) outlines how the researcher’s state, behavior and body language interferes with the participants when they are narrating (Engelsrud, 2005). As I gained confidence and skill, I managed to focus on the adolescent rather than the interview guide. This made it easier to recognize topics important to the adolescents. During the conversation, I could follow up the topics when
appropriate, and follow-up questions were adapted to each individual's ability and willingness to share thoughts and experiences. As I became more present, showed more interest and ensured time to answer the questions, the interviews became more like a conversation, like lifeworld, and the adolescents seemed more relaxed and were more willing to answer (Borjesson, 2013). Silence may be an important instrument in interviews/conversations (time to think and to have reflections), but silence can also be felt as a threat (Kvale & Brinkmann, 2009). It was a challenge to find the balance between good silence and silence that could be uncomfortable or potentially threatening to the adolescent, and occasionally I started talking a bit early, potentially interrupting a chain of thought. The focus of the interviews was not limited to challenges, but several reported being afraid that other people would think they were only moaning. Therefore, they did not wish to complain. It seemed as if they felt a relief to be allowed to talk about all the challenges in their everyday life. One of the adolescents replied that she felt relieved when given the opportunity to talk and be listened to. She also felt that the questions she was asked made her think about feelings and thoughts that she usually did not retrieve.

Other factors that might have influenced the interviews could be gender and age related. In both the pilot and the study interviews, I experienced that it was easier to have a conversation with the girls compared to the boys, especially among the youngest ones. The youngest boys were often reticent, responded to my questions with brief answers, and did not easily share their own thoughts or reflections. There is an age-related range in cognitive development and level of communication competency which also influences the relation between researcher and respondent (Kirk, 2007). A few girls started to cry during the interview. They were asked if they wanted to stop the interview, but they all wanted to continue. Two of them needed a break, but voluntarily came back and continued the interview. I experienced the connection with these girls as good, but to ensure that they did not leave the session with a bad feeling, they were asked how the interview experience had been and if the situation had been difficult for them. They all expressed that it had been a good experience, and one of them even started to tell some more, as this was not audio recorded.
3.4 Transcriptions
The interviews were tape recorded and transcribed word by word. By doing the transcription myself, I became familiar with the material. Occasionally, it was difficult to hear what the respondent said and in such cases, I made notes in the transcribed text. The reason for the difficulties could be a weak voice, environmental noise, speaking in chorus or a laugh. Laughter was frequently used when a respondent seemed uncertain or frustrated, to make some statements milder, or after a mutual understanding of a situation as humorous. Some respondents used irony or laughter, others emotional expressions like crying. Such situations were marked in the text as reflection notes.

Respondents came from different parts of the country and had different kinds of dialects. Norwegian “bokmål” was the transcribed language. The texts were cleaned and the respondent given a fictive name.

After each interview, I made research notes regarding my experience during the interview. The notes were typically about the arrangements, whether there were interruptions, and about the behavior of the adolescent. The notes made me aware of different aspects and made it possible to change the way I asked questions, or the way I responded to answers from the adolescent. In addition, reading the notes and transcribing the interviews made me adjust a couple of questions in the interview guide. For example, when I recognized that talking about friends was difficult, I changed the question by asking; “how would you describe a good friend?” This seemed easier to answer and often they started to talk about friends (or lack of friends) on their own initiative. Being flexible and creative in the interview setting is considered a strength (Sandelowski, 1993).

3.5 My preconceptions, skills and limitations
My clinical background as a nurse working with children and adolescents with CFS was a benefit in preparation of the PhD studies. It helped me find a focus for the studies; it made me curious about the adolescents’ own experiences and views. My experience also represented a basis when preparing the interview guide. However, my background included limitations in the sense that I thought I knew more than I actually did. During the research process, I now and then encountered my pre-
understanding and prejudices. The large number of uncertainties make CFS a difficult disease to understand, not only for patients and the public, but also for health professionals.

As the instrument in acquiring information (Kvale, 2009), my ability to facilitate an atmosphere, to create trust and a good rapport with the adolescents was crucial for collection of the information and knowledge. Upon inclusion, the procedures included taking blood samples. This was a task most of the adolescents feared. However, performing this procedure, I managed to create a kind of trust and alliance with the adolescents. I always informed them what I was going to do; asked what worried them and how they wanted me to do the procedure. Some wanted me to inform about every step of the procedure while others did not want to know anything. Some watched while others turned their heads away. My purpose was to let the adolescents have some sense of control over the situation. To deflect them, my research fellow or I always talked with them about what they liked to do or helped them imagine a joyful event or activity. In this way, the stressful event turned into a situation where we got the opportunity to become familiar with each other and to create trust and confidence. I believe this was an advantage for the adolescents and me for the interview setting.

The data and the information were created in a dialectic movement between the adolescent and me, or as Kvale (2009, p. 99) writes “in the interaction between the interviewer and the respondent”. I felt that I managed to create a good rapport with most of the adolescents, especially the girls. However, with some others I did not manage to create the same kind of relation. Maybe I was too nervous, did not have the skill to talk to the youngest boys, or was too bound up with the interview guide.

3.6 Analysis- A phenomenological hermeneutical method
To analyze lifeworld experiences, a phenomenological, hermeneutical approach inspired by Ricoeur and specifically developed for analyzing lifeworld interviews by Lindseth and Norberg (2004), was used. While hermeneutics is about the interpretation of text, phenomenology is about understanding good and bad experiences expressed in a text (Lindseth & Norberg 2004). The aim of the interviews with adolescents with CFS was to understand how they experienced living their adolescent life with
CFS. The purpose of the phenomenological approach in this study was not to describe and explain, but to understand the meaning of the experience of living with CFS, as it is expressed in the interview text. To achieve a comprehensive understanding of the lived experiences, three methodological steps were followed in the analysis: naive reading, thematic structural analysis and comprehensive understanding (Lindseth & Norberg, 2004).

3.6.1 Initial reading
The first step, working with the transcribed text, was as open-minded as possible, to read the text several times and to grasp a sense of the whole. In this setting, being open minded served to bracket my pre-understanding and to interpret what the text presents. Reflections were noted in the margins while reading, and discussed with my supervisors. Later on in the analysis, the notes were used to form themes and sub-themes. When no more reflections emerged, a summary for each interview was written. It was termed naive understanding (Lindseth & Norberg, 2004), and was used as a guide in the process of analysis.

3.6.2 Thematic structural analysis
Bearing the research question in mind, a thematic structural analysis was performed by identifying meaning units from the transcribed interviews. The meaning unit was as long (or short) as necessary to express a meaning. The meaning unit could be a few words, a sentence or a whole paragraph. Together with the naive understanding and reflection notes, the meaning units were reflected on in conjunction with the naive understanding and then condensed. The condensed meaning units were read through while looking for similarities and differences. Themes and sub-themes were identified, and written on “Post it”-stickers, before they were sorted. Some themes were hard to categorize because they covered more than one theme, or they could lead to change in a theme, providing a more suitable theme. Main themes that emerged as essential phenomena were finally added into the matrix. The phenomena “illness, body and me” from different respondents are presented as example in the appendix 3.
3.6.3 Comprehensive understanding
Both main themes, themes and sub-themes were summarized and reflected on in conjunction with the structural analysis, the authors’ pre-understanding, the literature and the naive understanding, resulting in a comprehensive understanding. The results are expressed in the findings and discussion in Paper 3.

3.7 Quantitative work (Papers II and III)
Based on the plurality of symptoms and disabilities in adolescents with CFS, the amount of tests and measures in the main project became extensive. This made it challenging to fill in all the questionnaires within the framework of time available with the adolescents. The majority of questionnaires were filled in by the adolescents at home and then returned to our research team in a pre-stamped envelope. Some questionnaires, such as the Brief Pain Inventory were filled in together with a researcher. In these cases the researcher read the question aloud while the participant answered by filling in the questionnaire. Measures used in the present work are a selection from the main project, planned for the present study and include the Brief Pain Inventory to explore pain, PedsQL to measure health related quality of life, the Mood and Feelings Questionnaire to measure depressive symptoms and single item questions to explore the frequency of pain. A well-known symptom in patients with CFS is hypersensitivity towards sound and light (Fukuda et al., 1994). We wanted to investigate if adolescents with CFS were hypersensitive to pain as well, demonstrated by the pressure pain threshold. These measures were performed during their stay at our hospital. All measures were carried out on a comparable group of healthy adolescents as well. Our reference group of healthy adolescents was smaller than the group of adolescents with CFS. Data from the Brief Pain Inventory and PedsQL (health related quality of life) and pressure pain threshold measurements, are only published in this thesis, while demographic data, the Mood and Feelings Questionnaire (depression) are presented in other papers from the research group of NorCAPITAL.
3.7.1 Sociodemographic measures
Some of the sociodemographic data considered relevant was gender, age, parents’ education, school absence and disease duration, and these data were self-reported. One of the researchers measured weight and height basis for computing body mass index.

3.7.2 Body mass index
Overweight and obesity might have an impact on adolescents’ health related quality of life (Buttitta, Iliescu, Rousseau, & Guerrien, 2014). Body mass index (BMI) was therefore included. BMI was calculated as weight in kilograms divided by height in squared meters and adjusted for age and gender in line with the recommendations from the Norwegian public authorities (The Norwegian Directorate of Health, 2010). Body mass index ≤ 25 was considered as a measure for normal weight, body mass index >25 as moderate overweight and body mass index ≥30 as severe overweight.

3.7.3 Brief Pain Inventory
The Brief Pain Inventory was used to assess the intensity of pain and to what extent pain interfered with different aspects of life (Cleeland & Ryan, 1994). The Norwegian version of the Brief Pain Inventory has been validated in patient with malign diseases (Klepstad et al., 2002), and in adults and youths with several chronic non-malign and musculoskeletal disorders (J. Engel, 2009; Tan, Jensen, Thornby, & Shanti, 2004; Williams & Arnold, 2011). The Brief Pain Inventory consists of an eleven-point numeric rating scale from 0 (no pain) to 10 (worst pain imaginable) The scale has been shown appropriate for children from 5 years of age (Gaffney, 2003). The responses to the questions can be expressed through a total pain severity score and a pain interference score. The total pain severity score is expressed as the mean of the four pain intensity items, while the total pain interference score is obtained by calculating the mean of the seven interference items (Williams & Arnold, 2011). The Brief Pain Inventory also consists of a body map in which the participant can indicate the location of pain by shading the areas corresponding to painful areas of their body. The body map is divided into seven areas; head, neck/shoulder, chest, back, abdomen, upper limb, lower limb (Figure 3). We only asked the participants to shade areas, without specifying a tissue source for the pain.
3.7.4 Frequency of Pain
Regarding pain frequency, we concentrated on headache, pain in muscles, pain in joint(s), and pain in the abdomen. The questions were obtained from a comprehensive CFS questionnaire that was used in the NorCAPITAL study (Sulheim et al., 2014). The questionnaire consisted of demographically related questions, frequency of common symptoms in CFS patients, including the eight accompanying symptoms of the CDC-definition of CFS. On a 0-5 point Likert scale (never/rarely present to present all of the time), participants are asked to rate how much of a problem each symptom presents.

3.7.5 Pressure pain thresholds
As part of the investigation of pain, we wanted to measure hypersensitivity towards pain in adolescents with CFS and healthy adolescents. Further, we wanted to see if there were any differences between the two groups. Pressure pain threshold is a reliable procedure to measure mechanical hyperalgesia in superficial structures like skin, nails and underlying muscles (Nie, Arendt-Nielsen, Andersen, & Graven-Nielsen, 2005). The International Association for the Study of Pain (1986) defines the pain threshold as “the minimum intensity of a stimulus that is perceived as painful.” (International Association for the Study of Pain, 1986). Pain thresholds were measured using a commercially available force transducer with a rubber tip of 0.5 cm² (Algometer, JTECH, medical, Salt Lake City, USA). The fingernail of the third finger, skin superficial to the trapezius (ascending part) and the supraspinatus muscles were the three pre-defined sites for the measures. We wanted to measure pressure pain thresholds on both symptomatic (trapezius and supraspinatus) and asymptomatic/remote (fingernails) places because this may indicate a general hypersensitivity (Nijs et al., 2012). We measured the thresholds bilaterally for every single person, repeated the measures and assessed all sites in the same order for every adolescent. The respondents were informed about the procedure, which was to increase the intensity of the pressure until the pressure pain threshold was reached. The participants were thoroughly instructed to indicate the pain threshold by saying “stop” or to use a word or sound of their choice. In between the two measurements, they filled in the BPI assessment form, which took about ten minutes to complete.
3.7.6 Pediatric quality of life inventory
The Pediatric Quality of Life Inventory (PedsQL) is a 23-item questionnaire developed to assess the overall HRQOL in children and adolescents aged between 5 and 18 years. The self-report questionnaire is available in different versions dependent on age (5–7, 8-12, 13–18 years) and is also available as proxy-reports (2–4, 5–7, 8–12, 13–18 years), assessing parents’ perceptions of their child’s HRQOL. Sub-grouping the questions enables assessment of the four HRQOL-domains: physical functioning, emotional functioning, social functioning and school functioning (Varni et al., 2001). In addition, a physical health summary score (eight items) and a psychosocial health summary score (15 items) can be computed. The later version for adolescents (13–18 years) was used in this study, and no proxy-reports were available. On a 0-4 point Likert scale (never a problem – almost always a problem), participants are asked to rate how much of a problem each item has been during the previous month. Items are reverse-scored and linearly transformed on a scale ranging from 0–100, in which higher scores indicate better HRQOL. Scale scores are computed as the sum of the items divided by the number of items answered (Varni et al., 2001).

3.7.7 Mood and Feelings Questionnaire
The Mood and Feelings Questionnaire is an instrument that measures levels of depressive symptoms in children and adolescents (Daviss et al., 2006). There are different versions for children and adolescents consisting of 33 items, and a version for proxies as well, consisting of 34 items. Only the self-measured version for children was used in this work (Paper 3). The alternative answers are ranked from 0–2; 0 = “not true”, 1= “sometimes” while 2= “true”. In the children and adolescent version, the total score ranges from 0 to 66. Daviss et al. (2006) suggest that a score $\geq 20$ implies presence of depressive symptoms to a degree that suggests mood disorders, while a higher cut-off of 29 indicates having major depressive symptoms (Daviss et al., 2006). We chose a cut-off $\geq 20$, hence this is the cut off used in the NorCAPITAL study.

3.8 Data analysis and statistical methods
Data analyses were performed using SPSS, version IBM Statistic 20 and 21. In this project, there were few missing data in the datasets; therefore, we did not use any data imputation methods except for
Paper 3 where values were imputed when the proportion of missing data was less than 10 percent for a given item. Missing values were estimated by calculating the mean of the item for all participants. There are many methodological problems connected to data imputation and they might be a threat to the statistical power (Fayers & Machin, 2009). Missing seldom occurs at random, and any simple imputation may therefore introduce a bias. Therefore, we invested a great deal of effort to achieve an almost complete data set and imputed only when the proportion of missing data was low.

In Paper 2, continuous variables are presented with medians and ranges while categorical variables are described as counts and percentages. Pain intensity and pain interference were measured on ordinal scales with a limited range, and group differences were therefore analyzed by a non-parametric test (Mann-Whitney-Wilcoxon test). To assess possible association between pairs of categorical variables, the $\chi^2$ test was applied. An average of two pain pressure threshold measurements was calculated for three body parts on each body side. As the values were normally distributed in both groups, they were compared using two independent samples $t$-tests.

To assess internal consistency of the instruments, Cronbach’s $\alpha$ was computed separately for cases and controls. An $\alpha$>0.7 was considered acceptable. All tests were two-sided and, due to multiple testing, only $p$ values <0.01 were considered statistically significant.

In Paper 3, continuous data (age and disease duration) are presented as means with $SD$ while categorical data (gender, parents’ education and adjusted BMI) are presented as numbers and percentages. Crude differences between cases and HCs concerning gender and BMI were assessed using the $\chi^2$ tests. Missing values were imputed when less than 10% of the values for all items given for the individual were missing. Regarding single items, there were only four values missing for cases and two missing for HCs. To replace missing values, we used the mean score for each HRQOL variable. To investigate the differences between CFS patients and HCs, we fitted a linear regression model for overall HRQOL (dependent variable) separately for each of the domains, and adjusted for
gender, depressive symptoms and BMI (in categories). BMI did not reach the level of statistical significance, and was therefore excluded from further analyses. The risk of having depressive symptoms (dichotomized dependent variables) was modeled using logistic regression models adjusted for gender and BMI. All the linear regression models, that is linear regression for HRQOL and the sub-categories, and the logistic regression models for HRQOL and depressive symptoms, fitted the data well (goodness of model fit). All residuals were approximately normally distributed in the linear regression models and the results are presented as estimates of beta (B) with 95% confidence intervals (CI). The results of logistic regression are presented as odds ratios (OR) with 95%CI. P-values <0.05 were considered statistically significant, and all tests were two-sided.

3.9 Ethical Considerations
3.9.1 Informed consent
Children might be physically or cognitive immature and might therefore have limited ability or rights to decide (Fossheim, Hølen, & Ingierd, 2013). In this study, we requested the minimum age of twelve years of age for inclusion. After oral and written information, written informed consent was given both by the adolescents and by their parents/next-of-kin. According to guidelines, parents/next of kin do not give their consent for healthy adolescents between 16 and 18 years, but because the NorCAPITAL project also included a drug intervention, informed consent was required for patients up to 18 is in line with the guidelines from The Norwegian Medicines Agency (SLV) (Statens legemiddelverk). The adolescents were given the opportunity to bring one of their parents to join the interview, but no one did. Information about the shape of and time limit for the interview, and their right to withdraw at any time, was given prior to the session. They were also told that they could have a break from the interview at any time. An important aim for the interviewer is to gain confidence from the adolescents (Kirk, 2007). Thus, the adolescents were told that they had to decide what to tell and that nothing of what they told would be looked upon as stupid or silly. The study was approved by the Norwegian Regional committee for Medical and Health Research Ethics (REK) and by the Norwegian Social Science Data Service (NSD).
3.9.2 Hearing the voice of children
In clinical work with children suffering from CFS and their parents, I have experienced that parents often speak on behalf of their children and some children do not speak up. I also have the impression that some children in the study were not familiar with speaking for themselves, and that this was not always due to shyness. As part of the medical examination, the parents were asked to leave the room so that the children could answer the questionnaire by themselves. In this setting, many children spoke more freely. The children’s and parents’ points of view are not always congruent and parents might not know their child as well as they believe. One mother told me that her child was shy and that I should not expect her to speak (or to tell me) very much. When we got on our own, the adolescent talked a lot, and she presented a very rich description of how life was. This may indicate that essential information from the child’s own point of view is not available when their parents are present and demonstrates the importance of giving the children the opportunity to speak freely.

Children’s right to participation and influence are embodied in the United Nations (UN) human rights articles (Convention on the Rights of the Child) and in Norwegian laws. In our society, children and adolescents are included in matters that concern them to a greater degree than they used to be. There are youth councils in municipalities and city districts and youth councils are established in several Norwegian hospitals. The Norwegian “barneombudet” [Office of the Commissioner for Children] stresses that children ought to be heard in matters that concern them. Rights are linked to individual autonomy and place requirements on the individual on the other hand Melheim (2014). Melheim (2014) discusses whether too much focus on rights might bring too much responsibility on the single child. Autonomy requires a balance between letting them speak up without laying too great a burden on them. We must not give them too much responsibility, but take into account their level of maturity and let them be heard.

In research, children and adolescents are considered a vulnerable group, and permission to interview children is sometimes difficult to receive (Fossheim et al., 2013). However, not to include children in research might exclude a large group of the Norwegian population. Often, children
experience participation in studies as useful (Dyregrov, Dyregrov, & Raundalen, 2000), which is demonstrated also in the present study (3.3.2). It is important to be sensitive to the uneven balance between a child and an adult researcher (Kirk, 2007). I ask the questions and they have a story I want to get in return. They are children, and it might be the parents who pushed them to participate. They are ill, and despite the careful information, some might have had difficulties foreseeing whether the interview would be to their benefit. An important task is to be sensitive towards the child, prepared for emotional expressions like crying, and to tell them that it is OK to stop the interview if they wish to. This is how the procedure was carried out in the present study. Efforts must be taken to create an atmosphere that ensures that the child experiences the interview setting as safe and controllable (Dyb i Fossheim, 2013).

Measuring pressure pain thresholds implies measuring “the minimum intensity of a stimulus that is perceived as painful” (3.7.5) and implies a stimulus that was experienced as unpleasant or slightly painful. The researcher was clear when informing about the procedure and explained carefully that they had to say stop at once when they felt that the pressure became painful. We did not intend to cause pain, and it was therefore important to ensure that they understood the procedure. It was our impression that all participants were comfortable with the procedure.
4 Findings

4.1 Summary of Paper 1
“Sometimes it feels as if the world goes on without me.” Adolescents’ Experiences of Living with Chronic Fatigue Syndrome.

The aim of this study was to explore the experience of being an adolescent with CFS. A semi-structured interview guide was used in the interviews of six boys and twelve girls, with an average age of 14.8 years, suffering from CFS. The interviews were analyzed with a hermeneutical-phenomenological approach, focusing on the life world of the adolescents. The purpose was to understand the lived experience as it was expressed by the adolescents through the transcribed interview text. They expressed that they felt alienated from life as it used to be, and alienated from their bodies because they could not recognize their own bodies’ reactions to normal activities. To “survive” the life as ill, they talked about the illness as something that had struck their bodies; but at the same time, the diseased body was not a part of what they defined as themselves. The diseased body made it impossible to participate in activities together with peers and resulted in a feeling of life passing by, leaving them behind and not as participants. Despite all the difficulties, the adolescents showed an important strength in maintaining hope and desire for their future.

4.2 Summary of Paper 2
Pain and Pressure Pain Thresholds in Adolescents with Chronic Fatigue Syndrome and Healthy Controls: A Cross Sectional Study

The aim of this study was to evaluate pain in adolescents with CFS compared to healthy adolescents, and more specifically explore: (1) the prevalence and location of pain symptoms, (2) pain severity and its interference in everyday life and (3) baseline pressure pain thresholds (PPTs).

This cross-sectional study used the questionnaire Brief Pain Inventory (BPI) to map the prevalence, location of, intensity and interference of pain, and a single item question about
frequencies of pain, and an Algometry to assess pressure pain thresholds (PPT) in 120 adolescents with CFS and 39 healthy adolescents.

Almost all adolescents with CFS were seriously influenced by pain on a weekly basis, and significantly differently from the HCs. Headache was the most common painful place, both in CFS patients and in HCs. In CFS patients, pain in muscles (62%), pain in joints (53%) and abdominal pain (49%) followed the headache. No HCs reported pain as a problem on a weekly basis. On the body map, almost 30% of adolescents with CFS marked more than four sites as painful, while none of the HCs did (Figure 3). The body map was divided into seven areas; head, neck/shoulders, chest, back, abdomen, upper limb and lower limb. There were significantly higher severity scores and pain interference scores in adolescents with CFS than in HCs. Among the patients, pain interfered the most with school attendance and general activity. Ability to enjoy life was the least affected task both in CFS patients and in HCs. Regarding PPT, the patients had significantly lower (almost 50%) PPTs on all measured locations compared with the HCs.

We found a higher prevalence of severe pain among adolescents with CFS and lowered pain thresholds compared to healthy controls. The total sum of bodily symptoms represented a heavy burden with large functional consequences. The large sample of patients together with few missing data strengthen the study, and make it possible to generalize the results.
4.3 Summary of Paper 3

*Health Related Quality of Life and Depression in Adolescents with Chronic Fatigue Syndrome: A Case-Control Study*

The aim of this study was to examine HRQOL and depressive symptoms in adolescents with CFS, and to compare HRQOL and depressive symptoms with a group of healthy adolescents. We hypothesized that adolescents with CFS report lower HRQOL than HCs and have a higher degree of depressive symptoms.

This cross sectional study measured HRQOL and depressive symptoms in 120 adolescents with CFS and 39 HCs. The questionnaires used were the Pediatric Quality of Life Inventory (PedsQL™) and The Mood and Feelings Questionnaire (MFQ).

Patients with CFS had slightly higher BMI (adjusted for gender and age) than the HCs, but the difference was not significant. Adolescents with CFS had significantly lower HRQOL than HCs, both overall and for all sub-domains. For PedsQL which ranges from 0–100, the CFS patients scored 44
points lower than the HCs for overall HRQOL, and for the domain physical health they scored as much as 60 per cent lower. Regarding school functioning, they scored 52 points lower and for emotional and social functioning they scored 29 and 27 points lower, respectively. The RMQ ranges from 0–66 and the cut-off was set to ≥20, which indicates depressive symptoms, and the CFS patients had higher scores on RMQ compared to HCs. We thus found more patients than healthy controls with depressive symptoms; with an eight times higher risk (OR=7.9, 95% CI 2.3-27.4).

However, we have only uncovered an additive effect of depressive symptoms and no interaction between having a higher level of depressive symptoms and being a CFS patient. Thus having a higher level of depressive symptoms had the same effect on HRQOL in CFS patients and HCs. Further, the strength and size of the association between being a patient and HRQOL was not changed when adjusted for depressive symptoms, so both depressive symptoms and being a patient were independently associated with lower levels of HRQOL.

Our study confirms findings from previous, smaller studies on HRQOL in adolescents with CFS and emphasizes that having CFS has a seriously negative impact on their HRQOL. Compared to healthy adolescents, those with CFS had an even poorer HRQOL than we expected. Physical function and school function were the domains with lowest scores. Even though depressive symptoms were found in the group of patients, depression could statistically not explain the poor HRQOL.
Figure 4: Health related quality of life of adolescents’ with CFS vs healthy controls
5 Methodological issues

Working in a large and interdisciplinary project implies advantages and disadvantages. The project consisted of six people, one leader of the project, a secretary, one master student and three PhD students. The group managed the project throughout the two and a half years of recruitment of study participants and data collection. Sharing this work was of benefit to all, and the project had the opportunity to use hospital facilities and collaborate with hospital staff.

The main project was an intervention study, but from which I used baseline data only. All questionnaires used in this thesis were chosen by the research group in the main project. If I had been more skilled in choosing different tools at that time, I might have picked different questionnaires. Working with a research group implies spending a great deal of time collecting data for others, which I did not use in the PhD work. One example is the hundreds of blood samples that I collected and prepared for further analysis. On the other hand, I am eligible for co-authorship of additional papers to the ones used in this thesis.

When discussing credibility, strengths and application in social sciences, the terms internal validity, reliability, objectivity and external validity are often used. In qualitative research, several authors have suggested other terms to describe these aspects (Polit & Beck, 2014). Corresponding to quality terms in quantitative research, Lincoln and Guba (1985) suggested four terms to evaluate trustworthiness in qualitative research: credibility, dependability, confirmability and transferability (Lincoln & Guba, 1985). Rolfe (2006) questions the usefulness of own criteria for reliability and validity in different paradigms and requests an overarching set of criteria (Rolfe, 2006); but at present there is still no agreement on this issue. Others highlight reflexivity as an important approach for evaluating quality in research (Jootun, McGhee, & Marland, 2009). In the following, I will elaborate on quality in mixed method (MM) research followed by quality in the qualitative study (Paper I) and the quantitative studies (Papers II and III).
5.1 Quality in mixed method research
This MM study has a convergent parallel mixed method design (Creswell, 2014), meaning that qualitative and quantitative data are provided simultaneously, analyses are done separately, and at the end the results are integrated through the discussion. To achieve validity in the convergent approach, Creswell emphasizes that validity should be based on both qualitative and quantitative principles, respectively. One issue that could potentially be a threat to validity is the uneven sample size between qualitative and quantitative data, making it difficult to compare data (Creswell, 2014).

In the present study, the sample size is different, but due to the purpose of the different research approaches, this should not be regarded as a problematic issue. Material that is based upon different sample size is not analyzed together and provides different types of knowledge. So instead of being a problem, this can be regarded as a strength due to a more complete understanding of the phenomena in the study. Combining qualitative interviews and psychometric procedures, an integration of findings will provide a more complete picture of the phenomenon of study. In mixed methods research, results from different approaches may be divergent or contradictory, which can lead to extra reflection, revised hypothesis, and further research; and possibly generate new theoretical insight (Lund, 2012). In the discussion section, both divergent and contradictory issues are presented and discussed.

Teddlie and Tashakkori (2009) use the term inference to evaluate quality in mixed method research, which consists of three related concepts: inference process, inference quality and inference transferability. The inference process refers to the research process, starting with planning of a project to the results of the study, resulting in making sense of the results of data analysis. Inference quality refers to the standards for evaluating the quality of conclusions that are made on the research findings, and is equivalent to internal validity and statistical conclusion validity in quantitative research, and credibility and trustworthiness in qualitative research. Inference transferability refers to generalizability and external validity in quantitative research and transferability in qualitative research; that is, in which degree conclusions may be applied to other
similar settings, people, time periods, contexts, and theoretical representations of the construct (Teddlie & Tashakkori, 2009). Quality in qualitative research and quantitative research has been explained in the sections 5.2 and 5.3 below.

One challenging task of mixed method approach has been the integration of the qualitative and quantitative findings in the discussion. The interviews provided new and exciting information about living with CFS and it was tempting to spend most time and effort on these. However, the quantitative material provided important information on both pain and HRQOL while the interviews provided extended information on the same phenomena. Some issues were dealt with through the interviews solely and in total; the qualitative material is slightly more weighted than the quantitative one, despite the 2:1 in favor of quantitative papers. Another challenge has been to find a common theoretical framework to discuss the findings. Methodologically, the biopsychosocial model is useful when focusing on a multifactorial disease. Still, the model does not suffice to frame the lifeworld brought through by the narratives. Phenomenology, as an additional philosophical approach, was considered suitable in the discussion. Yet another approach to discussing the findings has been examples from other people or other groups of patients not directly linked to adolescents with CFS. These have transfer value and were used to shed light on different phenomena in new ways. It was decided not to force the material into one specific theoretical framework despite the recommendations from Teddlie and Tashakkori (Teddlie and Tashakkori, 2009, p.286). Choosing one framework might have narrowed the possibility to look at CFS in adolescents from new perspectives. Instead, I took into account the advantages of mixed method research: different types of data provide different information and the combination might develop a stronger understanding of a problem (phenomenon) (Creswell, 2014). It is reasonable to think that different theoretical frameworks or approaches can be appropriate to discuss the findings and may expand our understanding, just as different types of data sources do. The procedure that is used in this thesis makes it possible to answer the research questions.
In the following, which was proposed by Creswell (2014), the quality in this work will be discussed using terminology for qualitative and quantitative methods respectively. The discussion of the research process will correspond to the term inference process.

5.2 Quality in qualitative research
5.2.1 Quality through reflexivity
Throughout the research process, I have endeavored to be as reflexive as possible, both orally and in writing. The terms credibility, dependability, reflexivity and authenticity will be discussed in this section.

5.2.2 Credibility
Credibility deals with the true value of data and interpretations of them (Polit & Beck, 2014) and if the findings are congruent to reality (Shenton, 2004). Credibility can be ensured through prolonged engagements, persistent observation, triangulation techniques, peer debriefing and member checking (Teddlie & Tashakkori, 2009). Malterud (2001) underpins the importance of reflexivity to ensure credibility; reflexivity includes the researcher’s preconceptions, reflections on how the researcher affects the research process, and transparency through documentation of the different stages of the research process (Malterud, 2001). Starting with how the researcher influences the different stages of the research process, I have reflected on this issue throughout the process. In the beginning of the thesis, I gave a brief introduction of my background making it possible for the reader to get a brief impression of it. In Chapters 3.3 to 3.6, descriptions of the interviews have been made, and my possible effect on the participants is made visible. Also, reflections about my skills and preconceptions are described together with descriptions of the analyses and choices made for the discussion.

Working with adolescents and their parents over a period of time has ensured prolonged engagements, which is about being familiar with the culture of participants ahead of data collection and with the participants of the study (Shenton, 2004). Prolonged engagement has taken place in two steps: working with children and adolescents ahead of the study made me familiar with the
group of patients, their parents and families. Different challenges were revealed, which created awareness about topics and areas in which there was lack of knowledge. Adolescents’ own point of view on living with CFS had hardly been explored, and interviews were decided to be a suitable method for obtaining such knowledge. The second step of prolonged engagement was when I prepared for meeting the patients included in the study. Information about their medical history was obtained by reading medical records and psychiatric reports before meeting the patient and the parents/next of kin. Meeting them when they got to the hospital in the morning, talking with them during procedures throughout their stay made me quite familiar with them. Working with an interdisciplinary team made it possible to discuss different challenges and problems. Further, different knowledge and experience made it possible to understand or solve these problems. Some of the parents needed to talk to someone without their child being present, and while the child went through some test with others from our research team, I got to know some of the parents as well. These talks provided different information, which consisted of challenges faced as a parent of a seriously ill child. Some themes, like lack of support as a parent, or the struggles between parents and school, are not always suitable to talk about when the child is present. Seeing this retrospectively it would have been interesting to interview some of the parents as well.

*Member checking and peer debriefing* are other techniques to ensure credibility. Member checking includes trustworthiness of interpretations and involves asking participants and other members of the social scene to secure accuracy of the themes, interpretations and conclusions. Peer debriefing is about having a senior researcher to clarify interpretations and identify possible sources of bias (Teddlie & Tashakkori, 2009).

Sometimes during the interviews it was difficult to hear and understand what the participant said. To clarify the uncertainty, I asked again or confirmed by repeating what they said, making it possible for the respondent to correct me. Member checking gives the informant the opportunity to validate the researcher’s interpretations (Polit & Beck, 2014). In preparing the research and the
interviews, I have discussed the work with my research fellows, healthcare professionals and my supervisors. In relation to the interviews, during the transcription and in the analysis, I have written notes and discussed these with my supervisors. Two of my supervisors read the transcribed interviews. Throughout the analysis, they read my written comments, and we discussed what I saw and what their point of view was. The goal was not total agreement, but to discuss our views and understanding of the text. Possessing different backgrounds, experiences and positions, we could obtain a broad illumination regarding different topics and themes. Working like this seemed useful. Though I did not necessarily realize what they saw, I could still understand what they meant and agree with their interpretation. A working group of PhD fellows and senior researchers further inspired me by challenging my ideas and thoughts. The purpose was to supplement and test our statements (Malterud, 2001). Letting others into parts of my work has been enlightening and has supported creativity and new thinking.

Because the verbal expression in the text was closely linked to the participants, it was emotionally challenging to read and analyze the text. I could hear their voices, see their faces and feel the atmosphere from the previous interview. In this process, questions from the supervisors were useful and made me aware of this influence and my pre-understanding. Working back and forth in the material, however, has shed light on the material from different angles and is in line with a hermeneutic research approach.

The credibility of this study could have been strengthened if my supervisors had listened to the interviews. Nevertheless, they did read the transcribed text and got a reliable impression by reading the thorough transcription.

5.2.3 Dependability
Dependability concerns the stability of data over time and condition, and whether the study can be repeated with the same or similar participants and in the same or similar condition by a different researcher (Polit & Beck, 2014). Because the conditions and the setting and the people in other interviews will differ, data can hardly be reproduced; the process within the study should be
reported in detail, making it possible for another researcher to repeat a similar work (Shenton, 2004). To demonstrate trustworthiness, effort has been made to ensure transparency. Throughout the research process, I have been thorough and systematic. The documentation of the research process have been done; from presentation of my background, development of the instruments and planning the study (together with the research group and my independent study) to description of procedures, analyses, interpretation and presentation of the results. This thesis makes it possible to see and follow the whole process and the different choices that were made.

Some of the interviews with the youngest boys are hampered by short answers, and their experiences might have been insufficiently narrated. All interviews are included in the analysis, and quotes from the boys are also used as examples. Nevertheless, when evaluating my skills in interviewing, better interviews with these boys could have provided additional information and knowledge. Also, the study might have been strengthened if the adolescents had been included in designing and planning of the study. This could have revealed important issues to focus on from their point of view. When health professionals set the premises, we might lose important perspectives.

The location for the interviews could have been more optimal and equal for all the participants. More comfortable and quiet environments could have improved some of the interviews and possibly elicited additional information. Despite this, I do not believe that additional information would have changed the results significantly.

5.2.4 Transferability and Confirmability
Transferability in qualitative research is about the extent to which the findings can be transferred to, or have applicability in other settings or groups in the same or in similar conditions (Guba and Lincoln, 1994). Transferability also concerns detailed descriptions of context and other aspects of the research setting so that other researchers can make comparisons. These are called thick descriptions (Teddli & Tashakkori, 2009). Examples and descriptions of the participants have been outlined so that readers can check the background for the discussion and the conclusion. In this thesis, thorough reflection and descriptions of the research process from the start of the study until the discussion
and the conclusion has been carried out and clarified. The reader might disagree or have other perspectives, but it will be possible to understand our view and see that there are several possible options for interpretation. Confirmability concerns objectivity, which is the accuracy, the relevance or meaning of the data and further, that there is congruence between the information given by the respondents and the interpretations of these data (Polit & Beck, 2014).

5.2.5 Authenticity
To secure trustworthiness, Guba and Lincoln (1994) added a fifth criterion which is about authenticity. Authenticity is about how fairly and faithful the researcher show a range of realities. The participants’ lives are made alive through the appearance of mood, feelings, experience, language and contexts of the life of the participants (Lincoln & Guba, 1985). I believe that the voices of the participants can be heard through the quotes and in the way the findings are discussed in Paper 1. A variety of moods and feelings were expressed through the narratives of their everyday lives, and among the feelings which are described is the crying of some of the participants (3.3.2), which is also discussed thoroughly below.

5.3 Quality in quantitative research
Reliability and validity are the preferred terms used to evaluate quality in quantitative research. Reliability is about the accuracy and consistency of information obtained in a study, and is also important concerning the interpretation of statistical analyses. Validity concerns the degree to which an instrument measures what it is intended to measure and the accuracy of interference in a study (Polit & Beck, 2014). All questionnaires had very few missing items, which strengthens our results. Trustworthiness regarding the quantitative data will be discussed according to reliability, internal validity, and external validity.

5.3.1 Reliability and validity of the instruments
To ensure reliability and validity it is important to use measures that are validated and psychometrically tested (Fayers & Machin, 2009). The measures used in this study have been translated into Norwegian and validated. Reliability refers to in which degree an instrument is
consistent, obtaining the same results when repeating the measure, given equal conditions (Fayers & Machin, 2009). Validation is important to ensure that the instrument measures what it is intended to measure (Polit & Beck, 2014). Missing data might be a threat to the statistical power (Fayers & Machin, 2009). To be able to compare results from patients with healthy adolescents, generic instruments were chosen. In the paragraphs below the validity and reliability of Pediatric Quality of Life Inventory, Brief Pain Inventory, pressure pain thresholds and the Mood and Feelings Questionnaire will be discussed.

5.3.2 Pediatric Quality of Life Inventory
In this study comparing data between diseased and healthy adolescents, the generic questionnaire Pediatric Quality of Life Inventory was the preferred questionnaire to measure health related quality of life. Accounting for missing data, scale scores were computed as the sum of the items divided by the number of items answered (Varni et al., 2001). The Pediatric Quality of Life Inventory has been validated and translated into several languages, and among them is Norwegian (Reinfjell et al., 2006). The World Health Organization emphasizes specific domains important to children and adolescents and the Pediatric Quality of life Inventory covers these domains which is physical functioning (8 items), emotional functioning (5 items), social functioning (5 items), and school functioning (5 items). Three of the subscales (emotional, social, and school functioning), are combined in a specific scale for psychosocial health (Varni et al., 2001). Even though there exist corresponding questionnaires for proxies, only the version for adolescents is used in Paper 3. Participants were asked to rate the severity of each item during the previous month by a Likert Scale from 0 (never a problem) to 5 (a lot of a problem). Items are reverse-scored and linearly transformed on a scale ranging from 0–100 (0=100, 1=75, 2=50, 3=25, 4=0), where higher scores indicate better health related quality of life. Each subscale score is computed as the sum of the items divided by the number of items answered (Varni et al., 2001). Missing values were estimated by calculating the mean of the items for all participants within each question respectively. Scale internal consistency was measured with Cronbach’s alpha, varying between 0.77 and 0.88, which is considered good (Reinfjell et al., 2006).
5.3.3 Brief Pain Inventory

Mapping pain, the Brief Pain Inventory (BPI) has demonstrated reliability and validity across languages and cultures (Cleeland & Ryan, 1994), and the NRS scales is a reliable measures of pain intensity in both children and adults (E. K. Breivik, Bjornsson, & Skovlund, 2000; Gaffney, 2003). Cronbach’s alpha has been calculated for several versions of the BPI. To make the questionnaire more age-relevant, we asked how pain affected school and homework instead of asking how pain affected work. We considered it irrelevant to ask about work in this age group. This will be a matter of definition, hence we define school and homework equal to an occupation. The purpose of the question was to evaluate how pain affects everyday obligations. In order to reduce the total burden of questions, we removed the question about pain interference with sleep and ended up with six interference scores. To ensure internal consistency, we computed Cronbach’s alpha for the six remaining questions, showing good internal validity. Cronbach’s alpha was computed separately for adolescents with CFS and healthy controls. The values were 0.89 and 0.87 for patients with CFS and healthy controls respectively, which is considered good (Fayers & Machin, 2009). In addition, it would actually have been of interest to measure pain interference with sleep. Modified versions of the brief pain inventory interference score have been used in previous studies with participants aged between 8 and 20 (J. M. Engel, Jensen, Ciol, & Bolen, 2012; J. M. Engel, Petrina, Dudgeon, & McKearnan, 2005). In Chapter 3.7.5, I described that the pressure pain threshold examinations were performed twice, and the respondents filled in the brief pain inventory in between the measures. This might have influenced the results, because the adolescents might still have felt the pressure from the algometry while filling in the questionnaire. On the other hand, all the questions except one were about pain during the previous week. Also, when asking about pain right now, twenty five percent answered that they had no pain at all, while sixty percent indicated pain less than three on the 0-10 scale. The distribution of the answers are outlined in appendix 4 (a) and 4 (b). This question was the single question that had the lowest pain scores compared to all the other questions.
5.3.4 Pressure pain thresholds
PPT is a reliable measure to test tolerance to painful pressure (Romundstad, Stubhaug, Niemi, Rosseland, & Breivik, 2006) and to test for hyperalgesia (Nie et al., 2005). To ensure validity, the pressure stimuli were applied twice to each spot and then averaged, a procedure that is commonly used in other studies to ensure reliability (Rombaut et al., 2014). The researcher was not blinded regarding CFS patients and HCs, and this could hypothetically interfere with the results. Nevertheless, the researchers endeavored as conscientiously as possible to apply the measures equally to patients with CFS and healthy controls. Pressure was only applied on the upper part of the body, showing a significantly lower pressure pain threshold compared to the healthy adolescents. It could have been interesting though to measure areas on the lower extremity as well to see if there were differences between the upper and lower parts of the body; this could have provided information about widespread pain and possibly strengthened validity. However, the adolescents went through multiple tests and examinations and we had to limit the examination. From a pragmatic perspective, we decided to limit the measurements to symptomatic and asymptomatic areas of the upper extremity.

5.3.5 The Mood and Feelings Questionnaire
MFQ has been used in several Norwegian studies (Sund, Larsson, & Wichstrom, 2001, 2003, 2011), and has shown good internal consistency (Sund et al., 2001). The wording in the Mood and Feelings Questionnaire is considered appropriate to the cognitive skills and development in the age group 8–18 years (Kovacs 1986 in Sundt 2006). Compared to a comparable study in adolescents with CFS (Bould et al., 2013), the prevalence of adolescents with depressive symptoms was higher in our patients with CFS. We might unintentionally have included patients with primary depression while a formal psychiatric assessment should have been conducted. Another explanation of the high prevalence of depressive symptoms might be that several single items in the Mood and Feelings Questionnaire are common in both depression and CFS (Sulheim et al., 2014).

Both the Mood and Feelings Questionnaire and the Pediatric Quality of Life Inventory, include questions concerning depression-like symptoms. These questions, however, were always
phrased differently in the two questionnaires and covered slightly different areas. The questions covering depression were also scored differently, and when assessing health related quality of life they were only a part of the overall score. Therefore, we concluded that it was meaningful to model associations between health related quality of life and depression (Paper 3).

Using different kinds of questionnaires to investigate a condition like CFS with its plurality of different symptoms highlights a challenge about overlapping symptoms. This might make visible a general challenge to assessment tools in research, rather than just a challenge to the present study.

5.3.6 Frequency of pain
Based upon a CFS symptom inventory for adults (Wagner et al., 2005), our research group developed a symptom inventory for adolescents with CFS, assessing the frequency of 24 common symptoms in this group of patients. The inventory consists of the eight accompanying symptoms of the CDC CFS definition, illness-related aspects like disease duration, and psychosocial aspects and has been applied in routine clinical practice at the hospital (Sulheim et al., 2014), and in previous studies (Sulheim, Hurum, Helland, Thaulow, & Wyller, 2012; Wyller & Helland, 2013). Single-item questions about pain (headache, abdomen, joints and muscles), were selected from this questionnaire and frequency of pain was measured on a five point Likert scale (0-5) ranging from “never/rarely” present to “present all the time”. Single item questions about pain have been shown to be reliable in measuring pain in children and adolescents (Roth-Isigkeit, Raspe, Stoven, Thyen, & Schmucker, 2003).

The comprehensive CFS questionnaire was combined with other questionnaires in the NorCAPITAL study (Sulheim et al., 2014), and three of them (BPI, MFQ and PedsQL) are used in the present study.

5.3.7 Transferability
Our study follows the international recommendations for children and adolescents although it uses wide criteria for inclusion. The NorCAPITAL study also has a relatively large study population compared to other studies, and the results should therefore be generalizable to adolescents with
CFS. There is, however, disagreement about the diagnostic criteria for CFS, and a review of case
definition of CFS/ME shows that studies have failed to identify subgroups of patients (Brurberg et al.,
2014). Although the majority of our study population fulfilled the CDC criteria for CFS, some will
argue that we have compared different subgroups of patients, implying that the results cannot be
generalized. It should be noted that adolescents with CFS participating in the NorCAPITAL study were
diagnosed by and recruited from their pediatrician or general practitioner. It is therefore likely that
the study population reflects the population of adolescents diagnosed with CFS in Norway.
6 General Discussion

Stories told by the adolescents reveal a troubled adolescent life with difficult feelings and thoughts. For the adolescents who were interviewed it seemed liberating to talk about their troubles to someone familiar with their condition. The experience of pain as a serious problem was disclosed by the questionnaires. Hypersensitivity towards stimuli like light and sound is another well-known problem in patients with CFS and measuring their pain threshold revealed hypersensitivity towards pressure as well. The discussion will revolve around the main findings from the qualitative and quantitative material, and pain will be discussed in a broader perspective, taking into account the complexity of the phenomenon not restricted to its physical appearance. A troubled life might be equally, or more, painful than muscle pain. The questionnaires address important areas, to which the interviews provide a more detailed and comprehensive insight. In relation to the problem statements and the aims of the studies, the findings will be discussed within the framework of the theoretical perspective and previous research presented in Chapter 2.0.

Adolescents with CFS are affected in several areas corresponding to the physical, emotional, mental, social and behavioral components in the domains of health related quality of life. Results from both questionnaires and the interviews reflect all these areas. School attendance and relations with friends are interfered with by the illness, which disturbs a “normal” adolescent life. School and social functioning, including family relations, depressive symptoms and gender differences are discussed in section 6.1.

An illness that is difficult to understand, without obvious and clear signs of a disease, might present challenges to the person who is ill. Words alone might be insufficient to express the challenges. Other forms of expression like dance, music or crying might be useful and feel like a relief, but not necessarily be appreciated or understood by others as alternative ways of expression. Different kinds of expressions emerged in the interviews and are discussed in section 6.2.
Pain and suffering will be discussed in Chapter 6.3. Pain might be well localized, but also difficult thoughts and a troubled life might be painful, and *suffering* is the term used when discussing pain in a broader sense. Development throughout adolescence might be challenging when afflicted with a long-lasting disease, and friends and development of identity will be discussed in Chapter 6.4. The different perspectives on illness and disease, together with how these perspectives might have consequences for the patients, will end the discussion (6.5).

6.1 Severely impaired health related quality of life
Even though we assumed health related quality of life to be lower in the group of patients compared with healthy adolescents, the health related quality of life was even worse than we expected. The adolescents with CFS scored low in all the health related quality of life domains, although physical functioning and school functioning had the lowest scores, far below those in healthy controls (Paper 3). On the overall health related quality of life, the girls demonstrated lower scores than the boys. This is the case both for adolescents with CFS and for the healthy controls, which is illustrated in Figure 3, Chapter 4.3. Emotional and social functioning were the domains in which adolescents with CFS scored the “best”. It is difficult to conclude on this result, but it might indicate that they managed some degree of social functioning despite reduced participation in teen venues like school (Paper 1). Even though the adolescents had a reduced possibility to be with friends, it might be that some of them had kept some good friends. The quality of peer relationship might play an important part due to their social functioning, but the *quality* of a peer relationship and health related quality of life has hardly been studied (Frisen, 2007). Still the difference was huge between adolescents with CFS and healthy controls also in these domains, which after all, underpin the poor emotional and social functioning. The interviews provide information that some of the adolescents realized that they appreciated their own family more than before they got ill and it might be that good relations with family to some degree compensate for the reduction in peer activities and peer relations. This can mean that the adolescents had adapted to life with their illness, and the more narrow frames of living. Without friends and peers, expectations might be changed in the way that they expected less,
and the peer orientation might have shifted to orientation towards their family instead. This does not mean that this was what they wanted, but that they were forced to think differently and made the best of their situation. It might also mean that they had developed and become more mature in some areas, which some of the respondents saw as an advantage. Nevertheless, it was obvious that they strove, and that they were emotionally troubled. The qualitative data provides extended insight into their emotional difficulties and into which ways emotions were expressed. Emotions and emotional expressions will be discussed more thoroughly in Chapter 6.2.

In the NorCAPITAL study, many of the participants reported interrupted school attendance (Sulheim et al., 2014). This is in line with other studies on adolescents with CFS (Bell et al., 2001; Kennedy et al., 2010; J. Richards, 2000). School is an arena for education, but equally important, an arena for meeting friends and for socialization. Low school attendance has further been associated with low mood and increased fatigue, which in turn may lead to worse physical functioning and reduced school attendance – a so called vicious circle (E. Crawley & Sterne, 2009; Kennedy et al., 2010). In Paper 2, adolescents with CFS reported that they were seriously impaired by pain and that pain had great functional consequences. The adolescents with CFS took for instance a significantly lower number of steps (less than 50%) per day than healthy controls (Sulheim et al., 2014). Low physical functioning and low school functioning might also lead to less participation in leisure activities, which is an important arena for teens to meet. In adolescents with CFS, the domain physical function is found to be the most seriously affected area of health related quality of life (Kennedy et al., 2010). In the material from the interviews, we found that the adolescents experienced losses in several important areas in life, which is consistent with findings from a study by Jelbert et al. (2010); when loosing contact with peers and school, adolescents with CFS lost the ability and freedom to carry out activities that they enjoyed (Jelbert et al., 2010). These losses have both educational and developmental consequences (Bell et al., 2001; E. Crawley & Sterne, 2009; Rangel et al., 2000). The loss in social competence and the loss in experience of peer fellowship might well lead to identification with the illness, instead of, for example, identification as a football player or a
musician. Being more dependent on and spending more time with their family will have consequences for the family structure. In the interviews, there were stories about siblings getting less attention; and one of the adolescents believed that she was the reason why her mother lost her job. If this assumption proves correct, this again would affect the family income and the economic resources of the whole family. The illness burden within the family will affect the health of the family (Rangel, Garralda, Jeffs, & Rose, 2005), and the inclusion of the family seems crucial for the family to be functional and supportive. The importance of family support of adolescents with CFS is shown through the effect of family-based treatment in adolescents with CFS (Chalder, 2002; M. E. Garralda & Rangel, 2004).

In adolescence there are several physiological, psychological and social changes which might be difficult to handle, leading to a reduction in well-being and health related quality of life (Bisegger et al., 2005; Haraldstad, Christophersen, Eide, Nativg, & Helseth, 2011). In particular, physical and psychological dimensions of health related quality of life have been found to be lower among girls compared to boys. This might be explained by more drastic hormonal and bodily changes (Bisegger et al., 2005); but another study suggest that the gender differences in psychological distress might reflect higher self-esteem among boys (Avison & Mcalpine, 1992). Another approach to understanding this difference might be through a gender perspective, which means that there are different expectations of boys and girls when it comes to expressions and actions. The more drastic hormonal changes in girls and the development from girl to woman might contribute to difficulties in keeping up with all the changes. One might feel different and strange, contributing to uncertainties about identity. Some girls with CFS said that they felt different from whom they used to be (Paper 1). Even though this might be due to the illness, it might as well have been a reinforcement of a pubertal uncertainty of identity. In healthy adolescents, it is more likely for girls to report negative health than boys (Meland, Haugland, & Breidablik, 2007), and this tends to increase with age. In the interviews, we experienced that the boys had shorter answers and less fruitful stories about living with CFS than did the girls. Girls telling more than boys probably means that more challenges are brought to light in
girls, rather than boys experiencing fewer difficulties. Bisegger et al. found improvement in social functioning in adolescents, and explained this by increased independence in deciding whom they wanted to be with, which again improved their social skills (Bisegger et al., 2005). For adolescents with CFS, this boost in new experiences followed by increased social functioning is lacking. Even though some might maintain some degree of social participation, this area should be of great concern.

A report from the Norwegian Center for Welfare and Labor Research (NOVA) (2013), states that adolescents in Norway are well adjusted, have good relations to their parents and that they are satisfied with school (NOVA, 2013). Nevertheless, the report also points to an area that should be of concern: more young people strive with mental health problems in their everyday life; they feel stressed, think everything is a struggle, and in general, they worry too much. The report reflects everyday life and mental health of Norwegian adolescents in general.

In the transition from childhood to adulthood, which represents a rapid change physically and psychologically, adolescents are a vulnerable group with the risk of developing a range of mental-health conditions (Kessler et al., 2005). All the rapid changes happening at the same time in adolescence means that getting an illness like CFS will have great consequences for adolescents.

In our study on health related quality of life and depression (Paper 3), we found that one third of the adolescents with CFS had depressive symptoms while eight percent of the healthy controls did. However, even though we found that depressive symptoms were an independent predictive factor for lower health related quality of life; depressive symptoms did not explain the poor health quality of life in the adolescents with CFS. Both depressive symptoms and being a patient were independently associated with lower levels of HRQOL. In our view, being a patient is by itself a major component contributing to a lower health related quality of life, as our findings cannot be explained only by depressive symptoms.
A range of difficult feelings is reported, both in the present and in other studies on adolescents with CFS (Fisher & Crawley, 2013; Jelbert et al., 2010). Generally, the occurrence of depression is found to be higher in adolescents with CFS than in healthy controls, as well as in adolescents with other chronic conditions (Bould et al., 2013; Rangel, Garralda, Hall, & Woodham, 2003; Smith, Martin-Herz, Womack, & Marsigan, 2003). Whether depression is present before the onset of CFS, or if it is an effect of being ill, is not clear (Bould et al., 2013), but in any case, anxiety and depression might be intensified as a result of social isolation (Fisher & Crawley, 2013).

6.2 Expressions and stories
As communication uses a multitude of expressions like words and tone of voice, emotions are expressed in several ways, not only as verbalized statements, but also as bodily expressions like dance, music or as tears or sobbing.

6.2.1 Bodily expressions
“I was at a camp...and I got a sign around my neck. On one side it said “out of order” and the other side said “in order” [...] and then they told me to turn the sign depending on my capacity”.

This girl probably expected too much from herself and her body had obvious signs of exhaustion when she had pushed her limits. Her friends were capable of observing this and instead of picking at her or verbally asking her every time they saw that she was tired, they helped her to accept her limitations. With a great deal of humor, her caring friends introduced the procedure with the signs. This quote might as well demonstrate the challenge of the visible and the invisible aspects of CFS.

A disease like CFS has the hallmark of exhaustion. The adolescents might be too tired to get out of bed or too exhausted to be with friends or participate in activities that previously were associated with pleasure. The exhausted body is not unique for adolescents with CFS. In my previous work with premature babies, I observed similar bodily states. When health care professionals, working in a neonatal intensive care unit (NICU) overloaded the premature babies with painful procedures or tasks necessary for their welfare or survival, the baby showed similar characteristics as
a person with CFS. What we might observe is a pale or gray skin color, a hypotonic body, closed eyes, and in addition, we can measure irregular pulse and blood pressure. The body no longer brings to the surface reactions if we continue to stimulate, and may reflect an overloaded human body. The overloaded human body is silent or muted but despite this, it is “screaming very loudly”. Normally, a person would cry out if there was something wrong or fight back if hurt. The silent expression is a very strong signal that should call upon us to stop stimulating. The overloaded human is dependent on other humans who want to see, who understand what is observed, and who might support the person in recovering. The difference though, between the premature babies and adolescents with CFS is that for the premature baby, the state is reversible within a relatively short period of time, while adolescents with CFS have a long lasting or chronic condition. Other differences are the social context and the cognitive, emotional development, which are far more developed in adolescents. It might seem strange to compare adolescents with CFS and premature babies, but the signs of exhaustion observed are similar despite obvious differences between the age groups. This might illustrate that expressions of exhaustion might not be restricted to patients with CFS, but rather a general bodily expression due to a stressor that is not manageable. Adolescents with CFS often pull themselves together when they are with other people. Afterwards they pay the price and might be stuck in bed for hours or days. Post-exertion malaise lasting more than 24 hours is a hallmark of CFS (Fukuda et al., 1994). A person with CFS might have weak signs of being ill, or there may be no signs at all. One of the findings from the interviews was formed as a question: “If the illness is not visible to others, does it exist?” As the example at the beginning of this chapter shows, the signs might be difficult for the ill person to accept. At the same time, the person is dependent on others who understand how it might be to be ill, despite the lack of obvious and “proper” signs of sickness. The girl in the example had good friends who cared about her and supported her. They probably contributed to her well-being, heightening her overall quality of life.

Some of the adolescent told that they could express themselves through music or other artistic expressions like singing or drawing. Because of the exhaustion, it was difficult to keep up with
activities that provided joy and pleasure. Even so, in the qualitative interviews, there were examples of spontaneity and joy when, for example, one of the girls told about the liberating feeling she had when she spontaneously started to dance in the living room at her home. The spontaneous dancing made it possible to forget her sufferings for short moments of time. In the qualitative paper, we discussed how dancing could be helpful to forget the illness and the suffering, and when experiencing such a liberating feeling the dance could provide rest and energy (Paper 1).

6.2.2 Crying as expression
As described in the Methods section, during the interviews, some of the adolescents started to cry, but this did not seem to be difficult for them. On the contrary, they expressed a wish to continue the interview and their stories. What did they express by crying? We might not fully understand why they cried, but the fact that they wanted to continue the talk indicates that they felt safe. In addition, notes in the transcribed interviews provide information about when they started to cry or what they talked about when starting to cry, which might contribute to our understanding. One of the adolescents started to cry when she told about all the troubles her mother went through because of her. Her mother was the only person that believed in her being ill and supported her, in contrast to the general practitioner and the local community. The tears possibly reflected a soreness but also expressed gratitude to her mother. Another adolescent gave me the impression that she was crying, but there were no tears. She “cried without tears”; her body behaved like the bodies of the others who cried. She was sitting there, telling about her life while resting, but expressing some kind soreness. I experienced this as crying, but even so, others might interpret this differently. The third girl wept silently and calmly, with tears that coursed down her cheeks now and then throughout the interview. Despite crying, they seemed comfortable in the setting. Crying and tears may occur when a person is overwhelmed by both negative and positive emotions (Vingerhoet, 2013), or when a message is difficult to express by words. A quote from the philosopher Hans-Georg Gadamer (1975) illustrates the difficulty of expressing emotions with words “Indeed, words often seem ill suited to express what we feel. In the face of the overwhelming presence of works of art, the task of expressing
in words what they say us seems like an infinite and hopeless undertaking.” (Gadamer 1975, p. 402).

The crying might help the listener to understand that the crying carries a message. The crying becomes the active part of the story being told. According to Lindseth and Nordberg (2004), we have to express what we experience to become aware of what the experience means. Further, the awareness itself leads to improvements. Crying as an emotional expression might have a stress-reducing function, leading to comfort, or it might communicate pain and discomfort resulting in care from others (Gracanin, Bylsma, & Vingerhoets, 2014). Further, Gracanin et al. hypothesize that crying might result in homeostatic regulation. One might be touched by something one (otherwise) is unaware of. Merleau-Ponty’s philosophy looks at the body as the primary source of feelings (Merleau-Ponty, 2002). In the moment, the adolescents become aware of what is bothering them; during the interview it also becomes obvious to me as the listener. When such a mutual understanding is achieved, a sense of community is obtained which possibly gives rise to confidence and trust. As the story is told and conveyed to another the message becomes real and acknowledged by the person telling the story. In this situation, the adolescents have managed to share something they were not able to express in words and, equally important, they have received new insight an insight first perceived by their bodies.

Before moving forward in the discussion, I find it necessary to deepen some of the theoretical views presented earlier. On pages 18–20, Chapter 2.7, I problematized the lack of a suitable vocabulary to express body and mind as one undivided and integrated unit. Melheim, 2014 suggests that a suitable term for such a unit is “the language of wholeness”. This language of wholeness is equal to a holistic language that can frame (and override) dualism, and might be in line with Merleau-Ponty’s philosophy of the “body”; in the meaning that we “are our bodies” (Merleau-Ponty, 2002). Seen in this perspective, we can use the term body when talking about a person in balance, which might bring us beyond the subject-object dichotomy. When talking about how we feel, we might for example say; “I am touched”. In our everyday vocabulary, this make sense to us.

One of the findings from the interviews was “the body, the illness and me”, which might underpin the
need to give different dimensions different names in an effort to make difficult phenomena comprehensible and understandable to us. We might rethink about this finding by thinking with Merleau-Ponty, and keeping the language of wholeness in mind. The finding and expression “the body, the illness and me” (Paper 1) might illustrate a person who is striving to understand different parts of being ill, unbalanced but trying to make sense of her situation. If the adolescent through narrating and through crying has achieved a greater understanding, the crying might function as a comprehensive expression or a comprehensive language which might stand in contrast to the divided, linguistic expression.

Bearing the above discussion in mind, bodily expressions like dance, music or even emotions like crying are important ways of expressing different sides of life, but which are underestimated ways of communication. Even with small children, we try to suppress crying rather than trying to understand what the crying means (Rossholt, 2010). Taking into account that humans often use other expressions than words, one can ask why we are not more sensitive towards these bodily expressions. The fact that we go to the theatre or to the opera and watch ballet, suggests that we understand bodily expressions and even appreciate them. We are touched, and feelings like tears, laughter, sadness and joy are evoked. This is a paradox when working with patients suffering from a condition like CFS. In the encounter with the patient, we ought to recognize feelings within ourselves in an effort to also understand the patient; but this probably challenges our own prejudices and attitudes to conditions like CFS. If accepting all the different feelings as bodily (anger, anxiety, grief and joy), and as a necessary and natural part of being humans, this challenge might be achievable. A study among children in kindergarten shows that anger is a less acceptable emotion than other feelings (Grindheim, 2014). The author says that there is a tendency in the Norwegian culture that anger is a less acceptable emotion to show. Anger is chosen as an example because it is an emotion that is very evident and potentially negative, as the illustration above shows. Other emotions might also be “unacceptable” due to culture, settings and people’s different preferences. Different kinds of feelings communicate different kinds of states and might carry with them important messages.
Favoring some emotions above others already from early childhood might affect the legitimacy of expressions of feelings. When some emotions are accepted while others are not, our way of handling our troubles might be affected. It might be that adolescents with CFS have challenges in expressing emotions, dependent on the people they are surrounded by and the environment they are part of.

The stories the adolescents are telling and the emotions expressed through the interviews make it obvious that they bear sadness. The illness is difficult to understand; they are accused of laziness, they lose friends and school attendance, they feel like outsiders and they feel that the world goes on without them (Paper 1). No wonder it seems hopeless to express all these difficulties using only words. To be able to help the adolescents express their situation and to make some sense out of their lives, it might be necessary to challenge our understanding and think again, as discussed in this section. The psychiatrist Trygve Braatøy (in Sviland, p. 148), argued that our prejudices are incorporated into our language, and that these linguistic prejudices have influenced our way of thinking: such as mind vs. body, objective signs vs. subjective expressions. For instance, our medical abstractions are not able to capture and explain the quality of passion and suffering in the way that art does. This means that there is a need to incorporate different theoretical views in an effort to broaden our understanding about CFS as disease. It must not be the responsibility of the adolescent alone to carry the burden of the incomprehensible.

Thorn (2000) suggests that adolescence is the broadest period of memory telling. If so, this might be seen as a resource, with storytelling potentially a fruitful and appropriate method for studying adolescents with CFS.

It might seem as if the adolescents with CFS have challenges to overcome. There might be several reasons: it might be difficult for them to understand themselves; emotions might be suppressed because of cultural and social expectations of what is allowed; the surroundings might present difficulties for understanding both the illness and non-verbal expressions. Difficult feelings
like uncertainty, loneliness and sadness due to relations with friends, family and school were discussed in Paper 1.

6.3 Pain and suffering
Even though fatigue is the main hallmark of CFS, the illness has a range of additional symptoms that all contribute to disability and suffering. Pain is probably the symptom that interferes the most, and for some patients it affects them more than the fatigue itself. We used the brief pain inventory to measure the frequency of headache, abdominal pain and musculoskeletal pain. We found that most of the adolescents had experienced pain in several parts of the body during the previous week. Almost one third of the adolescents with CFS had pain in more than four body sites, while 10 per cent reported pain in seven body parts (Figure 3, Chapter 4.2). Headache was most common type of pain, and this was also the case for healthy controls. Adolescents with CFS are thus severely affected both by fatigue and pain, meaning that they are suffering from more than one single health problem.

Some researchers have hypothesized that the pain in CFS is caused by increased sensitivity in the nervous system (Meeus & Nijs, 2007; Meeus et al., 2010; Nijs et al., 2012). In Paper 2, we investigated whether adolescents with CFS were more sensitive to pain stimuli compared to healthy adolescents. We measured pressure pain thresholds in both groups and found that the patients with CFS had far lower pain thresholds than the healthy adolescents. We discussed whether the lowered pressure pain thresholds could indicate a general sensitization of the nervous system in adolescents with CFS (Paper 2). General hypersensitivity has been suggested as a reason for pain in adult patients with CFS, as well as in patients with other pain conditions like Ehler-Danlos syndrome, widespread pain and fibromyalgia (Meeus & Nijs, 2007; Rombaut et al., 2014; Wolfe et al., 1990). Another potential mechanism for the pain is altered pain inhibition (Yarnitsky, 2010). Even though patients with CFS are sensitive to other stimuli like light and sound as well as pressure, we could not conclude which mechanism is involved given the design of this study. The NorCAPITAL study was based upon the theory of cognitive activation of stress (Ursin & Eriksen, 2004), and the theory of sustained arousal was hypothesized as a disease mechanism in CFS (Wyller et al., 2009). The hypothesis,
however, was not proved. Pain in CFS still remains unclear, but a multidimensional perspective seems reasonable, due to pain as a multidimensional concept.

As we planned this study, we believed that pain would be an important issue in the interviews with the adolescents (Paper 1). Despite our findings in Paper 2, showing that adolescents are severely influenced by and bothered by pain, this was not what they focused on. In the interviews, bodily pain was only discussed when addressed by the interviewer. This is an interesting finding taken into account how affected they were by pain. There may be several ways to understand this. Pain and pain thresholds were measured before the interviews took place, and the adolescents might have thought that physical pain was not or should not be an issue. Another explanation could be that physical pain was something they could overcome. This might seem odd, taking into account that pain in these patients is a serious problem, hence a third way of seeing it could be that other problems were even more important and preoccupied them. The themes from the interviews support the latter explanation. Existential issues of how the illness bothered them, and hindered them from living their lives with friends and attending school, were of greater concern (Paper 1).

Pain is usually localized in the body, but might also reflect difficult feelings and thoughts which might involve suffering. Pain is highlighted by Vetlesen (2004) as stemming from a physical trauma as well as from mental stress like loss, grief or “heartbreak” (Vetlesen, 2004). Within the frame of caring science, suffering is seen as a natural part of life, and Erikson (1995) argues that suffering might be described as the suffering of illness, the suffering of life and the suffering of care given (Eriksson, 1995). Adolescents with CFS might experience pain differently. Some might experience the “physical” pain as the worst, while others might suffer from difficult feelings and existential thoughts and experience this as painful. The pain that adolescents with CFS suffer from can stem from the illness, and the impact the illness has on their adolescent life might contribute to suffering from life. An interesting situation took place when one of the healthy adolescents was asked to fill in the body map part of the brief pain inventory. In the questionnaire, his scores were
pretty high on the 0-10 scale, but still he had trouble to decide which part of the body to shade. When asking him to explain why this was the case, he answered that he suffered from heartbreak.

When the body is healthy and without any unpleasant sensations, we are hardly aware of our body. It is not until we get ill and are afflicted by unpleasant symptoms like pain that we are reminded of the body, because the unpleasant symptoms make the body present, and may lead to another image of our body (Vetlesen, 2004). The body demands our attention and in such conditions, the person might experience that the body appears as “the other” as in an opposite position to self (Leder, p. 70). This was evident for some of the adolescents in this study. To deal with everyday life, they made a distinction between what they regarded as themselves, their body and the illness (Paper 1).

The previous section discusses an extended understanding of the concept of pain. I will return to pain as it was discussed in the beginning of this chapter, namely as selectable body locations. The pattern of illness has been found to be more cyclical than chronic in a pediatric CFS population (Gray & Rutter, 2007), and one can assume that symptoms like fatigue and pain might fluctuate with the illness with variation due to intensity. Even if this was the case for the patients in our study, they were still severely bothered by both fatigue and pain. Most patients in our study reported having pain approximately every day (Paper 2). Although the argument in the following addresses pain, this might as well be transferable to fatigue. Hence fatigue is the main hallmark; for some, the fatigue might be the overriding problem.

Pain steals focus and at its most severe, existence will be reduced to body (Vetlesen, 2004). This statement gets its relevance from the extreme cases of pain (like torture). Nevertheless, there are variations on the scale from no pain to extreme pain (and the same will be the case regarding fatigue), which means that how much focus unpleasant bodily sensations will have, will depend on both the stage of the illness together with the adolescent ability to focus elsewhere. As our findings show, adolescents with CFS are very aware of their bodies and they have different strategies to deal
with the illness, its unpleasant symptoms and consequence, which is reduced ability to participate in normal teenage activities. One of the adolescents in the study externalized the pain by placing the illness outside her body. The illness became something that she had, and that she had to deal with. At the same time, the illness was not a part of what she regard as herself, and she refused to let the illness be the commander. Due to the rapid change in physical appearance, adolescents’ overall self-image is closely tied to their body image (Frisen, 2007); which might be further complicated by CFS. Rethinking about their bodies is what some of the adolescents in this study did. Making a distinction between what they regarded as themselves, their body and the illness might be a challenging but yet an appropriate way of handling everyday life (Paper 1). Managing to look upon the illness in this way might have a positive impact, hence externalizing the illness has a positive influence on patients’ health related quality of life, while focusing on symptoms is associated with poor physical functioning (Gray & Rutter, 2007). However, thinking about the body as divided could on the contrary mean that the adolescents lacked ways to handle the illness. The illness made the person incoherent and divided; divided from thoughts, divided from the surroundings, and divided through the multiple painful body sites or body parts. Such is the maltreated “illness body” without coherence, without meaning, which can hardly be understood. All the difficulties the adolescents struggle with (Paper 1), together with pain (Paper 2) and the extremely affected (reduced) health related quality of life (Paper 3) makes adolescents with CFS suffer. The illness violates the body, just as the pain does.

### 6.4 Development of identity

When the adolescent project (making decisions for oneself, being more independent from parents and experiencing life together with friends) is disturbed and different from what was expected, the development is affected. Further, not being able to be with friends, feeling distrusted, feeling different and like outsiders, makes adolescents with CFS think differently about themselves. In our study, the adolescents felt that they had changed and described being another person than they used to be before they became ill, suggesting a change in identity. The lack of presence and impaired interaction with peers may have a serious impact on the development of identity and the
reorientation that occurs during adolescence. Changed identity, and confusion about identity, is also found in other studies on adolescents with CFS and other long term illnesses (Boice, 1998; Fisher & Crawley, 2013). I understand identity as a person’s awareness of who she or he is and what the person stands for. Identity might change or one might have different identities dependent on different settings. Development of identity can be illustrated by the use of Ricoeur’s (1992) work. Creation of identity might be seen as a dialectic process between identity as selfhood (ipse identity) and identity as sameness (idem identity) (Ricoeur, 1992). The dialectic process between stability and changeability is bound together in a meaningful whole through the stories we create and tell about ourselves (narrative identity) (Ricoeur, 1992). That the adolescents were clarifying their own position among peers, family and other people through telling their stories became evident in the qualitative material (Paper 1). Taking the reasoning further, the spontaneous dancing that one of the adolescents talked about, might be what ties the adolescent together in creation of a complete person as a meaningful and whole state of existence. Being in a state of completeness through, for instance, dancing (the moving body) makes the body a complete story and the self becomes a meaningful whole in contrast to the fragmented: body, illness and me. Thinking with Ricoeur like this shows that dance can represent narrative identity.

During adolescence a person normally passes from a state of being dependent on parents to autonomy (secession), and then attachment to others outside the family (Haavind & Øvreeide, 2008). According to Erikson, identity is formed during adolescence, and social relationships are therefore important during this stage (Erikson, 1968). The adolescents are occupied both with life right now and what might happen, who they are and existential thoughts like the meaning of life (Haavind & Øvreeide, 2008). Being chronically ill and worried about school, social life and the future will (despite maintaining hope for a better future), probably affect the development of personality. Most theorists assume that people’s tendencies of response are dependent on earlier experiences (vonTetzchner, 2012). Through cognitive work, they are trying to get what Antonovsky (1996) denotes a “sense of
coherence” (Antonovsky, 1996), in their lives. When approaching adulthood, adolescents are starting

to make/organize different parts of their life (past, present and future) into a meaningful whole.

As we understand, friends are one of the key factors regarding development, identity and
health related quality of life in adolescents, which makes it important to pick up and discuss this topic
further. In Paper 1 we asked if the adolescent could describe a good friend, and an answer would
typically be that a good friend is one who is there when you need her or him and who remembers
you even if you are not present. The subject of friends seemed difficult to talk about; some did not
experience loss of friends, while others either lost friends or found out who their true friend was.
Adolescents felt forgotten when they lost contact with peers. The experience of losing this contact
intensified the feeling of loneliness and the feeling of being outsiders. Even when they occasionally
managed to be with friends, for example when attending school, they did not feel like participants
because they had missed social experiences with their friends. Similar findings are found in other
studies on adolescents with CFS (Fisher & Crawley, 2013; Jelbert et al., 2010), where adolescents are
telling about losses of friends, social and academic loss and bullying from peers. In healthy
adolescents, friends are found to be one of the most important factors for health related quality of
life (Helseth & Misvaer, 2010). The orientation from parents towards peers and fellowship with
friends is a normal reorientation in adolescence, and the physical presence might seem crucial. The
English word “nobody” means a person of no importance (Online Etymology Dictionary) and both the
meaning of the word and the word itself illustrates the need of a body to be visible as a person.
Merleau-Ponty (2002) argues that we are present in the world through our bodies and our
appearance in the world is through our bodies (we are bodies). Being visible through our bodily
presence is essential to communicate with our surroundings. Frisen (2007) underlines that late
adolescence is one of the loneliest times in a person’s life, making them particularly vulnerable to
social isolation (Frisen, 2007). Adolescents who feel lonely and adolescents without a close friend
have a greater risk of developing mental difficulties (Hartberg & Hegna, 2014). When adolescence in
general is a lonely time, loneliness in adolescents with CFS might be even more intrusive. Even
though adolescents do not necessarily talk about difficult feelings with friends, they lose the sense of belonging in a community when not being present.

Having the opportunity to develop and fulfill the adolescent project is a matter of freedom, but adolescents with an illness do not necessarily have this opportunity. They are stuck in their own body and they are “stuck” with, and dependent, on their family because of their impaired body. Toombs (1993) argues that a person who is sick, is not free to do what he or she want, because the body may obstruct the intention of the person (Toombs, 1993).

Many of the adolescents with CFS felt alienated in their own bodies and from life as it used to be (Paper 1). Sveaneus (2000) says that the lived body is significantly involved in illness and is an important aspect of being-in-the-world. The body is experienced as a “‘broken tool’, which gives rise to helplessness, resistance and lack of control” (Svenaeus, 2000). Svenaeus elaborates further on Heidegger who argues that illness might be understood as unhomelike being-in-the-world (Svenaeus, 2000). According to Svenaeus, homelike is the opposite of unhomelike and can be equated with health. Further, homelike might be equivalent with positive health related quality of life, while unhomelike might concern poor health related quality of life. Echoing Heidegger and Svenaeus, adolescents demonstrated unhomelike being-in-the-world, but at the same time, they demonstrated health through the acceptance of their diseased body, as in Svenaeus’ term homelike being-in-the-world. I will argue that some of the adolescents in this study had adapted to their level of functioning (by reorienting and accepting the illness), and instead of fighting against the illness, they played along with the body. This might be a strength rather than a limitation. Being in this state, life and hope were brought back, which was reflected through dreams and hope for the future (Paper 1). Some of the adolescents with CFS managed to realize that that they had gained some important experiences during the illness period. Equally importantly, they managed to hold on to dreams about the future, hoping that their life then would not include the illness as it did at present (Paper 1). The adaption to the behavior of their body, the acceptance of the illness and the preservation of hope for
the future helps the adolescents to maintain their health. Seen in the perspective of WHO’s (p. 17) definition of mental health, they have realized their situation, which also means that they have the opportunity to realize their abilities. Further, they have managed to cope with the stresses that inflict their life. The WHO definition states that one should be able to cope with “normal” stresses of life. I think “normal” is a question of definition dependent on each individual’s situation in life. If supporting the adolescents in finding meaningful activities within their subjective limits, they might also fulfill the last part of the definition, which is to work productively and fruitfully, so that he or she can contribute to the individual’s community, which implies participation in activities with friends.

6.5 Nothing wrong

In the following discussion, it is necessary to bear in mind the definitions of the terms illness and disease as was outlined in the theoretical background (Chapter 2.8). “Illness” focuses on the subjective elements, while “disease” is used for the objective description of a malady. The use of the different terms might illustrates the distinction between them, as patients and health care professionals often perceive them. The terms are seen from different angles, which are not necessarily shared in a common understanding of a condition.

Another issue is the lack of words (Chapter 2.7) which would make us capable of naming and describing without using words which dichotomize. Even though I am aware of these issues, at present I do not believe we possess the language of wholeness that we need to bring about a common understanding of the topic. By restricting ourselves to words like “psychology” and “physiology” or “body” and “mind”, we risk perpetuating the dualistic view of humans as independent entities. Using words that dichotomize will probably affect the way we think (consciously or unconsciously). If we challenge ourselves to develop and to use words that could keep us aware of the complicated mechanism of the interplay within the human body, we might overcome some of the stigma attaching to conditions we cannot explain or prove (like diagnoses labeled MUS). The lack of words challenges the (conscious and unconscious) attention to the human as an integrated unit.
When others do not understand, it might be difficult for ill persons to trust their personal experiences. As one of the participants said, “everyone said there was nothing wrong with me, and then I started to believe that myself.” Through disbelief on the part of others, and having difficulties explaining the symptoms, the patients experience perceived illegitimacy of being ill with CFS (Fisher & Crawley, 2013). This is also the case for patients with pain without clear signs and medically explained reasons; they experience distrust from health care professionals (Ojala et al., 2015). An “explanation” that there is “nothing wrong” might be an example of different languages used by health care professionals and patients. Different understandings of medical jargon might give rise to misunderstanding, and might create distrust between patients and health care workers. One example might be the use of the term “medically unexplained symptoms” which is by some claimed to foster a dualistic (and hierarchical) view of a malady (Creed et al., 2010), which was probably not the intention by those who created the term. “Nothing wrong” might mean that the medical doctor has not been able to find structural changes or that there is nothing wrong with the available tests taken. Some might draw the erroneous conclusion that “nothing wrong” means that a patient is mentally ill. The conclusion might reflect a different understanding, but also misunderstanding, or a result of a medical hierarchy (Album & Westin, 2008). In the future, new research might explain that something is “wrong” or that not all bodily symptoms can be explained at the level of molecules and cells (Vogt, Ulvestad, Eriksen, & Getz, 2014). In some cases the statement might be based on thorough assessment and judgement, but psychological and sociological factors might also come into play, even though they do not reflect a mental illness, but a normal psychological reaction to different stressors. Linguistically, medically and existentially, the somatic jargon “nothing wrong” is misleading and wrong. This underpins the need of a renewal of, and a shared, medical language (Quintner et al., 2008), with an integrated vocabulary like a language of wholeness (Melheim, 2014), and removal of the prestige ranking of diseases (Album & Westin, 2008). A quote from one of the adolescents in the present study illustrates that CFS is low on the disease hierarchy. When he finally got a diagnosis, he stated this by explaining to me: “It turned out to be only ME.” Another way to
understand “only ME” is that being diagnosed with CFS might be experienced as a relief. Before she was diagnosed with CFS, one of the adolescents feared that she might have cancer and that she might die from it. Even though we no longer profess body and mind dualism, in practice the gap is still apparent. Vogt et al. (2015) suggest that instead of categorizing health problems as levels of parts, it might be fruitful to regard health problems as different manifestations of overarching constraints (Vogt et al., 2014). Seeing a person as being ill rather than a person having a disease has a long tradition in the discipline of nursing. This means that the emphasis is on the subjective experience rather than diagnosis, causal explanation or treatment of the disease (Nortvedt, 1998, p. 26).
Through the integration of the qualitative and quantitative work of this study, we have achieved a broader insight into, and more knowledge about, being an adolescent living with CFS. An important aspect is that the inability to participate in real life contributes to a feeling of loneliness, and of being different and an outsider, which affects social skills and development of identity. Difficult thoughts and feelings became evident during the interviews, and the adolescents’ poor health related quality of life became evident and was documented through the questionnaires. The development of identity is closely linked to issues like friends and school, as is the adolescents’ understanding of themselves. Because of the illness, their bodies behaved differently, and the alienated bodies challenged their self-understanding even further.

Even though some of the adolescents described losing friends, others experienced that some friends were faithful and maintained contact. Findings suggests that support in keeping up with friends and school, so that they feel like participants in life is essential for HRQOL. The experience of belonging might prevent mental health problems and possibly improve their health related quality of life. It is possible that peer relations of good quality can reduce the risk of depressive symptoms in adolescents with CFS, but the quality of peer relations is an area that is hardly explored (Frisen, 2007). One area for further research might be the importance of the quality of peer relations in adolescents with CFS. Another area that should be of great concern is efforts to keep the family healthy, functional and supportive.

Adolescents with CFS were seriously bothered by pain in their everyday lives and they had much lower pain thresholds compared to healthy adolescents. The pain mechanism in CFS remains unclear, and pain in adolescents with CFS is an area that should be investigated further. Despite the serious impact of the self-reported physical pain, the pain focus was different from what we expected. For adolescents with CFS, difficult feelings and existential thoughts might be equally, or even more, painful than the physically measured pain. The findings about the total burden of pain...
and suffering were one of the important benefits of this mixed method approach. A multidisciplinary approach targeting different difficulties living with the illness and its complications emerges as reasonable.

Difficulties because of the illness resulted in difficult thoughts, which were difficult to express using only words. The adolescents really made visible the different ways of expression, but towards which we might not be sensitive. Their stories were formed verbally, through nuances in the tone of voice, by crying and through their body language as it was observed during the interview. The different expressions, together with what they told about dance or the music, through which they felt they could express themselves, formed their stories and made some of their troubles visible. Different kinds of feelings communicate different states and carry with them different messages, which might be more or less acceptable to show. Further, it might be challenging for health care professionals to find sufficient time to become familiar with the individual patient’s way of expressing him or herself. Awareness towards different ways of expression should be prioritized, because suitable words to describe challenges might be difficult to find. If it is indeed the case as Thorn (2000) says, that adolescence is the broadest time of storytelling, storytelling could be used as a strength and resource in assessment and treatment of adolescents with CFS.

While ending this work, a proposal for new diagnostic criteria and a new term to replace CFS/ME has come from the Institute of Medicine (IOM). The committee appointed to do this work was The Committee on Diagnostic Criteria for ME/CFS (Institute of Medicine of the National Academies, 2015), and they have suggested the new name Systemic Exertion Intolerance Disease (SEID). The committee believes that the new name captures the central characteristics of the illness, and the new diagnostic criteria are intended to save time in the diagnostic process and to provide appropriate care. The different terms used when addressing a disease, the body and mind dualism and the disease hierarchy, have been problematized in the general discussion in this thesis, and the report from IOM shows the relevance and importance of this discussion. The committee goes far in
suggesting that CFS/ME is a physical disease, which might not improve the conditions of professional cooperation and disagreements related to this disease. Seeing this in a critical perspective, one might wonder if this will improve the reputation of a disease about which we still know too little. If the dichotomization is continued, disagreements might persist, and it will just be a question of time before the new name SEID becomes a stigmatized disease on the bottom of the disease hierarchy. It remains to be seen whether patients, patient organizations, researchers and health care professionals will embrace the renaming and new criteria. The new diagnostic criteria are still not validated, so the practical implications of the new diagnostic criteria are unknown.
References


Maloney, E. M., Boneva, R., Nater, U. M., & Reeves, W. C. (2009). Chronic Fatigue Syndrome and High Allostatic Load: Results From a Population-Based Case-Control Study in Georgia. Psychosomatic Medicine, 71(5), 549-556. doi: Doi 10.1097/Psy.0b013e3181a4fefa8


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Appendix 1
Regional komité for medisinsk forskningsetikk
Sør-Norge (REK Sør)
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E-post: rek-2@medisin.uio.no
Nettadresse: www.etikkom.no

Lege, Dr. med. Vegard Bruun Wyller
Barneklinikken
Rikshospitalet HF
0027 Oslo

Dato: 17.1.08
Deres ref.:
Vår ref.: S-07471a

S-07471a Sykdomsmekanismer hos ungdom med kronisk utmattelsessyndrom/myalgisk encefalopati (CFS/ME) [2.2007.2861]

Vi viser til bre datert 3.1.08 med følgende vedlegg: informasjonsskriv med samtykkeerklæring for foresatte og de eldste ungdommene og informasjonsskriv for de yngste ungdommene.

Komiteen tar svar på merknader til etterretning.

Komiteen har ingen merknader til de vedlagte informasjonsskriv.

Komiteen godkjenner at prosjektet gjennomføres og tilrår at forskningsbiobank opprettes.

Komiteen videresender skjema for opprettelse av forskningsbiobank og informasjonsskrivet samt komiteens vedtak til Sosial- og helsedirektoratet for endelig behandling av opprettelse av forskningsbiobanken.

Vi ønsker lykke til med prosjektet.

Med vennlig hilsen

Kristian Hagestad
Fylkeslege cand.med., spes. i samf.med
Leder

Jørgen Hardang
Sekretær

Kopi: Sosial- og helsedirektoratet, Postboks 7000, St. Olavs plass, 0130 Oslo
Appendix 2
Appendix 2

Intervjuguide

1. Fortell om deg selv
   (venner, familie, skole, fritidsaktiviteter)
2. Hva slags reaksjoner opplevde du å få når du fortalte at du var syk og hva slags sykdom du har?
   (lege, sykepleier, lærer, venner, familie)
3. Fortell om en hendelse eller reaksjon du husker godt
4. Hvordan opplevde du reaksjonen/hendelsen?
5. Har sykdommen betydd noe i forhold til tanken du har om deg selv og hvem du er? Hvordan er det å være deg (navnet på vedkommende)?
6. Hvis du tenker på en helt vanlig dag, fortell om hva som er en god dag og hva som er en dårlig dag. Hva tenker du var en bra og en dårlig dag før du ble syk?
7. Hvordan ser drømmedagen din ut?
8. Hva er det du opplever som vanskelig?
9. Er det noe som er umulig å gjøre for deg nå og er det noe som er umulig for deg å gjøre i fremtiden?
10. Dersom det er noe du skulle ønske du kunne gjøre, hva ville du gjøre da?
11. Hva er det du opplever som mest plagsomt ved sykdommen din?
12. Hva tenker du kunne vært annerledes ved livet ditt dersom du ikke hadde hatt de plagene du har nå som du er syk?
13. Hva er en god venn?
14. Er det noen (positive) erfaringer du har opplevd/fått som du tror ungdommer på din alder ikke har?
15. Hva er det som gjør deg glad eller gir deg en positiv opplevelse?
16. Hvis du kunne viderebringe noen råd til andre ungdommer som nettopp hadde fått diagnosen, hva ville du si til dem?
17. Hvis du kunne gi noen råd til de som jobber med ungdom som har kronisk utmattelsessyndrom, hva villed de rådene være? Er det noe de burde ha gjort annerledes og i så fall hva?
18. Er det noe du føler du ikke har fått sagt noe om, men som du gjerne vil si?
**Appendix 3: Example theme; The illness, the body and me**

<table>
<thead>
<tr>
<th>Sykdommen, kroppen og jeg</th>
<th>Noen ganger føles det som om verden går videre uten meg</th>
<th>Jeg bestemmer over kroppen og sykdommen kan gå og legge seg</th>
<th>Verden innenfor og verden utenfor (usynlighet)</th>
<th>Kroppen er så tydelig</th>
<th>Tap av seg selv/tanker som gjør dem verre eller bedre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lever i sin egen verden</td>
<td>Å ha en sykdom er et langsamt prosess</td>
<td>Lite eller ingen kontakt med venner</td>
<td>Tolker kroppens signaler</td>
<td>Opplevelse av seg selv som en annen</td>
<td></td>
</tr>
<tr>
<td>Tilsynelatende som kjedelig</td>
<td>Vil ikke tenke på sykdommen hele tiden for da får jeg ikke gjort noe gøy</td>
<td>Fravær skaper ikke-eksisنس</td>
<td>Valg for kroppen</td>
<td>Sykdommen har tatt fra ham den han var</td>
<td></td>
</tr>
<tr>
<td>Livet er ensformig med små variasjoner</td>
<td>Gir sykdommen motstand</td>
<td>Å bli husket på er avhengig om man er hyggelig</td>
<td>Slappe av når kroppen er sliten</td>
<td>Opplevelse av seg selv som en annen</td>
<td></td>
</tr>
<tr>
<td>Å stå stille uten å komme seg videre er vanskelig</td>
<td>Kroppen kan hjelpe til å være mest mulig frisk</td>
<td>Opplevelse av å være glemt av venner</td>
<td>Følelse av velvære når kroppen er ren</td>
<td>Identifiseres som en sykdom og ikke som en person</td>
<td></td>
</tr>
<tr>
<td>Observerer hva alle de andre gjør uten å kunne være med</td>
<td>Vil ikke være med på at sykdommen har regien</td>
<td>Viktige andre bryr seg ikke</td>
<td>En god dag er en dag der du føler deg som den du var før</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Følelse av å være utenfor og på siden av livet</td>
<td>Vil ikke at sykdom setter grenser for</td>
<td>Å ikke være informert om endringer som skjer i livet</td>
<td>Smerter støyer krefter fra kroppen</td>
<td>Andre tro og mening blir til slutt en sannhet</td>
<td></td>
</tr>
<tr>
<td>Tiden er lang når man venter</td>
<td>Taker sykdommen med</td>
<td>Bører smerten alene og våger ikke dele følelser med venner</td>
<td>Viktig å samarbeide med kroppen</td>
<td>Sykdommen har vært der så lenge at hun har blitt vant til den og den har blitt en del av henne</td>
<td></td>
</tr>
<tr>
<td>Tiden er lang når man kjeder seg</td>
<td>Et spill mellom seg selv og sykdommen</td>
<td>Melder seg ut og orker ikke delta i det virkelige livet</td>
<td>Jeg bestemmer over kroppen</td>
<td>Seg selv som nytt bekjentskap</td>
<td></td>
</tr>
<tr>
<td>Dagene er tomme og innholdslosse</td>
<td>Ingen vet hvordan det er</td>
<td>Vilje er ikke nok når kroppen ikke vil</td>
<td>Smertefullt og ikke være akseptert som den hun er med sin sykdom</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Har satt fremtiden på vent</td>
<td>Opplevelse av å ikke passe inn</td>
<td>Fanget i egen kropp</td>
<td>Tankene blir mørke og destruktive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>På en dårlig dag er det som å være i dvalomodus</td>
<td>Venner har ikke innsikt og forstår ikke</td>
<td>La kroppen hvile når den trenger det</td>
<td>Vanskelige tanker og usikre fremtidsutsikter gir alt mye verre</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lever livet passivt mottagende</td>
<td>Blir gradvis mer usynlig for andre</td>
<td>Hjelper kroppen til å bruke mindre energi på å fordøye maten</td>
<td>Alt oppleves mye verre når man blir liggende å tenke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opplevelse av en uendelighet av oppgaver</td>
<td>Å ikke bli sett og regnet med stjeler energi</td>
<td>Det er kroppen som er syk og ikke hodet</td>
<td>Livet uten sykdommen er vanskelig å forestille seg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Savn av det normale livet</td>
<td>Føler seg ensom og livet re urettferdig</td>
<td>Behov for bekräftelse på at kroppen er frisk</td>
<td>Å prioritere det sosiale, det som gir energi og glede har betydning for psykisk helse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opplever ingen mening med når man ikke kan gjøre det man vil</td>
<td>Kroppen svikter og det går ikke an å stole på den lengre</td>
<td>Kroppen setter grenser for friheten til å velge</td>
<td>Følelsom som sårbart svinger med sykdommen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Holder taket i livet</td>
<td>Ønsker at kroppen skal gjøre det hun vil uten at hun blir utsatt</td>
<td>Kroppen setter grenser for friheten til å velge</td>
<td>Positive følelser til det å ha energi</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Komme på høyde med livet igjen</td>
<td>Kroppen setter grenser for friheten til å velge</td>
<td>Han (kroppen) orker ikke</td>
<td>Blir gladere av å tenke på noe gøy à se frem til</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Livet kommer tilbake igjen</td>
<td>Han (kroppen) orker ikke</td>
<td>Kroppen vokser og det går ikke an å stole på den lengre</td>
<td>Utredningstiden preget av usikkerhet</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 4
Appendix 4a: Distribution of pain in adolescents with CFS measured by the Brief Pain Inventory

<table>
<thead>
<tr>
<th>Item</th>
<th>Patient (n=120)</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain worst</td>
<td>6 (5,1)</td>
<td>3 (2,5)</td>
</tr>
<tr>
<td>Pain least</td>
<td>40 (33,9)</td>
<td>2 (1,7)</td>
</tr>
<tr>
<td>Pain average</td>
<td>8 (6,8)</td>
<td>3 (2,5)</td>
</tr>
<tr>
<td>Pain now</td>
<td>30 (25,4)</td>
<td>2 (1,7)</td>
</tr>
<tr>
<td>General activity</td>
<td>23 (19,5)</td>
<td>2 (1,7)</td>
</tr>
<tr>
<td>Mood</td>
<td>19 (16,1)</td>
<td>2 (1,7)</td>
</tr>
<tr>
<td>Walking</td>
<td>39 (33,1)</td>
<td>2 (1,7)</td>
</tr>
<tr>
<td>School</td>
<td>22 (18,6)</td>
<td>2 (1,7)</td>
</tr>
<tr>
<td>Relation to others</td>
<td>45 (38,1)</td>
<td>2 (1,7)</td>
</tr>
<tr>
<td>Enjoy</td>
<td>35 (29,7)</td>
<td>2 (1,7)</td>
</tr>
</tbody>
</table>

Appendix 4b: Distribution of pain in healthy adolescents measured by the Brief Pain Inventory

<table>
<thead>
<tr>
<th>Item</th>
<th>Healthy (n=39)</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain worst</td>
<td>9 (23,1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pain least</td>
<td>27 (69,2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pain average</td>
<td>7 (17,9)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Pain now</td>
<td>27 (69,2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>General activity</td>
<td>18 (46,2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Mood</td>
<td>19 (48,7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Walking</td>
<td>22 (56,4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>School</td>
<td>22 (56,4)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Relation to others</td>
<td>27 (69,2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Enjoy</td>
<td>28 (71,8)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>