Pain, Symptoms and Health Related Quality of Life in Intensive Care Survivors

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Summary

A growing number of studies have addressed the long-term consequences of intensive care unit (ICU) treatment. However, at the start of the present study few studies had studied pain, symptoms and health related quality of life (HRQOL) in the same sample of ICU survivors. The aim was to explore: the prevalence of chronic pain in ICU survivors at 3 months and 1 year after ICU discharge, the association between pain and anxiety, depression, fatigue, sleep disturbance and post-traumatic stress symptoms (PTSS) in ICU survivors, and if HRQOL was different in ICU survivors compared to the general population and if social support, comorbidity and pain interference were associated with HRQOL in ICU survivors.

The study method was a mailed questionnaire, and data were collected at both 3 months and 1 year after discharge from study ICUs. The study sample was 118/89 adult ICU survivors from two mixed ICUs in Oslo University Hospital (OUS). The ICU survivors gave their written consent at 3 months after ICU discharge. The study was approved by The Regional Committee for Medical and Health Research Ethics and the Data Inspectorate at OUS. The study was also enlisted in Clinical Trials: NCT02279212.

Prevalence rates of intensive care survivors' symptoms at 3 months (n=118) were chronic pain 58 (49.2%), anxiety/depression 24/118 (20.8%), fatigue 18/118(15.3%), PTSS 15 (12.8%) and sleep disturbance 58/118 (49.2%). Prevalence rates at 1 year *(n*=89) changed only slightly; chronic pain 34 (38.2%), anxiety/depression 17 (20.0%), fatigue 12 (13.8%), PTSS 13 (15.1%) and sleep disturbance 40/89 (46.5%). Associations were strong between pain and presence of sleep disturbance, anxiety/depression, PTSS and fatigue. Shoulders were one of the most common pain locations at both 3 months and 1 year. Physical and mental HRQOL were both

reduced at both 3 months and 1 year in ICU survivors compared with the general population. This reduction was more pronounced at 3 months for physical HRQOL, while a small reduction in mental HRQOL was not clinically relevant. Social support was statistically significantly associated with increase in mental HRQOL at 3 months, while number of comorbidities was statistically significantly associated with a reduction in physical HRQOL at 3 months and 1 year and mental HRQOL at 1 year. Lastly, pain interference was statistically significantly associated with a reduction in physical HRQOL at 3 months and 1 year.

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Finally the day has arrived, many years of work have come to an end. I started out on a journey in 2007 when I got the initial funding to work out the study protocol. I soon learned that completing a PhD takes time, a lot of time. The inclusion of patients started in May 2010 and ended in January 2014. Why did it take so long? First of all I have had the privilege to work part-time as an ICU nurse throughout. This has kept me in touch with ICU medicine, nursing and all the ICU patients. It has also reminded me of who the main characters in this work really are: The ICU survivors. So my main thanks go to all the ICU patients/survivors and their family who have inspired me and enabled me to do this study. If the ICU survivors hadn´t participated, there would not have been any study.

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Acronyms and abbreviations

ARDS – Adult Respiratory Distress Symptom

BPI-SF – Brief Pain Inventory Short Form

CIPNM – Critical Illness Polyneuropathy/myopathy

ECMO – Extra Corporal Membrane Oxygenation

GSDS – General Sleep Disturbance Scale

HADS – Hospital Anxiety and Depression Scale

HRQOL – Health Related Quality of Life

IABP – Intra Aortic Balloon Pump

IASP – International Association for the Study of Pain

ICU – Intensive Care Unit

ICU LOS – Intensive Care Unit Length of Stay

LFS – Lee Fatigue Scale

PTSS/D – Post Traumatic Stress Symptoms/Disorder

SAPS II – Simplified Acute Physiology Score II

SF-12 – Short Form Health Survey 12

SOFA – Sequential Organ Failure Assessment

SPS – Social Provision Scale revised

TOUS – Theory of Unpleasant Symptoms

List of papers

I Prevalence, Location and Characteristics of Chronic Pain in Intensive Care Unit Survivors *in Pain Management Nursing (2017) doi.org/10.1016/j.pmn.2017.11.005*

(Reprinted with permission from Pain Management Nursing)

II Intensive Care Survivor-reported Symptoms: A Longitudinal Study of Survivors' Symptoms *in Nursing in Critical Care (2017) doi: 10.1111/nicc.12330*

(Reprinted with permission from Nursing in Critical Care)

III Health-Related Quality of Life in Intensive Care Survivors: Associations with Social Support, Comorbidity, and Pain Interference in *PLOS ONE (2018) doi.org/10.1371/journal.pone.0199656*

(Open access).

1.0 Introduction

Intensive Care Unit (ICU) patients are characterized by critical or life-threatening illness (1). There can be many causes for becoming an ICU patient; accidents, acute illness (e.g. cardiac infarction, sub arachnoid hemorrhage (SAH), a chronic illness that has worsened (e.g. acute or chronic liver failure), cancer, severe infections (e.g. sepsis) or recovery after major surgery or complications following surgery. Regardless of initial admission diagnosis in the ICU, the ICU patients may suffer from severe complications like multi-organ failure (MOF) (1). ICU patients can be of all ages, from newborn to very old. In 2007 the Norwegian Intensive Care Registry (NIR) documented over 10 000 ICU stays and over 55 000 ICU length of stay (ICU LOS) days in Norwegian ICUs. 12.1 % of ICU patients died in the ICU and an additional 5.7% died before discharge from hospital (2). This means that over 80 % of the ICU patients survived their critical illness and recovered to such an extent that they could be discharged from the hospital.

Intensive care medicine and ICUs became common during the 1950s -1960s (3), and for decades the success criteria for ICU treatment was a reduction in the 30 days mortality rate (3). As an ICU nurse working in the ICU, I have always wondered how the ICU patients experienced their quality of life after their stay in the ICU, and if they experienced different symptoms. I considered the 30 days mortality rate to be an insufficient measure of ICU treatment success. I wanted more details. This was the main driving force behind the present study. There has been a change over the last decade or two; more and more research has focused on the long-term outcome for this patient group (4). There are an increasing number of papers on quality of life, prevalence of depression, anxiety, post-traumatic stress disorder/symptoms (PTSD/PTSS) and critical illness polyneuropathy/myopathy (CIPNM) (5-10). Most of

these symptoms have been studied in isolation. We still have limited knowledge about the prevalence of pain and chronic pain, fatigue and sleep disturbance and, not least, how these different symptoms influence each other. The present study aims to increase knowledge regarding pain, different symptoms and health-related quality of life in IUC survivors, to help improve treatment and rehabilitation of ICU survivors.

2.0 Background

2.1 Intensive Care

When in the ICU, the ICU patients rely on life supporting technologies like ventilators, dialysis, Intra-Aortic Balloon Pump (IABP), Extra Corporal Membrane Oxygenation (ECMO) or other. They also need highly trained and competent personnel (e.g. different medical specialists, specially trained nurses, and physiotherapists). Furthermore, they need constant monitoring and different types of medication like antibiotics, sedatives, analgesics, inotropic medication etcetera. An ICU stay may last for just a few hours or for weeks and months. It is common to regard ICU stays shorter than 24 hours as post-operative stays. During their ICU stay these patients are deprived of their natural environment, including normal contact with relatives and their ability to perform normal activities (e.g. physical activity, eating, working, normal socializing) (11, 12). They are exposed to pain (13), noise (14, 15), sleep deprivation (16, 17) and disruption of normal routines (11). They may also experience a wide range of symptoms during their ICU stay, such as thirst, hunger, nausea, pain, sleep disturbance, anxiety, depression and other discomforts (13, 18, 19). Both the critical illness and different drugs used in the ICU may affect cognitive functioning, and a large proportion of ICU patients are at some time during the stay confused and diagnosed with delirium (4, 20-22)

2.2 Pain

Pain is defined by the International Association for the Study of Pain (IASP) as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage” (23). Pain is an important experience as it protects us from possible harm (e.g. burns, trauma). Pain is the body’s signal to the brain that something is

wrong and may cause harm to the organism (24). Pain is a subjective feeling/experience, and what is painful to me may not be painful to you. Different individuals may describe the same stimuli (pain) differently. Pain can be experienced as burning, throbbing, stabbing, etcetera (23).

Pain is divided into acute pain and chronic pain. Acute pain is defined by IASP as *" denoting pain that is caused by occurrences such as traumatic injury, surgical procedures, or medical disorders; clinical symptoms often include increased heart rate, blood pressure, and respiratory rate, shallow respiration, agitation or restlessness, facial grimaces, or splinting"* (23), and chronic pain is defined as *"pain exceeding an average healing period of 3–6 months"* (25). There are other definitions of chronic pain, but in the present study we used the one mentioned above. In the present study we used the term chronic pain, but other terms can also be used for the same phenomenon, such as persistent pain. It is also common to separate between cancer or malignant pain and non-cancer or non-malignant pain. In the present study we have primarily investigated non-cancer pain. Pain can also be classified according to the possible pathophysiology of the pain: nociceptive-, neuropathic-, idiopathic or nociplastic pain (23, 26). Nociceptive pain is pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors (23). Nociceptive pain may be brief or lengthy but it normally subsides when the lesion and inflammation is healed (26). Neuropathic pain is pain caused by a lesion or disease of the somatosensory neuro system (23). This may lead to hyper- and hypo- sensory phenomena. Neuropathic pain may be both spontaneous and provoked (26). Nociplastic pain is pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing activation of peripheral nociceptors, or evidence of disease or lesion of the

somatosensory system causing the pain (23). Idiopathic pain is recognized by unknown pathophysiology, but may also be both spontaneous and provoked, and acute or chronic (26). ICU patients may experience both acute and chronic pain in the ICU (27). Many ICU patients have experienced trauma, illness and surgery that may cause acute pain (e.g. fractures, surgery wounds, burn wounds, etcetera) and they may already have chronic pain from other conditions and illnesses (e.g. Rheumatoid Arthritis, migraine, cancer, etcetera). The pain may be either nociceptive, neuropathic or nociplastic in nature (26).

A common way to measure pain in awake patients in hospitals is by using the Numeric Rating Scale (NRS), which is an 11-point scale for patient self-reporting of pain (0 being no pain and 10 being worst pain imaginable (28) , based on this scale pain can also be described as mild (NRS 1-3), moderate (NRS 4-6) and severe (NRS 7-10) pain, like McCaffery & Beebe does (29). This present study defined mild, moderate and severe pain like McCaffery & Beebe (29).

The Global Burden of Disease Study (30) has studied the prevalence and impact of 354 different diseases and injuries in 195 countries/territories. Based on these findings, different pain conditions like headache and lower back pain were rated top three (from 1990 to 2017) as causes for years spent living with disability. There was an increase in lower back pain of 30 % from 1990 to 2017 and an increase of headaches of 34% in the same time period. These findings represent all ages and both sexes (30). A large European survey (31) found that chronic pain is a common health problem. Of the 46 394 participants 19 % had suffered from chronic pain over the last 6 months or longer. The same participants had also experienced chronic pain the last month and several times the last week. Their pain was 5 or more on the NRS (this was an inclusion criterium) (31). There were differences in

prevalence of chronic pain between the European countries. For instance, Norway reported a prevalence of 30 % chronic pain in the general population (representing the highest score), while Spain only reported 12 % chronic pain (31). Breivik et al (31) also found in a sub-sample (4839 participants) of interviewees that the participants with chronic pain reported other symptoms related to chronic pain, like depression (21%). The participants in the subgroup (31) also reported that they were less able or unable to work outside their home (61%) and 19% had lost their job or had to change jobs (13%) due to their pain.

While Breivik et al (31) studied the prevalence and impact of chronic pain, others have studied the economic costs of diagnosis related to chronic pain (32, 33). Gustavsson et al (32) studied socio-economic costs of diagnosis related to chronic pain in one part of Sweden in 840 000 participants, and found that the mean total cost was 6400 EUR/year. The mean cost was higher in cancer patients (10 400 EUR/year). Indirect costs like sick leave and early retirement were the largest part of the socio-economic cost (59%) (32). Another large (8412 participants) European study (33) on the economic costs of headache (a common source of chronic pain) found that the mean cost of migraines was 1222 EUR, tension headaches 303 EUR and 3561 EUR for headaches caused by medication overuse. For all these types of headaches the indirect costs, like absence from work and reduced work productivity, all amounted to more than 90 % of the costs (33). As many as 10-50 % of acute postoperative pain after common surgery may become persistent or chronic (34). Predictors of persistent/chronic post-surgical pain vary with different surgical procedures, but Bruce et al (35) summed up possible risk factors in 2011 as the following: genetic predispositions, demographic, clinical (pain history, type of surgery, anesthesia, acute pain severity) and psychological factors (vulnerability vs.

resilience). In a review from 2000 (36) different common surgeries were studied for predictors of chronic post-surgery pain. Several pain states were related to specific surgeries, but several predictors were related to other factors like the extent or intensity of acute post-operative pain, pain or symptoms before surgery, and nerve dysfunction. In addition to Perkins et al's (36) and Bruce et al's (35) findings, Kehlet (34) adds iatrogenic neuropathic pain, ongoing inflammation, intensity of acute pain, genetic factors, catastrophing, perceived social support and solicitous responding as possible risk factors of persistent post-surgical pain. Theunissen et al (37) found in their review of 29 studies that in 16 studies, pre-operative anxiety or pain catastrophing were significantly associated with higher rates of chronic post-surgical pain.

Previous studies from other patient groups have revealed that anxiety and depression correlate with chronic pain and insomnia (38-40). Chronic pain furthermore affected psychosocial wellbeing (41). In a large international study on patients seeking primary health care, Simon et al (39) found that 50 % of patients with depression had multiple medical symptoms like pain. Multiple medical symptoms may include aches and pain, lack of energy, disrupted sleep, change of appetite and palpitation (41). Bair et al (38) studied patients with depression and comorbidity, and found that 2/3 of patients with depression had one or more pain complaints. Bair et al (38) also found that depression occurs in up to 85 % of patients with pain disorders. For patients with anxiety, 1/3 of the patients also reported pain. Ohayon et al (40) found in a large study of people (N= 14915) in several European countries that of the 16.5 % respondents with symptoms of depression 27.6 % also reported one chronic painful physical condition. In the same study (40) study 4 % reported major

depression. These respondents with major depression had an increased risk of also reporting 1 chronic painful physical condition (OR 4.0 95% CI 3.5-4.7).

When we searched the literature for studies regarding pain and chronic pain in ICU survivors, we found numerous papers about post-operative pain and pain in the ICU (13, 42-52) but only two about chronic pain and pain in ICU survivors measured with a validated instrument for measuring pain (53, 54). Boyle (53) found that 28 % of ICU survivors reported chronic pain that influenced their quality of life. Kong (54) studied a subgroup of ICU survivors (stroke patients) and found the prevalence of pain to be 44%. Other studies have measured bodily pain as part of quality of life studies (55-62). They all show that different groups of ICU survivors (e.g. ARDS, trauma, prolonged ICU stay or mechanical ventilation) report more pain than the general population. Both Short Form Health Survey 36 (SF 36) and Short Form Health Survey 12 (SF 12) have bodily pain as part of their physical quality of life measure (63, 64). Schelling et al. (65) found that ICU survivors after Adult Respiratory Distress Syndrome (ARDS) had a reduction in physical function of 25% and a 40 % higher (absolute value) prevalence of chronic pain than an age- and gender-matched control group of the general population. The same patient group also had 27.5 % higher (absolute value) prevalence of PTSD than the control group (65).

2.3 Quality of Life (QOL) and Health Related Quality of Life (HRQOL)

Ferrans (66) defines QOL as a person's sense of satisfaction or dissatisfaction with areas in life that are important to the individual, which implies the person's subjective experience of QOL. This means that true QOL only can be measured by self-reporting (e.g. a questionnaire). Spilker (67) defines QOL as *a multi-dimensional*

concept with five major domains: physical or functional status, psychological status or wellbeing, social interactions, economic or vocational status and religious or spiritual status. Both these definitions are very broad, and many health care researchers have limited QOL to a narrower definition consisting of the domains that seem most relevant to health in the term HRQOL (68, 69). HRQOL is defined as a multi-dimensional and subjective concept describing a person's physiological and psychological status, functional ability, his/her wellbeing and social interaction (68). QOL is a subjective and composed concept which is influenced by other phenomena, like pain (70). HRQOL is studied extensively both in the general populations (71) and different patient groups (72-75). This present study has chosen the narrower concept of HRQOL, since we found it difficult to collect data on all aspects of the ICU survivor's life with regards to quality of life.

Previous research has also studied predictors or associations with changes in HRQOL. Loge et al (71) found that sociodemographic variables (e.g. age, sex, marital status and level of education) had an impact on physical and/or mental health in the Norwegian general population (n= 3500). From cancer patients we know that pain influences all the different dimensions of QOL (76). Irvine (73) found in his review of quality of life in patients with ulcerative colitis that the severity of the disease had the largest impact on quality of life, but also the type of treatment, side effects of treatment, adherence to treatment and psychosocial problems and comorbidity had an impact. Voll-Anerud et al (74) found that respiratory symptoms like breathlessness had a negative impact on both physical and mental health in both patients with asthma/COPD and subjects without. Voll-Anerud's study was conducted in Europe (n= 6009). Another European study found that chronic conditions (e.g. arthritis, chronic lung disease, congestive heart failure) had a negative impact on

HRQOL (n= 2031-4084) in different countries (72). Ribu et al (75) studied patients with diabetes and leg ulcers (n = 127) and found that elderly men living alone with low levels of education and no work had reduced HRQOL compared with both the general population (n= 5903) and a control group of diabetes patients without leg ulcers (n= 221). According to Dowdy et al.'s (77) large review on QOL in ICU survivors, several studies have been conducted to reveal predictors of QOL after ICU discharge. The results are not conclusive, but older age and severity of illness may have a negative association with physical health (77). In the same review age did not seem to be associated with mental health in the same way as physical health. Boyle et al. (53) found that younger age was associated with reduced physical health. Then again, Kaarlola et al. (78) studied QOL in older ICU survivors (65 years and older) and found an association between older age and reduced physical health, but the majority of the elderly ICU survivors rated their overall QOL as good.

It is well documented that ICU survivors have reduced HRQOL both shortly (6 months - 2 years) after the ICU stay (6, 7, 79), but HRQOL in ICU survivors was also found to be reduced up to 12 years after an ICU stay (5). Research regarding HRQOL in ICU survivors has also found that physical health is most reduced the first year, but physical health also shows greater improvement over time compared to baseline (pre ICU) (77, 79). Cuthberston et al. (80) studied QOL in ICU survivors up to 5 years after ICU discharge and found that physical health was significantly reduced at 3 months after discharge, but at 12 months the physical health was the same as premorbid status, before the physical health again declined from 2.5 years to 5 years. Mental health has shown to be less reduced in ICU survivors than physical health compared to the general population, and the reduction varies over time (80, 81). Cuthbertson et al. (80) found a reduction in mental health after ICU

discharge, but they also found that mental health improved at 6 months after ICU discharge and was now similar to the general population. Furthermore, research has shown that ICU survivors also have a lower HRQOL before the ICU stay, compared with the general population (7, 77, 81, 82).

2.4 Symptom Burden in ICU Survivors

A symptom is defined as: *"a subjective experience reflecting changes in the biopsychosocial functioning, sensations, or cognition of an individual. In contrast, a sign is defined as any abnormality indicative of disease that is detectable by the individual or others (83, 84)"*.

It seems self-evident that both symptoms and signs are important to ICU survivors, their relatives and health care workers, and that good communication about these is crucial. Earlier research on symptoms in ICU survivors has shown that they suffer from a variety of symptoms, such as anxiety, depression, pain and CIPNM (5, 9, 10). Prior to this study few studies had focused on more than one or two symptoms at the time (e.g. chronic pain, anxiety and depression, PTSD, sleep disturbance) (8, 9, 53, 85, 86). We only found one study prior to this present study on multiple symptoms, but that concerned symptoms during the ICU stay, not after the ICU discharge (19). During this present study, another pilot study by Choi et al (87) studied multiple symptoms in ICU survivors and found sleep disturbance, fatigue, weakness and pain to be the four most common.

Studies of multiple symptoms are known from cancer research, indicating that several symptoms may occur together and influence each other, increasing the symptom burden or influencing quality of life (88-91). Dodd et al (92) also suggests that multiple symptoms may have synergetic effects on patient outcome. Portenoy et

al (88) found that cancer patients may experience as many as median 11.0 (range 0-25) symptoms and Chang et al (89) found the median prevalence of symptoms in cancer patients to be 8.0 (range 0-30). Common symptoms in both these studies (88, 89) were lack of energy, pain, dry mouth, insomnia, psychological distress. In Portenoy et al's (88) study a number of symptoms was associated with reduced quality of life. Also Zoëga et al (91) found that a number of symptoms had a negative association with quality of life. Miaskowski et al. (93, 94) have done several studies on multiple co-occurring symptoms in different patient groups (e.g. oncology patients), and in Norway research has been carried out on multiple symptoms in breast cancer patients (95) and Chronic Obstructive Pulmonary Disease (COPD) patients (96).

The research on multiple symptoms conducted by Miaskowski and colleagues inspired us to study the following symptoms: anxiety, depression, post-traumatic stress symptoms, fatigue and sleep disturbance, which had already been studied in ICU survivors (8, 9, 85, 86), but at the start of this study the majority of these symptoms had been studied in isolation or in pairs. We thought that to study them as multiple symptoms instead of single symptoms would bring new or more knowledge to the understanding of ICU survivor's outcome. These symptoms are also common in patients with chronic pain (e.g. patients with fibromyalgia or chronic widespread pain) (97-99).

2.4.1 Anxiety and Depression

Anxiety can be understood as extreme apprehension and worry and is a normal reaction to stressful situations. Sometimes, however, the anxiety becomes excessive

and influences normal life in a negative way (100). Common anxiety symptoms are: hyperarousal and somatic tension like shortness of breath, feeling dizzy or lightheaded, dry mouth, trembling or shaking (101).

Depression is in this study understood as depressive symptomatology and not as major depression (which is thoroughly defined in for example ICD-10 and DSM-4). Common depressive symptoms are: anhedonia, lack of interest, low energy, having no fun, apathy, psychomotor retardation, hopelessness (101). It is important to draw the distinction between depressive symptoms and major depression, because the instrument used in this study to describe anxiety and depression (HADS) is insufficient to provide an anxiety or depression diagnosis. The prevalence of depression is reported in a range from 8-57% in ICU survivors (9) with a mean value of 28%. Scragg et al. (85) also reported a prevalence of depression at 30% and a prevalence of anxiety at 43% in a mixed ICU sample.

2.4.2 Fatigue

Fatigue can be described from two different perspectives: a physiological perspective and a psychiatric perspective. The physiologist describes fatigue as the end result of excessive energy consumption, depleted hormones, or the diminished ability of muscle cells to contract. The psychiatrist describes fatigue as a subjective state of weariness related to reduced motivation, prolonged mental activity, or boredom that occurs in situations such as chronic stress, anxiety or depression (102). Fatigue is a well-known symptom from research in cancer patients (103-105). When we planned this study, we were unable to find any specific research on fatigue in ICU survivors, but based on the physiological and psychiatric descriptions above, one could argue

that critical illness and an ICU stay may be associated with fatigue. During the study period we found two studies that will be mentioned in the discussion.

2.4.3 Sleep Disturbance

Sleep disturbance is defined as nonorganic insomnia: "*A condition of unsatisfactory quantity and/or quality of sleep, which persists for a considerable period of time, including difficulty falling asleep, difficulty staying asleep, or early final wakening. Insomnia is a common symptom of many mental and physical disorders* (106)". Previous research have found correlations between psychiatric diagnosis/symptoms (e.g. depression and anxiety) and insomnia (107, 108). In an old study of the general population (n= 7954) 10.2 % reported insomnia and 40 % of these also reported a psychiatric disorder. The respondents with insomnia were at a higher risk of developing depression (OR 39.8; 95% CI 19.8 to 80.0) (108). Ohayon et al (40) also studied the general population and found a prevalence of insomnia that affected the daytime living of 19.1%. The insomnia prevalence increases significantly with age. In more than 90 % the insomnia had lasted more than 6 months. About 28% of the respondents with insomnia also had a current diagnosis of mental disorder (107).

The ICU environment has been and remains a noisy and sleep-depriving environment, and this is associated with sleep disturbance in the ICU (86). Furthermore, the use of different medications, the critical illness in itself and non-synchronized cooperation of the ICU patient with the ventilator may be associated with sleep deprivation (86). Lee et al. (86) studied chronic sleep disturbance in ARDS survivors. They found that a small group (4.6%) of ARDS survivors suffer from chronic sleep disturbance several months after the ICU discharge. Orwelius et al. (109) found that sleep disturbance in ICU survivors was common (38%) and that

there was little change in sleep disturbance pre- and post-ICU stay. Women and individuals with concurrent diseases were at a higher risk of reporting sleep disturbance (109). Orwelius et al. (109) did not find any association between characteristics of the ICU stay (ICU LOS, admission diagnose) and sleep disturbance. During the study period we have found a few new research papers that will be mentioned in the discussion.

2.4.4 Post-Traumatic Stress Symptoms (PTSS)

Post-Traumatic Stress Disorder is defined as: "*Arises as a delayed or protracted response to a stressful event or situation (of either brief or long duration) of an exceptionally threatening or catastrophic nature, which is likely to cause pervasive distress in almost anyone. Typical features include episodes of repeated reliving of the trauma in intrusive memories ("flashbacks"), dreams or nightmares, occurring against the persisting background of a sense of "numbness" and emotional blunting, detachment from other people, unresponsiveness to surroundings, anhedonia, and avoidance of activities and situations reminiscent of the trauma. There is usually a state of autonomic hyperarousal with hypervigilance, an enhanced startle reaction, and insomnia (106)*". We used the term PTSS since it is not possible to diagnose someone with PTSD using only a questionnaire. The stressful event in question is the ICU stay/being critical ill. Davydow et al. (8) did a review on prevalence and predictors of PTSD/PTSS in ICU survivors and found a prevalence of 22 % of PTSS based on a questionnaire. If the diagnosis PTSD was given by a clinician, the prevalence was 19%. Prior psychopathology, increased use of benzodiazepine during the ICU stay, and unpleasant memories from the ICU (e.g. nightmares) were all predictors of developing PTSS post-ICU stay. The severity of the illness was not a

predictor. PTSS after ICU stay was associated with lower HRQOL. Myhren et al. (110) found a prevalence of PTSD in ICU survivors at 27%. They found no differences between medical, trauma or surgical ICU survivors. Deja et al. (111) reported a 29 % prevalence of PTSS in ARDS survivors. They found associations between PTSS and traumatic memories from the ICU stay and anxiety during the ICU stay.

2.5 Social Support

According to Cutrona (112) social support may be defined and operationalized in many ways, but there seems to be a consensus that social support is a multi-dimensional concept that includes the following functions; emotional substance, self-esteem building, provision of information and feedback, and tangible assistance (113). The definition of social support as a function makes it possible to generate hypotheses concerning the psychological processes and then again study the effect of social support. This present study chose to define the concept of a social network as *"the quantitative and structural aspect of human relationships"* (114) and the concept of social support as *"the qualitative aspect, the perceived social support, such as the content and availability of relationships with significant others"* (*114).* Previous research has found that level of social support may influence health status (115).

Research from the 1950-1970's found that more isolated or less socially integrated individuals had worse physical and mental health, and they had a higher mortality rate (116). A better social integration (e.g. married, close family, friends, group affiliations) could possibly buffer deteriorating health effects (116). Research on patients with cardiac diseases have shown that social support may predict better

health and better physical function (117). Cancer research has shown that help from friends and family is important for patient recovery and coping (118). ICU survivors often undergo dramatic changes in their health and functioning (119). Their social life may also be altered because of reduced contact with family and friends during their ICU and hospital stays, and because they are absent from work, school, and/or leisure activities. It may take a long time for these patients to regain normal activity levels, if they ever do (120). A study from Sweden (121) in 2011 found that the level of social integration significantly affected HRQOL in ICU survivors, but the effect was smaller than preexisting diseases. Still, the effect of social integration was larger than age, sex and ICU-related factors. Social integration did not affect HRQOL in the general reference group (121). This previous research inspired us to study social support and its association with HRQOL in ICU survivors (116, 117, 121).

2.6 Theory of Unpleasant Symptoms (TOUS)

The theoretical framework in this present study was Lenz et al.'s (122) updated Theory of Unpleasant Symptoms. This theory was chosen for the present study to improve the understanding of symptoms and how they interact with each other and their surroundings. This may again improve our understanding of the ICU survivor's symptom burden and hopefully improve post ICU care. TOUS is a middle-range theory which is both abstract and concrete, so it provides linkages with both research and clinical practice. The assumption behind the theory is that there are enough commonalities among different symptoms to make a theory that can explain and guide both research and clinical practice on many unpleasant symptoms, and not only one symptom at the time. This understanding of multiple symptoms seemed relevant to understanding the present study's findings on symptoms. The original TOUS was presented by Lenz et al. in 1995 (123), and was at that time a linear

model. The TOUS revised model has changed from linear to interactive to open for the experience of multiple symptoms (122).

TOUS has three major components: “the symptom that the individual is experiencing, the influencing factors that give rise to or affect the nature of the symptom experience, and the consequences of the symptom experience” (122).

Symptom is the central focus in the TOUS, and in the revised model it opens up for the coexistence of multiple symptoms. The multiple symptoms can be experienced simultaneously, but one symptom may also lead to or enhance another symptom. According to Lenz et al. (122), symptoms may differ from each other, but usually seem to have several dimensions in common. The different dimensions are intensity (strength/severity), timing (frequency/duration of occurrence), level of distress perceived (bothersomeness, degree of discomfort) and quality. These dimensions are assumed to be related to each other but also to be separable.

In the model (Figure 1), the cylinder in the middle shows the different symptoms which the individual experiences. This can be one single symptom or multiple symptoms. The symptoms can all be described with the different dimensions, and the dimensions can be different for each symptom, but also common among symptoms. To the left on Figure 1 we have the influencing factors (physiological, psychological, and situational factors). In the updated model these three factors influence the symptom, but they can also interact with each other. Different interventions on the influencing factors may again reduce or enhance the symptoms (e.g. enhanced social support in the situational factor may reduce anxiety in the psychological factor which again may reduce the symptom pain). The last part of the model is the performance, or the outcome/effect of the symptom experience. Performance includes both functional and cognitive activities. Functional activities

include physical or social activities, activities of daily living, interaction and role performance. Cognitive activity includes concentrating, thinking and problem-solving.

As mentioned earlier, the original TOUS was a straightforward, linear model. In the revised model, the different influencing factors may interact with each other and influence the symptoms, but the symptom experience may also have a reciprocal effect on the influencing factors (Hawthorne, MH et al. 1994, Pennebaker, JW 1982; in (122)). For instance, the experience of pain may have a reciprocal effect of psychological factors and enhance depression, and at the same time it may increase the distress of another symptom, such as fatigue. The different influences, interactions and feedbacks in the theory are illustrated in Figure 1.

Figure 1

The updated theory of unpleasant symptoms

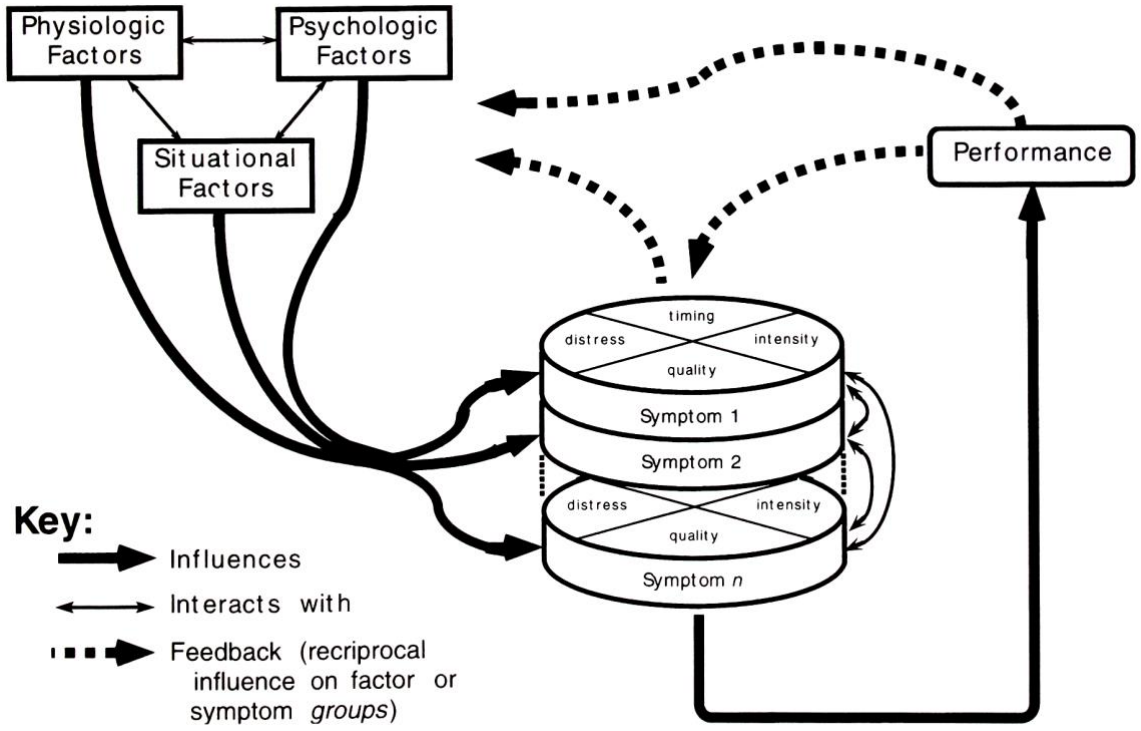


Figure reprinted with permission from the publisher. The original source for this figure is E.R Lenz et al in Advances in Nursing Science, Issue: Volume 19(3), March 1997, pp 14-27, Copyright © 1997 by Aspen Publisher, Inc. (122)

3.0 Research questions /Aims

The main aim of the present study was to investigate the prevalence of chronic pain after ICU treatment and to understand the impact of chronic pain on other symptoms and health related quality (HRQOL) of life up to 1 year after the ICU stay.

Based on the above, the main research questions of the papers included in this study were:

1. What is the prevalence of chronic pain in ICU survivors at 3 months and 1 year after ICU discharge?
2. What is the association between pain and anxiety, depression, fatigue, sleep disturbance and post-traumatic stress symptoms (PTSS) in ICU survivors, and does pain increase the risk of also reporting other symptoms?
3. Is HRQOL different in ICU survivors compared to the general population, and do social support, comorbidity and pain interference influence HRQOL in ICU survivors?

4.0 Methods

4.1 Study design

This study had a prospective, longitudinal design with two measurement time points: at 3 months and 1 year after discharge from the ICU. The data from the ICU stay were obtained from the patients' medical records after they had provided their informed consent. The rest of the data were obtained directly from the patients by questionnaire. Patients from two ICUs in Oslo University Hospital were included. The inclusion period was from May 2010 to January 2014.

4.2 Routine of inclusion

Three months after discharge from the ICU, all relevant patients were contacted by telephone, informed about the study, and asked if they wished to participate. If it was difficult to retrieve their phone number, the ICU survivors received study information and a consent form by ordinary mail. Of the 348 patients contacted, 193 consented to participate, while 118 patients completed the questionnaire at 3 months, and 89 patients completed it at 1 year after ICU discharge (figure 2).

4.3 Inclusion and exclusion criteria

Only adult patients who could read and write Norwegian and had been in the ICU for longer than 48 hours were asked to participate. Patients with reduced cognitive function and terminal patients were excluded. Only patients who consented received the questionnaire. Reduced cognitive function and terminal illness were determined based on information from the next of kin (e.g. from family members of ICU survivors who were not able to express their own will or were more or less comatose).

Figure 2

Flow chart of study sample

N = total study population in the two ICUs during the whole study period from May 2010 to January 2014.

4.4 Data collection

Data were collected at 3 months and 1 year after ICU discharge. The ICU survivors who consented to participate completed a questionnaire about demographic characteristics, comorbidity, pain and different symptoms like anxiety, depression, PTSS, sleep disturbance, fatigue and HRQOL, and social support. The ICU patients were screened in accordance with inclusion and exclusion criteria, and all suitable ICU survivors were contacted by phone three months after ICU discharge. If they consented to participate a questionnaire was sent to them by ordinary mail, and if they did not reply within 14 days the questionnaire was resent. The patients responded to the same questionnaire at 3 months and one year. The clinical characteristics regarding the ICU stay were collected from medical records retrospectively after the patients had consented to participate.

4.5 Inventory/Assessment instruments

The different instruments for assessment of demographic characteristics, clinical characteristics in the ICU, comorbidity, pain, symptoms, health-related quality of life and social support will be presented in this chapter, with the time of their application (Table 1).

Table 1

Overview over study instruments and when they were applied

	3 months	**1 year**
Demographic characteristics Age, sex, children, marital status, education level, employment and significant incidents in life	X	X
Clinical characteristics of the ICU stay (collected from medical records) Admission diagnosis ICU LOS MV days SAPS II and SOFA score Use of Fentanyl	X	
Comorbidity Self-administered Comorbidity Questionnaire (SCQ-18)	X	X
Pain Brief Pain Inventory Short Form (BPI-SF)	X	X
Anxiety and depression Hospital Anxiety and depression scale (HADS)	X	X
Post-traumatic stress symptoms Post-traumatic Stress Symptoms 10 (PTSS 10)	X	X
Sleep disturbance General Sleep Disturbance Scale (GSDS)	X	X
Fatigue Lee Fatigue Scale (LFS)	X	X
Health related quality of life Short Form Health Survey 12 (SF -12v1)	X	X
Social support Social Provision Scale revised (SPS)	X	X

All data were collected prospectively, except for clinical characteristics from the ICU stay that were collected retrospectively after ICU survivors' consent at 3 months.

4.5.1 Demographic, clinical characteristics and comorbidity

Demographic characteristics were collected at 3 months and 1 year after ICU discharge (Table 1). As a part of the clinical characteristics all patients were assessed using the Simplified Acute Physiology Score (SAPS II) and the Sequential Organ Failure Assessment (SOFA). SAPS II was originally developed to calculate the hospital mortality risk in ICU patients (124), and is valid and reliable in medical, surgical (124), and coronary ICU patients (125). The SOFA score describes different levels of organ failure over time in different patient groups and in individual patients with critical illness (126); it is valid and reliable in adult ICU patients (127). Both instruments may predict mortality on a group level (124, 126).

Comorbidities were assessed using a long version of the Self-administered Comorbidity Questionnaire (SCQ-18) 32, which includes 17 common and three optional medical conditions. In addition to assessing the presence of a comorbidity the questionnaire also assesses whether the participant received any treatment for the comorbidity, and whether the comorbidity limits daily activity (all yes/no question) (128). Only the sum of the total number of comorbidities was used in the present study.

4.5.2 Brief Pain Inventory Short Form (BPI-SF)

Pain occurrence, pain intensity, pain location, interference of pain with function, and pain relief were evaluated using the BPI-SF (129, 130). ICU survivors were asked to indicate whether they were in pain (yes/no). If they were in pain, they rated the severity of their average, least and worst pain during the last 24 hours, as well as their pain right now using a 0 (no pain) to 10 (the worst pain imaginable) numeric rating scale (NRS). Pain interference with the seven domains of functioning was rated using a 0 (does not interfere) to 10 (completely interferes) NRS. Pain relief was

rated using a 0% (no relief) to 100% (complete relief) scale. To identify pain locations the ICU survivors ticked boxes (names of different body parts) on a body chart. They could tick as many as they wanted. The BPI-SF has well-established validity and reliability in patients with cancer, including sensitivity to change in longitudinal studies (131-133), but also in patients with chronic non-cancer pain (134, 135). A modified version has also been used for postoperative patients in Norway (136).

Based on their responses to the BPI-SF, the patients were divided into two groups, a pain group and a no-pain group. The pain group consisted of all respondents who answered “yes” to the first BPI-SF question: [“Throughout our lives most of us have had pain from time to time such as minor headaches, sprains and toothaches. Have you had pain other than these everyday kinds of pains today?” (Yes/No)]. The no-pain group consisted of all respondents who answered “no” to the first BPI question or responded with “0” on all four dimensions. We also asked the participants about chronic pain prior to their ICU stay. This was reported retrospectively with a yes/no question in the questionnaire.

4.5.3 Hospital Anxiety and Depression Scale (HADS)

Anxiety and depression were measured with HADS(137). HADS contains 14 items that measure anxiety and depression on a scale from 0 (none) to 3 (very much). It is possible to calculate a total HADS score and sub score for anxiety and depression (137). The cut-off value for the total HADS score is 15 and the cut-off value for the sub scores is divided into below 8 (no treatment necessary), 8-10 (treatment may be necessary) and 11 or higher (treatment necessary). HADS is translated into Norwegian and found to be valid and reliable in the Norwegian population (138, 139).

4.5.4 Post Traumatic Stress Symptoms 10 (PTSS 10)

Post-traumatic stress symptoms was measured with the PTSS-10(140). The PTSS-10 contains 10 items on different symptoms of PTSS, such as sleep disturbance, nightmares, depression, guilt etc. Each question has a scale from 1 (none) to 7 (very much). The instrument was developed by Holen et al. (140) and is widely used both nationally and internationally. PTSS-10 has been tested as valid for identifying individuals with traumatic stress disorder (IS-03/2005) (141). A total score for all items was calculated. The cut-off value for the total PTSS 10 score was 35. Total PTSS 10 score ≥35 indicated PTSS that may need treatment.

4.5.5 General Sleep Disturbance Scale (GSDS)

Sleep was measured with General Sleep Disturbance Scale (GSDS)(142). The scale consists of 21 items about different sleeping habits. All items are Likert scales from never (0) to every day (7) (143). A total score was calculated and the cut-off value for a sleep disorder that needed treatment was 43. The GSDS has shown to be valid and reliable in healthy female nurses (142), patients with Parkinson´s disease (144) and cancer patients (145). The instrument is translated into Norwegian and has shown satisfactory psychometric properties (146).

4.5.6 Lee Fatigue Scale (LFS)

Fatigue and lack of energy were measured with the Lee fatigue scale (147). The Lee fatigue scale consists of 18 items describing fatigue and energy levels. All items are Likert scales from no symptom (0) to very high symptom (10). The 18 questions are divided in 13 about fatigue and 5 about lack of energy. This instrument operates with morning and evening cut-off scores; fatigue morning cut-off ≥3.2, fatigue evening cut-off ≥5.6, and energy morning cut-off ≤ 6.0 and energy evening ≤ 3.5 (148). In the

present study we did not know at what time of day the ICU survivors reported their symptoms, so we chose to use the evening cut-off scores. The instrument is found valid and reliable in cancer patients (143). The instrument is translated into Norwegian (unpublished material by T. M Ljoså and R. Andenæs, translation performed by the MAPI method).

4.5.7 Social Provision Scale revised (SPS)

Social provision was measured with the Social Provision Scale revised version (SPS), which contains 16 assertions on social support (113). Each assertion has four alternatives (strongly agree, agree, disagree, strongly disagree), and the patient chooses the alternative which best describes his/her social support (149). The 16 assertions were summed up into four individual provisions: reassurance of worth (assertions 5,7,10,13), attachment (assertions 2,11,12,14), nurturance (assertions 1,3,9,16) and social integration (assertions 4,6,8,15), in the same way as Bondevik (114). According to Weiss (150), Reassurance of worth means that other individuals accept and value your individual competence (e.g. working skills or other skills in leisure activities). Attachment means that individuals have relationship with other individuals which give them a feeling of security. Attachments make the individuals feel comfortable and at home. If attachment is absent individuals feel lonely and restless. Attachments can be formed by family or friends (150). Nurturance means that you as an adult have responsibility for the well-being of a child (150). Social integration, according to Weiss, means to take part in social networks (e.g. church, political party, sports club). True social integration means that the person may take part in social events and meet other that share the same interests. The result of absence of social integration may be boredom (150). One total social support score is available. This is a sum score where

64 is the top score. The higher the score, the higher the level of social support. The four individual provisions are also summed up in four scores with a max score of 16. Here, too, a higher score indicates a higher level of social support in that specific individual provision. Here there is no cut-off score (114). SPS is tested and found valid and reliable among the oldest elderly in Norway (114).

4.5.8 Short Form Health Survey 12 (SF12v1)

Health related quality of life was scored with SF 12 version 1, which measures total health status(64). SF 12 consists of 12 questions about the following eight health concepts: physical functioning, role-physical, bodily pain, general health, energy/fatigue, social functioning, role-emotional and mental health. These concepts are summed up in a physical component summary (PCS) and a mental component summary (MCS) (64). The SF 12 PCS and MCS are calculated using norm-based data from the 1998 general US population with a mean of 50 (SD 10). The cut-off score of the 1998 general US population is similar to the general Norwegian population, with a mean PCS of 50.3 (SD 8.8) and mean MCS 50.6 (SD 9.9) (151). Higher summary scores indicate better HRQOL. SF 12 is extensively used and validated for many patient groups as well as the general population and translated into many languages (151). SF 12 is found valid and reliable and to be a good alternative to the longer Short Form Health Survey 36 (SF 36) (64, 151). SF 12 is translated into Norwegian (71).

4.6 Analysis and power estimate

IBM SPSS (version 22; IBM SPSS, Armonk, NY: IBM Corp.) was used for statistical analyses. Sample characteristics are presented as means with standard deviation (SD) or proportions.

The aim of this study was to explore pain, other symptoms and quality of life in ICU-survivors. Thus, a formal power calculation was not appropriate. The main outcome of interest was estimation of the prevalence of pain. Thus, we calculated the number of respondents needed to get a reasonably narrow confidence interval around a point estimate of a proportion (prevalence of pain). Based on previous studies (53, 54) we assumed the true point estimate for chronic pain in ICU survivors to be within the interval from 20% to 80%. With 120 respondents the 95% confidence interval would stretch from ± 8.1 % to ± 8.9 % from any point estimate within this interval (nQuery Advisor 7.0, Cork, Ireland). We assumed that drop-outs could be expected in this population and decided to recruit at least 150 subjects.

4.6.1 Analysis paper 1

Sample characteristics are presented as means with standard deviation (SD) or proportions. Differences in continuous variables between groups were tested with the Student's *t*-test. The chi-square test or Fisher's exact test for contingency tables was used where appropriate to detect associations between categorical variables. Two-tailed *p*-values less than 0.05 were considered significant.

To identify independent risk factors for chronic pain 1 year after ICU discharge, logistic regression analysis was performed using a manual backward elimination procedure. Any variable with a p value < 0.25 in univariate analysis was a candidate for the multivariable model. The choice of variables in the univariate analysis was based on findings in previous research. Dowdy et al (77) identified age,

sex, ICU LOS, severity of illness (APACHE II) and time spent on ventilator as factors that may influence ICU outcome. Orwelius et al (7) state that preexisting diseases are another important factor that may influence HRQOL in ICU survivors. Levels of education have been shown in previous research to influence HRQOL (71). The following variables were included in the univariate regression model: age, sex, SAPS II score, SOFA score, level of education, number of comorbidities; ICU days; and use of fentanyl during the ICU stay (Table 7). The following independent risk factors were identified: ventilator days; SAPS II score; SOFA score; number of comorbidities; ICU days; and use of fentanyl during the ICU stay. High levels of education seemed to reduce the risk for chronic pain (Table 8). Multivariable analyses were preceded by estimation of the correlations between risk factors. Because of strong correlations between the SAPS II and SOFA scores (r = 0.61), and ventilator days and ICU days (r = 0.71), three multivariable models were needed to avoid multicollinearity.

4.6.2 Analysis paper 2

Sample characteristics are presented as means with standard deviation (SD) or proportions. In this paper we wanted to study associations between pain and symptoms like anxiety, depression, fatigue, lack of energy, sleep disturbance and PTSS so these were the variables chosen for the logistic regression model. To save statistical power we did not adjust for age and gender as they were not statistically significant in univariate analyses (Table 7). Associations between pain and selected symptoms were studied with univariate logistic regression analyses at both 3 months and 1year after ICU discharge. P-values <0.05 were considered statistically significant and all tests were two-sided. There was no need to use multiple regressions as none of the possible confounders (e.g. demographic and clinical data)

was statistically significant in the univariate analyses. These analyses were exploratory, thus no additional power estimation was performed (see 4.6).

4.6.3 Analysis paper 3

Sample characteristics are presented as the mean and SD, median and interquartile range (IQR), or proportions with percentages. Associations between social support, number of comorbidities, pain interference, and HRQOL were tested using univariate linear regression models at 3 months, and again at 1 year, after ICU discharge. To create the dependent variable as a continuous variable, ICU survivors in the no-pain group (based on BPI–SF) were assigned a pain interference score of 0. All other ICU survivors were included in the pain group. There was no need to use multiple regressions as none of the possible confounders (e.g. demographic and clinical data) was statistically significant in the univariate analyses. We chose to use the two pain interferences scores with the highest mean value in the regression model, because we believed that these pain interference scores would have the largest impact on HRQOL. We chose this option, rather than the mean of all seven pain interference scores, because the latter would be too general and inadequately describe the sample. To estimate the changes between measurements made 3 months and 1 year after discharge, we fitted the linear regression model for repeated measures (GLM) with diagonal covariance matrix. GLM does not require complete data so we were able to use all the observations and not just complete data (with values at both time points). A paired samples t-test requires data at both time points, thus in the eventuality of missing data the results could be biased. GLM uses all available data so imputation is not necessary. Simple imputation of missing data also often leads to bias, so it is not recommended. Values of $p < 0.05$ were considered statistically

significant, and all tests were two-sided. These analyses were exploratory, and thus no additional power estimation was performed (see 4.6 Analysis and power estimate).

4.7 Ethics

The study followed the Helsinki declaration. This study was approved by the Hospital Data Inspectorate and the Regional Committees for Medical Research Ethics in Norway South-B (reference number: 2012/4b S-07505b, first release 21.Dec.07). Only patients who gave their consent participated. There are ethical concerns related to research on ICU patients. When in the ICU the patients' ability to give informed consent is reduced due to the critical illness or the reduced level of consciousness (152). In the present study the former ICU patients consented 3 months after ICU discharge, as at this time many ICU survivors had regained their normal ability to give informed consent to participate in the study. The ICU survivors who had not regained their ability to consent were not included in the study. The consent was given in writing.

5.0 Summary of results

5.1 Internal consistency of the survey instruments and item missing

The relevant survey instruments were tested for internal consistency with Cronbach's alpha (153). Chronbach's alpha is not appropriate for all instruments e.g. Self-administered Comorbidity Questionnaire (SCQ-18) which is just a check list and where internal consistency is not expected. The internal consistency for BPI –SF intensity items was 0.92 and 0.88 for BPI-SF interference items, The Cronbach's alpha for HADS anxiety was 0.89 and 0.80 for HADS depression. In the present study we found the Cronbach's alpha for total PTSS 10 to be 0.87, and we found the Cronbach's alpha for total GSDS to be 0.66. The Cronbach's alpha for LFS fatigue was 0.95 and 0.88 for LFS energy, The Cronbach's alpha for total SPS revised was 0.83.

The survey instruments were checked for missing on each item and in general the item missing value was low. The item missing value for BPI, SF 12, HADS, PTSS 10, LFS, GSDS and SPS revised was all between 0-5 % for each item at both 3 months and one year. Only the SCQ-18 (comorbidity) had a higher item missing value. For the presence of comorbidity at 3 months the item missing value was between 17-22 % and for treatment and limitations of the comorbidity the item missing value was between 0- 2.5 %. At 1 year the item missing for presence of comorbidity was 10.1-16.9 %, and for treatment and limitations of the comorbidity the item missing value was between 0-6.7 %.

5.2 Demographic and clinical characteristics of the study sample

The demographic and clinical data are presented first, as these are common for all the three papers. There were no statistically significant differences between responders and non-responders regarding ICU-related clinical characteristics and demographic data at one year (Table 2). We were not allowed by the Ethics committee to record data on the ICU survivors that consented on the phone but did not reply to the questionnaire at 3 months, so we were not able to describe any potential differences between responders and non-responders at that time. At 3 months the mean age of the total sample was 55.1 year (SD 14.4) and 63.6 % were male. The majority had primary education as their highest level of education (50.9 %) (Table 3). Most ICU survivors were married or partnered and had children (80.5%). This number represents both under-aged children and adult children, 26.3% of the sample had children younger than 15 years. There were only small changes in demographic characteristics at 1 year (Table 4). The ICU survivors were also asked if they had experienced any significant negative incidents in their life the last 4 weeks, and 18.6% had experienced the death of a family member or close friend in that period. The total sample had a mean number of comorbidity of 2.27 (SD 1.65) and the ICU survivors with pain had significantly more comorbidities than the ICU survivors without pain. The most common comorbidities in the total sample were back/neck pain 30.9 % (n = 30), hypertension 29.9 % (n= 29), cardiac disease 27.6% (n= 27), headache 20.8 % (n= 20) and cancer 15.8 % (n= 15).

The two ICUs included in the study ICU admit both medical (39%) and surgical (61%) patients, as shown in Table 5. The three largest admission diagnosis groups were gastrointestinal, neurosurgery and infectious disease, another large group was cardiovascular. The gastrointestinal group consists of mostly hepatic failure/transplantation or other large gastrointestinal surgery (e.g. Whipple with

complications) or pancreatitis. The neurosurgery group consists of subarachnoid hemorrhage/ intracerebral hemorrhage or tumor cerebri, but no traumatic brain injury. Infectious diseases were mainly sepsis or adult respiratory distress syndrome. Cardiovascular cases were mainly patients suffering cardiac arrest who had been resuscitated. As shown in table 5 the admission diagnosis only influenced pain in a statistically significant way in the cardiovascular group (p value 0.05).

The patients had a mean SAPS II score of 44.9 (SD 16) and mean SOFA score of 8.8 (SD 3.4). The median ventilator time (days) in the ICU was 6.0 (Interquartile range [IQR] 3-12) and the median ICU LOS was 9.0 (IQR 5-15) (Table 5). There was no statistically significant difference between ICU survivors with or without pain regarding clinical ICU data.

Table 2

Relationship between responder and no responder on clinical and demographic data

	Responder	**Non-responder**	**p-value**
	n (%)	**n (%)**	
Sex			0.71
male	57 (64)	23 (60.5)	
female	32 (36)	15 (39.5)	
	Median (range)	**Median (range)**	
Age (years)	55 (22-79)	59 (20-81)	0.87
ICU LOS (days)	9 (3-57)	8 (3-18)	0.35
MV duration (days)	6 (0-35)	6 (0-17)	0.64
SAPS II score	42 (14-88)	40.5 (16-87)	0.21

Responder= respond to survey at 3 months and 1 year, no responder= respond to survey only at 3 months. ICU LOS = Intensive Care Unit length of stay. MV = mechanical ventilation. Statistical comparison: Mann Whitney Wilcoxon

Table 3

Demographic Characteristics of the Participants at 3 Months after ICU Discharge.

Characteristic	**Total Sample (n = 118)**		**Pain (n = 58)**		**No pain (n = 60)**		***p*-value**
	Mean (SD)	**Range**	**Mean (SD)**	**Range**	**Mean (SD)**	**Range**	
Age (years)	55.1 (14.4)	20 - 81	53.7 (13.1)	20 - 81	56.6 (15.4)	22 - 78	*0.29
Number of comorbidities	2.27 (1.65)	0 - 6	2.81 (1.58)	0 - 6	1.75 (1.55)	0 - 5	*<0.001
Sex	**n (%)**		**n (%)**		**n (%)**		
Male	75 (63.6)		33 (56.9)		42 (70)		**0.14
Female	43 (36.4)		25 (43.1)		18 (30)		
Education							
Primary	59 (50.9)		29 (50)		30 (51.7)		**0.89
Secondary	15 (12.9)		6 (10.3)		9 (15.5)		
University/college	42 (36.2)		23 (39.7)		19 (32.8)		
Marital status							
Married/partnered	74 (62.7)		35 (60.3)		39 (65)		**0.37
Divorced/separated/ Unmarried/widowed	44 (37.3)		23 (39.7)		21 (35)		

ICU = intensive care unit; SD = standard deviation. The participants were divided into pain and no-pain groups. Statistical comparison: *Independent sample t-test, **Pearson Chi-square.

Table 4

Demographic Characteristics of the Participants at 1 year after ICU Discharge.

Characteristic	**Total Sample (n =89)**		**Pain (n = 34)**		**No pain (n = 55)**		***p*-value**
	Mean (SD)	**Range**	**Mean (SD)**	**Range**	**Mean (SD)**	**Range**	
Age (years)	56.2 (14.4)	22 - 80	57.2 (11.2)	35 - 77	55.6 (16.2)	22 - 80	*0.57
Number of comorbidities	2.13 (1.99)	0 - 8	3.34 (2.03)	0 - 8	1.38 (1.56)	0 - 8	*<0.001
Sex	**n (%)**		**n (%)**		**n (%)**		
Male	57 (64.0)		21 (61.8)		36 (65.5)		**0.72
Female	32 (36.0)		13 (38.2)		19 (34.5)		
Education							
Primary	15 (17.6)		9 (28.1)		6 (11.3)		**0.08
Secondary	36 (42.2)		14 (43.8)		22 (41.5)		
University/college	34 (40.0)		9 (28.1)		25 (47.2)		
Marital status							
Married/partnered	57 (66.3)		25 (75.8)		32 (60.4)		**0.14
Divorced/separated/ Unmarried/widowed	29 (33.7)		8 (24.2)		21 (39.6)		

ICU = intensive care unit; SD = standard deviation. The participants were divided into pain and no-pain groups. Statistical comparison: *Independent sample t-test, **Pearson Chi-square.

Table 5

Clinical ICU Characteristics of the ICU survivors

Characteristic	**Total Sample (n = 118)**	**Pain (n = 58)**	**No Pain (n = 60)**	***p*-value**
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	
ICU LOS	9.0 (5.0–15.0)	10 (5.0–16.0)	8.0 (6.0–13.0)	²0.52
MV duration (days)	6.0 (3.0–12.0)	7.5 (3.0–14.0)	6.0 (3.0–10.8)	²0.29
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	
SAPS II	44.9 (16)	43.1 (14.5)	46.6 (17.3)	*0.23
SOFA score	8.8 (3.4)	8.7 (3.4)	8.8 (3.5)	*0.86
	n (%)	**n (%)**	**n (%)**	
Admission diagnosis:				
Cardiovascular	23 (19.5)	7 (12.1)	16 (26.7)	**0.05
Neurosurgery	29 (24.5)	16 (27.6)	13 (21.7)	**0.46
Infectious disease¹	28 (23.7)	15 (25.9)	13 (21.7)	**0.59
Gastrointestinal¤	30 (25.4)	16 (27.6)	14 (23.3)	**0.60
Other	8 (6.7)	4 (6.9)	4 (6.7)	
Patient groups:				
Surgical patients	72 (61)	36 (62.1)	36 (60)	**0.82
Medical patients	46 (39)	22 (37.9)	24 (40)	
Chronic pain prior to ICU stay	7 (7.5)	5 (11.4)	2 (4.1)	**0.25

ICU = intensive care unit; IQR = interquartile range; ICU LOS = ICU length of stay (in days); MV duration = mechanical ventilation (in days); SD = standard deviation. ¹ Infectious disease includes diagnoses such as pneumonia and sepsis. ¤ Gastrointestinal diseases were mostly hepatic failure and hepatic transplants. The total sample was divided into pain and no-pain groups.
Statistical comparison: ²Mann-Whitney U test. *Independent sample t-test, **Pearson Chi-square

5.3 Results Paper 1

Prevalence of pain was measured with BPI-SF chronic version, and at 3 months after ICU discharges 58 (49.2%) of 118 ICU survivors reported chronic pain. Of 89 ICU survivors, 34 (38.2%) reported chronic pain 1 year after ICU discharge. The prevalence of chronic pain prior to the ICU stay was measured retrospectively, and only 7 (7.5%) of the total sample reported chronic pain at 3 months after ICU discharge (Table 5).

5.3.1 Location and Characteristics of Pain

The BPI-SF scores at 3 months after discharge indicated that the ICU survivors who reported chronic pain suffered mild pain; the average score for the worst pain in the previous 24 hours was 4 on the NRS (0–10), and the average of the least pain was 1.5. Additional data on pain range not presented in the paper are added in Table 6. In the pain group, 52.5% of patients did not use any pain treatment at 3 months after discharge, and only 20% reported any effect of the pain treatment. About 25% of the patients used analgesics such as opioids, other pain medications, or a combination of the two, and 17% received either physiotherapy or a combination of physiotherapy and analgesics. Their pain was reported to have low (NRS 1-3) to moderate (NRS 4-6) levels of interference with their daily lives, and the pain interfered most with daily work and least with relationships with others (Table 6). The most common sites of pain were the shoulder/upper arm and the abdomen, with 29.3% reporting pain at each site (Fig. 3). At 3 months after discharge, the median number of sites of pain was 2.0 (IQR 1.5–4.0).

Table 6

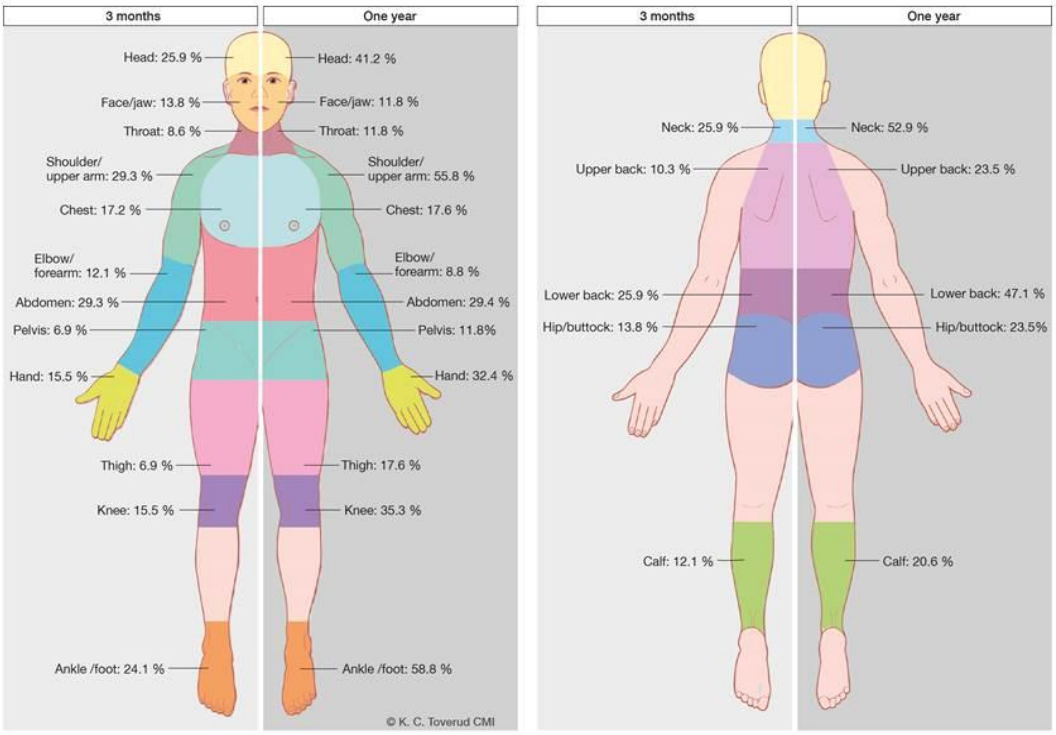
Pain Characteristics of the Intensive Care Survivors who report pain at 3 months and 1 year.

BPI-SF score	3 months (n = 58)		1 year (n = 34)	
	Mean (SD)	**Range**	**Mean (SD)**	**Range**
Pain intensity (0–10)				
Worst pain in the last 24 h	4.0 (2.6)	0 – 9	3.8 (2.8)	0 – 10
Least pain in the last 24 h	1.5 (1.7)	0 – 6	1.6(2.6)	0 – 10
Pain on average	3.4 (2.1)	0 – 5	3.3 (2.1)	0 – 10
Pain right now	2.5 (2.3)	0 – 8	2.8 (2.4)	0 – 10
Pain interference (0–10)				
Interference with general activity	3.3 (2.9)	0 – 10	3.7 (2.8)	0 – 10
Interference with mood	3.0 (2.7)	0 – 9	3.5 (2.6)	0 – 8
Interference with normal work	3.8 (3.1)	0 - 10	4.3 (2.9)	0 – 10
	Median (IQR)	**Range**	**Median (IQR)**	**Range**
Interference with walking ability	2.0 (0.0, 4.0)	0 – 10	2.5 (0.0, 5.0)	0 – 10
Interference with relationship with other people	1.0 (0.0, 3.5)	0 – 9	2.0 (0.0, 3.0)	0 – 7
Interference with sleep	2.0 (1.0, 6.0)	0 – 10	3.0 (2.0, 5.0)	0 – 10
Interference with enjoyment of life	2.0 (0.0, 5.0)	0 – 9	2.0 (1.0, 5.0)	0 – 8

SD = standard deviation; IQR = interquartile range.

FIGURE 3

Pain locations at 3 months and 1 year after ICU Discharge



At 3 months n= 58 and at 1 year n= 34. Bodily pain is presented as percent.

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Pain intensity at 1 year was similar to pain intensity at 3 months (Table 6). At the 1 year follow-up, 37% of the ICU survivors with pain reported that they did not use any pain treatment, and 20% reported that their method of pain relief was effective. There was an increase in the use of analgesics from 25% at 3 months to 33% at 1 year, and the proportion of patients using physiotherapy increased to 24%. The interference of pain with daily living was higher for all items after 1 year compared with after 3 months (Table 6). The most common site of pain at 1 year was the ankle/foot (58.8%), with the shoulder/upper arm as the second most common site (55.8%). The median number of sites of pain at 1 year increased to 3.0 (IQR 2.0–8.0).

5.3.2 Risk Factors for Chronic Pain at 1 year after ICU Discharge

Based on the univariate logistic regression model (Table 7, not included in the paper) the following three multivariable models showed effects with ORs that could be of clinical importance, although none of the associations reached statistical significance. Model A (Table 8) showed that ventilator time longer than 12 days (75th percentile) had an odds ratio (OR) of 2.31 for reporting chronic pain (95% confidence interval [CI] 0.88–6.05, p = 0.089). We also found that for each SD increase in the SAPS II, the OR for reporting chronic pain was 1.56 (95% CI 0.99–2.45, p = 0.058) (Table 8). Model B showed that for each SD increase in the SOFA score, the OR for reporting chronic pain was 1.63 (95% CI 0.99–2.67, p = 0.056). In contrast, high education seemed to reduce the risk of chronic pain with an OR of 0.45 (95% CI: 0.16–1.24, p = 0.12) (Table 8). Model C identified only ICU LOS longer than 15 days (75th percentile) as an independent risk factor for chronic pain (OR = 1.90, 95% CI 0.73–4.95, p = 0.19) (Table 8).

Table 7

Selected Risk Factors for Chronic Pain at 1 year Follow-up after ICU Discharge.

Univariate logistic regression analyses

Risk Factors	**OR**	**95% CI**	***p*-value**
Age increase pr. 5 year	1.04	(0.89, 1.21)	0.63
Sex	1.17	(0.48, 2.85)	0.73
SOFA pr. SD increase	1.52	(0.96, 2.39)	0.07
SAPS II pr. SD increase	1.46	(0.94, 2.27)	0.09
Ventilator days >75 percentile (12 days)	2.00	(0.79, 5.07)	0.14
ICU days >75 percentile (15 days)	1.76	(0.69, 4.51)	0.24
Use of Fentanyl (yes/no)	2.30	(0.58, 9.03)	0.23
Max. dose of Fentanyl/day	1.04	(0.72, 1.49)	0.85
Max. Fentanyl dose > 4 mg/day	0.86	(0.34, 2.28)	0.77
Higher education (university/collage)	0.45	(0.167, 1.20)	0.11

CI = confidence interval; SAPS II = Simplified Acute Physiology Score II; SOFA = Sequential Organ Failure Assessment; SD = standard deviation; ICU = intensive care unit. Statistical analysis: Univariate logistic regression.

Table 8

Risk Factors for Chronic Pain at 1 year Follow-up after ICU Discharge. Multiple logistic regressions

Risk Factors	OR	95% CI	*p*-value
Model a)			
Ventilator days >75 percentile (12 days)	2.31	(0.88, 6.05)	0.09
SAPS II pr. SD increase	1.56	(0.99, 2.45)	0.06
Model b)			
SOFA per SD increase	1.63	(0.99, 2.67)	0.06
Higher education (university/college)	0.451	(0.16, 1.12)	0.12
Model c)			
ICU days >75 percentile (15 days)	1.90	(0.73, 4.95)	0.19

CI = confidence interval; SAPS II = Simplified Acute Physiology Score II; SOFA = Sequential Organ Failure Assessment; SD = standard deviation; ICU = intensive care unit. Statistical analysis: Multiple logistic regressions.

5.4 Results Paper 2

At both time points ICU survivors with pain reported significantly higher anxiety (HADS A), depression (HADS D) and anxiety/depression (HADS Total), PTSS, sleep disturbance and fatigue compared to those who did not report pain at both 3 months and 1 year. LFS energy was not associated with reporting pain at either time point (Table 9).

5.4.1 Prevalence of anxiety and depression

In the total sample, the prevalence of anxiety/depression that may need treatment at 3 months (i.e. HADS score ≥15) was 20.8%. The prevalence of anxiety at 3 months based on a HADS A subscale ≥11 (i.e. treatment necessary) was 9.5%; this rate remained unchanged at 1 year. When we included those with scores 8–10 (i.e.

treatment may be necessary), the prevalence at 3 months rose to 24.1% and at 1 year there was a small increase to 28.3% (Table 10).

The prevalence rates for HADS D subscale ≥11 (i.e. treatment necessary) at 3 months was 5.1%, with a small decline to 4.6% at 1 year. When we included those who scored 8–10 (i.e. treatment may be necessary), the prevalence at 3 months rose to 15.4% and at 1 year there was a small decline to 12.8% (Table 10).

5.4.2 Prevalence of PTSS, sleep disturbance, fatigue and energy

For the whole sample, the prevalence of PTSS indicating that treatment may be needed (cutoff score ≥35) was 12.8% at 3 months; there was a small increase to 15.1% at 1 year. Our data revealed that severe sleep disturbance (cutoff score ≥43) reached a markedly higher prevalence rate than any other symptom: 49.2% at 3 months and 46.5% at 1 year. LFS sub-scores at 3 months showed that 15.3% of the sample experienced fatigue (cutoff ≥5.6) and 28.8% experienced energy levels below the cutoff value 3.5; there were small changes at 1 year, with the prevalence of both fatigue and energy declining to 13.8% and 21.1%, respectively (Table 10).

Table 9

Symptom scores for patients with or without pain after ICU discharge

3 months	**Pain (n = 58)** **Mean (SD)**	**No pain (n = 60)** **Mean (SD)**	***p*-value***
HADS Anxiety	6.23 (4.42)	3.5 (3.15)	<0.01
HADS Depression	5.18 (3.88)	3.2 (2.60)	0.03
HADS total	11.4 (7.67)	6.69(5.14)	<0.01
PTSS total	25.14 (11.43)	18.21 (7.72)	<0.01
GSDS total	49.73 (15.02)	35.79(12.79)	<0.01
LFS Fatigue	3.95 (2.39)	2.1 (1.64)	<0.01
LFS Energy	4.3 (1.99)	4.9 (1.90)	0.09
1 year	**Pain (n=34)** **Mean (SD)**	**No pain (n = 55)** **Mean (SD)**	
HADS Anxiety	6.15 (4.16)	3.88 (3.85)	0.01
HADS Depression	5.26 (3.24)	3.06 (2.84)	<0.01
HADS total	11.41 (6.5)	6.94 (5.69)	<0.01
PTSS total	25.29 (11.1)	19.04 (9.22)	0.02
GSDS total	47.06 (13.1)	37.22 (14.1)	0.01
LFS Fatigue	4.0 (2.29)	2.34 (1.93)	<0.01
LFS Energy	4.73 (1.99)	5.39 (2.18)	0.158

HADS, hospital anxiety and depression scale; PTSS, post-traumatic stress symptoms; GSDS, general sleep disorder scale; LFS, Lee fatigue scale. Statistical comparison: *Mann–Whitney U test.

Table 10

Symptom prevalence rates among ICU survivors

	3 months n = 118			**1 year** n = 89		
HADS	**HADS total**	**Anxiety**	**Depression**	**HADS total**	**Anxiety**	**Depression**
Mean (SD)	9.0 (6.9)	4.8 (4.1)	4.2 (3.4)	8.7 (6.4)	4.8 (4.1)	3.9 (3.2)
Median (IQR)	7.0 (4–14)	4.0 (1.3–7)	3.0 (1–6)	8.0 (3–13)	4.0 (1-8)	3.0 (3–6)
Score <8 n (%)		88 (75.9)	99 (84.6)		61 (71.8)	75 (87.2)
Score 8–10 n (%)		17 (14.7)	12 (10.3)		16 (18.8)	7 (8.1)
Score ≥11 n (%)		11 (9.5)	6 (5.1)		8 (9.4)	4 (4.7)
Score <15 n (%)	92 (79.3)			68 (80)		
Score ≥15 n (%)	24 (20.7)			17 (20)		
PTSS	**PTSS total**			**PTSS total**		
Mean (SD)	21.6 (10.3)			21.3 (10.4)		
Median (IQR)	20 (13–27)			17 (13–28)		
Score <35 n (%)	102 (87.2)			73 (84.9)		
Score ≥35 n (%)	15 (12.8)			13 (15.1)		
GSDS	**GSDS total**			**GSDS total**		
Mean (SD)	42.8 (15.5)			41.0 (14.4)		
Median (IQR)	41.5 (31–2.3)			40.0 (30–51)		
Score <43 n (%)	60 (50.8)			46 (53.5)		
Score ≥43 n (%)	58 (49.2)			40 (46.5)		
Lee fatigue		**Fatigue**	**Energy**		**Fatigue**	**Energy**
Mean (SD)		3.0 (2.2)	4.6 (2.0)		3.0 (2.2)	5.1 (2.1)
Median (IQR)		2.7 (1.2–4.6)	4.7 (3.4–6.1)		2.5 (1.1–5.0)	4.8 (3.6–6.6)
Score <5.6 n (%)		100 (84.7)			75 (86.2)	
Score ≥5.6 n (%)		18 (15.3)			12 (13.8)	
Score <3.5 n (%)			34 (28.8)			21 (24.1)
Score ≥3.5 n (%)			84 (71.2)			66 (75.9)

HADS, hospital anxiety and depression scale; GSDS, general sleep disturbance scale; PTSS, post-traumatic stress symptoms. Empty cells are not applicable.

5.4.3 Associations between pain and other symptoms in ICU survivors with pain

The presence of pain was significantly associated with all symptoms except energy at 3 months (Table 11). The odds ratios (ORs) for symptoms were relatively high, but their respective 95% CIs were wide, likely due to a limited sample size. The reason for the extremely high odds for fatigue for those who reported pain compared to those ICU survivors who did not report pain (OR, 24.46; p = 0.02) was that all but one participant who reported pain also reported experiencing fatigue.

Risk of anxiety and depression showed small changes from 3 months to 1 year, with depression no longer significant compared to the results at 3 months (Table 11). While sleep disturbance increased in OR and continued to be statistically significant, the OR of PTSS and fatigue declined (one-year fatigue was still statistically significant, but PTSS became borderline), OR of energy remained not statistically significant. At 1 year, the 95% CIs were wide due to sample size (Table 11).

5.4.4 Prevalence of multiple symptoms in ICU survivors with pain

As previously described, ICU survivors with pain had significantly higher odds for reporting symptoms, compared to ICU survivors without pain. Moreover, we found that 15% (n = 9) experienced at least three symptoms (e.g. sleep disturbance, fatigue and anxiety/depression) above the respective cut-off values, in addition to pain at 3 months after ICU discharge; at 1 year, 12% (n = 4) met these criteria.

Table 11

Risk of experiencing symptoms above cut-off value at 3 months and 1 year following ICU discharge in survivors who reported experiencing pain

	OR	**95% CI**	***p*-value**
3 months			
Anxiety	3.45	1.37–8.67	<0.01
Depression	3.25	1.08–9.81	0.04
Total anxiety/depression	5.40	1.85–15.72	<0.01
PTSS	4.87	1.30–18.30	0.01
Sleep disturbance	3.27	1.54–6.95	0.02
Fatigue	24.46	3.13–191.1	0.02
Energy	1.73	0.77–3.89	0.18
1 year			
Anxiety	3.68	1.37–9.90	0.01
Depression	2.01	0.56–7.21	0.28
Total anxiety/depression	5.02	1.57–16.01	<0.01
PTSS	2.89	0.86–9.76	0.09
Sleep disturbance	5.40	2.1–13.88	<0.01
Fatigue	6.0	1.49–24.14	0.01
Energy	1.59	0.59–4.29	0.36

PTSS, post-traumatic stress symptoms. Statistical analysis: Univariate logistic regression with pain as the dependent variable and covariates as independent variables.

5.5 Results Paper 3

Over all pain interference, number of comorbidities and social support was associated with HRQOL. The physical health was most affected, and pain interference had the largest negative association with Physical Component Summary (PCS).

5.5.1 Health related quality of life in ICU survivors

Overall the total sample showed that the ICU survivors had clinically and statistically significantly reduced HRQOL in PCS with a mean value of 39.3 (10.9) and a minor reduction of MCS with a mean value of 47.7 (10.9) at 3 months compared to norm data of mean 50 (SD 10). At 1 year the PCS mean value had increased to 43.4 (12.0) and the MCS mean value had normalized to 49.3 (10.3). We also found that the improvement in PCS was statistically significant from 3 months to 1 year ($p < 0.01$). In the MCS there also was a small improvement, but this was not statistically significant (Table 12).

5.5.2 Pain interference

The pain interference scores are listed in Table 6. The score was low (NRS 1-3) to medium (NRS 4-6) for all the 7 items (Table 6) and the two interference items with the highest mean score were impact on normal work 3.8 (SD 3.1) and daily activity 3.3 (SD 2.9) at 3 months after ICU discharge. Both mean scores had a small increase at 1 year 4.3 (SD 2.9) and 3.7 (SD 2.8) respectively.

5.5.3 Social support, comorbidity and pain interference's associations with HRQOL

The total social support had a statistically significant positive association with MCS at 3 months ($p < 0.01$), but not on the PCS at 3 months. The total social support had no statistically significant impact on PCS and MCS at 1 year (Table 13). Of the individual provisions, only attachment had a statistically significant negative association with PCS at 3 months ($p = 0.02$) and positive association with MCS on 1 year ($p = 0.03$) (Table 11). There was a statistically significant reduction in the total SPS scores from 3 months to 1 year after ICU discharge. Attachment also had a statistically significant reduction from 3 months to 1 year (Table 12).

The number of comorbidities had a statistically significant negative association with PCS at both times ($p < 0.01$) and on MCS at one year ($p = 0.01$) (Table 13). Both pain interference with normal work and daily activity were associated with a clinically relevant reduction on PCS score at 3 months and 1 year and both were statistically significant ($p< 0.01$). They also gave a relevant clinical reduction on the MCS score at 3 months and 1 year, but only pain interference with normal work was statistically significant at 3 months ($p= 0.03$) (Table 13).

Table12

Changes in social support and HRQOL from 3 months to 1 year after ICU discharge

	3 months n=118 Mean (SD)	1 year n= 89 Mean (SD)	95% CI	p-value
Total Social Provision score	56.1 (6.3)	54.0 (6.5)	[0.47; 3.63]	0.01
Individual provisions:				
• Reassurance of Worth (ROW)	14.7 (1.7)	14.4 (1.9)	[-0.11; 0.77]	0.13
• Attachment	14.9 (1.7)	13.2 (2.5)	[1.01; 2.27]	<0.01
• Nurturance	12.2 (2.7)	12.3 (2.8)	[-0.74; 0.53]	0.75
• Social integration	14.3 (1.7)	14.1 (1.8)	[-0.23; 0.59]	0.38
SF 12				
• PCS score	39.3 (10.9)	43.4 (12.0)	[-7.0; -2.2]	< 0.01
• MCS score	47.7 (10.9)	49.3 (10.3)	[-3.2; 1.4]	0.43

SD = standard deviation, 95 % CI= 95 % Confidence interval, SF 12 version 1 Physical Component Score (PCS) and Mental Component Score (MCS) relative to 1998 US Population baseline. SPS = Social Provision Score. Statistical comparison*: linear regression model for repeated measures (GLM)*

Table 13
Social support, comorbidity and pain interference's associations with HRQOL in ICU survivors

	Physical Component Score			Mental Component Score		
Variable	B	95% CI	p-value	B	95 % CI	p-value
3 months						
Total SPS score	-0.22	[- 0.51; 0.08]	0.15	0.60	[0.32; 0.89]	< 0.01
• Reassurance of worth	0.06	[-1.45; 1.58]	0.93	-0.01	[-1.58; 1.56]	0.99
• Attachment	-1.75	[-3.20; -0.31]	0.02	1.25	[-0.24; 2.75]	0.10
• Nurturance	-0.19	[-0.97; 0.59]	0.64	0.28	[-0.53; 1.08]	0.50
• Social integration	0.51	[-1.02; 2.04]	0.51	0.61	[-0.98; 2.19]	0.45
Number of comorbidity	-2.44	[-3.74; -1.14]	< 0.01	-1.19	[-2.53; 0.16]	0.08
Pain interference						
• Daily activity	-10.92	[-14.61;-7.24]	< 0.01	-3.93	[-8.22; 0.36]	0.72
• Normal work	-12.08	[-15.61;-8.56]	<0.01	-4.89	[-9.00;-0.78]	0.02
1 year						
Total SPS score	0.57	[-0.47, 0.58]	0.83	0.34	[-0.14, 0.82]	0.17
• Reassurance of worth	0.64	[-0.84; 2.13]	0.39	0.48	[-0.78; 1.73]	0.45
• Attachment	-0.41	[-1.58; 0.76]	0.49	1.09	[0.11; 2.08]	0.03
• Nurturance	0.09	[-0.85;1.02]	0.85	-0.08	[-0.87; 0.71]	0.84
• Social integration	-0.33	[-2.03; 1.36]	0.70	-0.50	[-1.92; 0.93]	0.49
Number of comorbidity	-3.25	[-4.40; -2.10]	<0.01	-1.66	[-2.63; -0.70]	0.01
Pain interference						
• Daily activity	-7.52	[-12.73;-2.30]	0.05	-2.48	[-7.88; 2.92]	0.36
• Normal work	-7.39	[-12.13;-2.66]	0.03	-1.93	[-6.85; 3.00]	0.44

95 % CI = 95 % Confidence interval, SF 12 version 1 Physical Component Score (PCS) and Mental Component Score (MCS) relative to 1998 US Population baseline. SPS = Social Provision Score. Statistical analysis: Univariate linear regression with PCS and MCS as the dependent variable and covariates as independent variables.

6.0 Discussion

The question that I had been asking myself all those years ago, before the study was planned and initiated, was: ” How are the ICU survivors doing after their ICU stay?” The fact that they were alive was not enough, and I was particularly interested in pain, symptoms and HRQOL. The study by Boyle et al. (53) inspired me to study pain and chronic pain, and there seems to be a short way from pain to other symptoms such as anxiety, depression, fatigue etc. The ultimate goal for all health care with a curative goal has to be adequate function and good quality of life for the individual who has received the health care in question, in this case intensive care treatment.

In the discussion I will try to answer my original question and the study’s aims in light of updated research. The first part will be a discussion about methodological issues, ethics and the term chronic pain.

6.1 Methodological considerations - Design

The present study’s goal was to improve the understanding of ICU survivors’ experience of pain, symptom burden and HRQOL after an ICU stay. We considered it best to obtain the information directly from the ICU survivors, not from health care professionals or their family members (proxies). Since Oslo University Hospital (OUS) receives patients from the largest health region in Norway, the South Eastern part of Norway (home to 2.9 million of Norway’s total population of 5.5 million), and in some cases from the whole country, a mailed survey seemed to be the most appropriate design to answer the research objectives.

An important part of planning this study was the selection of survey instruments; e.g. the collection of sufficient data and ensuring that the responder burden was not

too high (154). To our knowledge no survey instruments had been developed especially for the ICU survivors, so we used generic instruments that were widely used by other patient groups or by the general population. As ICU patients also are a heterogeneous group of patients, generic questionnaires were judged to be appropriate in the present thesis. The instruments were selected based on the following criteria:

- Collection of sufficient data
- Easy to understand
- Used in Norwegian samples version
- Not too comprehensive
- Showing satisfactory psychometric properties

We decided not to perform a pilot study, as similar surveys with similar numbers of questionnaires had been used on other patient groups by our research group (e.g. different groups of cancer patients and Chronic Obstructive Pulmonary Disease in not hospitalized patients) (95, 96, 155). Previous pilot tests did not reveal that the burden was too high, and there was an acceptable level of missing items. Thus, we did not believe that it would be different for the ICU survivors. As reported in results (5.1) the item missing value was low for all questionnaires except SCQ-18.

6.1.1 Study power calculation/estimate and statistical analyses

The aim of this study was to explore pain, other symptoms, and quality of life in ICU-survivors. Thus, a formal power calculation was not appropriate. The main outcome of interest was an estimation of the prevalence of pain. Such prevalence (proportion of patients experiencing pain) must be reported with a confidence interval which is dependent on both the number of respondents and the point estimate. Thus, we

calculated the number of respondents needed to get a reasonably narrow confidence interval around a point estimate of a proportion (prevalence of pain). Based on the available literature, we expected the prevalence of pain to be between 20 % to 80 %, and we calculated that 120 subjects would give a sufficiently narrow confidence interval. Our estimate for the prevalence of chronic pain fell within this interval with 49.2 % at 3 months and 38.2 % at 1 year. However, some of the potential risk factors for chronic pain (Table 8) might have been statistically significant with a larger sample. The results of our exploratory analysis show some large effects of clinical interest even if they were not statistically significant in our sample (Table 8).

All the study's statistical analyses were performed in close collaboration with two very experienced statisticians. The different analyses were chosen based on their recommendation of the most appropriate analyses to answer the different aims. Whether the data were normally distributed or not also affected which analyses were chosen and how the results were reported (e.g. mean/median).

In paper 1, multivariable analyses were preceded by an estimation of the correlations between risk factors. Because of strong correlations between the SAPS II and SOFA scores (r = 0.61), and ventilator days and ICU days (r = 0.71), three multivariable models were needed to avoid multicollinearity. In papers 2 and 3 we had originally planned to use multiple regression models, but since none of the demographic or clinical variables were statistically significant this approach was not appropriate. Instead, we used only univariate regression models.

In paper 3 we chose to use the two pain interferences scores with the highest mean value in the regression model instead of presence of pain, because we believed that these pain interference scores would have the largest impact on

HRQOL. We chose this, rather than the mean of all seven pain interference scores, because the latter would be too general and inadequately describe the sample.

Since we had 32% drop out from 3 months to 1 year, we fitted a linear regression model for repeated measures (GLM) with a diagonal covariance matrix to estimate the changes in HRQOL and social support between measurements 3 months and 1 year after discharge. GLM does not require complete data so we were able to use all the observations and not just complete data (with values at both time points). Paired samples t-test requires data at both time points thus in case of missing data the results could be biased. As GLM uses all available data, imputation is not necessary. Simple imputation of missing data also often leads to bias, therefore it is not recommended.

6.1.2 Study sample, period and recruitment

The decision to study pain, symptoms and HRQOL at 3 months and 1 year was based on the point at which acute pain changes from being acute to chronic (156). Furthermore, we reasoned that most ICU survivors were in rehabilitation at three months, while some had returned home. At one year, however, many ICU survivors' lives had in some way returned to normal, or to a "new normal life" after the critical illness.

In 2016 there were 15403 ICU stays in Norwegian hospitals, and 6383 were ICU stays in tertiary referral hospitals (2). Those 15403 ICU stays were distributed between 13679 ICU patients who had ICU stays longer than 24 hours (2). Compared to these large numbers this present study's 118 ICU survivors seem like a very small number, and it is possible to argue that the findings are not representative of the general Norwegian ICU population. It is, however, important to remember the present

study's inclusion and exclusion criteria. The NIR records include all patients with an ICU stay longer than 24 hours, and in the present study the ICU survivors had at least 48 hours in the ICU. This is an important difference. According to NIR, over 50 % of the ICU stays in Norway are shorter than 48 hours (2). In other words, the findings of the present study are not valid for the ICU survivors with an ICU stay shorter than 48 hours. The reason we chose this 48-hour limit was that we wanted to be sure to exclude the post-operative patients who sometimes stay overnight in the ICU. On the other hand, one may consider this a strength of the study, in that the present sample consists of quite severely ill former ICU patients. Even though the present study's findings are not representative for the total ICU population in Norway, it may still be representative for a comparable group of ICU patients from similar ICUs in Norway.

The choice of studying a mixed ICU survivor sample causes some challenges with regard to external validity. The sample was heterogeneous with regards to age, admission diagnosis, ICU LOS and time spent on mechanical ventilation (see results). It would most likely have been easier if we had studied ICU patients, who were admitted to elective surgery, but this would be a totally different sample and it would be difficult to generalize from this sample to the patients who were admitted as emergency ICU stays. The median ICU LOS days (9.0 (5-15)) and mechanical ventilator time days (6.0 (3-12)) are longer than median values for the Norwegian ICU population (median ICU LOS in Norwegian tertiary Hospitals was, in 2012, 2.2 days and the median ventilator time was 1 day), and the mean SAPS II (44.9) is also higher compared to the Norwegian ICU population (Norwegian tertiary Hospital mean SAPS II score 38) (2). There are several reasons for this. As mentioned above, we first excluded the ICU patients with stays shorter than 48 hours. Second, OUS is a

tertiary referral hospital and treats some of the most critically ill patients in South East Norway. And, compared to other similar hospitals in Norway, we have recruited a group of ICU survivors with severe illnesses. Previous research has shown that the most severely ill are a difficult group to study (157, 158).

A one-year inclusion period was initially considered to be sufficient, but the recruitment was slow and the study period ended up stretching from May 2010 to January 2014. This is a rather long period. In retrospect there were issues that could have been addressed differently. The ICU survivors could have been recruited from more than two ICUs in one hospital. The logistics of including more ICUs and hospitals were considered to be too extensive with new applications to Hospital boards, Regional Ethics Committee and local Hospital Data Inspectorate.

6.1.3 Validity and reliability of the instruments

Unfortunately few of the instruments are tested for reliability and validity for ICU survivors, but some have been used in research on ICU survivors: HADS (159) and PTSS 10 (160, 161). All the selected instruments were considered to have good psychometric properties (154), and for the main part were widely used and tested as valid and reliable for other patient groups and/or the normal population. The choice of instruments was also guided by the fact that other researchers, in the same research group, used many of the same instruments for the purpose of later comparison (95, 96, 162). A similar questionnaire package was pilot tested for layout and combinations of questionnaires in an oncology patient group (163) prior to the present study, and this was found to be sufficient. The overall missing items in the different instruments were under 5% on each item, which we deemed to constitute satisfactory internal validity. The comorbidity questionnaire (SCQ-18) had a much

higher item missing value than the other questionnaires. The missing value on each item for the SCQ 18 was between 10-22% (both 3 months and 1 year combined).

The included instruments were tested for internal consistency with the Coefficient alpha (Cronbach's alpha), which is a commonly used measure of reliability (154). Cronbach's alpha is defined as "*an estimate of the correlation between two random samples of items from a universe of items like those in the test (153)".* Cronbach's alpha is not appropriate for all questionnaires; SCQ-18 is just a list of different comorbidities and there is no expectation of internal consistency, and according to SF-12 different weighting of the score Cronbach's alpha is debatable(64). A Cronbach's alpha above 0.9 indicate an excellent internal consistency, between 0.8 – 0.9 indicate good internal consistency, between 0.7-0.8 indicate an acceptable internal consistency and a Cronbach's alpha between 0.6 – 0.7 indicates a questionable internal consistency. Cronbach's alpha below 0.6 indicates a poor or unacceptable internal consistency (164). This scale of quality of internal consistency must off course be interpreted with caution, since the number of items may inflate the value of Cronbach's alpha, and a narrow range may do the opposite(165). The Cronbach's alpha for the different instruments in the present study was good to excellent for all but GSDS, which had a Cronbach's alpha of 0.66. For comparing groups the Cronbach's alpha should be over 0.7, according to Bland and Altman (166).

Self-administered Comorbidity Questionnaire (SCQ-18)

There were some challenges associated with the Self-administered Comorbidity Questionnaire (SCQ-18). The questionnaire lists 17 comorbidities using a yes/no answer; if you answer yes, each comorbidity has two follow-up questions: Do you get

any treatment for the comorbidity, and does the comorbidity limit your activities? The consideration regarding this instrument was that it would provide us with more in-depth information on how the ICU survivors regarded their comorbidity. Other researchers have found that this instrument worked well (96), but we found the number of missing items to be quite high (Results 5.1), and maybe we could have extracted the same information from the medical records. One challenge with SCQ-18 is that one might misinterpret how to fill in the questionnaire. Some of the ICU survivors ticked the box that did not include the comorbidity, even if they said yes on the item asking for that they got treatment for it. That could mean that they did not have the disease anymore, but still received treatment, but it could also mean that they misinterpreted the questionnaire. A more precise way of collecting this information could be an electronic version where you only got the follow-up questions if you said that you had the disease. Another concern that could have been addressed is that SCQ-18 also consists of several comorbidities of pain (e.g. headache, back/neck pain, Rheumatoid Arthritis). Many of these constitute chronic pain illnesses and may interfere with the present study's findings of chronic pain (see discussion 6.4).

Brief Pain Inventory Short Form

The BPI–SF has well-established validity and reliability for patients with cancer, for whom it has shown sensitivity to change in longitudinal studies (131-133, 167), but also for people with chronic non-cancer pain (134, 135). BPI- SF measures the subjective intensity of pain and how pain interferes with function.

Since pain is subjective by nature, pain prevalence was dichotomized to be either present or absent, and this is of course simplifying pain. In a study with a

larger sample size one could have divided pain into mild (NRS 1-3), moderate (NRS 4-6) and severe (NRS 7-10), like McCaffery & Beebe (29) did, and compared these sub-groups. In the present study BPI-SF provided information on different aspects of pain in the ICU survivors, which we found interesting. The location (not related to the admission diagnosis), the low-to-moderate intensity score, the low use of analgesics and the low-to-moderate interference score in total, all contributed to more in-depth understanding of ICU survivors' pain. Furthermore, the low item missing value (See 5.1) is a sign of satisfactory internal validity. The internal consistency for BPI –SF intensity items was 0.92 and 0.88 for BPI-SF interference items, and we found these Cronbach's alphas satisfactory.

Short Form Health survey 12 version 1 (SF 12)

SF 12 is a generic and widely used instrument for measuring health status or HRQOL in many patient groups and the general population (95, 151, 162, 168). Even though SF 36 is much more frequently used when studying HRQOL in ICU survivors than SF 12, SF 12 was preferred over SF 36 only because it is shorter. Gandek et al. (151) have showed that SF 12 can replace SF 36 when studying physical component summary (PCS) and mental component summary (MCS) and they reproduce similar findings. The correlation between SF 36 and SF 12 is for PCS was high (0.95) and for MCS even higher (0.97) in a Norwegian population (151). All in all SF 12 worked well with a low item missing value of 0-5%, and the results of this present study are in line with previous studies that used SF 36 (77). We deliberately chose to use the SF 12v1 and not the SF12v2 because the SF 12 v1 is free of charge.

Hospital Anxiety and Depression Scale

HADS is also a widely used, relatively short instrument for self-reporting anxiety and depression. It consists of 7 questions about anxiety and 7 questions about depression (137, 139). HADS discriminated well between depression and anxiety, had a low item missing value and good internal consistency for the subscales (Cronbach's alpha anxiety 0.89, depression 0.80).

Post-Traumatic Stress Symptoms 10 (PTSS 10)

PTSS 10 is not an instrument for fine diagnostics, and this is why the term used is post-traumatic stress symptoms and not PTSD (disorder). When PTSS 10 is used on individuals who have been exposed to severe psychic trauma, few cases of false positive and false negative PTSS have been reported. If PTSS 10 is used in a broader context, like general crisis reactions, it seems as if there are more false positive reports of PTSS, but these can be sorted out in an in-depth interview. Whether an ICU stay may be characterized as a severe psychic trauma may be individual, and this may be the reason so few participants reported PTSS in this present study. One of PTSS 10's advantages is that it includes both depression and irritability, which are both important parts of the PTSD syndrome(141).

During the research process it has come to our attention that a newer version of the PTSS 10, designed for ICU survivors, was developed by Stoll et al. (161) in 1999, consisting of four more questions on traumatic events in the ICU (part A) of the questionnaire. The part B is the same as the original by Holen et al. (140) used in the present study. This is of course unfortunate, but overall the prevalence of PTSS was low in the present study, and as 10 of 14 questions are identical, we have reason to believe that the overall prevalence of PTSS is similar.

Lee fatigue scale (LFS)

LFS was chosen because it measures fatigue and energy level in an easy to understand and fast way, and is found to be valid and reliable in a healthy population and patients with sleep problems (102). Fatigue may be measured together with other symptoms and then often just with one question. The LFS, which contains 13 items on fatigue and 5 items on energy, was considered to be more robust than the one item instruments. As mentioned in the method section, we chose to use the evening cut off for fatigue and energy level, and we are aware that this cut off may have led to an overestimate of fatigue and energy level. Nevertheless, the prevalence of fatigue was relatively low compared to previous studies (87, 169). LFS had excellent internal consistency for the fatigue sub scale (0.95) and good internal consistency for the energy scale (0.88), so the internal validity was satisfactory and in accordance with a study of Norwegian women with breast cancer (170).

General sleep disturbance scale (GSDS)

General sleep disturbance scale was chosen to measure sleep disturbance as it is a validated instrument, translated into Norwegian and used on different populations: shift workers, pregnant women, residents in nursing homes, men with prostate cancer and people with psoriasis (94, 142, 146, 148, 171, 172). In this present study the item missing value was low (0%), which may indicate a good internal validity, but the internal consistency was only 0.66. Others have found the GSDS to be reliable for shift workers (0.88) (142, 171) and men with prostate cancer following radiation therapy (0.81)(148). Why the internal consistency was so low in this present sample we do not know, but caution should be taken when generalizing the findings on sleep disturbance.

Social Provision Scale revised (SPS)

Social Provision Scale revised was chosen to measure social support as it is a validated instrument, translated into Norwegian and used on different populations, either in its original form or in the revised version: college students, postpartum mothers, school teachers and the elderly (112, 114, 115, 173). It also appeared to be easy to understand and relatively short. The low item missing value (See 5.1) may indicate that the ICU survivors agreed and that the internal validity was good. The instrument also had a good internal consistency (Cronbach's alpha 0.83).

6.2 Ethics

ICU patients are a vulnerable patient group, because they are so severely ill. They are often unconscious for long periods during their ICU stay, due to sedation or the illness itself (e.g. brain hemorrhage). We also know from research that some ICU patients struggle to regain their usual level of cognitive function (174). All this is important to consider when researchers ask them to participate in studies and give informed consent. In the present study the ethical dimensions were considered before and during contact with ICU survivors. The research group concluded that the burden of the questionnaires would be quite low. When the ICU survivors received the survey in the mailbox, they had plenty of time to complete it (14 days) and they could complete it at home The different questions about pain, symptoms and HRQOL may have reminded them of their critical illness and how their life situation had changed, thus recalling unpleasant memories; on the other hand, such memories and such an understanding of their life situation were most likely already present. When the ICU survivors were contacted by phone, the information on the study was presented as neutrally as possible and with as little pressure as possible. If the

researcher sensed that the ICU survivor did not want to participate, but found it difficult to say so, the researcher emphasized that the participation was voluntary. The researcher's experience was that the ICU survivors who did not want to participate had no problem with saying so; the majority, however, was positive to research and wanted to participate. Some felt gratitude towards the hospital and the ICUs who had treated them and wanted to repay them with their participation. These ICU survivors were of course informed that the participation was voluntary, and that they should not feel obliged to participate due to gratitude. The research group thought that research on ICU survivors was important to improve future care for this group, and that no others could provide the information the ICU survivors provided.

6.3 Strengths and Limitations

The strength of the present study is that its sample consisted of former severely ill patients (see 6.1.1). This, however, may also be the reason for the response rate being 62%. Others (157, 158) have reported that the most severely ill are difficult to study, and the severity of the illnesses may explain our relatively low response rate and the relatively high dropout rate of 32 %. Even though the dropout rate was higher than wanted, there was no difference between dropout and study sample (Table 1). The strength of this present study is that it is prospective and longitudinal and that the item missing value was low (See 5.1) at both 3 months and one year.

A limitation to the study is the large group of ICU survivors we could not reach due to missing contact information (phone number). The primary contact with the ICU survivors was made by phone, and for some reason it is not common to record the ICU patients' phone number in their medical records. Despite reminders to the health care personnel to record phone numbers, many numbers were lacking. We searched

thoroughly in public phone records (1881, yellow pages etcetera), but still quite a few numbers were missing. In Norway today, you do not need to have your phone number in a public record if you do not want to. To the ICU survivors with lacking phone numbers we sent study information and consent form by ordinary mail, but unfortunately that approach did not yield any results. We did not contact next of kin, unless it was a spouse, as we did not have permission from REK to do so.

The survey as a method has its limitations. It is not possible to ask follow-up questions, and misunderstandings cannot be addressed. Surveys are also known to have a decreasing response rate and a high dropout rate, and this may threaten their ability to provide data that can be generalized. The qualitative interview is another method that could have been applied to this sample, but then again one would get different data, and it would be difficult to interview 118 ICU survivors. The method would be too time-consuming and too expensive as ICU survivors come from all over Norway, and the ability to generalize from qualitative data may be limited (175, 176). Since this was a study about pain, symptoms and HRQOL we thought, and still think, that self-reporting was the most appropriate choice with regards to presenting ICU survivors' subjective experience of pain, other symptoms and HRQOL. Other research (e.g. pain research) has shown that by proxy reporting does not yield the same results as self-reporting; by proxy reporting may both over- and under-report pain (177). Another possible limitation could be that the instruments are not tested for validity and reliability for an ICU population.

Another concern may be the external validity with regards to the study's sample. Comparable data from The Norwegian ICU registry includes ICU patients with stays longer than 24 hours (2), but in this present study all ICU survivors had ICU stays longer than 48 hours. This may challenge the external validity of the

present study, and we do not know if the present study's findings are valid for ICU survivors with shorter ICU stays than 48 hours. The ICU survivors in this present study were included after an ICU stay in OUS Rikshospitalet, which is a tertiary reference hospital in Norway. Thus, results of the present study may not apply to all ICU survivors in Norway. However, we believe the findings may be representative for other ICU survivors from comparable hospitals in Norway (e.g. other tertiary reference hospitals like Haukeland University Hospital, St Olavs Hospital, University Hospital of North Norway).

6.4 The concept of chronic pain – persistent pain – pain

There are some challenges associated with describing pain or chronic pain. By definition pain is a subjective phenomenon, and so is chronic pain (23). In the different pain societies and in research different terms have been used; chronic pain, persistent pain, acute pain (178). Pain is often measured with numeric instruments, such as NRS. There is, however, a challenge associated with this: If two people experience the same pain, they may rate it totally differently on the NRS scale. Acute pain may be more understandable than chronic or persistent pain. If you break an ankle or have surgery, the expectation is that this is painful and that you will need to take some form of analgesics. The pain will normally subside in a few days or weeks, until you are free of pain. Conversely, chronic pain is a bit more complex to comprehend. There are different definitions of when acute pain becomes chronic, both 3 and 6 months since the onset of pain are widely used time markers, but the International Association for the Study of Pain (IASP.org) also recognizes 1-12 months as the transition point from acute to chronic pain; it all depends on when normal healing has occurred (Classification of Chronic Pain IASP 2011). There has

been a growing objection to the term chronic pain due to how chronic pain is defined; as *"pain which persists past the normal time of healing"* (178). The time of healing is the problem. People with chronic pain often focus on the healing of tissue rather than learning how to cope with the chronic pain. Persistent pain is now more widely used, as this term does not include normal healing in its definition.

Another challenge associated with chronic pain is how to measure it (135). In the present study we asked the ICU survivors to report pain 3 months and 1 year after their ICU stay. The time point of 3 months was chosen based on one of the transition points from acute to chronic pain (25). The question still remains: Is it possible to measure chronic pain as an incidence report? Ideally, the ICU survivors would have reported their pain on a daily basis (or weekly) from ICU discharge and up to 3 months and maybe up to 1 year. However, this would have been too heavy a burden on the ICU survivors and focusing on pain every day may not have been good for them. The present study shares the challenge of how to report chronic pain with other studies (53, 54), and the question still stands: Has this study measured chronic pain or only the presence of pain? In most studies of persistent pain after surgery or ICU-treatment, the patients are asked to report presence of pain without questioning about duration and temporal pattern. In the study information where we explained the rationale of the study, the term chronic pain was used, and we asked the participants about previous chronic pain.

There was a large difference in the prevalence of chronic pain prior to the ICU stay and the prevalence after ICU discharge (see results). Based on this difference we have reason to believe that the pain measured was chronic, but measuring pain more often and in closer proximity to the ICU stay would have given us a higher certainty.

The choice of studying use of Fentanyl and the maximum doses of Fentanyl in the ICU as possible risk factors for chronic pain post-ICU was not as successful as we had hoped. This is in accordance with Hayhurst et al (179) who did not find any associations between opioid use in the ICU and pain intensity or pain interference at 3- and 12 months after the ICU stay.

6.5 General discussion

The short answer to the question, “How are the ICU survivors doing after their ICU stay?” for the sample in this present study is perhaps “Okay, fair, good”. The long answer is the discussion that follows below. How do the present study’s findings compare with updated research? Towards the end the discussion also includes a discussion on the present study’s results and the theory of unpleasant symptoms.

6.5.1 Pain in ICU survivors

The ICU survivors in the present study experienced pain after their ICU stay. The prevalence of pain at 3 months (49.2%) was the same or a bit higher than other studies (28% to 44%) (53, 54, 180), but the mean intensity and interference are low to moderate. Then again, if we study the range score of intensity and interference we find a large range for several for the scores (0-10) (Table 6). There are a few ICU survivors who experience both high pain intensity and interference, but the majority of ICU survivors do not. The study sample size was not large enough to perform sub-group analysis. The use of analgesics was also low to moderate. The reduction in pain prevalence at 1 year to 38.2% can be interpreted as recovery for the ICU survivor. The reduction in pain prevalence at 1 year is also the reason why I argue that the pain prevalence is mostly the same as in the studies mentioned above. It

might be the result of asking the ICU survivors about pain at different time points after the ICU stay. None of the other studies asked about pain before 6 months after the ICU stay (53, 54, 180).

One interesting finding in the present study is the most commonly reported pain locations in this sample: the shoulders/upper arms at both 3 months (29.3%) and 1 year (55.8%) and the ankles/feet and extremities at 1 year (Figure 3). These locations are not related to the admission diagnosis, but they may very well be connected to the critical illness or the ICU treatment. The presence of shoulder pain is the same as Battle et al. (180) found in their study, but the prevalence was higher in this present study. It is worth mentioning that shoulder pain is less common in the general population, only 9 % reported shoulder pain in a large European survey (31)

Only 7.5 % reported that they had chronic pain prior to the ICU stay. This prevalence of chronic pain is far lower than what is reported in Norwegian surveys, varying from 24 to 40 (31, 181, 182). Prevalence of chronic pain varies tremendously between studies (from 8 to 64 % in a recent meta-analysis) (183) and is dependent on different definitions of chronic pain and different methodology (183). The chronic pain prevalence score in this study may be biased by the retrospective report and the most plausible explanation for this is the theory of response shift (184, 185). The theory of response shift suggests that a life-changing event like an ICU stay may change the way a person thinks about his or her past health. The person adapts to the new reality and so health complaints from before the ICU stay seem to be trivial and of minor importance (184).

An interesting study from Latronico et al. (186) found that ICU survivors may have pathology in the small nerve fibers which again may cause pain post-ICU. It is well established that many ICU survivors suffer from CIPNM, which today often is

referred to as intensive care acquired weakness, which often affects the extremities (187-189). The present study did not perform any neurophysiology examinations, but the findings of Latronico et al. (186) are quite interesting and may provide a physiological explanation for the presence of pain among ICU survivors.

6.5.2 Other symptoms in ICU survivors

The prevalence and level of symptoms in the present study is on the low side compared to previous international studies. Previous studies have found a prevalence of anxiety of approx. 42-43% (85, 190) and a prevalence of depression in the range of 8 to 57 (9, 85, 159, 190), and the present study found a prevalence of anxiety of 24.1% at 3 months with a small increase to 28.3% at 1 year, and a prevalence of depression of 15.4 % and 12.8 % respectively. Milton et al. (191) found, in a mixed ICU population from Sweden, a prevalence of anxiety of 16% with a HADS A cutoff of >7 and a prevalence of depression of 21% (HADS D cutoff >7) at 3 months. Milton et al. (191) also found a prevalence of PTSS of 13% (PTSS 10 part B cutoff >34). When comparing the present study with Milton et al. (191), it seems as if Norwegian ICU survivors experience more anxiety, the same level of PTSS, but are less depressed than the Swedes. Compared to the rest of the world's population, Norwegians and Swedes are regarded as very similar people from very similar societies, so the explanation would not seem to be cultural, although upon closer scrutiny Scandinavian populations do show variations between nations. We do not know why Scandinavians report less anxiety and depression than other populations, but high living standards, high-quality and free public health care might contribute to this phenomenon (192). The Scandinavian populations also score high on happiness and satisfaction with life (193).

In addition to pain, sleep disturbance was the most prevalent symptom among the ICU survivors in the present study, with 49.2% at 3 months and 46.5 % at 1 year. Sleep disturbance seems to be a prominent problem for ICU survivors in other recent research (194). Altman et al.'s review from 2017 (194) found severe sleep disturbance at approx. 3 months to be in the range of 34-64%, and in the range of 10-61% after 6 months. They also found that sleep disturbance declined over time. These findings correspond well with the findings of the present study.

There was an association between the prevalence of pain and all symptoms except lack of energy. Research on other patient groups has found an association between pain and other symptoms (195-197). We do not know, however, whether the pain came first and then the other symptoms followed, or vice versa. Neither do we know whether there is some physiological trait (e.g. genes) that makes some individuals predisposed for developing pain, depression and fatigue with the right exposure. Miaskowski et al. (93, 94) have done several studies on multiple co-occurring symptoms. Multiple symptoms indicate that several symptoms occur together and influence each other and increase the symptom burden. The present study also found a few individuals who suffered from a multiple co-occurring symptom burden with four symptoms or more.

The term multiple co-occurring symptoms is not used frequently regarding ICU survivors, but there has been more and more research in recent years on Post Intensive Care Syndrome (PICS). PICS is defined as *"new or worsening impairment in physical, cognitive, or mental health status arising after critical illness and persisting after the ICU discharge* (198)". ICU-acquired neuromuscular weakness is a part of PICS. PICS may be another approach to study some of the same phenomena. Multiple symptoms studied with a self-reporting questionnaire is an

important part of PICS, but physiological tests such as neurophysiology tests, walking test and tests of muscular strength alongside cognitive tests must also be performed to complete the picture. If these tests should become part of standard post-ICU care, multidisciplinary follow-up clinics for ICU survivors must be established. So far this is not standard care in Norway. ICU follow-up clinics are established in other countries.

6.5.3 Health-related quality of life

ICU survivors in the present study experienced reduced physical and mental HRQOL, but the reduction in mental HRQOL was so small that it was within the SD of the mean MCS of the normal population. There was an improvement in both scores from 3 months to 1 year. Previous research has found a statistically significant reduction in both physical and mental HRQOL and an improvement over time in both physical and mental health (6, 53, 199). This finding also appears in a Norwegian population of ICU survivors (5), and new research from Scotland (200). Why this particular sample of ICU survivors reports a smaller reduction in MCS may be associated with the high level of social support (total SPS score and sub provisions) in the present study. The positive effect of social support on health outcomes and HRQOL has been shown in previous research on other patient groups (117, 201, 202).

The present study compared HRQOL in ICU survivors with results from a norm-based population. Other researchers have, however, found that preexisting comorbidity is associated with lower HRQOL: The more comorbidity, the larger reduction in HRQOL (7, 82). This finding was confirmed by Griffith et al. (200) in 2018.

Pain interference with normal work and daily activity had the largest negative association with physical HRQOL at both time points, and even though the pain interference increased from 3 months to 1 year, the association with HRQOL was reduced. This finding may seem contradictory, but the theory of response shift (185) may provide a possible explanation for this. With regard to the pain interference score, the ICU survivors may have expected the pain to improve from 3 months to 1 year, but then, at 1 year, the ICU survivors may have accepted the pain and its interference as having become chronic/persistent. However, the theory of response shift argues that the life-changing event, critical illness, leads to a change in the perception of the ICU survivors' life and health status, so even though the pain interference was higher, the association with physical HRQOL was less. The here and now are more important than what was before the critical illness.

6.6 The present study's findings and TOUS

TOUS as a mid-range theory may help us to understand this present study's findings. The concept of the symptom in TOUS is understood as more than just an isolated symptom, like pain, for instance. Pain as a symptom may appear alone or together with other symptoms, such as fatigue and sleep disturbance, and the symptoms may all interact with each other. If you are in pain, it is well known that falling asleep is difficult. As discussed earlier, pain is a complex symptom, difficult to understand and do research on, because it is so subjective in its description (6.4 and 6.5.1). When pain is understood as a symptom in TOUS, it becomes clearer that it is unwise to try to understand pain as an isolated phenomenon, and better to try to understand pain in relation with other symptoms and influencing factors. In the present study we did not investigate the different dimensions of the symptoms, so I will not comment on

intensity, distress, timing and quality, other than stating that they may or may not vary from symptom to symptom. The different dimensions may also vary over time, according to Lenz (122). The influencing factors may be the ICU survivor's physical HRQOL, his/her mental HRQOL, and the situational factors may be other resources around the ICU survivor, such as family, social support, rehabilitation facilities etc. All these factors may influence the different symptoms that the ICU survivor experiences. If the ICU survivor is depressed, the mental HRQOL can be reduced. This reduction in mental HRQOL may again influence pain, sleep disturbance and fatigue. If the physical HRQOL is reduced, the ICU survivor is not able to walk the way he/she used to, which could also influence symptoms like pain and sleep, and possibly interact with mental HRQOL. In paper 3 of the present study, pain interference influenced both statistically significant and clinically relevant HRQOL, especially physical HRQOL. HRQOL is here interpreted as the performance part of TOUS. Both mental and physical HRQOL may have a reciprocal influence on both the symptoms and the different influencing factors, so that physical HRQOL may influence pain and psychological and physiological factors and mental HRQOL may also influence fatigue, sleep disturbance and how the ICU survivor relates to his or her social network (situational factor). Since TOUS is a mid-range theory it can also be of use in a more clinical setting than research. Modern health care is often organized in outpatient clinics for the various organs (e.g. gastro-, surgical, heart failure, orthopedics, pain, etcetera). This type of organization makes it easy to lose perspective of the patient's total health status, and the different physicians and nurses may only see what they are looking for in relation to their particular "organ". If TOUS was used as a framework to understand symptoms in outpatient clinics, maybe it would be easier to see the whole picture, i.e. the individual's total HRQOL.

7.0 Conclusion

The prevalence of chronic pain in ICU survivors was 49.2 % at 3 months and the prevalence of chronic pain was reduced to 38.2 % at 1 year. Pain was strongly associated with anxiety, depression, PTSS, fatigue and sleep disturbance at both 3 months and 1 year after ICU discharge. HRQOL was reduced in the ICU survivors at 3 months and 1 year; the greatest reduction was in physical HRQOL at 3 months. Pain interference had the largest negative association with reduction in physical HRQOL, but comorbidities also had a negative association with physical HRQOL. Social support on the other hand had a positive association with mental health at 3 months. Despite this, ICU survivors in our study seems to manage life fairly well, and pain and HRQOL improved during the first year after ICU-discharge.

7.1 Further research

There is still a need for more in-depth understanding of the recovery and rehabilitation of ICU survivors. The high prevalence of shoulder pain in the present study needs further investigation, for example through thorough clinical examination, before we can find possible causes and develop interventions that may reduce this pain. We also still have more work to do to improve their physical HRQOL post-ICU. The challenge is the heterogeneity within the group of ICU survivors and how to reach the ones who need help. One size does not fit all, and we need to develop tools to identify the ICU survivors who may benefit from targeted interventions. It seems evident that we need to develop and examine the effectiveness of individual follow-up treatment and care for the ICU survivors.

7.2 Clinical implications

Even though this was an exploratory study and not designed to test an intervention, we think that our findings are interesting for health care professionals and ICU survivors. Follow-up programs for ICU survivors are of increasing interest. The result of the present thesis adds to already existing information on ICU survivors' outcome. The results may enable multi-disciplinary health care professionals to identify individual challenges regarding pain, symptoms and HRQOL after an ICU stay. This could eventually lead to better care for the ICU-survivors.

8.0 Errata

In paper 3 there is an error in table 2 in the tables sub text. It's stated that the statistical comparison was paired samples t-test. This in not correct and should be linear regression model for repeated measures (GLM). This is corrected in table 7 in the synopsis.

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III

PLOS ONE

RESEARCH ARTICLE

Health-related quality of life in intensive care survivors: Associations with social support, comorbidity, and pain interference

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Abstract

Background

Experiences during a stay in the intensive care unit (ICU), including pain, delirium, physical deterioration, and the critical illness itself, may all influence survivors' health-related quality of life (HRQOL). However, few studies have examined the influence of social support, comorbidity, and pain interference on ICU survivors' HRQOL.

Objectives

To investigate possible associations between social support, number of comorbidities, and pain interference on HRQOL in ICU survivors.

Methods

ICU survivors responded to a survey 3 months (n = 118) and 1 year (n = 89) after ICU discharge. HRQOL was measured using the Short Form Health Survey-12 (v1), social support using the revised Social Provision Scale, pain interference using the Brief Pain Inventory–Short Form, and comorbidities using the Self-Administered Comorbidity Questionnaire.

Results

Physical and mental HRQOL were reduced at both 3 months and 1 year in ICU survivors compared with the general population. This reduction was more pronounced at 3 months for physical HRQOL, while a small reduction in mental HRQOL was not clinically relevant. Social support was statistical significantly positively associated with mental HRQOL at 3 months, while number of comorbidities was statistical significantly associated with a reduction in physical HRQOL at 3 months and 1 year and mental HRQOL at 1 year. Lastly pain

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interference was significantly associated with a reduction in physical HRQOL at 3 months and 1 year.

Conclusions

ICU survivors primarily report reduced physical HRQOL. Social support was positively associated with mental HRQOL, while number of comorbidities, and pain interference were all significantly associated with a reduction in HRQOL. Pain interference was associated with the largest reduction in HRQOL.

Introduction

Today, most intensive care unit (ICU) patients survive their ICU stay [1], although they may experience critical illness, trauma, or deterioration of chronic disease, and many require support with a ventilator, vasoactive drugs, or dialysis. During their ICU stay, patients may experience sleep deprivation [2–4], pain [5], discomfort [6], delirium [5], and physical deterioration [7]. All of these experiences, and the critical illness itself, may negatively be associated with ICU survivors' health-related quality of life (HRQOL) long after their ICU stay [8–16]. Previous research on this population has demonstrated that preexisting disease or comorbidity has a negative impact on HRQOL following an ICU stay [8, 17, 18], and that chronic pain had a negative impact on HRQOL [19]. Quality of life (QOL) is a multidimensional concept that, in its broadest interpretation, comprises almost every aspect of life, includes numerous definitions [20, 21]. For the purposes of this study, we used the definition of QOL that regards a person's sense of satisfaction or dissatisfaction with areas of life that are important to them [22]. HRQOL, then, is QOL in the context of health and illness [23].

Research on patients with cardiac diseases have shown that social support may predict better health and better physical function [24]. Cancer research has shown that help from friends and family is important for patient recovery and coping [25]. ICU survivors often undergo dramatic changes in health and functioning [26–28]. Their social life may also be altered because of reduced contact with family and friends during their ICU and hospital stays, and because they are absent from work, school, and/or leisure activities. It may take a long time for these patients to regain normal activity levels, if they ever do [29, 30]. We hypothesized that these factors could explain changes in HRQOL. Previous research [31] found that instrumental and emotional social support influence HRQOL in ICU survivors; however, to our knowledge, little other research has been conducted on social support in ICU survivors and its impact on HRQOL. The aim of the present study was to investigate a possible association between social support, pain interference, and comorbidity on HRQOL 3 months and 1 year after ICU discharge.

Material and methods

This was an exploratory study with a longitudinal design and two data collection time points: 3 months and 1 year following ICU discharge.

Settings and sample

ICU survivors from two mixed surgical and medical ICUs (ICU 1 and ICU 2) at Oslo University Hospital, a tertiary referral hospital, were included. ICU 1 and ICU 2 have 11 and 9 beds,

respectively, and neither treats trauma patients. The study took place from May 2010 to January 2014. ICU survivors aged 18 years or older with an ICU stay longer than 48 hours were invited to participate. The other inclusion criterion was the ability to read, write, and understand spoken Norwegian, so that the participant could complete the study questionnaires; patients with reduced cognitive function or terminal illness were excluded. Level of cognitive function and/or terminally ill status was established with assistance from the ICU survivor's next of kin if they were unable to speak with the investigator (AKL) over the phone. Of the 348 patients contacted, 193 consented to participate. Among these, 118 and 89 patients completed the questionnaires at 3 months and at 1 year, respectively.

Data collection

Three months after discharge, all eligible patients were contacted by telephone, informed about the study, and invited to participate. The ICU survivors who consented to participate got the questionnaire, study information in writing and informed consent by mail. If the ICU survivors did not reply within 14 days they got the questionnaire, information and consent form once more. The first author (AKL) used ICU electronic medical records to collect information on diagnosis, length of ICU stay, days on ventilation, and disease severity. Study participants completed questionnaires regarding HRQOL, social support, and pain interference; they also reported demographics (i.e., age, sex, education, marital status, and children), and comorbidities.

Severity of disease during intensive care unit stay. Two measures were used to assess disease severity during ICU stay: the Simplified Acute Physiology Score II (SAPS II) and the Sequential Organ Failure Assessment (SOFA) score. The SAPS II was developed to quantify the likelihood of hospital mortality in ICU patients [32] and is based on multiple parameter values (vital signs, Glasgow Coma Scale, and the presence of malignancy or human immunodeficiency virus infection) measured during the first 24 hours after ICU admission. These values are summed for a total SAPS II (range 0–163), with a higher score indicating greater severity of illness. SAPS II has been shown valid and reliable for use in medical, surgical [32], and coronary ICU patients [33]. A SAPS II score of 29 indicate a mortality of 10% and if the SAPS II score increase to 40 the morality also increases to 25%. If the SAPS II score increase to 64 and above the morality increase to 75% [32].The SOFA score describes different levels of organ failure over time, as well as the risk of death from sepsis, and has been used with many critically ill patients and patient groups [34]. The SOFA score has been shown valid and reliable in adult ICU patients [35]. The SOFA score is based on respiratory, cardiovascular, hepatic, coagulation, renal, and cognitive failure, each rated on a 4-point scale (total score range 0–24). A higher SOFA score indicates a higher level of organ failure and a higher risk of death. SOFA score of 0–6 may on a group level indicate mortality of 10%. If the SOFA score increase to 7–9 mortality increases to 15–20%, and SOFA score of above 15 indicates mortality of above 90% [35]. Both SAPS II and SOFA scores provide information about critical illness severity and can be used to predict mortality.

Comorbidities. Comorbidities were assessed using the Self-Administered Comorbidity Questionnaire (SCQ) [36], which includes 13 common and three optional medical conditions. The SCQ allows the informant to report both severity of comorbidities and their impacts on their daily life. For this study, four common comorbidities (headache, skin diseases, bowel diseases, and muscular diseases) were added to the standard 13. Only the total number of comorbidities was used in our analyses, but the most common comorbidities are presented.

Heath-related quality of life. HRQOL was scored using the Short Form Health Survey-12 (v1) (SF-12), which measures total health status. The SF-12 (v1) consists of 12 questions

about eight health concepts: physical functioning, role-physical, bodily pain, general health, energy/fatigue, social functioning, role-emotional, and mental health. These concepts are summed to create a Physical Component Summary (PCS) and a Mental Component Summary (MCS) [37]. The SF-12 PCS and MCS are calculated using norm-based data from the 1998 general US population, with a mean of 50 (standard deviation [SD] 10), which is similar to the general Norwegian population, which has a mean PCS of 50.3 (SD 8.8) and mean MCS of 50.6 (SD 9.9) [38]. The mean cutoff score of 50 means that if the study sample scores a mean value for PCS below 50, then they have reduced physical health compared with the general population; if the study sample scores higher than 50, then they have better physical health compared with the general population. This also applies to the MCS. Higher summary scores indicate better HRQOL. The SF-12 is widely used and has been validated for use in many patient groups, as well as the general population, and has been translated into many languages, including Norwegian [38]. The SF-12 has specifically been shown to be valid and reliable in relation to, and to be a good alternative for, the longer SF-36 [37, 38].Based on recommendation from Ware et al [39] a reduction of 5.0 in PCS and MCS score was considered to be clinical relevant in this present study.

Social support. Social support was measured using the revised version of the Social Provision Scale (SPS) [40–42]. The revised SPS consists of 16 assertions about social support that may apply to the individual. Responses options include: strongly disagree, disagree, agree, and strongly agree, representing the degree to which each assertion describes the individual's social support situation. A high score indicates a high level of social support [43]. The 16 assertions are summed to create four provisions—reassurance of worth, attachment, nurturance, and social integration—each of which has a maximum score of 16, consistent with previous research [43]. The total SPS score is calculated by summing the scores of the four provisions (maximum score 64). The revised SPS has been shown to be valid and reliable for use with older adults living in Norway [43], and the original SPS has been used in studies of hospital nurses [44], pregnant women, first time mothers [45], and schoolteachers [46]. The primary differences between the original and revised SPS are the decrease from six to four provisions, respectively, and a change in total score from a maximum of 96 in the original to 64 in the revised version. There are no cut off value to this instrument [43].

Pain interference. Pain was evaluated using the Brief Pain Inventory–Short Form (BPI–SF) [47, 48]. The BPI–SF assesses pain occurrence, intensity, location, relief, and interference with function. The BPI–SF has well-established validity and reliability in different patient groups [49–54]. The ICU survivors in our sample were divided into groups based on their answer to the first BPI–SF question, "Do you have pain?" The pain group included those who responded "yes", and the no-pain group included those who responded "no" or whose scores were "0" on all four dimensions, consistent with previous use of the instrument [55, 56]. Pain interference with the seven functional domains was rated on a numerical rating scale from 0 (does not interfere) to 10 (completely interferes). In our analyses, we only used the pain interference score of the two highest interference score. We chose this, rather than the mean of all seven pain interference scores (in BPI-SF), because the latter would be too general and inadequately describe the sample.

Ethics

The study was approved by the Hospital Data Inspectorate and the Regional Committees for Medical Research Ethics in Norway (reference number 2012/4b S-07505b). Only patients who gave informed consent participated; written consent was administered 3 months after ICU discharge. The study is also registered in Clinical Trials: NCT02279212.

Statistical analyses

Sample characteristics are presented as the mean and standard deviation (SD), median and interquartile range (IQR), or proportions with percentages. Associations between social support, number of comorbidities, pain interference, and HRQOL were tested using a linear regression model at 3 months, and again at 1 year, after ICU discharge. For the linear regression analysis, ICU survivors in the no-pain group (based on BPI–SF) were assigned a pain interference score of 0. P-values < 0.05 were considered statistically significant, and all tests were two-sided. All analyses were performed using IBM SPSS (version 23; IBM SPSS, Armonk, NY, USA).

Results

Demographic- and clinical characteristics of the sample

The mean age of the sample was 55.1 years (SD 14.4), 63.6% (n = 75) were male, 62.7% (n = 74) were married or had a partner, and 77.1% (n = 91) had children (either young or adult children) (Table 1). The mean SAPS II and SOFA score was 44.9 (SD 16) and 8.8 (SD

Table 1. Survivors' demographics, clinical characteristics, and social provision scale scores 3 months after intensive care unit discharge.

Characteristics	3 months
	Mean (SD)
Age	55.1 (14.4)
Number of comorbidities	2.0 (1.6)
Sex	**n (%)**
Male	75 (63.6)
Female	43 (36.4)
Education	
Primary	59 (50.9)
Secondary	15 (12.9)
University/College	42 (36.2)
Marital status	
Married/partnered	74 (62.7)
Divorced/separated/widowed/unmarried	44 (37.3)
Children	95 (80.5)
Children younger than 15 years old	31 (26.3)
Children older than 15 years old/adult children	64 (54.2)
No children	23 (19.5)
Significant negative life incidents (during last 4 weeks)	
Death in family or close friend	18 (18.6)
Severe financial problems or living conditions	4 (4.2)
Clinical characteristics	**Median (IQR)**
ICU LOS (days)	9 (5–15)
MV duration (days)	6 (3–12)
	Mean (SD)
SOFA score	8.8 (3.4)
SAPS II score	44.9 (16.0)

SD = standard deviation, IQR = interquartile range, ICU LOS = Intensive care unit length of stay, MV = mechanical ventilation, SOFA = Sequential Organ Failure Assessment, SAPS II = Simplified Acute Physiology Score II

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3.4), respectively. The median number of days on a ventilator in the ICU was 6.0 (IQR 3–12), and the median ICU length of stay (LOS) was 9.0 (IQR 5–15). The mean number of comorbidities was 2.3 (SD 1.7), most common of which were back/neck pain at 30.9% (n = 30), hypertension at 29.9% (n = 29), cardiac disease at 27.6% (n = 27), headache at 20.8% (n = 20), and cancer at 15.8% (n = 15). The two interference items with the highest mean scores were "interference with normal work" and "interference with daily activity" after ICU discharge and both mean scores increased slightly compared with 1 year [57].

Health-related quality of life in intensive care unit survivors at 3 months and 1 year

Overall, we found that compared with normative values (mean 50, SD 10), ICU survivors had a clinically relevant reduction in HRQOL PCS scores (mean 39.3, SD 10.9) and a minor reduction in HRQOL MCS scores (mean 47.7, SD 10.9) at 3 months. At 1 year, the mean PCS score increased to 43.4 (SD 12.0), and the mean MCS score normalized at 49.3 (SD 10.3). The improvement in PCS scores from 3 months to 1 year was statistically significant ($p < 0.01$), however the small improvement in MCS scores did not reach the level of statistical significance (Table 2).

Influence of social support, comorbidities, and pain interference on health-related quality of life

Total social support had a statistically significant positive association with MCS at 3 months ($p < 0.01$), but not on PCS at 3 months. Total social support was not statistically significantly associated with either PCS or MCS at 1 year (Table 3). Of the individual provisions, only attachment was statistically significant negatively associated with PCS at 3 months ($p = 0.02$) and a positively associated with MCS at 1 year ($p = 0.03$) (Table 3). There was a statistically significant reduction in total SPS scores from 3 months to 1 year, and in attachment from 3 months to 1 year (Table 2).

Number of comorbidities was statistically significantly negatively associated with PCS at both time points ($p < 0.01$) and with MCS at 1 year ($p = 0.01$) (Table 3). Pain interference with both normal work and daily activity was associated with a clinically relevant and statistically significant reduction in PCS at 3 months ($p < 0.01$, each) and 1 year (p = 0.03 and p = 0.05,

Table 2. Changes in social support and health-related quality of life from 3 months to 1 year after intensive care unit discharge.

	3 months n = 118 Mean (SD)	1 year n = 89 Mean (SD)	95% CI	p-value
Total SPS score	56.1 (6.3)	54.0 (6.5)	[0.47; 3.63]	0.01
Individual provisions				
Reassurance of worth	14.7 (1.7)	14.4 (1.9)	[−0.11; 0.77]	0.13
Attachment	14.9 (1.7)	13.2 (2.5)	[1.01; 2.27]	<0.01
Nurturance	12.2 (2.7)	12.3 (2.8)	[−0.74; 0.53]	0.75
Social integration	14.3 (1.7)	14.1 (1.8)	[−0.23; 0.59]	0.38
SF-12				
PCS score	39.3 (10.9)	43.4 (12.0)	[−7.0; −2.2]	<0.01
MCS score	47.7 (10.9)	49.3 (10.3)	[−3.2; 1.4]	0.43

SD = standard deviation, 95% CI = 95% confidence interval, SF-12 version 1 Physical Component Summary (PCS) and Mental Component Summary (MCS) relative to 1998 US Population baseline, SPS = revised Social Provision Scale. Statistical test: paired samples t-test, SF-12 = Short Form Health Survey-12

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Table 3. Influence of social support, comorbidity, and pain interference on health-related quality of life 3 months and 1 year after intensive care unit discharge.

	Physical Component Score			Mental Component Score		
Variable	**B**	**95%CI**	**p-value**	**B**	**95%CI**	**p-value**
3 months						
Total SPS score	-0.22	[−0.51; 0.08]	0.15	0.60	[0.32; 0.89]	<0.01
Reassurance of worth	0.06	[−1.45; 1.58]	0.93	-0.01	[−1.58; 1.56]	0.99
Attachment	−1.75	[−3.20; -0.31]	0.02	1.25	[−0.24; 2.75]	0.10
Nurturance	-0.19	[−0.97; 0.59]	0.64	0.28	[−0.53; 1.08]	0.50
Social integration	0.51	[−1.02; 2.04]	0.51	0.61	[−0.98; 2.19]	0.45
Number of comorbidities	−2.44	[−3.74; −1.14]	<0.01	−1.19	[−2.53; 0.16]	0.08
Pain int.–Daily activity	-10.92	[−14.61; −7.24]	<0.01	-3.93	[−8.22; 0.36]	0.72
Pain int.- Normal work	−12.08	[−15.61; −8.56]	<0.01	−4.89	[−9.00; −0.78]	0.02
1 year						
Total SPS score	0.57	[−0.47, 0.58]	0.83	0.34	[−0.14, 0.82]	0.17
Reassurance of worth	0.64	[−0.84; 2.13]	0.39	0.48	[−0.78; 1.73]	0.45
Attachment	−0.41	[−1.58; 0.76]	0.49	1.09	[0.11; 2.08]	0.03
Nurturance	0.09	[−0.85; 1.02]	0.85	−0.08	[−0.87; 0.71]	0.84
Social integration	−0.33	[−2.03; 1.36]	0.70	−0.50	[−1.92; 0.93]	0.49
Number of comorbidities	−3.25	[−4.40; −2.10]	<0.01	−1.66	[−2.63; −0.70]	0.01
Pain int. -Daily activity	−7.52	[−12.73; −2.30]	0.05	−2.48	[−7.88; 2.92]	0.36
Pain int.- Normal work	−7.39	[−12.13; −2.66]	0.03	−1.93	[−6.85; 3.00]	0.44

95% CI = 95% confidence interval, SF-12 version 1 Physical Component Summary (PCS) and Mental Component Summary (MCS) relative to 1998 US Population baseline, SPS = revised Social Provision Scale. Pain int. = pain interference. Statistical analysis: Linear regression

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respectively). Only pain interference with normal work's association with MCS was statistically significant at 3 months ($p = 0.02$) (Table 3).

Discussion

We found statistically significant and clinically relevant reduction in PCS for the ICU survivors compared with the normative population at both 3 months and 1 year after ICU discharge, but only a minor reduction in MCS. Further, there was a statistically significant reduction in total social support from 3 months to 1 year. Only one of the provisions, attachment, was statistically significantly associated with PCS at 3 months and with MCS at 1 year.

Our findings on HRQOL are consistent with previous studies over the last two decades [13–15, 21, 58–60]. The general findings from previous studies of ICU survivors have shown a large reduction in physical HRQOL after an ICU stay [15, 58–60], whereas the reduction in mental HRQOL is commonly found to be smaller. Our sample of ICU survivors' mental health was similar to the normative population 1 year after discharge. The theory of response shifts [61] may explain our participants' unchanged mental HRQOL reports. According to theory of response shifts [61], ICU survivors change their internal standards, values, and conceptualization of QOL—a response shift—and thus may report their MCS similar to that of the normative population.

One explanation for the finding that social support decreased from 3 months to 1 years, is that at 3 months, the ICU survivors were still in a rehabilitation situation, during which family and friends might have been aware that social support was more important, whereas at 1 year, this need for support may have normalized, and friends and family would likely have shifted

their focus from the ICU survivor's rehabilitation to normal activities, possibly leading the ICU survivor to perceive less social support and feel less attached to their social network.

It is difficult to compare our SPS and individual provision scores with other studies in which the original SPS was used, because the instruments have different maximum scores. However, if we compare our data with those of first time mothers [45], it appears that our ICU survivors perceived a higher level of total social support and scored higher on all provisions, except nurturance, compared with first time mothers. Both of these groups have undergone life-changing events, but with very different consequences. ICU survivors are in a rehabilitation situation, trying to regain their normal lives, whereas new mothers are learning new skills and adapting to a new life. This may be the reason ICU survivors score higher on social support. Even though social support influences HRQOL, and some aspects of that influence were statistically significant, it was moderate and of questionable clinical relevance (Table 3). Other researchers, including Tilburg [31], have found that social support has a positive impact on HRQOL. Our interpretation is that social support matters, but since our relatively small sample scored high on most of the individual provisions, there may have been a ceiling effect.

The ICU survivors in the present study also scored high on every SPS provision. This might be explained by the fact that most of these ICU survivors were married or had a partner, had children (young and/or adult), and were middle-aged, suggesting that they had networks of family, friends, and colleagues. The one individual provision on which they scored lower was nurturance. This might be explained by the mean age of the ICU survivors: many had adult children who did not need parental care in the same ways as when they were children. Some of the older ICU survivors may also have received nurturing from their adult children.

Number of comorbidities was statistically significantly associated with PCS at both time points and on MCS at 1 year. Orwelius et al. [17] found that preexisting disease had a significant influence on HRQOL after an ICU stay, and emphasized the importance of considering comorbidities when discussing outcomes in ICU survivors. We agree that this is an important consideration, especially when discussing physical HRQOL, since PCS seems most impacted by comorbidity. In regard of what is a clinical relevant change in HRQOL we chose to rely on Ware's [39] suggestion from 1993 with a 5 point change in PCS or MCS. Based on this limit the number of comorbidity did not have a clinically relevant association with HRQOL, but others have argued that for an individual smaller change (1–2 points) could be of relevance [62]. The theory of response shift may be the reason here [62].

Pain interference had the largest association with HRQOL, and specifically on PCS. These findings are in accordance with previous research [19]. As mentioned above, the reduction in PCS was larger at 3 months than at 1 year. Of interest, the pain interference score increased from 3 months to 1 year, but had less association with PCS. We can only speculate that there is a change from rehabilitation and hope of returning to life as it was before the ICU stay at 3 months, to acceptance that life has changed at 1 year. This may have led to the improved HRQOL scores in our results and others, and may help to explain why those who experience pain interference feel that the pain has a larger influence on their life, but less impact on their HRQOL. This phenomenon could be due to yet another response shift [61].

Based on these findings and previous research [13, 14, 21, 58, 63], it seems that what most ICU-survivors need is rehabilitation of physical health. Previous research [59] has found that HRQOL improves even from ICU discharge to hospital discharge, and suggested that rehabilitation must start early. Another study [64] found that early mobilization in the ICU improved physical function after ICU discharge. Early mobilization in the ICU seems to be one way of improving physical HRQOL after an ICU stay, and this may be a specific topic for further research. Unfortunately, there is still no high-quality intervention to improve HRQOL in ICU survivors. This may be a subject for future research.

Limitations

First, we did not have pre-admission baseline measurements with which to compare HRQOL and social support, number of comorbidity and pain interference because nearly all ICU admissions are the result of emergencies. Collecting any baseline data from ICU survivors is difficult, but previous studies have shown that this population has lower HRQOL than the normative population, even before their ICU stay [8, 17]. Second, we compared PCS and MCS derived from our sample with 1996 normative US data. Ideally, we would have used normative Norwegian data but, as mentioned above, Norwegian cutoff scores are similar to the US data [38]. Finally, our drop-out rate at 1 year was relatively high (32%). These factors may have resulted in a selection bias, though we did not find any differences between responders and non-responders at 1 year with regard to gender (p-value 0.71), age (p-value 0.87), ICU LOS (p-value 0.35), MV days (p-value 0.64) and SPAPS II score (p-value 0.21). More details are presented in supplementary material to Langerud et al [65]. Therefore, we assume that our results might be generalizable to other ICU survivors. Others have reported that the most severely ill are difficult to study [66, 67]; therefore, illness severity may explain our relatively high dropout rate.

Conclusions

Physical HRQOL was reduced in ICU survivors at 3 months and 1 year compared to the normative population. These patients' mental HRQOL was, from a clinical perspective, similar to that of the normative population. Social support was positively associated with mental HRQOL, while number of comorbidities, and pain interference were all significantly associated with a reduction in HRQOL. Pain interference was associated with the largest reduction in HRQOL.

Supporting information

S1 Request. For partisipation in research project.
(DOCX)

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13018

Fylles ut av Kontor for Klinisk Forskning

Reg. Nr: | | | |

Oppfølgingsskjema:

☐ 3 mnd etter utskrivelse fra ICU ☐ 1 år etter utskrivelse fra ICU **Initialer:** | | | |

2010 NEUPAQ studien

NEVROPATI, SMERTE OG LIVSKVALITET HOS INTENSIVPASIENTER

DATO FOR UTFYLLING: | | | . | | | . | | | | |

dag *måned* *år*

(Fylles ut av pasient)

Vennligst les hvert spørsmål nøye før du svarer. Hvis du er usikker hva du skal svare på et spørsmål, svar så godt du kan. Husk at det er ingen riktige eller gale svar.

Dine svar på dette spørreskjemaet vil bli behandlet strengt konfidensielt, og de vil bare bli brukt til forskning. Informasjonen du gir vil bli bearbeidet sammen med svarene fra andre pasienter som også fyller ut skjemaet, slik at det ikke blir mulig å finne tilbake til svarene fra enkeltpersoner.

Utfylling av skjema:

1. Bruk bare blå eller sort kulepenn (ikke blyant)
2. Kryss innenfor rutene: ☒
3. Skjemaet må ikke brettes (gir streker i skjemaet ved optisk lesing)
4. Skriv tydelig!
5. Utfylt skjema bes returnert i vedlagte ferdig frankerte svarkonvolutt

Prosjektleder: Audun Stubhaug, overlege dr. med

Stipendiat: Anne Kathrine Langerud, MSc

Reg. Nr: ☐☐☐

BAKGRUNNSOPPLYSNINGER

Vennligst sett kryss eller fyll inn det som passer

1. Kjønn ☐ Mann ☐ Kvinne

2. Hvilket år er du født? *(F.eks. 1961)*

☐☐☐☐
år

3. Hvem bor du sammen med? (sett ett eller flere kryss)

- ☐ Ektefelle/samboer
- ☐ Barn/svigerbarn
- ☐ Bor alene
- ☐ Søster/bror
- ☐ Annen familie/slekt
- ☐ Bor på institusjon
- ☐ Andre

4. Hva er din sivilstand?

- ☐ Gift/registrert partner
- ☐ Ugift
- ☐ Enke/enkemann
- ☐ Skilt
- ☐ Separert

5. Har du barn? ☐ Ja ☐ Nei

6. Hvis du har barn, hvor mange barn har du daglig ansvar for innenfor følgende aldersgrupper:

0-5 år	6-10 år	11-15 år
☐☐ (antall)	☐☐ (antall)	☐☐ (antall)

UTDANNING

7. Hvilken utdanning er den <u>høyeste</u> du har <u>fullført</u>? (Sett kun <u>ett</u> kryss)

- ☐ Grunnskole 7-10, framhaldsskole, folkehøgskole
- ☐ Real- eller middelskole, yrkesskole, Ett- eller toårig videregående skole
- ☐ Artium, økonomisk gymnas eller allmennfaglig retning i videregående skole
- ☐ Høgskole eller universitet, mindre enn 4 år
- ☐ Høgskole eller universitet, 4 år eller mer

ARBEID

8. Hva slags arbeidssituasjon har du nå? (Sett ett eller flere kryss)

- ☐ Lønnet arbeid
- ☐ Selvstendig næringsdrivende
- ☐ Heltids husarbeid
- ☐ Utdanning, militærtjeneste
- ☐ Arbeidsledig, permittert
- ☐ Pensjonist/trygdet

ARBEID *forts.*

9. Hvis du er eller har vært i inntektsgivende arbeid, kan du angi hvilken av disse yrkeskategoriene ditt yrke faller innenfor?

(Hvis du ikke er i arbeid nå, svarer du ut fra det yrket du hadde sist.)

☐ Spesialarbeider, ufaglært arbeider

☐ Fagarbeider, håndverker, formann

☐ Underordnet funksjonær (butikk, kontor, offentlige tjenester)

☐ Fagfunksjonær (f.eks. sykepleier, tekniker, lærer)

☐ Overordnet stilling i offentlig eller privat virksomhet

☐ Gårdbruker eller skogeier

☐ Fisker

☐ Selvstendig i akademisk erverv (f.eks. tannlege, advokat)

☐ Annen selvstendig næringsvirksomhet

☐ Selvstendig næringsdrivende (f.eks. industri, transport, handel)

☐ Har ikke hatt innteksgivende arbeid (f.eks. pga. heltids husarbeid, studier, trygd)

SYKDOM

10. Har du noen sykdom eller lidelse av mer varig natur, noen medfødt sykdom eller virkninger av skade?

Vi tenker på vanskeligheter/begrensninger av mer varig karakter. Med varig karakter menes at de har vart eller forventes å vare i 6 måneder eller mer.

☐ Ja ☐ Nei

11. Er du ofte syk?

☐ Ja ☐ Nei

12. Har du eller har du hatt: (sett ett eller flere kryss)

Hjerteinfarkt?	☐ Ja	☐ Nei
Hjertekrampe (angina pektoris)?	☐ Ja	☐ Nei
Hjerneslag/hjerneblødning?	☐ Ja	☐ Nei
Sukkersyke (diabetes)?	☐ Ja	☐ Nei
Kreft?	☐ Ja	☐ Nei
Beinskjørhet (osteoporose)?	☐ Ja	☐ Nei
Fibromyalgi?	☐ Ja	☐ Nei
Kronisk smertesykdom?	☐ Ja	☐ Nei
Leddgikt (revmatoid artritt)?	☐ Ja	☐ Nei
Slitasjegikt (artrose)?	☐ Ja	☐ Nei
Bechtrews sykdom?	☐ Ja	☐ Nei
Andre langvarige skjelett- eller muskelsykdommer?	☐ Ja	☐ Nei
Psykisk lidelse?	☐ Ja	☐ Nei
Mave- eller tarmsykdom?	☐ Ja	☐ Nei
Astma?	☐ Ja	☐ Nei

ANDRE HENDELSER I LIVET

13. Sett kryss hvis du i den senere tiden (de siste 4 uker) har opplevd noen av følgende hendleser:

Giftet deg/flyttet sammen med samboer	☐ Ja	☐ Nei
Fått barn	☐ Ja	☐ Nei
Dødsfall familie/nære venner	☐ Ja	☐ Nei
Alvorlig bomessige eller økonomiske problemer	☐ Ja	☐ Nei
Andre betydelige livshendelser	☐ Ja	☐ Nei

Reg. Nr: ☐☐☐

TILLEGGSSYKDOMMER (SCQ-18)

Det følgende er en liste over vanlige medisinske problemer. Sett ett kryss for hvert problem om hvorvidt du har problemet nå (ja eller nei). Hvis du HAR problemet, så svar på spørsmålene om behandling og aktiviteter til høyre. Hvis du IKKE HAR problemet, gå videre til neste problem.

Problem	HAR DU PROBLEMET?	HVIS JA: Får du behandling for det?	HVIS JA: Begrenser det dine aktiviteter?
1. Hjertesykdom	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
2. Høyt blodtrykk	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
3. Lungesykdom	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
4. Kreft	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
5. Diabetes	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
6. Magesår/magesykdom	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
7. Tarmsykdom	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
8. Nyresykdom	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
9. Leversykdom	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
10. Anemi eller annen blodsykdom	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
11. Hodepine	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
12. Depresjon	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
13. Slitasjegikt/artrose	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
14. Rygg/nakkesmerter	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
15. Leddgikt/revmatoid artritt	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
16. Sykdom i bindevev eller muskulatur	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
17. Hudlidelser	☐ Ja ☐ Nei	☐ Ja ☐ Nei	☐ Ja ☐ Nei
18. Andre medisinske problemer (angi)			
		☐ Ja ☐ Nei	☐ Ja ☐ Nei
		☐ Ja ☐ Nei	☐ Ja ☐ Nei
		☐ Ja ☐ Nei	☐ Ja ☐ Nei

Reg. Nr: | | | |

FUNKSJONSTILSTAND (KARNOFSKY)

Sett ett kryss i den ruten som passer best.

100 ☐ Normal, ingen plager eller subjektive tegn på sykdom

90 ☐ Klarer normal aktivitet, sykdommen gir lite symptomer

80 ☐ Klarer med nød normal aktivitet. Sykdommen gir en del symptomer

70 ☐ Klarer meg selv, ute av stand til normal aktivitet eller aktivt arbeide

60 ☐ Trenger noe assistanse, men klarer stort sett å tilfredsstille egne behov

50 ☐ Trenger betydelig hjelp og stadig medisinsk omsorg

40 ☐ Ufør, trenger spesiell hjelp og omsorg

Reg. Nr: ☐☐☐

SPØRRESKJEMA FOR SYMPTOMER PÅ NEVROPATISK SMERTE

Du lider av smerter som skyldes skade eller sykdom i nervesystemet. Disse smertene kan være av ulike typer. Du kan ha plutselig innsettende smerte, dvs. smerte utløst uten stimulering. Den kan være langvarig eller opptre som kortvarige anfall. Du kan også ha smerte fremkalt eller forsterket ved lett stryking, trykk, eller kontakt med kulde i det smertefulle området. Du kan kjenne en eller flere typer smerter. Dette spørreskjemaet er utviklet for å hjelpe legen din til bedre å kunne vurdere og behandle forskjellige typer smerter som du kan oppleve.

Vi ønsker å vite om du kjenner plutselig innsettende smerter, dvs. smerter uten forutgående stimulering. For hvert av de følgende spørsmålene, ber vi deg velge det tallet som beskriver et ***gjennomsnitt av hvor intense dine plutselig innsettende smerter har vært i de siste 24 timene.*** *Velg tallet 0 hvis du ikke har kjent slik smerte. (Sett ett kryss)*

1. Kjennes smertene dine som om de er brennende?

	0	1	2	3	4	5	6	7	8	9	10	
Ikke brennende	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Verst brennende du kan tenke deg**

2. Kjennes smertene dine som om de er knipende?

	0	1	2	3	4	5	6	7	8	9	10	
Ikke knipende	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Verst knipende du kan tenke deg**

3. Kjennes smertene dine som om de er trykkende?

	0	1	2	3	4	5	6	7	8	9	10	
Ikke trykkende	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Verst trykkende du kan tenke deg**

4. I de siste 24 timene har dine plutselig innsettende smerter vært til stede:
Velg det svaret som best beskriver ditt tilfelle.

☐ Hele tiden

☐ Mellom 8 og 12 timer

☐ Mellom 4 og 7 timer

☐ Mellom 1 og 3 timer

☐ Mindre enn 1 time

Reg. Nr: ☐☐☐

*Vi ønsker å vite om du har kortvarige smerteanfall. For hvert av de følgende spørsmålene ber vi deg velge det tallet som best beskriver et **gjennomsnitt av hvor intense dine smerteanfall har vært i de siste 24 timene.** Velg tallet 0 hvis du ikke har kjent slik smerte. (Sett ett kryss)*

5. Kjennes smertene dine ut som elektriske støt?

	0	1	2	3	4	5	6	7	8	9	10	
Ikke elektriske støt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Verst elektriske støt du kan tenke deg**

6. Kjennes smertene dine ut som stikkede?

	0	1	2	3	4	5	6	7	8	9	10	
Ikke stikkende	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Verst stikkende du kan tenke deg**

7. I løpet av de siste 24 timene, hvor mange slike smerteanfall har du hatt? Velg det svaret som best beskriver ditt tilfelle.

- ☐ Mer enn 20
- ☐ Mellom 11 og 20
- ☐ Mellom 6 og 10
- ☐ Mellom 1 og 5
- ☐ Ingen smerteanfall

---

*Vi ønsker å vite om smertene dine er fremkalt eller forsterket ved lett stryking, trykk, kontakt med kulde i det smertefulle området. For hvert av de følgende spørsmålene ber vi deg velge det tallet som best beskriver et **gjennomsnitt av hvor intense din fremkalte smerter har vært i de siste 24 timene.** Velg tallet 0 hvis du ikke har kjent slik smerte. (Sett ett kryss)*

8. Er smertene dine fremkalt eller forsterket ved lett stryking på det smertefulle området?

	0	1	2	3	4	5	6	7	8	9	10	
Ingen smerte	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Verste smerte du kan tenke deg**

9. Er smertene dine fremkalt eller forsterket ved trykk på det smertefulle området?

	0	1	2	3	4	5	6	7	8	9	10	
Ingen smerte	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Verste smerte du kan tenke deg**

10. Er smertene dine fremkalt eller forsterket ved kontakt med noe kaldt på det smertefulle området?

	0	1	2	3	4	5	6	7	8	9	10	
Ingen smerte	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Verste smerte du kan tenke deg**

---

*Vi ønsker å vite om du føler spesielle sansefornemmelser i det **smertefulle området.** For hvert av de følgende spørsmålene, vennligst velg det tallet som best beskriver et **gjennomsnitt av hvor intense dine spesielle sansefornemmelser har vært i de siste 24 timene.** Velg tallet 0 hvis du ikke har kjent slik sansefornemmelse. (Sett ett kryss)*

11. Kjenner du prikking og nålestikk?

	0	1	2	3	4	5	6	7	8	9	10	
Ingen prikking eller nålestikk	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Verste prikking og nålestikk du kan tenke deg**

12. Kjenner du kribling?

	0	1	2	3	4	5	6	7	8	9	10	
Ingen kribling	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Verste kribling du kan tenke deg**

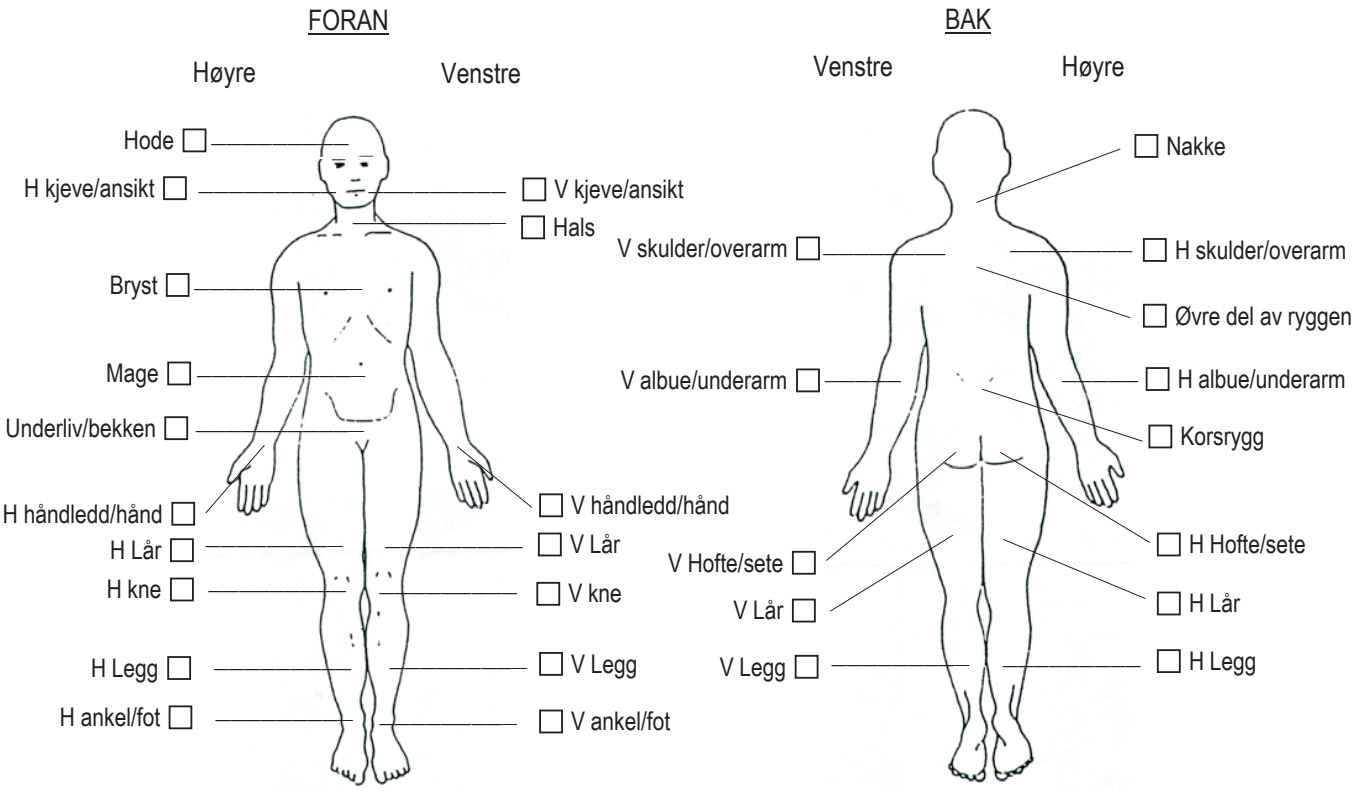
Reg. Nr: | | | |

SMERTER (BPI)

1. Gjennom livet har de fleste av oss hatt smerter (som lett hodepine, forstuelser eller tannpine).
Har du i dag smerter av et annet slag enn slike dagligdagse smerter?

☐ Ja ☐ Nei **Hvis NEI, gå til side 12**

2. Dersom du har hatt smerter den siste uken, hvor har du hatt disse plagene?
Vennligst sett et eller flere kryss.



3. Vennligst sett ett kryss i den ruten som best beskriver de sterkeste smertene du har hatt i løpet av de siste 24 timer.

Ingen smerter	0	1	2	3	4	5	6	7	8	9	10	Verst tenkelige smerter
	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	

4. Vennligst sett ett kryss i den ruten som best beskriver de svakeste smertene du har hatt i løpet av de siste 24 timer.

Ingen smerter	0	1	2	3	4	5	6	7	8	9	10	Verst tenkelige smerter
	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	

5. Vennligst sett ett kryss i den ruten som best angir hvor sterke smerter du har i gjennomsnitt.

Ingen smerter	0	1	2	3	4	5	6	7	8	9	10	Verst tenkelige smerter
	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	

6. Vennligst sett ett kryss i den ruten som best angir hvor sterke smerter du har akkurat nå.

Ingen smerter	0	1	2	3	4	5	6	7	8	9	10	Verst tenkelige smerter
	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	

7. Hvilken behandling eller medisiner får du for å lindre smertene dine?

8. I hvor stor grad har behandling eller medisiner lindret smertene dine de siste 24 timene? Vennligst sett ett kryss i den ruten med prosenttallet som viser hvor stor smertelindring du har fått.

Ingen lindring	0%	10%	20%	30%	40%	50%	60%	70%	80%	90%	100%	Fullstendig lindring
	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	

Reg. Nr: ☐☐☐

Sett ett kryss i den ruten som for de siste 24 timene best beskriver hvor mye smertene har virket inn på:

9. Daglig aktivitet

	0	1	2	3	4	5	6	7	8	9	10	
Ikke påvirket	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Fullstendig påvirket**

10. Humør

	0	1	2	3	4	5	6	7	8	9	10	
Ikke påvirket	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Fullstendig påvirket**

11. Evne til å gå

	0	1	2	3	4	5	6	7	8	9	10	
Ikke påvirket	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Fullstendig påvirket**

12. Vanlig arbeid (gjelder både arbeid utenfor hjemmet og husarbeid)

	0	1	2	3	4	5	6	7	8	9	10	
Ikke påvirket	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Fullstendig påvirket**

13. Forhold til andre mennesker

	0	1	2	3	4	5	6	7	8	9	10	
Ikke påvirket	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Fullstendig påvirket**

14. Søvn

	0	1	2	3	4	5	6	7	8	9	10	
Ikke påvirket	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Fullstendig påvirket**

15. Livsglede

	0	1	2	3	4	5	6	7	8	9	10	
Ikke påvirket	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Fullstendig påvirket**

Reg. Nr: ☐☐☐

SPØRRESKJEMA OM HELSE (SF-12)

INTRODUKSJON: Dette spørreskjemaet handler om hvordan du ser på din egen helse. Disse opplysningene vil hjelpe oss til å få vite hvordan du har det og hvordan du er i stand til å utføre dine daglige gjøremål.

Hvert spørsmål skal besvares ved å sette ett kryss i den ruten som passer best for deg. Hvis du er usikker på hva du vil svare, vennligst svar så godt du kan.

1. Stort sett vil du si at din helse er:

☐ Utmerket ☐ Meget god ☐ God ☐ Nokså god ☐ Dårlig

De neste spørsmålene handler om aktiviteter som du kanskje utfører i løpet av en vanlig uke. Er din helse slik at den begrenser deg i utførelsen av disse aktivitetene nå? Hvis ja, hvor mye?

	Ja, begrenser meg mye	Ja, begrenser meg litt	Nei, begrenser meg ikke i det hele tatt
2. Moderate aktiviteter som å flytte et bord, støvsuge, gå en tur eller drive med hagearbeid	☐	☐	☐
3. Gå opp trappen flere etasjer	☐	☐	☐

I løpet av den siste uken, har du hatt noen av de følgende problemer i ditt arbeid eller i andre av dine daglige gjøremål på grunn av din fysiske helse?

	Ja	Nei
4. Du har utrettet mindre enn du hadde ønsket	☐	☐
5. Du har vært hindret i å utføre visse typer arbeid eller gjøremål	☐	☐

I løpet av de siste 4 ukene, har du hatt noen av de følgende problemer i ditt arbeid eller andre av dine daglige gjøremål på grunn av følelsesmessige problemer (som for eksempel å være deprimert eller engstelig)?

	Ja	Nei
6. Du har utrettet mindre enn du hadde ønsket	☐	☐
7. Du har utført arbeidet eller andre gjøremål mindre grundig enn vanlig	☐	☐

8. I løpet av de siste 4 ukene, hvor mye har smerter påvirket ditt vanlige arbeid (gjelder både arbeid utenfor hjemmet og husarbeid)?

☐ Ikke i det hele tatt ☐ Litt ☐ En del ☐ Mye ☐ Svært mye

De neste spørsmålene handler om hvordan du har følt deg og hvordan du har hatt det de siste 4 ukene.
For hvert spørsmål, vennligst velg det svaralternativet som best beskriver hvordan du har hatt det.
Hvor ofte i løpet av de siste 4 ukene har du:

	Hele tiden	Nesten hele tiden	Mye av tiden	En del av tiden	Litt av tiden	Ikke i det hele tatt
9. Følt deg rolig og harmonisk	☐	☐	☐	☐	☐	☐
10. Hatt mye overskudd	☐	☐	☐	☐	☐	☐
11. Følt deg nedenfor og trist	☐	☐	☐	☐	☐	☐

12. I løpet av de siste 4 ukene, hvor mye av tiden har din fysiske helse eller følelsesmessige problemer påvirket din sosiale omgang (som det å besøke venner, slektinger osv)?

☐ Hele tiden ☐ Nesten hele tiden ☐ En del av tiden ☐ Litt av tiden ☐ Ikke i det hele tatt

Reg. Nr: | | | |

ANGST- OG DEPRESJONSSKALA (HADS)

Her kommer noen spørsmål om hvorledes du føler deg. For hvert spørsmål setter du kryss for ett av de fire svarene som best beskriver dine følelser den siste uken. Ikke tenk for lenge på svaret - de spontane svarene er best.

1. Jeg føler meg nervøs og urolig

- ☐ Mesteparten av tiden
- ☐ Mye av tiden
- ☐ Fra tid til annen
- ☐ Ikke i det hele tatt

2. Jeg gleder meg forsatt over tingene slik jeg pleide før

- ☐ Avgjort like mye
- ☐ Ikke fullt så mye
- ☐ Bare lite grann
- ☐ Ikke i det hele tatt

3. Jeg har en urofølelse som om noe forferdelig kommer til å skje

- ☐ Helt sikkert og svært ille
- ☐ Ja, men ikke så veldig ille
- ☐ Litt ille, men det bekymrer meg ikke så mye
- ☐ Ikke i det hele tatt

4. Jeg kan le og se det morsomme i situasjoner

- ☐ Like mye som jeg alltid har gjort
- ☐ Ikke like mye nå som før
- ☐ Avgjort ikke så mye som før
- ☐ Ikke i det hele tatt

5. Jeg har hodet fullt av bekymringer

- ☐ Veldig ofte
- ☐ Ganske ofte
- ☐ Av og til
- ☐ En gang i blant

6. Jeg er i godt humør

- ☐ Aldri
- ☐ Noen ganger
- ☐ Ganske ofte
- ☐ For det meste

7. Jeg kan sitte i fred og ro og kjenne meg avslappet

- ☐ Ja, helt klart
- ☐ Vanligvis
- ☐ Ikke så ofte
- ☐ Ikke i det hele tatt

8. Jeg føler meg som om alt går langsommere

- ☐ Nesten hele tiden
- ☐ Svært ofte
- ☐ Fra tid til annen
- ☐ Ikke i det hele tatt

9. Jeg føler meg urolig som om jeg har sommerfugler i magen

- ☐ Ikke i det hele tatt
- ☐ Fra tid til annen
- ☐ Ganske ofte
- ☐ Svært ofte

10. Jeg bryr meg ikke lenger om hvordan jeg ser ut

- ☐ Ja, helt klart
- ☐ Jeg bryr meg ikke så mye som jeg burde
- ☐ Det kan godt hende jeg ikke bryr meg nok
- ☐ Jeg bryr meg om utseendet like mye som jeg alltid har gjort

11. Jeg er rastløs som om jeg stadig må være aktiv

- ☐ Uten tvil svært mye
- ☐ Ganske mye
- ☐ Ikke så veldig mye
- ☐ Ikke i det hele tatt

12. Jeg ser med glede frem til hendelser og ting

- ☐ Like mye som jeg alltid har gjort
- ☐ Heller mindre enn jeg pleier
- ☐ Avgjort mindre enn jeg pleier
- ☐ Nesten ikke i det hele tatt

13. Jeg kan plutselig få en følelse av panikk

- ☐ Uten tvil svært ofte
- ☐ Svært ofte
- ☐ Ikke så veldig ofte
- ☐ Ikke i det hele tatt

14. Jeg kan glede meg over gode bøker, radio og TV

- ☐ Ofte
- ☐ Fra tid til annen
- ☐ Ikke så ofte
- ☐ Svært sjelden

Reg. Nr: | | | |

POSTTRAUMATIC STRESS DISORDER (PTSD 10)

Vi vil her be deg angi hvor ofte eller i hvor stor grad du har opplevd nedenforstående fenomener den siste uken. Vær vennlig å besvar alle spørsmålene. *(Sett ett kryss)*

I løpet av de siste syv dager har jeg vært plaget av:

1. Søvnproblemer

Aldri/ sjelden	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	**Meget ofte**

2. Drømmer med mareritt

Aldri/ sjelden	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	**Meget ofte**

3. Depresjon, følt meg nedtrykt

Overhodet ikke	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	**Svært mye**

4. Skvetten ved plutselig lyder eller brå bevegelser

Overhodet ikke	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	**Svært mye**

5. Tendens til å isolere meg fra andre

Overhodet ikke	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	**Svært mye**

Reg. Nr: ☐☐☐

POSTTRAUMATIC STRESS DISORDER *forts.*

6. Irritabilitet (blir lett irritert eller rasende)

Aldri/ sjelden ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 **Meget ofte**

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7. At følelsene svinger mye opp og ned

Overhodet ikke ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 **Svært mye**

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8. Dårlig samvittighet, selvbebreidelser, skyldfølelse

Overhodet ikke ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 **Svært mye**

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9. Frykt for steder eller situasjoner som kan minne om hendelsen (intensivoppholdet)

Overhodet ikke ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 **Svært mye**

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10. Anspenhet i kroppen

Svært mye ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7 **Svært mye**

Reg. Nr: ☐☐☐

SØVNPROBLEMER (LEE SØVNFORSTYRRELSESSKALA)

Tenk tilbake på den siste uken. Hvor mange dager har du: *(sett ett kryss i den aktuelle ruten)*

	Aldri							Hver dag
1. Hatt problemer med å sovne	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
2. Våknet i løpet av søvnperioden	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
3. Våknet for tidlig og fikk ikke til å sovne igjen	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
4. Følt deg uthvilt når du våkner på slutten av en søvnperiode	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
5. Sovet dårlig	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
6. Følt deg søvnig i løpet av dagen	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
7. Kjempet for å holde deg våken gjennom dagen	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
8. Følt deg irritabel i løpet av dagen	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
9. Følt deg trøtt eller utmattet i løpet av dagen	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
10. Følt deg tilfreds med søvnkvaliteten	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
11. Følt deg våken og energisk gjennom dagen	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
12. Fått for mye søvn	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
13. Fått for lite søvn	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
14. Tatt en blund til planlagt tid	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
15. Sovnet uten at det var planlagt	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
16. Drukket alkohol for å få til å sovne	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
17. Brukt tobakk for å få til å sovne	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
18. Brukt andre stimuli for å sovne (f.eks: avslapping, musikk, lesing)	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
19. Brukt naturmedisinske midler for å sovne	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
20. Brukt reseptbelagt sovemedisin for å få til å sovne	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
21. Brukt Paracet eller annet smertestillende for å sove	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐

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TRETTHET (LFS)

Vi ønsker å vite mer om energinivået ditt. Nedenfor er det 18 utsagn vi ber deg svare på.

INSTRUKSJONER: For hvert utsagn nedenfor -
Sett ett kryss i den ruten som best indikerer hvordan du føler deg akkurat nå.

1.												
Ikke sliten i det hele tatt	**0** ☐	**1** ☐	**2** ☐	**3** ☐	**4** ☐	**5** ☐	**6** ☐	**7** ☐	**8** ☐	**9** ☐	**10** ☐	**Svært sliten**
2.												
Ikke trøtt i det hele tatt	**0** ☐	**1** ☐	**2** ☐	**3** ☐	**4** ☐	**5** ☐	**6** ☐	**7** ☐	**8** ☐	**9** ☐	**10** ☐	**Svært trøtt**
3.												
Ikke døsig i det hele tatt	**0** ☐	**1** ☐	**2** ☐	**3** ☐	**4** ☐	**5** ☐	**6** ☐	**7** ☐	**8** ☐	**9** ☐	**10** ☐	**Svært døsig**
4.												
Ikke utmattet i det hele tatt	**0** ☐	**1** ☐	**2** ☐	**3** ☐	**4** ☐	**5** ☐	**6** ☐	**7** ☐	**8** ☐	**9** ☐	**10** ☐	**Svært utmattet**
5.												
Ikke utslitt i det hele tatt	**0** ☐	**1** ☐	**2** ☐	**3** ☐	**4** ☐	**5** ☐	**6** ☐	**7** ☐	**8** ☐	**9** ☐	**10** ☐	**Svært utslitt**
6.												
Ikke energisk i det hele tatt	**0** ☐	**1** ☐	**2** ☐	**3** ☐	**4** ☐	**5** ☐	**6** ☐	**7** ☐	**8** ☐	**9** ☐	**10** ☐	**Svært energisk**
7.												
Ikke aktiv i det hele tatt	**0** ☐	**1** ☐	**2** ☐	**3** ☐	**4** ☐	**5** ☐	**6** ☐	**7** ☐	**8** ☐	**9** ☐	**10** ☐	**Svært aktiv**
8.												
Ikke sprek i det hele tatt	**0** ☐	**1** ☐	**2** ☐	**3** ☐	**4** ☐	**5** ☐	**6** ☐	**7** ☐	**8** ☐	**9** ☐	**10** ☐	**Svært sprek**
9.												
Ikke effektiv i det hele tatt	**0** ☐	**1** ☐	**2** ☐	**3** ☐	**4** ☐	**5** ☐	**6** ☐	**7** ☐	**8** ☐	**9** ☐	**10** ☐	**Svært effektiv**

10.

	0	1	2	3	4	5	6	7	8	9	10	
Ikke livlig i det hele tatt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Svært livlig**

11.

	0	1	2	3	4	5	6	7	8	9	10	
Ikke utkjørt i det hele tatt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Svært utkjørt**

12.

	0	1	2	3	4	5	6	7	8	9	10	
Ikke utslått i det hele tatt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Svært utslått**

13.

	0	1	2	3	4	5	6	7	8	9	10	
Å holde øynene åpne er ikke anstrengende i det hele tatt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Å holde øynene åpne er veldig anstrengende**

14.

	0	1	2	3	4	5	6	7	8	9	10	
Å bevege kroppen er ikke anstrengende i det hele tatt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Å bevege kroppen er veldig anstrengende**

15.

	0	1	2	3	4	5	6	7	8	9	10	
Å konsentrere seg er ikke anstrengende i det hele tatt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Å konsentrere seg er veldig anstrengende**

16.

	0	1	2	3	4	5	6	7	8	9	10	
Å holde i gang en samtale er ikke anstrengende i det hele tatt	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Å holde i gang en samtale er veldig anstrengende**

17.

	0	1	2	3	4	5	6	7	8	9	10	
Jeg har absolutt ikke noe behov for å lukke øynene	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Jeg har et veldig sterkt behov for å lukke øynene**

18.

	0	1	2	3	4	5	6	7	8	9	10	
Jeg har absolutt ikke noe behov for å legge meg nedpå	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	**Jeg har et veldig sterkt behov for å legge meg nedpå**

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SOSIAL STØTTE (SOCIAL PROVISION SCALE)

Alle mennesker har sin egen oppfatning om forskjellige ting. Nå følger et antall påstander og spørsmål som handler om holdninger, interesser og følelser. Det finnes ingen "rette" eller "gale" svar. Deres svar beskriver bare hvordan De tenker og føler i ulike situasjoner: Visse påstander eller spørsmål kan kanskje føles fremmede, men forsøk likevel å besvare dem.

Sett ett kryss i den ruten som best beskriver hvordan du har det.

	Stemmer helt	Stemmer delvis	Stemmer neppe	Stemmer ikke i det hele tatt
1. Det er personer som er avhengige av min hjelp.	☐	☐	☐	☐
2. Det føles om om jeg ikke har nær personlig kontakt med andre mennesker.	☐	☐	☐	☐
3. Jeg føler meg personlig ansvarlig for et annet menneskes velbefinnende.	☐	☐	☐	☐
4. Jeg føler at andre i mine omgivelser deler mine meninger.	☐	☐	☐	☐
5. Det føles som om andre mennesker ikke respekterer det jeg kan.	☐	☐	☐	☐
6. Jeg kjenner personer som liker de samme sosiale aktiviteter som meg.	☐	☐	☐	☐
7. Jeg har bekjente som verdsetter min dyktighet og mine kunnskaper.	☐	☐	☐	☐
8. Det finnes ingen som deler mine interesser og anliggender.	☐	☐	☐	☐
9. Det er ingen som er avhengig av meg for sitt velbefinnende.	☐	☐	☐	☐
10. Det føles som om andre mennesker betrakter meg som udugelig.	☐	☐	☐	☐
11. Det er mennesker som gir meg en følelse av trygghet og velbefinnende.	☐	☐	☐	☐

Reg. Nr: | | | |

SOSIAL STØTTE *forts.*

	Stemmer helt	Stemmer delvis	Stemmer neppe	Stemmer ikke i det hele tatt
12. Jeg har en sterk følelsemessig nærhet i det minste til et annet menneske.	☐	☐	☐	☐
13. Det er personer som setter pris på mine talenter og evner.	☐	☐	☐	☐
14. Det er ingen som jeg føler fortrolighet til.	☐	☐	☐	☐
15. Jeg kjenner ingen som liker å gjøre det samme som meg.	☐	☐	☐	☐
16. Inger behøver lenger min omtanke og omsorg.	☐	☐	☐	☐

Vennligst legg ferdig utfylt spørreskjema i svarkonvolutten. Porto er betalt.

Tusen takk for hjelpen!

Kontaktinformasjon:

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FORESPØRSEL OM DELTAGELSE I FORSKNINGSPROSJEKT

Prosjekttittel:

NEVROPATI, SMERTE OG LIVSKVALITET HOS INTENSIVPASIENTER (NEUPAQ)

En studie for å kartlegge forekomst og konsekvenser av kronisk smerte hos pasienter som overlever intensivbehandling.

I denne studien ønsker vi å vite mer om hvordan du som pasient har det etter oppholdet på intensiv. Hensikten er at vi som helsepersonell skal få mer kunnskap om senvirkninger av intensivbehandling som igjen kan gjøre oss bedre i stand til å yte bedre behandling/oppfølging til dere pasienter. Per i dag har vi ingen systematisk oppfølging av pasienter som har vært inneliggende på intensivavdelingen. Deltakelse i studien er basert på frivillighet.

Studien går ut på at pasienter som har ligget på Generell Intensiv ved Oslo Universitetssykehus Rikshospitalet i perioden 2010-2012 svarer på noen spørreskjema 3 måneder etter utskrivelse fra Generell Intensiv ved Oslo Universitetssykehus Rikshospitalet og at de samme spørreskjemaene besvares 1 år etter utskrivelse fra Generell Intensiv. Spørreskjemaene tar ca 30-45 minutter å fylle ut og spørsmålene omhandler din opplevelse av smerte, livskvalitet, angst, depresjon og posttraumatisk stress. I tillegg følger det med en smertedagbok som fylles ut hver kveld i en uke. Dette tar maks 5 min hver kveld.
Når man blir kritisk syk kan det oppstå skade på muskler og nervefibre. Dette kalles ”critical illness neuro-myopathy”. Ved ”critical illness neuro-myopathy” kan de tynne nervefibrene være skadet. Dette vil kunne gjelde de tynne nervefibre som leder temperatur- og smerte impulser fra huden og inn til sentralnervesystemet og det vil kunne gjelde de tynne utoverledene nervefibre som regulerer svette.

Vi ber også om tillatelse til å innhente informasjon om ditt opphold på intensiv fra din journal. Vi er ute etter informasjon om hva som feilte deg, hvor lenge du lå på respirator, hva slags innstillinger respiratoren hadde, hvilke medisiner du fikk, om du fikk dialyse, om du hadde infeksjoner osv.

Oppbevaring av data

Informasjon om deg og dine svar på spørreskjemaene vil oppbevares forsvarlig innelåst og med begrenset adgang til de som gjennomfører forskningen. Data vil bli slettet etter publisering og senest innen 31.12.2020. Du har rett til informasjon om utfallet av studien og du har rett til å få innsyn i hvilke opplysninger som er registrert om deg. Du har rett til å få rettet eventuelle feil i opplysningene vi har registret om deg.

Vi ber også om tillatelse til å innhente data fra din journal i ettertid hvis det skulle vise seg å være noe informasjon om din behandling som vi mangler. Alle som arbeider med studien er helsepersonell som har taushetsplikt og informasjonen vil bli behandlet konfidensielt.
I samsvar med nasjonale og internasjonale retningslinjer for forskningsetikk, vil vi med dette be om din tillatelse til å benytte dataene fra oppholdet på intensiv og svarene dine på spørreundersøkelsen i dette forskningsprosjektet. Data som samles inn i denne studien vil kun brukes i tråd med studiens hensikt.
Alle lagrede opplysninger vil være avidentifiserte. Ingen pasienter vil kunne gjenkjennes når studieresultatene publiseres.

Etikk

Det er helt frivillig å delta. Du står på ethvert tidspunkt helt fritt til å si nei til deltagelse i studien, og data lagret med tanke på denne studien vil da bli slettet. Dette vil ikke ha noen innvirkning på den fortsatte oppfølgingen og behandlingen av deg og din tilstand. Du trenger ikke å oppgi noen grunn for at du vil trekke deg fra studien. Dersom du ønsker å tilbakekalle samtykket, kan du kreve å få de innsamlede data slettet eller utlevert. Dersom opplysningene allerede har inngått i vitenskapelige arbeider, har du imidlertid ikke adgang til å tilbakekalle samtykket eller kreve destruksjon av biologisk materiale, sletting eller utlevering av data (jf Bioteknologiloven §§11-14).

Studien har fått godkjenning fra den regionale komiteen for medisinsk forskningsetikk (REK Sør), og fra sykehusets personvernombud som ivaretar Oslo Universitetssykehus Rikshospitalet HF sitt databehandlingsansvar på vegne av Datatilsynet.

Ansvarlig lege for studien er seksjonsoverlege Audun Stubhaug, (Akuttklinikken Oslo Universitetssykehus Rikshospitalet).

Spørsmål om studien kan rettes til Anne Kathrine Langerud, intensivsykepleier ved Akuttklinikken Oslo Universitetssykehus Rikshospitalet. Tlf 93229832

Øvrige medarbeidere er Seniorforsker Tone Rustøen ved senter for pasientmedvirkning og sykepleieforskning ved Oslo Universitetssykehus Rikshospitalet.

Databehandlingsansvarlig er Oslo Universitetssykehus Rikshospitalet ved administrerende direktør.

Studien vil bli publisert i internasjonale tidskrift i form av flere vitenskaplige artikler. Disse vil inngå i flere doktorgrader (PhD).

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Anne Kathrine Langerud	Audun Stubhaug
Intensivsykepleier/PhD stipendiat	Prof. Dr.med.

Denne siden fylles ut, rives løs og sendes inn sammen med evt. spørreskjema og smertedagbok.

SAMTYKKEERKLÆRING for studien:

NEVROPATI, SMERTE OG LIVSKVALITET HOS INTENSIVPASIENTER
En studie for å kartlegge forekomst og konsekvenser av kronisk nevropatisk smerte hos pasienter som overlever intensivbehandling.

Jeg bekrefter med dette å ha mottatt skriftlig og muntlig informasjon om studien, og er inneforstått med at jeg når som helst kan trekke meg fra studien uten konsekvenser for meg og behandling av min tilstand. Jeg er inneforstått med at deltakelse i studien er frivilllig. Jeg er inneforstått med at jeg kan be om at innsamlet materiale slettes, dog ikke etter at resultatene er publisert.

Ja takk, jeg ønsker å delta i NEUPAQ studien. ……. (sett kryss)

Nei takk, jeg ønsker ikke å delta i NEUPAQ studien ……. (sett kryss)

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Navn (blokkbokstaver) Fødselsdato

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Signatur Dato

Jeg bekrefter å ha gitt skriftlig og muntlig informasjon om studien

Studie.medarb. ---------- Dato ----------