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Pre and post–injury health in persons with whiplash: The Hunt Study

Exploration of the functional somatic model for chronic whiplash

Thesis for the degree of Philosophiae Doctor

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Norwegian University of Science and Technology
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Helsetilstand hos personer med nakkesleng, før og etter traumet.
HUNT studien.
Utforskning av kronisk nakkesleng som en funksjonell somatisk lidelse.

Kronisk nakkesleng utgjør en stor belastning både for den enkelte og for helsevesenet i de fleste vestlige lander. Tilstanden er karakterisert ved en mengde ulike symptomer fra hele kroppen, tilsynelatende uten tilsvarende påvisbare skader. Symptomene vedvarer tross ulike former for behandling og er forbundet med stor uførhet og psykososiale problemer. Det er foreslått to motstridende modeller til å forklare kronisk nakkesleng: den organiske modell, som forklarer symptomene med biomekaniske krefter mot nakken, og den funksjonelle somatiske modell, som forklarer symptomene som uttrykk for psykososiale faktorer og en sykeliggjøring hos personen.

Formålet med avhandlingen var å utforske hypoteser basert på den funksjonelle modellen.

Hovedfunn

1) Vi fant en økt forekomst av angst og depresjon hos mennesker som hadde opplevd nakkesleng for minst to år siden. Denne økte forekomst kunne delvis forklares av nakkesmerter og hodepine, hvilket er tilsvarende andre kroniske smertelidelser.

2) Sammenlignet med andre kroniske smertelidelser fant vi at kronisk nakkesleng ligner mer på en funksjonell smertelidelse (fibromyalgi) enn en organisk smertelidelse (leddgikt) ved å ha symptomer fra hele kroppen og også økt angst og depresjon.

3) Angst og depresjon før traumet synes å forutsier det å rapportere nakkesleng senere.

4) Dårlig helse før traumet er forbundet med økt risiko for senere å rapportere nakkesleng.

5) Det å rapportere nakkesleng er forbundet med økt risiko for å få uførepensjon 2 år senere, også for nakkesleng uten nakkesmerter

Konklusjon

Nakkesleng er en kompleks lidelse som er forbundet med symptomer på dårlig helse og funksjonssvikt allerede før traumet og som viser et bredt spekter av symptomer både fysiske og psykiske etter skaden. Angst og depresjon før skaden synes å predikerer selv-rapportert nakkesleng. Funnene gir støtte til en funksjonell somatisk forståelse av kronisk nakkesleng og antyder dermed faktorer å være oppmerksom på ved vurdering og behandling av pasienter med nakkeslengskader.

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SUMMARY

Objective

Chronic whiplash is a burden both to the individual and to the health care system in most western countries. The condition is characterized by a great variety of symptoms from all over the body, apparently without attending objective signs, making it difficult to relate the symptoms to the neck injury. The symptoms are persisting, in spite of different treatment approaches and are associated with gross disability and psychosocial problems. It has been difficult to explain these findings and that is where scientific debate has centred. Two opposing models have been proposed: the organic model, which explains the symptoms with the mechanical forces transmitted during a collision, and the functional somatic model, which explains the symptoms as expression of psychosocial factors and a sick role adopted of the individual. The aim of the thesis is to explore hypotheses derived from the functional somatic model: that whiplash is associated with an increased prevalence of anxiety and depression and that pre-injury anxiety and depression predict subsequent report of whiplash, that pre-injury poor health is associated with the report of whiplash, and that chronic whiplash is characterized by a great array of different symptoms. Finally, it is an aim to explore the association between self-reported whiplash and subsequent disability pension award.

Method

All studies in the thesis are based on the Health Study of Nord-Trøndelag (HUNT), which is a large population-based survey. The first two studies used cross-sectional designs based on the HUNT 2 study (1995-97), while the last two studies had a prospective longitudinal design, including baseline data from the HUNT 1 study (1984-86) and outcome data from the HUNT 2 study. Information on whiplash was included in the HUNT 2 study. In the two prospective studies, the whiplash group was restricted to individuals reporting a whiplash injury between HUNT 1 and HUNT 2. To explore the predictive significance of self-reported whiplash for later disability award, we used baseline data from the HUNT 2 study and outcome data from the Registries of the National Insurance Administration. In all the studies, we used binary logistic regression to explore our research questions, adjusting for possibly confounding factors like age,

gender, education, marital status and alcohol problems. Information on anxiety and depression was based on two different instruments: the Anxiety and Depression Index – 12 (ADI-12) in the HUNT 1 study and the Hospital Anxiety and Depression Scale (HADS) in the HUNT 2 study. Information on symptoms, diagnoses, subjective health, use of health services and use of medication were self-reported without objective confirmation.

Results

We found, in the first study, an increased prevalence of anxiety disorder and depression in individuals reporting whiplash injuries happening more than two years ago. The increased prevalence of these disorders was partly explained by neck pain and headache, which was in accordance with findings from other chronic pain disorders. This conclusion was further explored in the second study where we compared the symptom profile of chronic whiplash with the profile of two chronic pain disorders, an organic pain disorder (rheumatoid arthritis) and a functional somatic pain disorder (fibromyalgia). Results indicated that the symptom profile of chronic whiplash was more alike the profile of fibromyalgia than rheumatoid arthritis. The chronic whiplash group had a significantly higher prevalence of symptoms from all body parts, across all organ systems, and also mental symptoms, compared to a control group without fibromyalgia, rheumatoid arthritis and whiplash. The fibromyalgia group had an even higher prevalence of all symptoms than the whiplash group, while the rheumatoid arthritis group showed an increase in particularly pain and stiffness symptoms. The perception of chronic whiplash as a functional somatic disorder was further explored in the third and the fourth study by examining the predictive significance of pre-injury health on the report of whiplash. We found, in the third study, that pre-injury anxiety and depression predicted the report of whiplash. The strength of the association of pre-injury case-level anxiety and depression with incident whiplash was comparable to the previously reported cross-sectional association of anxiety and depression with chronic whiplash in the first study. Also pre-injury health, as a broader concept, was also strongly associated with incident whiplash and particularly with “whiplash with neck pain”. The association between pre-injury health and ‘whiplash with neck pain’ could not be explained by the neck pain. Finally, the third study indicated a strong association

between self-reported whiplash and subsequent disability pension award, even in the absence of neck pain.

Conclusions

Whiplash is a complex disorder which is associated with symptoms of poor health and impairment already before the trauma, and which demonstrates a wide array of symptoms from all over the body after the injury. Pre-injury anxiety and depression predicts subsequent self-reported whiplash and individuals with whiplash have an increased prevalence of anxiety and depression long time after the injury. Award of disability pension is increased following self-reported whiplash, even in the absence of neck pain. This picture seems to give strongest support to the functional somatic model of chronic whiplash.

CONTENTS

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ABBREVIATIONS

ADI-12	Anxiety and Depression Index, 12 questions
ACT	Acceptance and Commitment therapy
CBT	Cognitive Behavior Therapy
DSM-III	Diagnostic and Statistical manual of Mental disorders, Third edition
DSM-IV	Diagnostic and Statistical manual of Mental disorders, Fourth edition
GP	General Practitioner
HADS	Hospital Anxiety and Depression Scale
HADS-A	Hospital Anxiety and Depression Scale, anxiety module
HADS-D	Hospital Anxiety and Depression Scale, depression module
HUNT	The Health Study of Nord-Trøndelag
HUNT 1	The Health Study of Nord-Trøndelag , first wave, 1984-86
HUNT 2	The Health Study of Nord-Trøndelag , seond wave, 1995-97
HUNT 3	The Health Study of Nord-Trøndelag , third wave, 2008-2008
ICD-8	International Classification of Diseases, eighth edition
ICD-9	International Classification of Diseases, ninth edition
ICD-10	International Classification of Diseases, tenth edition
NTNU	Norwegian University of Science and Technology, Trondheim, Norway
OR	Odds Ratio
PTSD	Post Traumatic Stress Disorder
SCL-25	Hopkins Symptom Check List, 25 questions
SF-36	Short Form 36 questionnaire
RA	Rheumatoid Arthritis
REK	Regional Committee for Medical Research Etics
RR	Relative Risk
WAD	Whiplash Associated Disorders

LIST OF PAPERS

1. Wenzel HG, Haug TT, Mykletun A, Dahl AA (2002) A population study of anxiety and depression among persons who report whiplash traumas. J Psychosom Res 53: 831-835.
2. Wenzel HG, Mykletun A, Nilsen TIL (2009) Symptom profile of persons self-reporting whiplash: a Norwegian population-based study (HUNT 2). Eur Spine J 18: 1363-1370.
3. Mykletun A, Glozier N. Wenzel HG, Øverland S, Harvey SB, Wessely S, Hotopf M. (2011) Reverse causality in the association between whiplash and anxiety and depression. The HUNT study. Spine 36: 1380-1386.
4. Wenzel HG, Vasseljen O, Mykletun A, Nilsen TIL. (2011) Pre-injury health related factors in relation to self-reported whiplash: Longitudinal data from the HUNT study, Norway. Eur Spine J, DOI: 10.1007/s00586-012-2186-2

1 BACKGROUND

1.1 Whiplash

The term “whiplash” was first used by H.E. Crowe [1] in 1928 at a symposium on traffic accidents held in San Francisco. Before “whiplash” was used, the injury was referred to as “railway spine” to describe common injuries of persons involved in train accidents at the turn of the 20th century [2]. Crowe did not refer to the injury as such, but to the motion that the head and neck underwent in conjunction with a collision. Since the mechanism of indirect cervical spine trauma resembles that of a whip lash, namely, a relatively minor force at the handle of the whip leading to a much larger and more rapid movement at the end of the whip, the term whiplash was used to describe both the motor pattern and injury mechanism associated with indirect cervical trauma. Since the term was introduced the meaning of it has expanded even further, and by now, the term is used by many to describe both the injury mechanism and the symptoms after the injury.

In 1995, the Quebec Task Force on Whiplash-Associated Disorders (WAD) has redefined the term as “an acceleration-deceleration mechanism of energy transfer to the neck which may result from rear-end or side impact, predominantly in motor vehicle accidents, and from other mishaps”. The energy transfer may result in bony or soft tissue injuries (whiplash injury), which may in turn lead to a wide variety of clinical manifestations termed WAD [3].

To assist health care workers in making therapeutic decisions the Quebec Task Force further proposed a classification of WAD:

- Grade 0: no neck complaints and no physical signs.
- Grade I: neck pain, stiffness or tenderness, but no physical signs.
- Grade II: neck complaints accompanied by decreased range of motion and point tenderness (musculoskeletal signs).
- Grade III: neck complaints accompanied by neurological signs such as decreased or absent deep tendon reflexes, weakness and/or sensory deficits.
- Grade IV: neck complaints accompanied by fracture or dislocation.

Other symptoms can be present in all grades, and a wide variety of symptoms has been documented in several studies, both in the acute phase [4] and in the chronic phase [5]. Grade I and II comprises 80% of all whiplash injuries [6], and these are the grades included in most research on WAD [7-10]. The prognostic significance of the classification has been examined, however results have been inconclusive [11,12]. A Norwegian expert panel estimated an approximate number of 2000 new cases of acute WAD (grade I and II) per year in Norway [13]
The WAD classification system also included a grading system for the amount of time since the onset of symptoms arising from 1-5. Grade 1 is an acute problem of less than 4 days, grade 5 is a chronic problem exceeding 6 moths [3].

A Swedish medical task force recently developed a consensus on early whiplash and argued that the diagnosis of whiplash injury would acquire a more exact and realistic meaning by deleting grades 0 and IV. Misunderstandings may occur when individuals presenting no symptoms or physical signs (grade 0) are classified as having a WAD disorder. They further argued that the term "whiplash trauma" should be reserved for indirect traumas to the neck, and fractures and dislocations (grade IV) are rarely the results of indirect traumas and might rather be classified in terms of morphological findings [14]. In the International Classification of Diseases, whiplash is classified as S 13.4, distortion of the cervical spine [15].

1.1.1 Acute whiplash

The acute phase after a whiplash trauma, lasting up to 6 weeks is called acute whiplash. The most common symptoms are pain in the neck, but also pain in the shoulder, back, headache, dizziness, paraesthesiae, vertigo or cognitive/psychological symptoms[16]. Symptoms gradually appear during the first week, with almost 75% of the neck pain starting within two days [17] and then they start subsiding again with a gradually recovery during the following weeks [10,18,19]. The condition seems to stabilize within 3 months, though a certain fluctuation in the severity of symptoms may persist even after this time [20,21]. There is no doubt or discussion about the acute whiplash, which may be considered in the same way as other strain and sprains in the body. These early

symptoms are rather similar among patients and do not vary much between different countries, in contrast to the chronic whiplash.

1.1.2 Chronic whiplash

The course after a whiplash injury is for many persons characterized by rapid recovery during the first three months. However, up to 50% of cases, particularly in most western countries, develop into chronic WAD [17,22,23]. The Quebec Task Force defined chronic WAD as "the presence of pain, restriction of motion or other symptoms six months or more after a whiplash injury, sufficient to hinder return to normal activities such as driving, usual occupation and leisure" [3]. Synonyms for chronic WAD are "chronic whiplash", and "late whiplash syndrome" [24,25]. The effect of treatment is not documented. Thus a recent critical literature review did not find support for clearly effective conservative treatments of acute, sub-acute or chronic symptoms of WAD [26]. Early, aggressive care instead has been associated with prolonged recovery [27-29].

Chronic WAD is characterized by a great variety of symptoms, psychosocial problems and gross disability, apparently without attending objective signs. The symptoms derive from all body parts and include all organ systems, including mental symptoms, making it difficult to relate them to the neck injury [30-33]. Many patients also report neuropsychological complaints, however with no documented neuropsychological impairments [34,35]. Simultaneously, there is evidence for development of a widespread sensory hypersensitivity, indicating disturbances in central nervous pain processing [36-38].

In our studies, the questions on whiplash and symptoms were independent. Thus we do not know whether the symptoms were related to the whiplash injury or not. Some of them probably will be, as indicated in the second study, however other symptoms might not be related to the injury, as the prevalence of symptoms in the population is high [39-41]. Thus, in the thesis, I have decided to use the term whiplash instead of WAD.

1.2 Incidence and prevalence

The most common sources consulted when estimating the number of whiplash injuries are police reports, emergency ward visits, and insurance claims regarding such injuries, but also information from general practitioners (GP) and population studies should be considered. Despite increasing collision severity, the injury severity in vehicle occupants has decreased in the last 25 years. In contrast, the incidence of WAD has increased. These disorders seem to follow low velocity collisions on many occasions; however it has not been possible to document any association between velocity change and severity of symptoms [9]

The information indicates that the number of whiplash injuries has increased dramatically in many countries during the last decades and such injuries now represent the largest part of all road traffic injuries [42]. In a best evidence synthesis it was found that the cumulated annual incidence increased from 83 per 100 000 inhabitants (1985-1986) , to 142 per 100 000 (1988-1990), to 147 per 100 000 (1990-1991), and to 302 per 100 000 (1997-1998) [43] and it seems to have increased further after 2000 [44]. However, the annual incidence rates of whiplash injuries show large variation across different studies and countries with rates varying between 28 per 100 000 and 834 per 100 0000 [16]. About 90% of cases are attending emergency room health care and about 10% are visiting the general practitioner [45,46].

The incidence of chronic whiplash differs considerably between countries, with 40-50% of individuals in most western countries developing lasting symptoms after a whiplash injury [22], while other countries, e.g. Lithuania, Greek and Germany report of approximately no persons with lasting symptoms [18,47-49]. It has been proposed that this wide range of recovery rates might reflect different perceptions of whiplash in the populations as well as different compensation systems [49], however, the varying rates reported in the literature might also, at least partly, be accounted for by the lack of a standardised definition of recovery after acute whiplash.

1.3 Societal costs of chronic whiplash

Chronic whiplash represents a considerable burden to the society, both health care systems, insurance systems and compensation systems [50]. Whiplash is for many persons associated with persistent pain, disability and considerably emotional distress. The condition is costly in most western countries, which was shown in a comparative study of the societal costs of minor cervical spine injuries in 10 European countries. The percentage minor cervical injuries constituted of all bodily injuries was on a mean 40% and the average cost per claim was € 9.000. Results further showed a great variation between the different countries, which was interpreted in light of differences in cultural attitudes [42].

1.4 Outcome of whiplash

1.4.1 Neck pain

Neck symptoms in terms of pain and stiffness are the most prominent symptoms associated with whiplash injuries [51]. There is further evidence for reduced head steadiness [52] and altered movement patterns in the neck [53,54], possibly aimed at minimizing the use of painful muscles. This change in motor patterns is in accordance with both the (neurophysiological) 'pain adaption model' and (cognitive behavioural) 'fear avoidance model'. In a best evidence synthesis, Caroll et al. [22] reported that approximately 50% of those with whiplash will report neck pain symptoms one year after their injury. However, only 12% of subjects reported daily neck pain and only 9% reported significant health impairment due to the collision [17,22]. Studies with longer time follow up suggest that whiplash symptoms can persist or recur over the long term. At seven years post-injury, almost 40% of those making a claim after a traffic related whiplash injury reported often or always having neck pain, compared with less than 15% of a matched cohort who had been in a car crash with no whiplash. People with neck pain were also more likely to have pain in other parts of the body [55]and to report general ill health [22].

These findings should be interpreted in light of the background prevalence of neck pain which also shows a persistent or recurrent course, both in the general population [56] and in workers [57]. However, chronic neck pain secondary to trauma (including

whiplash trauma) seems to differ from spontaneous chronic neck pain in several respects, such as self-perceived health, working ability, personality profile and cerebral expression of pain. The chronic whiplash patients seem to be more vulnerable and have impaired illness behaviour [34].

1.4.1.1 Neck pain in the general population

A best evidence synthesis found that most estimates of 12-months prevalence of neck pain range from 30% to 50% among adults in the general population. The 12-months prevalence of neck pain, limiting activities, among adults ranged from 1.7% (limited ability to work due to neck pain) to 11.5% (limited activities due to neck pain) [58]. Most cases of neck pain fit into the category of non-specific neck pain, with a multifactorial and poorly understood etiology [34,59]. Clinical and radiographic examinations seldom show organic lesions to be responsible for the symptoms, and instead psychosocial and cultural factors have been proposed to be contributory factors. Also alterations in the central nervous system (neural sensitization) have been suggested as an explanation for the persistence of pain [34].

1.4.2 Mood symptoms

There is a strong association between the report of somatic health problems and anxiety and depression [60,61], and research has indicated that the depression is not just a comorbid disorder, however interacts with the chronic pain to increase morbidity and mortality. Thus the temporal relationship between depression and chronic pain is not clear. It has further been suggested that there is qualitative differences between depression as a result of chronic pain and depression as a primary psychiatric disorder. "Affective distress" which incorporates wider emotions such as anger, frustration, fear and sadness might be a better term than "depression" in chronic pain patients [62].

Correspondingly, several studies have documented an increased prevalence of anxiety and depression in whiplash [21,63,64]. Carroll et al. [65] found in a one year follow up of individuals making an injury claim for traffic related whiplash injuries that 44.9% had developed depression within six weeks after their injury compared to 10.6% reporting mental health problems within six months before the injury. This

symptomatology was persistent throughout the one year follow up in 18% of subjects, and it followed a recurrent course in another 18%. However, Côté [31] did not find any association between whiplash and depressive symptoms.
Both pre-injury psychological problems and poor general health as well as post-injury symptoms and anxiety have been associated with development and persistence of depression after a whiplash injury [65,66], while the effect of chronic pain was considered to be less important [65].

1.4.3 Other symptoms and signs

Clinically, whiplash patients also present with headache, jaw pain, interscapular pain, shoulder pain, thoracic pain, low back pain, spinal pain, stomachache, nausea, paraesthesiae, sensory hypersensitivity, vertigo, dizziness, eye symptoms, hearing symptoms, fatigue, sleeping problems, memory problems, cognitive dysfunction, depressive moods, and anxiety [4,5,14,67]. These symptoms however have to be interpreted in light of the high prevalence of symptoms in the population [39,41], particularly different chronic pain conditions [68]. Some studies also emphasize the traumatic effect of the motor vehicle accident resulting in stress responses continuing into Post Traumatic Stress Disorder (PTSD) [69,70]

1.4.4 Quality of life

Chronic pain disorders experience a great impact on quality of life in the patients [37,71] which has been shown by the Short Form 36 (SF-36)[72]. This is one of the most widely used generic instrument for measuring perceived health status in various diseases and conditions, and has also been suggested to be the most appropriate generic instrument for use in musculoskeletal disorders. In a comparative study of four groups of female patients with chronic non-malignant pain syndromes (low back pain, endometriosis, rheumatoid arthritis and whiplash/fibromyalgia), results showed that the whiplash / fibromyalgia group experienced the greatest impact of their disorder on quality of life, particularly relating to vitality, social function, emotional problems, and mental health status, which emphasizes the nature of this complicated pain syndrome and the related management problems [37]. Research has indicated that significant improvement occur as time progressed for the dimensions of role physical and bodily

pain. In contrast, no significant improvement occur over time for the dimensions of physical function, general health, role emotional, vitality, social function and mental health [71].

Whiplash patients also have clear symptoms of psychological distress as indicated by the Symptom Check List 90 revised version (SCL-90-R). Particularly the somatisation scale, the obsessive scale and the depressive scale have been elevated [73,74]. The somatisation score might indicate a tendency to experience and report non-physical symptoms which might be explained by an increased psychobiological sensitivity to minor or even normal changes in bodily signals, the obsessive score might indicate an increased tendency to worry and ruminate about the impact of the trauma and its consequences, and the depressive score might indicate anger, sadness and helplessness as a result of the pain, disability and reduced quality of life[73,74].

1.5 Recovery

Several different definitions of recovery after a whiplash injury have been used in the prognostic whiplash literature. A recent systematic review found 30 different methods for defining recovery [75]. Most of these concerned body structure and function with restricted participation being the second most common definition followed by activity limitations. However, even within each domain, there was wide variability in the cut-off values for dichotomizing a group as recovered or not recovered. This lack of a standardized definition of recovery after a whiplash injury might be an important reason for the wide range of recovery rates reported in the literature. There is further a risk that the emphasis on symptoms in the current literature neglects other important aspects of health [75]. The most commonly used outcome measures include neck pain[30,76,64], disability [30,64], return to work [76,77] and quality of life [8,78,79]. Recovery rates and prognostic factors for these different measures might differ considerably. Typically, individuals rather quickly return to work though they are still disabled and have considerable activity limitations. Often neck pain and reduced quality of life are the most persistent symptoms [23,71]. Most symptoms stabilize at three months, however, for many individuals the severity of symptoms will fluctuate during the following years and less than 50% of individuals will experience the same severity of symptoms after

two years as they did at three months, both improvement and deterioration is possible [21,80].

1.6 Prognostic factors

During the last decades a large number of studies have been performed on prognostic factors in whiplash, including large population-based studies, clinical studies and critical reviews covering more than 100 different prognostic factors [81].

1.6.1 Demographic and socioeconomic factors

Evidence concerning the prognostic significance of demographic and socioeconomic factors is inconsistent. Some studies find that female gender is a risk factor for neck pain, disability, mood disorder and prolonged claim closure [23,30,32,82-84], while other studies have not been able to confirm these associations [10,22,64,81]. Thus, it is difficult to draw any valid conclusions, however, it could be mentioned that some studies have shown that females with whiplash have a higher prevalence of pre-injury neck pain, other health problems and visits to the GP [83,78], which is in accordance with the general tendency of females to report more somatic problems than males [60]. Also, evidence concerning the effect of age is conflicting. Some studies report that older age is a risk factor for poor outcome after a whiplash injury [17,32,85], while other studies do not find any association between age and outcome [10,22,64,81,84]. It has been proposed to explain the positive findings with degenerative changes in the cervical columna; however, MRI studies have not been able to document any relation between degenerative changes and symptoms after a whiplash trauma [7].

Evidence concerning the significance of education has also been conflicting. Lower level of education has in some studies been reported as a prognostic factor for neck pain, disability and mood symptoms [23,30]. However, in a best evidence synthesis of prognostic factors in whiplash, Carroll et al. [22] could not find support for this as evidence was inconsistent. It is not clear what is the reason for the associations found, however it may be related to coping abilities [82,86] or it may be related to occupation [87]. Hunter [88] studied the effect of demographic factors on the report of chronic pain and found conflicting evidence of a correlation with chronic pain.

1.6.2 Pre-injury health

Pre-accidental factors may play a role in predicting both injury vulnerability and prognosis.

There seem to be strong evidence that pre-injury poor health, health seeking behaviour and neck pain are predictive for post-injury neck pain, widespread pain and disability [20,22,89-91]. Accordingly, there was consensus among an expert panel, in a Delphi Poll, that a long history of sick leave before the accident was considered as a risk factor for disability in whiplash [92]. However, Hendriks et al. [23] did not find any relation between functional recovery in whiplash and self-reported pre-injury neck pain, headache, participation problems, comorbidity and use of pain medication.

Considering the effect of pre-injury health, it is important to be aware of the risk of underreport of pre-accidental symptoms, when the information is reported retrospectively. Carragee [93] found that the self-reported prevalence of axial pain and drug, alcohol and psychological problems was much less than the documented prevalence in prior medical records and expected prevalence in age- and sex –matched populations. This effect was seen most strongly in individuals filling compensation claims. Studies using pre-accidental reported information have supported the significance of pre-injury factors. Lankester et al. [94] and Turner et al. [85] used information from General Practioner (GP) reports and found that both physical and psychological outcome was associated with pre-injury musculoskeletal complaints [85] and with pre-injury back pain, high frequency of GP attendance and anxiety and depression symptoms [94].

Some of these findings may reflect difficulties in distinguishing pre-injury symptoms from post-injury symptoms, however findings could also reflect a more pronounced vulnerability to the effects of neck injury in case of a motor vehicle collision [89,95].

1.6.3 Collision related factors

Most evidence suggest that collision related factors such as direction of the collision, position in the vehicle, head rest, seat belt, and awareness of the collision have no

significance for outcome [10,22,30,32,90]. Furthermore, it has not been possible to find any association between accident forces and outcome [10,17,76,84]. Two empirical studies lend further support to these findings:
In a questionnaire cohort study of drivers in a car crashing contest, which replicates an accidental whiplash injury, there were no chronic symptoms or disability. The results were explained by the fact that the sports driver is not fearful or angered and is highly motivated to ignore minor symptoms, and to avoid an illness role [96]. In an experimental study, subjects were exposed to placebo collisions that almost completely lacked biomechanical stress. Approximately 20% of subjects indicated whiplash related symptoms, even though no biomechanical potential for injury existed. However, it was found that certain psychological profiles, characterized by a tendency for psychosomatic disorder and emotional instability, placed an individual at higher risk for development of symptoms after a whiplash injury [97].

1.6.4 Organic injuries

Throughout many years, a large number of publications have focused on structural changes in soft tissues in the cervical spine in patients with whiplash. It has not been possible to detect pathology connected to the injury or to predict symptom development and outcome from MR or other imaging techniques [7,98,99]. However, one study group have used fluoroscopically guided, controlled diagnostic blocks and identified lesions in the facet joints as the single most common basis for chronic neck pain after whiplash accounting for at least 50% of cases [100]. These findings have been replicated by another study group, however the effect was only transient and the nerve root blocks could not be recommended as a treatment approach [101,102]. No studies have been able to document any association between organic findings related to the injury and that wide array of other symptoms other than neck pain, present in whiplash injuries.

1.6.5 Initial symptoms

There is consistent evidence that greater initial pain, more symptoms and greater initial disability predict slower recovery after whiplash, both in critical reviews [22,32,24] and in empirical studies [17,23,30,103]. The findings were supported by consensus in an

expert panel in a Delphi Poll, which proposed that high severity of injury, and presence of constant neck pain since the accident was considered as prognostic for pain and disability in whiplash [92].

1.6.6 Psychological factors

There is strong evidence that adjustment to chronic illness is best explained using a biopsychosocial framework, incorporating both psychological and social factors [104,105]. Sullivan [64] found that psychological variables (catastrophizing, anxiety and depression) accounted for 18% of variance in pain ratings and for 37% of variance in perceived disability in patients referred to a speciality pain clinic with a diagnosis of whiplash injury. Even after controlling for the effect of pain, psychological variables accounted for 27% of variance in disability rating, while pain alone only accounted for 14%. Several studies have indicated that psychosocial factors are more important predictors for outcome than collision related and demographic factors [10,77].

1.6.6.1 Emotional factors

Several studies report that depression is an important influencing factor in perceived health and quality of life in whiplash [78,62]. Even minor deviations in depressive symptoms have an effect and should be taken seriously [78]. Generally, emotional distress has a close interaction with pain and might predispose individuals to experience pain, precipitate symptoms, amplify the intensity of pain and be a perpetuating factor. Thus it was shown that depression predicted the occurrence of low back pain three years later. Depression being a much stronger predictor than both clinical and anatomical risk factors [106].

It has further been shown that depressive symptomatology is an effect modifier on the effect of coping in whiplash. Without depressive symptomatology, those using high levels of passive coping recovered 37% slower than those using low levels of passive coping, while, in the presence of depressive symptomatology, those using high levels of passive coping recovered 75% more slowly than those using low levels of passive coping [107].

1.6.6.2 Cognitive factors

There is strong evidence that cognitive factors have great prognostic significance in whiplash and other chronic conditions. Illness beliefs are important as a framework for interpretation of the illness threat, to guide illness behaviour and determine coping, and have been associated with both disability and quality of life, independent of disease severity [105,108,109]. Clinical research on chronic whiplash has particularly emphasized the prognostic significance of catastrophizing [64,78], positive expectations for recovery [110-112], self-efficacy [8,113,114], and helplessness [30]. These cognitive factors are particularly important as research has indicated that beliefs concerning whiplash and recovery after a whiplash injury might be very pessimistic in the population [115]. Evidence has suggested that there might be a close association between negative expectations for recovery and high levels of passive coping after a whiplash injury [116]. However, these beliefs seem to vary in different cultures [47,48] as do also the reported incidence and prognosis of whiplash. Also the belief that one has a serious disease, the expectation that the condition will worsen, magnification of symptoms and attribution of sensations and minor bodily symptoms to the injury has been associated with prognosis after a whiplash injury [104].

1.6.6.3 Coping

Several studies have documented the significance of coping in the adjustment to chronic pain [117,118] and in the prognosis of whiplash. Particularly, passive coping strategies have been shown to be detrimental to recovery after a whiplash trauma [82,107], while the effect of active coping strategies are less clear [82,119]. One mechanism of the effect of coping style on recovery might be that high levels of passive coping predict non-compliance with active rehabilitation and instead reliance on medication and rest [120]. It has further been shown that the use of different coping strategies increases over time after the whiplash injury [86]. Correspondingly, the proportion of variance in disability shared with coping also increases over time with 12% at inception, and 54% at 1 year follow up. The quality of coping attempts seem to be more important than the quantity [86].

1.6.7 Societal factors

1.6.7.1 Compensation

Both the compensation process, including litigation, and the compensation system have been associated with recovery after a whiplash injury.

Being involved in litigation and particularly consulting a lawyer has been associated with delayed recovery [27,76,84,121], independent of bodily pain and limitations due to emotional problems [76].

Compensation systems which depend on bodily symptoms have been shown to prolong recovery time. In a comparative study from Spain and Portugal, results showed that the registered incidence of whiplash traumas was higher and the recovery time was significantly longer in Spain where compensation after whiplash is dependent on and increased by the report of bodily symptoms, which is not the case in Portugal [122]. Correspondingly, it was shown that the incidence of claims decreased and the median time to claim closure decreased when the compensation system was changed from a tort system to a no-fault system [123]. In a tort system, people who are injured in a traffic collision may sue the driver at fault for the collision for additional compensation for pain and suffering which is not possible in a no-fault system [22]. Results were interpreted as indicating that a compensation system in which financial compensation is determined by the continued presence of pain and suffering provides barriers to recovery and may promote persistent illness and disability.

Evidence from critical reviews concerning the prognostic significance of compensation claims is contrasting. Coté [32] concluded that there is evidence that compensation is associated with outcome in whiplash, while Scholten-Peeters [81] concluded that compensation had no significance.

1.6.7.2 Cultural factors

Internationally, the rate of chronic pain after motor vehicle collisions is dramatically lower in Greece and Lithuania than in Canada and the United Kingdom [18]. These international differences have been attributed, in part, to differences in culture, beliefs and attitudes regarding the risk of developing chronic symptoms [124]. E.g media

attention and widespread impression that whiplash injury is serious and debilitating are factors that may raise the risk of long-term problems [14].
.However, the differences in reported recovery rates might also be due to other factors, e.g. methodological issues such as differences in sampling frames and sampling procedures, and differences in case definitions or measurements procedures [22]. Also differences in the context in which an injury occurs or differences in policies relevant to compensation for traffic collisions might be important, as mentioned above.

1.7 Explanatory models for chronic whiplash

It is largely unknown why certain individuals exposed to whiplash trauma develop pronounced, long-term symptoms; however, it is evident that both biological factors, psychological factors and psychosocial factors have to be considered. Many explanations have been presented over the years falling in two different categories, either organic models, relating the symptoms to organic injuries to particular structures in the neck as a result of biomechanical forces, and functional models focusing on psychological and psychosocial explanations, representing a 'functional somatic disorder'.

1.7.1 The organic model for chronic whiplash

First, it should be mentioned that pathoanatomical explanations of the symptomatology have often been based on experimental animal studies, cadaver studies, post-mortem observations, and findings at surgery. However, one should be careful when extrapolating the results of these studies and observations to the clinical situation [14]. Keeping this in mind, it is proposed that some symptoms of whiplash injury likely have organic bases that are related to the forces transmitted during a collision exposure and that some whiplash injuries likely do not resolve for organic reasons [16]. This latter proposition is supported by the delayed recovery and higher chronicity rates for patients with more severe initial symptoms [81,24,125]. Several anatomical sites of whiplash injury have been proposed (the facet joints, the ligaments and intervertebral discs, the vertebral artery, the nerve root and the muscles), each with its own clinical evidence, relevant anatomy, mechanism and tolerance to injury [16,126]. From all of these anatomical sites, except the muscles, the possible duration of injury and pain are

supposed to be more than six months [16]. Possibly, but less commonly, also the sympathetic trunk, brain, inner ear, and esophagus may be damaged as well [126]. Most of these proposed injuries are based on theoretical speculations , and it has been difficult to document the existence of the injuries.

Imaging techniques have not been able to determine the cause of neck pain in whiplash [126], however, double-blind, controlled, fluoroscopically guided diagnostic blocks, have indicated that facet joint pain is a common basis for chronic neck pain after whiplash, accounting for at least 50% of cases. No diagnostic techniques of comparable validity exist for diagnosing pain stemming from disks, ligaments, or muscles, thus the pathological significance of these structures remain unknown [100].
There also seem to be a lack of evidence linking the supposed injuries to the symptoms presented after whiplash injury. Tears of muscles and ligaments are acceptable, possible causes of pain. Analogous with injuries to these tissues elsewhere in the body, and being vascular structures, muscles and ligaments would be expected to heal over several weeks with scar formation and loss of pain. Such a pattern would be consistent with the observation that the majority of patients quickly recover after whiplash injury [126]. Minor, occult fractures would also follow this pattern with painless function following healing after 6-8 weeks. On the other hand, injuries to the facet joints or intervertebral discs would be expected to have a different prognosis. Discs are avascular, and tears to the annulus fibrosus or separation of the disc from the adjacent vertebral body are unlikely to heal, yet these structures are innervated and therefore constitute an anatomical substrate for pain. Therefore, patients with injuries to the discs or joints may be expected to have prolonged pain with little chance of healing or spontaneous recovery [127,128].

The headache has been perceived as referred pain from injury to some cervical structure. The weakness has been explained as a pain related reflex inhibition of muscle systems that act on or in conjunction with the neck; and the paraesthesiae has been explained as a thoracic outlet syndrome. Exactly how these symptoms develop, however, remains speculative. Symptoms other than pain may occur through damage to the sympathetic trunk, brain, inner ear and esophagus. Most of these symptoms present

as subjective sensations with unclear organic findings and the pathophysiological explanations have been tentative and speculative with unclear objective evidence [127].

1.7.2 The functional somatic model for chronic whiplash.

The term ‘functional somatic disorder’ or ‘functional somatic syndrome’ has been applied to several related syndromes characterized more by symptoms, suffering, and disability than by disease-specific, demonstrable abnormalities of structure and function [129]. Several functional somatic disorders have been described e.g. multiple chemical sensitivity, sick building syndrome, Gulf War syndrome, chronic whiplash, chronic fatigue syndrome, irritable bowel syndrome, and fibromyalgia. Research has shown that they share similar phenomenologies, high rates of co-occurrence and overlap, similar epidemiologic characteristics, and higher-than-expected prevalence of psychiatric comorbidity. Though no organic cause apparently can be found, many such patients are severely disabled, and their symptoms are often refractory to reassurance, explanation, and standard treatment [129,130].

The functional somatic disorder is supposed to be based on common, subjective and unexplained symptoms. Such symptoms are endemic in the society, probably derived from normal physiological sensations and are usually perceived as harmless [39-41]. However, a process of symptom amplification might be initiated resulting in a changed perception of the symptoms as threatening, and as a consequence a self-perpetuating cycle develops. This cycle is supposed to be driven by the belief that one has a serious disease; which is likely to worsen, and the adoption of a "sick role". These threatening perceptions might result in the development of a functional somatic disorder in which the symptoms are incorrectly attributed to serious abnormality e.g. a neck injury after a whiplash trauma [96,119,129]. This was illustrated in a study comparing health related quality of life in patients with sprain of the neck and a control group from the general population. Results showed that role limitations due to physical problem differed considerably between the whiplash group and the control group, though physical functioning did not differ between the groups. This discrepancy was explained by a selective perception of the complaints, attribution of complaints to the accident and illness behavior in the group with sprain of the neck. It was also remarked that even

individuals without complaints after the whiplash injury experienced worse health-related quality of life than the reference population [79].

Functional disorders are no new phenomenon e.g. there are similarities between the 'railway spine syndrome', common in the early 20th century and the chronic whiplash syndrome. However, for the last 3 decades there has been an increased focus on the functional disorders as an adaptation to life, stresses, emotions and expectations [129,130].

The psychobiological mechanism for the functional somatic disorders is suggested to be central sensitization in neural loops resulting in widespread and persistent pain and disability [131,132].
This central sensitisation is supposed to be dependent on cognitive factors, e.g. interpretation of pain and illness perceptions and maintained by sustained attention and arousal [39,133]. Thus, negative expectations of recovery shortly after the whiplash injury have been associated with symptoms of central sensitisation three months later [134]. In agreement with the suggestion of central sensitization, empirical evidence has pointed to abnormalities in the serotonergic CNS pathways in functional somatic disorders [130]. In some cases, the functional somatic disorder might be triggered by an organic stressors e.g. a motor vehicle accident, resulting in activating of the stress response system in the body and maintained by a dysregulation of this stress response system as well as contributing psychosocial factors [119,133].

There is strong evidence for an increased level of anxiety and depression in functional somatic disorders [135], which has been demonstrated for chronic fatigue syndrome [136], for functional dyspepsia [137], and for irritable bowel syndrome [138,139]. The psychiatric symptoms seem to be present prior to the functional symptoms and there appear to be a dose-response relation between the severity of psychiatric symptoms and the functional symptoms [136,138].

2 AIM OF THE THESIS

The two models for chronic whiplash have different implications both concerning risk factors, prognostic factors and treatment. Typically, the organic model might focus on collision related factors. The most important prognostic factors would be expected to be the severity of the injury, as measured by the WAD grade, initial neck pain intensity, neck disability, and radicular symptoms [140]. Neck pain intensity would be particularly important, as it seems to be central in the induction of other related symptoms. The recommended treatment would be analgesics in the acute phase, followed by early activation, physiotherapy and manual therapy in a multimodal intervention program emphasizing improved function [126]. In the more chronic phase it might be recommended to anesthetize the painful joints by blocks of the spinal nerves that supply the zygapophysial joints [128]. Sick leave, compensation and eventually disability pension would be natural components of the approach to persons with whiplash injuries, according to the organic model.

In contrast, the functional somatic model would be expected to focus on risk factors of a psycho-social character e.g emotional distress and life problems, somatization and the cultural perception of a whiplash injury as a serious illness with poor prognosis. Also prognostic factors would be expected to have a psychosocial character, e.g. emotional factors, cognitive factors, behavioral factors as well as maladaptive coping strategies as described above. Treatment recommendations would aim at correcting erroneous conceptions of whiplash, reducing distress, reducing symptom focus, avoiding unnecessary medical treatment and reducing sick leave as well as compensation and litigation processes. An important principle would be to resume normal activities as fast as possible. Compensation systems should be designed with no focus on pain and suffering [141].

Thus it is evident that the two models have great practical implications both for policy makers, the health service system and treatment approaches. These are implications which are very different for the two models. Therefore, it is important to explore further which model is the best one fitting with clinical evidence. The aim of this thesis is to explore hypotheses derived from the functional somatic model for chronic whiplash:

1) Is the prevalence of anxiety and depression increased after a whiplash injury?
2) Is chronic whiplash characterized by a great array of different symptoms?
3a) Is pre-injury anxiety and depression associated with subsequent self-reported whiplash?
3b) Is self-reported whiplash associated with subsequent disability pension award?
4) Is poor pre-injury health associated with subsequent self-reported whiplash?

3 MATERIAL AND METHODS

3.1 The Health Study of Nord-Trøndelag (HUNT)

The Health Study of Nord-Trøndelag consists of population based cross-sectional surveys conducted within the county of Nord-Trøndelag, Norway. Nord-Trøndelag is located in the central part of Norway. The county has coastal and typical inland areas, and also more densely populated areas, but has no big city with over 50 000 residents. It has a population of 126 000, and the geographical, demographic and occupational structure is fairly representative of Norway as a whole. The Health Study is a collaboration between the HUNT Research Centre, Faculty of Medicine, Norwegian University of Science and Technology; The Norwegian Institute of Public Health; and Nord-Trøndelag County Council. The study has till now three waves: the HUNT 1 study performed 1984-86, the HUNT 2 study performed 1995-97 and the HUNT 3 study performed 2006-08 [142]. The HUNT 2 study and the HUNT 3 study were more comprehensive than the HUNT 1 study. The questionnaires were larger and the objectives were expanded. The present thesis is based on information from the HUNT 1 and the HUNT 2 studies.

Based on updated population register lists, all inhabitants aged 20 years and above in the 24 municipalities of the Nord-Trøndelag County received an invitation by mail to take part in the HUNT study with an appointment date and time for physical examination that included measurements of height, weight, blood pressure, and blood glucose.. The invitation also included a questionnaire that should be filled in and delivered at the examination. The methods for data collection were largely similar in HUNT 1 and HUNT 2, mainly through self-reported information by use of questionnaires and clinical examinations.

At HUNT 1, 74 599 persons (88.1%) participated in some part of the study. The participation was highest in the middle age groups. It was lower among men, among young people and old people, among those who were unmarried, divorced or separated, and among those living in the largest municipalities. Detailed analyses of the non-participants indicated four main reasons for non-participation; some were too busy, some had moved, some were not interested and some had health problems. There were no indication that the health status of the ”busy”, “moved” and “not interested differed from that of the participants. These groups made up all together 63% of the non-participants. As a group, the non-participants demonstrated increased mortality and morbidity compared to the participants. Accordingly, the participants at the health study were more “healthy” than the total population of the county. However, the increased mortality and morbidity, affected only 12% of the non-participants, and only elderly people, and it was concluded that the data from the Nord-Trøndelag Health Survey should make a solid basis for the studies in epidemiology and health services research as well as different types of follow-up studies [143]

At HUNT 2, 65 604 persons (70.6%) chose to participate in some part of the study. The participation rate was higher among women than men, and lowest among the youngest. The low level of participation among the youngest individuals was in part caused by difficulties in obtaining directories of residency in these age cohorts due to studies, military services, long vacations, and temporary jobs in other counties or abroad. In individuals within working age, the main reason for not attending the study was lack of time, emigration from the county, being busy at work, that they had forgotten, or no reason at all. Among the age group of 70 years and older, many reported regular follow ups by physicians or at the hospital, and therefore did not see any need to attend. Some individuals (10%) could not attend because they were immobilized due to disease, and some (4%) refused due to long waiting time at the screening site. Rather few (9%) reported that the study was unnecessary or simply that they were unwilling to participate [144].

The papers were based on three different deliveries of data from the HUNT research center. This resulted in minor discrepancies between the numbers of participants and individuals with whiplash, anxiety and depression in the studies. However, it is not likely that these discrepancies have had any marked impact on the results or the interpretation.

3.2 Registries of the National Insurance Administration.

Information on disability pension award was used in the third study exploring the predictive value of self-reported whiplash for later disability award. Data from the HUNT study were linked to the Registries of the National Insurance Administration by employing personal identification 11-digit numbers. The disability registries contain information on date of disability pension award, proportion of disability (50-100% disabled), and up to two diagnoses warranting disability pension for each application. Multiple applications are common due to changes in diagnosis and degree, as many are initially awarded a partial pension. Accumulated, across the disability pension population, most individuals are recipient of 100% disability pension. Individuals awarded disability pension before participating in the HUNT study and start of the follow up period could be identified and were excluded from the study.

3.3 Study variables

Table 1: Variables used in the studies:

	Exposure	**Outcome**
Study 1	Whiplash	Anxiety, depression (HADS)
Study 2	Chronic pain conditions	Symptoms
Study 3a	Anxiety, depression (ADI-12)	Whiplash
Study 3b	Whiplash	Disability pension award (1997-99)
Study 4	Subjective health	Whiplash, neck pain

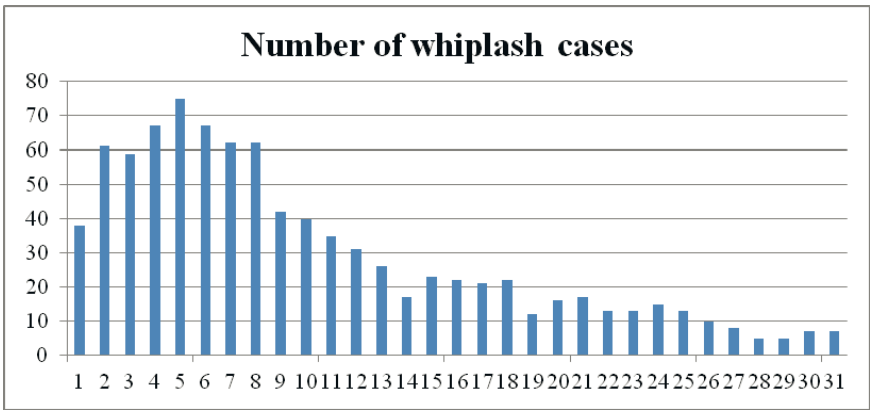
To explore the first and the second aims, we used cross sectional designs, including data from HUNT 2. To explore the third and the fourth aims we used prospective designs,

including data from HUNT 1, HUNT 2 and the National Insurance Administration registry.

3.3.1 Whiplash

Information on whiplash was self-reported in the HUNT 2 study based on the following questions: "Have you ever had neck injury (whiplash)?" and if Yes: "Please indicate your age for last episode of whiplash". All grades of whiplash were included in the registration, from grade 0 with no symptoms to grade IV with fractures and dislocation. Analyses showed that the self-report of whiplash was not evenly distributed, but showed a decreasing incidence with increasing time since the whiplash trauma. This finding indicates an underreport of whiplash, particularly for cases happening more than 9 years ago, see Figure 1.

Figure 1 Number of whiplash cases with years since whiplash trauma.



To estimate the significance of 'chronic whiplash' in the second and the fourth study we used the clinical approximation 'whiplash and long term neck pain'.

3.3.2 Hospital Anxiety and Depression Scale (HADS)

HADS is a self-report questionnaire comprising of 14 four-point Likert-scaled items, seven for anxiety (HADS-A) and seven for depression (HADS-D) formulated in a language that is readily understandable [145]. To avoid false positive cases in the

contexts of somatic illness, no somatic items or items regarding sleeping difficulties are included [146]). Symptoms of severe psychopathology are not included in HADS, and this makes HADS more sensitive to milder psychopathology, thus avoiding the "floor effect" that has been frequently observed when psychiatric rating scales have been used in nonpsychiatric samples. HADS is well accepted in both psychiatric and non-psychiatric settings and is completed in 2-6 minutes [147].

Table 2: HADS items

Scale / item	Text
A / 1	I feel tense or wound up
A / 3	I get a sort of frightened feeling as if something awful is about to happen
A / 5	Worrying thoughts go through my mind
A / 7	I can sit at ease and feel relaxed
A / 9	I get a sort of frightened feeling like 'butterflies' in the stomach
A / 11	I feel restless as if I have to be on the move
A / 13	I get sudden feelings of panic
D / 2	I still enjoy things I used to enjoy
D / 4	I can laugh and see the funny side of things
D / 6	I feel cheerful
D / 8	I feel as if I am slowed down
D / 10	I have lost interest in my appearance
D / 12	I look forward with enjoyment to things
D / 14	I can enjoy a good book or TV programme

Questions are answered on a four point scale from 0 to 3, labels varying between items. Item 2, 4, 6, 7, 12 and 14 are reversed before summation.

The psychometric properties of HADS have been studied in the HUNT sample, in sub-samples defined by clinical (both mental and physical) characteristics, and in sub-groups defined by age and gender[148]. Results confirmed the two factors solution according to the originally proposed model in HADS [146]. The internal consistency, as

measured with the Cronbach's Coefficent Alpha, was good with values of 0.80 and 0.76 in the anxiety and depression scales respectively [148].

The seven items of HADS-D are related to anhedonia, lowered mood and psychomotor retardation, which are all diagnostic criteria of depression in ICD-10 [15] and DSM-IV [149]. Six of the seven items of HADS-A are criteria of general anxiety disorder in both diagnostic manuals. According to a literature review covering 31 studies, HADS has shown good case-finding properties for anxiety and depression in patient populations in primary care as well as in hospital settings [150]. A cut off score for possible cases of anxiety disorder and depression was recommended at scores $\geq$ 8 on each subscale, and $\geq$ 14 of the HADS total score [150], giving an optimal balance between sensitivity and specificity according to the DSM-III and IV, ICD-8 and -9.
A valid HADS-A or HADS-D score was defined as at least five or six completed items on each subscale. Those who filled in five or six items were also included in the study and their score was based on the sum of valid items multiplicated with 7/5 or 7/6 respectively.

3.3.3 Chronic pain disorders

Information on the "exposure" variable in the second study was obtained from the HUNT 2 study and included information on three study groups with chronic pain: chronic whiplash, fibromyalgia (a functional somatic disorder) and rheumatoid arthritis (an organic pain disorder).

Chronic whiplash was defined as the report of whiplash and the report of long-term neck pain. Information on neck pain was recorded in the HUNT 2 study based on the following questions: "During the last year, have you had pain and/or stiffness in the muscles or limbs, which has lasted for at least three consecutive months?" and if yes "where did you have these complaints?" with "neck" as the chosen option. The pain and/or stiffness were graded by the question: "Have the disorders reduced your level of work in the last year?" with the response categories: (a) 'no, not significantly', (b) 'to some degree', (c) 'significantly', and (d) 'don't know'. However this grading was not

used in the study because it was not indicated which body region the recording was referring to.

Fibromyalgia is a common, female dominated disorder with unclear organic aetiology, however a growing literature has suggested that psychological factors might be important in its initiation and maintenance [151]. A hallmark of the disorder is the presence of central non-nociceptive pain [131] resulting in chronic widespread pain and the finding of tender points on examination without identifiable tissue inflammation or damage [152,153]. The condition is further marked by a large number of medically unexplained symptoms from differing organ systems and increased prevalence of all psychiatric diagnoses. The functional disability is often seriously affected with a level of social, family and occupational impairment that is equal or greater that that reported by patients with advanced coronary artery disease, despite the absence of verifiable anatomical disease [151]. Recent research has indicated that fibromyalgia might be, at least in part, a disorder of central pain processing that produces heightened responses to painful stimuli (hyperalgesia) and painful responses to nonpainful stimuli (allodynia) [131,152]. The condition has been referred to as both a functional somatic disorder [129] and a central sensitization syndrome [154,132]. The condition was reported by the question: "Has the doctor ever said that you have/have had any of these diseases?" with 'Fibromyalgia (fibrositis/chronic pain syndrome)' as the chosen option.

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammatory polyarthritis. The hallmark of RA is symmetrical synovial proliferation and tenderness of multiple joints, particularly the small joints of the hands and feet, in addition to radiographic changes of erosions and bony decalcification. Pain in the joints is universal in patients with RA. However, the quality of the pain may vary depending on the type of joint involvement [155]. The clinical course is often complicated marked by joint deformity, restriction of movement, joint replacement surgery and long courses of anti-inflammatory drug therapy with attendant side effects [151]. This condition was also recorded by the question "Has the doctor ever said that you have/have had any of these diseases?" but with 'Arthritis (rheumatoid arthritis)' as the chosen option. Thus

both these latter diagnoses should be physician diagnosed, though self-reported by the participants.

We chose fibromyalgia and RA as comparison groups as both represents chronic, painful conditions. This comparison has been used also in earlier studies [151], which showed significant differences between the two conditions. Individuals with fibromyalgia had significant higher lifetime prevalence rates of psychiatric diagnoses and medically unexplained physical symptoms, and they showed significant higher levels of pain, poorer quality of sleep, perceived loss of control over their illness and impaired coping [151]. Results further showed that the number of medically unexplained symptoms was the best predictor of disease group.

Cases of comorbidity between the three diagnoses were excluded as we wanted to observe the effect of the different diagnoses most clearly. Beside these groups we included a control group with none of these diagnoses.

3.3.4 ADI-12

Information on anxiety and depression as exposure / predictor variables in the third study was obtained from the HUNT 1 study and based on ADI-12, which is a one-dimensional anxiety and depression symptom index. This measure has been validated against the Hopkins Symptom Checklist 25 (SCL-25) in a subsample re-examined two years after baseline screening (r=0.82) [156]. The ADI-12 also correlated well (r=0.46) with the Hospital and Anxiety Scale (HADS) [148,150] measured 11 years later in the HUNT 2 study [157]. Five of the items correspond with ICD-10 criteria of depressive episode (F32), and three items correspond with the ICD-10 criteria for generalized anxiety disorder (F41.1) [15]. Two items are related to feelings of being under pressure, one to the use of tranquilizers or sleeping pills, and one to being more aware of responsibilities than others [157]. The individual items in the ADI-12 are weighted by use of principal component analysis [156].

Table 3: ADI-12 items

Scale / item	Text
ADI 1	Over the last month, have you suffered from nervousness (irritability, anxiety, tension or restlessness)?
ADI 2	Do you mostly feel strong and fit, or tired and worn out?
ADI 3	Do you often feel lonely?
ADI 4	Do you have any long-term disease, damage or injury of a physical or mental nature which impairs your functions in everyday life? – restriction on account of mental illness.
ADI 5	Do you by and large feel calm and good about yourself?
ADI 6	Have you had any problem falling asleep or sleep disorders during the course of the last month?
ADI 7	Would you say that over the last year you have pushed yourself or steadily urged yourself forward?
ADI 8	Are you constantly short of time even when it comes to day-to-day tasks?
ADI 9	Do you have a tendency to take your duties more seriously than other people?
ADI 10	When you think about your life at the moment, would you say that you by and large are satisfied with life, or are you mostly dissatisfied?
ADI 11	Would you say that you are usually cheerful or dejected?
ADI 12	How often have you used analgesics or hypnotics during the last month?

As it may be remarked – ADI 4 and ADI 12 are also used as variables of pre-injury subjective health in the fourth study.

According to previous practice, the ADI-12 was used as a categorical variable with cut off at the 80th percentile for case-level, and also as a continuous z-scored variable for symptom load of anxiety and depression [157].

3.3.5 Symptoms

Information on symptoms as "outcome" variables in the second study was obtained from the HUNT 2 study and based on self-report. The information was classified into three groups: (a) pain and stiffness in different body areas; (b) other symptoms, including gastrointestinal symptoms, palpitations, and breathlessness; and (c) mental health.

The questions about musculoskeletal complaints were adopted from the Standardized Nordic Questionnaires, which quantifies musculoskeletal pain and activity prevention in 9 body regions [158]. A modified version of the questionnaires was evaluated in a group of outpatients with upper limb and neck complaints. Results showed good sensitivity and repeatability, however low specifity. It was concluded that the questionnaire was likely to have a high utility in screening and surveillance [159] .

Participants were asked: "During the last year, have you had pain and/or stiffness in the muscles or limbs, which has lasted for at least three consecutive months?, and if Yes "Where did you have these complaints?" with the response options: (a) neck, (b) shoulders, (c) elbows, (d) wrists, hands, (e) chest/stomach, (f) upper part of back, (g) lumbar region, (h) hips, (i) knees, and (j) ankles, feet. The severity of the specific pain and/or stiffness was not graded. The participants were further asked: "Have you been troubled by headache in the last 12 months?" including both 'attack (migraine)' and 'other types of headache'. Only 'other types of headache' were included in the study

Other symptoms were recorded by asking: "To what degree have you had these disorders in the last 12 months?" with the response options: (a) 'nausea', (b) 'heartburn/regurgitation of acid', (c) 'diarrhoea', (d) 'feeling of heaviness in the stomach', (e) 'palpitations', and (f) 'breathlessness'. The symptom intensity was grades as (a) 'not at all', (b) 'slightly', and (c) 'very much' as response options. For analytical purposes, the two latter categories were collapsed in the study.

Finally, mental health was recorded by the HADS, please see above.

3.3.6 Pre-injury subjective health

Information on pre-injury health as exposure / predictor variables in the fourth study was obtained from the HUNT 1 study and covered subjective health, physical impairment, mental impairment, visiting a general practioner (GP), hospitalisation, use

of analgesics and use of tranquilizers. Subjective health was recorded by asking participants:"How do you feel at present?" with the response options: a) 'Poorly', b) 'Not very well, c) 'well and d) 'Very well'. Impairment was recorded by first asking: " Do you have any long-term disease, damage or injury of a physical or mental nature which impairs your functions in everyday life?" and if confirmed, then asking which kind of impairment. The present study presents the results concerning 'impairment on account of physical disease' and 'impairment on account of mental illness'. Use of health services was recorded by asking participants: "In the course of the last 12 months, have you been to the general practitioner (community doctor, private doctor, locum?" and "Have you been hospitalized in the last 5 years?" Use of medication was recorded by asking: "How often have you used analgesics during the last months?" and "how often have you used tranquilizers during the last month? " with the response options: 'never', 'less than weekly', 'weekly' and 'daily'. In the analyses the two last categories were collapsed. The information concerned primarily self-reported health and the reliability as well as the validity in relation to objectively confirmed measures of health was not known.

3.4 Research Strategy

The two first studies use cross sectional designs while the two later studies use prospective longitudinal designs (in the form of historical cohort designs).

Cross-sectional designs

In the first study we used anxiety and depression symptoms as outcome variable and the self-report of whiplash with different timeframes since the whiplash injury as exposure variable (potential risk factor); and in the second study we used the report of different symptoms as outcome variable and the diagnostic entity as exposure variable (potential risk factor). However, a major drawback of cross-sectional studies is that one cannot be sure of the direction of causality when an association is present as the exposure and outcome are measured simultaneously [160].

Cohort studies

The great advantage of cohort studies is that the temporal relation is clarified as the exposure variables are measured before the exposure variables [161].

In the third and the fourth study we used historical cohort designs with self-reported whiplash at HUNT 2 as outcome variable and respectively anxiety and depression measured at HUNT 1 as exposure variable in the third study and subjective health reported at HUNT 1 as exposure variables in the fourth study. The historical cohort study design has several advantages, first it include minimal observer- and recall bias as the specific hypotheses of interest are not known for the participants and even not exposure status; secondly it is less costly than the population cohort study. In addition, we also used a historical cohort study design with self-reported whiplash as exposure variable and subsequent disability award as outcome variable in an exploration of the clinical validity of self-reported whiplash, in the study 3b.

Typically, prospective cohort designs are very costly and time consuming [161], however current Norwegian research policy allows to link data sources like the HUNT study and public registries, as it was done in the study 3b. Another problem with cohort studies is a risk of selection bias due to incomplete follow up [161]. The possibility of record linkage in Norway also reduces this problem, as it is possible to identify outcomes in national registries, however incomplete follow up might still be a problem in the HUNT 1 – HUNT 2 linkage, as it is not possible to follow persons outside the county.

3.5 Statistical analyses

To estimate the effect of the different exposure variables we used logistic regression models in all the studies. The logistic regression model is based on the linear regression model, however a logit transformation is performed meaning that the model predicts the log of the odds of the outcome instead of the risk of the outcome. The model makes it possible to estimate the Odds Ratio (OR) for the effect of the exposure variable. When the prevalence of the outcome is low, the OR is further a good approximation of the relative risk (RR) [162,163]. All analyses were adjusted for potential confounders, please see below.

3.6 Ethics

The HUNT study (including all sub-studies) was approved by the Data Inspectorate of Norway and recommended by the Regional Committee for Medical Research Etics (REK Central Norway). Each participant signed a written consent including the use of all data for research purposes and the linking of their data to other registers. This issue is, however, also subject to approval of the Data Inspectorate for each record linkage of data sources. All involved researchers work with files where names and personal identification numbers have been removed [144].

4 RESULTS

4.1 Anxiety and depression in persons self-reporting a whiplash trauma

Among 61 110 individuals who attended the HUNT 2 study, 1704 individuals (2.8%) self-reported a whiplash injury. The prevalence of whiplash injury was approximately equal among men and women, and highest in the youngest age group. Among those indicating a whiplash injury, 158 subjects reported this injury to have happened within the last two years, 838 subjects reported more than 2 years since the trauma, and 708 subjects did not give any time interval.

The proportion of HUNT 2 attendants that fulfilled the criterion for a possible anxiety disorder (HADS-A $\geq$ 8) was 15.5%, and 10.9% fulfilled the criterion for depression (HADS-D $\geq$ 8). In the whiplash group, both these proportions were significantly elevated to 24.2% and 15.0%, respectively. Logistic regression showed a significantly increased risk of possible anxiety disorder and depression (HADS-A $\geq$ 8 and HADS-D $\geq$ 8) in the groups reporting whiplash trauma more than 2 years ago, or without any indication of time period (OR in the range 1.71-1.87). There was no increased risk of anxiety and depression in those who reported whiplash less than 2 years ago. The OR for anxiety disorder was slightly higher than for depression. Adjustment for age and gender did not alter the results; however adjustment for symptoms of headache and neck pain reduced the effect on both anxiety disorder and depression for whiplash traumas more than 2 years ago to OR 1.22 for depression and 1.33 for anxiety. The effect of whiplash without indication of time period was not significant.

Results thus indicate that the prevalence of anxiety and depression is elevated in the group of individuals with a long time interval after the whiplash group. This group may correspond to those individuals with chronic whiplash.

It should be mentioned, that one of the aims was to "test the hypothesis that the prevalences of anxiety disorders and depression are elevated also before the whiplash injury". We did not do this since this study is cross-sectional, making it impossible to explore causal relations.

We concluded that whiplash injuries might be considered as a chronic pain disorder.

4.2 Symptom profile of persons self-reporting a whiplash trauma.

The study population was divided into three study groups: 785 persons with chronic whiplash, 1 095 persons with fibromyalgia and 958 with rheumatoid arthritis; and a control group of 52 208 persons without any of these disorders.

All three study groups had a significant higher prevalence of symptoms compared to the control group. This included both pain and stiffness symptoms from all over the body, gastrointestinal and cardiopulmonary symptoms and mental symptoms. Analyses showed that the adjusted OR for the chronic whiplash group and the fibromyalgia group were the most elevated (adjusted OR 6.87-9.58 and 19.09-19.93 respectively for pain and stiffness, adjusted OR 1.73-3.22 and 2.65-3.30 respectively for gastrointestinal and cardiopulmonary symptoms, and adjusted OR 2.03-2.13 and 2.96-3.09 respectively for mental symptoms), compared to the rheumatoid arthritis group (adjusted OR 3.62-4.90 for pain and stiffness except joint pain, which showed an adjusted OR of 7.77, adjusted OR 1.53-2.12 for other symptoms and adjusted OR 1.38-1.39 for mental symptoms).

The adjustment for demographic and socioeconomic variables did only affect the results marginally concerning the pain and stiffness symptoms and the gastrointestinal and cardiopulmonary symptoms; while the adjustment for demographic variables slightly

attenuated the associations concerning anxiety and depression and further adjustment for socioeconomic variables did not change the results.

We concluded that chronic whiplash had a symptom profile more alike a functional somatic disorder than an organic pain disorder.

4.3 Reverse causality in the association between whiplash and anxiety and depression.

Among 37 792 persons included in the study, 277 reported a whiplash trauma in the time period between HUNT 1 and HUNT 2. We found that baseline anxiety and depression increased the likelihood of reporting an incident whiplash injury at follow up. Adjusted for age and gender, this was found both for the 80th percentile case-level cut off (OR= 1.60) and also for the z-scored scale-score of anxiety and depressive symptoms (OR=1.25 per standard deviation increase in the scale score). The presence of alcohol problems did not confound this association.

Disability pension award during the two year follow up after HUNT 2 was strongly increased in those reporting whiplash injury with neck pain (OR=6.54), and also in whiplash without neck pain (OR=3.48). The association between 'whiplash without neck pain' and disability pension award was comparable to the association of neck pain and disability pension award (OR=3.44). An analysis of the diagnoses of the disability pension awarded to persons reporting whiplash showed that these were divided on 27 different diagnoses, 40.7% musculoskeletal disorders, 23.8% injury related diagnoses and 15.2% mental disorders.

We concluded that the results suggest reverse causality, that is, increased risk of future self-reported whiplash in individuals who already have symptoms of anxiety and depression. Beside that, self-reported whiplash was associated with increased risk of subsequent disability pension award.

4.4 The association between pre-injury health and self-reported whiplash.

Among 40 751 persons included in the study 304 individuals reported a whiplash trauma in the time period between HUNT 1 and HUNT 2. Among these persons, 197 individuals further reported long-term neck pain. There was a strong association between baseline subjective health and incident whiplash (adjusted OR=3.07 for not so good health/poor health compared to very good health), and particularly between baseline subjective health and 'whiplash with neck pain' (adjusted OR=5.70, correspondingly). Both physical impairment and mental impairment was associated with incident whiplash (adjusted OR= 2.69 and adjusted OR=2.49, respectively for moderate/severe impairment compared to no impairment) and with 'whiplash with neck pain' (adjusted OR= 3.48 and adjusted OR=3.02, respectively).

The association between use of health services and incident whiplash, and between use of health services and 'whiplash with neck pain' was a bit weaker; and we now found no significant difference in the strength of the associations for all whiplash and 'whiplash with neck pain' (OR=1.47-1.53 and OR=1.50-1.66, respectively.

Use of medication also showed a strong association with incident whiplash and particularly with 'whiplash with neck pain' (OR=1.97-2.07) for the association between weekly use of tranquilizers or painkillers and incident whiplash; and OR =2.42-2.75 for the association between weekly use of tranquilizers or painkillers and 'whiplash with neck pain'.

To explore the significance of neck pain on the associations, we performed all the analyses in a subpopulation of persons with neck pain. The association between subjective health and chronic whiplash was weakened by this procedure, however still significant (OR=1.86-2.31) while the association between more objective measures like use of health services and use of medication and chronic whiplash were not significant.

We concluded that the results indicated that individuals reporting whiplash might have adopted an illness role, already before the trauma.

5 DISCUSSION

5.1 Main results

The main result of this thesis is that health problems typically seen in chronic whiplash, is present already before the whiplash incident. Before the whiplash trauma, we found increased incidence of poor subjective health, physical and mental impairment and increased use of analgesics and tranquilizers, compared to individuals not reporting a whiplash trauma. Individuals reporting chronic whiplash were characterized by a great array of symptoms from all over the body, across all organ systems, and also mental symptoms. Rightfully, it may be objected that self-reported whiplash has challenges regarding validity and reliability. However, the clinical relevance of this construct was demonstrated by its strong association with subsequent disability pension award, even in the absence of neck pain. These results are in accordance with our hypotheses and giving support to the functional somatic model of chronic whiplash.

5.2 Strength and limitations

The main strength of the studies is that the information on pre-injury health was reported before the report of the whiplash injury, thus increasing the reliability of the information and avoiding the risk of underreport of symptoms reported retrospectively [93]. The self-report of symptoms was neither linked to the report of whiplash, which should minimize the risk of attribution and symptom accentuation [104] nor to any litigation, compensation or insurance process, which should avoid the increase in report of post-injury symptoms due to pending litigation processes [32,141,164]. The information was further reported as part of a general health survey and neither participants nor administrators were aware of any specific focus or hypothesis. Ascertainment of disability pension status at baseline and at follow up in the third study was obtained from the National Insurance Administration. These data are complete (including those moving to other parts of the country) and should not be influenced by exposure status. The prospective longitudinal design used in the third and the fourth studies also made it possible to explore causal relationships between variables.
An additional strength is the population based design with a large number of participants and a high response rate. Usually, the response rate may be very low (30-40%) for postal questionnaires [160], however in the HUNT studies, the questionnaires

had to be delivered at the physical examination, which increased the response rate to 71-88% for the two studies.

The studies also include different limitations. The non-participants in the health studies might induce a participation bias. There is evidence that the health of non-participants is poorer than the health of participants [165], which was also indicated in our study [143]. However, as the impaired health only concerned a minor part of the non-participants, and primarily individuals not so often involved in motor vehicle collisions, we accept the data as satisfactory for our studies. Besides that, participation bias is probably a greater threat to the validity of prevalence studies than to studies of associations between exposures and outcomes.

All information from the HUNT studies included in the thesis was self-reported with no objective confirmation. This concerned both information on whiplash, symptoms, diagnoses, impairment, use of health services and medication. This introduces the possibility of information bias. However, this type of assessment also has the advantage to permit assessment of several domains of functioning that would not otherwise be possible [79]

Whiplash injuries may have different grades as indicated above, however we did not have any possibility to ascertain the severity and grade of the whiplash injuries. Consequently, it may be difficult to know exactly the validity of the findings. As indicated above, we found evidence of a significant underreport of whiplash injuries. These false negative cases might be explained by a memory bias concerning accidents happening several years ago, probably meaning that predominantly symptomatic cases are remembered and reported. Concerning more recent cases, self-reported information of motor vehicle collision injuries is rather consistent with information from official collision data [166]. However, the possibility of false positive cases cannot be excluded, neither. These cases might be explained as an attribution bias, meaning that symptoms and distress with no relation to whiplash are attributed to a whiplash injury and thus reported as whiplash. Both biases would result in an over-report of symptomatic cases

and thus result in an overestimation of the true relation between whiplash and the symptoms.

We defined chronic whiplash as the self-report of a whiplash injury and long-term neck pain. However, we did not know if the neck pain was really related to the injury, as the prevalence of neck pain in the population is high [34,58]. However, the second study showed that the prevalence of both neck pain and also other symptoms was significantly higher than the prevalence in a population with no whiplash injuries, which supports the validity of our definition. As a control of other variables to neck pain in the second study, we also selected a subgroup of individuals excluding cases of Mb Becterew, arthrosis and muscle disease and performed all analyses also on this group. This did not change our results. In an effort to increase the probability of an association between the report of whiplash and the report of neck pain in the fourth study, we selected a subsample of individuals excluding cases happening more than five years ago. This resulted in an accentuation of the associations found in the main analyses including all individuals reporting a whiplash injury in the time period between HUNT 1 and HUNT 2.

We further included all cases of whiplash in the definition of chronic whiplash in the second and the fourth study, thus also more acute cases, though the definition of "chronic" indicates that symptoms have lasted at least 6 months. However, the proportion of individuals still in the acute phase was negligible, and research has further documented that symptoms stabilize within three months after the whiplash injury [20,21], thus we found this definition of chronic whiplash acceptable.

Symptoms, diagnoses and pre-injury health were also self-reported. Many symptoms are subjective and cannot be confirmed or disconfirmed but have to be accepted at face value. They may be important exactly because of their subjective character, e.g. as manifestations of an illness role with an increased focus on somatic sensations, magnification and attribution as proposed in the functional somatic model [96,129].

Self-report of both pain and symptoms however may represent a problem of reliability as indicated by Carey et al [167] who matched the telephonic report of low back pain symptoms against Medical Centre records and found that by about 1 year there was almost 20% under reporting as well as an almost identical forward telescoping of symptoms. Correspondingly, Waddell et al [168] noted that history beyond one year was likely to be unreliable. In our studies information on symptoms was based on a much shorter time period (HADS, ADI-12) or the symptoms had to be clinically significant or lasting at least three consecutive months during the last year, which should increase the reliability of the information. The validity of the self-report of symptoms also might be affected by a demand characteristic encouraging an affirmative response, as a result of the direct questioning of the symptoms. Supporting the validity of the information, Ngo [169], found that information on self-perceived recovery in patients with whiplash associated disorders has adequate reliability for use in epidemiological research.

The diagnoses were supposed to be physician diagnosed, though they were self-reported in the HUNT study. Self-report of physical diagnoses implies a problem of reliability [170]. Research has shown, that many persons are not correctly informed about their diagnoses, and both under-report and over-report do occur [171]. It is however likely that the misclassification was random and non-differential, resulting in an underestimation of the true association between diagnoses and symptoms.

Symptoms of anxiety and depression were measured by two different instruments; ADI-12 in HUNT 1 and HADS in HUNT 2. The ADI-12 is a post hoc established measure, though with fairly good psychometric properties, however not as good as the HADS. This may have biased the comparison in favour of a stronger cross sectional association in study one compared to the prospective association found in the fourth study.

As a measure of work-related disability in general, the validity of disability pension award might be questionable. National policies for awarding disability pension adhere to the medical model, where physicians are appointed to a gate-keeping function with the purpose of restricting disability pensions to individuals with a work-related

impairment. However, physicians may be caught in conflicting roles between gate-keeping for national authorities and being the advocate of the patient. Finally, there is a possible under-utilization of disability pension award in individuals on unemployment benefit or in individuals supported financially within the family. These factors are reducing the validity of disability pension award as a measure of work-related disability, thus weakening the possible effect of self-reported whiplash and neck pain on disability pension award.

We adjusted all our analyses for potential confounders e.g socio-demographic factors, and for neck pain and headache in the first study and for alcohol problems at baseline in the third study. However, also other factors may have been relevant, however not possible to include in the analyses because of missing information in the HUNT studies which are general health surveys performed without specific research hypotheses, thus residual confounding cannot be excluded.

5.3 Interpretation of the results

Results indicated that whiplash is more likely to be reported in persons with pre-injury impaired health or anxiety and depression. Whether, this increased prevalence of reporting really does reflect an increased prevalence of whiplash or an increased prevalence of reporting whiplash is difficult to tell. Impaired concentration, attention and reactivity are common symptoms in anxiety and depression as well as consequences of medication. Thus the responsiveness in the traffic might be reduced making it more likely to experience a whiplash injury [172]. However, it should be remembered that a whiplash injury is usually the result of a rear end collision, making it less dependent on the attention of the driver in the exposed car.

However, the results might also reflect an increased prevalence of reporting whiplash. Subjective health complaints are common in the population, primarily musculoskeletal and pseudo-neurological complaints [39,41]. It is possible that persons with subjective health complaints are more focused on bodily symptoms and thus more observant of potential injurious events, and as a consequence are more likely to report a whiplash injury after a motor vehicle collision; while the rest of the population is less aware of

minor injuries and complaints and thus less likely to report a whiplash injury [96,129]. Also, anxiety and depression is common in the population [173]. This emotional distress might be expressed as somatic symptoms [40,174], e.g. attributed to a minor neck injury and reported as whiplash [129,130]. This would be false positive cases, representing an attribution bias.

In the chronic whiplash condition, we observed an increased prevalence of anxiety 25.2% and depression15.5% compared to the prevalence observed in the no whiplash group of 15.3% and 10.8% respectively. Other studies have reported the prevalence of post-injury depression to be 55% to 60% and the prevalence of PTSD to be 39%. A history of pre-injury depression was an important risk factor for the development of both post-injury depression and PTSD [175]. Both these studies were from clinical samples, which might explain the high prevalence of mental problem compared to our study which is population based.

It is common to find an increased prevalence of anxiety and depression in individuals with somatic health problems [135,176,61,177]. Escobar [40] found that 3 or more general symptoms are associated with increased levels of anxiety and depression, increased level of mental suffering and use of health services independent of whether the symptoms are medically explained or not. In our study we found a mean of 5.3 symptoms in individuals reporting whiplash. It has further been indicated that there is a linear relation between number of somatic symptoms and dimensional anxiety and depression [135]. Evidence has indicated that the psychiatric symptoms seem to be present prior to functional symptoms [136,138], which is in accordance with our findings. Finally, it should be mentioned that the finding in our first study of a significant underreport of whiplash might contribute to the finding of an increased prevalence of symptoms, including anxiety and depression, in chronic whiplash. The reason for this underreport might be a memory bias, meaning that minor injuries with no or little symptoms are easily forgotten, while more symptomatic cases will be remembered and reported. However, it is not likely that a memory bias would be able to account for all the increased prevalence of symptoms in the chronic whiplash condition.

We found an increased prevalence of symptoms from all over the body in the chronic whiplash condition compared to the population (population except individuals with whiplash trauma, fibromyalgia or rheumatoid arthritis). This finding is in agreement with findings from other studies of whiplash [4,5], and it has been suggested that WAD should be appreciated as a systemic illness, a syndrome extending well beyond what can be labeled as a neck injury [4]. We also observed an increased prevalence of symptoms in the two other pain conditions. It is well known that fibromyalgia is associated with other somatic symptoms than just pain [131,152]. However, also rheumatoid arthritis might be associated with other symptoms. The explanation for this finding might be consequences of the illness and its treatment. NSAID for example might induce both dyspnoe and gastrointestinal symptoms. Besides that, the chronic pain disorder might have induced neuronal changes resulting in hyperexitability of the central nervous system and as a consequence a lower threshold of perceiving symptoms [106].

This increased prevalence of symptoms has to be seen against the prevalence of symptoms in the population [39-41]. In a cross sectional study from Norway of subjective health complaints in the population, Ihlebæk [41] found that 80% reported musculoskeletal complaints, 65% "pseudo-neurological" complaints (tiredness, depression, dizziness), and 60% gastrointestinal complaints. However, the prevalence of substantial complaints was much lower: 13% reported musculoskeletal complaints, 5% "pseudo-neurological" complaints, and 4% gastrointestinal complaints. Such symptoms are usually based on normal bodily sensations which are usually not paid attention to [4,129]. However, our findings showed that the prevalence of symptoms were significantly higher than the prevalence in the population, particularly for the chronic whiplash group and for the fibromyalgia group.

The explanation for this might be a somato-sensory amplification as an adaption to life, emotions and distress, as it has been described for the functional somatic syndromes [96]. This theory is in agreement with our findings of both increased level of pre-injury anxiety and depression and increase report of pre-injury poor health. However, due to

limitations of the data, we had no possibility to explore whether the poor health was related to identifiable organic pathology or represented functional symptoms.

Recent developments in the research on functional somatic disorders [130] as well as research on the development of persistent symptoms after a motor vehicle collision [119,133,154] have further suggested that the symptoms are not due to tissue abnormality but rather reflects alterations in central nervous function related to sensory processing, autonomic regulation and neuro-endocrine function. These alterations seem to be similar to alterations found in chronic pain condition [106] and might explain the increase prevalence of symptoms also in the organic pain disorder.

The clinical relevance of self-reported whiplash was documented as a risk factor for disability pension award. This effect was observed even in the absence of neck pain, which suggest that there are some other factors which might explain the findings. This was explored in an analysis of the disability diagnoses in the whiplash group. Results showed that these covered a wide specter of diagnoses, primarily musculoskeletal and mental disorders in addition to injury-related diagnoses. It is well known that anxiety and depression are recognized as among the strongest risk factors for disability pension [178].

5.4 Evaluating the findings in relation to the organic model of chronic whiplash

In our analyses thus far, we have explored hypotheses derived from the functional somatic model of chronic whiplash. Our results could not falsify these hypotheses, thus adding support to the functional somatic model. We did not intend to explore the organic model; however it would be interesting to evaluate the findings also in relation to the organic model of chronic whiplash.

The findings of increased prevalence of anxiety and depression in whiplash, in the first study, might also be in accordance with an organic model. It is well known that anxiety and depression are increased in conditions with persistent pain and disability, particularly in the chronic phase [106]. It was further concluded that chronic whiplash should be considered in the same way as other chronic pain disorders. As described

above, chronic pain disorders might be based on both organic factors as well as psychosocial factors.

The symptom profiles in the second study were accentuated for all study groups compared to the control group. Thus also the organic pain disorder (rheumatoid arthritis) showed an increased prevalence of symptoms from all over the body and through all organ systems, including mental symptom, though less than the chronic whiplash group and less than the fibromyalgia group. Thus also findings from the second study might be in accordance with an organic model for chronic whiplash.

The predictive significance of anxiety and depression, as found in the third study, however is not in accordance with an organic model for chronic whiplash. Before the injury, there should be no difference between the general population and individuals which will later report a whiplash injury.

The same argument can be used in relation to the increased prevalence of poor pre-injury subjective health and use of health services found in fourth study. This finding is not in agreement with an organic model for chronic whiplash.

Thus some of the results are in agreement with an organic model, while other results are in contrast to this model. It is however not possible to draw any valid conclusions from this evaluation which is based on results from studies exploring the functional model of chronic whiplash.

5.5 Conclusion

Whiplash is a complex disorder which is associated with symptoms of poor health and impairment already before the trauma, and which demonstrates a wide array of symptoms from all over the body after the injury. Pre-injury anxiety and depression predicts subsequent self-reported whiplash and individuals with whiplash have an increased prevalence of anxiety and depression long time after the injury. Award of disability pension is increased following self-reported whiplash, even in the absence of

neck pain. This picture seems to give strongest support to the functional somatic model of chronic whiplash.

5.6 Clinical implications

There is still an ongoing debate regarding the etiology of chronic whiplash. The two models (the functional model and the biomechanical model) offer opposite and competing explanations regarding this etiology. In the future, a settlement of the dispute between these two models will have clinical implications of major significance. By testing hypotheses derived from the functional model for whiplash, my thesis is one contribution to this ongoing debate. My thesis has limited if any clinical implications on its own, but as a contribution to the debate between the two models, it may have so in the future.

Specifically, my thesis has provided evidence that health problems often seen in whiplash injury may be present already many years before the whiplash incident. The results from our studies indicate that it is important to be aware of possible pre-injury health problems, both somatic and mental, which might indicate a more severe course of whiplash with lasting symptoms. These problems have to be identified as early as possible, and to be attended to. It will be important to be aware not only of neck pain and stiffness but also of other symptoms from all over the body. The best way to respond to these is probably by normalizing and informing. Finally, be aware of anxiety and depression in chronic whiplash, which has to be treated on its own.

5.7 Future research

The conflict between the functional and the organic model for whiplash is by no means settled, and thus, research cannot yet give anything but ambiguous and conflicting advice to clinicians, national authorities and the public. Thus, there is a need for further studies exploring the understanding of chronic whiplash, particularly the relative empirical relevance of the functional somatic model and the organic model for chronic whiplash.

This research should as far as it is possible include prospective population-based studies which could explore causal relations between potential predictive and prognostic factors for whiplash and the development after the injury. Information on pre-injury factors should be recorded before the injury. The research should use a grading both of the whiplash injury and of complaints, differentiating trivial and disabling conditions, and outcome should be measured by validated instruments which have proven their psychometric value in the whiplash condition. The research should include multivariate models making it possible to explore the significance of each different variable.

REFERENCES

1. Crowe H (1928) Injuries to the cervical spine. Paper presented at the Presentation to the annual meeting of the Western Orthopedic Association, San Francisco,

2. Eck J, C. , Hodges S, D. , Humphreys SC (2001) Whiplash: A review of a commonly misunderstood injury. American Journal of Medicine 110:651-656

3. Spitzer WO, Skovron ML, Salmi LR, Cassidy JD, Duranceau J, Suissa S, Zeiss E (1995) Scientific monograph on the quebec task force on whiplash-associated disorders: Redefining "whiplash" and its management. Spine 20 (suppl):1-73

4. Ferrari R, Russell AS, Carroll LJ, Cassidy JD (2005b) A re-examination of the whiplash associated disorders (wad) as a systemic illness. Ann Rheum Dis 64:1337-1342

5. Berglund A, Alfredsson L, Jensen I, Cassidy JD, Nygren Å (2001) The association between exposure to a rear-end collision and future health complaints. Journa of Clinical Epidemiology 54:851-856

6. Ferrari R (2003a) Myths of whiplash. Surg J R Coll Surg Edinb Irel 1 (2):99-103

7. Borchgrevink G, Smevik O, Haave I, Haraldseth O, Nordby A, Lereim I (1997a) Mri of cerebrum and cervical columna within two days after whiplash neck sprain injury. Injury 28 (5-6):331-335

8. Käll LB (2008) Psychological determinants of quality of life in patients with whiplash assoociated disorders - a prospective study. Disability and Rehabilitation:1-10

9. Radanov BP, Begré S, Sturzenegger M, Augustiny KF (1996) Course of psychological variables in whiplash injury--a 2-year follow-up with age, gender and education pair-matched patients. Pain 64 (3):429-434

10. Richter M, Ferrari R, Otte D, Kuensebeck H-W, Blauth M, Krettek C (2004) Correlation of clinical findings, collision parameters, and psychological factors in the outcome of whiplash associated disorders. J Neurol Neurosurg Psychiatry 75 (5):758-764

11. Hartling L, Brison RJ, Ardern C, Pickett W (2001) Prognostic value of the quebec classification of whiplash-associated disorders. Spine 26 (1):36-41

12. Kivioja J, Jensen I, Lindgren U (2008) Neither the wad-classification nor the quebec task force follow-up regiment seems to be important for the outcome after a whiplash

injury. A prospective study on 186 consecutive patients. . Eur Spine J 17:930-935. doi:10.1007/s00586-008-0675-0
13. Rø, M., Borchgrevink G, Dæhli B, Finset A, Lilleås F, Laake K, Nyland H, Loeb M (2000) Nakkeslengskade, diagnostikk og evaluering vol STF 78 A00405. SINTEF Unimed, Norsk Pasientregister,
14. Jansen G, Edlund C, CGrane P, Hildingsson C, Karlberg M, Link H, Mawe U, K. P, Rydevik B, Sterner Y (2008) Whiplash injuries: Diagnosis and early mangement. The swedish society of medicine and the whiplash commision medicl task force. . Eur Spine J 17 (Suppl 3):S355-417
15. WHO (1994) International classification of diseases version 10.
16. Siegmund G, Winkelstein R, Ivancic P, Svensson M, Vasavada A (2009) The anatomy and biomechanics of acute and chronic whiplash injury. Traffic Inj Prev 10:101-112
17. Pobereskin LH (2005) Whiplash following rear end collisions: A prospective cohort study. J Neurol Neurosurg Psychiatry 76 (8):1146-1151
18. Obelieniene D, Schrader H, Bovim G, Miseviciene I, Sand T (1999) Pain after whiplash: A prospective controlled inception cohort study. J Neurol Neurosurg Psychiatry 66:279-283
19. Shannon AL, Ferrari R, Russell AS (2006) Alberta rodeo athletes do not develop the chronic whiplash syndrome. J Rheumatol 33:975-977
20. Kamper SJ, Rebbeck TJ, Maher CG, McAuley JH, Sterling M (2008) Course and prognostic factors of whiplash: A systematic review and meta-analysis. Pain 138 (3):617-629
21. Tomlinson PJ, Gargan MF, Bannister GC (2005) The fluctuation in recovery following whiplash injury 7.5-year prospective review. Injury Int J Care Injured 36 (6):758-761
22. Carroll LJ, Holm LW, Hogg-Johnson S, Coté P, Cassidy JD, Halderman S, Nordin M, Hurwitz EL, Carragee EJ, van der Velde G, Peloso PM, Guzman J (2008c) Course and prognostic factors for neck pain in whiplash-associated disorders (wad): Results of the bone and joint decade 2000-2010 task force on neck pain and its associated disorders. Spine 33 (Suppl 4):S83-92

23. Hendriks EJM, Scholten-Peeters GGM, Windt DAWMvd, Neeleman-van der Steen CWM, Oostendorp RAB, Verhagen AP (2005) Prognostic factors for poor recovery in acute whiplash patients. Pain 114 (1-2):408-416
24. Williams M, Williamson E, Gates S, Lamb SE, Cooke M (2007) A systematic literature review of physical prognostic factors for the development of late whiplash syndrome. Spine 32 (25):E764-780
25. Williamson E, Williams M, Gates S, Lamb SE (2007) A systematic literature review of psychological factors and the development of late whiplash syndrome. Pain 135 (1-2):20-30
26. Conservative treatments for whiplash. (2007) John Wiley & Sons, Ltd.
27. Cassidy JD, Coté P (2008) Is it time for a population health approach to neck pain? J Manipulative Physicol Ther, vol 31. doi:10.1016/j.jmpt.2008.06.008
28. Coté P, Hogg-Johnson S, Cassidy J, Carroll L, Frank J, Bombardier C (2005) Inital patterns of clinical care and recovery from whiplash injuries: A population-based cohort study. Arch Intern Med 165:2257-2263
29. Coté P, Hogg-Johnson S, Cassidy J, Carroll L, Frank J, Bombardier C (2007) Early aggressive care and delayed recovery from whiplash: Isolated finding or reproducible result? Arthritis Rheum 57 (861-8). doi:10.1002/art.22775
30. Berglund A, Bodin L, Jensen I, Wiklund A, Alfredsson L (2006) The influence of prognostic factors on neck pain intensity, disability, anxiety and depression over a 2-year period in subjects with acute whiplash injury. Pain 125 (3):244-256
31. Coté P, Cassidy JD, Carrol L (2000) Is a lifetime history of neck injury in a traffic collision associated with prevalent neck pain, headache and depressive symptomatology? Accident Analysis and Prevention 32:151-159
32. Coté P, Cassidy JD, Carroll LJ, Frank JW, Bombardier C (2001a) A systematic review of the prognosis of acute whiplash and a new conceptual framework to synthesize the literature. Spine 26 (19):E445-458
33. Lovell ME, Galasko CSB (2002) Whiplash disorders - a review. Injury, Int J Care Injured 33:97-100. doi:10.1016/S0020-1383(01)00111-5
34. Guez M (2006) Chronic neck pain. An epidemiological, psychological and spect study with emphasis on whiplash associated disorders. Acta Orthopedica Supplementum 77 (320):3-33

35. Lees-Haley P, Brown R (1993) Neuropsychological complaint base rates of 170 personal injury claimants. Archives of clinical neuropsychology 8 (3):203-209
36. Banic B, Petersen-Felix S, Andersen OK, Radanov BP, Villiger PM, Arendt-Nielsen L, Curatolo M (2004) Evidence for spinal cord hypersensitivity in chronic pain after whiplash injury and in fibromyalgia. Pain 107:7-15
37. Laursen BS, Bajaj P, Olesen AS, Delmar C, Arendt-Nielsen L (2005) Health related quality of life and quantitative pain measurement in females with chronic non-malignant pain. European Journal of Pain 9:267-275
38. McCaffrey R, Frock TL, Garguilo H (2003) Understanding chronic pain and the mind-body connection. Holist Nurs Pract 17 (6):281-287
39. Eriksen HR, Svendsrød R, Ursin G, Ursin H (1998) Prevalence of subjective health complaints in the nordic european countries in 1993. European Journal of Public Health 8 (4):294-298
40. Escobar J, Cook B, Chen C-N, Gara M, A., Algría M, Interian A, Diaz E (2010) Whether medically unexplained or not, three or more concurrent somatic symptoms predict psychopathology and service use in community populations. J Psychosom Research 69:1-8. doi:10.1016/j.psychores.2010.01.001
41. Ihlebæk c, Eriksen HR, Ursin H (2002) Prevalence of subjective health complaints (shc) in norway. Scand J Public Health 30:20-29. doi:10.1177/14034948020300010701
42. Chappuis G, Soltermanna B (2008) Number and cost of claims linked to minor cervical trauma in europe: Results from the comparative study by cea, aredoc and ceredoc. Eur Spine J 17:1350-1357. doi:10.1007/s00586-008-0732-8
43. Holm LW, Carroll LJ, Cassidy JD, Hogg-Johnson S, Coté P, Guzman J, Peloso P, Nordin M, van der Velde G, Carragee E, Halderman S (2008a) The burden and determinants of neck pain in whiplash-associated disorders after traffic collisions: Results of the bone and joint decade 2000-2010 task force on neck pain and its associated disorders. Spine 33 (Suppl 4):S52-59
44. Bener A, Rahman YS, Mitra B (2009) Incidence and severity of head and neck injuries in victims of road traffic crashes: In an economically developed country. Int Emerg Nurs 17 (1):52-59
45. Bylund P, Björnstig U (1998) Sick leave and disability pension among passenger car occupants injured in urban traffic. Spine 23:1023-1028

46. Sterner Y, Toolanen G, Gerdle B, Hildingsson C (2003) The incidence of whiplash trauma and the effect of different factors on recovery. Journal of Spinal Disorders & Techniques 16 (2):195-199
47. Ferrari R, Constantoyannis C, Papadakis N (2003b) Laypersons' expectation of the sequelae of whiplash injury: A cross-cultural comparative study between canada and greece. Medical Science Monitor 3:CL 120-124
48. Ferrari R, Lang C (2005a) A cross-cultural comparison between canada and germany of symptom expectation for whiplash injury. J Spinal Disord Tech 18:92-97
49. Schrader H, Obelieniene D, Bovim G, Surkiene D, Mickeviciene D, Mickeviciene I (1996) Natural evolution of late whiplash syndrome outside the medicolegal context. Lancet 347 (9010):1207-1211
50. Borchgrevink G, Lereim I, Røyneland L, Bjørndal A, Haraldseth O (1996) National health insurance consumption and chronic symptoms following mild neck sprain injuries in car collisions. Scand J Soc Med 24 (4):264-271
51. Wallin MK, Raak RI (2008) Quality of life in subgroups of individuals with whiplash associated disorders. Eur J Pain 12 (7):842-849
52. Woodhouse A, Liljebäck., Vasseljen O (2010) Reduced head steadiness in whiplash and chronic non-traumatic neck pain patients. J Rehabil Med 42:35-41
53. Nederhand MJ, Hermens HJ, IJzerman MJ, Turk DC, Zilvold G (2003) Chronic neck pain disability due to an acute whiplash injury. Pain 102 (1-2):63-71
54. Woodhouse A, Vasseljen O (2008) Altered motor control patterns in whiplash and chronic neck pain. BMC Musculoskelet Disorder 9:90
55. Hincapié CA, Cassidy JD, Coté P, Carroll LJ, Guzmán J (2010) Whiplash injury is more than neck pain: A population-based study of pain localization after traffic injury. JOEM 52 (4):434-440. doi:10.1097/JOM.0b013e3181bb806d
56. Carroll LJ, Hogg-Johnson S, van der Velde G, Haldeman S, Holm LW, Carragee EJ, Hurwitz EL, Côté P, Nordin M, Peloso PM, Guzman J, Cassidy JD (2008e) Course and prognostic factors for neck pain in the general population. Results from the bone and joint decade 2000-2010 task force on neck pain and its associated disorders. Spine 33 (45):S75-82
57. Carroll LJ, Hogg-Johnson S, Coté P, van der Velde G, Holm LW, Carragee EJ, Hurwitz EL, Peolsson M, Cassidy JD, Guzman J, Nordin M, Halderman S (2008b)

Course and prognostic factors for neck pain in workers: Results of the bone and joint decade 2000-2010 task force on neck pain and its associated disorders. Spine 33 (Suppl 4):S93-100. doi:10.1097/BRS.0b013e31816445d4
58. Hogg-Johnson S, van der Velde G, Carroll LJ, Holm LW, Cassidy JD, Guzman J, Coté P, Halderman S, Ammendolia C, Carragee E, Hurwitz E, Nordin M, Peloso P (2008) The burden and determinants of neck pain in the general population: Results of the bone and joint decade 2000-2010 task force on neck pain and its associated disorders. Spine 33 (Suppl 4):S39-51
59. Binder A (2007) The diagnosis and treatment of nonspecific neck pain and whiplash. Eura Medicophys 43:79-89
60. Stordal E, Bjelland I, Dahl AA, Mykletun A (2003a) Anxiety and depression in individuals with somatic health problems. The nord-trøndelag health study (hunt). Scand J Prim Health Care 21 (3):136-141
61. Löve B, Spitzere R, Williams J, Mussell M, Schellberg D, Kroenke K (2008) Depression, anxiety and somatization in primary care: Syndrome overlap and functional impairment. Gen Hosp Psychiatry, vol 30. doi:10.1016/j.genhosppsych. 2008.01.001
62. Börsbo B, Peolsson M, Gerdie B (2008) Catastrophizing, depression, and pain: Correlation with and influence on quality of life and health - a study of chronic whiplash associated disorders. J Rehabil Med 40 (7):562-569. doi:10.2340/16501977-0207
63. Fishbain D, Cutler R, Rosomoff H, Rosomoff R (1997) Chronic pain-associated depression: Antecedent or consequence of chronic pain? A review. Clin J Pain 13:116-137
64. Sullivan MJL, Stanish W, Sullivan ME, Tripp D (2002b) Differential predictors of pain and disability in patients with whiplash injuries. Pain Res Manage 7 (2):68-74
65. Carroll LJ, Cassidy JD, Coté P (2006b) Frequency, timing and course of depressive symptomatology after whiplash. Spine 31 (16):E551-556
66. Phillips LA, Carroll LJ, Cassidy JD, Coté P (2010) Whiplash-associated disorders: Who gets depressed? Who stays depressed? Eur Spine J 19 (6):945-956. doi:10.1007/s00586-010-1276-2

67. Krohne K, Ihlebæk C (2010) Maintaining a balance: A focus group study on living and coping with chronic whiplash-associated disorder. BMC Musculoskeletal Disorders 11:158. doi:10.1186/1471-2472-11-158
68. Tsang A, von Korff M, Lee S, Alonso J, Karam E, Angermeyer M, Borges G, Bromet E, Demytteneare K, de Girolamo G, de Graaf R, Gureje O, Lepine J, Haro J, Levinson D, Oakley Browne M, Posada-Villa J, Seedat S, Watanabe M (2008) Common chronic pain conditions in developed and developing countries: Gender and age differences and comorbidity with depression-anxiety disorders. J Pain 9 (10):883-891. doi:10.1016/j.jpain.2008.05.005
69. Merrick D, Stalnacke B-M (2010) Five years post whiplash injury: Symptoms and psychological factors in recovered versus non-recovered. BMC Research Notes 3:190. doi:10.1186/1756-0500-3-190
70. Sulllivan M, Thibault P, Simmonds M, Milioto M, Cantin A, Velly A (2009) Pain, perceived injustice and the persistence of post-traumatic stress symptoms during the course of rehabilitation for whiplash injuries. Pain 145 (3):325-331
71. Rebbeck T, Sindhusake D, Cameron ID, Rubin G, Feyer AM, Walsh J, Gold M, Schofield WN (2006) A prospective cohort study of health outcomes following whiplash associated disorders in an australian population. Injury Prevention 12 (2):93-98
72. Ware JrJE (2000) Sf-36 health survey update. Spine 25 (24):3130-3139
73. Krogstad BS, Jokstad A, Dahl BL, Soboleva U (1998) Somatic complaints, psychological distress, and treatment outcome in two groups of tmd patients, one previously subjected to whiplash injury. J Orofacial Pain 12:136-144
74. Wallis BJ, Lord SM, Barnsley L, Bogduk N (1998) The psychological profiles of patients with whiplash-associated headache. Cephalalgia 18 (2):101-105
75. Walton D (2008) A review of the definition of 'recovery' used in prognostic studies on whiplash using an icf framework. Disability and Rehabilitation:1-15. doi:10.1080/09638280802404128
76. Gun R, Townsend., Osti OL, O'Riordan A, Mpelasoka F, Eckerwall CGM, Smyth JF (2005) Risk factors for prolonged disability after whiplash injury: A prospective study. Spine 30 (4):386-391

77. Heikkilä H, Heikkilä E, Eisemann M (1998) Predictive factors for the outcome of a multidisciplinary pain rehabilitation programme on sick-leave and life satisfaction in patients with whiplash trauma and other myofascial pain: A follow-up study. Clinical Rehabilitation 12:487-496
78. Peolsson M, Gerdie B (2004) Coping in patients with chronic whiplash-associated disorders: A descriptive study. J Rehabil Med 36 (1):28-35
79. Versteegen GJ, Dijkstra PU, Jaspers JPC, Meijler WJ, tenDuis HJ, Klip EC (2003) Sprain of the neck: Quality of life and psychological functioning. A 4-year retrospective study. Quality of Life Research 12 (3):335-343
80. Gargan MF, Bannister GC (1994) The rate of recovery following whiplash injury. Spine 3:162-164
81. Scholten-Peeters G, G M., Verhagen AP, Bekkering GE, Windt DAWMvd, Barnsley L, Oosendorp RAB, Hendriks EJM (2003) Prognostic factors of whiplash-associated disorders: A systematic review of prospective cohort studies. Pain 104 (1-2):303-322
82. Buitenhuis J, Spanjer J, Fidler V (2003) Recovery from acute whiplash. The role of coping styles. Spine 28 (9):896-901
83. Kivioja J, Jensen I, Lindgren U (2005) Early coping strategies do not influence the prognosis after whiplash injuries. Injury Int J Care Injured 36:935-940
84. Osti OL, Gun RT, Abraham G, Pratt NL, Eckerwall G, Nakamura H (2005) Potential risk factors for prolonged recovery following whiplash injury. Eur Spine J 14:90-94
85. Turner MA, Taylor PJ, Neal LA (2003) Physical and psychiatric predictors of late whiplash syndrome. Injury 34 (6):434-437
86. Söderlund A, Lindberg P (2003) Whiplash-associated disorders-predicting disability from a process-oriented perspective of coping. Clinical Rehabilitation 17 (1):101-107
87. Hagan K, Naqui S, Lovell ME (2007) Relationship between occupation, social class and time taken off work following a whiplash injury. Ann R Coll Surg Engl 89 (6):624-626
88. Hunter J (2001) Demographic variables and chronic pain. Clin J Pain 17 (Suppl 4):S14-19

89. Holm LW, Carroll LJ, Cassidy JD, Ahlbom A (2007) Factors influencing neck pain intensity in whiplash-associated disorders in sweden. Clin J Pain 27 (7):591-597. doi:10.1097/AJP.0b013e318100181f
90. Atherton K, Wiles NJ, Lecky FE, Hawes SJ, Silman AJ, Macfarlane GJ, Jones GT (2006) Predictors of persistent neck pain after whiplash injury. Emerg Med J 23:195-201. doi:10.1136/emj.2005.027102
91. Wynne-Jones G, Jones G, Wiles N, Silman A, Marfarlane G (2006) Predicting the new onset of widespread pain following a motor vehicle collision. J Rheumatol 33 (5):968-974
92. Miró J, Nieto R, Huguet A (2008) Predictive factors of chronic pain and disability in whiplash: A delphi poll. European Journal of Pain 12 (1):30-47
93. Carragee EJ (2008) Validity of self-reported history in patients with acute back or neck pain after motor vehicle accidents. The Spine Journal 8 (2):311-319
94. Lankester BJA, Garneti N, Gargan MF, Bannister GC (2006) Factors predicting outcome after injury in subjects pursuing litigation. Eur Spine J 15 (6):902-907. doi:10.107/s00586-005-0936-0
95. Lankester BJA, Garneti N, Bannister GC (2004) The classification of outcome following whiplash injury--a comparison of methods. Eur Spine J 13 (7):605-609
96. Berry H (2000) Chronic whiplash syndrome as a functional disorder. Arch Neurol 57:592-594
97. Castro WHM, Meyer SJ, Becke MER, Nentwig CG, Hein MF, Ercan BI, Thomann S, Wessels U, Du Chesne AE (2001) No stress-no whiplash? Prevalence of "whiplash" symptoms following exposure to a placebo rear-end collision. Int J Lega Med 114 (6):316-322
98. Myran R, Kvistad K, Nygård O, Andresen H, Folvik M, Zwart J (2008) Magnetic resonance imaging assessment of the alar ligament in whiplash injuries: A case-control study. Spine 33 (18):2012-2016
99. Myran R, Zwart J, Kvistad K, Folvik M, Lydersen S, Rø M, Woodhouse A, Nygård O (2011) Clinical characteristics, pain, and disability in relation to alar ligament mri findings. Spine 36 (13):E862-867
100. Bogduk N, Teasell R (2000) Whiplash. The evidence for an organic etiology. Arch Neurol 57:590-591

101. Slipman C, Lipetz J, Jackson H, Plastaras C, Vresilovic E (2001) Outcomes of therapeutic selective nerve root blocks for whiplash induced cervical radicular pain. Pain Physician 4 (2):167-174
102. Slipman C, Lipetz J, DePalma J, Jackson H (2004) Therapeutic selective nerve root block in the nonsurgical treatment of traumatically induced cervical spondylotic radicular pain. Am J Phys Med Rehabil 83 (6):446-454
103. Suissa S (2003) Risk factors of poor prognosis after whiplash injury. Pain Res Manage 8 (2):69-75
104. Ferrari R, Schrader H (2001d) The late whiplash syndrome: A biopsychosocial approach. J Neurol Psychiatry 70 (722-6)
105. Graves H, Scott D, Lempp H, Weinman J (2009) Illness beliefs predict disability in rheumatoid arthritis. J Psychosom Res 67 (5):417-423
106. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC (2007) The biopsychosocial approach to chronic pain: Scientific advances and future directions. Psychological Bulletin 133 (4):518-624
107. Carroll LJ, Cassidy JD, Coté P (2006a) The role of pain coping strategies in prognosis after whiplash injury: Passive coping predicts slowed recovery. Pain 124 (1-2):18-26
108. Jopson N, Moss-Morris R (2003) The role of illness severity and illness representations in adjusting to multiple sclerosis.. J Psychosom Res 54 (6):503-511
109. Juergens M, Seekatz B, Moosdorf R, Petrie K, Rief W (2010) Illness beliefs before cardiac surgery predict disability, quality of life, and depression 3 months later. J Psychosom Res 68 (6):553-560
110. Carroll LJ, Holm LW, Ferrari R, Ozegovic D, Cassidy JD (2009) Recovery in whiplash-associated disorders: Do you get what you expect? J Rheumatol 36 (5):1063-1070
111. Holm LW, Carroll LJ, Cassidy JD, Skillgate E, Ahlbom A (2008b) Expectations for recovery important in the prognosis of whiplash injuries. PLoS Medicine 5 (5):e105 (0767-0767). doi:10.1371/journal.pmed.0050105
112. Ozegovic D, Carroll LJ, Cassidy JD (2009) Does expecting mean achieving? The association between expecting to return to work and recovery in whiplash assoociated

disorders: A population-based prospective cohort study. Eur Spine J 18 (6):893-899. doi:0.1007/s00586-009-0954-4
113. Bunketorp L, Lindh M, Carlsson J, Stener-Victorin E (2006) The perception of pain and pain-related cognitions in subacute whiplash-associated disorders: Its influence on prolonged disability. Disabil Rehabil 28:271-279
114. Asghari A, Nicholas MK (2001) Pain self-efficacy beliefs and pain behaviour. A prospective study. Pain 94:85-100
115. Bostick GP, Ferrari R, Carrol LJ, Russell AS, Buchbinder R, Krawciw D, Gross DP (2009) A population-based survey of beliefs about neck pain from whiplash injury, work-related neck pain, and work-related upper extremity pain. European Journal of Pain 13 (3):300-304. doi:10.1016/j.epain.2008.04.003
116. Ferrari R, Russell A (2010e) Correlations between coping styles and symptom expectation for whiplash injury. Clin Rheumatol 29 (11):1245-1249. doi:10.1007/s10067-010-1443-1
117. Jensen MP, Turner JA, Romano JM, Karyly P (1991) Coping with chronic pain: A critical review. Pain, vol 47.
118. Carroll L, Mercado A, Cassidy J, Coté P (2002) A population-based study of factors associated with combinations of active and passive coping with neck and low back pain. J Rehabil Med 34 (2):67-72
119. McLean SA, Clauw DJ (2004) Predicting chronic symptoms after an acute "stressor"-lessioins learned from 3 medical conditions. Med Hypotheses 63 (4):653-658. doi:10.1016/j.mehy.2004.03.022
120. Ferrari R, Louw D (2011) Coping style as a predictor of compliance with referral to active rehabilitation in whiplash patients. Clin Rheumatolog 30 (9):1221-1225. doi:10.1007/s10067-011-1742-1
121. Joslin CC, Khan SN, Bannister GC (2004) Long-term disability after neck injury. A comparative study. The Journal of Bone and Joint surgery 86-B:1032-1034
122. Represas C, Vieira DN, Magalhães T, Dias R, Frazão S, Suárez-Peñaranda JM, Rodríguez-Calvo MS, Concheiro L, Muñoz JI (2008) No cash no whiplash?: Influence of the legal system on the incidence of whiplash injury. Journal of Forensic and Legal Medicine 15:353-355. doi:10.1016/j.jflm.2007.12.016

123. Cassidy JD, Carroll LJ, Coté P, Lemstra M, Berglund A, Nygren Å (2000) Effect of eliminating compensation for pain and suffering on the outcome of insurance claims for whiplash injury. N Engl J Med 342 (1179-86)
124. Ferrari R, Russell AS (1999c) Epidemiology of whiplash: An international dilemma. Ann Rheum Dis 58:1-5
125. Suissa S, Harder S, Veilleux M (2001) The relation between initial symptoms and signs and the prognosis of whiplash. Eur Spine J 10 (1):44-49
126. Barnsley L (2011) Whiplash. In: Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH (eds) Rheumatology, vol 1. Mosby, Elsevier, Philadelphia, pp 655-666
127. Barnsley L, Lord S, Bogduk N (1994) Whiplash injury. Pain 58:283-307
128. Schofferman J, Bogduk N, Slosar P (2007) Chronic whiplash and whiplash-associated disorders: An evidence-based approach. J Am Acad Orthop Surg 115 (10):596-606
129. Barsky AJ, Borus JF (1999) Functional somatic syndromes. Ann Intern Med 130:910-921
130. Wessely S, Nimnuan C, Sharpe M (1999) Functional somatic syndromes: One or many? Lancet 354:936-939
131. McLean SA, Clauw DJ (2005a) Biomedical models of fibromyalgia. Disabil Rehabil 27 (12):659-665. doi:10.1080/09638280400009048
132. Yunus MB (2008) Central sensitivity syndromes: A new paradigm and group nosology for fibromyalgia and overlapping conditions, and the related issue of disease versus illness. Sem Arthritis Rheum 37 (6):339-352. doi:10.1016/j.semarthrit.2007.09.003
133. McLean SA, Clauw DJ, Abelson JL, Liberzon I (2005b) The development of persistent pain and psychological morbidity after motor vehicle collision: Integrating the potential role of stress response systems into a biopsychosocial model. Psychosomatic Medicine 67:783-790
134. Ferrari R (2010b) Predicting central sensitisation - whiplash patients. Aust Fam Physician 39 (11):863-866

135. Haug TT, Mykletun A, Dahl AA (2004) The association between anxiety, depression, and somatic symptoms in a large population: The hunt-ii study. Psychosomatic Medicine 66:845-851
136. Harvey S, Wadsworth M, Wessely S, Hotopf M (2008) The relationship between prior psychiatric disorder and chronic fatigue: Evidence from a national birth cohort study. Psychological Medicine 38 (7):933-940
137. Haug TT, Mykletun A, Dahl AA (2002c) Are anxiety and depression related to gastrointestinal symptoms in the general population? Scand J Gastroenterol 37:294-298
138. Walker EA, Roy-Byrne PP, Katon WJ, Li L, Amos D, Jiranek G (1990) Psychiatric illness and irritable bowel syndrome: A comparison with inflammatory bowel disease. Am J Psychiatry 147 (12):1656-1661
139. Mykletun A, Jacka F, Williams L, Pasco J, Henry M, Nicholson G, Kotowicz M, Berk M (2010) Prevalence of mood and anxiety disorder in self reported irritable bowel syndrome (ibs). An epidemiological population based study of women. BMC Gastroenterol 10:88. doi:10.1186/1471-230X-10-88
140. Guzman J, Halderman S, Carroll LJ, Carragee EJ, Hurwitz EL, Peloso PM, Nordin M, Cassidy JD, Holm LW, Coté P, van der Velde G, Hogg-Johnson S (2008) Clinical practice implications of the bone and joint decade 2000-2010 task force on neck pain and its associated disorders: From concepts and findings to recommendations. Spine 33 (Suppl 4):S199-213
141. Aceves-Avila FJ, Ferrari R, Ramos-Remus C (2004) New insights into culture driven disorders. Best Practice & Clinical Rheumatology 18 (2):155-171
142. Forskningssenter H (2009) Hunt helseundersøkelsen i nord-trøndelag - lokalt, nasjonalt og internasjonalt fremragende. Hunt og ntnu mot 2020. Status og muligheter.
143. Holmen J, Midthjell K, Bjartveit K, Hjort PF, Lund-Larsen PG, Mooun T, Næss S, Waalder H, Th. (1990) The nord-trøndelag health survey 1984-86. Purpose, background and methods. Participation, non-participation and frequency distributions. Report 4/90. HUNT research centre,
144. Holmen J, Midthjell K, Krüger Ø, Langhammer A, Holmen T, Bratberg G, Vatten L, Lund-Larsen P (2003) The nord-trøndelag health study 1995-97 (hunt 2): Objectives, contents, methods and participation. Norsk epidemiologi 13:19-32

145. Snaith PR, Zigmond AS (1994) The hospital anxiety and depression scale manual. Windsor,
146. Zigmond AS, Snaith RP (1983) The hospital anxiety and depression scale. Acta Psychiatr Scand 67:361-370
147. Hermann C (1997) International experiences with the hospital anxiety and depression scale - a review of validation data and clinical results. J Psychosom Research 42 (1):17-41
148. Mykletun A, Stordal Ø, Dahl AA (2001) Hospital anxiety and depression (had) scale: Factor structure, item analysis and internal consistency in a large population. British Journal of Psychiatry 179:540-544
149. Association AP (1994) Diagnostic and statistical manual of mental disorders, fourth edition. Americal Psychiatric Association, Washington DC
150. Bjelland I, Dahl AA, Haug TT, Neckelmann D (2002) The validity of the hospital anxiety and depression scale. An updated literature review. Journal of Psychosomatic Research 52 (2):69-77
151. Walker EA, Keegan D, Gardner G, Sullivan M, Katon WJ, Bernstein D (1997) Psychosocial factors in fibromyalgia compared with rheumatoid arthritis: I. Psychiatric diagnoses and functional disability. Psychosomatic Medicine 59:565-571
152. Clauw DJ (2009) Fibromyalgia: An overview. The American Journal of Medicine 122 (12A):S3-13. doi:10.1016/j.amjmed.2009.09.006
153. Clauw DJ (2011) Fibromyalgia and related syndromes. In: Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH (eds) Rheumatology, vol 1. Mosby Elsevier, Philadelphia, pp 769-791
154. McLean SA, Williams DA, Clauw DJ (2005c) Fibromyalgia after motor vehicle collision: Evidence and implications. Traffic Inj Prev 6 (2):97-104
155. Brasington RD (2011) Clinical features of rheumatoid arthritis. In: Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH (eds) Rheumatology, vol 1. Mosby Elsevier, Philadelphia, pp 829-839
156. Tambs K, Moum T (1993) Low genetic effect and age-specific family effect for symptoms of anxiety and depression in nuclear families, halfsibs and twins. Journal of Affective Disorders 27:183-195

157. Hildrum B, Mykletun A, Holmen J, Dahl AA (2008) Effect of anxiety and depression on blood pressure: 11-year longitudinal population study. British Journal of Psychiatry 193 (2):108-113. doi:10.1192/bjp.bp.107.045013
158. Kuorinka I, Jonsson B, Kilbom A, Vinterberg H, Biering-Sørensen F, Andersson G, Jørgensen K (1987) Standardised nordic questionnaire for the analysis of musculoskeletal symptoms. Applied ergonomics 18:233-237
159. Palmer K, Smith G, Kellingray S, Cooper C (1999) Repeatability and validity of an upper limb and neck discomfort questionnaire: The utility of the standardized nordic questionnaire. Occup Med (London) 49 (3):171-175. doi:10.1093/occmed/49.3.171
160. Prince M (2003c) Cross-sectional surveys. In: Prince M, Steward R, Ford T, Hotopf M (eds) Practical psychiatric epidemiology. Oxford University Press, London, pp 111-132
161. Weich S, Prince M (2003) Cohort studies. In: Prince M, Steward R, Ford T, Hotopf M (eds) Practical psychiatric epidemiology. Oxford University Press, London, pp 13-41
162. Rothman KJ (2002) Using regression models in epidemiologic analysis. In: Rothman K (ed) Epidemiology and introduction. Oxford University Press, Oxford, pp 180-197
163. Rosner B (2006) Multiple logistic regression. In: Carolyn Crockett AD, Daniel Geller (ed) Fundmentals of biostatistics. Thomson Brooks, Duxbury, pp 668-676
164. Øverland S, Glozier N, Henderson M, Mæland JG, Hotopf M, Mykletun A (2008) Health status before, during and after disability; pension award: The hordaland health study (husk). Occupational and Environmental Medicine 65 (11):769-773. doi:10.1136/oem.2007.037861
165. Knudsen A, Hotopf M, Skogen J, Øverland S, Mykletun A (2010) The health status of non-participants in a population-based health study. The hordaland health study. Am J Epid 172 (11):1306-1314. doi:10.1093/aje/kwq257
166. Roberts S, Vingilis E, Wilk P, Seeley J (2008) A comparison of self-reported motor vehicle collision injuries compared with official collision data: An analysis of age and sex trends using the canadian national population health survey and transport canada data. Accid Anal Prev 40:559-566

167. Carey TS, Garrett J, Jackman A, Sanders L, Kalsbeek W (1995) Reporting of acute low back pain in a telephone interview. Identification of potential biases. . Spine 20 (7):787-790
168. Waddell G, Main CJ, Morris EW, Venner RM, Rae PS, Sharmy SH, Galloway H (1982) Normality and reliability in the clinical assessment of backache. Br Med J 284 (6328):1519-1523
169. Ngo T, Stupar M, Coté P, Boyle E, Shearer H (2010) A study of the test-retest reliability of the self-perceived general recovery and self-perceived change in neck pain questions in patients with recent whiplash disorders. Eur Spine J 19 (6):957-962. doi:10.1007/s00586-010-1289-x
170. Prince M (2003a) Measurement in psychiatry. In: Prince M, Steward R, Ford T, Hotopf M (eds) Practical psychiatric epidemiology. Oxford London, pp 13-41
171. Nord C, Mykletun A, Fosså SD (2003) Cancer patients' awareness about their diagnosis: A population-based study. J Public Health Med 25 (4):313-317. doi:10.1093/pubmed/fdg076
172. Brunnauer A, Laux G, Geiger E, Soyka M, Möller H (2006) Antidepressants and driving ability: Results from a clinical study. The Journal of Clinical Psychiatry 67 (11):1776-1781
173. Kringlen E, Torgersen S, Cramer V (2001) A norwegian psychiatric epidemiological study. Am J Psychiatry 158 (7):1091-1098
174. Simon GE, von Korff M, Piccinelli M, Fullerton C, Ormel J (1999) An international study of the relation between somatic symptoms and depression. The New England Journal of Medicine 341 (18):1329-1335
175. Blanchard EB, Hickling EJ, Taylor AE, Loos WR (1995) Psychiatric morbidity associated with motor vehicle accidents. J Nerv Ment Dis 183 (8):495-504
176. Härter MC, Conway KP, Merikangas KR (2003) Associations between anxiety disorders and physical illness. Eur Arch Psychiatry Clin Neurosci 253:313-320
177. Stordal E, Mykletun A, Dahl AA (2003b) The association between age and depression in the general population: A multivariate examination. Acta Psychiatr Scand 1007:132-141
178. Mykletun A, Overland S, Dahl AA, Krokstad S, Bjerkeset O, Glozier N, Aarø LE, Prince M (2006b) A population-based cohort study of the effect of common mental

disorders on disability pension awards.T. The American Journal of Psychiatry 163 (8):1412-1418

Paper I

ELSEVIER

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A population study of anxiety and depression among persons who report whiplash traumas

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Abstract

The purpose of this study was to explore whether self-reported whiplash traumas were associated with increased prevalence of anxiety disorder and depression. A cross-sectional design ($N = 61{,}110$) based on data from the health study (HUNT-II) was used. Anxiety and depression were measured with the Hospital Anxiety and Depression Scale (HADS). A positive association was found between whiplash traumas and anxiety disorder and depression in traumas that happened more than 2 years ago, but not in more recent whiplash traumas. Some of the association between whiplash traumas and anxiety and depression is due to neck pain and headache. Two different explanations, the ''memory bias'' and the ''attribution'' hypothesis, are discussed as explanations of these results.

Keywords: Whiplash; Anxiety; Depression; Headache; Neck pain

Introduction

''Whiplash'' is not a diagnosis, but describes a mechanism of trauma with sudden acceleration–deceleration forces acting on the neck and upper trunk, exerting a ''lash-like'' effect on the neck. The typical trauma is a road traffic accident with a rear-end collision. The whiplash trauma is essentially transient and benign, and the majority of patients recover within 2 years. [1,14]. However, a sizeable proportion, especially among those managed in hospitals or specialist services, describes persisting physical and psychological problems that may result in disability and litigation for personal injury. In a prospective study from an English emergency ward [4], 47% of whiplash patients were still symptomatic after 1 year, and 61% after 2 years, however, only 1% had persistently disabling symptoms. Most patients have reached their final state within 2 years. The persistent whiplash syndrome could be considered in the same way as other disorders with a close interaction of physical, psychological, and social variables [10,13].

Mental symptoms after whiplash traumas are common. In a 1-year follow-up study from an English emergency department [12], 40% of the patients had clinically significant mental problems, and 12% fulfilled the diagnostic criteria for a mood disorder diagnosed by the Present State Examination, compared to 5% in the general population. Nineteen percent of the patients developed a phobic travel anxiety, and 5% manifested symptoms of posttraumatic stress disorder. However, patients who suffer from mood disorder at 1-year follow-up showed substantial predisposing and maintaining factors of the mental disorder, independent of the road traffic accident [11,13].

Several factors might relate to the mental symptoms associated with the whiplash syndrome, and the significance of the trauma in itself is uncertain. Malt [10], in a prospective study of accidental injured adults in Norway, found no more mental disorders than could be expected after illness in general. The most important pathogenic factor, in his study, seemed to be the chronic pain, which could follow the injury. Chronic pain was shown to be closely related to mental problems.

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Table 1
Prevalence of whiplash traumas according to age and gender

		N total	*N* (%) whiplash	*N* (%) HADS-A ≥ 8	*N* (%) HADS-D ≥ 8
Total		61,110	1704 (2.8)	9479 (15.5)	6643 (10.9)
Gender	Males	28,927	847 (2.9)	3606 (12.5)	3244 (11.2)
	Females	32,183	857 (2.7)	5873 (18.2)	3399 (10.6)
Age	18–39 years	20,010	588 (3.2)	3006 (15.0)	1145 (5.7)
	40–59 years	24,126	761 (2.1)	4087 (16.9)	2734 (11.3)
	60–89 years	16,974	355 (2.8)	2386 (14.1)	2764 (16.3)

All chi-square asymp. significance $<.05$ (two-sided).

This study examined self-reported whiplash traumas in a large community population. The aim of this study was to: (a) estimate the prevalence of self-reported whiplash injuries in this population; (b) test the hypothesis that such traumas were associated with increased prevalence of anxiety disorders and depression after the trauma; and (c) test the hypothesis that the prevalences of anxiety disorders and depression are elevated also before the whiplash injury.

Material and methodology

Based on updated population register lists, all inhabitants aged 20 years and above in the 24 municipalities of Nord-Trøndelag County received a mailed, personal invitation to take part in the Health Study of Nord-Trøndelag County 1995–1997 (HUNT-II), with an appointment date and time for physical examination carried out locally. The invitation also included a questionnaire that should be filled in and brought to the appointment.

Population register lists were found in all municipalities and were based on unique personal identification numbers. According to these lists, 92,100 individuals aged 20 to 89 were eligible for HUNT-II, and 61,110 participated in the study with valid responses on all relevant variables (66.4%).

Description of Hospital Anxiety and Depression Scale (HADS)

HADS consists of 14 items, seven for anxiety (HADS-A) and seven for depression (HADS-D) formulated in a language that is readily understandable [19]. Symptoms of severe psychopathology are not included in HADS, and this makes HADS more sensitive to milder psychopathology, thus avoiding the "floor effect" that has been frequently observed when psychiatric rating scales have been used in nonpsychiatric samples. HADS is well accepted in both psychiatric and nonpsychiatric settings and is completed in 2–6 min [6,13]. The psychometric properties of HADS are examined in HUNT-II and are considered as good [15]. The cutoff level for possible cases of anxiety disorder and depression is recommended at scores ≥ 8 on each subscale, and ≥ 14 of the HADS total score [2,17]. A valid HADS-A or HADS-D rating was defined as at least five completed items on each subscale. Those who filled in five or six items were also included in the study, and their score was based on the sum of valid items multiplied with 7/5 or 7/6, respectively.

Description of relevant items from the questionnaire

Whiplash injuries were investigated with the following questions: "Have you ever experienced whiplash?" and "Age for last episode of whiplash." No answer on the whiplash question was counted as "No"; and cases with indication of "Age for last episode of whiplash," but no response to the first whiplash question, were counted as "Yes." Based on the responses to these questions, the material was divided into four groups: "no whiplash," "up to 2 years since whiplash," "more than 2 years since whiplash," and "time since whiplash unknown." Headache was recorded with the question: "Have you been bothered by headache during the last 12 month?" Headache included both migraine and other forms of headache. Neck pain was recorded with the questions: "Have you had aches in muscles and/or joints during the last month? If yes, please

Table 2
Prevalence of anxiety and depression according to whiplash trauma

	HADS-A ≥ 8			HADS-D ≥ 8			HADS total ≥ 14		
	N	%	95% CI	*N*	%	95% CI	*N*	%	95% CI
Total (61,110)	9479	15.5	15.2–15.8	6643	10.9	10.6–11.1	9031	14.8	14.5–15.1
No whiplash	9067	15.3	15.0–15.6	6387	10.8	10.5–11.0	8658	14.6	14.3–14.9
Whiplash (1704)	412	24.2	22.1–26.2	256	15.0	13.3–16.7	373	21.9	19.9–23.6
0–2 years ago (158)	27	17.1	11.1–23.0	15	9.5	4.9–14.1	21	13.3	7.9–18.6
>2 years ago (838)	211	25.2	22.2–28.1	130	15.5	13.1–18.0	189	22.6	19.7–25.4
No date reg. (708)	174	24.6	21.4–27.8	111	15.7	13.0–18.4	163	23.0	19.9–26.1

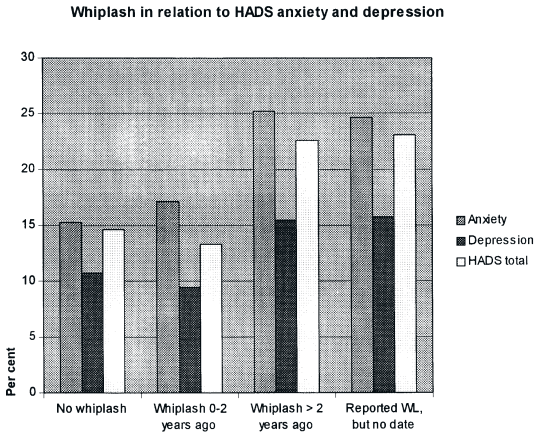

Fig. 1.

indicate where," with nine different alternative body parts including the neck.

Weighting procedures

Weighting according to the procedure used in National Comorbidity Study [8] was performed to adjust for difference in response rate according to age and gender, and also for age and gender differences between the population of Nord-Trøndelag County and the population of Norway aged 20 years and above. The weighting procedure was based on the National Population Statistics of 1996. Weighting did not alter any conclusions, and reported results are nonweighted.

Statistics

A binary blockwise logistic regression analysis with three models was performed to explore the risk for anxiety disorder and depression when controlled for the effect of other relevant variables. Model 1 showed the crude effect of the whiplash trauma, Model 2 with adjustment for gender and age, and Model 3 with additional adjustment for headache and neck pain. The level of significance was set to $P \leq .05$.

Ethics

HUNT-II was approved by the National Data Inspectorate and the Board of Research Ethics in Health region IV of Norway.

Results

Totally, 1704 subjects (2.8%) of the 61.110 who attended the HUNT study, self-reported a whiplash trauma, and 996 also reported their age at the (first) whiplash injury. The prevalences were approximately equal among men and women, and highest in the youngest age group (Table 1). One hundred fifty-eight subjects reported that the time since the trauma was within 2 years, 838 subjects reported more than 2 years since the trauma, and 708 subjects did not give any time interval.

The proportion of HUNT attendants that fulfilled the criterion for a possible anxiety disorder (HADS-A ≥ 8) was 15.5%, and 10.9% fulfilled the criterion for depression (HADS-D ≥ 8). In the whiplash group, both these propor-

Table 3
Anxiety and depression in accordance to whiplash: a multivariate model

	Model 1: crude effects		Model 2: adjusted age and gender		Model 3: adjusted age, gender, headache, neck pain	
	Exp(*B*)	95% CI	Exp(*B*)	95% CI	Exp(*B*)	95% CI
HADS ≥ 14						
No whiplash (WL)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)
WL 0–2 years ago	0.90	0.57–1.42	0.98	0.62–1.56	0.68	0.43–1.09
WL >2 years ago	1.71*	1.45–2.01	1.78*	1.51–2.09	1.26*	1.07–1.49
WL, no date reg.	1.75*	1.47–2.09	1.76*	1.47–2.10	1.18	0.99–1.42
Anxiety						
No whiplash (WL)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)
WL 0–2 years ago	1.14	0.76–1.73	1.13	0.74–1.71	0.76	0.51–1.18
WL >2 years ago	1.87*	1.60–2.19	1.89*	1.61–2.21	1.33*	1.13–1.56
WL, no date reg.	1.81*	1.52–2.15	1.81*	1.52–2.15	1.21*	1.01–1.44
Depression						
No whiplash (WL)	1.00	(Ref.)	1.00	(Ref.)	1.00	(Ref.)
WL 0–2 years ago	0.87	0.51–1.48	1.07	0.62–1.83	0.79	0.46–1.36
WL >2 years ago	1.52*	1.26–1.84	1.64*	1.35–1.98	1.22*	1.01–1.46
WL, no date reg.	1.54*	1.26–1.89	1.55*	1.26–1.91	1.11	0.90–1.37

Effects are odds ratios (OR) obtained from logistic regression analyses. Reference category is "no history of whiplash."

* $P < .05$. Anxiety and depression are measured by HADS. $N = 61{,}110$.

tions were significantly elevated to 24.2% and 15.0%, respectively (Table 2). Subjects with a recent whiplash injury (≤ 2 years ago) reported HADS-scores no different from the group without whiplash traumas, while those who reported whiplash for more than 2 years ago or without specification of age by whiplash injury reported an elevated anxiety and depression score (Fig. 1).

Model 1 in Table 3 showed a significantly increased risk of possible anxiety disorder and depression (HADS-A and HADS-D ≥ 8) in the groups reporting whiplash trauma more than 2 years ago, or without any date given [Odds Ratios (OR) in the range 1.71–1.87]. In accordance with the prevalences indicated in Table 2, there was no increased whiplash risk in those who reported whiplash less than 2 years ago. The ORs for anxiety disorders were slightly higher than for depression. In Model 2, the effects were adjusted for age and gender, and this did not alter the results from Model 1. Adjustment for symptoms of headache and neck pain reduced the effects on both anxiety disorder and depression for whiplash traumas more than 2 years ago, to OR 1.22 for depression and 1.33 for anxiety. The effect of whiplash without a specified date on depression was nonsignificant.

Discussion

We found a prevalence of whiplash traumas of 2.8%, which was much lower than expected according to the literature. From Table 2, we estimated the yearly incidence of whiplash trauma to be 0.13%, since 158 of the 61,110 attendants reported a whiplash trauma within the last 2 years. If we assume the proportion of drivers and the risk of a whiplash trauma to be equal in all age groups, and the period of active driving to be 60 years, the expected prevalence of whiplash traumas should be 7.8%. The discrepancy between the observed and the expected prevalence indicates a marked underreporting of whiplash traumas in our study. Côte et al. [3] reported that 15.9% in a population-based cross-sectional survey had a lifetime history of neck injury after a traffic accident. We found increased prevalence of anxiety disorder and depression when the trauma was more than 2 years ago or the time was not given. However, in the short time group, the incidence of anxiety disorder and depression was not significantly increased.

This study examined a large unselected population, which gave a unique opportunity to study the occurrence of mental symptoms after whiplash traumas. However, our study design also has some definite methodological shortcomings. The judgement of a whiplash trauma was left up to the attendants and, thereby, lacked a medical confirmation. The definition was entirely subjective, and we had to accept individual differences in what was perceived as a "whiplash trauma." Another problem has to do with long-term recall and retrospective evaluations. Finally, it is important to mention that other factors aside from whiplash trauma and its consequences might also have significance in the occurrence of mental disorders after whiplash traumas. Malt [10] stressed the importance of correcting for other life events during the follow-up period, and Mayou et al. [11] mentioned chronic social difficulties as an important factor for such disorders. In our study, we did not have such information, but we assumed that the distribution of such factors in the whiplash group was no different from the population, and rated this methodological weakness insignificant.

To explain the assumed underreporting and the increased prevalence of anxiety disorder and depression in the long time and unknown time whiplash groups, we suggest a "memory bias hypothesis," which proposes that minor traumas with few symptoms are easily forgotten as time passes, and consequently, they will not be reported. The "memory bias hypothesis" explains why traumas that occurred more than 2 years ago and without a given time frame have a higher prevalence of anxiety disorders and depression than more recent whiplash traumas. However, we also entertain an alternative hypothesis to explain these findings, namely, the "attribution hypothesis," which proposes that preexisting mental symptoms, before the whiplash trauma, are the main cause of the symptoms that are attributed to that injury. Because of these preexisting symptoms, the subjects are more observant on trauma, and look for an explanation of their symptoms. This could result in overrepresentations of subjects with manifest symptoms, among those reporting a whiplash trauma. However, we had no possibility to test this hypothesis in our study, as we did not know whether the anxiety disorder or depression had been present before or only after the trauma. The attribution hypothesis is in agreement with observations made by Côte et al. [3], who found a substantial amount of coexisting health problems in subjects who reported a neck injury compared to persons without such injury. Schrader et al. [18], in a study of the natural evolution of late whiplash syndrome outside the medico-legal context, found that chronic symptoms were not usually caused by car accidents. Expectation of disability, a family history of and attribution of preexisting symptoms to the trauma may be more important determinants for the evolution of the late whiplash syndrome. Malt [10] also reported that in some cases the patient attributed distress present before the accident to consequences of the injury. In the crude analyses, we found that the whiplash traumas were associated with anxiety disorder and depression in the long-term and unspecified term groups. However, when we controlled for the effect of somatic complaints, headache, and neck pain, this association was reduced for anxiety disorders and disappeared for depression. This result indicated that the injury per se was not the main cause of the mental symptoms, but rather the somatic complaints that could be a consequence of the trauma. The relationship between chronic pain and mental disorders is well established [9]. For example, Holroyd et al. [7], in a study of individuals with chronic tension-type headaches in the general popu-

lation, found that they were 3–15 times more likely than matched controls to receive a diagnosis of anxiety or mood disorder, with almost half of them showing clinically significant levels of anxiety and depression. Gureje et al. [5] demonstrated a strong longitudinal relationship between persistent pain and mental disorder, however, the relationship seemed to be symmetrical. Pain predicted the later onset of a mental disorder just as well as a mental disorder predicted the onset of persistent pain. In a comparison of Symptom Checklist 90-profiles from patients with chronic pain from whiplash traumas and patients with other musculoskeletal injuries, Peebles et al. [16] found no support for a distinctive profile for whiplash patients. Instead, the results suggested that the psychological consequences of experiencing chronic pain from whiplash-associated disorders were similar to the psychological consequences of chronic pain from other musculoskeletal injuries.

In conclusion, our findings suggested an increased prevalence of anxiety disorders and depression after self-reported whiplash traumas that happened more than 2 years ago. However, when we controlled for possible confounders, the mental disorders could be explained by the effect of pains and aches from the head and neck. This result suggested that whiplash traumas should be considered in the same way as other chronic pain syndromes.

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References

[1] Barrett K, Buxton N, Redmond AD, Jones JM, Boughey A, Ward AB. A comparison of symptoms experienced following minor head injury and acute neck strain (whiplash injury). J Accid Emerg Med 1995;12:173–6.
[2] Bjelland I, Dahl AA, Haug TT, Neckelmann DOG. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res 2002;52:69–77.
[3] Côte P, Cassidy JD, Carroll L. Is lifetime history of neck injury in a traffic collision associated with prevalent neck pain, headache and depressive symptomatology? Accid Anal Prev 2000;32:151–9.
[4] Gargan MF, Bannister GC. The rate of recovery following whiplash injury. Eur Spine J 1994;3:162–4.
[5] Gureje O, Simon GE, Von Korff M. A cross-national study of the course of persistent pain in primary care. Pain 2001;92:195–200.
[6] Herman C. International experiences with the Hospital Anxiety and Depression Scale — a review of validation data and clinical results. J Psychosom Res 1997;42:17–41.
[7] Holroyd KA, Stensland M, Lipchik GL, Hill KR, O'Donnell FS, Cordingley G. Psychosocial correlates and impact of chronic tension-type headaches. Headache 2000;40:3–16.
[8] Kessler RC, McGonagle KA, Zhao KA, Nelson CB, Hughes M, Eshleman S, Wittchen HU, Kendler KS. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: results from the National Comorbidity Survey. Arch Gen Psychiatry 1994;51:8–19.
[9] Lee J, Giles K, Drummond PD. Psychological disturbances and an exaggerated response to pain in patients with whiplash injury. J Psychosom Res 1993;37:105–10.
[10] Malt U. The long-term psychiatric consequences of accidental injury. Br J Psychiatry 1993;153:810–8.
[11] Mayou R, Bryant B, Duthie R. Psychiatric consequences of road traffic accidents. Br Med J 1993;307:647–51.
[12] Mayou R, Bryant B. Outcome of ''whiplash'' neck injury. Injury 1996;27:617–23.
[13] Mayou R, Radanov BP. Whiplash neck injury. J Psychosom Res 1996;40:461–74.
[14] Mayou R, Tyndel S, Bryant B. Long-term outcome of motor vehicle accident injury. Psychosom Med 1997;59:578–84.
[15] Mykletun A, Stordal E, Dahl AA. The Hospital Anxiety and Depression Scale (HAD): factor structure, item analyses, and internal consistency in a large population. Br J Psychiatry 2001;179:540–4.
[16] Peebles JE, McWilliams LA, MacLennan R. A comparison of symptom checklist 90-revised profiles from patients with chronic pain from whiplash and patients with other musculo-skeletal injuries. Spine 2001;26:766–70.
[17] Radanov BP, Begré S, Sturzenegger M, Augustiny KF. Course of psychological variables in whiplash injury — a 2 year follow-up with age, gender and education pair-matched patients. Pain 1996;64:429–34.
[18] Schrader H, Obelieniene D, Bovim G, Surkiene D, Mickeviciene D, Miseviciene I, Sand T. Natural evolution of late whiplash syndrome outside the medicolegal context. Lancet 1996;347:1207–11.
[19] Snaith RP, Zigmond AS. The Hospital Anxiety and Depression Scale manual. Windsor: NFER-NELSON, 1994.

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ORIGINAL ARTICLE

Symptom profile of persons self-reporting whiplash: a Norwegian population-based study (HUNT 2)

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Abstract The aetiology of chronic whiplash associated disorder (WAD) is unclear and the condition has been perceived both as a chronic pain disorder, based on the injury to the neck, and as a functional somatic disorder. Based on the hypothesis that chronic WAD should be perceived as a functional somatic syndrome, we compared the symptom profile of persons with chronic WAD with the profile of persons with a functional somatic disorder, and with the profile of persons with an organic pain disorder. A sample of 55,046 persons participating in a Norwegian population-based health study (HUNT 2) was divided into four study groups: chronic WAD, fibromyalgia, rheumatoid arthritis, and controls (none of these disorders). Symptoms were categorized as pain and stiffness, cardiopulmonary and gastrointestinal symptoms, and mental disorders. Odds ratios (ORs) with 95% confidence intervals (CIs) from logistic regression were used to compare the prevalence of symptoms among the groups. The chronic WAD group had a significantly higher prevalence of symptoms from all body parts, across organ systems and also mental symptoms, compared to the control group. The fibromyalgia group had an even higher prevalence of all symptoms, while the rheumatoid arthritis group showed an increase in the prevalence of particularly pain and stiffness symptoms and also a minor increase in the prevalence of other symptoms compared to the control group. We conclude that this study provide evidence in favour of the hypothesis that chronic WAD should be perceived as a functional somatic syndrome. Persons with chronic WAD had a symptom profile more similar to people with a functional somatic disorder than an organic pain disorder, consisting of a wide array of symptoms, not only predominantly pain symptoms.

Keywords Whiplash · Symptom profile · Functional disorder · Pain disorder

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Introduction

The term 'whiplash associated disorders' (WAD) was introduced in 1995 by the Quebec Task force as a grading system for whiplash associated disorders ranging from grade 0 with no symptoms to grade IV with neck pain or stiffness associated with cervical dislocation or fracture [39]. Grades I

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and II which include only soft tissue injuries represent almost 90% of whiplash injuries and represent what is usually associated with the term WAD [22]. The incidence of WAD has increased rapidly during the last 20 years and is now estimated to be approximately 4 per 1,000 persons in Western countries [2, 11, 14, 26].

Several studies have investigated the course and the prognosis of whiplash, and it has been reported that 14–50% of acute WAD progress to chronic WAD [2, 12, 21, 35] with 28% of residual symptoms being intrusive and 12% being severe [19, 21]. Typically the symptoms also change character, from symptoms located to the neck and head, to more complex somatic symptoms as well as several problems of a psychosocial character often accompanied by gross disability [4, 11, 17, 40].

To explain the wide variety of symptoms, without clear objective findings, their long-lasting character as well as varying prevalence of chronic WAD in different cultures it has been necessary to take a biopsychosocial perspective on the disorder, suggesting that symptoms arise from and are modulated by pathology, psychological factors, and social context [18, 28]. Some authors have perceived the condition as a chronic pain condition [27, 28, 33, 34] based on the injury to the neck and surrounding structures, while others suggest that chronic WAD should be considered a functional somatic syndrome.

The chronic pain disorder could be described by a biopsychsocial pain model: nociceptive stimuli reach the brain through affective pathways, are evaluated and interpreted in the central nervous system, and then relayed back through efferent pathways in the peripheral nervous system. The pain threshold may vary with psychological and cultural factors as indicated by the gate control theory and the effect of different neurotransmitters. However the pain experience has a distinct quality, and should not be mistaken as other kind of sensations or symptoms [20, 28].

The term functional somatic syndrome is defined as a condition, which involve disturbance of function without physical abnormality [5]. Several different functional somatic syndromes have been described among these fibromyalgia and chronic whiplash [3]. All these syndromes are characterized by a great array of different and diffuse symptoms. On the basis of a literature review, Wessely et al. [41] concluded that a substantial overlap exists between the individual syndromes and that the similarities between them outweigh the differences. Similarities were apparent in case definition, reported symptoms, and non-symptom associations.

For a long time researchers have tried to find structural changes in the neck suspecting that occult lesions in discs, ligaments, and joints were the cause of WAD symptoms [24]. Improvements in medical imaging techniques have made it possible to visualize small lesions in the cervicocranial junctions, although these findings may not differ from those found in persons without whiplash trauma [8, 16]. Thus, it has not been possible to document any causal connection between these findings and the symptoms of WAD [30]. Moreover, symptoms arising from the neck constitute only a small part of the wide variety of symptoms described for WAD [4, 17].

Given these findings, we hypothesised that chronic WAD should be perceived primarily as a functional somatic syndrome. To explore this hypothesis we used information from a large health study that was conducted in Norway between 1995 and 1997 to compare the symptom profile of persons with chronic WAD to that of people with either a functional somatic syndrome (fibromyalgia), an organic pain disorder (rheumatoid arthritis), or a control group without any of these disorders.

Materials and methods

Study population

Between 1995 and 1997, all inhabitants aged 20 years or more who lived in the county of Nord-Trøndelag, Norway, were invited to participate in the second wave of the Nord-Trøndelag Health Study (HUNT 2). The Nord-Trøndelag Health Study (The HUNT Study) is a collaboration between the HUNT Research Centre, Faculty of Medicine, Norwegian University of Science and Technology, The Norwegian Institute of Public Health, and Nord-Trøndelag County Council.

Among the 92,936 persons who were eligible to participate, 65,604 (70.6%) accepted the invitation, filled in questionnaires, and attended a clinical examination. The clinical examination included standardized measures of height, weight, hip and waist circumference, blood pressure, and heart rate. Additionally, a blood sample was drawn and stored in a freezer for later analysis. Briefly, information was collected on a range of lifestyle and health-related factors. Included in this study were persons who had answered questions concerning whiplash, fibromyalgia, and rheumatoid arthritis. For the purpose of the present study, we were interested in persons reporting either chronic WAD (defined as the report of a whiplash trauma and long-term neck pain) or fibromyalgia or rheumatoid arthritis or none of these disorders. Consequently only persons answering these questions were included, cases of comorbidity were excluded, and persons reporting whiplash but no long-term neck pain were also excluded. This left us with 55,046 persons (26,599 males and 28,447 females) who were available for statistical analysis (Fig. 1).

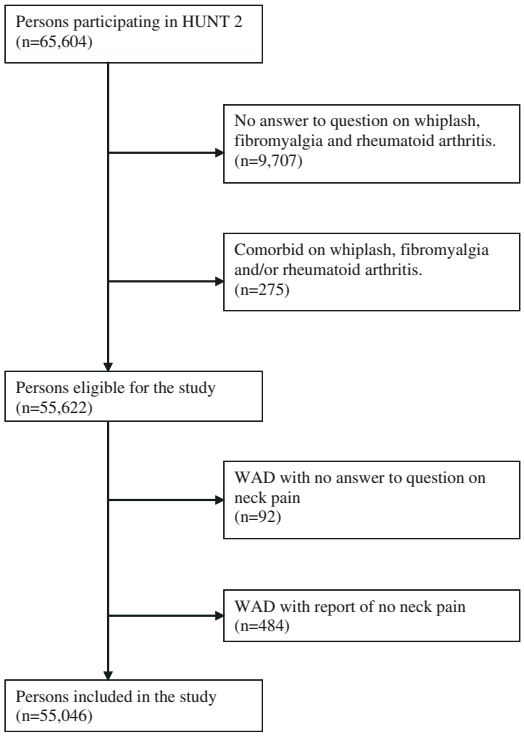

Fig. 1 Flow diagram of inclusion and exclusion of participants to the study

Study variables

Whiplash trauma was self-reported and defined by the question "Have you ever had neck injury (whiplash)?" Those who responded confirmatively on this question and who further reported neck pain and stiffness for at least three consecutive months during the last year were defined as having chronic WAD and were included in the present study. The participants were also asked to report physician diagnosed fibromyalgia and rheumatoid arthritis. Based on their response, the participants were classified into four mutually exclusive groups: (a) a reference group with none of these disorders, (b) chronic WAD, (c) fibromyalgia, and (d) rheumatoid arthritis.

Symptoms were self-reported and classified into three groups: (a) pain and stiffness in different body areas; (b) other symptoms, including gastrointestinal symptoms, palpitations, and breathlessness; and (c) mental health.

Participants were asked: "During the last year, have you had pain and/or stiffness in the muscles and limbs, which has lasted for at least three consecutive months?" and if YES: "Where did you have these complaints?" and "Please, indicate the region for which the complaints lasted longest". The participants were also asked "Have you been troubled by headaches in the last 12 months?" (both attacks (migraines) and "other types of headaches"). Only "other types of headaches" were included in this study.

Other symptoms were registered by asking: "To what degree have you had these disorders in the last 12 months?" with "not at all", "slightly", and "very much" as response options. For analytical purposes, the two latter categories were collapsed.

Mental health was recorded by the 'Hospital Anxiety and Depression Scale' (HADS), which is a self-report questionnaire consisting of 14 four-point Likert-scaled items, 7 for anxiety and 7 for depression. No somatic items are included. According to a recent literature review, the HADS showed good case-finding properties for anxiety and depression in primary care and somatic patient sample. A cut-off score of 8 on both subscales was found to give an optimal balance between sensitivity and specificity at about 0.80 for, respectively, depression and anxiety according to DSM-III, DSM-IV, ICD-8, and ICD-9 [7]. Case-finding properties of HADS are found to be comparable to or better than that of general practitioners in clinical examinations [31]. Further, the psychometric properties in terms of factor structure and internal consistency of sub-scales are found to be good [29]. In accordance with previous studies using HADS, a valid HADS subscale rating was defined as at least five completed items, one or two missing responses substituted by the individual's own mean score on valid responses [23].

There are some missing responses to variables on different symptoms as is indicated in the tables. In the analyses these values are not included, and only valid responses are considered.

Statistics

We used logistic regression analyses to compute odds ratios (ORs) and 95% confidence intervals (CIs) for symptoms in the different study groups (fibromyalgia, rheumatoid arthritis, and chronic WAD) using the control group as the reference group. The analyses were performed with two different adjustments in addition to the crude analyses. First we adjusted for the effect of demographic factors (i.e. age and gender) and secondly, we adjusted for social factors (i.e. marital status and education).

In supplementary analyses we excluded all cases of arthrosis, morbus Becterew, or muscle disease from the material and then performed all analyses again to explore the potential effect these other musculo-skeletal disorders may have had on the results. SPSS 14.0 for Windows (Copyright (c) SPSS Inc., 1989–2005) was used in the analyses.

Ethics

The study was approved by the Regional Committee for Medical Research Ethics. All participants gave their written informed consent.

Results

In this population-based study of 55,046 individuals, we identified 785 persons with chronic WAD, 1,095 with fibromyalgia, 958 with rheumatoid arthritis, and a control group of 52,208 persons with none of these disorders. Characteristics of the study population are presented in Table 1. Overall, the rheumatoid arthritis group was older than the other groups; the proportion of females was higher in the fibromyalgia group than in the other groups, and the educational level seemed to be lower in the fibromyalgia group and the rheumatoid group than in the other groups.

The chronic WAD group had higher prevalence of reported pain and stiffness in various body parts, compared to the control group (adjusted OR = 6.87, 95% CI 5.62–8.41 for pain in the elbows to adjusted OR = 9.58, 95% CI 7.91–11.60 for lumbar pain) (Table 2). This also included body parts, which should have no relation to the whiplash trauma, e.g. the hips (adjusted OR = 7.03, 95% CI 5.81–8.51). Compared to the control group, people with fibromyalgia reported an even higher prevalence of pain and stiffness than people with chronic whiplash (adjusted OR = 17.09, 95% CI 14.60–20.01 for thoracic pain to adjusted OR = 17.93, 95% CI 15.08–21.32 for hip pain). People with rheumatoid arthritis also showed a higher prevalence of pain and stiffness compared to the control group, however, less than the chronic WAD group (adjusted OR = 3.62, 95% CI 3.10–4.21 for lumbar pain to adjusted OR = 4.90, 95% CI 4.19–5.73 for hip pain) except for pain in the elbow where the OR was equal to the OR for chronic WAD. The findings were only marginally confounded by age, gender, education, and marital status.

All three study groups had a higher prevalence of gastrointestinal symptoms and symptoms related to the cardiopulmonary system than the control group (Table 3), although the associations were weaker than for the pain and stiffness symptoms (Table 2). The ORs for the chronic WAD group and the fibromyalgia group were the most elevated. Compared to the control group, people with chronic WAD had an adjusted OR = 1.73 (95% CI, 1.46–2.06) for diarrhoea and an adjusted OR = 3.22 (95% CI, 2.66–3.91) for palpitations. The adjusted ORs for people with fibromyalgia were 2.65 (95% CI, 2.30–3.04) for diarrhoea and 3.30 (95% CI, 2.79–3.89) for dyspnoea, while the ORs for rheumatoid arthritis were somewhat lower (adjusted OR = 1.53, 95% CI 1.31–1.79 for palpitations to adjusted OR = 2.12, 95% CI 1.75–2.57 for dyspnoea). Adjustments for age, gender, education, and marital status had only marginal influence on the results.

Compared to the control group, there was a marked increase in prevalence of anxiety and depression in the chronic WAD group (adjusted OR = 2.03, 95% CI 1.66–2.48 for depression to adjusted OR = 2.13, 95% CI 1.78–2.55 for anxiety) and in the fibromyalgia group (adjusted OR = 2.96, 95% CI 2.56–3.41 for depression to adjusted OR = 3.09, 95% CI 2.65–3.61 for anxiety) (Table 4). The rheumatoid arthritis group had a somewhat smaller increase in the prevalence of symptoms compared to the control group (adjusted OR = 1.38, 95% CI 1.14–1.67 for depression to adjusted OR = 1.39, 95% CI 1.14–1.69 for anxiety). Adjustment for age and gender slightly attenuated the results, while adjustment for education and marital status did not change the results.

In a supplementary analysis, we adjusted for a variable indicating time since the trauma (0–2, 3–5, 6–10, 11–20, >20 years, and no time period indicated), but we observed no material change in the estimated associations (data not shown).

Discussion

We hypothesised that chronic WAD should be perceived primarily as a functional somatic syndrome and expected to find that the profile of the chronic WAD was more similar to the profile of fibromyalgia with symptoms from all body regions, including regions that could not be directly related

Table 1 Demographic characteristics of study groups

	Control group	Chronic WAD	Fibromyalgia	Rheumatoid arthritis
No. of participants	52,208	785	1,095	958
Mean age at baseline, years (SD)	47.9 (16.7)	47.6 (14.9)	50.4 (12.3)	58.0 (17.5)
Percent females	50.7	48.4	87.9	63.6
Percent married	59.9	62.2	69.5	62.1
Percent with higher[a] education	20.9	18.9	12.0	11.1

WAD Whiplash associated disorders

[a] Defined as college or university

Table 2 Odds ratio (OR) and 95% confidence interval (CI) for reporting pain and stiffness in different parts of the body

	No. with symptoms	No. without symptoms	Model a		Model b		Model c	
			OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Elbow pain								
Control group	3,430	37,681	1.00	(Reference)	1.00	(Reference)	1.00	(Reference)
Chronic WAD	167	277	6.62	(5.45–8.05)	6.77	(5.56–8.24)	6.87	(5.62–8.41)
Fibromyalgia	518	293	19.42	(16.76–22.51)	18.51	(15.93–21.51)	17.38	(14.90–20.28)
Rheumatoid arthritis	318	378	9.24	(7.93–10.77)	7.91	(6.77–9.25)	7.77	(6.62–9.13)
Thoracic pain								
Control group	2,060	38,256	1.00	(Reference)	1.00	(Reference)	1.00	(Reference)
Chronic WAD	117	286	7.60	(6.10–9.46)	7.77	(6.23–9.69)	7.84	(6.26–9.82)
Fibromyalgia	374	371	18.72	(16.11–21.76)	17.85	(15.30–20.82)	17.09	(14.60–20.01)
Rheumatoid arthritis	136	483	5.23	(4.30–6.36)	4.42	(3.62–5.39)	4.37	(3.56–5.36)
Lumbar pain								
Control group	10,357	34,826	1.00	(Reference)	1.00	(Reference)	1.00	(Reference)
Chronic WAD	415	152	9.18	(7.61–11.07)	9.55	(7.91–11.53)	9.58	(7.91–11.60)
Fibromyalgia	810	146	18.66	(15.62–22.28)	17.31	(14.48–20.70)	17.32	(14.41–20.83)
Rheumatoid arthritis	421	330	4.29	(3.71–4.96)	3.64	(3.14–4.22)	3.62	(3.10–4.21)
Hip pain								
Control group	7,192	36,283	1.00	(Reference)	1.00	(Reference)	1.00	(Reference)
Chronic WAD	264	215	6.20	(5.17–7.43)	6.90	(5.72–8.33)	7.03	(5.81–8.51)
Fibromyalgia	752	175	21.68	(18.36–25.60)	18.39	(15.53–21.78)	17.93	(15.08–21.32)
Rheumatoid arthritis	423	339	6.30	(5.45–7.28)	4.97	(4.27–5.78)	4.90	(4.19–5.73)

CI Confidence interval, *WAD* whiplash associated disorders

Model a: Crude effect

Model b: Adjusted for demographic variables (age and gender)

Model c: Adjusted for demographic variables (age and gender) and socio-economic variables (marital status and education)

to the injury. Our results were in favour of this hypothesis, showing that the chronic WAD group had a significantly higher prevalence of symptoms from all body parts, across organ systems, and also mental symptoms, compared to the control group. The fibromyalgia group had an even higher prevalence of all symptoms, while the rheumatoid arthritis group showed an increase in the prevalence of particularly pain and stiffness symptoms and also a minor increase in the prevalence of other symptoms compared to the control group.

The findings are in accordance with previous studies which have also reported a wide range of symptoms in WAD. Ferrari et al. [17] found that neck pain was only one of many diffuse and intense symptoms. However, these results were obtained only 1 month post-collision and might thus be influenced by pending litigation. In a population-based survey, Coté et al. [11] found that persons self-reporting a previous whiplash trauma also reported considerable comorbidity of other health complaints, all with frequencies significantly greater than the no whiplash group. Berglund et al. [4] focused specifically on the chronic whiplash syndrome in a cohort study of persons involved in a rear-end collision, and found increased risks of headache, thoracic, and low back pain, as well as fatigue, sleep disturbance, and ill health.

Subjective health complaints are also common in the general population. Eriksen et al. [15] reported from surveys in the Nordic countries that as many as 75% of the sample had at least some subjective health complaint for the previous 30 days, with headache (42%) and neck pain (32%) as two of the most common complaints. Haug et al. [23] reported from the HUNT study that 22.2% of the population reported at least five somatic symptoms, which could not be related to any known somatic disease. These high prevalences should be taken into account in the interpretation of the results. However, the results from the present study showed that the prevalence of symptoms in the chronic WAD group was significantly higher than in the control group.

The major strength of the study is the large number of participants and the population-based design. The report of symptoms was not linked to the previous whiplash trauma in the questionnaire, which should minimize the risk for attribution and symptom accentuating. Neither was the

Table 3 Odds ratio (OR) and 95% confidence interval (CI) for reporting various symptoms and complaints

	No. with symptoms	No. without symptoms	Model a		Model b		Model c	
			OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Nausea								
Control group	5,873	42,492	1.00	(Reference)	1.00	(Reference)	1.00	(Reference)
Chronic WAD	204	527	2.80	(2.38–3.30)	2.94	(2.48–3.48)	3.01	(2.54–3.56)
Fibromyalgia	320	677	3.42	(2.99–3.92)	2.87	(2.50–3.29)	2.90	(2.52–3.33)
Rheumatoid arthritis	164	703	1.69	(1.42–2.01)	1.86	(1.56–2.22)	1.81	(1.51–2.17)
Diarrhoea								
Control group	7,629	40,785	1.00	(Reference)	1.00	(Reference)	1.00	(Reference)
Chronic WAD	176	541	1.74	(1.47–2.07)	1.74	(1.46–2.06)	1.73	(1.46–2.06)
Fibromyalgia	312	676	2.47	(2.15–2.83)	2.60	(2.27–2.98)	2.65	(2.30–3.04)
Rheumatoid arthritis	185	691	1.43	(1.22–1.69)	1.58	(1.34–1.86)	1.56	(1.32–1.85)
Palpitation								
Control group	7,944	40,728	1.00	(Reference)	1.00	(Reference)	1.00	(Reference)
Chronic WAD	224	501	2.29	(1.96–2.69)	2.36	(2.01–2.77)	2.41	(2.05–2.83)
Fibromyalgia	429	587	3.75	(3.30–4.25)	3.11	(2.74–3.54)	3.09	(2.71–3.52)
Rheumatoid arthritis	240	651	1.89	(1.63–2.20)	1.59	(1.37–1.85)	1.53	(1.31–1.79)
Dyspnoea								
Control group	3,445	44,601	1.00	(Reference)	1.00	(Reference)	1.00	(Reference)
Chronic WAD	138	572	3.12	(2.59–3.77)	3.16	(2.61–3.82)	3.22	(2.66–3.91)
Fibromyalgia	199	777	3.32	(2.83–3.89)	3.31	(2.81–3.89)	3.30	(2.79–3.89)
Rheumatoid arthritis	140	726	2.50	(2.08–3.00)	2.22	(1.85–2.68)	2.12	(1.75–2.57)

CI Confidence interval, *WAD* whiplash associated disorders

Model a: Crude effect

Model b: Adjusted for demographic variables (age and gender)

Model c: Adjusted for demographic variables (age and gender) and socio-economic variables (marital status and education)

Table 4 Odds ratio (OR) and 95% confidence interval (CI) for reporting anxiety and depression

	No. with symptoms	No. without symptoms	Model a		Model b		Model c	
			OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
HADS-A $\geq$ 8								
Control group	5,954	39,273	1.00	(Reference)	1.00	(Reference)	1.00	(Reference)
Chronic WAD	166	517	2.12	(1.77–2.53)	2.14	(1.79–2.56)	2.13	(1.78–2.55)
Fibromyalgia	306	621	3.25	(2.83–3.74)	2.92	(2.53–3.36)	2.96	(2.56–3.41)
Rheumatoid arthritis	140	650	1.42	(1.18–1.71)	1.42	(1.18–1.71)	1.38	(1.14–1.67)
HADS-D $\geq$ 8								
Control group	4,409	43,978	1.00	(Reference)	1.00	(Reference)	1.00	(Reference)
Chronic WAD	126	621	2.02	(1.67–2.46)	2.06	(1.69–2.51)	2.03	(1.66–2.48)
Fibromyalgia	241	781	3.08	(2.66–3.57)	3.12	(2.68–3.63)	3.09	(2.65–3.61)
Rheumatoid arthritis	139	724	1.92	(1.59–2.30)	1.49	(1.24–1.80)	1.39	(1.14–1.69)

CI Confidence interval, *HADS* Hospital And Depression Scale, *WAD* whiplash associated disorders

Model a: Crude effect

Model b: Adjusted for demographic variables (age and gender)

Model c: Adjusted for demographic variables (age and gender) and socio-economic variables (marital status and education)

study related to any litigation, compensation, or insurance process, which is known to be related to increased symptom reporting [1, 12, 16, 32].

The study also has some limitations. First, information on both the disorders and the symptoms and complaints was self-reported with no objective confirmation. We

further defined chronic WAD as having a previous whiplash trauma and additionally reporting long-term neck pain. However we had no information whether the neck pain was in fact related to the whiplash trauma or whether it was pre-existent or had other causes. Neck pain is very common in the population [15, 38], thus our definition may have contributed to an overestimation of the prevalence of chronic WAD in the data. As a control for the effect of other causes to neck pain we performed all analyses with a material excluding cases of Mb Becterew, arthrosis, and muscle disease. This did not change our results.

Chronic WAD is defined as symptoms lasting more than 6 months after the trauma, although in this study we included all persons self-reporting a whiplash trauma who also reported long-term neck pain. It is thus possible that some persons were still in the acute WAD phase and could have a pending litigation that in turn might influence the reporting of symptoms [6, 10, 36, 37]. However, 94% of the chronic WAD group reported that the trauma occurred at least 2 years ago. A systematic review and meta-analysis of prospective cohort studies of subjects with acute whiplash injuries found that pain, disability, and recovery stabilize within the first 3 months after the trauma [25].

The work and compensation situation may be important for the symptom report, as the work situation may imply job demands which result in physical strain and mental stress with resulting symptoms, while sickness leave with resulting sickness compensation or disability pension award may reduce this strain and stress. In a best evidence synthesis on the burden and determinants of neck pain in workers Coté et al. [13] found that risk factors associated with neck pain included predominantly psychosocial factors. Moreover, Carroll et al. [9] reported that the prognosis of neck pain was linked to few workplace or physical job demands, and that workers with little influence on their own work situation had a slightly poorer prognosis. Unfortunately, this kind of information was not available in the present study, and could not be taken into account in the analysis presented.

In our analyses we excluded cases of comorbidity between the three disorders in the study groups. Part of this comorbidity may not be incidental. As indicated in the results, the prevalence of symptoms in the fibromyalgia group was very high and would probably have overshadowed the effect of the other comorbid groups. Thus excluding comorbidity means that we were able to observe the effect of the other study groups more clearly. Finally, the potential for residual confounding by other unknown or unmeasured factors cannot be excluded in this kind of study.

Conclusion

We found the hypothesis of chronic WAD as a functional somatic disorder was supported. The symptom profile showed a wide array of symptoms, not only predominantly pain symptoms.

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References

1. Aceves-Avila FJ, Ferrari R, Ramos-Rebus C (2004) New insights into culture driven disorders. Best Pract Res Clin Rheumatol 18:55–71
2. Barnsley L, Lord S, Bogduk N (1994) Whiplash injury. Pain 58:283–397
3. Barsky AJ, Borus JF (1999) Functional somatic syndromes. Ann Intern Med 130:910–921
4. Berglund A, Alfredsson L, Jensen I, Cassidy JD, Nygren Å (2001) The association between exposure to a rear-end collision and future health complaints. J Clin Epidemiol 54:851–856
5. Berry H (2000) Chronic whiplash syndrome as a functional disorder. Arch Neurol 57:592–594
6. Binder LM, Rohling ML (1996) Money matters; a meta-analytic review of the effects of financial incentives on recovery after closed-head injury. Am J Psychiatry 153(1):7.10
7. Bjelland I, Dahl AA, Haug TT, Neckelmann D (2002) The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res 52:69–77
8. Borchgrevink G, Smevik O, Haave I, Haraldseth O, Nordby A, Lereim I (1997) MRI of cerebrum and cervical columna within two days after whiplash neck sprain injury. Injury 28(5–6):331–335
9. Carroll LJ, Hogg-Johnson S, Coté P, van der Velde G, Holm LW, Carragee EJ, Hurwitz EL, Peolsson M, Cassidy JD, Guzman J, Nordin M, Halderman S (2008) Course and prognostic factors for neck pain in workers: results of the Bone and Joint Decade 2000–2010 Task Force on Neck Pain and Its Associated Disorders. Spine 33(S4):S91–S100
10. Cassidy JD, Carroll LJ, Coté P, Lemstra M, Berglund A, Nygren Å (2000) Effect of eliminating compensation for pain and suffering on the outcome of insurance claims for whiplash injury. N Eng J Med 342:1179–1186
11. Coté P, Cassity JD, Carroll L (2000) Is a lifetime history of neck injury in a traffic collision associated with prevalent neck pain, headache and depressive symptomatology? Accid Anal Prev 32:151–159
12. Côté P, Cassity JD, Coté P, Frank JW, Bombardier C (2001) A systematic review of the prognosis of acute whiplash and a new conceptual framework to synthesize the literature. Spine 26:E445–E458
13. Côté P, van der Velde G, Cassidy JD, Carroll LJ, Hogg-Johnson S, Holm LW, Carragee EJ, Haldeman S, Nordin M, Hurwitz EL, Guzman J, Peloso PM (2008) The burden and determinants of neck pain in workers: results of the Bone and Joint Decade 2000–2010 Task Force on Neck Pain and Its Associated Disorders. Spine 33(S4):S61–S74

14. Eck JC, Hodges SD, Humphreys SC (2001) Whiplash: a review of a commonly misunderstood injury. Am J Med 10:651–656
15. Eriksen HR, Svendsrød R, Ursin G, Ursin H (1998) Prevalence of subjective health complaints in the Nordic European countries in 1993. J Public Health 8:294–298
16. Ferrari R (1999) The whiplash encyclopedia. The facts and myths of whiplash. Aspen Publishers, Maryland
17. Ferrari R, Russel AS, Carroll LJ, Cassity JD (2005) A re-examination of the whiplash associated disorders (WAD) as a systemic illness. Ann Rheum Dis 64:1337–1342
18. Ferrari R, Schrader H (2001) The late whiplash syndrome: a biopsychosocial approach. J Neurol Neurosurg Psychiatry 70:722–726
19. Gargan MF, Bannister GC (1990) Long-term prognosis of soft-tissue injuries of the neck. J Bone Joint Surg Br 72:901–903
20. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC (2007) The biopsychosocial approach to chronic pain: scientific advances and future directions. Psychol Bull 133:518–624
21. Guez M, Hildingsson C, Nilsson M, Toolanen G (2002) The prevalence of neck pain. A population-based study from northern Sweden. Acta Orthop Scand 73:455–459
22. Harting L, Brison RJ, Ardern C, Pickett W (2001) Prognostic value of the Quebec classification of whiplash-associated disorders. Spine 26:36–41
23. Haug TT, Mykletun A, Dahl AA (2004) The association between anxiety, depression, and somatic symptoms in a large population: the HUNT-II study. Psychosom Med 66:845–851
24. Johnson G (1996) Hyperextension soft tissue injuries of the cervical spine—a review. J Accid Emerg Med 13:3–8
25. Kamper SJ, Rebbeck TJ, Maher CG, McAuley JH, Sterling M (2008) Course and prognostic factors of whiplash: a systematic review and meta-analysis. Pain 138(3):617–629
26. Lovell ME, Galasko CSB (2002) Whiplash disorders—a review. Injury 33:97–100
27. Mayou R, Bryant B (2002) Psychiatry of whiplash neck injury. Br J Psychiatry 180:441–448
28. McLean SA, Clauw DJ, Abelson JL, Liberzon I (2005) The development of persistent pain and psychological morbidity after motor vehicle collision: integrating the potential role of stress response systems into a biopsychosocial model. Psychosom Med 67:783–790
29. Mykletun A, Stordal Ø, Dahl AA (2001) Hospital Anxiety and Depression (HAD) scale: factor structure, item analysis and internal consistency in a large population. Br J Psychiatry 179:540–544
30. Obelieneiene D, Schrader H, Bovim G, Miseviciene I, Sand T (1999) Pain after whiplash: a prospective controlled inception cohort study. J Neurol Neurosurg Psychiatry 66:279–283
31. Olssøn I, Mykletun A, Dahl AA (2005) The Hospital Anxiety and Depression rating Scale: a cross-sectional study of psychometrics and case finding abilities in general practice. BMC Psychiatry 5:46
32. Overlang S, Grozier N, Hendeson M, Mæland JG, Hotopf M, Mykletun A (2008) Health status before, during and after disability pension award: the Hordaland Health Study (HUSK). Occup Environ Med 65:769–773
33. Peebles JE, McWilliams LA, MacLennan R (2001) A comparison of symptom checklist 90-revised profiles from patients with chronic pain from whiplash and patients with other musculoskeletal injuries. Spine 26:766–770
34. Radanov BP, Stefano GD, Schnidrig A, Ballinari P (1991) Role of psychosocial stress in recovery from common whiplash. Lancet 338:712–715
35. Rebbeck T, Sindhusake D, Cameron ID, Rubin G, Feyer A-M, Walsh J, Gold M, Schofield WN (2006) A prospective cohort study of health outcome following whiplash associated disorders in an Australian population. Inj Prev 12:93–98
36. Represas C, Vieira DN, Magalhães T, Dias R, Frazão S, Suárez-Peñaranda JM, Rodrigues-Calvo MS, Concheiro L, Muñoz MD (2008) No cash no whiplash? Influence of the legal system on the incidence of whiplash injury. J Forensic Leg Med 15:353–355
37. Rohling ML, Binder LM, Langhinrichsen-Rohling J (1995) Money matters: a meta-analytic review of the association between financial compensation and the experience and treatment of chronic pain. Health Psychol 14(6):537–547
38. Schrader H, Obelieniene D, Bovim G, Surkiene D, Mickeviciene D, Mckeviciene I (1996) Natural evolution of late whiplash syndrome outside the medicolegal context. Lancet 347:1207–1211
39. Spitzer WO, Skovron ML, Salmi LR, Cassidy JD, Duranceau J, Suissa S, Zeiss E (1995) Scientific monograph of the Quebec Task Force on Whiplash-Associated Disorders: redefining "whiplash" and its management. Spine 20:S1–S73
40. Wenzel HG, Haug TT, Mykletun A, Dahl AA (2002) A population study of anxiety and depression among persons who report whiplash traumas. J Psychosom Res 53:831–835
41. Wessely S, Nimnuan C, Sharpe M (1999) Functional somatic syndromes: one or many? Lancet 354:936–939

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