Moderate-to-severe traumatic brain injury in Eastern Norway: trends and challenges

Nada Hadzic-Andelic

Doctoral thesis

The Faculty of Medicine, University of Oslo
Department of Physical Medicine and Rehabilitation, Oslo University Hospital, Ulleval

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ABSTRACT

In recent years, there has been an ongoing debate in the health region of Eastern Norway concerning the management of patients with Traumatic Brain Injury (TBI), in order to better understand the extent of problems with management and to identify the high-risk groups. The debate has been hampered by a shortage of population-based studies of the TBI epidemiology, and a scarcity of information regarding the outcomes and the occurrence of disability in the Norwegian TBI population.

The overall aim of this thesis was to describe epidemiological trends of hospital-treated TBI, TBI-related disabilities and health-related quality of life after moderate-to-severe TBI.

The study findings indicated a trend towards a decreasing incidence of hospital-treated TBI in Norway, as reported in other countries. The study showed a bimodal age distribution, as the elderly and young children are those most affected by TBIs. Falls comprise the most frequent cause of TBI-related hospitalization. Transport accidents were the main cause of TBI in the 15-54 year age groups. A considerable number of the patients showed alcohol and drug use upon admission to the hospital. The majority of hospitalised patients had mild TBI. The elderly were more often found to have intracranial lesions. The majority of patients who were discharged to local care facilities belonged to the moderate-to-severe TBI group. At the one-year follow-up, patients with moderate-to-severe TBI were highly independent in physical but not cognitive activities. Social integration was not complete, and many patients reported participation restrictions. Better physical and mental health was associated with more severe injuries and higher levels of activities and productivity. Participation in productive activities was the strongest individual predictor of the physical and mental health dimensions. A majority of patients had good recovery or moderate disability at ten-year follow-up. However, health-related quality of life (HRQL) was significantly reduced in TBI survivors at one-year and ten-year follow-ups compared to the general Norwegian population.

Our findings suggest that more effective programs related to falls and transport accidents are needed. Due to the extent of the use of alcohol and drugs at the time of injury, preventive efforts targeting risk populations are needed. To optimise the physical and mental health outcomes, clinicians need to ensure that the disability and health needs of patients with less severe intracranial injuries are identified and treated during the post-acute...
period. The decreased HRQL in the TBI survivors in the long-term perspective suggests the importance of support and care-availability in the “chronic” stage of TBI as well.
LIST OF PAPERS

This thesis is based on the following papers, referred to in the text by Roman numbers.


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1. INTRODUCTION AND BACKGROUND

Traumatic Brain Injury (TBI) is a worldwide public health problem, with a high mortality among the most severely injured patients (1). TBI can result in long-term physical, cognitive, behavioural and emotional problems that affect a patient’s ability to perform daily activities and return to work, even among those with mild TBI (2;3). As a result, the socioeconomic costs of TBI are considerable (4). Knowledge of the incidence, causes and consequences of TBI is needed for the prevention, care, rehabilitation and effective services for TBI patients.

In recent years, there has been an ongoing debate in the health region of Eastern Norway concerning the means by which the management of patients with TBI could be improved. The debate has been hampered by a shortage of population-based studies of the TBI epidemiology and a scarcity of information on the outcome and disability in the Norwegian TBI population. Indeed, an accurate documentation of the outcomes in this population has never been performed in Eastern Norway, and the body of knowledge is mainly founded on studies conducted in other countries. In order to understand the extent of the problems and to identify the high-risk groups, it would be necessary to identify the regional impact of TBI. Such knowledge may be helpful when planning injury prevention and improving the acute care, rehabilitation and long-term care facilities.

The present thesis addresses some of the challenges mentioned above by describing epidemiological trends of TBI, TBI-related disability and self-reported health and well-being. According to the NIH (National Institute of Health, USA) (5), the 30 areas of research needed to guide the rehabilitation of patients with TBI were addressed at a consensus conference in 1998. The purpose of this thesis was to contribute to the following areas of research: epidemiological studies on the risk factors and incidence of TBI, the relationship between substance abuse and TBI, the long-term consequences of TBI, and the predictors of health-related quality of life for TBI survivors.

1.1 Definition of TBI

The case definition of TBI has varied among epidemiological studies, creating some difficulties in comparing their findings (6). In an effort to standardise the epidemiological
case definition of TBI, the Guidelines for Surveillance of Central Nervous System Injury by the Centers for Disease Control and Prevention (CDC) was published in 1995 (7). The CDC defined TBI as “damage to brain tissue caused by external mechanical force as evidenced by: loss of consciousness due to brain trauma, amnesia, other neurological or neuropsychological abnormalities, skull fracture and diagnosed intracranial lesions or death” (8).

TBI may also be defined by the codes of the International Classification of Diseases (ICD-10) that specify the clinical features of brain injury (9). According to the ICD codes, skull fractures, brain concussions, brain contusions, and other intracranial injuries, including subarachnoid, subdural, and extradural haematomas and diffuse injuries, are included. Its clinical utility is thus limited when assessing the possible outcomes. However, the ICD classification has proven to be practicable for epidemiological studies (10).

1.2 Criteria for the classification of TBI

The assessment of the TBI severity is of fundamental importance in clinical management, as well as for the design of clinical trials aimed at developing novel therapies (11). The methods used to classify the severity of TBI have included the assessment of the following: a) clinical indices of severity, most often used in clinical research to compare patients among centres; b) pathoanatomic type, most often used to describe injuries for acute management; and c) physical mechanism (i.e., causative forces associated with injury), most often used in the biomechanics and prevention fields (12;13).

To date, the majority of clinical treatment trials for TBI have classified and included patients based on the neurological injury severity criteria (14). The most commonly used neurological injury severity scale for adults is the Glasgow Coma Scale (GCS), which assesses the level of consciousness after TBI (15). This scale is based on eye opening and motor and verbal responses. Mild TBI is defined as a state with GCS scores of 13-15, whereas scores of 9-12 and 3-8 define moderate and severe TBI, respectively. The GCS has high inter-observer reliability, and is useful in predicting mortality (14). However, GCS has several important limitations, particularly in patients who are intoxicated or who require pharmacological sedation or paralysis due to intubation (12;16;17). Infants, young children and patients with pre-existing neurological impairments are difficult to assess with the GCS (13). The GCS is also a poor discriminator for less severe TBI, which accounts for 80-90 %
As shown by Balestreri et al. (16), the predictive value of the GCS should be carefully reconsidered when building prognostic models. A new assessment tool, the Full Outline UnResponsiveness (FOUR) score, appears to provide more specific information and accounts for patient intubations. In addition, the FOUR score tool is nearly as user-friendly as the GCS, but it will require further validation before it can be widely embraced (18).

A number of scales are also available that assess extracranial injuries and physiological instability, including the Abbreviated Injury Scale (AIS) and Injury Severity Score (ISS) (19, 20). The AIS is widely used in trauma centre studies to define the severity of injury in different body regions. The AIS has been recognised as a good prognostic tool regarding mortality (21) and functional outcome (22). The AIS-head is part of the AIS, and the rating of severity is based on a combination of anatomic lesions and impairment of consciousness. The ISS is designed to quantify the severity of multiple body region injuries and is based on the AIS codes. The AIS-head and ISS, in addition to the GCS, could be used to rate the severity of TBI and overall trauma for selecting and stratifying patients for clinical trials (11). However, the AIS-head is dependent on the duration of consciousness, and therefore, it does not completely eliminate the bias of using physiologic scores (23). The AIS manual does not specifically address how to code individuals who are pharmacological paralysed or intubated (24). Further, the AIS-head cannot be based on clinical diagnoses but must be verified by the neuroimaging or surgery.

A pathoanatomic classification describes the location or anatomical features of the TBI. In many acute TBI studies, the description of the pathoanatomic type of injury is done using the Marshall score for computed tomography (CT) findings (25). The Marshall classification focuses on the presence or absence of a mass lesion and differentiates diffuse injuries by signs of increased intracranial pressure. When applied to CT scans of early severe and moderate TBI, the Marshall score has been shown to predict both the risk of increased intracranial pressure and the outcome in adults (13). The Marshall classification system is widely used, but has many recognised and accepted limitations. This classification fails to account for several important characteristics of the injury, such as the nature and location of contusions or the type of intracranial bleeding (26), and has difficulties in classifying patients with multiple injury types and standardisation of certain features of the CT scan (13). The Rotterdam score (27) is a more recent and standardized CT-based classification, which uses combinations of findings to predict the outcomes. This system
overcomes some of the limitations of the Marshall score, but it has not yet been fully validated, and more studies are required (13).

An alternative approach is to classify patients by prognostic risk. Well-validated models developed on large patient samples are available (28). According to Maas et al. (12;28), a “prognostic classification can serve as an objective basis for comparison of different TBI series, form the basis for quality assessment of the delivery of health care, and aid the analysis of clinical trials”.

In addition, the presence and duration of posttraumatic amnesia (PTA) are often used as tools for classifying TBI (29). The duration of the PTA is related to the severity of the injury and has shown a robust correlation with treatment costs. The PTA is also a reliable index of outcome prediction, related to both earlier and later stages after injury (30;31).

1.3 TBI-closed and penetrating injuries

TBIs can be divided into penetrating and closed (blunt) head traumas. These may occur with or without simultaneous fracture of the cranial bones (32). Penetrating head trauma occurs when the scalp and skull are compromised, and brain tissue is exposed to the external environment. In terms of outcome, the early mortality rate after a penetrating injury is much higher than that of a closed injury (33). Among the survivors, however, the penetrating injuries often give rather distinct symptoms, and often the patients will recover spontaneously. In closed TBI, the brain is subjected to mechanical forces, in terms of being pushed against the skull bone (coup-counter-coup injuries); another mechanism that causes injury is the shearing and twisting of neural fibres as a result of the movement of the brain (diffuse axonal injury). There is also the risk of haemorrhage leading to haematoma, which can cause increasing intracranial pressure and lesions to the neurons. This implies both the development of discrete symptoms, because of the damage of specific sites of the brain, and more diffuse and generalised impairment from the more widespread type of damage caused by axonal tearing (34). The physiological response to primary damage of the neuronal tissue, such as cerebral oedema, increased intracranial pressure (ICP), cerebral ischemia, hypotension, and infection, are the most common causes of secondary injury (35;36).

Systemic changes in temperature, haemodynamics, and pulmonary status may also lead to secondary brain injury. These secondary injuries are what the caregiver must anticipate and prevent in order to provide the optimum environment for a positive patient outcome (35).
1.4 Epidemiological aspects of TBI

The measurement of the TBI incidence (rate of occurrence of new cases in a specified period of time) and prevalence (proportion of a population with TBI-related disability) requires population-based studies either on the entire population of interest or a representative sample of that population (37). Complete registration of the occurrences of TBI is not feasible as most individuals with mild TBI are not admitted to hospitals, and the majority of these injuries are never medically diagnosed. In particular, older people and subjects injured at home are less likely to seek medical care (38). Most published rates include hospitalised patients regardless of outcome (39). The number of hospital-admitted TBI patients is an important indicator of the impact of local injuries on hospital resources (9).

According to a review article of the European studies published in 2006, the annual incidence of TBI (hospitalised and fatal) in Europe was 235 per 100,000 in population per year (range 91 to 546 per 100,000) (39). The former rate from Spain included hospital admissions only, while the later rate from Western Sweden included hospital admissions, emergency department visits, and deaths. In the Scandinavian countries, the annual incidence of hospital-admitted TBI has been reported to vary from 95/100,000 (40) to 546/100,000 (41). In three previous Norwegian regional studies based on hospital-treated head injuries conducted in 1974, 1979 and 1993, the annual incidence rates were 236, 200 and 169 per 100,000, respectively (42-44). The same pattern of TBI incidence was also found in a national study in Denmark over the same time period: 265/100,000 in 1979-81 and 157/100,000 in 1991-93 (45). In Finland, a national study that enrolled only patients who were registered for the first time in the Hospital Discharge Register reported a substantially lower incidence of 101/100,000 in 1991-2005 (46). A national study in Sweden using the Hospital Discharge Register showed a stable hospital discharge incidence, which was on average 259/100,000 in 1987-2000 (47).

The studies from the U.S. suggest that the rates of TBI-related hospitalisation have decreased substantially in the last two decades. Thurman and Guerrero (37) found that the incidence of hospitalisation associated with TBI decreased 51% from 1980 to 1995 (from 199/100,000 to 98/100,000). However, this was mainly due to a decrease in the incidence of hospitalisation for mild TBI (hospitalisations for mild and moderate TBI decreased 61% and 19%, respectively, while hospitalisation for severe TBI increased 90% during that period).
A recent published report from the U.S. (48) estimated the average incidence rate of TBI-related hospitalisation to 79/100,000 (range 50.6-96.9). The decreasing trends for the TBI numbers in the U.S. over the past two decades appear to be due to a mix of widespread implementation of prevention measures, safety legislations, and public education initiatives; improvements and wider availability of emergency medical systems and regional trauma centres; improvements in neuro-critical care and the implementation of evidence-based treatment guidelines for severe TBI (49). It also appears to be the result of changes in admission policies that discourages inpatient care for less severe TBI and promotes the use of outpatient facilities for these patients (8).

The groups at high risk of TBI are males and individuals living in regions characterised by socio-economic deprivation (50). Males have approximately twice the rate of TBI as women (50). This pattern may reflect differences in risk-taking behaviour and different hazards associated with occupational exposures (6). A tri-modal age-specific TBI incidence is quite often seen in population-based studies with peaks in early childhood, late adolescence/early adulthood and in the elderly (51;52).

Falls are the leading cause of TBI in Northern Europe (9;39;43;53;54), and in the U.S. (1;48), resulting in an enormous financial cost for society. In Southern Europe, traffic accidents constitute the vast majority of TBI cases and continue to be the main cause of severe and fatal injuries (9;39;55). Excluding the UK, violence-related injuries are not as great a problem in Europe, which is quite different from the U.S. figures (56).

Mild TBI accounts for 80-90% of all head injuries, according to several international studies (9;51;57;58). In Europe, the ratio of hospitalised patients with severe, moderate and mild TBI is 1:1.5:22 (39). A large number of people with mild TBI may not go to the hospital at all or they may be discharged without follow-up. Approximately 10-15% of patients have more severe injuries requiring specialist care (12;59). The patients with moderate and severe TBI often have associated injuries and continuing medical and surgical needs (60).

The TBI mortality rates vary by the severity of the injury. Severe TBI is associated with a 30-50% death rate among hospitalised patients. This is most strongly associated with a high ICP (61). For hospitalised patients with moderate TBI, the death rates are 7-9%, generally due to associated trauma or complications (62). The average mortality of TBI in Europe has been estimated to be about 15/100,000 per year (39). For the period from 1987 to 2000, the
The median mortality rate was estimated to be 11.5/100,000 in Scandinavia and 10.5/100,000 in Norway (63). The case fatality rate (CFR) is the simplest epidemiological measure of the severity, as well as a measure of the gross outcome following TBI. The overall CFR in Europe (which reflects both in-hospital and out-hospital deaths) is estimated to be 11 per 100 persons with TBI. Meanwhile, the average in-hospital CFR in Europe is estimated to be 2.7 per 100 hospitalised patients (39). Nestvold et al. (39;44) reported a total CFR of 4.1 and an in-hospital CFR of 1.4 in Akershus County in 1974. The TBI-related mortality in the U.S. declined 22.6% from 1979 to 1992, and 11.4% from 1989 to 1998 (due to the downward trend of TBI in mortality rates with a concurrent increase in severe TBI hospitalisation rates) (37). As cited in the literature, the cause for these decreases is likely due to injury prevention efforts, compulsory safety laws (e.g., seatbelt, helmet, and drunk driving laws), engineered solutions (e.g., airbags), and improved treatment for alcohol and drug problems (52).

As mentioned above, the previous Norwegian studies on the TBI incidence were conducted between 15 and 30 years ago (42-44). The incidence of TBI hospitalisations has never been investigated in the Oslo region, and research is needed for current information about this population, as well as for updated incidence trends in a Scandinavian population.

**1.5 Substance use and TBI**

Substance use (encompassing both alcohol and/or other psychoactive substances) is commonly associated with trauma (64;65). The number of patients that have used substances while sustaining TBI is considerable, with an estimated 36-51% showing some signs of substance use upon emergency admission to the hospital (66;67).

Most studies related to substance consumption have focused on selected TBI populations, such as victims of road traffic crashes (68), falls (69) or assaults (70). In the recent literature, it has been debated whether the influence of alcohol increases (68) or decreases (71) the risk of more severe injuries or if it has no effect (72). The different views are primarily due to the variations in the data collected and a lack of consistency in methodology and outcomes. As reported by Parry-Jones et al. (67), most of the studies are conducted in the U.S., which may limit the applicability of these findings to non-American countries, “given the potential influence of cultural factors on patterns of alcohol and drug consumption” (73).
Several studies have assessed a link between substance use and clinical measures of TBI severity (66;67;74), but the data from Europe are limited (39;75). However, there have been a few studies on the effects of substance use on anatomical brain injury based on a CT classification (68;76). A study by Cunningham et al. (68) reported that persons involved in motor vehicle accidents who tested positive for alcohol were approximately twice as likely to have more severe CT injuries than those who tested negative for alcohol. Ruff et al. (76) found that alcohol abuse before the injury, rather than alcohol intoxication levels at the time of injury, had a significant effect on the severity of the intracranial injuries.

It is important to study the impact of substance consumption on the TBI severity in different countries because of variations in the cultural acceptance of substance use; in addition, this can be used to identify significant substance abuse among TBI patients and identify those who might benefit from an intervention.

1.6 TBI health care

Patients with TBI who are admitted for acute hospital care can range from those who need a period of observation (to recognise secondary neurological deterioration and neurosurgical complications that may ensue after a delay), to those with co-morbidities that require hospital care, to those with more severe TBI that requires intensive care management (77). The focus of acute TBI management is to control the ICP and cerebral perfusion pressure and prevent complications (e.g., cardiovascular, pulmonary, and musculoskeletal) (35;36). Acute neurosurgical and intensive care for patients with TBI have improved over the last two decades with better survival and outcomes (78). Much of the treatment has evolved towards standardised approaches that follow international and national guidelines. The international guidelines for severe head injury are mostly evidence-based and address specific aspects of management (79;80). The national guidelines focus more on organisational issues, such as admission and referral policy; however, these remain limited to the constraints of the existing trauma systems, and clear statements on the best trauma organisation are often avoided (12;81).

The provision of a continuum of care for persons with TBI is an enormous challenge given the number of people affected by the disorders (patients, family members and others), the potential long-term course of recovery, the possible life-long effects (often beginning at an earlier stage of life), and the wide variety of types of brain damage, clinical effects, and associated problems (77;82). The health care for TBI involves the coordination of numerous
services utilising many disciplines across the range of severities and course of recovery. These services include prevention; emergency; acute care; early and later rehabilitation; vocational, educational, and community support; and long-term care. An understanding of the brain injury, its clinical consequences, associated problems and complications, and natural history of recovery helps in applying the proper services for patients along the continuum of care, and helps ensure more effective use of resources (77).

1.7 Disability following TBI

Following the acute stage, residual motor, sensory, behavioural and cognitive deficits may remain. While the majority of patients with mild TBI recover rapidly and return to their premorbid activities, a small group may continue to experience cognitive, emotional and physical impairments (83). In a study of mainly mild TBI cases (n=6783), it was found that only 4.9% had a disability that required in-hospital rehabilitation (84). In contrast, a large proportion of moderately to severely injured patients are left with permanent impairments that profoundly affect their ability for self-care, mobility, and reintegration to society (83), and these patients generally require TBI rehabilitation. Most patients are in need of both in-patient and outpatient services with an emphasis on community re-entry and vocational training (82). TBI rehabilitation is based on the philosophy of interdisciplinary, team-based, and goal-oriented services that aim to reduce disability and improve functioning within person’s environment and from his/her perspective (85).

The outcome after TBI refers to the extent of impairment and disability after there has been an opportunity for recovery (7). There is no single measure of positive or negative TBI outcome. For TBI survivors, a modest amount of independence may be considered positive, whereas for the society as a whole, economic independence may be the desired outcome (86).

Disablement models are a meaningful way to determine and evaluate the consequences of disease and injury (87). In rehabilitation medicine it has become a common practice to classify the consequences of disease according to the framework of the International Classification of Functioning, Disability, and Health (ICF) (88-90). The ICF attempts to achieve a synthesis between the different perspectives of health from a biological, individual and social perspective (90). The ICF model emphasises the relation between disease and disability in a social context, but it has some weaknesses, especially in the degree to which it allows for the patients’ subjective experiences (91).
The ICF has three major domains, body structure/function, activities and participation. These domains interact with each other, and are influenced by both environmental and personal factors. Within the ICF, disability is defined as “an umbrella term for impairments in body functions and structures, limitation in activities and restriction in participation” (88). The multidimensional view of disability may help care providers to find a common language, define common rehabilitation goals, and coordinate treatment.

**Impairments** as defined by the ICF are problems in the body functions and structure with a significant deviation or loss. Almost all patients surviving after a moderate or severe TBI suffer a number of impairments: physical (i.e., ambulation, balance, coordination, and fine motor skills), behavioural (i.e., impulsivity), cognitive (i.e., disruption in learning and memory, processing speed, and executive functioning) and emotional changes (i.e., depression) (92). The associated injuries may have an impact on the level of impairment (2;14). For example, a patient with significant orthopaedic injuries may have weight-bearing limitations that contribute to the level of impairment (93).

It is generally agreed that physical impairments have less influence on outcome than cognitive and behavioural impairments (94), even thought the impact of physical impairments can not be neglected (95). In a study of subjective perception of recovery after TBI, Powell et al. (96) found that even though physical concerns were dominant during the first year after TBI, they decreased over time, while the awareness of cognitive-related concerns increased with time.

Cognitive dysfunction is the most common impairment after TBI. Neuropsychological assessment is widely used in the rehabilitation setting in order to evaluate cognitive abilities and possible dysfunction. The utility of neuropsychological testing is diminished by the fact that only a subset of patients are able to be tested sub-acute; therefore, the results of the neuropsychological studies are not relevant to the significant number of patients who are not testable during the in-patient rehabilitation (97). However, neuropsychological assessments have been shown to have good predictive value for the functional outcome at the one-year follow-up (98). Significant cognitive impairments in verbal memory tests, complex attention and executive functioning were found at the one-year follow-up in severe TBI cases (99). In a study of cognitive functioning at ten years after TBI, the greater injury severity correlated significantly with the poorer test performances in all assessed cognitive
domains (processing speed, memory and executive function), showing that many deficits persist over time (100).

Emotional dysfunction after TBI, as expressed by the depression rates, appears to vary considerably in different studies (100-102) due to the differences in methodology and selection criteria. Seel et al. (103) studied 666 patients with moderate-to-severe TBI at 10-126 months post-injury and found that 27% of the patients had major depressive disorders according to the diagnostic framework of the Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM-IV). Neither time since injury nor severity of injury were correlated with depression. In another study by Seel et al. (102), 37% of patients were classified as depressed using the Beck Depression Inventory (BDI). The onset of depression in the acute recovery stage has been linked to neurophysiologic changes, whereas a later onset of depression has been shown to be associated with psychosocial factors (104). Moreover, it has been reported that depression may have a negative influence on the patient’s daily activities, participation and social interaction (100;101).

One of the most important neurological complications of TBI is posttraumatic epilepsy, accounting for 20% of the symptomatic epilepsy in the general population. Posttraumatic epilepsy is relatively common after TBI with a reported incidence of early (<1 week) epilepsy of 2 to17%, and late epilepsy of 2 to >30% (105). Vespa et al. (106) found posttraumatic epilepsy in 22% of 94 patients with moderate and severe TBI. Skandsen et al. (107) followed 94 patients (aged 1-88 year) with severe TBI 3-8 years after injury and found an epilepsy rate of 23%. Various factors have been associated with the increased seizures risk including the following: GCS <10, cortical contusions, depressed skull fracture, epidural, subdural, or intracranial haematoma, penetrating head injury, or seizures within 24 h of injury (108). In the case of both moderate and severe TBI, the increased risk of late epilepsy lasts for up to approximately ten years after the injury (109). Asikainen et al. (110) reported that epilepsy worsens the functional outcome in TBI survivors.

The ICF defines activity limitations as difficulties that an individual may have in the performance of activities. The TBI outcome related to the level of activity is mostly reported as the independence in daily activities (111). In the literature, a substantial percentage of TBI survivors reported activity limitation at one-year post-injury (3;112). However, Dikmen et al. (113) investigated a group of 31 patients with moderate-to-severe TBI and found that 68% of the patients were independent in everyday life at the one-year
follow-up. In a population-based study by Whiteneck et al. (112), 37% of all participants scored 5 or lower on at least one Functional Independence Measure (FIM) item (114), indicating an activity limitation that requires assistance from another person. The FIM cognitive subscale showed a higher percentage of people with scores of 5 on individual items (31%) compared to the FIM physical subscale (15%). Statistically significant differences in the need for assistance were demonstrated among groups defined by injury severity, age and gender in the analyses of the physical and cognitive FIM items. More of the patients with severe TBI needed assistance, as well as older persons and women. Olver et al. (115) has demonstrated that patients can make significant improvements in activities of daily living between 2 and 5 years after injury. A study conducted by Dawson et al. (116) showed that 15% of the participants reported a need for assistance with personal care at 13 years after TBI.

Participation restrictions are defined as problems an individual may have in the manner or extent of involvement in life situations. Substantial restrictions in the community integration after TBI have been reported in previous studies (3;116;117). Huebner et al. (117) reported that 20% of survivors never go out for leisure activities, another 20% never visit friends and relatives, and 12% seldom or never travel outside the home. Corrigan et al. (3) found a stable level of societal functioning in the first five years following TBI, but these levels generally averaged below the normative comparisons. The long-term follow-up data on participation in social activities present a picture of a very isolated group of people; 27% reported never socialising with relatives or friends at home, and almost 20% reported never visiting family or friends (116). However, it has been reported that being in a relationship before injury, potentially reduced the level of independent community involvement of the patients with TBI, if a partner carried out social and domestic task (118).

A major segment of the ICF participation domain is devoted to employment (88). Previous studies have documented that returning to work is one of the most important contributors for successful community reintegration (51). The employment rates vary from 12-70% depending on the injury severity and the time of follow-up (83;119-122). In a follow-up study of 1591 people with mixed TBI severity, it was found that 68% of the participants were employed at the time of the injury (112). Of those who were employed pre-injury, 76% reported employment at one-year post-injury (78% for moderate and 47% for severe TBI group), but the employment was not necessarily by the same employer or in the same
position as before their injuries. Significant differences in the return to work rates were demonstrated among groups defined by severity of injury and gender. Those with more severe injuries and women were less likely to be employed at one-year post-injury than those with less severe injuries and men. In a follow-up study of 72 patients with moderate-to-severe TBI, the employment rate was 21% at one-year after injury (123). Some studies have reported a deterioration in the employment status over time (115) despite improvements in general functioning (115;124). In a Swedish study of TBI (125), 70% returned to work or education within 5-8 years after injury. A study that evaluated the employment status in severe TBI found that 39% did not work at all ten years after injury; moreover, it was found that there were few changes in the employment outcome after the first years (126). It has been reported that many of those who return to work have to change the task they perform and/or reduce their working hours (83). However, the factors related to employment are complex. Studying the relationship between TBI, function and employment in different countries may shed light on this issue.

1.8 Health-related quality of life after TBI

Despite the fact that TBI is known to have long-lasting social, physical and health-related consequences, the outcome studies in the TBI literature traditionally focus on employment status and cognitive functioning (30). Fuhrer (127) raised the argument that the measures of outcomes are incomplete if the subjective well-being of the individual is not considered. Consensus (128) also noted that the patient’s self-reported quality of life values are necessary in TBI research. The quality of life as an outcome measure is important for both patients and clinicians, since one of the primary goals of rehabilitation is to give TBI survivors a meaningful existence and a life within their expectations. The factors that contribute to quality of life could guide the interventions for improving physical, cognitive and emotional status, along with the environmental factors.

The concept of quality of life is broad, and there are many different definitions in the literature. The World Health Organization (WHO) has defined quality of life as “individuals’ perception of their position in life in the contest of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns” (129). The quality of life after TBI is considered to be related to attaining a healthy and productive life-style (130), and it is increasingly being used as the ultimate goal of rehabilitation.
The measures of quality of life can be grouped into objective measures (which are outsider defined, where the patient’s quality of life is assessed by an outsider) and subjective measures (which are insider-defined, i.e., self reported) (131). Brown et al. (132) believed that the objective measures tell little about how people with impairment or disability experience their life situation, and therefore, they are not useful in rehabilitation planning and evaluation. The subjective perspective of a patient with regard to health functioning and well-being is frequently called the health-related quality of life (HRQL) (133). The dimensions related to quality of life or subjective well-being that are independent of or not directly associated with health are not comprised by the HRQL concept. Because the patients are the experts for their own well-being and functioning, their self-reports play an important role in capturing the impact of the HRQL of health conditions and treatment regimes (134).

The perceived health-related functioning in both physical and mental domains may change over time because the recovery from TBI is a complex and lengthy process. The rate of recovery may vary due to a number of factors, including the severity of the brain injury, time since injury, the domain of functioning that is being assessed, and the measure used for the assessment.

The TBI survivors rate their HRQL lower than non-disabled persons (132;135;136). There are several studies that have described the factors that influence the HRQL or satisfaction with life in people with TBI (86;136-139). They showed that improved physical functioning, perceived mental health, participation in work and leisure, and social support increased the HRQL and life satisfaction. The higher ratings of life satisfaction were significantly associated with employment and an absence of pre-injury substance abuse (130). Seibert et al. (140) found that gender differences influenced the perception of the quality of life at one year after injury, with significantly more females (69%) reporting a worse overall quality of life than males (21%). Dijkers (141) also reported that gender influences the quality of life.

Brown and Vandergoot (142) reported a tendency for more severely injured people to estimate their life satisfaction as being good or unaffected, while the people with mild injury seemed to experience a more negative influence on their life satisfaction after brain injury. This is in accordance with Koskinen (143), who found that those with more grave intracranial damage had a rather high quality of life despite the severe brain injury.
The prediction of adjustment and well-being following TBI is essential to the development of meaningful psychological and medical interventions and informed health policy, especially when considering the health-related quality of life as a relevant TBI outcome. The impact of a TBI-related disability on the self-reported health and well-being has received limited investigation, and studies from Scandinavia are lacking. Studies from different countries are required to provide “a more accurate reflection of the population’s needs, allowing better understanding of regional, national and international differences and needs in the area of TBI rehabilitation” (89).

Despite its importance, studies on the perceived health-related quality of life at many years after TBI are still limited in number (2;119-121). The description of the HRQL on a mild TBI population from Sweden is available (144), but the profile on a moderate-to-severe TBI population from Scandinavia is lacking. There are a few recently published Scandinavians studies that comprise long-term recovery after TBI (107;145;146), but the data from the working-age population at ten years after moderate-to-severe TBI is limited.

2. GENERAL AIM AND SPECIFIC RESEARCH QUESTIONS

The overall aim of this research project was to describe the epidemiological trends of hospital-treated TBI, TBI-related disabilities and health-related quality of life after moderate-to-severe TBI.

More specifically, the research questions were as follows:

- What is the incidence of hospital-treated TBI in the Oslo population? (paper I)
- What is the spectrum and injury severity in this TBI population? (paper I)
- What is the occurrence of substance use and pre-injury substance abuse in moderate-to-severe TBI? (paper II)
- How does substance consumption at the time of injury and pre-injury substance abuse affect the severity of the intracranial injury? (paper II)
- What is the extent of the TBI-related disability, as defined by the ICF, at one year after moderate-to-severe TBI? (paper III)
- What is the use of rehabilitation services at the one-year follow-up? (paper III)
- What is the impact of the TBI-related disability on the physical and mental domains of health at the one-year follow-up? (paper III)
- What is the functional outcome ten years after moderate-to-severe TBI? (paper IV)
Which factors influence the HRQL ten years after moderate-to-severe TBI? (paper IV)

3. SUBJECTS AND METHODS

3.1 Study population

The studies were conducted in the TBI population treated at the Oslo University Hospital, Ulleval. The first of these studies was an unselected population-based study of patients with acute TBI from Oslo (paper I); the others studies included TBI patients from Oslo/Eastern Norway selected according to age (16-55 years) and injury severity inclusion criteria (moderate-to-severe TBI) (papers II-IV). The Oslo University Hospital, Ulleval, is the major trauma (neurotrauma) hospital for 534,129 inhabitants in Oslo (260,731 males and 273,398 females) and is also the Trauma Referral Centre for the South-East region of Norway with a population of nearly 2.6 million (1.8 million in the East and 0.8 million in the South region), i.e., half of the Norwegian population.

3.2 Patients and design of the population-based study, Paper I

Paper I presents the prospective study on the incidence of hospital-treated TBI, and it includes persons residing in Oslo at the time of the injury, who were hospitalised with acute TBI during the period from May 15, 2005 to May 14, 2006. The electronic patient register from the hospital emergency room was searched two times weekly to identify all patients admitted to the hospital with acute TBI of any severity level. TBI was defined as head trauma with a loss of consciousness or PTA, skull fracture, or objective neurological findings. The following ICD-10 codes were used: S02.0-S02.9 (skull and facial fractures), S06.0-S06.9 (intracranial injuries), S07-S07.1, S07.8, S07.9 (crushing injury of the head), S09.7-S09.9 (other and unspecified injuries of the head), T04 (crushing injuries involving the head with neck) and T06 (injuries of the brain and cranial nerve). The patients were registered in the study with the most severe TBI diagnosis given during their stay in the hospital, according to the following hierarchy: contusions/diffuse brain lesions (S06.1-S06.3, S06.7-S06.9, S06.7, S07.1, S09.7, T04.0 and T06.0), traumatic intracranial haemorrhages (S06.4-S06.6), cranial fractures (S02.0, S02.1 and S02.7-S02.9) and concussions (S06.0) (147). The medical records of a total of 1816 patients were reviewed. Patients with isolated injuries to the scalp, isolated facial and jaw fractures, chronic subdural haematomas, anoxia and birth trauma, were excluded. The patients with multiple
admissions for the same injury, those admitted to the hospital later than 48 hours after the trauma and patients not residing in Oslo were also excluded. Only 445 patients met the inclusion criteria. The initial severity of the TBI was measured by the GCS score given upon admission to the hospital or by the pre-intubation values assigned at the site of the injury.

3.3 Patients and design of studies on selected TBI populations, Papers II-IV

Papers II and III present prospective studies of patients with moderate-to-severe TBI admitted to the Oslo University Hospital, Ulleval, during a period of 2 years starting in May 2005.

In the study assessing the association between substance use and severity of TBI (paper II), the following inclusion criteria were used: patients age 16-55 years, reside in the Eastern region of Norway, admitted with ICD-10 diagnoses of intracranial injuries (S06.0-S06.9) within 24 hours of injury, considered to have moderate-to-severe TBI (GCS 3-12), known status of substance use at the time of injury, and CT scan of the brain performed within 24 hours post-injury. We excluded patients with co-morbidities that may interfere with the assessment of the TBI consequences, such as neurological disorders/injuries and known psychiatric diseases (n=11). We also omitted patients who were homeless or with unknown addresses (e.g., previously diagnosed severe substance abuse disorders) and those who were incarcerated (n=18).

Over the study period, 48 patients with moderate TBI and 99 patients with severe TBI who were admitted to the hospital met the inclusion criteria. Of these, 27 patients (12 in the moderate and 15 in the severe TBI group) were not willing to participate in the study. Thus, 120 patients were initially included. Subsequently, we excluded four patients with missing CT data and five with unknown substance use status at the time of injury; thus, a total of 111 patients were assessed in paper II. A detailed comparison between the participants and non-participants with moderate TBI showed no statistically significant differences in age, gender, GCS, external cause of injury and substance use. A higher number of patients in the participating group had more severe intracranial pathologies, but no statistically significant difference was revealed (p=0.06). In the severe group, there was no difference in participating vs. non-participating groups regarding age, gender, substance use and
intracranial pathology. A significantly higher number of participants had a lower GCS (p=0.02) and were injured in traffic accidents (p=0.05).

The one-year follow-up study (paper III), which assessed the TBI-related disabilities and subjective reported health and well-being, was done on the same population as in paper II. Of the patients who fulfilled the inclusion criteria, 27 refused to participate as mentioned above (18% of 147). A total of 21 patients died during acute care, and two died in post-acute care (19% of 120). Four patients dropped out of the study before the one-year follow-up (4% of 97). The data collection was performed at one year post-injury and included 93 patients. Eight patients (9% of 93) with severe communication disabilities were unable to participate; thus, 85 patients were assessed in paper III.

The long-term follow-up study concerning the functional outcome and health-related quality of life (paper IV) was a retrospective study of patients admitted to the Neurosurgical Department, Ulleval University Hospital, with moderate-to-severe TBI from January 1995 to December 1996; the follow-up period for this study was ten years after the injury. The inclusion and exclusion criteria were similar to those in paper II-III. The patients were identified from the hospital discharge register if they had ICD-9 diagnosis codes indicating head injury, skull fractures and intracranial injuries (800-801.9; 803-804.9; 850-854.9). All medical records were reviewed for the accuracy of coding and the severity of the TBI. The review of 499 medical records (242 patients injured in 1995 and 257 injured in 1996) resulted in 136 eligible participants with diagnostic codes of intracranial injuries. Of these, 26 (19%) had died after discharge from the hospital; the remaining 110 survivors were invited by mail to participate in the study. Eighty replies (73%) were received. Of these, 16 (20%) refused participation, and 64 agreed to take part in the study and were scheduled for an interview. The interviews were conducted during the summer/winter months of 2005/2006. Two patients were excluded after the interviews due to co-morbidities; thus, 62 patients, 30 with severe and 32 with moderate TBI, were evaluated for their long-term outcome.

3.4 Data collection

Data was collected during the acute hospital stay (papers I-III), at one year post-injury (papers III), and at ten years post-injury (paper IV). The patient outcomes were assessed by clinical evaluation, interviews and self-reported questionnaires.
At the one-year follow-up, the patients were interviewed and evaluated by N. Andelic at the outpatient department or the rehabilitation hospital at which they were admitted for a clinical follow-up assessment. Four interviews were conducted in the patients’ homes at their request.

At the ten-year follow-up, the majority of the interviews (81%) were performed as a face-to-face interview in the hospital or in the patient’s home; 16% were conducted via telephone.

3.5 Measures and instruments

3.5.1 Pre-injury socio-demographic characteristics and injury characteristics

The baseline information including socio-demographic and injury characteristics was based on a systematic medical chart review and/or on data from the Trauma Register at the Oslo University Hospital, Ulleval. The marital status was classified as married, single or living with parents. The education was categorised as 0-9, 10-12 or ≥13 years. The employment status was categorised as employed full-time, employed part-time, unemployed or retired. Students were regarded as full-time/part-time employees.

The causes of injury were classified as transport/traffic accidents (irrespective of type), falls (irrespective of height), assault, and others, with sports injuries considered as subgroups of the other causes (paper I, III and IV). In paper II, the cause of injury was dichotomised into traffic accidents and other causes.

The substance use (encompassing both alcohol and/or other psychoactive substances) in paper II was assessed by clinical judgment (65) when the hospital admission records reflected blood alcohol concentration (BAC) or a positive drug screen, when a physician verified influence by examining the patient, or when the patient reported recent substance ingestion. A dichotomous classification was also used for the substance use (yes/no).

The CAGE questionnaire (Cut down, Annoyed, Guilty, Eye-opener)

The CAGE questionnaire was used as the standard patient interview for the screening of pre-injury substance abuse in our TBI population (148) (paper II). The CAGE consists of four questions that address the lifetime drinking experience (CAGE-alcohol). The questions are also modified to address the drug use experience (CAGE-drug). The CAGE is popular
in a clinical setting because of its brief administration time (149). Previous studies have shown that the CAGE may be a useful screening test for substance abuse in the TBI population (150). A score of 2 or more is considered a cut-off score indicating clinically significant alcohol and/or drug problems (149). The CAGE interviews were administered as part of the follow-up study.

3.5.2 Injury severity variables

*The Glasgow coma scale (GCS)* (15) was used to assess the initial severity of the TBI in all papers. The GCS is described thoroughly in the introduction.

*CT head scan*

The TBI severity in papers II-III was defined by the structural brain damage shown on the CT scans. The patients underwent a CT head scan shortly after admission. A second scan was obtained within 6-24 hours after injury. The findings from the first and second CT scans were categorised according to the diagnostic categories of types of anatomical abnormalities as classified by Marshall et al. (25). The scores from the “worst” CT were used in the final analyses (151). The original *Marshall classification* ranges from 1 to 4, with separate categories for any lesion that is surgically evacuated and non-evacuated mass lesions. Few patients were observed in category 4 and in separate categories, thus precluding analyses in all the Marshall categories. Therefore, the original Marshall classification was subdivided into two groups (68). The first group included patients with a Marshall score <3 (less severe brain injury) and the second group included those with a Marshall score ≥3 (more severe brain injury with significant intracranial abnormalities).

*The Injury Severity Score (ISS)*

The ISS was used in papers II-III to indicate the overall trauma severity (20). The ISS is an anatomical scoring system that provides an overall score for patients with multiple injuries. Each injury is assigned to an Abbreviated Injury Scale (AIS) that classifies the individual injuries by body region on a 6-point ordinal severity scale (19). The ISS score ranges from 1 to 75 (best to worst) and is calculated using the sum of the squares of the highest AIS score in the three different body regions. An ISS of 15 or greater is universally accepted as a definition of a major trauma patient. The trauma scores were extracted from the hospital’s Trauma Register.
3.5.3 Post-injury variables

We requested information about the duration of treatment (e.g., length of stay in acute and rehabilitation hospitals) and discharge place.

In paper III, we collected information about access to the community-based rehabilitation services at the one-year follow-up assessment as an indicator of the environmental support. The use of rehabilitation services related to TBI was dichotomised into yes/no variables. The types of services were divided into the following: daycare (nurse and/or personal assistant), physiotherapy, occupational therapy, speech therapy, psychologist, social worker and others.

3.5.4 Outcome variables

Beck Depression Inventory (BDI)

Depression was assessed using the BDI (152) at one and ten years post-injury (papers III-IV). The BDI is a 21-item self-report instrument designed to screen for depression, with primarily cognitive and affective symptoms. Although the inventory is widely used for psychiatric populations, it may be an effective screening tool for self-reported depression in the TBI populations (153), and it has been used previously in TBI research (102;153). The BDI scores range from 0-63, and scores above 12 indicate depression (154).

The post-traumatic epilepsy was defined as two or more unprovoked seizures after TBI that were causally related to the trauma itself (paper IV) (105). The patient medical records were examined for confirmation of the diagnosis.

Functional Independence Measure (FIM)

The FIM is an 18-item scale that assesses specific activities of daily living (ADL): self-care, sphincter control, mobility, communication, cognition and social adjustment (114). Each FIM item is rated on an ordinal scale from 7 to 1. A score of 7 or 6 is categorised as ‘not needing personal assistance’ and 5 or less as ‘needing assistance’ (ranging from cueing and guidance to total dependence). The FIM consists of two subscales, the FIM Motor (FIM-M: 13 items) and the FIM Cognitive (FIM-COG: 5 items). The FIM-M scores range from 13 to 91, and the FIM-COG scores range from 5 to 35; higher scores indicate greater independence. Corrigan et al. (155) confirmed the validity of the FIM for patients with TBI. Because the motor and cognitive abilities may change differently over time, both the FIM-
M and FIM-COG were used in the analyses (138). Ceiling effects of the FIM have been reported due to the complex functional nature of TBI (156). N. Andelic, a certified FIM rater, performed the FIM scoring. The FIM was used as a measure of activity limitations in paper III.

Community Integration Questionnaire (CIQ)

The CIQ is designed to assess reintegration into the community after TBI and is frequently applied in TBI research (157). It is a 15-item scale designed to assess home integration (range 0-10), social integration (range 0-12) and productive activities (range 0-7). A higher score indicates greater integration. As the CIQ home integration subscales assess activities rather than participation (158), we used the CIQ social integration and CIQ productivity subscales as measures of participation restrictions in paper III.

The Glasgow Outcome Scale-Extended (GOS-E)

The GOS-E (159) was used to evaluate the global functional outcome in paper IV. The GOS-E defines areas of independence, work, social and leisure activities, family and return to normal life. The GOS-E is an 8-point ordinal scale with higher scores associated with better outcome. The patients are divided into the following outcome categories: 1=dead, 2=vegetative state, 3=lower severe disability, 4=upper severe disability, 5=lower moderate disability, 6=upper moderate disability, 7=lower good recovery and 8=upper good recovery.

The Medical Outcomes 36-Item Short Form Health Survey (SF-36)

The SF-36 is a widely used health outcome measure (160), which has also been validated for the TBI population (135). The items are designed to measure health related functioning and well-being along eight sub-scales. The physical domain consists of physical functioning (PF), role-physical functioning (RP), bodily pain (BP) and general health (GH). Vitality (VT), social functioning (SF), role-emotional functioning (RE), and mental health (MH) are the dimensions of the mental health domain. The scale range is 0-100 from worst to best. The scoring and calculation of the scales were performed according to the Wares survey-manual (160) in both papers III and IV. The subscales can be aggregated into summary scores that represent the two main dimensions of health: a physical component summary (PCS) and a mental component summary (MCS), which are calculated as the weighted sums of the subscale scores (160). The literature highlights the discrepancies between the scores on the individual scales and the component summaries (161). The emotional role limitation
and mental health scales have negative effect on the PCS, whereas physical functioning, physical role limitation and bodily pain have a negative effect on the MCS. Consequently, improved scores on the scales within one domain reduced the component score for the other domain. Recent research has investigated the factor structure by making comparisons between the models with correlated (oblique solution) and uncorrelated (orthogonal solution) PCS and MCS factors. The model using the oblique solution reduced the negative weights that caused inconsistencies in the scale and summary scores. As recommended by Hann and Reeves (162), we used the oblique model for calculating the physical and mental component scores in paper III. The resulting scores were converted to a scale with a mean value of 50 and a standard deviation of 10. These scores were computed at the SF-36 website (http://www.sf-36.org/nbscalc/index.stml) and were based on the Norwegian norms. The physical and mental health summary scores less than 40 (> 1 SD below general population norms) indicate poorer health (163).

3.6 Statistical analyses

A variety of analyses were used in this study. All statistical analyses were performed with SPSS 13.0-15.0 (SPSS Inc., Chicago, IL, USA).

The descriptive data are presented as proportions, mean values with standard deviations (SD) or medians with 25th and 75th percentile values (25%, 75%). In general, the statistical comparisons between participants and non-participants or between other groups of patients were performed using the Mann-Whitney U test or the independent samples t-test (for normally distributed data). The Chi-square test for contingency tables was used to detect associations between the categorical independent variables (papers I-IV). Spearman’s correlation coefficient was used to analyse the association between the different variables in the SF-36 and when analysing the differences in the SF-36 dimensions between the subgroups within patients who filled out the questionnaire. Due to the number of tests performed, a significance level of 0.01 was set in the analysis of the SF-36 scales differences (paper IV). A significance level of 5% was used (p = 0.05) in the other papers I-III.

In paper I, the incidence of hospital-treated TBI per 100,000 in population per year was calculated on the basis of the number of new hospital-treated cases with acute TBI residing in Oslo and from information on the demographic data of the Oslo population from Statistics Norway, 2005 (534,129 inhabitants). The case fatality rate was calculated using
the following formula: \( \frac{\text{fatal injury}}{\text{fatal injury} + \text{non-fatal injury}} \times 100 \). Multiple linear regression analysis was performed to determine whether the association between the length of the hospital stay and the GCS remained significant after adjusting for age, gender and associated injuries. The length of the hospital stay was log-transformed when performing the linear regression analyses, as this variable was skewed.

In paper II, logistic regression analyses were used to evaluate the effects of substance use at the time of injury and pre-injury substance abuse on the TBI severity, and the odds ratios (OR) with confidence intervals (95% CI) were calculated. The substance use and pre-injury substance abuse (from the CAGE questionnaire) were entered as the predictor variables and were analysed separately (crude OR) against the Marshall groups, which comprised the dependent variable. The possible confounding variables studied in the multivariate regression analysis (adjusted OR) were gender and age, as well as education levels and cause of injury (as these differed significantly in the two severity groups). The final regression analysis was also adjusted for substance use and pre-injury substance abuse. Age was recorded in four categories (in ten-year intervals), and cause of injury was dichotomised into traffic accidents and other causes. The categories with the highest number of patients were used as the reference groups. For the categories of substance use and CAGE, the reference group consisted of patients who screened negative for substance use and abuse.

In paper III, simple linear regression was used to explore the relationship between each of the independent variables (demographic variables, ISS, CT head, FIM-M, FIM-COG, CIQ social participation, and CIQ productivity) and dependent variables (SF-36 physical and mental component oblique scores). Multiple regression analyses were carried out using a hierarchical approach (a block-wise analysis). The independent variables were entered in four separate blocks based on the ICF conceptual model, and two regression models were built. The results are presented as adjusted \( R^2 \) and standardised beta (\( \beta \)). Before conducting the multiple regression analysis, the possible multicollinearity of the independent variables was examined using the variance inflation factor (VIF). The distribution of the residuals was examined for normality. The influential data points were examined using Cook’s distance (D). A power analysis (a priori) showed that for a multiple regression analysis with eight predictors, a sample size of 83 would be required if an effect size of 0.2 was achieved at a power of 0.80 and alpha of 0.05.
3.7 Legal and ethical aspects

All studies were conducted according to the Declaration of Helsinki, and the patients gave their written consent in follow-up studies. The Regional Committee for Medical Research Ethics, South-East Norway, evaluated and approved the project. The Norwegian Data Inspectorate endorsed the project.

4. SUMMARIES OF MAIN RESULTS

4.1 Paper I

In this paper, we presented the incidence of the hospital-treated TBI in an Oslo population, and we described the severity of the injury and the outcome of the patient’s acute medical care.

The 445 patients identified represent an annual incidence of 83.3/100,000. The median age was 29 years. The male: female ratio was 1.8:1.0. The highest incidence of TBI hospitalisation was found in elderly males and young children. The most common causes of TBI were falls (51%) and transport accidents (29.7%). The majority of patients were classified as mild (86%) according to the GCS. Contusions and intracranial haemorrhages were found in 12.3% of cases with mild TBI. Intracranial lesions were found more often in the elderly. The case fatality rate was 2.0 per 100 hospitalised patients and was highest in the elderly. The length of the hospital stay and the proportion of discharged patients to local care/in-patient rehabilitation increased significantly with the severity of the TBI and with advanced age (≥75 years).

We concluded that the incidence of hospital-treated TBI is considerably lower than that found in previous studies from Norway and Scandinavia. Despite the apparent decline in the TBI hospitalisation rates, our findings should draw attention to the need for more effective preventive programs related to falls. Studies that assess the long-term consequences for the elderly TBI patients are also needed.

4.2 Paper II

In this paper, we assessed the occurrence of substance use at the time of injury and of pre-injury substance abuse in patients with TBI. The effects of acute substance consumption at the time of injury and pre-injury substance abuse on the TBI severity were also investigated.
We hypothesised that patients who consumed substances at the time of injury (controlling for age, gender and cause of injury) would have CT evidence of more severe anatomical brain injuries than their non-influenced counterparts.

The TBI severity was defined by the modified Marshall classification into less severe (score < 3) and more severe brain injuries (score ≥ 3), based on the structural brain damages shown on a CT scan. The clinical definition of substance use was applied. The pre-injury substance abuse was screened using the CAGE questionnaire.

A total of 111 patients with a mean age of 32.2 (SD 11.6) were included. Of all patients, 50 (45%) were in the less severe TBI group, and 61 (55%) were in the more severe TBI group. In addition, 47% of the patients were under the influence of a substance at the time of injury. Significant pre-injury substance abuse (CAGE ≥ 2) was reported by 26% of the patients. Substance use at the time of injury was more frequent in the less severe group (p = 0.01). The frequency of pre-injury substance abuse was higher in the more severe group (30% vs. 23%). In a logistic regression model, the acute substance use at the time of injury tended to decrease the probability of a more severe intracranial injury, but the effect was not statistically significant after adjusting for age, gender, education, cause of injury and substance abuse (OR = 0.39; 95% CI 0.11-1.35, p = 0.14). The patients with positive screens for pre-injury substance abuse (CAGE ≥ 2) were more likely to have a more severe TBI in the adjusted regression analyses (OR = 4.05; 95% CI 1.10-15.64, p = 0.04).

We concluded that acute substance use was more frequent in patients with less severe TBI that was caused by low-energy events, such as falls, violence and sport accidents. Pre-injury substance abuse increased the probability of a more severe TBI that was caused by high-energy trauma, such as motor vehicle accidents and falls from higher levels. Preventive efforts to reduce the substance consumption and abuse in the at-risk populations are needed.

4.3 Paper III

The purpose of this study was to assess the disability and the physical and mental health status at one year after TBI, using the International Classification of Functioning, Disability and Health (ICF) as a conceptual model for understanding the TBI disability. Based on previous research, we hypothesised that the participation in productive activities would be the strongest predictor of both health dimensions.
The severity of structural brain damage (from a CT of the head) and overall trauma (from the ISS) were used as the indices of body structure impairments. The activity limitations were measured by the Functional Independence Measure (FIM), and the participation restrictions were assessed via the Community Integration Questionnaire (CIQ). The physical and mental health dimensions as reported on the SF-36 questionnaire were chosen as the outcome measures.

There were 85 patients with mean age of 31 years (SD 11.0) included in this study. About half of the patients sustained severe TBI with significant intracranial abnormalities, as found on the CT head scans. Almost 75% of the patients were defined to have major trauma according to the ISS. Half of the patients had additional orthopaedic injuries. The mean length of hospital stay in acute care was 24.0 \pm 21.0 days. Of these 85 patients, 65% received in-patient rehabilitation (92% of those with severe TBI and 44% of those with less severe TBI). The mean length of the inpatient rehabilitation stay was 57.0 \pm 38.0 days. Roughly one-quarter of the patients reported a disability requiring personal assistance at the one-year follow-up. One-third of the patients had major problems with social integration, and 42% were not working. Nearly half of the patients reported poor physical health, and 37% reported poor mental health. Regression models, including demographics, impairments, activity limitations and participation restrictions, accounted for 50% of the variance in physical health and 35% of the variance in mental health. More severe impairments, fewer activity limitations and fewer participation restrictions equated to better overall health. Participation in productive activities was the strongest individual predictor of the physical and mental health dimensions ($\beta =0.55$, $p<0.001$ and $\beta=0.40$, $p=0.001$, respectively).

The results demonstrated that a significant proportion of TBI survivors face substantial disabilities and impaired overall health at one year after injury. To optimise the health and well-being outcomes, clinicians need to ensure that the health needs of the patients with less severe TBI are identified and treated during the post-acute period.

4.4 Paper IV

In this paper, we present the functional outcomes and health-related quality of life (HRQL) at ten years after moderate-to-severe TBI.
The functional status was measured by the Glasgow Outcome Scale-Extended (GOS-E), and the HRQL was measured by the SF-36 questionnaire.

The 30 survivors with severe and 32 with moderate TBI were included. The mean age at the time of follow-up was 40.8 years. The frequency of epilepsy was 19%, and the depression rate was 31%. A majority had good recovery (48%) or moderate disability (44%). The employment rate was 58%. Of the patients with a GOS-E = 6, 27% received full disability pension, even if they had partial working capacity. The functional status and employment rate were associated with the initial TBI severity. The study patients had significantly lower scores in all SF-36 dimensions when compared to the general Norwegian population. However, there was no statistically significant difference between the SF-36 scores in the moderate and severe TBI patients. Depressed patients scored significantly worse in all SF-36 dimensions. The patients with good recovery showed significantly better scores in seven SF-36 dimensions than patients with moderate and severe disability. With the exception of BP, employed patients showed better scores than unemployed.

We concluded that the study population is still in their most productive years at the ten-year follow-up, and vocational rehabilitation should be considered at this stage of the injury. The decreased HRQL suggested the importance of support and care-availability in the “chronic” stage of TBI as well.

5. GENERAL DISCUSSION

In this thesis, the trends in TBI hospitalisations, the effects of substance use on the TBI severity and the disability following TBI have been studied. A special emphasis has been placed on the health and health-related quality of life after TBI. The quality of the data sources and the main findings of this research will be discussed.

5.1 Quality of Data Sources

5.1.1 Study population

According to Altman (164), if the sample is not representative of the population, "the results will be unreliable and of dubious worth". This problem is usually referred to as selection bias. There are many sources of selection bias, including non-random sample, number of non-participants, difficulties in tracing patients omitted and number of drop-outs.
The data in this dissertation were collected from the hospital-admitted acute TBIs at the Oslo University Hospital, Ulleval. Ulleval is the major trauma hospital and the only hospital in Oslo for the neurosurgical care of acute TBI. There are three other general hospitals in Oslo that provide secondary hospital care of the TBI patients living in Oslo. About one-quarter of the TBI patients from Oslo are discharged to these hospitals following acute hospitalisation at Ulleval. In the planning phase of paper I, the authorities of these local hospitals were contacted to check their policy regarding the management of patients with acute TBI. If the TBI diagnosis is suspected in patients referred to these hospitals, the policy is to transfer them to Ulleval for neurosurgical evaluation, surveillance and treatment. Therefore, we consider that the patients included in this study were representative of the whole Oslo population. We also considered that the Oslo population is representative of a big-city population in Scandinavia in terms of the gender and age distribution in the population (sources: Statistics Norway, Sweden, Denmark, 2005), in addition to the urbanity of the region and availability of emergency services and Level I trauma centres.

A major problem with the epidemiological studies is associated with the inconsistencies in the TBI definitions and the classification of injury severity (165). Confusion also exists regarding head injury (HI) and TBI. HI is a non-specific and antiquated term that includes clinically evident external injuries to the face, scalp, and calvarium, such as lacerations, contusions, abrasions, and fractures, and it may or may not be associated with TBI (50). The subjects were included in the study of hospital-treated TBI in the Oslo population if they had an acute TBI followed by admission to the hospital (paper I). According to Jennett (9), higher incidences are reported in the studies that identify TBI cases by hospital admissions, by discharge register or by routine ICD coding than in the studies that review medical case records. The former studies could be biased because of double counting of patients with multiple hospital admissions and also by the inclusion of late admissions due to delayed complications. The hospital admission policies and access to health care systems also vary within and between different countries (9;39;43;166).

The TBI incidence calculation in our study may be limited by several factors. Our data provides no information about the number of persons with acute TBI treated in local emergency departments or other outpatient facilities (The Emergency Medical Agency, Oslo) or those persons who did not seek medical care. However, according to the existing literature, most of this underestimation likely consists of milder forms of TBI (6). The Oslo-
residing patients that sustained milder injuries outside their home region and were not treated in the Oslo University Hospital, Ulleval, could not be identified. However, the number of patients included in our study is in accordance with information on the hospital-treated persons residing in Oslo with traumatic intracranial injuries in Oslo hospitals in 2005 (Source: Statistics Norway 2005).

Age-exclusion criteria were applied to the study populations in papers II-IV, and patients representing the age range of 16-55 years were recruited. This was first done due to the experience from another TBI project conducted at the Ulleval in 2001 (167;168) and because the TBI literature shows the highest rates of morbidity, mortality and persistent functional impairment for this group (37). Secondly, the alcohol and substance uses differ between the populations according to age, such as children and the elderly. Thirdly, the co-morbidities that may influence the assessment of the TBI consequences are more frequent in the elderly. Finally, the assessment of the employment rate after the TBI is an important study outcome; therefore, a follow-up of this sample during their productive years (10-15 years after injury) was planned.

In papers II-IV, we included patients with a diagnosis of intracranial injuries considered as moderate-to-severe TBI (GCS 3-12). Permanent disability is common in moderate-to-severe TBI, and studies from Norway/Scandinavia were limited for this population. The moderate-to-severe TBI population included in this project was representative of the population in East Norway that is in need of acute neurosurgical care (irrespective of the treatment they received after discharge from acute hospitalisation) as our hospital is the only neurotrauma hospital in this region.

5.1.2 Patients and design

Of the 1,099 patients with a TBI diagnosis admitted to the hospital over a period of one year, 41.3% did not live in Oslo, 13% had chronic subdural haematomas, 3.3% had multiple admissions for the same injury and 1.9% were admitted to the hospital later than 48 h after the trauma. The remaining 40.5% (445 patients) met the inclusion criteria (paper I).

During the inclusion period for papers II-III, we identified 147 candidates eligible for the study. The refusal rate was 18% (n=27). In paper II, we included 111 patients, and 14 (13%) of these died after inclusion. Of the 97 TBI survivors, 85 completed the one-year follow-up and were included in paper III. The severity of the TBI has limited those patients who could
respond to the SF-36 questionnaire. Consequently, eight survivors with severe communication problems were not included in this study. The reason for the withdrawal of four other patients was unknown.

The response rate of the retrospectively identified moderate-to-severe TBI cohort in paper IV was 73%, and three-quarters of these were included in the study. One of the most crucial sources of bias in cohort studies is a lack of follow-up. According to Corrigan et al. (169), “one third to one half of subjects in long-term outcomes of TBI are not included in outcome samples because of inability to track subjects after they leave inpatients treatment”. However, the participation rate in this long-term follow-up study was in accordance with (121) or even higher (100) that other similar TBI studies.

Compared with many international studies, papers II-IV have a relatively low number of participants. However, the material across the studies represents a good spectrum of consecutive Norwegian TBI patients in a Trauma Referral Centre, and the demographic and injury-related data are comparable with that in the literature from other countries (22, 26).

The strength of our studies is that they comprise the patients hospitalised with acute TBI at the Trauma Referral Centre, irrespective of the treatment they received after discharge from the acute hospitalisation. The studies that include only persons with TBI who received comprehensive inpatient rehabilitation services may lead to overestimation of the severity of the disability and the associated need for services (112).

The data in papers I-III were sampled within a prospective cohort design. This implies that certain criteria for the data collection were established in advance, which secures the relevance and completeness of the data.

The data in paper IV were sampled with a retrospective cohort design, which may have influenced the accuracy of the inclusion procedure and the classification of the injuries. The severity of TBI in this study was defined by the GCS given at the emergency admission to the hospital because it was difficult to obtain the acute CT data for all participants. However, it is possible that the more severely affected patients were more likely to enter a retrospective study such as this.
5.1.3 Measures and instruments

Due to the use of the clinical definition of substance use in paper II and other factors, such as a lack of BAC levels and toxicological screening in all patients, our results regarding substance use should be interpreted with caution. As a result, we made no distinction between the types of used substances when analysing the probability of a more severe TBI. The lower sensitivity of the CAGE-drug questionnaire as compared to the CAGE-alcohol questionnaire (150) is a methodological limitation, as was the cut-off score used. We based our CAGE screening on a self-report from the patients; therefore, under-reporting of illicit drug use is probable.

Injury severity variables

In paper I, the patients were registered with the most severe TBI diagnosis given to the patient during their stay at the hospital. As mentioned in the introduction, the ICD-10 codes allow for differentiation between contusions, intracranial haemorrhages, cranial fractures and concussions. The ICD-10 diagnoses were in accordance with the findings of the CT head scans performed on admission.

The GCS has become the standard method for assessing the initial TBI severity, which aids in comparing findings in and across countries and world regions (39) (paper I). Prior studies have documented the problems in obtaining an accurate GCS score for TBI (12). Higher blood alcohol levels affect the consciousness of the TBI patients, and at the time of hospital admission, it may be difficult to evaluate which symptoms are due to the head injury and which are due to alcohol intoxication (170). Thus, alcohol-influenced patients may be more likely to be admitted, even if they have a very minor TBI (170). In this thesis, however, we did not include patients with mild TBI in the follow-up studies. We defined the severity of brain injury by the structural damage shown on the CT head scans in papers II-III, as the level of consciousness might be obscured in acute settings by the above mentioned factors (12). Despite the limitations of the Marshall classification addressed in the introduction, there is evidence that the CT scans can assist in discriminating less severe and more severe TBI (25;68). The CT evaluations and the Marshall classifications were done by the same neuroradiologist (T. Jerstad), thus eliminating any inter-rater bias.
Our population consisted of both isolated TBI and TBI with multiple injuries. Although TBI was the primary diagnosis in this population, concomitant extracranial injuries may confound the interpretation of the long-term functional outcome of the TBI (112;171).

Outcome variables

It was previously reported that the BDI has low sensitivity in terms of discriminating depressed from non-depressed persons and the BDI may be measuring the hyperreactivity to symptoms instead of depression (172). This may lead to a greater number of individuals falsely classified as depressed (153). In contrast, Green et al. (153) reported that the BDI was useful in screening for depression in TBI. However, the depression rate of the present studies should be interpreted with caution as only the BDI was used for depression screening.

As reported in the literature (173), the FIM has a ceiling effect at one-year post-injury. The cognitive function in paper III was evaluated by the cognitive FIM items. The FIM-COG is of the limited sensitivity (155). Thus, the cognitive dysfunction in this study may be underestimated. However, this project was not designed to evaluate the neuropsychological outcome after the TBI, as neuropsychologist S. Sigurdardottir has done this in another study on the same population (174;175). The clinical evaluation, including the assessment of the FIM and the GOS-E, was performed by the same person (N. Andelic), thus eliminating any inter-rater bias (papers III-IV).

The GOS-E as a relatively crude measure of global function has been criticised for ceiling effects and for being insensitive to subtle but functionally limited deficits in cognition, mood and behaviour (176). However, the implementation of a structured interview has resulted in the improved inter-rater reliability of the GOSE (159).

While the CIQ measures the person’s level of involvement in activities associated with community integration, low scores may not reflect an actual failure to reintegrate as a result of the TBI. Rather, the scores reflect the distribution of responsibilities in the family at pre-injury or may highlight personal choice or circumstances (177;178).

The SF-36 is a generic instrument that assesses the HRQL across different health conditions, (healthy versus ill). The disadvantage of using generic measures, as cited by Petersen and Bullinger (134), “is that small changes in HRQL of specific patient groups
may not be detected in specific populations. On the other hand, while condition-specific instruments may provide clinically relevant information, comparison across health conditions will not be possible” (128). Bullinger and the TBI consensus group (128) have recommended that the assessment of the HRQL include both generic and condition-specific instruments. Among the generic instruments the SF-36 should be considered. However, the condition-specific instrument Quality of Life in Brain Injury (QOLIBRI) was just in the development phase when this project was planned and thus could not be used in this study (179).

Several studies have pointed out that the SF-36 does not address the cognitive aspects of the quality of life (134;158;180). According to van Baalen et al. (181), “although some health concepts like sleep, cognitive functioning, health distress, self-esteem, eating and communication are not measured specifically, the SF-36 scales have been proven to be associated with these concepts”.

5.2 Statistical analyses

Although the study sample was relatively small, we used multiple regressions modelling in papers II and III, and we adjusted for factors commonly assumed to contribute to the predictions. Such analyses seemed to be the best method to answer our research questions. To increase our confidence in the quality of the analyses, we used a conservative approach (with the number of subjects at least ten times the number of included variables). We inspected the graphs of the residuals, investigated the effects of extreme values or outliers on the adjusted models, and compared data with and without logarithmic transformation when necessary.

In paper II, a multiple logistic regression analysis was used to calculate the effects of substance use and pre-injury substance abuse on the intracranial brain injury severity. When constructing the adjusted model, several of the covariate variables were collapsed into fewer categories, thus ensuring a sufficient ratio of the number of subjects relative to the number of included variables.

In paper III, a hierarchical block regression model was used. This implies that the independent variables were categorised into blocks according to a theoretical model, in this case the ICF, before the blocks were entered in a predetermined order. In this procedure, the
ICF provided a well-organised model to classify and group the independent variables. The regression analysis provided the opportunity to estimate the contribution of each block.

Like many international studies on similar topics, our papers have a low number of participants, but clinically relevant associations have been detected. However, there may be less strong but still clinically relevant associations that have not been detected in our studies.

All questionnaire data and clinical evaluation were collected at the same point. The results, especially of the regression analyses, should therefore be interpreted with caution. Further investigation, including larger samples and multiple measurement time points, are required to confirm our findings.

5.3 Epidemiological aspects of hospital-treated TBI

When this thesis was planned, there were no studies that described the TBI population from Oslo, and the existing data from an urban area of East Norway was from 1974 (44). There was also a need for updated studies on the TBI hospitalisation trends in a Scandinavian population. In paper I, we found that the estimated annual incidence of hospital-treated patients with acute TBI in Oslo was considerably lower than the rates reported in previous population-based studies in Scandinavia and Northern Europe (41-45;47). However, our results were in accordance with a recently published report from the U.S. (48). The study findings indicated a trend towards a decreasing incidence of hospital-treated TBI in Norway, perhaps due to the effectiveness of preventive traffic accident legislation, as reported in other countries, with a subsequent decrease in road traffic accidents (48;55;182;183). The density of road traffic in Norway has increased substantially over the last ten years, but the risk of injuries and death in road traffic accidents has declined from 0.400 to 0.288 per million-vehicle kilometres for the same period of time (184). Our findings may also indicate changes in the hospital TBI admissions practices, hopefully due to the implementation of guidelines for the initial management of minimal, mild and moderate head injuries in Scandinavia (81), as well as guidelines for severe TBI (49). In addition, our findings may indicate a decrease of the TBI mortality rates in Norway during the last 10-15 years (63).
The present study showed a bimodal age distribution, as the elderly and young children are those most affected by TBIs, in agreement with other studies (57;183;185;186). The large number of TBI in the elderly could be associated with the trend of ageing in the population (1;57). In contrast to the previous Norwegian and international studies, we found a lower incidence in the 15-29 year age group, probably due to the decline in transport-related TBI incidence, as previously pointed out. The incidence was highest among males, which is a finding reported both in national and international studies (39;47;57;183).

Falls comprise the most frequent cause of TBI-related hospitalisation, followed by transport accidents, which is consistent with previous studies from Norway (43), Scandinavia (47;147) and recent reports from the U.S. (1;48;186). Transport accidents were the main cause of TBI in the 15-54 year age groups. Age-related transport accidents were, however, the highest in young men from 20-29 years old, similar to that reported in other studies in Europe (39) and the U.S. (1;48). The incidence of assaults was higher in this study than in the Northern Norway (43) and U.S. studies (185;186), but a similar incidence was found in Europe (39) and Sweden (41). In this study, alcohol influence was found in as many as 82% of victims of assault.

After the publication of our paper, Heskestad et al. (187) reported a considerably higher incidence of hospital admitted head injuries in the Stavanger region in 2003 (157/100.000). The use of different case definitions (head injury in the study by Heskestad and TBI in our study) and exclusion criteria might explain these differences. However, the trends toward a higher incidence in the elderly and falls as the main cause of injury were consistent in both studies.

The largest proportion of cases in paper I were classified as mild TBI, according to the GCS scores (86%). According to the ICD-10 diagnoses of intracranial injuries used in the study, it could be expected that 12% of patients with mild TBI, 80% of those with moderate TBI and 93% of those with severe TBI will have long-term loss of functioning. Concussions and intracranial haemorrhages were most common in the elderly. Our results support the finding of TBI severity trends observed in the elderly (45;54).

The average CFR in paper I was low; it was mostly related to falls in severely injured and elderly patients, but it was also related to an increased number of medical complications in these patients. Many studies in Europe (9;39;42;44;183), as well as Australia (39), have shown that the CFR has been stable over the last years. The CFR in the present study is
consistent with these rates. The deaths prior to hospitalisation were not accounted for in the present study. The in-hospital mortality has been shown to account for one-third of the total deaths from TBI (9;182;188), and thus, the overall mortality in Oslo can be estimated to be 5.0 per 100,000 inhabitants. This is slightly lower than reported in another Norwegian study from Oslo’s surrounding county, which found 6.6 per 100,000 (39;44), and the urban mortality rate in Australia, which was 6.4 per 100,000 (189). Our estimated rate for overall mortality is in accordance with the rates reported in 1996 from France (5.2 per 100,000) (9;39), and Western Sweden, which was 4.0 per 100,000 (41). However, our estimated mortality rate is considerably lower than the median TBI mortality rate in Scandinavia (11.5/100,000) and in Norway (10.5/100,000), which were estimated for the period 1987-2000 (63). It is possible that the mortality rates in Oslo are lower than in other areas of Norway. Oslo is an urban region with a wide availability of emergency medical services and the Trauma Referral Centre. Thus, the lowest mortality from transport accidents in Norway is found in Oslo (Source: Statistics Norway, 2005).

The length of hospital stay and discharge place were both closely related to the injury severity. Consequently, admission for 24 hours observation was the most common hospital stay. A previous Norwegian study from 1993 showed similar findings for the length of hospital stay (43). As expected, the median duration of the hospital stay was highest in the severe TBI patients. The elderly patients in the age group 75+ years had the longest hospitalisation, as found in several international studies (51;55;185). A large number of patients were discharged to their homes, as reported in others studies (48;185;186). However, 25% of patients were discharged to local care hospitals, nursing homes and other care facilities, and 75% of these were in moderate-to-severe TBI groups.

5.4 Substance use and TBI

When this thesis was planned, there was a need for TBI studies from Europe on the roles of important exposure factors, such as alcohol (39). Studies on the impact of substance use on TBI were also lacking in Norway.

Almost half of the patients showed substance use upon admission to the hospital (paper II). The proportion of patients found to be under the influence of alcohol was 35%, which is higher than in previous Norwegian studies (43;190). This result may be explained by a trend towards increasing alcohol consumption in the general Norwegian population during the
last few decades (191), as a result of the increased number of more regular drinkers (192), and the higher consumption in the Oslo/Eastern Norway than in other regions (193). The alcohol consumption rate was, however, within the range of those reported in a recent review of TBI epidemiology in Europe (24-51%) (39) and in other international studies (66;67). The study also confirmed that alcohol is the most common substance used in the TBI population (67;71).

The use of other psychoactive substances was found in 12% of the total TBI sample. This rate is lower than those presented in international studies (74), and it may be biased by the clinical routines on admission and the clinical definition of substance use. In agreement with the studies on illicit drug use in the TBI populations (74), cannabis was the most frequently detected drug. It is well known that cannabis is the most frequently used illegal drug in the general population in Norway (194).

The proportion of patients that use substances while driving motor vehicles was four times higher in the present study than in a recent study on the prevalence of alcohol and illicit drugs among motor vehicle drivers (aged ≤ 54 years) in South-Eastern Norway (194). Our findings may indicate that the persons who sustain TBIs are not representative of the general population. However, a considerably lower proportion of traffic injury cases in this study were alcohol-influenced compared to that found in the older TBI literature (74). This may represent the lowering of the legal limit for the BAC from 0.5 to 0.2 mg/g in 2001 (194), the effectiveness of campaigns and programs for reducing drinking and driving, and a decrease in the incidence of traffic-related TBI during the last decades.

The proportion of patients with substance use was significantly higher in the less severe TBI group. Falls and other injuries were the main causes of injury in this severity group. The percentage of patients under the influence of alcohol upon admission who were injured by falls or assaulted was in agreement with other Nordic studies (43;72). Northern European countries are often characterised as nations with infrequent but heavy episodes of drinking (“dry” culture), with a higher tolerance toward excessive drinking, and higher frequencies of alcohol-related injuries than Southern European countries, where the use of alcohol is more integrated into everyday life (“wet” culture) (195).

We expected that the substance use at the time of injury could have a potentiating effect on the anatomical brain injury, as measured by the findings on the “worst” head CT scan within 24 hours of the injury (68). Contrary to the expectation, substance use tends to decrease the probability of a more severe intracranial injury in the adjusted logistic
regression (OR=0.39). However, a strong conclusion should not be drawn due to the insufficient statistical power (power 0.58, alpha 0.05).

It has been reported that acute alcohol intoxication exerts both detrimental and beneficial effects on the injury severity and outcome of TBI, although the mechanisms have not been determined. The hypothesis that alcohol-inebriated victims injured by falls on stairs sustain more severe intracranial injuries because of a delayed reaction time and inadequate protection reflexes was not confirmed (69). Smink et al. (196) could not demonstrate a relation between the alcohol concentration and the severity of traffic accidents. Furthermore, alcohol and methamphetamine use were found to be associated with decreased mortality in a retrospective study of severe TBI (71). Ruff et al. (76) also found that alcohol intoxication at the time of injury “was not associated with poor outcome in those who survived long enough to reach hospital”. Based on experimental research, Kelly (197) reported that acute alcohol intoxication may have neuroprotective effects in traumatic brain injuries as a result of the “ethanol-induced inhibition of N-methyl-D aspartate receptor-mediated (NMDA) excitotoxicity”. Dose-dependent effects have also been reported, with a better outcome in the animals influenced by low- and moderate ethanol doses than in the no and high ethanol dose groups (198). According to Tien et al. (23), a low to moderate BAC may be beneficial in the patients with severe brain injury from blunt head trauma, while a high BAC seems to have a deleterious effect on the in-hospital death rate in these patients. Although the focus of our study was not to assess whether the BAC levels impact the severity of the structural brain injury, the mean BAC level was found to be similar in both severity groups.

Screening from the CAGE questionnaire showed that 26% of the patients reported pre-injury substance abuse (problems with alcohol and/or other substances) (paper II). Approximately two-thirds of these subjects misused alcohol. This study showed a lower proportion of pre-injury substance abuse than in the TBI literature review from 1994-2004 (67). The rate was also slightly lower than in a recent study on the TBI population from Australia (73). In our study, we omitted patients with a pre-existing substance abuse disorder, which could explain these lower rates. If we include those patients with a CAGE score of one (8 patients, 9%), those omitted with pre-diagnosed severe substance abuse disorders (14 patients, 14%) and the pre-injury substance misuse group (26%), a total proportion of 49% reached the range of estimates presented in the literature (67;73). The prior history of substance abuse is found less often in persons treated in the Trauma Referral
Centres than in the rehabilitation populations (66). However, the occurrence rate of pre-injury substance abuse in this study was higher than in a Danish study (199), where 5.8% of the intracranial lesions group were diagnosed with substance misuse by the ICD-9 criteria. In our study, 26% of all patients with ICD-10 diagnoses of intracranial lesions had a positive CAGE screening for pre-injury substance problems.

The CAGE positivity is usually equivalent to being a heavy drinker (200). When we extracted the results of patients with a positive CAGE alcohol, the proportion was more than two times higher than the rate of heavy drinkers found in a Norwegian survey in 1998 (191). One population at risk of pre-injury substance misuse in this study was males younger than 35 years of age with a lower education level (< 12 years). The other population was single males, older than 35 years with a high school education. It has previously been reported that drinking serves as an important social function for young people (73), and increased consumption of alcohol is found in subjects with a higher level of education and higher income (191;193).

We found in the adjusted regression analysis that the patients with pre-injury substance problems showed significantly increased probability of more severe TBI as compared to their counterparts (OR 4.05). Chronic alcohol use has consistently been found to be associated with more severe TBI. Ronty et al. (75) reported that pre-injury alcohol abuse precipitated the development of more severe structural traumatic brain damage on the CT examinations. A strong association between the history of excessive alcohol use, the poor outcome for all types of intracranial diagnoses and the greater prevalence of a mass lesion was reported by Ruff at al. (76). Several other studies have reported an association between alcohol abuse and the greater severity of TBI as measured by posttraumatic amnesia, neuropsychological tests and global functioning (66;67;74). According to previous experimental studies, chronic alcohol exposure may exacerbate the TBI, probably as the “effect of imbalance of up-regulation of NMDA receptor activity and down-regulation of gamma-aminobutyric acid (GABA) receptor function resulting in excitotoxicity” (197).

In the adjusted regression analyses, females tended to have an increased probability of more severe intracranial injury, in agreement with the study on females under 50 years of age (201). The older age tended to increase the probability of more severe intracranial injuries. Other studies have reported that increasing age is related to poorer outcome after TBI (202). Of all patients with severe intracranial injuries, 20% were young adults living with parents.
and attending secondary school. School education programs about the effects of and dangers associated with alcohol consumption and drug use are “a key component in preventing substance abuse in this population” (74).

The considerable number of patients with substance use in the present study shows that the use of alcohol and drugs is one of the major risk factors for TBI (23;66;72). The health related- and psycho-social consequences of TBI, as well as the economical burden of these injuries underline the importance of preventive efforts targeting risk populations.

The association shown in this study between the pre-injury substance abuse and more severe intracranial injuries highlights the importance of identifying persons at risk who would benefit from an intervention related to their substance abuse. A routine alcohol and psychoactive substance use and substance abuse screening of the TBI patients at the emergency admission may pinpoint this population (64).

5.5 Disability following moderate-to-severe TBI

When this thesis was planned, there were several studies from Norway regarding the disability after mild TBI (167;168), while the studies on moderate-to-severe TBI was lacking. Moderate-to-severe TBI is known to have long-lasting social, physical and health-related consequences. Of the patients with such injuries from the population-based study (paper I), 75% were in need of further hospital care at local hospitals at the time of discharge. Papers III and IV were designed to follow-up the moderate-to-severe TBI population at one and ten years after injury.

TBI-related disability as defined by the ICF is essential for understanding the TBI consequences for daily life. In the early phase, the detection of impairments and limitations in basic activities is necessary for diagnostic and prognostic purposes, as well as for planning of intervention. In the later phases, the return to daily activities of living and the participation in community life are the most relevant aims of rehabilitation, and therefore, the outcome measures should reflect this (203).

5.5.1 TBI-related disability one year after injury

Although a large number of participants reported no disabilities in terms of motor activity limitations, a significant proportion of the TBI survivors face substantial cognitive disabilities as measured by the FIM at one year after injury (paper III). It is generally
considered to be more difficult to compensate for an inability to perform daily life activities arising from cognitive impairments than to compensate for limitations caused by physical impairments (204). One-fifth of the participants reported a disability that required personal assistance in the cognitive ADL. A similar profile of activity limitations at one year after injury was found in other studies (3;205). The study by Whiteneck et al. (112) reported 37% of patients with disabilities. The lower rates in our study may be explained by the different methodologies used and also the exclusion of patients with considerable communication problems. However, the proportion of activity limitations in our study was likely underestimated as the FIM instrument is of limited value due to a ceiling effect at one year post-injury (173) (paper III).

Social integration was not complete at one year after the injury, and many patients reported productivity restrictions. Two-thirds of the patients reported at least two problems regarding social integration. Only 10% of the patients reached a maximum score on the CIQ productivity scale. These results and the average total CIQ score of 15 were consistent with previous studies (3;123;206). Lower CIQ home integration score was found in those who were living with parents or significant others without participating in domestic tasks even though being able to, in agreement with other studies (2;118). However, it has been reported that being in a relationship before injury, potentially reduced the level of independent community involvement of the patients with TBI, if a partner carried out social and domestic task (177).

Of patients working at the time of injury (82%), one-third was out of work one year later; 37% were working full-time, and 26% had part-time jobs or were studying. The employment rate in Norway for full-time work (age 15-74) in 2007 was 73% (Statistics Norway, 2008). Our rates of employment were roughly comparable with the estimates from a US population-based study (112), but they were more than two times higher than those reported in another prospective study of recovery after moderate-to-severe TBI (123). However, half of the patients with initial severe TBI were not productive one year after the injury, while 25% returned to full-time work, in accordance with previously reported rates (207).
5.5.2 Environmental support one year after injury

Roughly 75% of the patients in the severe TBI group and 48% of those with less severe TBI received rehabilitation services one year after the injury. The survivors with more severe TBIs tended to remain functionally dependent and often required more extensive services (86). More than 33% of these patients received several services. As reported in other studies, however, the most notable service was the use of physiotherapy (121). This may be due to the fact that many patients had additional orthopaedic injuries. Despite the frequent service use, it seems that the rehabilitation and support needs are not covered. For instance, only 6% of the patients with major social integration problems received organised social support.

5.5.3 TBI consequences ten years after injury

The occurrence of posttraumatic epilepsy was roughly comparable with the results of late seizures in adults reported by both Asikainen et al. (110) and a recent Norwegian study of patients with severe TBI at 3-7 years after injury (107) (paper IV). The percentage of patients with epilepsy who received anti-epileptic treatment at the follow-up was also comparable with the former study (110). Epilepsy was correlated with the injury severity, intracranial lesions and craniectomy, in agreement with the previous studies (105;110). Our study showed slightly better general functioning for the patients who did not have epilepsy. This is consistent with the study from Finland mentioned above (110). However, there was no correlation between the epilepsy and the employment outcome in these two studies. Epilepsy was managed by medication, and the patients seemed to have acceptable follow-up routines.

Based on the BDI scores, we found that the depression rate at ten-year follow-up was three to five times higher than the rate in the Norwegian rural and urban population (208). However, the rate was in the lower range of the previous estimates, suggesting that 25-60% of the TBI patients develop depression within eight years post-injury (101;102). The results should be interpreted with caution as we used only the BDI scores for depression screening. However, this underlines the importance of assessment for clinical depression in a long-term perspective and the need for intervention in this segment of the TBI population.
Activity limitations and participation restrictions at ten years after injury were measured by the GOS-E and the employment rates. One half of the patients scored in the good recovery categories. This is in agreement with a recent study from Australia (100). Only 8% of the patients in our study suffered from severe disability, compared with 5% in the former study. Our GOS-E data of the patients with severe TBI were comparable with the study by Wood et al. (209). As in other studies, the initial injury severity was related to the functional outcome at follow-up (24;120;145). Although a large number of participants reported good global functioning at the ten-year follow-up, there are still patients with severe disabilities who require 24-hour support in the community.

A total employment rate of 58% was found, with 45% of patients in full-time jobs at ten years post-injury. These rates were better than those presented by Colantonio et al. (31% of the patients < 65 years were in full-time jobs at 14 years post-injury) (121). An Australian study showed slightly higher rates than ours (66%), but they included patients at all severity levels of TBI (100). Wood and Rutterford (209), reported that 41% of those with severe TBI were employed 17 years after injury. This agrees with our results of 40% of working patients in the severe TBI group. However, the employment rates were higher in our severe TBI population than those reported from the Middle region of Norway (107). The variation observed in the employment rates between these two studies may likely be explained by the different designs and follow-up periods as well as better opportunities for employment in our region. The work-disablement in the patients in this study is probably a consequence of their TBI condition itself rather than of the other multiple injuries. One-fifth of the patients had multiple injuries; four of these were permanently disabled at follow-up and suffered from subsequent issues related to the severe TBI. However, 27% of the patients with a GOS-E score of six received full disability pension, even though they had partial working capacity. These subjects are still in the productive age, and vocational rehabilitation should also be considered at this post-injury stage.

It is notable that nearly similar employment rates were found in our prospective follow-up study one year after TBI (paper III). It has previously been reported that there are few changes in employment outcome after the first years post-injury (210). However, improvements in the acute care of TBI during the last decade may lead to a better outcome in the populations like our prospective cohort (211).
The findings of considerable disability at both one year and ten years after TBI injury are particularly notable given the fact that this sample was composed of subjects who were enrolled at the time of injury based on the characteristics of their injury. Thus, they were not selected because they were involved in rehabilitation or had been presented for follow-up because of complicated recovery or specific complaints about functioning (133).

5.6 Health-related quality of life after moderate-to-severe TBI

The health and health-related quality of life after TBI are the most important focus of this thesis (papers III-IV). Health is a major aspect to quality of life, and the HRQL tools have been used as health outcome measures in TBI studies (212). These outcomes are important for both patients and clinicians, since one of the primary goals of rehabilitation is to give TBI survivors a meaningful existence and a life within their expectations. The factors that contribute to the health-related quality of life could guide interventions for improving physical, cognitive and emotional status, as well as environmental factors.

The self-reports on health and well-being (SF-36) were in general within the impaired range compared to the general Norwegian population, both at the one-year and ten-year follow-ups (paper III and IV) (154). Other studies have also reported that individuals with TBI rate their quality of life lower than non-disabled persons (142;213). Our results seem to be comparable to those reported in the TBI population in the USA in both earlier and later post-injury phases (3;135).

Almost half of the patients reported poor physical health, while one-third reported poor mental health at one year after TBI (paper III). The patients under 31 years of age reported better overall health than those above 31 years of age. Other studies have shown better mental health in older TBI subjects compared to the younger TBI subjects (163). In the general Norwegian population, worse physical health with increasing age was reported, and mental health was the only scale in which there was no statistically significant differences between different age groups (214).

Males experienced better physical health than females (paper III and IV), and a similar trend was observed both in the general population (214) and in other TBI studies (116;163). More problems with the physical role functioning reported by females in our studies may be associated with the trouble they have in fulfilling domestic roles after the injury (116). Among the patients who reported poor physical health, 60% had less severe TBI. Of these,
62% did not receive inpatient rehabilitation, and 38% did not receive any type of rehabilitation services at follow-up. Among the patients with poor mental health, 58% were in the group with less severe brain injuries. Half of these did not receive inpatient TBI rehabilitation, and 44% did not receive any type of rehabilitation services at follow-up. A similar trend was observed in another study, which reported that less than half of the patients with poor mental health received any mental services (163). Consequently, mental services were one of the most prevalent types of unmet needs reported by the TBI survivors (163). In the severe TBI group, the majority of those who reported poor overall health attended the rehabilitation programs at the time of follow-up.

Peters (87) advocated for the inclusion of the subjective experience of persons with disabilities in the models of disablement. We investigated the impact of disability on the self-reported health and well-being using the ICF as a conceptual model for understanding the TBI disability (paper III). The ICF worked well as a conceptual model because the disability dimensions identified at one year after TBI were related to the physical and mental health outcomes. Statistically significant models for the physical and mental health were found. The higher levels of activity and participation were the strongest predictors of better overall health. The model for physical health, which covered data on the demographics, impairments, activity limitations and participation restrictions, accounted for 50% of the variance, whereas the model for mental health accounted for 35%. One of the reasons why a large proportion of the variance remained unexplained, particularly in the model of mental health, is that cognitive function was evaluated by the cognitive items of the FIM, which may be of limited sensitivity one year after injury (3;155;215). Physical and mental health is a multidimensional phenomena assumed to be influenced by many factors. Some of the remaining explanatory factors may be related to personal factors (e.g., interpersonal relations (117;130)) or environmental conditions (e.g., quality of environment, care giving and current living situation (138)). Clearly, mental health is influenced by other factors with important clinical implications (e.g., depression and other life event stressors), which have not been captured by this model. Other studies have shown that depression tends to be strongly associated with the subjective quality of life, accounting for nearly 50% of the variance (216). In a sample of patients with moderate-to-severe TBI, Findler et al. (135) reported significant correlations between the scores on the SF-36 mental health subscale and the BDI (r=-0.60). Depression was not used in the analyses in paper I because of the high correlation between the BDI and MCS in our data. Further, we applied similar
regression models to both health outcomes to demonstrate that certain factors are common and consistently important.

The associations between the different measures of disability and the self-reported health outcomes are complex. The variables associated with better physical health included the following: male gender, more severe TBI and overall trauma, higher level of motor ability and participation in productive activities. Better mental health was related to more severe TBI, a higher level of cognitive ability and participation in productive activities. As expected, participation in productive activities was the strongest individual explanatory variable in both health models. Somewhat controversially, our results suggest that the patients with more severe impairment experience better overall health at one year post-injury, likely due to the reduced awareness of the functional consequences of the disability. According to the study by Flashman and McAllister (217), “up to 45% of individuals with moderate-to-severe TBI demonstrated reduced awareness or complete lack of awareness of their deficits”. Impaired memory to recall the frequency of problems within the SF-36 domains may also influence these results (2). An alternative explanation could be related to the different levels of expectations and different coping and adaptive mechanisms (218). Individuals who are afflicted with fewer problems overall may be more bothered by these symptoms (2) and may have more difficulties in coping (218). According to Webb et al. (86), “persons sustaining mild or moderate TBIs are less likely to receive formal rehabilitation services than those with more severe, irreversible brain damage, thus limiting further their ability to regain their former quality of life”.

The association shown between the severity of injury and the physical and mental health in this study is in contrast with the previously mentioned findings of Dijkers (141), but it is in agreement with those reported by Koskinen (143). Several other studies have also found a negative relationship between the injury severity and the quality of life, with a higher perceived quality of life in the more severely injured patients (136;142).

At the ten-year follow-up, there was no statistically significant difference between the SF-36 scores in the moderate and severe TBI groups (paper IV). One possible explanation suggests that the association with injury variables dissolves over time, or perhaps other variables become more important for the health-related quality of life at a later stage (219). However, strong associations were observed between the depression (BDI screening) and SF-36 scale scores. Further, the disability as assessed by the GOS-E was also strongly
correlated with SF-36 scores. The patients with good recovery reported significantly better HRQL, both in the physical and mental health domains.

Being employed or productive has been found to be positively associated with the quality of life in several studies in different countries (51). These findings seem to be consistent over time post-injury. At the ten-year follow-up, the employed TBI survivors reported significantly better physical function and physical and emotional role functions than the unemployed patients (paper IV).

Our finding supported the proposal of other studies that productivity is the most important contributor for the better self-reported health, the social, psychological and economic well-being and the health-related quality of life both in the earlier and later stages of recovery (83).

6. CONCLUSIONS AND IMPLICATIONS
The following conclusions referring to the research questions can be provided from the present thesis:

- The incidence of hospital-treated TBI is considerably lower than that found in previous Norwegian studies. Falls were considered the most common external cause of TBI in both the youngest and the elderly. The proportion of the transport accidents was highest in young men aged 20-29 years. The majority of hospitalised patients have mild TBI. The elderly were more often found to have intracranial lesions.

- Acute substance use was more frequent in patients with less severe intracranial injuries. Contrary to the expectations, substance use tends to decrease the probability of more severe intracranial injury. However, the analysis has insufficient statistical power, and we could not conclude that the substance influence had a beneficial effect on the structural brain injury.

- Pre-injury substance abuse increased the probability of more severe TBI that was caused by high-energy trauma, such as traffic accidents and falls from higher levels.

- One of the populations at-risk of pre-injury substance abuse was males younger than 35 years with a lower education level. The other population was single males older than 35 years with a high school education.
At the one-year follow-up, the patients were highly independent in the physical but not cognitive activities. Social integration was not completed, and many patients reported productivity restrictions.

Better physical and mental health was associated with more severe injuries and higher levels of activity and productivity.

As expected, participation in productive activities was the strongest individual predictor of the physical and mental health dimensions.

The use of rehabilitation services at the one-year follow-up reflects the severity of the injury. Many patients with less severe TBI who reported impaired overall health did not receive any type of rehabilitation during the first year after injury.

A majority of the patients had good recovery (48%) or moderate disability (44%) at the ten-year follow-up.

The functional and employment status at the ten-year follow-up were associated with the initial injury severity in contrast to the HRQL.

A good recovery and no depression were associated with a better HRQL, and employment was associated with better physical and emotional role functions ten years after TBI.

The HRQL was significantly reduced in the TBI survivors at the one-year and ten-year follow-up compared to the general Norwegian population.

6.1 Implications

This thesis provides data that are of potential importance to both health authorities and clinicians. Our findings suggest that more effective preventive programs related to falls are needed for both the youngest and the elderly. A higher number of elderly TBI patients will require acute care and rehabilitation services in the future, as the population is ageing. The prevention strategies related to the environment, as well as adequate medical evaluation and treatment of co-morbid conditions, will probably reduce the incidence of falls in the elderly. Welfares programs and a multidisciplinary approach to this type of problem in the elderly should be considered. The preventive programs related to transport accidents in younger adults is also needed.
Due to the extent of the use of alcohol and drugs at the time of injury and the fact that this is one of the major risk factors for TBI, preventive efforts targeting risk populations are also needed. A routine alcohol and psychoactive substance screening of the TBI patients at the emergency admission may pinpoint the population who would benefit from an intervention related to substance abuse.

This thesis presents a descriptive overview of the key outcomes at one and ten years after moderate and severe TBI. It is notable that many patients with less severe intracranial injuries who reported impaired overall health at the one-year follow-up did not receive any type of rehabilitation after their injuries. To optimise the physical and mental health outcomes, clinicians need to ensure that the disability and health needs of these patients are identified and treated during the post-acute period. The decreased HRQL in the TBI survivors in the long-term perspective study suggests the importance of support and care-availability in the “chronic” stage of TBI as well.

Due to its complexity, the rehabilitation of the TBI patients should involve a continuum of care, from the acute, inpatient stage to the reintegration in community. Only through an integrated and systematic effort will we be able to achieve the optimal results in improving the functional capacity and health-related quality of life for this profoundly affected patient population. It is our goal that this knowledge will lead to better care for the TBI population in our health region.
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Effects of acute substance use and pre-injury substance abuse on traumatic brain injury severity in adults admitted to a trauma centre

Nada Andelic*1, Tone Jerstad 2, Solrun Sigurdardottir 3, Anne-Kristine Schanke 3, Leiv Sandvik4,5, Cecilie Roe 1,6

1Department of Physical Medicine and Rehabilitation, Oslo University Hospital, Ulleval, Norway
2Department of Neuroradiology, Oslo University Hospital, Ulleval, Norway;
3Sunnaas Rehabilitation Hospital, Nesoddtangen, Norway;
4Centre for Clinical Research, Oslo University Hospital, Ulleval, Norway;
5Faculty of Dentistry, University of Oslo, Norway;
6Faculty of Medicine, University of Oslo, Norway

E-mail addresses:
NA: nada.andelic@ulleval.no*
TJ: tone.jerstad@ulleval.no
SS: solrun.sigurdardottir@sunnaas.no
AKS: anne-kristine.schanke@sunnaas.no
LS: leiv.sandvik@ulleval.no
CR: cecilie.roe@ulleval.no

*Corresponding author
Abstract

Background: The aims of this study were to describe the occurrence of substance use at the time of injury and pre-injury substance abuse in patients with moderate-to-severe traumatic brain injury (TBI). Effects of acute substance use and pre-injury substance abuse on TBI severity were also investigated.

Methods: A prospective study of 111 patients, aged 16-55 years, injured from May 2005 to May 2007 and hospitalised at the Trauma Referral Centre in Eastern Norway with acute TBI (Glasgow Coma Scale 3-12). Based on structural brain damages shown on a computed tomography (CT) scan, TBI severity was defined by modified Marshall classification as less severe (score <3) and more severe (score ≥3). Clinical definition of substance use (alcohol and/or other psychoactive substances) was applied when hospital admission records reflected blood alcohol levels or a positive drug screen, or when a physician verified influence by examining the patient. Pre-injury substance abuse (alcohol and drug problems) was screened by using the CAGE questionnaire.

Results: Forty-seven percent of patients were positive for substance use on admission to hospital. Significant pre-injury substance abuse was reported by 26% of patients. Substance use at the time of injury was more frequent in the less severe group (p=0.01). The frequency of pre-injury substance abuse was higher in the more severe group (30% vs. 23%). In a logistic regression model, acute substance use at time of injury tended to decrease the probability of more severe intracranial injury, but the effect was not statistically significant after adjusting for age, gender, education, cause of injury and substance abuse, OR= 0.39; 95% CI 0.11-1.35, p=0.14. Patients with positive screens for pre-injury substance abuse (CAGE ≥2) were more
likely to have more severe TBI in the adjusted regression analyses, OR=4.05; 95% CI 1.10-15.64, p=0.04.

**Conclusions:** Acute substance use was more frequent in patients with less severe TBI caused by low-energy events such as falls, violence and sport accidents. Pre-injury substance abuse increased the probability of more severe TBI caused by high-energy trauma such as motor vehicle accidents and falls from higher levels. Preventive efforts to reduce substance consumption and abuse in at-risk populations are needed.
Background

Substance use (encompassing both alcohol and/or other psychoactive substances) is commonly associated with trauma [1,2]. The number of patients who have used substances while sustaining traumatic brain injury (TBI) is considerable, with an estimate of 36-51% showing some substance use on emergency admission to hospital [3,4].

Most studies related to substance consumption have focused on selected TBI populations such as victims of road traffic crashes [5], falls [6] or assaults [7]. In recent literature it has been debated whether the influence of alcohol increases [5] or decreases [8] the risk of more severe injuries, or if it has no effect [9]. The different views are primarily due to variations in the data collected, and a lack of consistency in methodology and outcomes. As reported by Parry-Jones et al. [4], most of the studies are conducted in the USA, which may limit applicability of findings to non-American countries, “given the potential influence of cultural factors on patterns of alcohol and drug consumption”[10].

Methods used to classify severity of head injury have included assessment of level of consciousness by the Glasgow Coma Scale (GCS) [11] or assessment of structural brain damage revealed on neuroimaging scans such as computed tomography (CT classification) [12]. The level of consciousness might be obscured in the acute phase due to substance use, in contrast to a more objective assessment of structural brain injury [13].

Several studies have assessed a link between substance use and clinical measures of TBI severity [3,4,14], but the data from Europe are limited [15]. However, there have been a few
studies on the effects of substance use on anatomical brain injury based on CT classification [5,16]. A study by Cunningham et al. [5] reported that persons involved in motor vehicle accidents having tested positive for alcohol were approximately twice as likely to have more severe CT injuries than those who tested negative for alcohol. Ruff et al. [16] found that alcohol abuse before the injury, rather than alcohol intoxication levels at the time of injury, had a significant effect on the severity of intracranial injuries.

It is important to study the impact of substance consumption on TBI severity in different countries because of varieties in cultural acceptance of substances use, and also in order to identify significant abuse among TBI patients and identify those who might benefit from intervention. The present study is one of the few to date that have described the effects of substance use at the time of injury and pre-injury substance abuse on the level of anatomical brain injury severity shown on a CT head scan, across different causes of TBI.

The objectives of this study were:

1. To describe the occurrence of substance use at the time of injury in the moderate-to-severe TBI population admitted to the Trauma Referral Centre.

2. To detect patients at risk of having pre-injury substance misuse.

3. To determine whether substance consumption at the time of injury and pre-injury substance abuse affect the severity of TBI as measured by structural brain damage on the CT scan. On the basis of Cunningham’s study [5], we hypothesised that patients who had consumed substances at time of injury (controlling for age, gender and cause of injury) would have CT evidence of more severe anatomical brain injury as compared to their non-influenced counterparts.
Methods

This prospective study was part of a larger TBI project that comprises patients with acute TBI admitted to Oslo University Hospital, Ulleval, Norway during a period of 2 years, starting in May 2005. This hospital is the Trauma Referral Centre for the South-East region of Norway with a population of nearly 2.6 million (1.8 million in the East and 0.8 million in the South region). The definition of TBI and inclusion procedures have been described elsewhere [17,18]. Briefly, the study inclusion criteria were: (a) patients aged 16-55 years; (b) admitted with ICD-10 diagnoses S06.0-S06.9 within 24 hours of injury; considered as (c) moderate-to-severe TBI; (d) with known status of substance use at the time of injury (e) with CT scan of the brain performed within 24 hours post-injury; and (f) residing in East Norway. The initial severity of TBI was assessed by the GCS either at the time of emergency admission to the hospital or based on pre-intubation values assigned at the site of injury; GCS 3-8 represents severe and 9-12 moderate TBI [11]. In this study TBI severity was defined as structural brain damage shown on a CT scan using the Marshall classification, which is described more thoroughly below. We excluded patients with co-morbidities that might interfere with assessment of TBI consequences such as neurological disorders/injuries (n=5) and known psychiatric diseases (n=6). We omitted patients with previously diagnosed severe substance abuse disorders who were homeless or with unknown address (n=14), and those being incarcerated (n=4).

Over the inclusion period, 48 patients with moderate TBI and 99 patients with severe TBI who met the inclusion criteria were admitted to the hospital. Of these, 27 patients (12 in the moderate and 15 in severe TBI group) were not willing to participate in the study. A detailed comparison between participants and non-participants with moderate TBI showed no
statistically significant differences in age, gender, GCS, cause of injury and substance use. In the participating group, a higher number had more severe intracranial pathology, but no statistically significant difference was revealed ($p=0.06$). In the severe group there was no difference between participating and non-participating patients with regard to age, gender, substance use and intracranial pathology. A significantly higher number of participants had lower GCS ($p=0.02$), and were injured in traffic accidents ($p=0.05$).

Finally, we excluded four patients with missing CT and five with unknown substance use status on admission; thus, 111 patients were assessed in this study.

The study was approved by the Regional Committee for Medical Research Ethics, East Norway and the Norwegian Data Inspectorate.

**Measures**

Baseline information including pre- and injury-related factors (e.g., socio-demographic and injury characteristics) was determined based on a systematic medical chart review and/or on data from the Trauma Register at Oslo University Hospital, Ulleval. The causes of injury were classified as follows: traffic accidents (irrespective of type), falls (irrespective of height) and others; assault and sport injuries were considered as subgroups of other causes.

The Injury Severity Score (ISS) was used to indicated overall trauma severity [19]. The ISS is an anatomical scoring system that provides an overall score for patients with multiple injuries. Each injury is assigned to an Abbreviated Injury Scale (AIS) that classifies individual injuries by body regions on a 6-point ordinal severity scale [20]. The ISS scores range from 1 to 75.
(best to worst) and are calculated by using the sum of the squares of the highest AIS scores in three different body regions. An ISS of 15 or greater is universally accepted as a definition of a major trauma patient. Trauma scores were extracted from the hospital’s Trauma Register.

**Substance use**

According to the definition of clinical judgment of substance use used by Bracken et al. [2], classifications were made when hospital admission records reflected blood alcohol levels or a positive drug screen, or when a physician verified influence by examining the patient, or when the patient reported recent substance ingestion. In this study we used dichotomous classification for substance use: yes/no. We decided to use the clinical definition of substance use to enhance the utility of physician observations “which reflect concern that different substances not detected on routine laboratory testing may indeed have influenced the patients, and that physicians are required to treat the patients before laboratory results are available” [2]. However, many patients are routinely tested for alcohol ingestion during clinical TBI assessment on emergency admission to the hospital (enzymatic method). The toxicology screening for other substances is done on clinical indications (immunological screening method in urine). If present, blood alcohol concentrations (BAC) as well as screening of the other substances in urine analyses were derived from admission laboratory files.

**Pre-injury substance abuse**

We used the CAGE questionnaire (Cut down, Annoyed, Guilty, Eye-opener) as a standard patients interview for screening pre-injury substance abuse in our TBI population [21]. The CAGE consists of four questions that address the lifetime drinking experience. Questions are also modified to address drug use experience. The CAGE is popular in clinical settings because of
its brief administration time [22]. Previous studies have shown that the CAGE may be a useful screening test for substance abuse in the TBI population [23]. A score of 2 or more is considered a cut-off score indicating clinically significant alcohol and/or drug problems [22]. The CAGE interviews were administrated as part of a follow-up study and were available for 88 patients.

**Structural brain damage (CT)**

TBI severity was measured by the structural brain damage shown on head CT scan. Patients underwent a CT head scan shortly after admission. A second CT was obtained within 6-24 hours after injury. Findings from the first and second CT scans were categorised according to diagnostic categories of types of anatomical abnormalities as classified by Marshall et al. [12]. A neuroradiologist (the second author) reviewed the CT findings. Scores from the “worst” CT were used in the final analyses [24]. The original Marshall classification ranges from 1 to 4, with separate categories for any lesion that is surgically evacuated and non-evacuated mass lesions. Few patients were observed in category 4 and in separate categories (table 1), thus precluding analyses in all the Marshall categories. Therefore, the original Marshall classification was subdivided into two groups [5]. The first group included patients with Marshall score <3 (less severe brain injury) and the second group included those with Marshall score ≥3 (more severe brain injury with significant intracranial abnormalities).

*Insert table 1 about here*
Statistical analysis

Descriptive data are presented using the proportions and mean values with standard deviations (SD), or the median with interquartile range (the 25th and 75th percentile values). The Mann Whitney U-test was used to compare differences between participants and non-participants, and when analysing differences between modified Marshall groups regarding gender and length of acute hospital stay. T-tests were used when analysing differences in age, GCS, ISS and BAC levels. Further, the Chi-square test with contingency tables was applied when studying associations between categorical independent variables.

Logistic regression analyses was used to evaluate effects of substance use at the time of injury and pre-injury substance abuse on TBI severity, and odds ratios (OR) with confidence intervals (95% CI) were calculated. Substance use and pre-injury substance abuse were entered as predictor variables and analysed separately (crude OR) against the Marshall groups, which comprised the dependent variable. Possible confounding variables studied in the multivariate regression analysis (adjusted OR) were gender and age, as well as education levels and the cause of injury (as these differed significantly in the two severity groups). The final regression analysis was also adjusted for substance use and pre-injury substance abuse. Age was recorded in four categories (in 10-year intervals) and cause of injury was dichotomised into traffic accidents and others. The categories with highest number of patients were reference groups. For the categories substance use and CAGE, the reference group consisted of patients who screened negative for substance use and abuse. All statistical tests were two-sided and the 5% significance level was used. Statistical analyses were performed using SPSS for Windows, version 14 (SPSS Inc, Chicago, IL).
Results

Demographic and injury characteristics

Table 2 shows the main demographic and injury characteristics of all study patients (n=111) in relation to anatomical severity of TBI as measured by the modified Marshall classification (score <3 less severe, score ≥3 more severe TBI). Fifty-five percent of the patients (n=61) had severe anatomical injuries on initial CT scan. There was no statistically significant age difference (p=0.69) between the two severity groups, while the gender difference approached significance (p=0.08). Education was significantly lower in the group with more severe injuries (p=0.002). Furthermore, no significant differences were found in marital and employment status (p=0.54 and p=0.40, respectively). Two-thirds of the patients in the group with more severe injuries were involved in traffic accidents. The GCS and ISS scores differed significantly between the severity groups, as did the length of acute hospital stay (see table 2).

Insert table 2 about here

Substance use

Forty-seven percent of all the patients used some kind of substances at the time of injury; alcohol ingestion was found in 35%, influence by other substances in 8%, and combined consumption in 4% of patients. Figure 1 shows the frequency of substance use in the severity groups (using Marshall Classification).

Insert figure 1 about here
Seventy-five percent of results regarding substance use were derived from blood or urine analyses and 25% by clinical judgment. There was no statistically significant difference regarding severity of intracranial injuries between tested and non-tested patients in the group considered as positive for substance use ($\chi^2 = 1.34$, $p=0.25$). BAC levels were available in 31 of 39 patients considered as alcohol-influenced. In 87% of these, the BAC was >100mg/g; with mean BAC values of 185 mg/g in the less severe group and 210 mg/g in the more severe group, $p=0.44$). Of eight patients who were not BAC tested, six were in the more severe TBI group. Of six patients tested for use of other substances, four were in the more severe group. Of seven patients who self-reported drug use at the time of injury, three were in the severe TBI group. One of four patients with combined alcohol and drug use was in the more severe TBI group. Cannabis was the most commonly detected substance (54%) followed by benzodiazepines (46%), amphetamine (31%), barbiturates, cocaine and LSD (24%) and methadone (8%). Only 12% of the females were in the positive substance use group. The mean age was similar in both the substance-positive and substance-negative groups [31.8 years (SD 11.5) vs. 32.6 years (SD 11.8), $p=0.70$]. Sixty percent of substance positive patients were under 35 years of age. Alcohol ingestion was strongly related to the cause of injury; 29% of patients injured in traffic accidents were in the positive group, in contrast to 71% of those injured in falls and 92% of assault patients ($\chi^2=25.01$, $p=0.001$). There were no differences in the mean GCS scores between substance-positive and negative groups [6.9 (SD 3.2) vs. 7.2 (SD 3.1) respectively, $p=0.72$]. Patients in the substance-negative group had higher mean ISS than those in the positive group with a statistically significant difference [33.3 (SD 13.9) vs. 27.4 (SD12.3), $p=0.02$]. Substance use was significantly higher in the less severe Marshall group (60% vs. 36 % $p=0.01$). The median length of acute hospital stay differed significantly between substance-
positive and substance-negative groups (6 days, interquartile range 11 vs. 8 days, interquartile range 11, p=0.001).

**Pre-injury substance abuse**

CAGE data were available in 80% (n=88) of all the patients. Of the remaining 23 patients, 13 were deceased, eight were not able to participate in the interview because of communication disorders and two dropped out. Positive screening for pre-injury substance problems (CAGE cut-off ≥2) was found in 26% of patients (n=23). Of these, 13 were influenced by alcohol on admission, five by other substances and two by poly-substances ($\chi^2=20.4$, p=0.001). Only 3 females were in the CAGE risk group. The mean age in the CAGE positive group was 33.6 years (SD 12.1) vs. 30.1 years (SD 11.1) in the negative CAGE group (p=0.22). Eleven patients in the risk group were injured in traffic accidents, nine in falls and three in assaults. Eighty-four percent of patients with lower education level in the age group younger than 35 years of age were at risk of having significant pre-injury substance abuse, as well as 60% of the patients above 35 years with higher education level (≥13 years). The mean GCS was similar in both CAGE groups [CAGE<2: 7.6 (SD 3.1) vs. CAGE≥2: 7.7 (SD 3.1), p=0.93]. The mean ISS was not found to be significantly higher in patients with a positive CAGE screen [CAGE≥2: 30.1 (SD 12.3) vs. CAGE<2: 28.9 (SD 14.0), p=0.62]. The proportion of patients with positive CAGE was found to be higher in the more severe group as compared to the less severe group (30% vs. 23%, p=0.45). The median length of hospital stay was one day longer in the CAGE positive group (9 days, interquartile range 12 vs. 8 days, interquartile range 10, p=0.56).

The unadjusted and adjusted effects of acute substance use and pre-injury substance abuse on the unfavourable intracranial severity group (Marshall ≥3) are shown in table 3. Binary logistic
regression analyses included the 88 patients with available CAGE data. In both unadjusted and adjusted models, substance use on admission tend to decrease the probability of more severe intracranial injuries (OR 0.52; 95% CI 0.23-1.24, p=0.14 and OR 0.39; 95% CI 0.11-1.35, p=0.13, respectively). In the regression analyses adjusted for age, gender, education, substance use at time of injury and cause of injury, pre-injury substance abuse (CAGE ≥2) significantly increased the probability of more severe TBI (OR 4.05; 95% CI 1.05-15.64, p=0.04).

According to covariate analysed female gender, age group 46-55 years, lower education level and traffic accidents tend to increase the probability of more severe TBI (data not shown). The final adjusted regression model predicted more severe TBI in 70% of cases.

*Insert table 3 about here*

Discussion

**Demographic and injury characteristics**

Demographic and injury characteristics in the present study of a TBI cohort aged 16-55 years admitted to the Trauma Referral Centre with acute TBI are comparable to those of other TBI populations [8,13]. All subjects from East Norway with moderate-to-severe TBI (GCS 3-12) in need for acute neurosurgical check-up and care are referred to this Trauma Referral Centre. Participants in this study were representative of their cohort; the refusal rate was about 20% as in existing literature [25], and the substance use at the time of injury did not differ between participants and non-participants.

The level of consciousness might be obscured in acute settings due to substance use at the time of injury, medical sedation or paralysis [13]. In this study, the mean GCS score did not differ significantly between the substance-positive and substance-negative groups of patients,
agreeing with results reported by Sperry [26]. In contrast, assessment of structural brain damage by neuroimaging is not influenced by state of consciousness. Therefore, we defined the severity of TBI in this study by structural brain damage as shown on CT scans. There is evidence that the CT scan can assist in discriminating less severe from more severe TBI using the Marshall scores as a standard measure of anatomical classification of severity [5]. Fifty-five percent of patients in this study had injuries that could be categorised as more severe.

**Substance use**

In this study, almost half of the patients showed substance use upon admission to the hospital. The proportion of patients found to be under the influence of alcohol was 35%, which is higher than in previous Norwegian studies [27,28]. A trend towards increasing alcohol consumption in the general Norwegian population during the last decades [29] as a result of the increased number of regular drinkers [30] as well as higher consumption in Oslo/Eastern Norway than in other regions may explain this result [31]. Norway is, however, in the lower range of international statistics on alcohol consumption as compared to other Western countries [31]. This could be explained by limitation in availability of alcohol, as well as the high taxation on alcoholic beverages in Norway. The alcohol consumption rate shown in this study was within the range of those reported in a recent review of TBI epidemiology in Europe (24-51%) [15] and other international studies [3,4]. This study also confirms that alcohol is the most common substance used in the TBI population [4,8].

The use of other psychoactive substances was found in 12% of the total TBI sample. This rate is lower than those presented in international studies [14], and is biased by clinical routines on admission and the clinical definition of substance use. In agreement with studies on illicit drug use in TBI populations [14], cannabis was the most frequently detected drug. It is well known
that cannabis is the most frequently used illegal drug in the general population in Norway [32].
The proportion of patients that use substances while driving motor vehicles was more than five
times higher in the present study than in a recent study on the prevalence of alcohol and illicit
drugs among motor vehicle drivers (aged ≤ 54 years) in South-Eastern Norway [32]. Our
findings may indicate that persons who sustain TBI are not representative of the general
population. However, a considerably lower proportion of traffic injury cases in this study were
alcohol-influenced than in older TBI literature [14]. This may represent the reduction of the
legal limit for BAC from 0.5 to 0.2 mg/g in 2001 [32], effectiveness of campaigns and
programmes for reducing drinking and driving, and a decrease in the incidence of traffic-related
TBI during the last decades [17].
The proportion of patients with substance use was significantly higher in the less severe
Marshall group. Falls and other injuries were the main causes of injury in this severity group.
The percentage of patients under the influence of alcohol on admission and injured by falls or
assaulted was in agreement with other Nordic studies [9,28]. Northern European countries are
often characterised as nations with infrequent but heavy episodes of drinking (“dry” culture),
with higher tolerance toward excessive drinking, and higher frequencies of alcohol-related
injuries than Southern European countries where alcohol use is more integrated into everyday
life (“wet” culture) [33].

As hypothesised previously, we expected that substance use on admission could have a
potentiating effect on anatomical brain injury, as measured by findings on the “worst” head CT
scan within 24 hours of injury [5]. Contrary to expectation, substance use tended to decrease
the probability of more severe intracranial injury in the adjusted logistic regression (OR=0.39).
However, strong conclusion should not be drawn due to insufficient statistical power in the analysis (power 0.58, alpha 0.05) [34]. Cunningham`s results [5] showing that alcohol potentiated the severity of TBI among victims of motor vehicle crashes were not replicated in this study.

It has been reported that acute alcohol intoxication exerts both detrimental and beneficial effects on the injury severity and outcome of TBI, although mechanisms have not been determined. The hypothesis that alcohol-inebriated victims injured by falls on stairs sustain more severe intracranial injuries because of delayed reaction time and inadequate protection reflexes was not supported [6]. Smink et al. [35] could not demonstrate a relationship between alcohol concentration and the severity of traffic accidents. Furthermore, alcohol and methamphetamine use was found to be associated with decreased mortality in a retrospective study of severe TBI [8]. Ruff et al. [16] also found that alcohol intoxication at the time of injury “was not associated with poor outcome in those who survived long enough to reach hospital”.

Based on experimental research, Kelly [36] reported that acute alcohol intoxication may have neuroprotective effects in traumatic brain injuries as a result of “ethanol-induced inhibition of N-methyl-D aspartate receptor-mediated (NMDA) excitotoxicity”. Dose-dependent effects are also reported, with a better outcome in animals obtained with low and moderate ethanol doses as compared to no- and high-ethanol groups [37]. According to Tien et al. [38], low to moderate BAC may be beneficial in patients with severe brain injury from blunt head trauma, while high BAC seems to have a deleterious effect on in-hospital death in these patients. Although the focus of our study was not to assess whether BAC levels impact the severity of structural brain injury, the mean BAC level was found to be similar in both severity groups.
The considerable number of patients with substance use in the present study shows that the use of alcohol and drugs is a major risk factors for TBI [3,9,38]. Health-related and psycho-social consequences of TBI, as well as the economical burden of these injuries underline the importance of preventive efforts targeting at-risk populations.

**Pre-injury substance misuse**

Screening by the CAGE questionnaire showed that 26% of patients reported pre-injury substance abuse (problems with alcohol and/or other substances). Around two-thirds of these patients misused alcohol. This study shows a lower proportion of pre-injury substance misuse than in TBI literature (40-55%) reviewed from 1994-2004 [4]. This rate is also slightly lower than that reported in a recent study on a TBI population from Australia (21% alcohol and 9% drug dependence) [10]. In our study, we omitted patients with pre-existing substance abuse disorders, which could explain these lower rates. Lower sensitivity of the CAGE-drug questionnaire as compared to the CAGE-alcohol questionnaire [23] is a methodological limitation, as the cut-off score used. If we include patients with a CAGE score of one (8 patients, 9%), those omitted due to pre-diagnosed severe substance abuse disorders (14 patients, 14%) and the pre-injury substance misuse group (26%), a total proportion of 49% reached the range of estimates presented in the literature [4,10]. We based our findings on self-reports from the patients (the CAGE interview), thus possibly under-reporting illicit drug use, since patients may be unwilling to report engagement in illegal activities [4]. Prior history of substance abuse is less often found in persons treated in Trauma Referral Centres than in rehabilitation populations [3]. However, the occurrence rate of pre-injury substance abuse in this study is higher than in a Danish study [39], where 5.8% of the intracranial lesions group were diagnosed with substance misuse by the ICD-9 criteria. In our study, 26% of all patients
with ICD-10 diagnoses of intracranial lesions had a positive CAGE screening for pre-injury substance problems.

CAGE positivity is usually equivalent to being a heavy drinker [40]. When we extracted results of patients with positive CAGE-alcohol, the proportion shown was more than two times higher than the rate of heavy drinkers found in a Norwegian survey in 1998 [29]. One population at risk of pre-injury substance misuse in this study was a male, younger than 35 years of age, with a lower education level (≤12 years). The other population was single males, older than 35 years, with a high school education. It has previously been reported that drinking serves an important social function for young people [10], and that increased consumption of alcohol is found in subjects with a higher level of education and higher income [29,31].

We found in the adjusted regression analysis that patients with pre-injury substance problems showed significantly increased probability of more severe TBI as compared to their counterparts (OR 4.05). Chronic alcohol use has consistently been found to be associated with more severe traumatic brain injuries. Ronty et al. [41] reported that pre-injury alcohol abuse precipitated the development of more severe structural traumatic brain damage on CT examinations. A strong association between history of excessive alcohol use and poor outcome for all types of intracranial diagnoses and greater prevalence of mass lesion was reported by Ruff et al. [16]. Several other studies have reported an association between alcohol abuse and greater severity of TBI as measured by posttraumatic amnesia, neuropsychological tests and global functioning [3,4,14]. According to previous experimental studies, chronic alcohol exposure may exacerbate TBI, probably as the “effect of imbalance of up-regulation of NMDA receptor activity and down-regulation of gamma-aminobutyric acid (GABA) receptor function resulting in excitotoxicity” [36].
The association shown in this study between pre-injury substance abuse and more severe intracranial injuries underlines the importance of identifying persons at risk who would benefit from intervention related to substance abuse. A routine alcohol and psychoactive substance screening of TBI patients at the emergency admission may pinpoint this population [1].

In the adjusted regression analyses, female gender tended to have increased probability of more severe intracranial injury, in agreement with a previous study on females under 50 years of age [42]. Older age tended to increase the probability of more severe intracranial injuries. Other studies have reported that increasing age is related to poorer outcome after TBI [43]. Of all patients with severe intracranial injuries, 20% were young adults living with parents and attending secondary school. School education programmes about the effects and dangers associated with alcohol consumption and drug use are “a key component in preventing substance abuse in this population” [14].

This study has several limitations that should be addressed. It is a selected cohort study describing a TBI population aged 16-55 years. The study assesses the severity of anatomical brain injury as shown on CT at a fixed point of time (within 24 hours of injury), but not clinical course and outcome of TBI. Our results should be interpreted with caution because of the clinical definition of substance use, lack of BAC levels and toxicology screenings in all patients, as well as the small number of participants. Therefore, we made no distinction between the types of substances used when analysing the probability of more severe TBI. The frequency of pre-injury substance problems is slightly underestimated due to the exclusion criteria which resulted in omission of 14 patients with previously diagnosed severe substance
abuse. Ten of these suffered from severe TBI supporting the association between pre-injury substance abuse and severe structural brain injury shown by the study. Self-reported screening instruments might under-report pre-injury use of alcohol and, especially, of illicit drugs. Limitations of the CAGE questionnaire are described above. Clinical interviews based on the DSM-IV diagnostic criteria may provide a reliable measure of substance abuse disorders. However, a replication of the study is needed before the present findings can be considered as a verified hypothesis.

**Conclusion**

One in two patients was under the influence on admission, and one in five abused substances pre-injury. Substance use on admission was more frequent in less severe TBI caused mostly by low-energy events such as falls, violence and sport accidents. Pre-injury substance abuse increased the probability of more severe structural brain injuries. These were mostly results of high-energy events such as motor vehicle accidents and falls from higher levels. Targeting preventive efforts to reduce substance use and misuse in the TBI population in general is needed in order to minimise the number of injuries and consequences including the socio-economic burden. In view of the trend of aging in the general population and the differences in the mechanism of injuries between younger and older individuals, studies on the association between substance use and TBI in the elderly are also needed.

**Competing interests**

The authors declare that they have no competing interests.
Authors’ contributions

NA and CR were responsible for the conception and design of the study. NA and SS collected data. TJ reviewed the CT findings and performed Marshall Classification. LS helped with statistical analysis and interpretation of data. SS and AKS participated in the study design. All authors contributed to the analysis and interpretation of data that was initially performed by NA. NA, SS and CR drafted the manuscript and all authors reviewed it critically for intellectual content and have given final approval of the version to be published.

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Figure 1 Frequency of substance use by modified Marshall classification into less severe (score <3) and more severe TBI (score ≥3)
Table 1 Distribution of “worst” CT scan findings assigned by Marshall score (N=111)

<table>
<thead>
<tr>
<th>Marshall score</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14</td>
<td>(13)</td>
</tr>
<tr>
<td>2</td>
<td>36</td>
<td>(32)</td>
</tr>
<tr>
<td>3</td>
<td>43</td>
<td>(39)</td>
</tr>
<tr>
<td>4</td>
<td>18</td>
<td>(16)</td>
</tr>
</tbody>
</table>

1  No visible intracranial pathology
2  Cisterns present with midline shift 0-5 mm; no high or mixed density lesion > 25 ml.
3  Cisterns compressed or absent with midline shift 0-5 mm.
4  Midline shift > 5 mm; or surgically evacuated lesion; and non-evacuated high or mixed density lesion > 25 ml
Table 2 Demographic and injury characteristics in relation to Marshall groups (score <3, less severe, score ≥3 more severe TBI)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Less severe TBI (n=50) (%)</th>
<th>More severe TBI (n=61) (%)</th>
<th>p-value</th>
<th>Total (N=111) (%)</th>
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<tbody>
<tr>
<td>Gender</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>43 (86)</td>
<td>44 (72)</td>
<td>0.08</td>
<td>87 (78)</td>
</tr>
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<td>Female</td>
<td>7 (14)</td>
<td>17 (28)</td>
<td></td>
<td>24 (22)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
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<td></td>
<td>32.2±11.6</td>
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<tr>
<td>Education</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>0-9 years</td>
<td>11 (22)</td>
<td>4 (6)</td>
<td></td>
<td>15 (14)</td>
</tr>
<tr>
<td>10-12 years</td>
<td>14 (28)</td>
<td>33 (54)</td>
<td></td>
<td>47 (42)</td>
</tr>
<tr>
<td>≥13 years</td>
<td>25 (50)</td>
<td>18 (30)</td>
<td></td>
<td>43 (39)</td>
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<td>6 (5)</td>
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<tr>
<td>Marital status</td>
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<td>Married/live with</td>
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<td>35 (59)</td>
<td></td>
<td>62 (56)</td>
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<td>Divorced</td>
<td>4 (8)</td>
<td>7 (12)</td>
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<td>11 (10)</td>
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<td>Live alone</td>
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<td>17 (29)</td>
<td></td>
<td>36 (32)</td>
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<td>2 (3)</td>
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<td>46 (81)</td>
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<td>85 (77)</td>
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<td>6 (11)</td>
<td></td>
<td>9 (8)</td>
</tr>
<tr>
<td>Retired/ Disabled</td>
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<td>5 (9)</td>
<td></td>
<td>13 (12)</td>
</tr>
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<td>4 (7)</td>
<td></td>
<td>4 (2)</td>
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<tr>
<td>Cause of injury</td>
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<td></td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Traffic accidents</td>
<td>23 (46)</td>
<td>42 (69)</td>
<td></td>
<td>65 (59)</td>
</tr>
<tr>
<td>Falls</td>
<td>17 (34)</td>
<td>11 (18)</td>
<td></td>
<td>28 (25)</td>
</tr>
<tr>
<td>Others</td>
<td>10 (20)</td>
<td>8 (13)</td>
<td></td>
<td>18 (16)</td>
</tr>
<tr>
<td>Substance use</td>
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<td></td>
</tr>
<tr>
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<td>20 (40)</td>
<td>39 (64)</td>
<td></td>
<td>59 (53)</td>
</tr>
<tr>
<td>Yes</td>
<td>30 (60)</td>
<td>22 (36)</td>
<td></td>
<td>52 (47)</td>
</tr>
<tr>
<td>Glasgow coma scale (GCS)</td>
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</tr>
<tr>
<td>Mean±SD</td>
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<td>5.5±2.5</td>
<td></td>
<td>7.0±3.2</td>
</tr>
<tr>
<td>Injury severity score (ISS)</td>
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<tr>
<td>Mean</td>
<td>25.2±14.6</td>
<td>35.0±10.7</td>
<td></td>
<td>30.6±13.5</td>
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<td>Length of hospital stay (days)</td>
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</tr>
<tr>
<td>Median</td>
<td>5</td>
<td>12</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Interquartile Range</td>
<td>6</td>
<td>12</td>
<td>11</td>
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</table>
Table 3 Risk for severe TBI (Marshal ≥3) associated with substance use at time of injury and pre-injury substance abuse  (n=88)

<table>
<thead>
<tr>
<th>Substance use</th>
<th>Number of cases</th>
<th>Less severe TBI</th>
<th>More severe TBI</th>
<th>OR (95% CI)</th>
<th>OR (95% CI)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>Unadjusted</td>
<td>Adjusted for age and gender</td>
<td>Adjusted for age, gender, education, cause of injury, subst. use /CAGE</td>
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<tr>
<td>No</td>
<td>43 (49)</td>
<td>20 (42)</td>
<td>23 (58)</td>
<td>1*</td>
<td>1*</td>
<td>1*</td>
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<tr>
<td>Yes</td>
<td>45 (51)</td>
<td>28 (58)</td>
<td>17 (42)</td>
<td>0.52 (0.23-1.24)</td>
<td>0.60 (0.24-1.53)</td>
<td>0.39 (0.11-1.35)</td>
</tr>
<tr>
<td>CAGE &lt; 2</td>
<td>65 (74)</td>
<td>37 (77)</td>
<td>28 (70)</td>
<td>1*</td>
<td>1*</td>
<td>1*</td>
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<tr>
<td>≥ 2</td>
<td>23 (26)</td>
<td>11 (23)</td>
<td>12 (30)</td>
<td>1.44 (0.56-3.74)</td>
<td>1.66 (0.60-4.61)</td>
<td>4.05 (1.05-15.64)</td>
</tr>
</tbody>
</table>

The data are presented as OR (odds ratio). *Reference category. OR greater than 1 increases probability of severe TBI. OR less than 1 decreases the probability of severe TBI.
Disability, physical health and mental health one year after traumatic brain injury

Nada Andelic a, Solrun Sigurdardottir b, Anne-Kristine Schanke b, Leiv Sandvik c,d, Unni Sveen a, Cecilie Roe a,e

aDepartment of Physical Medicine and Rehabilitation, Oslo University Hospital, Ulleval, Norway
bSunnaas Rehabilitation Hospital, Nesoddtangen, Norway
cCentre for Clinical Research, Oslo University Hospital, Ulleval, Norway
dFaculty of Dentistry, University of Oslo, Norway
eFaculty of Medicine, University of Oslo, Norway

Corresponding author:
Nada Andelic
Department of Physical Medicine and Rehabilitation, Oslo University Hospital, Ulleval 0407 Oslo, Norway
Phone: +47 22118687; Fax: +47 22115022;
E-mail: nada.andelic@ulleval.no
Abstract

*Purpose:* The purpose of this study was to assess disability and the physical and mental health status 1 year after traumatic brain injury (TBI), using the International Classification of Functioning, Disability and Health (ICF) as a conceptual model for understanding TBI disability.

*Methods:* A prospective study of 85 patients with moderate-to-severe TBI (aged 16-55 years) due to injury occurring from May 2005 to May 2007 and hospitalised at the Trauma Referral Centre in Eastern Norway were included. The severity of structural brain damage and overall trauma were used as indices of body structure impairments. Activity limitations were measured by the Functional Independence Measure (FIM), and participation restrictions were assessed via the Community Integration Questionnaire (CIQ). Physical and mental health dimensions as reported on the Medical Outcome Survey Short-Form (SF-36) were chosen as outcome measures.

*Results:* Roughly one quarter of the patients reported disability requiring personal assistance. One third had major problems with social integration, and 42% were not working. Nearly half of the patients reported poor physical health, and 37% reported poor mental health. Regression models, including demographics, impairments, activity limitations and participation restrictions, accounted for 50% of the variance in physical health and 35% of the variance in mental health. More severe impairments, fewer activity limitations and fewer participation restrictions equated to better overall health.

*Conclusions:* The results demonstrated that a significant proportion of TBI survivors face substantial disability and impaired overall health 1 year after injury. To optimise health and
well being outcomes, clinicians need to ensure that health needs of patients with less severe TBI are identified and treated during the post-acute period.
Introduction

Traumatic brain injury (TBI) is known to have long-lasting social, physical and health-related consequences. However, outcome studies in the TBI literature traditionally focus on employment status and cognitive functioning (1). Fuhrer (2) raised the point that measures of outcomes are incomplete if the subjective well-being of the individual is not considered. Consensus (3) also noted that patients’ self-reported health-related quality of life values are necessary in TBI research. Quality of life as an outcome measure is important for both patients and clinicians since one of the primary goals of rehabilitation is to give TBI survivors a meaningful existence and a life within their expectations (4). The factors that contribute to health-related quality of life could guide interventions for improving physical, cognitive and emotional status along with environmental factors.

The World Health Organisation (WHO) developed the ‘International Classification of Functioning, Disability, and Health’ (ICF) framework to describe the functional consequences of various health conditions (5-7). The ICF has three main domains: body structures/functions, activities and participation. These domains interact with each other and are also influenced by environmental and personal factors. Within the ICF, disability is defined as ‘an umbrella term for impairments in body functions and structures, limitations in activities and restrictions in participation’ (5). The multidimensional view of disability may help care providers to find a common language, define common rehabilitation goals and coordinate treatment amongst those with injuries. Disability measures can be linked to the ICF in order to better reflect the different aspects of health (6).

Several studies have described factors that influence health-related quality of life or satisfaction with life in people with TBI (4;8-15). The studies showed that improved physical functioning,
perceived mental health, participation in work and leisure and social support were associated with better quality of life and life satisfaction. In a review by Dijkers (13), substantial variation in health-related quality of life after TBI was noted; however, injury severity did not predict subjective well-being. Koskinen (16) found that participants who had more grave intracranial damage had a rather high quality of life despite the severe brain injury. However, a limited number of studies have used the ICF terminology to frame quality of life outcomes. Pearce and Hanks (10) examined which disability components of the ICF are most predictive of global life satisfaction after TBI. It was shown that a combination of all ICF components and demographic factors significantly predicted life satisfaction and accounted for 17% of the variance. Restriction of participation in life activities was found to have the greatest impact on life satisfaction. A study by Huebner et al. (8) supports the premise that participation is associated with a high quality of life.

The impact of TBI-related disability on self-reported health and well-being has received limited investigation, and studies from Scandinavia are lacking. Studies from different countries are required to provide ‘a more accurate reflection of population needs, allowing better understanding of regional, national and international differences and needs in the area of brain injury rehabilitation’ (6). We decided to use the ICF model to characterise TBI consequences, expecting that this bio-psycho-social approach would allow us to understand the extent of disability at the 1-year follow-up time point. Exploring TBI disability in this context is useful when discussing appropriate care and support programmes as well as when making rehabilitation goal priorities.
The overall purpose of this study was to assess disability and health 1 year after TBI using the ICF as a conceptual model for understanding TBI disability. Specifically, this study examines the impact of impairments, activity limitations and participation restrictions on physical and mental domains of health. Based on previous research, we hypothesised that participation in productive activities would be the strongest predictor of both health dimensions.

**Material and Methods**

*Participants*

This prospective cohort study is part of a larger TBI research project comprising patients with acute TBI admitted to Oslo University Hospital, Ulleval during a period of 2 years starting in May 2005. This hospital is the Trauma Referral Centre for the South-East region of Norway with a population of nearly 2.6 million (1.8 million in the East and 0.8 million in South region). The study inclusion criteria were patients (a) aged 16-55 years, (b) residing in East region of Norway, (c) admitted with ICD-10 diagnoses S06.0-S06.9 within 24 hours of injury and (d) considered to have moderate-to-severe TBI. The initial severity of TBI was assessed by the Glasgow Coma Scale (GCS), either at the time of emergency admission to the hospital or from pre-intubation values assigned at the site of injury; a GCS score of 3-8 represents severe and 9-12 moderate TBI (17). In this study, TBI severity was defined as structural brain damage shown on a CT scan using the Marshall classification as described more thoroughly later.

We omitted patients with serious co-morbidities interfering with assessment of TBI-related disabilities such as: (a) previous neurological disorders, (b) associated spinal cord injuries and (c) previously diagnosed severe psychiatric and substance abuse disorders.
Of all the patients who fulfilled the inclusion criteria, 27 refused participation (18% of 147). A total of 21 patients died during the acute care, and two died in post-acute care (19% of 120). Four patients dropped out of the study before the one-year follow up (4% of 97). Data collection was performed 1 year post-injury and included 93 patients. Eight patients (9% of 93) with severe communication disabilities were unable to participate; thus, 85 patients were assessed in this study.

The study was approved by the Regional Committee for Medical Research Ethics, East Norway and the Norwegian Data Inspectorate. Written informed consent was obtained from all participating patients.

**Procedure**

Demographic variables (age, gender, education, marital status, employment), GCS, Injury Severity Score (ISS) and Computed tomography (CT) of the head were collected during acute TBI admissions. At the 1-year follow-up, patients were interviewed and examined by the first author at the outpatient department or rehabilitation hospital at which they had been admitted for a clinical follow-up assessment. Four such interviews were conducted in the patients’ homes at their request.

**The conceptual model**

The ICF was used as a conceptual model to frame TBI disabilities at the 1-year follow-up time point (Table1). Our model posits different dimensions of disability that are expected to influence the health and well-being of TBI survivors.

*Insert table 1 about here*
The following sets were used: demographic characteristics, impairments, limitations in activity and restrictions in participation. Although a validated instrument was not available to measure overall body functions at follow-up, we used the severity of structural brain damage and the overall trauma severity as indices of impairments in body structures. Limitations in functional ability and restrictions in social integration and productivity reflect activity and participation disabilities. The instruments used are described later.

Impairments

Structural brain damage (CT)

Patients underwent a CT scan of the head shortly after the acute admission. A second CT was obtained within 6-24 hours after injury. Findings from the first and second CT scans were categorised according to diagnostic categories of types of anatomical abnormalities as classified by Marshall et al. (18). Scores from the ‘worst’ CT scan were used in this study. A neuroradiologist reviewed the CT findings. The original Marshall classification ranges from 1 to 4, with separate categories for any lesion that is surgically evacuated and non-evacuated mass lesions. For the purpose of this study, the CT findings were divided into two groups: less severe brain injury (no intracranial injuries and small lesions, Marshall 1 and 2) and more severe brain injury (significant intracranial abnormalities, Marshall 3 and 4).

Injury Severity Score (ISS)

The ISS is an anatomical scoring system that provides an overall score for patients with multiple injuries (19). Each injury is assigned to an Abbreviated Injury Scale (AIS) that classifies individual injuries by body regions on a 6-point ordinal severity scale (20). The ISS
scores range from 1 to 75 (best to worst) and are calculated by using the sum of the squares of the highest AIS scores in the three different body regions. An ISS of 15 or higher is universally accepted as a definition for a major trauma patient. Trauma scores were extracted from the hospital’s Trauma Register.

Activity limitations

Functional Independence Measure (FIM)

The FIM is an 18-items scale assessing specific activities of daily living (ADL): self-care, sphincter control, mobility, communication, cognition and social adjustment (21). Each FIM item is rated on an ordinal scale from 7 to 1. A score of 7 or 6 is categorised as ‘not needing personal assistance’ and 5 or less as ‘needing assistance’ (ranging from cueing and guidance to total dependence). The FIM consists of two subscales, the FIM Motor (FIM-M: 13 items) and FIM Cognitive (FIM-COG: 5 items). FIM-M scores range from 13 to 91, and FIM-COG scores range from 5 to 35; higher scores indicate greater independence. Because motor and cognitive abilities may change differently over time, both the FIM-M and FIM-COG were used in the analyses (10). The first author, who is a certified FIM rater, performed the FIM scoring.

Participation restrictions

Community Integration Questionnaire (CIQ)

The CIQ is designed to assess reintegration into the community after TBI and is frequently applied in TBI research (22). It is a 15-item scale designed to assess home integration (range 0-10), social integration (range 0-12) and productive activities (range 0-7). A higher score indicates greater integration. As the CIQ home integration subscales assess activities rather
than participation (23), we used the CIQ social integration and CIQ productivity subscales as measures of participation in this study.

*Environmental support*

Rehabilitation services

We collected information about access to the community-based rehabilitation services at the 1-year follow-up assessment as an indicator of the environmental support. The use of rehabilitation services related to TBI was dichotomised into yes/no variables. Types of services were divided into: daycare (nurse and/or personal assistant), physiotherapy, occupational therapy, speech therapy, psychologist, social worker and others.

*Outcome of medical health (SF-36)*

The Medical Outcomes 36-Item Short Form Health Survey (SF-36) is a widely used health outcome measure (24) that is also validated for the TBI population (25). The items are designed to measure health-related functioning and well-being along eight subscales. The scale range is 0-100 (worst to best). Subscales can be aggregated into summary scores that represent the two main dimensions of health: the physical component summary (PCS) and mental component summary (MCS) are calculated as weighted sums of the subscale scores (24). The literature highlights discrepancies between scores on individual scales and component summaries (26). The emotional role limitation and mental health scales have negative loading on the PCS, whereas physical functioning, physical role limitation and bodily pain have negative loading on the MCS. Consequently, improved scores on the scales within one domain reduce the component score for the other domain. Recent literature has investigated the factor structure by
making comparisons between models with correlated (oblique solution) and uncorrelated (orthogonal solution) PCS and MCS factors. The model using an oblique solution reduced the negative weights that caused inconsistencies in scale and summary scores. As recommended by Hann and Reeves (27), we used the oblique model for calculating physical and mental component scores (r=0.51) in this study. The resulting scores were converted to a scale with a mean value of 50 and standard deviation of 10. These scores were computed at the SF-36 web site (http://www.sf-36.org/nbcalc/index.stml) and are based on Norwegian norms. Physical and mental health summary scores less than 40 (> 1 SD below general population norms) indicate poor health (9).

Statistical analysis
Descriptive statistics were calculated for the dependent and independent variables. Data inspection for assumption violation resulted in a logarithmical transformation of the FIM-M and FIM-COG scores. Simple linear regression was used to explore the relationship between each of the independent variables (demographic variables, ISS, CT head, FIM-M, FIM-COG, CIQ social participation and CIQ productivity) and dependent variables (SF-36 physical and mental component oblique scores). We decided to apply similar regression models to both health outcomes to demonstrate that certain factors are common and consistently important. Marital status, education, CT head and ISS did not reach the probability level of <0.10. However, CT and ISS were forced into regression analyses as impairment indicators. Multiple regression analyses were carried out using a hierarchical approach (a block-wise analysis). The independent variables were entered in four separate blocks based on the ICF conceptual model (Table 1), and two regression models were built. The results are presented as adjusted R² and
standardised Beta (β) values. The expected direction of standardised Beta-weights is positive for the FIM and CIQ measures and negative for the CT head and ISS, indicating that less disability equated to better physical and mental health. Before conducting the multiple regression analysis, possible multicollinearity of the independent variables was examined using the variance inflation factor (VIF). The distribution of the residuals was examined for normality, and influential data points were examined using Cook’s distance. All statistical tests were two-sided, and a 5% significance level was used. Statistical analyses were performed using SPSS for Windows, version 14 (SPSS Inc, Chicago, IL).

Results

Table 2 presents the demographic and injury characteristics of the study patients. Roughly 75% of patients were male. The mean age was 31 years; half of the patients were younger than 31 years.

*Insert table 2 about here*

Impairments

About half of the patients sustained severe TBI with significant intracranial abnormalities, as found on CT head scans. Almost 75% of patients were defined to have major trauma according to the ISS. Half of the patients had additional orthopaedic injuries (3% spine fractures, 7% extremity fractures and 39% multiple injuries). The mean length of hospital stay in acute care was 24.0±21.0 days. Sixty-five percent of all patients received inpatient rehabilitation (92% of those with severe TBI and 44% of those with less severe TBI). The mean length of rehabilitation stay was 57.0±38.0 days.
An overview of disabilities, rehabilitation services and SF-36 scores at the 1-year follow-up is shown in Table 3.

Insert table 3 about here

Activity limitations
Roughly 75% of the patients approached the maximum score of the FIM-M, meaning that participants were highly independent in motor function. In contrast, only half of the patients reached the maximum FIM-COG score of 35. A higher percentage of patients required assistance (scores ≤5 or less) with individual FIM-COG (18%) than FIM-M (6%) items.

Participation restrictions
Maximal social integration scores were found in 20% of patients. Thirty-five percent of patients were considered to have major problems with social integration (CIQ social integration score <9). According to the CIQ productivity subscale, 40% of all patients worked more than 20 hours per week and 18% less than 20 hours at the 1-year follow-up.

Environmental support
At the 1-year follow-up, 58% of all patients had access to community-based rehabilitation services for dealing with the consequences of TBI; of these, 39% used more than one service. The most frequently applied service was physiotherapy (86%), used four times more often than occupational therapy (20%). Day care and psychological treatment were used equally, each by one-quarter of the patients.
**Physical and mental health**

Compared with the general population, the sample of TBI patients in this study had impaired overall health as measured by the SF-36 (the general population data are not shown). Forty-six percent of the patients reported poor physical health, and 37% reported poor mental health (mean scores <40). Good physical health (mean score >40) was more often reported by males (60%) than females (30%). Patients older than 31 years reported poorer physical and mental health than younger patients (59% vs. 39% and 45% vs. 27%, respectively). Among the 42 patients who reported poor physical health, 60% had less severe TBI. Of these, 62% did not receive inpatient rehabilitation and 38% did not receive any type of rehabilitation services at follow-up. Among the 31 patients with poor mental health, 58% were in the group with less severe brain injury. Half of these did not receive inpatient TBI rehabilitation, and 44% did not receive any type of rehabilitation services at follow-up. In the severe TBI group, the majority of those who reported poor health attended rehabilitation programs at follow-up.

**Multiple regression analyses**

Results of the hierarchical regression models designed to explain the impact of TBI disability on physical and mental health are presented in Table 4. The collinearity diagnostic indicated an acceptable degree of collinearity (all VIFs <2.5). No single case within the data exceeded an undue influence on the model, based on Cook’s distance (D <0.13).

*Insert table 4 and table 5 about here*

Demographics (age and gender), activity limitation (FIM-M and FIM-COG) and participation restriction (CIQ social integration and CIQ productivity) added significant variance to the model with physical health as the dependent variable. The final model explained a total of 50%
of the variance in the physical health (p<0.001). The most important individual variable was productivity (CIQ), followed by gender, severity of brain injury (CT), motor functional ability (FIM-M) and severity of overall trauma (ISS). The model with mental health as a dependant variable revealed that activity limitation was the strongest model predictor (20%), followed by participation restriction (14%). Demographics and impairment did not add a significant R² change to the model. The explanatory power of the final mental health model was 35% (p<0.001), with productivity (CIQ), cognitive functional ability (FIM-COG) and brain injury severity (CT) as the three significant individual variables. The standardised Beta values of the FIM-M and CIQ subscales were positive in the physical health model (Table 5), indicating that better motor functional ability and less participation restriction equated to better physical health. Better cognitive functional ability and less participation restriction equated to better mental health. However, the β-values were positive for the CT head scans and ISS, suggesting that patients with more severe injuries reported better overall health.

Discussion

This study applied the ICF model to investigate the impact of disability after moderate-to-severe TBI on physical and mental health outcomes. In agreement with other TBI studies, patients face substantial disability and impaired overall health at 1 year of follow-up (28-30). The ICF domain of activities and participation accounted for a large proportion of variance in physical and mental health, whereas productivity was the strongest individual explanatory variable. The findings will be discussed in detail later.
Impairments

The impairment measures used in this study warrant a discussion. The GCS is the most commonly used TBI impairment instrument (11). However, prior studies have recognised problems in obtaining accurate scores for the GCS. The level of consciousness might be obscured in the acute settings due to substance influence, medical sedation or paralysis, in contrast to the more objective structural brain injury shown on CT head scans (31). There is evidence that the CT scan can assist in discriminating less severe versus more severe TBI using the Marshall Classification (18). Therefore, we used CT data as an indicator of structural brain damage. In this study, 60% of the patients had a GCS score in the severe TBI range. However, CT scans showed that only 44% of patients had injuries that could be categorised as more severe. Many TBI survivors recruited from a trauma centre have orthopaedic injuries in addition to head injuries. The patients with orthopaedic injuries may have limitations that contribute to their levels of impairment (11). As almost half of the patients in this study had associated orthopaedic injuries, we also used the ISS as a measure of impairment.

Activity limitations

With regard to activity limitations, the FIM-M and FIM-COG mean values were in the independence range and similar to those found in Corrigan’s study (28). Roughly 25% of our patients reported disability requiring personal assistance in physical and/or cognitive ADL, in contrast to the 37% of patients reported in the study by Whiteneck (30). Lower rates in this study may be explained by the different methodologies used or the fact that we excluded patients with considerable communication problems. As the FIM is of limited value due to the
ceiling effect 1 year after injury, however, the degree of activity limitation is likely underestimated (32).

**Participation restrictions**

Social integration was not achieved by all patients 1 year post-injury, and many patients reported productivity restrictions. Roughly 66% of the patients reported at least two problems regarding social integration. Only 10% of patients reached a maximum score on the CIQ productivity scale. These results and the average CIQ total score of 15 are consistent with previous studies (28;33). Of patients working at the time of injury, 37% were not working one year later, 37% were working full-time and 26% had part-time jobs or were studying. These rates of employment are roughly comparable with estimates from a USA population-based study (30), but they are more than two times higher than those reported in another prospective study of recovery after moderate-to-severe TBI (33). However, half of the patients with initial severe TBI were not productive 1 year after injury; in accordance with previously reported rates, 25% returned to full-time work (34). It is well recognised that many of those returning to work after TBI have condition-related difficulties, such as reduced cognitive capability, in their employment settings (29).

**Physical and mental health**

In this study, TBI patient self-reported health status was more often within the impaired range than that of the general Norwegian population (35). However, our results seem to be comparable to those reported in the TBI population in the USA at 1 year post-injury (28). Almost half of the patients reported poor physical health whereas one third reported poor
mental health in this study. Patients under 31 years of age reported better overall health than those above 31 years. Other studies showed better mental health in older than younger TBI subjects (9). Worse physical health with increasing age was reported in the general population, and mental health was the only subscale (SF-36) in which there were no statistically significant differences between the age groups (36). Males experienced better physical health than females, and a similar trend was observed in the general population (35) and other TBI studies (9;29). The increased problems with physical role functioning reported by females in this study may be associated with difficulties in fulfilling domestic roles after injury (29). Poorer overall health was, however, more often reported in groups with less severe injury (15). More insight and better memory to recall the frequency of problems within the SF-36 domains may in part explain these results. Some studies have indicated that those patients with milder injuries who are afflicted with fewer problems may be more bothered by these problems (11). According to Webb et al. (15), ‘persons sustaining mild or moderate TBIs are less likely to receive formal rehabilitation services than those with more severe, irreversible brain damage, thus limiting further their ability to regain their former quality of life’.

Environmental support

Roughly 75% of patients in the severe TBI group and 48% of those with less severe TBI received rehabilitation services 1 year after injury. Survivors with more severe TBI tend to remain functionally dependent and often require more extensive services (15). More than 33% of these patients received several services. As reported in other studies, however, the most notable is the use of physiotherapy (37). This may be due to the fact that many patients had additional orthopaedic injuries. Despite the frequent service use, it seems that rehabilitation and
support needs are not covered. Only 6% of patients with major social integration problems received organised social support. Roughly 66% of these patients also reported poor mental health. Of patients who reported poor mental health, one third did not receive any type of service at the 1-year follow-up. A similar trend was observed in another study, which reported that less than half of patients with poor mental health received any mental services (9). Consequently, mental services were one of the most prevalent types of unmet needs reported by TBI survivors (9).

The conceptual model

The ICF worked well as a conceptual model, because the disability dimensions identified 1 year after TBI were related to physical and mental health outcomes. Statistically significant models for physical and mental health were found. Higher level of activities and participation were the strongest predictors of better overall health. The model for physical health, covering data on demographics, impairments, activity limitations and participation restrictions, accounted for 50% of the variance, whereas the model for mental health accounted for 35%. One of the reasons why a large proportion of the variance remained unexplained, particularly in the model of mental health, is that cognitive function was evaluated by the cognitive items of the FIM, which is of limited sensitivity (28). Physical and mental health is a multidimensional phenomena assumed to be influenced by many factors. Some of the remaining explanatory factors may be related to personal factors (e.g. interpersonal relations (8;12)), or environmental conditions (e.g. quality of environment, care giving and current living situation (10)). Clearly, mental health is influenced by other factors with important clinical implications (e.g. depression and other life event stressors), which have not been captured by this model. Other
studies have shown that depression tends to be strongly associated with subjective quality of life, accounting for nearly 50% of the variance (38). In a sample of patients with moderate-to-severe TBI, Findler et al. (25) reported significant correlations between scores on the SF-36 mental health subscale and the Beck Depression Inventory (BDI) (r=-0.60). Depression was not used in the analyses in this study because of the high correlation between the BDI and MCS (r=-0.79). Further, we applied similar regression models to both health outcomes to demonstrate that certain factors are common and consistently important.

Because of the wide variation in study designs related to inclusion procedures, the use of different methodology and outcome measures, the comparison of our findings with those from previous studies is difficult. The conceptual approach and ICF components used in this study are similar to the study of Pearce and Hanks (10). As these studies measured different dimensions of quality of life, however, the outcomes are not comparable. The explanatory power of the model in Pearce’s study is more limited, as > 82% of the variance of life satisfaction remained unexplained.

Associations between different measures of disability and self-reported health outcomes are complex. Variables associated with better physical health included: male gender, more severe TBI and overall trauma, higher level of motor ability and participation in productive activities. Better mental health was related to more severe TBI, a higher level of cognitive ability and participation in productive activities. Somewhat controversially, the β-values were positive for the CT head scans and ISS. This result suggests that patients with more severe impairment experienced better overall health 1 year post-injury, likely due to reduced awareness of the
functional consequences of the disability. According to the study by Flashman and McAllister (39), ‘up to 45% of individuals with moderate-to-severe TBI demonstrated reduced awareness or complete lack of awareness of their deficits’. Impaired memory to recall the frequency of problems within SF-36 domains may also influence these results (11). As expected, participation in productive activities was the strongest individual explanatory variable in both health models. Our findings support the conclusions from other studies that productivity is the most important contributor for better self-reported health, well-being and quality of life (10-12;40).

The association shown between the severity of injury and physical and mental health in this study is in contrast with previously mentioned findings of Dijkers (13), but in agreement with those reported by Koskinen (16). In a retrospective study of moderate-to-severe TBI 10 years after the injury, an association between TBI severity and SF-36 items was not found (40). One possible explanation suggests that the association with injury variables dissolves over time, or perhaps other variables become more important for health-related quality of life at a later stage (41).

Despite the low ‘lost to follow-up’ rate (12% of those surviving at 1 year post-injury) in this prospective study, several limitations should be considered when interpreting our results. This is a selected cohort study describing a population aged 16-55 years with moderate-to-severe TBI. The severity of TBI was limited those patients who could respond to the SF-36 questionnaire. Consequently, eight survivors with severe TBI were not included in the study. The small sample size limited the number of explanatory variables (e.g., environmental factors) that could be used in the regression analyses. The FIM is of limited value due to the ceiling
effect 1 year post-injury (32). However, our cohort had demographic and injury characteristics similar to those of the general TBI population, making the study results generalisable.

**Conclusion**

At the 1-year follow-up, patients were highly independent in physical but not cognitive activities. Social integration was not completed, and many patients reported productivity restrictions. Better physical and mental health was related to more severe injury and higher levels of activities and productivity. The use of rehabilitation services reflects the severity of the injury. It is notable that many patients with less severe TBI who reported impaired overall health did not receive any type of rehabilitation after their injury. To optimise physical and mental health outcomes, clinicians need to ensure that the disability and health needs of these patients are identified and treated during the post-acute period.

**Acknowledgements**

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**Conflict of interest:** None.
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Table 1 TBI-related disability and measures used

<table>
<thead>
<tr>
<th>ICF components</th>
<th>Measures</th>
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<tr>
<td>Demographics</td>
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<tr>
<td></td>
<td>Gender</td>
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<tr>
<td>Impaired body structures</td>
<td>CT</td>
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<tr>
<td></td>
<td>ISS</td>
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<tr>
<td>Activity limitations</td>
<td>FIM-M</td>
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<td></td>
<td>FIM-COG</td>
</tr>
<tr>
<td>Participation restrictions</td>
<td>CIQ social participation</td>
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<td></td>
<td>CIQ productivity</td>
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Table 2 Demographic and injury-related characteristics of the participants (n=85)

<table>
<thead>
<tr>
<th>Variables</th>
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</thead>
<tbody>
<tr>
<td><strong>Gender, n (%)</strong></td>
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<td></td>
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<tr>
<td>Male</td>
<td>65 (76.0)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>20 (24.0)</td>
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<tr>
<td><strong>Age at onset (years), mean (range)</strong></td>
<td>31 (16-55)</td>
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<tr>
<td><strong>Marital status (pre-injury), n (%)</strong></td>
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<tr>
<td>Married/partnership/live with</td>
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<tr>
<td>Unmarried/widowed/divorced</td>
<td>36 (42.0)</td>
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</tr>
<tr>
<td><strong>Education (pre-injury), n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-12 years</td>
<td>45 (53.0)</td>
<td></td>
</tr>
<tr>
<td>≥13 years</td>
<td>40 (47.0)</td>
<td></td>
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<tr>
<td><strong>Employed (pre-injury), n (%)</strong></td>
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</tr>
<tr>
<td>Full-time</td>
<td>66 (77.0)</td>
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<tr>
<td>Part-time</td>
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<tr>
<td>Unemployed</td>
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<tr>
<td>Sick leave/disability pension</td>
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<tr>
<td><strong>Cause of injury, n (%)</strong></td>
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<td></td>
</tr>
<tr>
<td>Traffic accidents</td>
<td>50 (59.0)</td>
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<td>Fall</td>
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<td>Assaults</td>
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<tr>
<td>Other</td>
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<tr>
<td><strong>Severity of injury</strong></td>
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<tr>
<td>GCS, mean (SD)</td>
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<tr>
<td>ISS, mean (range)</td>
<td>28.6 (4-59)</td>
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<tr>
<td><strong>CT head (Marshall classification), n (%)</strong></td>
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</tr>
<tr>
<td>1. No visible intracranial pathology</td>
<td>15 (17.0)</td>
<td></td>
</tr>
<tr>
<td>2. Cisterns present with midline shift 0-5mm;</td>
<td>32 (38.0)</td>
<td></td>
</tr>
<tr>
<td>No high or mixed density lesion &gt; 25ml.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Cisterns compressed or absent with midline shift 0-5 mm</td>
<td>33 (39.0)</td>
<td></td>
</tr>
<tr>
<td>4. Midline shift &gt; 5 mm;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgically evacuated mass lesion</td>
<td>5 (6.0)</td>
<td></td>
</tr>
<tr>
<td>Non-evacuated high or mixed density lesion &gt; 25 ml</td>
<td>0 (0.0)</td>
<td></td>
</tr>
</tbody>
</table>
Table 3 Descriptive statistics of disabilities, rehabilitation services and physical and mental health one year after TBI (n=85)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Activity limitation, mean (range)</th>
<th>Participation restriction, mean (range)</th>
<th>Rehabilitation services, n (%)</th>
<th>SF-36 NBS (norm based scores), mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FIM-M</td>
<td>89.0 (58-91)</td>
<td>FIM-COG</td>
<td>32.0 (19-35)</td>
</tr>
</tbody>
</table>
Table 4 Hierarchical multiple regressions of the ICF components on the physical and mental health scores (n=85)

<table>
<thead>
<tr>
<th>Step</th>
<th>Variables</th>
<th>Physical health(^a)</th>
<th>Mental health(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(R^2) change</td>
<td>(R^2) change</td>
</tr>
<tr>
<td>1</td>
<td>Demographics</td>
<td>0.13 (p=0.003)</td>
<td>0.05 (p=0.12)</td>
</tr>
<tr>
<td>2</td>
<td>Body structures impairment</td>
<td>0.03 (p=0.27)</td>
<td>0.02 (p=0.37)</td>
</tr>
<tr>
<td>3</td>
<td>Activity limitations</td>
<td>0.18 (p&lt;0.001)</td>
<td>0.20 (p&lt;0.001)</td>
</tr>
<tr>
<td>4</td>
<td>Participation restrictions</td>
<td>0.20 (p&lt;0.001)</td>
<td>0.14 (p=0.001)</td>
</tr>
</tbody>
</table>

\(^a\) Physical health \(R^2=0.54\); adjusted \(R^2=0.50\)

\(^b\) Mental health \(R^2=0.41\); adjusted \(R^2=0.35\)
Table 5 Association between dependent and independent variables.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Physical health $\beta$ (p=0.18)</th>
<th>Mental health $\beta$ (p=0.79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.11</td>
<td>0.03</td>
</tr>
<tr>
<td>Gender</td>
<td>-0.27 (p=0.001)</td>
<td>-0.13 (p=0.16)</td>
</tr>
<tr>
<td>ISS</td>
<td>0.17 (p=0.04)</td>
<td>0.18 (p=0.07)</td>
</tr>
<tr>
<td>CT head</td>
<td>0.27 (p=0.004)</td>
<td>0.21 (p=0.05)</td>
</tr>
<tr>
<td>FIM-M</td>
<td>0.24 (p=0.02)</td>
<td>-0.12 (p=0.35)</td>
</tr>
<tr>
<td>FIM-COG</td>
<td>-0.02 (p=0.88)</td>
<td>0.27 (p=0.05)</td>
</tr>
<tr>
<td>CIQ social integration</td>
<td>0.02 (p=0.85)</td>
<td>0.17 (p=0.12)</td>
</tr>
<tr>
<td>CIQ productivity</td>
<td>0.55 (p&lt;0.001)</td>
<td>0.40 (p=0.001)</td>
</tr>
</tbody>
</table>

$\beta$-values and $p$-values of independent variables are given for the final multiple regression models.