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ALCOHOL MISUSE IN RELATION TO TRAUMATIC BRAIN INJURY

THE NORTHERN FINLAND 1966 BIRTH COHORT STUDY
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The Northern Finland 1966 birth cohort study

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Abstract

Traumatic brain injury (TBI) is often the leading cause of death and the most common cause of permanent disability in children and young adults. The hospital admission rates as well as the incidence and mortality rates of TBI vary enormously in different countries and populations. Even though alcohol misuse is a well-known modifiable risk factor for TBI and other injuries, few studies have been carried out on drinking patterns in relation to TBI, alcohol's role in recurrent brain injuries as well as TBI in relation to alcohol use in children and adolescents.

The Northern Finland 1966 Birth Cohort was used to study the epidemiology and recurrence of TBI as well as alcohol use by children with TBI by the age of 14 years and those who sustained TBI later in life. The role of parents' alcohol misuse on children's TBI was also studied.

The incidence of TBI in the whole study population was 118/100 000 person-years (PY), and the pediatric incidence of TBI (children aged under 16 years) was 130/100 000 PY. Up to the age of 10 years, the occurrence of TBI did not differ by gender, but after that age, boys and men had a higher incidence compared to girls and women. Mortality from TBI in the whole study population was 14/100 000 PY. Parental alcohol misuse and male gender were significant risk factors for the occurrence of TBI in childhood. Drinking to intoxication at the age of 14 years was a more common habit of TBI subjects than controls, especially among girls. Frequent alcohol drinking and drunkenness reported at the age of 14 years as well as male gender were independent predictors of TBI later in life. An alcohol-related first TBI and urban place of birth were found to be significant risk factors for recurrent TBI. A significant positive correlation between first and recurrent TBIs with respect to alcohol involvement was observed.

Alcohol drinking and parental alcohol misuse should be recognized among children and adolescents with acute TBI. Because alcohol drinking predicts the recurrence of TBI, a brief intervention focused on drinking habits is needed as an immediate preventive measure.

Keywords: adolescents, alcohol drinking habits, children, incidence, mortality, traumatic brain injury, young adults
To my family
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Oulu, May

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Abbreviations

AIS<sub>head</sub> Abbreviated Injury Scale for head injuries
CI confidence interval
ED emergency department
FHDR Finnish Hospital Discharge Register
GCS Glasgow Coma Scale
HR hazard ratio
ICD International Classification of Diseases, Injuries and Causes of Death
LOC loss of consciousness
NA not available
PTA post-traumatic amnesia
PY person-years
RR risk ratio
<sub>r</sub> Spearman rank-order correlation coefficient
SR-related sport- and recreation-related
TBI traumatic brain injury
List of original publications

This thesis is based on the following publications, which are referred to in the text by their Roman numerals I–IV:


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1 Introduction

Traumatic brain injury (TBI) is the leading cause of death and the most common cause of permanent disability in children, adolescents, and young adults (Kraus 1993, Jennet 1996). In the United States, TBI represents the most frequent cause of hospital admission for nervous system disease (Marshall 2000). Even if not fatal, TBI frequently causes not only personal suffering but also a considerable societal burden because it may result in long-term disability. It is expensive for the community because of the high costs of acute care and rehabilitation and the loss of productivity (Berg 2005). The societal cost in the United States has been estimated to be 85 000 000 million dollars per year (Singh et al. 2006), and even pediatric traumatic brain injury accounts for more than 1 000 000 million dollars in total hospital charges annually (Schneier et al. 2006). In Europe, we still lack good estimates for the total costs of TBI (Berg et al. 2005).

Alcohol misuse is a well-known modifiable risk factor for injuries. During the past decades, acute alcohol consumption has been identified as a significant contributor to both unintentional and intentional injuries (Honkanen & Visuri 1976, Wagner et al. 2000). Approximately 50% of trauma patients have alcohol-related injuries on admission (London & Battistella 2007). Adolescents who begin alcohol drinking before the age of 14 years has been found to have an almost three-fold risk for some kind of alcohol-related injury during their lives compared to those who begin alcohol drinking after the age of 14 years (Hingson 2000). TBI is frequently associated with heavy drinking and alcoholism, but studies that report on occasional hazardous drinking of young people leading to TBI are lacking.

Millions of US children are exposed to parents who are problem drinkers (Bijur et al. 1992), and parental alcoholism has been found to correlate positively with children’s injuries, abuse, and neglect (Widom et al. 2001, Villalba-Cota et al. 2004). Children of mothers classified as problem drinkers have been reported to have a more than twofold risk of injury (Bijur et al. 1992). Violence is a frequent cause of injuries in families with alcohol problems (Crandall et al. 2006, Stewart et al. 2004, Hanson et al. 2006). Even though head injury is the leading cause of death in abused children under 2 years of age (Rubin et al. 2003), it has not been reported whether parental alcohol misuse also predicts traumatic brain injuries in older children.

Pre-injury alcohol abuse has been reported to be a frequent habit among brain-injured subjects. Alcohol drinking often decreases after the injury, but
relatively soon returns to the pre-injury level (Dikmen 1995). Much less is known about the drinking habits of the TBI subjects who do not have pre-injury alcohol misuse, and studies that report the drinking habits of children with TBI are lacking totally. Recurrent brain injuries are often reported among male athletes (Salcido et al. 1992, Zemper 2003, Guskiewicz et al. 2003), but studies of recurrent brain injuries due to alcohol drinking are almost non-existent (Hillbom & Holm 1986).

Almost all reports dealing with head injury are, in fact, concerned with brain injury (Kraus 1993). Hence, in this doctoral thesis, the terms ‘head injury’ and ‘brain injury’ are used synonymously. The present study is an epidemiological study of TBI in a birth cohort over a long follow-up time. It focused on alcohol drinking during childhood and adolescence in relation to the occurrence and recurrence of TBI.
2 Review of the literature

2.1 Traumatic brain injury

2.1.1 Definition of TBI

Traumatic brain injury (TBI) is defined as a closed (blunt) or penetrating head trauma. It may occur with or without simultaneous fracture of cranial bones (Engberg 1995). In closed injuries, brain injury is caused by blunt force contact, acceleration/deceleration of the brain within the skull, or a combination of both. Penetrating injury occurs when the scalp and skull are compromised and brain tissue is exposed to the external environment, resulting in the introduction of a foreign object into or through the skull cavity (Bandak 1995 & Sosin et al. 1995). The operational definition of TBI in the Finnish Adult TBI guidelines (2003) incorporates a verified history of trauma to the head followed by at least one of the following conditions: 1) even a short period of altered consciousness, 2) any kind of memory loss before or after the trauma, 3) alteration of mental functioning (for example, confusion or disorientation) in connection with the trauma, or 4) a temporary or permanent neurological sign or symptom indicating local brain injury (Aikuisiän aivovammojen käypähoito, Guidelines 2003). Brain injuries can also be defined by the codes of the International Classification of Diseases (ICD) that specify the location of injury (Jennet 1996). According to the ICD codes, skull fractures, brain contusions, brain concussions, and other intracranial injuries, including subarachnoid, subdural, and extradural hematomas and diffuse axonal injuries, are included.

2.1.2 Incidence rate of TBI

An incident case is defined as a new diagnosis of TBI in a specified period of time. Most published rates include hospitalized patients and deaths identified from local registers. The incidence of TBI varies widely in different studies, depending on the inclusion criteria (Table 1). Some studies report all brain injuries according to the ICD codes, as some studies report brain injuries that show evidence of LOC or have a certain GCS value.
### Table 1. Incidence studies of TBI.

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Source population</th>
<th>Case criteria</th>
<th>Incidence rate/10^5 person years (PY)</th>
<th>Age and gender features, not available (na)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alaranta et al.</td>
<td>All residents of Finland injured in 1991–1995</td>
<td>ICD-9 codes 800–801, 803, 850–854 first-time admissions</td>
<td>95–100</td>
<td>Male:female rate ratio of 1.5:1. Highest rates for males at ages 0–9, 10–19, 40–49 and for females at ages 0–9 and 70+</td>
</tr>
<tr>
<td>Bazarian et al.</td>
<td>All patients in ED USA 1998–2000</td>
<td>ICD-9 800,801,803,850 + intracranial injury unspecified, head injury unspecified</td>
<td>503</td>
<td>Highest occurrence in males aged under 5</td>
</tr>
<tr>
<td>Engberg</td>
<td>Residents of Fredriksborg County, Denmark 1988</td>
<td>ED and intensive care admitted patients, ICD-9 diagnosis 851–854.</td>
<td>22.6</td>
<td>Male:female rate ratio 2.1:1. Highest rates for both genders +65</td>
</tr>
<tr>
<td>Author(s)</td>
<td>Source population</td>
<td>Case criteria</td>
<td>Incidence rate/10^5 person years (PY)</td>
<td>Age and gender features, not available (na)</td>
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</tr>
<tr>
<td>Ingebritsen et al. (1998)</td>
<td>Population of Tromsø and 16 surrounding municipalities Norway 1993</td>
<td>Hospital/ED-treated head injury defined as physical damage to the brain or skull by external force</td>
<td>229 (all) 169 (hospital admissions)</td>
<td>Male/female rate ratio 1.7:1. Highest rates for men ages 10–24 and 80+, for women ages 0–4, 85+</td>
</tr>
<tr>
<td>Kraus et al. (1986)</td>
<td>San Diego County, USA 1981</td>
<td>Children ≤ 15 years ED visits, hospitalizations, death certificates, nursing home and extended-care records</td>
<td>185</td>
<td>Male/female rate 1.7:1.</td>
</tr>
<tr>
<td>Langlois et al. (2005)</td>
<td>Three National Center for Health statistics USA 1995–2001</td>
<td>Hospitalizations and deaths among 0–14 years</td>
<td>63 (hospit.) 4.5 (deaths)</td>
<td>Highest rates ages 0–4</td>
</tr>
<tr>
<td>Maegle et al. 2007</td>
<td>130 000 prehospital emergencies in Germany1990–1999</td>
<td>GCS ≤ 8 or AIS_head ≥ 2 with confirmed TBI</td>
<td>7.3</td>
<td>Males 73%, average age 40.3</td>
</tr>
<tr>
<td>Meerhoff et al. (2000)</td>
<td>Catchment area of the Academic Hospital Maastricht, Netherland, 1997</td>
<td>Traumatic head or brain injury patients who were hospital-admitted</td>
<td>88</td>
<td>Mean age 30 years, 67% were men</td>
</tr>
<tr>
<td>Sallee et al. (2000)</td>
<td>Alaska residents 1196–1998</td>
<td>Hospital admissions or out-of-hospital deaths with TBI</td>
<td>105</td>
<td>na</td>
</tr>
<tr>
<td>Author(s) (year)</td>
<td>Source population</td>
<td>Case criteria</td>
<td>Incidence rate/10^5 person years (PY)</td>
<td>Age and gender features, not available (na)</td>
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</tr>
<tr>
<td>Tate et al. (1998)</td>
<td>Residents in the North Coast Health Region, Australia 1988</td>
<td>Hospital-treated head traumas according to medical records confirming diagnosis of brain injury</td>
<td>100</td>
<td>na</td>
</tr>
<tr>
<td>Tiret et al. (1990)</td>
<td>Residents of Aquitano Region, France 1986</td>
<td>Hospital admissions and death certificates. Contusions, lacerations, skull fractures, or brain injuries and/or LOC after a relevant injury</td>
<td>282</td>
<td>Male:female rate ratio 2.08:1. Highest rates at ages 0–4, 15–24, 75+</td>
</tr>
<tr>
<td>Vasquez-Barquero et al. (1992)</td>
<td>All residents of Cantabria, Spain 1988</td>
<td>University Hospital admissions &lt; 24 hours from injury with LOC, skull fracture, objective neurologic findings attributed to head injury including in-hospital deaths</td>
<td>91</td>
<td>Male:female rate ratio 2.87:1. Highest rates at ages 0–15 and 15–24 for both genders</td>
</tr>
</tbody>
</table>

na = not available

Higher incidence rates are reported from surveys based on routine international classifications of disease coding (ICD coding) than those based on hospital case records (Jennet 1996). In Scandinavia, TBI incidence has been reported to vary from 95/100 000 PY (Alaranta et al. 2000) to 546/100 000 PY (Andersson et al. 2003). A recent study from Finland (Koskinen & Alaranta 2008) reported an average incidence of 101/100 000 during 1991–2005. The average incidence of annual pediatric TBI has been reported to be 180/100 000 PY, calculated from nine different studies in USA 1980–1989 (Kraus 1995). Complete registration of the occurrence of TBI, however, is not practicable because most of the mild brain injuries are not treated at hospitals, and the great majority of these injuries are never medically diagnosed. Especially older people and subjects injured at home are less likely to seek care (Setnik & Bazarian 2007).

### 2.1.3 Severity of TBI

Brain injuries cover a wide range of severity from patients who die before admission to hospital to those with such mild injuries that they never seek health care. Most brain injuries admitted to hospital are mild. The severity of TBI can be
defined in several ways, but TBIs have traditionally been classified as mild, moderate, and severe (Vos et al. 2002). The basis for severity description is usually either the Glasgow Coma Scale score (GCS) (Teasdale & Jennet 1974), the length of post-traumatic amnesia (PTA) (Russel & Smith 1961), or loss of consciousness (LOC). Also, ICD codes have been used to describe the severity of TBI. ICD-9 850 (brain concussion) and 800, 801, 803 (skull fractures) have been used to cover mild TBI, while 851–854 cover the more severe cases (intracranial injuries) (Jennet 1981). The ICD classification has proved to be practicable for epidemiological studies (Sosin et al. 1989). The average ratio of mild to moderate and severe TBI has been reported to be 22:1.5:1, accordingly 90%, 6%, and 4% (Tagliaferri et al. 2005). The average incidence of mild TBI has been reported to be 503.1 /100 000 PY (Bazarian et al. 2005), and the average incidence of severe brain injury has been estimated as 7.3 /100 000 PY (Maeglele et al. 2007).

In Finland, about 1000 people die from brain injury annually (Alaranta et al. 2002). The mortality rates in Central Europe range from 5.2/100 000 PY in France (including only deaths in hospital) (Masson et al. 2001) to 24.4/100 000 PY in Italy (including also pre-hospital deaths) (Servadei et al. 1988). The average mortality of TBI has been estimated to be about 15/100 000 per year (Tagliaferri et al. 2005). Deaths that occur before admission to hospital account for two-thirds or more of all deaths from brain injury in the United States and Australia, 45% of those in the United Kingdom (Jennet 1996), and 28% of deaths in Europe (Maegale et al. 2007). These differences in prehospital death rates can be due to the possibility that some prehospital death patients might have had brain injury but TBI has not been the primary cause of death (Maegale et al. 2007). Instead, penetrating injuries due to violence increase the mortality rates and this type of death (especially firearm related TBI) is common in the United States (Sosin et al. 1995). It has been reported that five out of nine potentially preventable deaths occur as a result of delay in transfer (Benzel et al. 1991) and this can be related to the fact that many of these incidents are suicides and homicides. Previous studies have also shown that young men have higher mortality rates than young women (Jennet 1996). Pediatric (0–17 years) mortality from TBI has been estimated to be 2.6/100 000 PY in Sweden (Emanuelsson & von Wendt 1997) and 8.1/100 000 PY in the United States during 1987–1988 (Kraus 1995).
2.1.4 External causes of TBI

The main external causes of TBI are motor vehicle accidents, falls, recreational injuries, and violence. The frequency of external causes varies from one study to another due to their different inclusion criteria and age and sex distributions. In the general population, including elderly people, falls comprise the most frequent cause of TBI (Andersson et al. 2003, Alaranta et al. 2000). Falls and road traffic accidents are the most frequent causes of severe brain injuries (Hillier et al. 1997, Masson et al. 2001). Traffic accidents have been reported to be the main cause of TBI in France and Australia (Tiret et al. 1990, Hillier et al. 1997). Intentional injuries (homicide and suicide) comprise about 1–15% of all external causes of TBI (Tagliaferri et al. 2005). Intentional injuries leading to TBI occur particularly among young people, minorities, and males (Wagner et al. 2000). In Glasgow, up to 28% of the external causes of TBI have been reported to be assault/violence (Thornhill et al. 2000). The major causes of pediatric brain injuries in the United States are falls (35%), recreational activities (29%), and motor vehicle accidents (24%) (Kraus et al. 1986). In Sweden, traffic accounts for 60%, falls for 22%, sports for 7%, object hitting the head for 3%, violence for 2%, and unknown causes for 6% of pediatric TBI cases (Emanuelson & von Wendt 1997). According to a recent report from the United States, sport- and recreation-related (SR-related) brain injuries comprised 5.1% of all TBIs, and the highest rates of SR-related TBI emergency department visits occurred among those aged 10–14 years, followed by those aged 15–19 years (Centers for Disease Control and Prevention (CDC) 2007).

2.1.5 Recurrent TBI

There have been relatively few reports about recurrent brain injuries. Most of the recurrent brain injury studies report on cases of concussion among young male athletes (Zemper 2003, Guskiewicz et al. 2003). Recurrence of injury and the possibility that previous TBI may increase the risk of subsequent injury have been mentioned occasionally in the literature (Salcido & Costich 1992). A recent study from Canada reported evidence that having a head injury increases a child’s risk of sustaining a subsequent head injury (Swaine et al. 2007). The risk of a second head injury among those with a previous head injury has been found to be threefold compared to the uninjured population, and the risk rises to eight times the normal risk after two traumatic brain injuries (Annegers et al. 1980). In the
same study, a head injury after the age of 25 was found to generate a fivefold increased risk of subsequent injury. This was explained by behavioral characteristics such as use of alcohol. The role of alcohol in traumatic brain injury recurrence remains unclear, however, because only a few studies have been conducted on recurrent brain traumas in relation to alcohol consumption (Hillbom & Holm 1986, Drubach et al. 1993). Recurrent head injuries were found to be more frequent in alcoholics than in non-alcoholic subjects. No studies have reported on recurrent brain injuries and occasional hazardous drinking among non-alcoholic persons.

2.1.6 Socio-demographic data and TBI

According to several studies, the age-specific incidence of TBI is highest for males aged 15–24 years (Engberg & Teasdale 2001, Vasquez-Barquero et al. 1992), and some studies also report the maximum incidence for females in this age group (Klauber 1981, Kraus 1986, MacKenzie et al. 1989). However, some other studies show higher incidence rates for those aged less than 15 years (Jennet & MacMillan 1981, Engberg & Teasdale 2001). In many studies, the brain injury rate has been estimated to be higher among men than among women. In Spain, for instance, the rate is 2.7 times higher among men than women (Vazquez-Barquero et al. 1990), whereas in Norway the corresponding figure is 1.7 (Ingebritsen et al. 1998). The following pre-morbid factors of TBI subjects other than age and gender have been reported: personality, family characteristics, and socioeconomic circumstances (Wagner et al. 2000). Studies on children have revealed a higher incidence of pre-morbid behavior problems (Craft et al. 1972) and poorer school attainment (Chadwick et al. 1981) among TBI patients compared to non-TBI subjects. Unemployment, lower family incomes (Durkin 1998), and single-parent families have also been associated with TBI in children (Klonoff 1971, Rubin et al. 2003). Poor academic performance (Engberg 1995), high frequency of pre-morbid abuse, and social problems (Engberg 1995, Rimel et al. 1983) are frequent among adult TBI patients.

2.2 Alcohol and TBI

Adolescents’ misuse of alcohol is nowadays very common in USA (Naimi et al. 2003, Spear 2002) as well as in other countries, including Finland (Lamminpää & Vilska 1990, Official Statistics of Finland 2002). The typical drinking pattern of
adolescents is binge drinking (five or more drinks on one drinking occasion), and this pattern of drinking is often associated with other types of risky behavior. Higher volume per drinking occasion and higher proportions of binge drinking occasions to all drinking occasions have been reported from United Kingdom, Sweden and Finland compared to Italy, France and Germany (Kuntsche et al. 2004). However, the lowest frequencies of drinking were found in Finland and Sweden as the highest frequency of drinking has been reported from Italy (Kuntsche et al. 2004).

Adolescents are more inclined toward risky behavior and risky decision making than adults, and peer influence plays an important role in their behavior (Gardner & Steinberg 2005). Alcohol misuse is known to be associated with many high-risk activities such as violence and reckless driving (Quinlan et al. 2005), and alcohol and substance users often engage in risk-taking behaviors (Desrichard & Denarie 2005). These observations may hold for both genders (Kelly et al. 2005). The number of lives lost through needless deaths associated with this type of risky behavior may be high among adolescents.

2.2.1 Socio-demographic factors and drinking during adolescence

Drunkenness among adolescents increased in the 1980s and 1990s in Finland (Rimpelä et al. 1997) and the other Nordic countries (Andersson & Hibell 1995). This was attributed to the increased alcohol availability (Edwards et al. 1994) and the liberalized alcohol policy in general (Rahkonen & Ahlström 1989). The known socio-demographic background variables of adolescents’ alcohol drinking are age, gender, religion, family structure, and socioeconomic status as well as parental unemployment and residential urbanization (Isohanni et al. 1994, Lintonen et al. 2000). Observations differ somewhat regarding father’s/parents’ educational background. Some studies suggest that high parental education associates with a high level of alcohol consumption (Dantzer et al. 2006), whereas others report an association between low parental education and excessive alcohol drinking (Droomers et al. 2003). Male gender and early onset of alcohol consumption seem to predict alcohol abuse later on in life (Andersen et al. 2003, Fergusson et al. 1995, Warner & White 2003). Heavy drinking of 15-year-old Finns has been associated with poor school achievement (Laukkanen et al. 2001), but alcohol consumption varies geographically in Finland. Alcohol consumption has been shown to be lowest in the rural areas of Northern Finland (Winter et al. 2002), which makes the present study of particular interest.
2.2.2 Alcohol involvement at injury

Drinking before the age of 21 years has been found to associate with a tendency to sustain some kind of injury and especially alcohol-related injuries (Hingson et al. 2000). Acute alcohol consumption is also known to increase two- to three-fold the risk of injury after six hours of alcohol drinking (Watt et al. 2004, McLeod et al. 1999), and the risk of injury has been reported to be significantly higher (OR 9.6) for women than for men (OR 2.1) (McLeod et al. 1999). Alcohol is an important contributory cause of head injury, and its influence has been best documented for road accidents, especially for drivers (Jennet 1996). Alcohol involvement has been reported to associate with 41% of brain injuries in the USA (Levy et al. 2004). In Spain, 51% of TBI patients admitted to hospital during one year were intoxicated (Vazquez-Barquero et al. 1992). In the 1980s, 29% of hospitalized traffic accident subjects with TBI had blood alcohol concentrations that exceeded the legal limit (0.5‰) in Denmark (Engberg 1995), and in Ireland 31% of TBI patients had ingested alcohol prior to their injury (O’Brien et al. 1996). A TBI study from Norway reported that 24% of the injuries involved alcohol, and they occurred most commonly among males being assaulted (Ingebritsen et al. 1998). According to a cross-national study of injuries, drunkenness was positively (p < 0.01) and consistently (8/8 countries) associated with injuries caused by fighting, but not with school and sport-related injuries (Picket et al. 2005).

2.2.3 Drinking habits before and after TBI

Little is known about the drinking habits of adolescents before and particularly after sustaining a TBI. In adults, pre-morbid alcohol abuse is frequent among head injured patients (Dikmen et al. 1995, Kolakowsky-Hayner et al. 1999). Both alcohol abuse and drug use have been reported to be common before sustaining TBI (Bombardier et al. 2002). In this study by Bombardier, 59 percent of acute TBI rehabilitation patients (n = 142) were considered problem drinkers, and they usually reported episodic heavy drinking instead of serious physical alcohol dependence. They were also frequently engaged in high-risk behaviours such as drunk driving.

Several studies have shown a transient decrease of alcohol drinking after TBI among adults (Kreutzer et al. 1996, Dunn et al. 2003, Dikmen et al. 1995). However, as soon as four months after the injury, alcohol abuse often returns to
the pre-injury level (Dunn et al. 2003). Men and persons with a history of pre-injury heavy drinking also run a high risk for long-term alcohol abuse post-injury (Kreutzer et al. 1996). Three clinical predictors of hazardous drinking during one year after the injury have been reported: any positive blood alcohol concentration at admission, non-prescription drug abuse one month before injury, and suffering an intentional injury (Dunn et al. 2003). It has also been reported that a significant percentage (20%) of persons who are heavy drinkers after TBI reported only light drinking or even abstinence prior to TBI (Corrigan et al. 1995). In another study, about 25% of TBI patients reported heavy drinking and significant problems related to drinking during the first year after their injury (Bombardier et al. 2003).

2.2.4 Parents’ alcohol misuse and TBI of their children

Parental alcoholism has been reported to associate positively with children’s injuries, not only abuse, but also neglect (Bijur et al. 1992, Widom & Hiller-Sturmhöfel 2001, Villalba-Cota et al. 2004). Children of problem drinker mothers have a 2.1-fold risk of serious injury compared to children of non-drinker mothers, and children whose both parents are problem drinkers are at an even higher risk (Bijur et al. 1992). In a study of 173 abused infants, nearly one-third of inflicted head injuries were missed on their initial admission to medical care (Jenny et al. 1999), and 25% of these infants were re-injured before they were appropriately diagnosed. Nearly 10% of these missed cases suffered a fatal injury after their initial presentation. Occult head injuries (Rubin et al. 2003) and also other injuries (Durkin et al. 1998) have been reported to appear particularly among children aged less than one year. Although parental alcoholism has been reported to associate with different types of injuries, no particular emphasis has been placed on brain injuries.
3 Aims of the study

The main purpose of this study was to evaluate the relationship between brain injuries and alcohol consumption in the Northern Finland Birth Cohort 1966. The numbers I–IV hereafter refer to the original publications. The specific aims of the individual studies were:

2. To find out the risk factors for recurrent traumatic brain injuries (TBI) in adolescents and young adults (II).
3. To assess the psychosocial factors that predicted the occurrence of TBI in childhood, especially the relationship between parental alcohol misuse and the childhood TBI (III).
4. To assess how TBI sustained during childhood and parental alcohol misuse influence drinking habits of adolescents at the age of 14 years (III).
5. To assess relationships between psychosocial factors, drinking habits at the age of 14 years and the risk of traumatic brain injury later in life (IV).
4 Subjects and methods

4.1 Study design

The original purpose of the Northern Finland 1966 Birth Cohort was to enable description and analysis of the risk factors for perinatal deaths and low birth weight, and it was collected by Professor (emerita) Paula Rantakallio. This epidemiological study population represents a longitudinal and prospective one-year birth-cohort design (Rantakallio 1988). The Northern Finland Birth Cohort includes 12,058 subjects (6,169 boys, 5,889 girls) born in the two northernmost provinces (Oulu and Lapland) of Finland in 1966. Geographically, the area covers about half of Finland, and the population living in this area is genetically rather homogenous and comprises slightly more than one-fifth of the total population of the country. In 1966, the population of the area was roughly 604,000, and 204,000 of them were urban dwellers. The cohort covers 96% of all children born in this area in 1966. The cohort members have been followed since their birth by means of different questionnaires. In 1966, information about the children’s families was collected by the antenatal clinics on a questionnaire (Rantakallio 1969). The mother’s demographic characteristics and obstetric history as well as the parents’ occupational and vocational status and family’s overall social status were recorded. The first follow-up of the cohort was done in 1967 at the age of one year. A questionnaire was filled in by public health nurses for 90.8% of all the children alive at this age. The second follow-up was done at the age of 14 years. In 1980 and early 1981, when the children were 14 years old, a questionnaire was completed for 97% of the living cohort members. This questionnaire elicited information about the child’s general health, growth, school performance, and smoking and drinking habits as well as the parents’ social status. Data were gathered from the cohort members after obtaining informed consent. The study protocol was approved by the Ethical Committee of Oulu University Hospital. The study population and the data collection procedure are presented schematically in Figure 1.
4.2 Subjects

Table 2 presents the subjects’ baseline characteristics. We used the record linkage technique and obtained data from the Finnish Hospital Discharge Register (hereafter FHDR), the Registry for Causes of Death maintained by Statistics Finland, and the hospital records. Based on the Finnish identity code system, all the diagnoses given at discharge are available in the FHDR, which covers all hospital and health center visits in the country. Outpatient visits and emergency visits at hospitals shorter than 24 hours are not recorded. Patient records of the TBI patients were gathered from all hospitals and health centers in Finland. A total of 457 TBI patients were identified who had been admitted into hospitals or health centers for at least 24 hours because of TBI, including the subjects who succumbed to the index injury either at hospital or at the scene. Altogether 10 197 non-injured subjects who answered the alcohol questions formed the control group in studies III and IV.
Table 2. Subjects’ baseline characteristics and duration of follow-up (I–IV).

<table>
<thead>
<tr>
<th>Study</th>
<th>Gender men/women</th>
<th>Age at injury (mean ± SD)</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>I TBI-patients (n = 457)</td>
<td>304/153</td>
<td>15 ± 8</td>
<td>34 years</td>
</tr>
<tr>
<td>II TBI single group (n = 215)</td>
<td>154/61</td>
<td>20 ± 5</td>
<td>22 years</td>
</tr>
<tr>
<td></td>
<td>TBI recurrent group (n = 21)</td>
<td>14/7</td>
<td>21 ± 6</td>
</tr>
<tr>
<td>III TBI-patients (n = 176)</td>
<td>106/70</td>
<td>8 ± 3</td>
<td>14 years</td>
</tr>
<tr>
<td></td>
<td>Subjects without TBI (n = 10 197)</td>
<td>5040/5157</td>
<td></td>
</tr>
<tr>
<td>IV TBI patients (n = 227)</td>
<td>164/63</td>
<td>22 ± 5</td>
<td>21 years</td>
</tr>
<tr>
<td></td>
<td>Subjects without TBI (n = 10 197)</td>
<td>5040/5157</td>
<td></td>
</tr>
</tbody>
</table>

We used the International Classification of Diseases coding (ICD) and analyzed the following diagnoses: ICD-8 (until 1986) and ICD-9 (1987–1995): 800, 801, 803, 850 and 851–854, ICD 10 (after 1995): S02.0–S02.11, S06.0–S06.9, S07.1 (Table 3). Accordingly, the subjects with the diagnoses of skull fracture, brain contusion, brain concussion, and other intracranial injuries, including hematomas, were included. As to assaults and suicides, penetrating brain injuries caused by shooting were included, but anoxic injuries caused by strangling or suicides by hanging were excluded. TBIs were defined into three categories according to severity: mild (concussions and skull fractures), moderate-to-severe (contusions, intracranial hematomas, and diffuse axonal injuries), and fatal injuries. Fifty-five of the subjects succumbed to the index injury (one with brain contusion died of liver rupture).

Table 3. The International Classification of Diseases coding (ICD).

<table>
<thead>
<tr>
<th>ICD 8</th>
<th>ICD 9</th>
<th>ICD 10</th>
<th>Injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>800</td>
<td>8000–8003</td>
<td>S02.0–</td>
<td>Fracture of vault of skull</td>
</tr>
<tr>
<td>801</td>
<td>8010–8013</td>
<td>S02.11</td>
<td>Fracture of base of skull</td>
</tr>
<tr>
<td>803</td>
<td>8030–8033</td>
<td>Other skull fractures</td>
<td></td>
</tr>
<tr>
<td>850</td>
<td>8500–8501</td>
<td>S06.0</td>
<td>Concussion</td>
</tr>
<tr>
<td>851</td>
<td>8510–8519</td>
<td>S06.3</td>
<td>Contusion</td>
</tr>
<tr>
<td>852, 853</td>
<td>8520–8525, 8530–8531</td>
<td>S06.4–S06.6, S06.7–S06.9</td>
<td>Traumatic hematomas of brain</td>
</tr>
<tr>
<td>854</td>
<td>8540–8541</td>
<td>S06.1–S06.2, S07.1</td>
<td>Other intracranial injury Crushing injury of head</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
External causes of injuries were gathered from the FHDR and hospital records. The ICD codes used were motor vehicle accidents (E800A–830A), falls (E880A–889A), and intentional injuries (E950A–969A). Sport and occupational accidents were recorded from the hospital records, and they did not have an ICD code for external causes of injuries. External causes of injuries were available for 326/457 subjects (72%). Data of alcohol consumption immediately before the occurrence of the index trauma were available for 374/457 (82%) subjects. Thirty-two TBI subjects did not give permission to retrieve their hospital records.

4.3 Study variables

4.3.1 Measurement of alcohol consumption (III, IV)

Data of alcohol consumption immediately before the occurrence of the index trauma was recorded either from the FHDR (ICD-9 980 and ICD-10 T51, acute alcohol intoxication) or hospital records. If the hospital records were used a mention of alcohol use before injury was recorded. Children under the age of 12 years were recorded as non-alcohol involvement cases.

Measurement of alcohol consumption was done with a postal questionnaire at the age of 14. The frequency and pattern of alcohol use were inquired with two different questions: "Have you ever drunk alcohol?" and "Have you ever been drunk?" The alternative answers to the question concerning the frequency of alcohol use were: 1) never, 2) I have tried once, 3) I have tried once or more often, 4) I drink alcohol about once a month, and 5) I drink alcohol every week. The responses to the questions concerning the frequency of alcohol consumption were divided into three categories as follows: never (alternative 1), infrequently (alternatives 2–3), and frequently (alternatives 4–5). Six reply alternatives were given for the question concerning drinking to intoxication (getting drunk): 1) never, 2) slightly drunk once, 3) slightly drunk twice or more often, 4) heavily drunk once, 5) heavily drunk two to four times, and 6) heavily drunk often. The answers were divided into two categories: 1) never drunk, 2) drunk (alternatives 2–6).

Parental alcohol misuse was recorded from the FHDR during 1966–1980. The ICD 8 diagnoses 291 (alcoholic psychosis), 303 (alcohol dependence syndromes), 571 (alcoholic liver diseases), 577–579 (alcoholic pancreatic disease), and 980 (acute alcohol intoxication) were considered indicative of a family
history of alcohol misuse. Accordingly, those alcohol related diagnosis that were treated at the hospitals were included. All those alcohol misuse cases which did not lead to a hospital admission were not included. This certainly brings some inaccuracy in the figures of parental alcohol misuse; those cases treated outside hospitals were missing. Children’s alcohol involvement during the index trauma was recorded from the FHDR or hospital records (I, II, IV).

4.3.2 Confounding variables

The following confounding variables were gathered from two different questionnaires, one completed by the parents during pregnancy or soon after birth and the other by the subjects at the age of 14.

Pregnancy and antenatal data (II, III, IV)

Pregnancy and antenatal data of the cohort members’ mothers was collected by the antenatal clinics on a questionnaire. Efforts were made to obtain this information at the 24th to 28th gestational weeks, but whenever this failed, the questionnaire was completed later in the pregnancy or after the delivery, which was the case for 10.1% of the mothers. Information on the child’s (cohort member) gender, date of birth, birth weight, death, illness, etc., was collected during routine visits to the antenatal clinics or hospitals, which entered it on their files. Of this data, we used the child’s place of birth, the mother’s civil status, and the father’s occupation as confounding factors in the studies II, III, and IV.

We used the following information drawn from the antenatal data: Fathers’ occupations were divided into four categories: 1) academic, including all university level education (5 years), 2) skilled workers, including vocational education (3 years), 3) unskilled workers, including persons without professional education and students, and 4) farmers. Family background was divided into two categories: 1) one-parent family, including all children having been born to a single mother, 2) two-parent family, including families with both a mother and a father at the time of birth. Place of birth was divided into 1) urban and 2) rural.
Health study of adolescents at the age of 14 (III, IV)

The health study of the adolescents at the age of 14 was conducted as a postal questionnaire survey. Data of growth and health, living habits, school performance, and family conditions were included. The children’s addresses and mortality data were obtained from the National Population Centre of Finland and the Central Statistical Office of Finland by sending the subjects’ identity codes to these authorities. A re-inquiry was sent to the non-responding adolescents. The addresses were not available for 14 subjects living abroad. We used the following information: fathers’ occupation, family background, and place of residence. School performance was recorded as 1) “basic” if the child was at or above his/her age-appropriate level and 2) “less than basic” if the child had attended a special school for disabled children or was on a lower than the age-appropriate class level.

4.4 Statistical methods

Fisher's exact test and Pearson’s $\chi^2$ test were used as appropriate in all studies. The incidence and mortality rates of TBI were calculated as the number of TBI cases divided by the person time for the entire cohort separately for men and women (I) as well as in each exposure category (drinking pattern and frequency) (IV). The cumulative incidence curves of TBI (I, IV) and mortality due to TBI in the cohort (I) were calculated up to the last follow-up by using the Kaplan-Meier product limit method, and the log-rank test was used to determine the statistical significance between the groups with different drinking patterns (IV). The probabilities for sustaining a recurrent TBI during the follow-up time were compared between those with and without alcohol involvement using the Kaplan-Meier survival curves and the differences between the groups being tested by a two-tailed log-rank test (II).

The Cox proportional-hazards model was used to identify factors predicting the recurrence of TBI (II) and the risk of TBI in childhood (III) and later in young adulthood (IV). All the results were expressed as hazard ratios (HR) with 95% confidence intervals. The following variables were used to produce the adjusted relative risks: severity and external cause of injury (II), relation of first injury to alcohol (II), family background (II, III, IV), place of birth (II, III, IV), father’s occupation (III, IV), family background (II, III, IV), place of residence (III, IV), family history of alcohol misuse (III) and gender (II, III, IV). Log-binomial
regression analysis was used to analyze the association between brain injury and drinking to intoxication at the age of 14 years after adjustment for confounding factors (III). All statistical tests were 2-tailed, and p < 0.05 indicated statistical significance. All analyses were performed using SPSS, versions 12.0–14.0 and Stata software, version 7 (Stata Corp., College Station, Texas) for Windows.
5 Results

5.1 Incidence of TBI (I)

A total of 457 subjects (304 men) out of 12,058 (3.8%) sustained TBI during 1966–2000. Fifty-five subjects (0.45%) succumbed to the injury. All but one of the deaths resulted from TBI, the single exception being a patient who died from liver rupture even though she also had brain contusion. As expected, mild injuries were most frequent (78.1%). Mild TBIs comprised concussions and skull fractures, whereas moderate-to-severe brain injuries included patients with brain contusions, intracranial hematomas, and diffuse traumatic axonal injuries (9.8%). Fatal injuries comprised 12.1% of all brain injuries. The baseline characteristics of these subjects are presented in Table 4.

Table 4. Baseline characteristics of the study population with TBI.

<table>
<thead>
<tr>
<th>Gender</th>
<th>TBI</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discharge diagnosis</td>
<td></td>
<td>n = 304 (%)</td>
<td>n = 153 (%)</td>
<td>n = 457 (%)</td>
</tr>
<tr>
<td>Mild TBI*</td>
<td></td>
<td>230 (75.6)</td>
<td>127 (83.0)</td>
<td>357 (78.1)</td>
</tr>
<tr>
<td>Moderate-to-severe TBI†</td>
<td></td>
<td>33 (10.9)</td>
<td>12 (7.8)</td>
<td>45 (9.8)</td>
</tr>
<tr>
<td>Fatal TBI</td>
<td></td>
<td>41 (13.5)</td>
<td>14 (9.2)</td>
<td>55 (12.1)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>304 (100)</td>
<td>153 (100)</td>
<td>457 (100)</td>
</tr>
<tr>
<td>External cause of injury</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor vehicle accidents</td>
<td></td>
<td>92 (39.8)</td>
<td>44 (46.3)</td>
<td>136 (41.7)</td>
</tr>
<tr>
<td>Fall accidents</td>
<td></td>
<td>55 (23.8)</td>
<td>29 (30.5)</td>
<td>84 (25.8)</td>
</tr>
<tr>
<td>Intentional injuries‡**</td>
<td></td>
<td>40 (17.4)</td>
<td>9 (9.5)</td>
<td>49 (15.0)</td>
</tr>
<tr>
<td>Sport accidents</td>
<td></td>
<td>30 (13.0)</td>
<td>11 (11.6)</td>
<td>41 (12.6)</td>
</tr>
<tr>
<td>Occupational &amp; other</td>
<td></td>
<td>14 (6.0)</td>
<td>2 (2.1)</td>
<td>16 (4.9)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>231 (100)</td>
<td>95 (100)</td>
<td>326 (100)</td>
</tr>
<tr>
<td>Alcohol drinking before injury</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes**</td>
<td></td>
<td>36 (11.8)</td>
<td>7 (4.6)</td>
<td>43 (9.4)</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td>209 (68.8)</td>
<td>122 (79.7)</td>
<td>331 (72.4)</td>
</tr>
<tr>
<td>Missing information</td>
<td></td>
<td>59 (19.4)</td>
<td>24 (15.7)</td>
<td>83 (18.2)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>304 (100)</td>
<td>153 (100)</td>
<td>457 (100)</td>
</tr>
</tbody>
</table>

* Discharge diagnosis was concussion or skull fracture without intracranial injury
† Discharge diagnosis was brain contusion, intracranial hematoma with or without skull fracture, or diffuse traumatic axonal injury
‡ Suicides and homicides
** p < 0.01 between men and women
The incidence of TBI in the whole study population was 118/100 000 PY (95% CI 108–130). Men had an incidence of 153/100 000 PY (95% CI 137–171), whereas women displayed a much lower incidence of 82/100 000 PY (95% CI 70–96). The pediatric incidence of TBI (children under the age of 16 years) was 130/100 000 PY (95% CI 115–148), with boys having a higher incidence (155/100 000 PY, 95% CI 132–183) than girls (104/100 000 PY, 95% CI 85–128). Up to the age of 10 years, the occurrence of TBI did not differ by gender, and the injuries were usually mild. After the age of 10 years, however, boys started to sustain brain injuries more frequently than girls (Fig 2). Young men aged 18 to 23 years had more often (32%) moderate-to-severe and fatal injuries than women (11%). After the age of 25 years, the incidence of TBI decreased in both genders. Infants and adults aged 32–34 years seemed to sustain brain injury least often. Assuming that all those with mild TBI recovered without permanent sequelae, and that all those with moderate-to-severe TBI had permanent sequelae, an estimated prevalence (subjects with permanent sequelae) of TBI at the age of 34 years was 269/100 000 PY.
5.2 Mortality from TBI (I)

Mortality from TBI in the whole study population was 14/100 000 PY (95% CI 11–18). Cumulative mortality is shown in Figure 2. Proportionate mortality (i.e. the proportion of TBI mortality out of total mortality in the cohort) was 12%. The figure was almost 7-fold among young adults compared to children and 10- to 3-fold among men and women aged 16–34 years compared to boys and girls ≤15 years. Fatal injuries were especially common in subjects aged 16–34 years. In this age group, 45 subjects succumbed to brain injury. Alcohol was frequently
associated with fatal injuries (50%), particularly with suicides (78%). TBI mortality and proportionate mortality ratios by age and gender are presented in Table 5.
### Table 5. TBI deaths, mortality and proportionate mortality ratio by age and gender.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TBI/all</td>
<td>Mortality per 100 000/PY (95% CI)</td>
<td>PMR*</td>
</tr>
<tr>
<td>0–15</td>
<td>4/156</td>
<td>4 (2–12)</td>
<td>2.6</td>
</tr>
<tr>
<td>16–34</td>
<td>37/135</td>
<td>19 (14–27)</td>
<td>27.4</td>
</tr>
<tr>
<td>0–34</td>
<td>41/291</td>
<td>21 (15–28)</td>
<td>14.1</td>
</tr>
</tbody>
</table>

*PMR = proportionate mortality ratio = percent of TBI deaths out of all deaths in the cohort.

PY = Person-years, CI = confidence interval
5.3 External causes of injuries (I, II, IV)

The most frequent external causes of injuries in the whole study population were traffic accidents, followed by falls, intentional injuries, and sport injuries (Table 4). In children aged under 16 years, traffic injuries (40%), falls (37%), and sport injuries (16%) accounted for the majority of brain injuries. No significant gender differences in the external causes of pediatric injuries were seen. In young adults (16 to 34 years old), traffic injuries (44%) were the most frequent external cause of injury, followed by intentional injuries (25%), falls (16%), and sport injuries (9%). Intentional injuries were significantly (p < 0.01) more frequent among men than women, and almost 50% of them were fatal. The external cause of fatal injuries was known in 38 of the cases. Suicide was the most frequent cause (58%) of death, but traffic accidents (29%) and other causes (13%) occurred as well. Suicides were committed by 21 men (all with firearms) and 1 woman (situation unknown).

5.4 TBI and alcohol

5.4.1 Alcohol involvement at injury (I, II, III, IV)

According to the FHDR (Finnish Hospital Discharge Register) and/or hospital records, at least 43/457 (9%) injuries occurred under the influence of alcohol (2 in children, 41 in young adults). Intentional injuries (57%), but not falls (14%) and traffic accidents (7%), were frequently associated with alcohol. Men had been drinking alcohol at the time of injury significantly more often than women (Table 4). Unfortunately, we did not have alcohol data available for 83 (18%) patients because this information was frequently lacking in the hospital records.

5.4.2 Alcohol drinking and recurrent TBI (II)

Of the 236 TBI patients who had survived the first-ever TBI after the age of 11 years, 21 sustained a recurrent TBI, and three of them also suffered a second recurrent TBI during the follow-up period. The Cox proportional-hazards model indicated that an alcohol-related first injury (RR 4.41, 95% CI 1.53–12.70) and an urban place of birth (RR 4.39, 95% CI 1.68–11.48) were significant independent predictors of recurrent TBI. A significant positive correlation between the first
and recurrent TBIs with respect to alcohol involvement ($rs = 0.61$, $p = 0.003$) was also observed.

During the follow-up time, nine out of 36 subjects (25%) with and 12 out of 200 (6%) without an alcohol-related first TBI experienced a recurrence. Thus, the cumulative incidence proportion (%) of recurrent TBI was 4 times higher for those with alcohol-related first injury. The Kaplan-Meier survival curves in Figure 3 show much lower probabilities for avoiding a repeated TBI among patients with alcohol involvement than among those without, especially after the first 5 years since the primary TBI.

**Fig. 3.** Kaplan-Meier curves showing the proportions of patients remaining without TBI recurrence according to alcohol involvement in the first injury.
5.4.3 Parental alcohol misuse as a predictor for TBI in childhood (III)

Diagnoses indicative of alcohol misuse were recorded for 556 parents of the whole cohort population during the period from 1966 to 1980. TBI children had significantly (p < 0.001) more frequently parents with alcohol misuse compared to control children (9.7% vs. 5.0%). By using the Cox proportional hazards model and adjusting for place of residence, family background, and father’s occupation at birth, we found parental alcohol misuse (RR 1.99, CI 1.19–3.33) and male gender (RR 1.53, CI 1.12–2.08) to be significant (p < 0.05) risk factors for the occurrence of TBI in childhood (Table 6).

Table 6. Factors predictive of a risk of brain injury in childhood.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR (95% CI)</td>
<td>p</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girls</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Boys</td>
<td>1.53 (1.13–2.08)</td>
<td>0.006</td>
</tr>
<tr>
<td>Parental alcohol misuse *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Yes</td>
<td>1.90 (1.13–3.17)</td>
<td>0.015</td>
</tr>
<tr>
<td>Fathers’ occupation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Academic</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Skilled worker</td>
<td>1.03 (0.71–1.48)</td>
<td>0.198</td>
</tr>
<tr>
<td>Unskilled worker</td>
<td>2.45 (0.78–7.72)</td>
<td>0.893</td>
</tr>
<tr>
<td>Farmers</td>
<td>0.73 (0.47–1.14)</td>
<td>0.127</td>
</tr>
<tr>
<td>Family background</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two-parent family</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>One-parent family</td>
<td>1.05 (0.50–2.23)</td>
<td>0.905</td>
</tr>
<tr>
<td>Place of residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Urban</td>
<td>1.13 (0.83–1.54)</td>
<td>0.434</td>
</tr>
</tbody>
</table>

*Recorded for the period from 1966 to 1980.

RR = Risk Ratio
CI = confidence interval

5.4.4 Drinking habits of TBI subjects injured as children (III)

Drinking to intoxication, reported at the age of 14 years, was a more common habit among the TBI subjects (34%) than the controls (25%). The proportion of those who had never been drunk was higher among the controls than the TBI subjects (75% vs. 66%), whereas having been drunk at least once or more often
was more frequent in the TBI group. TBI girls reported more frequently drinking to intoxication than control girls. TBI boys also reported more frequently drinking to intoxication than control boys, but the difference was not statistically significant. The frequency of drinking occasions did not significantly differ between the groups. Frequent drinking (once a month or more often) was reported by 3% of TBI subjects and 2% of controls. According to the hospital records, only two TBI subjects were alcohol-intoxicated when injured. Drinking to intoxication at the age of 14 years significantly associated with parental alcohol misuse (RR 1.62, CI 1.34–1.96), belonging to a one-parent family (RR 1.80, CI 1.61–2.02), and mild TBI (RR 1.67, CI 1.20–2.33) (Table 7). There was a significant correlation between parental alcohol misuse and drinking to intoxication at the age of 14 years among both those with TBI ($r_s = 0.275$, $p < 0.001$) and those without TBI ($r_s = 0.064$, $p < 0.001$). In fact, separate analyses (data not shown) of TBI subjects and controls showed 7.5- and 1.6-fold risks for drinking to intoxication for subjects with a background of parental alcohol misuse.

Table 7. Factors associating with drinking to intoxication at the age of 14.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate</th>
<th></th>
<th>Multivariate</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR (95% CI)</td>
<td>p</td>
<td>RR (95% CI)</td>
<td>p</td>
</tr>
<tr>
<td>Brain injury</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Mild</td>
<td>1.75 (1.27–2.42)</td>
<td>&lt; 0.001</td>
<td>1.67 (1.20–2.33)</td>
<td>0.002</td>
</tr>
<tr>
<td>Moderate/Severe</td>
<td>0.61 (0.13–2.78)</td>
<td>0.517</td>
<td>0.62 (0.14–2.87)</td>
<td>0.542</td>
</tr>
<tr>
<td>Fathers’ occupation*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Academic</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Farmer</td>
<td>0.58 (0.49–0.69)</td>
<td>&lt; 0.001</td>
<td>0.68 (0.57–0.81)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Skilled worker</td>
<td>0.99 (0.88–1.10)</td>
<td>0.800</td>
<td>0.99 (0.89–1.11)</td>
<td>0.904</td>
</tr>
<tr>
<td>Unskilled worker</td>
<td>1.12 (0.99–1.26)</td>
<td>0.069</td>
<td>1.01 (0.89–1.15)</td>
<td>0.844</td>
</tr>
<tr>
<td>Family background*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two-parent family</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>One-parent family</td>
<td>1.95 (1.75–2.16)</td>
<td>&lt; 0.001</td>
<td>1.80 (1.61–2.02)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Place of residence*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Urban</td>
<td>1.31 (1.20–1.44)</td>
<td>&lt; 0.001</td>
<td>1.20 (1.10–1.32)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>School performance*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Special school</td>
<td>0.63 (0.49–0.80)</td>
<td>&lt; 0.001</td>
<td>0.53 (0.41–0.69)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girls</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Boys</td>
<td>1.00 (0.92–1.10)</td>
<td>0.945</td>
<td>1.04 (0.95–1.13)</td>
<td>0.452</td>
</tr>
<tr>
<td>Parental alcohol misuse</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Yes</td>
<td>1.92 (1.60–2.31)</td>
<td>&lt; 0.001</td>
<td>1.62 (1.34–1.96)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

*Recorded at the age of 14 years and analyzed by a log-binomial regression model
5.4.5 Alcohol drinking as a risk factor for TBI later in life (IV)

The habit of frequent drinking and drinking to intoxication at the age of 14 years or before increased the risk for TBI during adolescence and young adulthood (Figure 4). Information about drinking habits was obtained from 227 subjects who sustained a brain injury after the age of 14 years (and before they were 34 years old). A total of 2.4% of the children reported frequent drinking. Having been drunk before the age of 14 years was more prevalent among the brain-injured boys, whereas the brain-injured girls seemed to have been more often frequent drinkers compared to the boys and the non-injured girls before the age of 14 years. Compared with never-drinkers, those who drank alcohol once a month or more often (= frequent drinkers) or had sometimes been drunk before the age of 14 years had an increased crude relative risk of TBI during the follow-up time of 21 years (RR 2.04; 95% CI 1.06–3.93 and 1.42; 95%CI 1.08–1.88 for frequent alcohol use and drunkenness, respectively). Adjusted (for fathers’ occupation, family background, place of residence, and school performance) RRs for TBI during the 21-year follow-up were 2.21 (CI 1.14–4.29) and 1.35 (CI 1.01–1.79), respectively.
Fig. 4. The TBI incidence rate ratios after the age of 14 for those who had been drunk and those who reported that they had not been drunk in their childhood.

Independent risk factors for TBI occurring after the age of 14 years are presented in Table 8. We used two different models to study this issue by taking into account confounding variables recorded at birth (model 1) or at the age of 14 years (model 2). In both models, frequent drinking and drinking to intoxication were significant predictors for TBI later in life. In addition, male gender and belonging to a one-parent family (only at the age of 14 years) were significant predictors for TBI later on (Table 8).
Table 8. Independent predictors for TBI occurring after the age of 14 years.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td><strong>Drinking status</strong></td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Never</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infrequent drinker</td>
<td>1.17 (0.88–1.55)</td>
<td>1.14 (0.87–1.51)</td>
</tr>
<tr>
<td>Frequent drinker</td>
<td>2.23 (1.15–4.32)</td>
<td>2.21 (1.14–4.29)</td>
</tr>
<tr>
<td><strong>Drunkenness</strong></td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.38 (1.04–1.84)</td>
<td>1.35 (1.01–1.79)</td>
</tr>
<tr>
<td><strong>Father’s occupation</strong></td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Farmer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unskilled worker</td>
<td>1.05 (0.70–1.57)</td>
<td>0.99 (0.63–1.57)</td>
</tr>
<tr>
<td>Skilled worker</td>
<td>1.03 (0.69–1.53)</td>
<td>0.64 (0.41–1.01)</td>
</tr>
<tr>
<td>Academic</td>
<td>0.81 (0.52–1.25)</td>
<td>0.79 (0.50–1.25)</td>
</tr>
<tr>
<td><strong>Family background</strong></td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Two-parent family</td>
<td></td>
<td></td>
</tr>
<tr>
<td>One-parent family</td>
<td>1.09 (0.55–1.25)</td>
<td>1.60 (1.17–2.19)</td>
</tr>
<tr>
<td><strong>Place of residence</strong></td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Urban</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>1.08 (0.80–1.47)</td>
<td>0.95 (0.72–1.25)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Girls</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>2.62 (1.95–3.51)</td>
<td>2.61 (1.95–3.50)</td>
</tr>
</tbody>
</table>

Father’s occupation, family background, and place of residence at birth (model 1) and at the age of 14 (model 2).

1 If the father’s occupational status was not known, the mother’s respective information was used.
6 Discussion

6.1 Epidemiology of traumatic brain injury

6.1.1 Incidence, prevalence, and mortality

The annual incidence of traumatic brain injury in the whole study population of the Northern Finland 1966 Birth Cohort was 118/100 000 PY. Men had a higher annual incidence of 153/100 000 PY, whereas women had a much lower annual incidence of 82/100 000 PY. The pediatric incidence of TBI (children aged under 16 years) was 130/100 000 PY, with boys having a higher incidence than girls. Assuming that all those with mild TBI recovered without permanent sequelae, and that all those with moderate-to-severe TBI had permanent sequelae, the estimated prevalence of TBI patients with permanent sequelae at the age of 34 years was 269/100 000 PY. Mortality from TBI in the whole study population was 14/100 000 PY. Fatal injuries were especially common in subjects aged 16–34 years, and alcohol was frequently associated with fatal injuries (50%), particularly with suicides (78%). Traffic accidents were the most frequent external cause of injuries in the whole study population, followed by falls, intentional injuries, and sport injuries.

The overall incidence of TBI agrees well with previous findings from a cross-sectional study of all Finnish residents injured between 1991 and 2005 (Alaranta et al. 2000, Koskinen & Alaranta 2008). The incidence of TBI in this study was somewhat lower than the incidences reported from the United States, Australia, and Central Europe. The annual incidence figure has been reported to be 200/100 000 PY in the United States, 322/100 000 PY in Southern Australia (Hillier et al. 1997), 281/100 000 PY in France (Tiret et al. 1990), and 250 /100 000 PY in Italy (Servadei et al. 2002). This variation in incidence rates is partly due to the use of different inclusion criteria in the studies. In France, fatal cases prior to hospitalization were also included (Tiret et al. 1990). In Italy, the two study areas were popular tourist areas, which may explain the higher incidence figures (Servadei et al. 2002). The Italian higher incidence rates can also be explained by the fact that all age groups were included in these studies. If older age groups are included, higher incidence rates of TBI are reported (Engberg 1995). Higher incidence rates have been reported from studies based on routine use of ICD coding compared to case records (Jennet 1996). However, some
studies report only brain contusions, hematomas and other intracranial injuries, some only include patients with loss of consciousness or post-traumatic amnesia, and yet some others include only patients with intracranial lesions on CT scan.

The annual incidence of TBI was strongly influenced by age and gender. Most studies of TBI report that boys have higher incidences than girls (Durkin et al. 1998). In this study, however, traumatic brain injuries were sustained equally often by boys and girls under the age of 11 years. Both genders showed a distinct peak at the age of 6–7 years (i.e. at the age of school entry). Thereafter, boys showed a somewhat higher incidence than girls, but with no significant differences in severity and external cause. Incidence among those aged under 16 years, i.e. pediatric incidence, was 130/100 000 PY. This figure is also lower than the average incidence (180/100 000 PY) calculated from nine studies performed in the USA in 1980–1989 (Kraus 1986). The incidence figures of children aged 0–14 years from Iceland are similar to those reported from the the United States: 170/100 000 PY (Arnarson & Halldorsson 1995).

The mortality of children aged under 16 was 6/100 000 PY, which is slightly higher than the mortality reported earlier from Sweden (2.6/100 000 PY), but similar to the corresponding figures from the United States (5.8/100 000 PY) and Spain (6.3/100 000 PY) (Emanuelsson & vonWendt 1997, Kraus et al. 1990, Vazquez-Barquero et al. 1990). Mortality varied notably by age and gender. Mortality was 10-fold among young men compared to boys, but 3-fold among young women compared to girls. Previous studies have also shown that young men have higher mortality rates than young women. A striking finding of our study was the high number of fatal TBIs due to suicides committed by young men. Both traffic accidents and injuries due to assaults have been reported as causes of death in many previous papers on brain injury in this age group, but suicides have remained a less recognized cause (Thornhill et al. 2000, Masson et al. 2001, Potenza et al. 2004). The finding about a high suicide rate is not surprising in the light of the fact that Finland had the highest suicide rate in the European Union in 1997 (Chishti et al. 2003). Alcohol-related accidental and violent deaths show a decreasing trend in 1991–1995 in Finland, particularly among men (Herttua et al. 2007), whereas deaths due to alcohol-related liver diseases increased. This decreasing trend in alcohol-related deaths was connected to a severe economical depression in Finland those years (Herttua et al. 2007). However, in 2004–2006 the alcohol related deaths increased 22% in Finland (Päihdetilastollinen vuosikirja 2007) and in 2006 about 1000 people succumbed due to violence and accidents under the influence of alcohol in Finland.
6.1.2 External causes

Among young adults (16 to 34 years old), the most frequent external causes of injuries were traffic accidents (44%), followed by intentional injuries (25%), falls (16%), and sport injuries (9%). This is in line with previous studies and is explained by the fact that the study population comprised only young subjects. The only exception compared to previous studies was the high incidence of intentional injuries among 16- to 34-year-old men in our study (25%). This is a markedly higher percentage than most of those previously reported and probably due to the fact that Finland has the highest suicide rate in Europe (Chishti et al. 2003). Overall, in this age group, men had more severe injuries than women, which is also due to the high frequency of intentional injuries among men. Intentional injuries were significantly (p < 0.01) more frequent among men, and almost 50% of them were fatal. In Glasgow intentional injuries comprised 28% of all TBI external causes (Thornhill et al. 2000), whereas in Sweden 15% of all external causes has been reported to be intentional injuries (Kleiven et al. 2003) and in Italy (Servadei 2002), France (Masson et al. 2001) and Norway (Ingebritsen et al. 1998) the corresponding figure has been reported to be less than 10%. Traffic accidents are usually also associated with more severe injuries. Unfortunately, we had no situational data about these accidents, but other authors have pointed out the devastating role of the risky driving habits of young men, particularly those who are newly licensed (Laapotti & Keskinen 1998, Ferguson 2003). Among children aged under 16 years, traffic injuries (40%), falls (37%), and sport injuries (16%) accounted for the majority of brain injuries. The corresponding figures in a study from San Diego County (California, USA) were 29%, 35%, and 24% (Kraus 1986). In our study, intentional injuries were rare in this age group (4%). The injuries of children were usually mild, and no significant gender differences in severity or external cause were seen.

6.1.3 Alcohol involvement at injury

According to the FHDR and/or hospital records, at least 43/457 (9%) injuries occurred under the influence of alcohol (2 in children, 41 in young adults). Men had been drinking alcohol at the time of the injury significantly more often than women. The figures are low, but it should be borne in mind that the analysis also included children. In the older age groups, intentional injuries (57%) associated
frequently with alcohol, but falls (14%) and traffic accidents (7%) associated less frequently with alcohol drinking.

It has been reported that approximately every second head injury takes place under the influence of alcohol, and only two thirds occur in addicted drinkers (Kolakowsky-Hayner et al. 1999, Brismar et al. 1983, Honkanen & Visuri 1976). In Finland, alcohol drinking is closely associated with adolescent violence. The male/female ratio for violent incidents among Finnish adolescents is almost 2:1 (Mattila et al. 2005). The numbers of fights, assaults, homicides, and suicides are probably increased by alcohol drinking. This is in line with the studies that report drunkenness to be positively associated with fighting injuries in several countries (Pickett et al. 2005). Alcohol encourages young people to engage in risk-taking behaviors. In Denmark in 1987, alcohol involvement at injury was seen in 17.7% of male and 4.6% of female motor vehicle drivers (Engberg 1995). In Finland, 49% of all male drivers’ loss-of-control accidents occurred under the influence of alcohol, whereas 7% of female drivers’ accidents involved alcohol (Laapotti & Keskinen 1998). In the United States, 41% of traffic deaths were alcohol-related in 2002 (Quinlan et al. 2005). Alcohol is also frequently involved in traffic injuries among pedestrians and cyclists (Jennet 1996).

6.2 Recurrence of TBI

In this study a relationship was found between alcohol drinking and recurrence of TBI. An alcohol-related first injury and an urban place of birth were significant independent predictors of recurrent TBI. The first TBI related to alcohol drinking was predictive of recurrent TBI, which was often similarly alcohol-related. The proportional cumulative incidence of recurrent TBI was 4 times higher for those with alcohol-related first injury, especially after the first 5 years since the first TBI.

6.2.1 Alcohol is a risk factor for TBI recurrence

Previous reports have shown that recurrent traumatic brain injuries occur in a significant portion of trauma patients, especially in specific populations, such as child abuse victims and athletes (Weber 2007). Surprisingly few reports have dealt with the recurrence of TBI in relation to hazardous alcohol consumption. Corrigan (1995) states in his review article that a history of substance abuse is associated with repeated head injuries, and an early study reported an almost
fourfold frequency of recurrent head injuries in alcoholics compared to non-alcoholic subjects (Hillbom & Holm 1986). Likewise, two subsequent studies showed that substance abusers admitted for rehabilitation were more prone to repeated TBI (Drubach et al. 1993, Wong et al. 1993). The present study, however, is the first to point to an increased likelihood of repeated head injuries in subjects who were not chronic alcoholics, but were under the influence of alcohol when sustaining their first TBI. Previous investigations have shown that the risk of injury in general is more closely related to acute than long-term exposure to alcohol (Watt et al. 2004, McLeod 1999, Vinson et al. 2003).

6.2.2 Severity of TBI and subsequent drinking

In this study the patients who have a mild-to-moderate first alcohol-related TBI seem to possess a high risk of suffering a recurrent alcohol-related TBI. Other investigators have reported that patients with more severe head injuries seem to reduce their drinking more markedly than those with less severe head injuries (Dikmen et al. 1995). In fact, drinking and alcohol-related problems have been reported to decrease substantially after a TBI (Bombardier et al. 2003). A hazardous drinking pattern usually returns to the pre-injury level soon after the injury unless preventive measures are taken (Dunn et al. 2003), and this occurs more easily among the subjects with better physical functioning (Horner et al. 2005). In study II, both the first and the subsequent TBI, if alcohol-related, were usually mild, and the patients were not chronic alcoholics. Such patients provide an easy-to-access and important group for immediate preventive measures.

6.3 Predictors for TBI during childhood

Both parental alcohol misuse and male gender caused an almost two-fold risk for the occurrence of TBI during childhood. The parents of the TBI subjects showed significantly more often alcohol misuse than the parents of the control subjects. Separate analyses of the TBI subjects and controls showed 7.5- and 1.6-fold risks for drinking to intoxication for the subjects with a background of parental alcohol misuse.
6.3.1 Effect of gender

Male gender appeared to be a risk factor for traumatic brain injury. Up to the age of 10 years, the occurrence of TBI did not differ by gender. After the age of 10 years, however, boys started to sustain brain injuries more frequently than girls. This is in line with the research results from Norway (Ingebritsen 1998), whereas Alaranta et al. (2000) found the peak occurrence of TBI among boys under the age of ten years. Young men aged 18 to 23 years had more often moderate-to-severe and fatal injuries than women. The higher TBI incidence of men can be explained by the more frequent occurrence of violence among men. Deaths associated with head injury have been found to be three times more frequent among men than women, especially in age group of 25–34 years (Sosin et al. 1989). The risk of firearm accidents leading to brain injury has been reported to be almost 6-fold and the risk of motor vehicle accidents almost 3-fold among men compared to women (Sosin et al. 1989). Wagner et al. (2000) reported that, in the United States, 73% of intentional brain injuries occurred among men in 1994–1998. Wong et al. (1993) reported that TBI men have a history of alcohol misuse before injury more often than TBI women, whereas TBI women have less often alcohol-related injuries. After the age of 25, the incidence of TBI decreased in both genders.

6.3.2 Effect of parental alcohol misuse

Alcohol drinking did not cause TBI in childhood in this cohort. Seventy-three per cent of the TBI subjects sustained their injury while ≤10 years old. Those who were intoxicated when injured were > 10 years old. However, parental alcohol misuse predicted the occurrence of TBI before the age of 14. Parental alcoholism may be associated with physical abuse or neglect of children, both of which conditions expose children to a risk of injury (Widom & Hiller-Sturmhöfe 2001, Villalba-Cota 2004, Rivara 1998). Violence is a frequent cause of injuries in families with alcohol problems (Crandall et al. 2006 & Hanson et al. 2006), and head injury is the leading cause of death in abused children under 2 years of age (Rubin et al. 2003). Children of mothers classified as problem drinkers have been reported to have more than twice the average risk of injury (Bijur et al. 1992). Unfortunately, we did not have any situational data regarding violent parental behaviour in relation to the traumas. Therefore, we do not know how often parents were responsible for the injuries leading to TBI in our cohort. It is also
well known that child abuse is very difficult to certify, and not all abused children are seen at hospitals.

6.4 Alcohol drinking and TBI during adolescence and early adulthood

Adolescents who had sustained TBI during childhood reported significantly more often drinking to intoxication at the age of 14 years than those without TBI. Drinking to intoxication among such adolescents seemed to associate with parental alcohol misuse, belonging to a one-parent family, and mild but not severe TBI. The drinking patterns differed slightly between the boys and the girls who had sustained TBI, the girls having been more often frequent drinkers compared to the boys, who reported more often drunkenness. On the other hand, alcohol drinking before the age of 14 years was a significant and independent risk factor for TBI later in life. Both frequent drinking and drunkenness before the age of 14 years seemed to increase this risk. Gender did not have any significant influence on the habit of drinking to intoxication. Another factor that seemed to increase the risk of TBI was a single-parent family background at the age of 14 years.

6.4.1 Alcohol drinking after TBI sustained during childhood

Reports of alcohol drinking by TBI subjects who have been injured as children are lacking. In this study, most TBI subjects were not intoxicated by alcohol when injured. In adolescence, however, they reported drinking to intoxication significantly more frequently than the controls. Other studies have shown a transient decrease of alcohol drinking after TBI, but these studies include adults and not children (Kreutzer et al. 1996, Dunn et al. 2003, Dikmen et al. 1995).

The effects of TBI on children have traditionally been regarded as less serious than those of similar injuries sustained during adulthood. This model of thinking may also explain the neglect of certain problems of TBI children, such as their poor social functioning, which includes a harmful alcohol drinking pattern. Self-esteem and adaptive behavior have been reported to be significantly lower among TBI children than their healthy counterparts, and loneliness has been reported more frequently among TBI children (Andrews et al. 1998). These factors can eventually be associated with problem drinking later in life among those children in our cohort who sustained TBI as a child.
6.4.2 Drinking habits during childhood predict TBI later in life

Hazardous drinking habits before the age of 14 years significantly increased the risk for TBI in adolescence and young adulthood. Alcohol use nowadays begins earlier than ever. It has been reported that even children under the age of 12 drink alcohol (Donovan 2007). Adolescents’ alcohol use has been studied for a long time in Finland. In 1981, among 14-year-olds, monthly drunkenness was reported by 13% of boys and 6% of girls (Lintonen et al. 2000). In the 1990s, monthly alcohol use continued to increase among 14-year-olds and 16-year-old girls. By now, girls have reached and exceeded the drunkenness figures of boys. A recent study from Finland showed that 14-year-old girls drink to be really drunk at least once a month, i.e. even more often than 14-year-old boys, as 13% of girls and 7% of boys reported heavy drunkenness every month (Lamminpää 2004). In the United States, a total of 30.6% of adolescents reported drinking until drunkenness in 2003 (Centers for Disease Control and Prevention 2004), and there is a trend showing that even girls and young women do so (Pritchard & Cox 2007). This study revealed the alarming finding of the frequent drinking habit of the 14-year-old girls who sustained TBI in early adulthood. Although drunkenness predicted TBI in boys, it may also predict it among girls. It is likely that girls also engage in drinking alcohol to be drunk, although they reported it less often in our survey. Accordingly, special attention should be paid to adolescent girls because heavy drinking is associated with more severe psychosocial dysfunction (school problems, poor social skills) among girls than boys (Laukkanen et al. 2001).

6.4.3 Role of other types of risky behavior

Alcohol misuse is known to be associated with high-risk activities such as violence and reckless driving (Quinlan et al. 2005). Alcohol drinking to the point of drunkenness is especially harmful for adolescents because they are more inclined toward risky behaviors and risky decision-making than adults. On the other hand, earlier studies have shown that risk-taking personality is associated with excessive alcohol drinking (Kuntche et al. 2004) and risk of injuries (Kelly et al. 2005). Early onset of drinking increases the risk for unintentional injury involvement after drinking (Hingson et al. 2000). A case series from our hospital showed that binge drinking is a major risk factor for head trauma, assaults, falls, and biking accidents, which are the most typical causes of injury in people aged
It is obvious that children under the age of 14 years drink alcohol to be drunk and thereby engage in risky behaviours.

### 6.4.4 Role of psychosocial factors

In this study, the children of one-parent families reported drinking to intoxication more often than the children of two-parent families. The findings also suggest that belonging to a single-parent family in adolescence does have an impact on the risk of sustaining brain injury later on. Family problems have been associated with excessive alcohol drinking among children and adolescents. Broken family has been found to be an underlying factor in about 45% of the cases of adolescents’ heavy drinking (Lamminpää & Vilska 1990). In Finland, the risk of hazardous alcohol drinking among teenagers who belong to a broken family has been reported to be 10 to 20% compared to those who have a standard family (Isohanni et al. 1994). However, a Swedish study revealed no association between binge drinking and single-parent family background among adolescents aged 12–18 years (Lundborg 2002). Less has been written about brain injuries and belonging to single-parent family. One study reported that, compared to controls, TBI children more often belong to a single-parent family (Klonoff 1971), and this finding is in line with our study result.

Many of the head-injured subjects are not dependent drinkers, and harmful alcohol consumption also includes occasional drinking until drunkenness, i.e. leisure time and/or weekend drinking. It is well known that injuries do not happen only to alcohol-addicted persons but also to hazardous drinkers. This holds particularly for teenagers and young adults. Alcohol intoxications of teenagers are treated in Finnish hospitals quite frequently. The frequency of subjects aged 10–15 years amounted to 39.0/100 000 PY (Lamminpää 2004). Consumption of alcoholic beverages at the age of 15 years has been reported to increase the risk of drinking alcohol weekly at the age of 19 years (Andersen et al. 2003). Accordingly, young teenagers’ heavy alcohol drinking is not just a passing phenomenon. This phenomenon has been also acknowledged in Finland. Heavy drinking is likely to continue among both men and women in adulthood if drinking is started early in adolescence. Socio-emotional behavior or school performance at the age of 8 years did not predict the age of onset of drinking (Pitkänen et al. 2005).
6.5 Strengths and weaknesses of the study

The strength of this study is the relatively large, unselected birth cohort with a homogeneous ethnic background and a long follow-up period. The cohort covers approximately 96% of all births in that area during 1966. The database of the psychosocial and family characteristics of the cohort members at birth is almost complete, and a large proportion of all cohort members returned the 14-HSAQ questionnaire. The use of general hospital discharge registers as the database for epidemiological studies of brain injuries has been criticized. However, having more than one year’s cross-sectional data makes the results more reliable (Alaranta et al. 2000). Although the NHDR was used, it was possible to confirm the majority of the diagnoses and about 70% of the external causes from the hospital records. The follow-up period was long (from 1966 to 2000), and GCS was recorded irregularly or not at all in Finnish hospitals during the 1960’s and 1970’s. Accordingly, GCS scores were not available from all the subjects, and therefore the hospital discharge diagnoses were used to describe the severity of brain injury. It is possible that especially many concussion patients are missed, because they are not recorded in hospital registers. On the other hand, we should also remember that the GCS is often not applicable to young children or cannot be computed reliably because of the patients’ condition or the circumstances surrounding resuscitation efforts (Cuff et al. 2007). There can also be a problem when ICD-9 codes are used, this coding system appear to be inaccurate in the identification of mild TBI patients (Bazarian et al. 2006). Unfortunately, however, this coding system was the only one available at the time of the study period.

In rural Ostrobothnia, which constituted the main geographical source of our study population, alcohol consumption has been fairly low compared to the other parts of Finland (Winter et al. 2002). Accordingly, these results probably underestimate the problem of alcohol drinking in relation to brain injuries in other parts of Finland, and the situation may be even more alarming in the cities of southern Finland, where alcohol consumption is higher. On the other hand, observations in this study cannot be interpreted to suggest a similar risk in countries where the culture favors moderate drinking. The practice of using postal questionnaires may also be open to criticism. However, this method has been found sufficiently reliable for epidemiological applications (Johnson & Mott 2001). One of the limitations related to the recurrence of TBI is that the series were relatively small because recurrent brain injury as a phenomenon is quite uncommon (except in sport injuries), and it could be better studied in larger series.
There are also other possible TBI risk factors that we were not able to record. Information about risk-taking behaviors (Kelly et al. 2005), different driving styles (Verschuur & Hurts 2008) or depression among suicide TBI cases (Nrugham et al. 2008) was not available. Also information about weather conditions during driving, slippery roads, biking during winter was lacking. These are all factors that can cause accidents. The missing data of alcohol intoxication at the time of index injury as well as parental alcohol misuse are certainly also limitations of this study. Most of the parental alcohol misuse cases do not come to knowledge because these people do not seek help and are not treated at hospitals.

6.6 Future perspectives

Injury prevention is one of the most important preventive challenges for health care staff. Because alcohol is involved in a variety of injuries, including TBI, there is a need for education, legislation and environmental modification. Attention should be paid to the alcohol drinking of children and adolescents who attend emergency surgical wards. Interventions are needed to prevent their alcohol drinking. Many of the brain injuries of young people could probably be avoided if there were stricter constraints on the availability of alcohol and the acceptability of alcohol drinking. Even though we did not have an opportunity to use alcohol brief interventions focused on adolescents and young adults presenting hazardous alcohol drinking in the present study, the results suggest a need for such interventions. Alcohol interventions are associated with a reduction in alcohol drinking and a reduced risk of trauma recidivism (Gentilello et al. 1999). Interventions are also needed because alcohol intoxication is a confounding factor in the treatment of especially severe TBI patients (Golan et al. 2007). Unfortunately, however, alcohol problems are not routinely addressed in trauma centers, and alcohol counselling is even rarer (Gentilello et al. 1999). In UK brief interventions have been reported to decrease alcohol consumption over the following 6 months, and reduce re-attendance at the emergency department (Crawford et al. 2004). As even occasional drinking to intoxication will increase the risk of TBI and recurrent injuries, brief interventions should be focused on adolescents and young adults presenting with an alcohol-related visit to an emergency hospital. This could reduce the medical and social burden on the community due to the frequently very high medical expenses of TBI patients’ acute care and rehabilitation.
7 Conclusions

1. The incidence of TBI, 118/100 000/person-years, was slightly higher than earlier reported in Finland. However, it varied between the genders and age groups in such a way that the peak incidence occurred at the age of 6–7 years in both genders. Subsequent peaks were observed among boys aged 10 to 13 years and among young men aged 18 to 23 years. After the age of 25 years, the incidence of TBI decreased in both genders. Mortality from TBI in the whole study population was 14/100 000 PY. The figure was almost 7-fold among young adults compared to children and 10- to 3-fold among men and women aged 16–34 years compared to boys and girls ≤15 years.

2. Recurrent brain injuries appear outside sport arenas, too, and alcohol is significantly related to the recurrence of TBI. First TBI related to alcohol drinking was predictive of recurrent TBI, which was often similarly alcohol-related.

3. Parental alcohol misuse is a predictor for TBI in childhood. The parents of TBI subjects reported significantly more often alcohol misuse than the parents of controls. The subjects who sustained mild TBI during childhood drank for intoxication before the age of 14 years more often than the adolescents without TBI.

4. The habit of frequent drinking and drinking to intoxication before the age of 14 years seem to increase the risk for TBI in adolescence and young adulthood. Having been drunk was more prevalent among the brain-injured boys, whereas the brain-injured girls seemed to have been more often frequent drinkers compared to the boys and the non-injured girls.
References


Appendix

NUORTEN TERVEYSTUTKIMUS


KASVUJA TERVEYS

6-8. Paino __________ kg
9-11. Mitattu __________ kuu 19
12-14. Pituus __________ cm
15-17. Mitattu __________ kuu 19

18. Kuulo on
   □ normaali
   □ lievästi alentunut
   □ selvästi alentunut
   □ olen kuuro

20. Näkö on
   □ normaali
   □ lasien avulla normaali
   □ alentunut
   □ olen sokea

19. Käytätkö kuulolaitetta?
   □ kyllä
   □ ei

21. Käytätkö silmälaseja?
   □ kyllä
   □ ei

22-24. Onko sinulla jokin pitkäaikaisaaras (esim. allergia, sokeritauti, astma, epilepsia, reuma tms) tai vanma (esim. loukkavika, jalkaprotoesi tms)?
Jos on niin muka!

25. Oletko käynyt lääkärin vastaanotolla (terveyskeskuksessa, sairaalan poliklinikalla, yksityislääkärillä) syyslukukauden 1980 aikana (koululääkärin huokatarkastuksia ei lasketa mukaan)?
Jos on, kuinka monta kertaa?

26-28. Jos olet käynyt, minkä vuoksi?

29. Oletko ollut sairaalassa vuodeosastolla hoitettavana syyslukukauden 1980 aikana (pelkä poliklinikka- kääntyn) merkitään edellisen kohtaan 25.1?
Jos on, kuinka monta kertaa?

30-32. Jos olet, minkä vuoksi?
### 33. Onko sinulla ollut syyslukukauden 1980 aikana yakä, nuhka tai äänenkääyttyä?

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<td>kerran</td>
<td>2</td>
<td>1-3 päivä</td>
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<td>3</td>
<td>kahdesti</td>
<td>3</td>
<td>4-10 päivä</td>
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<td>4</td>
<td>kolmesti tai useamm</td>
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<td>yli 10 päivä</td>
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### 34. Oletko ollut sairauden tai varmman vanksi pois koulusta syyslukukauden 1980 aikana yhteensä

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### HARRASTUKSET

#### 35. Kuinka uskia harrastat yhtä tai useampaa urheilulajia kouluajan ulkopuolella yhteenä?

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<td>kahdesti viikossa</td>
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<td>kerran viikossa</td>
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<td>5</td>
<td>joka toinen viikko</td>
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<td>6</td>
<td>kerran kuukausi</td>
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<td>7</td>
<td>yteensä en olenkaan</td>
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#### 36. Pääasialliset urheilulajit ovat?

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#### 37. Kuulutko johonkin urheiluseuraan?

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#### 38. Oletko saanut ioksuspalvelun urheilusuorituskesteistä?

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<td>3</td>
<td>kolmesti tai useamminkin</td>
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#### 39. Kevätluukukauden 1980 todistuksen numero voimistelussa ja urheilussa

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#### 40. Tupakoito

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<td>3</td>
<td>olen kokeillut kahdesti tai useammin</td>
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<td>5</td>
<td>poitan noin kahdesti viikossa</td>
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<td>poitan joka päivä 1-5 savuketta</td>
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<td>poitan päivittäin 6-10 savuketta</td>
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<td>8</td>
<td>poitan päivittäin yli 10 savuketta</td>
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#### 41. Alkoholin naauttiminen (olut tai muu alkoholipitoisen juoma)

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<td>olen naauttinut monta kertaa</td>
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<td>4</td>
<td>käytän kuukausittain</td>
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<td>5</td>
<td>käytän väkkojaan</td>
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72
42. Muut päihteet (esim. timmeri, haumaavat lääkkeet)

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43. Oletko ollut alkoholin aiheuttamassa huma-

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<td>kerran lievästi päihittyyn</td>
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KOULUNKAYNTI

44. Monenellako luokalla olet nyt? |

45. Koulu nimi ____________________________

46. Montako vuotta täsit sinä vuonna aloitet kuolen?

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47. Oletko jäänyt joskus luokalle?

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48-49. Mikä oli kevätodistuksesi keskiarvo 1980 lukuvuonna?

50-51. kaikissa aincissa ____________? (ellet muista tarkoin kirjoita eteen: ns: esim. m:n 6.5)

PERHE

52-53. Montako osta lasten perhessoj ollon ollut kaikkiaan? ________________ Listaa

54-55. Asuuuko joku lapsista jo poissa kodista? Moniko? ________________

(ellei asu merkitse –)

56-57. Onko joku lapsista kuolut? Montako?

(ellei ole merkitse –)

58-59. Äiti on 1 elossa 2 kuollut 3 elää, muttei asu kotona

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60. Äiti

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<td>1</td>
<td>on kotona (koitilii)</td>
<td>2</td>
<td>on työssä kodin ulkopuolella (merkitse tähän rasti myös jos äidillä on uus työ esiin, uus kampaama mikä ei ole teidän asunnossa)</td>
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61. Äidin nykyinen ammatti (jos äidillä on ammatti, kerro se vaikkei hän olisi työssä)

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65. Isän nykyinen ammatti

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66. Isän tupakuisto

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Jos haluat antaa lisätietoja jostaan asusta, kirjoita ne tähän.

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/ 1981

allekirjoitus

KUUMAT VASTAUKSISTASI. POSTITA LOMAKE OHEISTA KIRJEKUORTA KÄYTTÄEN.
Original publications

This thesis is based on the following publications, which are referred to in the text by their Roman numerals I–IV:


Reprinted with permission from Karger (I), Taylor & Francis Group (III) and Elsevier (IV).

Original publications are not included in the electronic version of the dissertation.
955. Löfgren, Eeva (2007) Effects of epilepsy and antiepileptic medication on reproductive function
959. Papponen, Hinni (2008) The muscle specific chloride channel ClC-1 and myotonia congenita in Northern Finland
962. Dunder, Teija (2008) Environment and atopy and asthma in childhood. The effect of dietary fats, common infections and asthma treatment practises on morbidity rates
964. Rysä, Jaana (2008) Gene expression profiling in experimental models of cardiac load
967. Huilaja, Laura (2008) Collagen XVII and pathomechanisms of junctional epidermolysis bullosa and gestational pemphigoid
969. Junetii, Hanna (2008) Association of respiratory syncyial virus infection with asthma and atopic allergy
Satu Winqvist

ALCOHOL MISUSE IN RELATION TO TRAUMATIC BRAIN INJURY

THE NORTHERN FINLAND 1966 BIRTH COHORT STUDY