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SUBJECTIVE MEASURES OF BINGE DRINKING AND ADVERSE HEALTH OUTCOMES

SELF-REPORTED INTOXICATIONS, HANGOVERS, AND ALCOHOL-INDUCED PASS-OUTS AS INDICATORS OF AT-RISK DRINKING PATTERNS IN THE FINNISH ADULT POPULATION

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ACADEMIC DISSERTATION

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ABSTRACT

Alcohol consumption is a major cause for disease and ill health in terms of disability, morbidity, and mortality. Accumulating epidemiological evidence shows that the public health burden of alcohol-related harm cannot be accurately described merely as a function of total intake, but variability in drinking patterns needs to be taken into account as well.

Given the importance of alcohol intoxication in determining the population burden of alcohol-related harm, the purpose of this study is to validate three subjective measures of binge drinking, i.e. subjectively defined intoxications/drunkenness, hangovers, and alcohol-induced pass-outs as indicators of at-risk drinking patterns. There are no previous prospective studies, which would have assessed the relative performance of these three separate indicators in the same study.

This study used data from the *Health and Social Support Study* (HeSSup), which consists of a baseline measurement in 1998 (n=25 901), and a repeated measurement after five years in 2003 (n=19 629). The postal survey data was linked with follow-up information from the national hospital discharge register and from the national cause-of-death register. The baseline sample was stratified by gender and four age groups (aged 20–24, 30–34, 40–44, 50–54 years at baseline). Measures of alcohol use included beverage-specific average total intake, overall frequency of drinking, frequency of intoxications/drunkenness, frequency of hangovers, and frequency of alcohol-induced pass-outs. International Classification of Diseases, tenth revision (ICD-10), Finnish modification codes were used to identify cause-specific hospitalizations and deaths. The data were analysed using multivariate regression models.

The results showed that subjects at higher frequency levels of a given binge drinking measure drank on average more than subjects at lower frequency levels. Hangover frequency levels were associated with slightly higher average intake than the corresponding frequency levels of intoxication, suggesting that hangovers, on average, reflected somewhat heavier drinking than intoxications. The results showed that all three binge drinking measures were markedly more frequently reported by persons who were diagnosed with an alcohol-specific diagnosis than by persons who were not. The relative differences were largest in high-frequency binge drinking, and in binge drinking measures potentially capturing higher intensity binge drinking, i.e. in hangovers and pass-outs. For example, half (52%) of the persons who received an alcohol-specific diagnosis during the seven-year follow-up period reported experiencing an alcohol-induced pass-out at least twice during the past 12 months, whereas only one in every ten persons (9%) among those who did not receive an alcohol-specific diagnosis reported experiencing pass-outs as often. The results on the ability of each binge drinking measure to predict adverse health outcomes showed coherent and consistent relations. In predicting future alcohol-specific diagnoses, symptoms of depression, and

suboptimal subjective health, all three binge drinking measures showed positive graded relations (dose-response).

The results of this study, therefore, support the feasibility and utility of using these three measures, i.e. self-reported frequencies of subjectively defined intoxications/drunkenness, hangovers, and alcohol-induced pass-outs, as indicators of at-risk drinking patterns in epidemiological research. The results demonstrated that in terms of methodological performance, the three indicators were complementary to each other, meaning that each measure contained additional information of the risk of adverse health outcomes that was not captured by the other two indicators, or by total intake. Self-reported intoxications, alcohol-induced hangovers, and alcohol-induced pass-outs had both diagnostic and prognostic utility in identifying harmful alcohol drinking patterns at population level.

Because asking about the number of drinking occasions leading to intoxication, experiencing a hangover, or passing out as a consequence of drinking is much simpler and quicker than asking about quantities of intake of various different beverage types and beverage ethanol strengths, these results have important implications to clinical and public health practice as well. Public health messages aimed to reduce alcohol-related harm should be formulated to encourage avoiding/cutting-down drinking until intoxication in general, but highlighting the prognostic role of experiencing alcohol-induced hangovers and alcohol-induced pass-outs could potentially enhance that message further as these indicators could serve as face valid self-screening instruments.

TIIVISTELMÄ

Alkoholin kulutus on merkittävä terveysongelmien aiheuttaja, niin toimintakyvyn, sairastavuuden kuin kuolleisuudenkin näkökulmasta. Useat epidemiologiset tutkimukset osoittavat, että alkoholin aiheuttamia kansanterveydellisiä haittoja ei voida kuvata tarkasti pelkästään kokonaiskulutuksen kautta, vaan myös juomatapa tulee huomioida.

Koska humalajuominen on merkittävä riskitekijä alkoholihaitoille, tämän tutkimuksen tarkoituksena on validoida kolme subjektiivista humalajuomisen mittaria: humaltumistiheys, krapulatiheys ja sammumistiheys. Tämä on ensimmäinen seurantatutkimus, jossa on voitu samalla aineistolla selvittää näiden kolmen mittarin toimivuutta ja keskinäistä paremmuutta haitallisen juomatavan indikaattoreina.

Tässä tutkimuksessa käytettiin *Sosiaalisen tuen terveysvaikutukset* (HeSSup) – aineistoa, joka käsittää lähtötason mittauksen vuonna 1998 (n=25 901) ja toistomittauksen viiden vuoden jälkeen vuonna 2003 (n=19 629). Aineiston keräysvaiheessa aineisto stratifioitiin sukupuolen ja neljän ikäryhmän mukaan (ikäryhmät 20–24, 30–34, 40–44, 50–54 lähtötason mittauksessa). Postikyselyyn vastanneiden tiedot liitettiin rekisteritietoihin sairaalahoidoista ja kuolemansyistä. Alkoholin kulutuksen mittarit olivat keskimääräinen kokonaiskulutus juomalajeittain, juomistiheys, humaltumistiheys, krapulatiheys, ja sammumistiheys. Sairaalahoitojaksojen ja kuolemien syyt perustuivat kansainvälisen tautiluokituksen (ICD-10) suomalaiseen versioon. Aineisto analysoitiin käyttämällä regressiomalleja.

Tulokset osoittivat, että kunkin mittarin ylemmillä tiheystasoilla olevat vastaajat joivat keskimäärin enemmän kuin vastaajat alemmilla tiheystasoilla. Krapulatiheystasot olivat yhteydessä hieman korkeampiin kulutusmääriin kuin vastaavat humalatiheystasot, mikä antoi viitteitä siitä, että krapulajuomiskerroilla kulutettiin keskimäärin enemmän alkoholia kuin humalajuomiskerroilla. Tulokset osoittivat, että vastaajat jotka saivat seurannan aikana alkoholiin liittyvän diagnoosin, raportoivat selvästi enemmän kaikkia kolmea humalajuomistyyppiä, kuin vastaajat, jotka eivät saaneet vastaavaa diagnoosia. Suhteelliset erot kolmen humalajuomistyypin yleisyydessä olivat suurimmillaan ylemmillä humalajuomistiheystasoilla, ja mittareissa, jotka potentiaalisesti kuvasivat korkeampaa humalajuomisintensiteettiä (krapulat ja sammumiset). Esimerkiksi alkoholiin liittyvän diagnoosin seitsemän vuoden seuranta-aikana saaneista puolet (52%) raportoi sammuneensa vähintään kaksi kertaa kuluneen 12 kuukauden aikana, kun taas niistä, jotka eivät saaneet vastaavaa diagnoosia, vain joka kymmenes (9%) raportoi sammuneensa yhtä usein. Tulokset osoittivat, että kaikki kolme humalajuomisen mittaria ennusti alkoholihaittoja yhtenäisesti ja johdonmukaisesti. Kaikki kolme humalajuomisen mittaria ennusti alkoholiin liittyviä diagnooseja, masennuksen oireita ja huonoksi koettua terveyttä annos-vaste suhteella.

Tämän tutkimuksen tulokset tukevat itseilmoitetun subjektiivisen humalatiheyden, krapulatiheyden ja sammumistiheyden soveltuvuutta ja käyttökelpoisuutta haitallisen juomatavan osoittimina epidemiologisissa tutkimuksissa. Tulokset osoittivat, että menetelmällisestä näkökulmasta käsin nämä kolme humalajuomisen mittaria täydensivät toisiaan. Tämä tarkoittaa, että kukin mittari sisälsi lisäinformaatiota alkoholihaittojen riskistä, jota toiset mittarit -tai keskimääräinen kokonaiskulutus- eivät kyenneet selittämään. Itseilmoitettu humalatiheys, krapulatiheys ja sammumistiheys osoittivat sekä diagnostista että prognostista käyttökelpoisuutta haitallisen juomatavan tunnistamisessa väestötasolla.

Koska humaltumiseen, krapulan kokemiseen ja sammumiseen johtavien juomiskertojen lukumäärän kysyminen on huomattavasti yksinkertaisempaa ja nopeampaa kuin vaihteleviin juomalajeihin ja etanolipitoisuuksiin perustuvan kokonaiskulutuksen kysyminen, näillä tuloksilla on myös käytännön merkitystä kliiniselle ja kansanterveydelliselle työlle. Alkoholihaittojen ehkäisyyn pyrkivän kansanterveydellisen viestin tulisi kannustaa välttämään ja vähentämään humalajuomista yleensä, mutta krapulan kokemisen ja sammumisten haittoja ennustavan roolin esille tuominen voisi vahvistaa tätä viestiä entisestään, koska nämä juomatapaindikaattorit voisivat toimia ymmärrettävinä ja hyväksyttävinä itse toteutetun haitallisen juomatavan tunnistamisen keinoina.

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LIST OF ORIGINAL PUBLICATIONS

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I Paljärvi T, Suominen S, Car J, Koskenvuo M. (2013) Socioeconomic disadvantage and indicators or risky alcohol-drinking patterns. Alcohol Alcohol 48:207–14.

II Paljärvi T, Mäkelä P, Poikolainen K, Suominen S, Car J, Koskenvuo M. (2012) Subjective measures of binge drinking and alcohol-specific adverse health outcomes: a prospective cohort study. Addiction 107:323–30.

III Paljärvi T, Suominen S, Car J, Mäkelä P, Koskenvuo M. (2011) Subjective measures of binge drinking, suboptimal subjective health and alcohol-specific hospitalizations among working-aged adults: a prospective cohort study. Alcohol Alcohol 46:607–13.

IV Paljärvi T, Koskenvuo M, Poikolainen K, Kauhanen J, Sillanmäki L, Mäkelä P. (2009) Binge drinking and depressive symptoms: a 5-year population-based cohort study. Addiction 104:1168–78.

The publications are referred to in the text by their roman numerals (sub-studies I-IV). These original publications have been reproduced with the permission of the copyright holders.

ABBREVIATIONS

AHS	Acute Hangover Scale
AHSS	Alcohol Hangover Severity Scale
AUC	Area under the receiver operating characteristics curve
AUD	Alcohol use disorder
AUDIT	Alcohol Use Disorders Identification Test
BAC	Blood alcohol concentration
BAL	Blood alcohol level
BDI	Beck Depression Inventory
CI	Confidence interval
CNS	Central nervous system
CVD	Cardiovascular disease
DSM	Diagnostic and Statistical Manual of Mental Disorders
DUI	Driving under influence [of alcohol]
DWI	Driving while intoxicated
HeSSup	Health and Social Support study
HR	Hazard ratio
HSS	Hangover Symptoms Scale
ICD	International Classification of Diseases
IHD	Isheamic heart disease
LD	Lethal dose
NIAAA	National Institute on Alcohol Abuse and Alcoholism
OCVD	Other cardiovascular disease
OR	Odds ratio
ROC	Receiver operating characteristics curve
T1	Time 1 (1998)
T2	Time 2 (2003)
UM-CIDI	University of Michigan version of the Composite International Diagnostic Interview

1 INTRODUCTION

Among alcohol drinkers, the risk of alcohol-related harm generally increases with increasing levels of alcohol consumption (Room *et al.* 2005, Rehm *et al.* 2010). This dose-response relation between level of total alcohol consumption and alcohol-related harm means that heavy drinkers have a greater risk of experiencing adverse outcomes due to their drinking compared to drinkers at lower consumption levels.

Estimates of the number of heavy drinkers in Finland vary, e.g. depending on how heavy drinking is defined, but conservative estimates based on total volume of consumption suggest that the prevalence of heavy drinking is around 5–10% (Mäkelä *et al.* 2010, p.196). Despite being a small minority, heavy drinkers consume the majority of all alcohol consumed in Finland. It has been estimated that drinkers at the highest 10% of the total intake distribution consume about half, and drinkers at the highest 20% of the intake distribution consume about two-thirds of all alcohol consumed in Finland (Mäkelä *et al.* 2010, p.196).

The above would seem to suggest that, as the majority of alcohol is consumed by heavy drinkers who have the greatest risk of experiencing alcohol-related harm, much of the alcohol-related harm at the population level would come from a small group of high-risk drinkers. Empirical evidence, however, has shown that despite the fact that the relative risk of harm is typically higher among heavy drinkers, the majority of the burden of harm at the population level comes from non-heavy drinkers (Skog 1999, Rossow & Romelsjö 2006). The main explanation of this notion, sometimes referred to as prevention paradox, is merely that the group of non-heavy drinkers, which is not risk-free, is much larger than the group of heavy drinkers, and therefore it contributes more to the burden of harm in absolute numbers than heavy drinkers. The prevention paradox is to a large extent explained by drinking patterns involving infrequent heavy drinking occasions, i.e. binge drinking occasions (Poikolainen *et al.* 2007).

From a public health perspective, alcohol-related harm in Finland is thus not only a problem of a small minority of alcohol dependent and heavy drinkers, but a collective problem facing the society as a whole. Accumulating evidence shows that the public health burden of alcohol-related harm cannot be accurately described merely as a function of total intake, but variability in drinking patterns needs to be taken into account as well (Rehm *et al.* 2010). Evidence-based national alcohol policy therefore needs reliable information on the complex and multidimensional relation between alcohol use and various types of harm; within and across all consumption levels and in particular in relation to binge drinking.

Given the importance of alcohol intoxication in determining the population burden of alcohol-related harm, the purpose of this study is to validate three subjective measures of binge drinking, i.e. subjective intoxications, hangovers, and alcohol-induced pass-outs as indicators of at-risk drinking patterns.

2 BACKGROUND

2.1 ALCOHOL-RELATED ADVERSE HEALTH OUTCOMES

Alcohol consumption is a major cause for disease and ill health in terms of disability, morbidity, and mortality (Room *et al.* 2005, Parry *et al.* 2011). In Finland, alcohol has been the leading cause of death among working aged (aged 15–64 years) men and women during the past several years.

Marked population group differences exist in the contribution of alcohol to burden of disease, e.g. by gender, age, socioeconomic status, and ethnic background. These demographic factors reflect differences in the prevalence of alcohol consumption, differences in volume and patterns of drinking, but also other wider determinants of health affecting the likelihood of onset and course of disease.

Alcohol has been identified as a risk factor in over 200 disease codes in the International Classification of Diseases, tenth revision, ICD-10 (Rehm *et al.* 2010). For the majority of health outcomes, the effect of alcohol is detrimental, and the risk of adverse health outcomes increases with increasing dose of alcohol (dose-response relation). Besides adverse effects on incidence, alcohol has potentially detrimental effects on the course and severity of symptoms of numerous medical conditions. Accumulating evidence suggests that for some disease outcomes, alcohol may also have beneficial effects, such as for the incidence of coronary heart disease, diabetes mellitus, and possibly also for dementia (Rehm *et al.* 2010). The potential beneficial effects of alcohol are confined to habitual light drinkers who avoid heavy drinking occasions.

Two dimensions of alcohol exposure are important in determining the health risks resulting from alcohol consumption, namely overall volume of intake and pattern of drinking. Pattern of drinking involving heavy drinking occasions, i.e. binge drinking occasions, has been shown to better determine the risk of injury (Cherpitel 2007) and ischemic heart disease (Roerecke & Rehm 2010) than overall volume of drinking.

Diseases and conditions related to alcohol can be grouped into two categories reflecting the assumed causal role of alcohol. For the purpose of highlighting the importance of alcohol as a preventable cause of disease burden, alcohol has been included in the name of some disease categories. These medical conditions are related to alcohol by definition, and these diagnostic categories are thus referred to as wholly (100%) alcohol-attributable health conditions (Rehm *et al.* 2010). The underlying assumption is that should alcohol have been eliminated as a risk factor, these health conditions would not have occurred. Table 1 lists the ICD-10, Finnish modification medical conditions which are alcohol-specific by definition.

Table 1 Alcohol-specific medical conditions by definition in the International Classification of Diseases, tenth revision (ICD-10), Finnish modification.

ICD-10 code	Label	Additional details
E24.4	*Alcohol-induced pseudo-Cushing's syndrome*	
F10 (F10.0-F10.9)	*Mental and behavioural disorders due to alcohol use*	Separate codes for acute intoxication, harmful use, dependence syndrome, withdrawal state, withdrawal state with delirium, psychotic disorder, amnesic syndrome, residual and late onset psychotic disorder, other mental and behavioural disorder, unspecified mental and behavioural disorder
G31.2	*Degeneration of nervous system due to alcohol*	
G40.51	*Epileptic seizures related to alcohol*	
G62.1	*Alcoholic polyneuropathy*	
G72.1	*Alcoholic myopathy*	
I42.6	*Alcoholic cardiomyopathy*	
K29.2	*Alcoholic gastritis*	
K70 (K70.0-K70.9)	*Alcoholic liver disease*	Includes codes for alcoholic fatty liver, alcoholic hepatitis, alcoholic fibrosis and sclerosis of liver, alcoholic cirrhosis of liver, alcoholic hepatic failure, unspecified alcoholic liver disease
K85.2	*Alcohol-induced acute pancreatitis*	
K86.0 (K86.00-K86.08)	*Alcohol-induced pancreatitis*	Includes codes for alcohol-induced acute pancreatitis, late effects of (recurrent) alcohol-induced pancreatitis, alcohol-induced chronic pancreatitis
O35.4	*Maternal care for (suspected) damage to foetus from alcohol*	
P04.3	*Foetus and newborn affected by maternal use of alcohol*	
Q86.0	*Foetal alcohol syndrome (dysmorphic)*	
R78.0	*Finding of ethanol in blood*	
T51 (T51.0-T51.9)	*Toxic effect of alcohol*	Includes codes for ethanol, methanol, 2-propanol, fusel oil, other alcohols, unspecified alcohols
X45	*Accidental poisoning by and exposure to alcohol*	
Y90 (Y90.0-Y90.9)	*Evidence of alcohol involvement determined by blood alcohol concentration*	Includes nine codes for various BAC levels, and a code for undetermined BAC
Y91 (Y91.0-Y91.9)	*Evidence of alcohol involvement determined by observed degree of intoxication*	Includes four codes for observed degree of intoxication ranging from mild to severe, and a code for undetermined intoxication

Source: Finnish version of the International Statistical Classification of Diseases and Related Health Problems, tenth revision (ICD-10), third edition, 2011.

In addition to the alcohol-specific health outcomes, alcohol may act as a contributing causal risk factor in the disease processes of various communicable and non-communicable diseases, and in the causal processes of unintentional and intentional injuries. For these medical conditions, alcohol is seen as being part of a constellation of various component causes, which together contribute to the incidence of a disease condition. Table 2 lists the medical conditions for which alcohol has been established as a causal component risk factor in previous reviews and meta-analyses (Rehm *et al.* 2010), and table 3 lists medical conditions for which some evidence exists on the suspected role of alcohol as a risk factor (Rehm *et al.* 2010), but the evidence is less conclusive than that for the medical conditions given in table 2.

Table 2 Alcohol as an established risk factor for incidence, excluding alcohol-specific medical conditions.

Diseases and conditions	Additional details
Infectious diseases	Tuberculosis, pneumonia
Cancers	Cancers of the mouth, pharynx, oesophagus, larynx, liver, colorectal, female breast
Cardiovascular conditions	Arrhythmia, hypertensive heart disease, ischaemic heart disease, stroke
Epilepsy	
Perinatal conditions	Low birth weight
Unintentional injuries	Accidents such as road and transport, falls, drowning, heat and fire, cold
Intentional injuries	Suicide, self-inflicted injuries
Assault injuries	Injuries resulting from interpersonal violence

Source: Rehm *et al.* 2010.

Table 3 Alcohol as a suspected risk factor for incidence, excluding alcohol-specific medical conditions and other established medical conditions.

Diseases and conditions	Additional details
Infectious diseases	Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS)
Cancers	Cancers of the stomach, trachea, bronchus, and lung
Unipolar depressive disorders	
Cardiovascular conditions	Non-alcoholic cardiomyopathy, heart failure
Oesophageal varices	
Psoriasis	

Source: Rehm *et al.* 2010.

2.2 MECHANISMS OF ALCOHOL-RELATED HARM

The main causal mechanisms of alcohol-related harm resulting from alcohol exposure are toxic effects of ethanol and its metabolites on human tissue and organs, alcohol intoxication (inebriation/drunkenness), and alcohol dependence syndrome and addiction. Due to its pharmacokinetic properties (i.e. mechanisms of absorption and distribution in the body) alcohol can affect all body tissues and organs, and therefore the potential adverse effects of alcohol can also be wide-ranging and complex. Figure 1 shows a conceptual model of the causal processes of alcohol-related harm involving alcohol exposure, mediating factors, and different types of alcohol-related adverse outcomes (Babor *et al.* 2010).

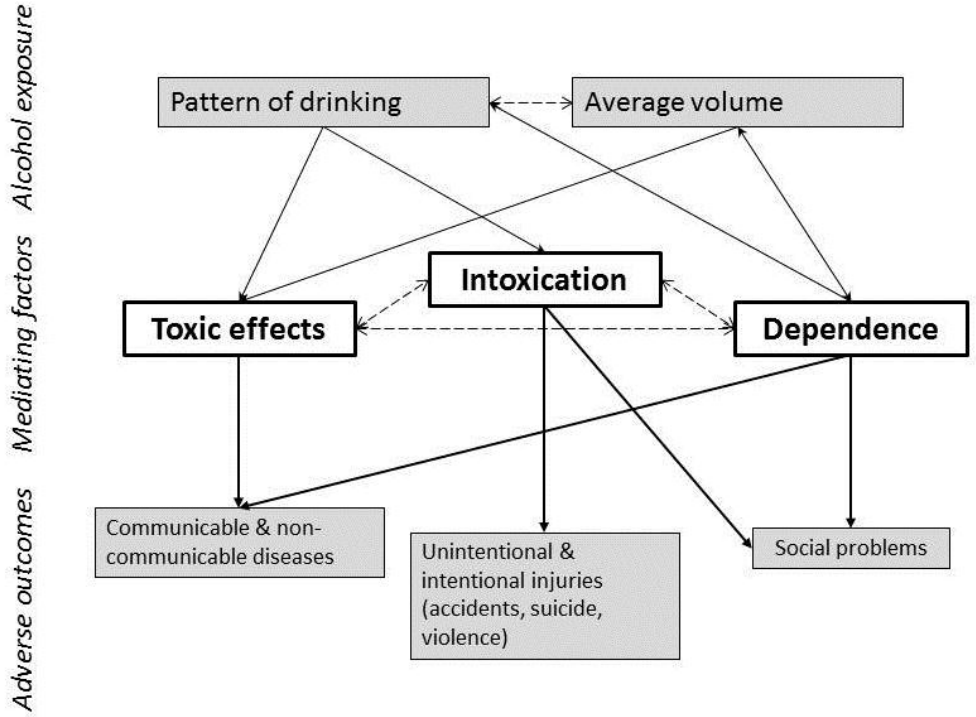

Figure 1 Conceptual presentation of the causal process of alcohol-related harm. Modified from Babor *et al.* 2010.

Toxic effects

Toxic effects of alcohol can be divided into two domains based on a function of time. Acute toxic effects result from ingesting large quantities of alcohol within a short period of time. Examples of acute toxic effects of alcohol are alcohol poisoning, acute pancreatitis, acute hepatitis, and cardiac arrhythmia. Long-term exposure of even small quantities of alcohol can have cumulative adverse effects on tissues across the body. Typical adverse disease outcomes of sustained toxic effects of alcohol are cirrhosis of the liver and alcohol-related cancers. Acute toxic effects of alcohol can have synergistic effects with

long-term alcohol exposure in causing alcohol-related harm. For example, a single heavy drinking occasion (acute toxicity) in a person suffering from liver cirrhosis can cause a fatal liver failure.

Intoxication

The intoxicating effect of alcohol has been acknowledged as an important mechanism of alcohol-related harm, and it is also often the main motivation for alcohol consumption. Alcohol intoxication is an ambiguous term, and the definition of intoxication depends on the context in which the term is used, e.g. whether used in medical, legal, or social context. At low levels of blood alcohol concentration (BAC) the intoxicating effects of alcohol are generally experienced as beneficial and desirable, including experiences such as euphoria, relaxation, and loss of social inhibitions. These perceived beneficial effects of mild alcohol intoxication may, however, act as an incentive to sustained and increasing use of alcohol, and therefore contribute to development of alcohol dependence.

From a perspective of alcohol-related harm, alcohol intoxication is typically defined as an outcome of a drinking pattern leading to high BAC. Alcohol intoxication therefore refers to a threshold of BAC, after which the adverse effects of intoxication become substantial. Alcohol intoxication as a psychological, behavioural, and functional state is an important contributing factor in unintentional and intentional injuries, and in interpersonal and social harm. Recent evidence also suggests that alcohol intoxication is an important factor in determining the risk of adverse cardiovascular outcomes (Roercke & Rehm 2010, Hillbom *et al.* 2011).

Dependence

The core symptom of alcohol dependence syndrome is alcohol craving, i.e. a strong desire or a sense of compulsion to use alcohol. Other symptoms of alcohol dependence syndrome, according to the ICD-10, are impaired capacity to control alcohol use, withdrawal symptoms, tolerance to effects of alcohol, preoccupation with alcohol use, and persistent alcohol use despite clear signs of alcohol-related harm. Three of the above six symptoms need to co-occur for a clinical diagnosis of alcohol dependence. Sustained alcohol use alongside perceived effects of alcohol and neuroadaptation contribute to the development of alcohol dependence, in particular among those with a hereditary vulnerability to alcohol dependence. The term alcohol addiction is sometimes used as synonymous to alcohol dependence (alcoholism), but it is a narrower term referring mainly to alcohol craving. Alcohol dependence maintains and increases alcohol consumption and therefore predisposes to the toxic effects of alcohol, but it is also a significant source of wide-ranging social problems.

2.3 ALCOHOL INTOXICATION

Alcohol is a psychoactive substance, which means that as a result of its effects on the functioning of the central nervous system (CNS), it alters affect/mood, cognition, judgement, perception, level of consciousness, and behaviour. Based on its pharmacodynamic properties, alcohol is classed as a CNS depressant. For example, alcohol in the brain suppresses activity on brain areas involved in regulating inhibition and judgement (Vonghia *et al.* 2008). However, these CNS depressant effects can be experienced as stimulating during rising blood alcohol level (Ray *et al.* 2009).

Alcohol intoxication is an outcome of a drinking pattern resulting in blood alcohol (ethanol) concentration levels (BAC/BAL) high enough to produce marked short-term functional impairment in psychological and psychomotor performance (table 4). The term alcohol intoxication can be used to refer to a degree/level of intoxication on a BAC continuum, or to a specific cut-off value of BAC, indicating a threshold for 'being intoxicated' or being 'under the influence' of alcohol. Threshold values for alcohol intoxication are used particularly in defining intoxication for drunk driving laws (e.g. driving while intoxicated, DWI, or driving under the influence, DUI).

From a legal perspective, a person is deemed as intoxicated when his/her ability to drive and operate a motor vehicle is impaired to an extent which results in significantly increased risk of causing harm to others and to oneself (Brick & Erickson 2009). Alcohol-induced impairment observable in laboratory settings, particularly in complex tasks, start typically at BAC levels as low as 0.02-0.03% (Breitmeier *et al.* 2007). The BAC threshold used to define intoxication in DWI laws varies considerably across countries; in most countries between 0% and 0.08%. The legal definition of being 'intoxicated' may therefore differ markedly from a layperson's definition of someone being intoxicated/drunk.

Table 4 Main domains of impairment related to alcohol intoxication.

Type of functional impairment	Description
Psychomotor impairment	Impaired fine and gross motor coordination, impaired balance and movement, impairment in tasks requiring divided attention
Reaction time	Lengthened reaction time
Judgement	Impaired judgement related to risk-taking behaviours, e.g. whether to drive a car, whether to continue drinking
Emotional changes	Changes in emotions, mood, and social interaction.

Source: Brick & Erickson 2009, Babor *et al.* 2010, Rubenzer 2011.

Blood alcohol concentration

BAC is used as an objective measure of alcohol intoxication. BAC is an estimate of the amount of alcohol absorbed in the body, and it is usually expressed as mass of ethanol per volume of blood. There is no single generally accepted convention to express BAC levels. For example, the same BAC can be expressed either as mg/100mL, mg/dL, g/dL, g/L, as a percent (%), or as per mille (‰). In addition to direct measurement from blood samples, BAC can be estimated from samples of breath, saliva, and urine, or it can be calculated retrospectively using a validated formula (Widmark calculation).

A BAC curve describes the blood alcohol concentration as a function of time, i.e. the change in BAC resulting from differences in rates of absorption into blood, temporary distribution to body tissues, and elimination (mainly via metabolism, but also partly via excretion into urine and breath). The BAC curve has three stages as shown in figure 2. A steep ascending limb of the BAC curve reflects rapid rate of absorption. Alcohol is absorbed to blood by diffusion mainly from the upper small intestine due to its large surface area and rich blood supply. The rate of absorption from the small intestine is regulated by gastric emptying (Hillbom & Wallgren 1978) which is influenced, for example by quantity and type of food consumed concurrently with alcohol. Drinking on an empty stomach allows rapid absorption of alcohol from the small intestine and results in steeply ascending BAC. The peak/plateau of the BAC curve represents the highest BAC reached during a given drinking occasion. At plateau (dashed line in figure 2), the rate of absorption equals to that of elimination, which keeps the BAC at a constant level for a period of time. During the descending limb of the BAC curve the rate of elimination is higher than that of absorption reflecting the removal of alcohol from the blood. Various individual and situational factors affect the level of BAC and shape of the BAC curve (table 5).

The CNS depressant effects of alcohol lead to functional impairment even at low BAC levels (below 0.05%). As the impairing effects of alcohol intoxication are mostly dose-related, the manifestation of alcohol intoxication, i.e. the signs and symptoms of intoxication are also time-related, depending on the phase of the BAC curve (figure 2). At low BAC levels and during the ascending BAC curve, the effects of alcohol are typically manifested through stimulation and euphoria, whereas at high BAC levels and during the descending BAC curve, the effects are manifested through sedation and dysphoria. This duality in the manifestation of alcohol intoxication is referred to as the biphasic effects of alcohol (Martin *et al.* 1993, Addicott *et al.* 2007). There is, however, marked between-person variability in the manifestation of alcohol intoxication during both limbs of the BAC curve (Holdstock *et al.* 2000, Marczinski & Fillmore 2009, Morean & Corbin 2010, Wetherill *et al.* 2012).

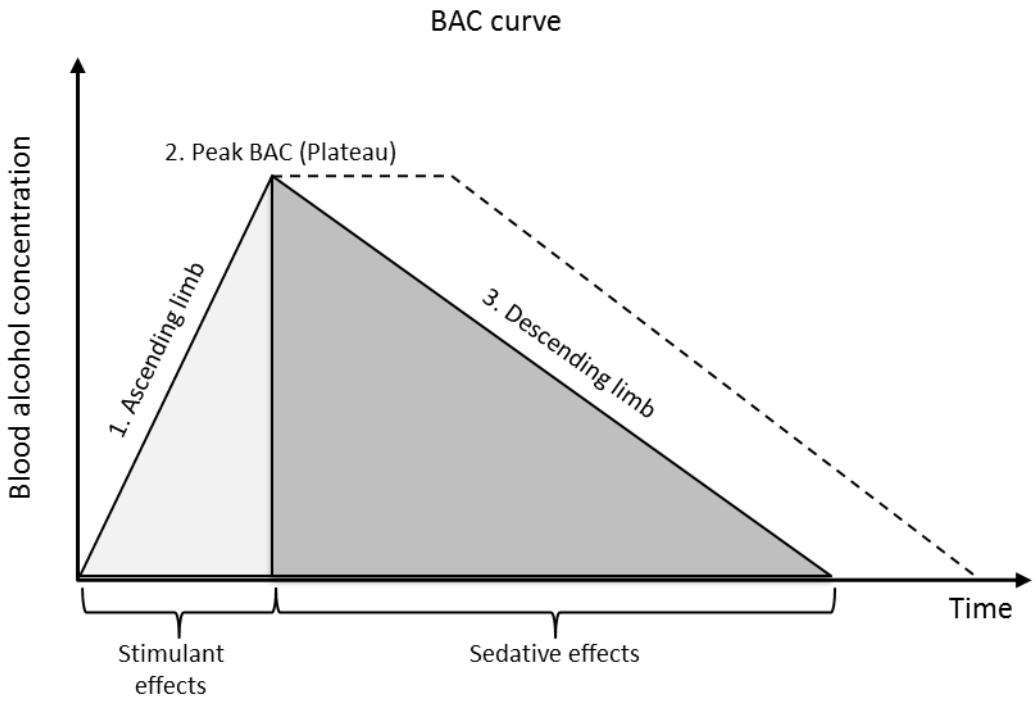

Figure 2 Theoretical representation of the biphasic blood alcohol concentration curve.

Table 5 Factors affecting the level of BAC.

Factor	Description
Volume of intake	Number of standard drinks consumed on a given drinking occasion (grams of absolute alcohol per drinking occasion), or dose of ethanol (grams of ethanol per kg of body mass).
Rate of intake	Higher rate of intake leads to a more rapidly increasing BAC and to a higher peak BAC.
Beverage ethanol content (strength)	Higher strength alcoholic drinks have a potential to produce higher BACs due to higher ethanol content per volume of alcoholic drink, but the relation seems to depend for e.g. on whether alcohol is consumed on an empty stomach or not.
Consumption of food	Concurrent consumption of food decreases the rate of ethanol absorption compared to drinking on an empty stomach, and therefore produces a lower BAC.
Gender	Women have, on average, a lower body water content and a higher body fat content, which leads to a higher BAC than in men, when consuming the same amount of alcohol.
Body mass and composition	Higher body water content (a larger body size/mass) leads to a lower BAC, whereas a higher body fat content leads to a higher BAC.
Tolerance	In persons who have developed metabolic tolerance due to long-term alcohol exposure, the liver can metabolize alcohol more quickly and therefore contribute to a lower BAC (Tabakoff *et al.* 1986).

Source: Eckardt *et al.* 1998, Tabakoff *et al.* 1986.

Signs and symptoms of alcohol intoxication

Signs of alcohol intoxication refer to the impaired CNS function caused by alcohol, which can be observed using either laboratory tests, validated field tests (standardized field sobriety tests), or by using subjective evaluation

based on visible signs of intoxication. Visible signs of alcohol intoxication are those behavioural and physical signs used to make judgements as to whether a person is intoxicated or not, and/or to assess the degree of intoxication. Symptoms of alcohol intoxication refer to the self-perceived effects of alcohol. These symptoms are not necessarily visible to an observer. For example, vomiting can be seen both as a sign and symptom of alcohol intoxication, but nausea is only a symptom, because the presence of nausea is difficult to observe. (Brick & Erickson 2009, Rubenzer 2011)

Observer assessment of signs of intoxication

When an observer without access to objective BAC indicators is trying to subjectively judge whether a person is intoxicated or not, the evaluation is mainly based on behavioural visible manifestations assumed to be alcohol-induced, i.e. the signs of alcohol intoxication. Alcohol-induced sedation, i.e. the signs associated with high BAC levels and/or signs occurring during the descending limb of the BAC curve are more frequently interpreted to be indicative of alcohol intoxication than other signs (Brick & Erickson 2009). Such signs include slurred/stammering speech, body sway, impaired walking, clumsiness, smell of alcohol on the breath, and red eyes. Signs related to the ascending limb of the BAC curve, i.e. the stimulating effects are less frequently interpreted to be indicative of alcohol intoxication (Brick & Erickson 2009). None of the signs alone provide a single accurate method for determining alcohol intoxication. Also situational cues have an important role in assuming whether the signs are interpreted as alcohol-induced (Brick & Erickson 2009).

Research has consistently shown that even trained observers face marked difficulties in correctly judging a person as intoxicated when the BAC is below 0.10%, and good observer accuracy in subjective observer judgement of alcohol intoxication is not achieved until the target person has a BAC of around 0.15% (Brick & Erickson 2009). At this BAC level the alcohol-induced psychomotor functional impairment is substantial for the majority of drinkers, also among those who have developed mild to moderate alcohol tolerance, and most of the visible signs are reliably judged as alcohol-induced. However, only at a BAC of 0.20% or higher, almost all persons are accurately identified as intoxicated, with an exception of a small number of persons who have developed marked alcohol tolerance (Brick & Erickson 2009). Therefore, from the point of view of an observer judgement, when alcohol intoxication seems obvious, the actual BAC is probably closer to 0.20% than 0.10%.

Self-perceived symptoms of intoxication

Symptoms of alcohol intoxication refer to symptoms that persons use themselves to assess whether he or she is intoxicated/drunk or not. The signs of alcohol intoxication are basically dichotomous from the point of view of an observer, the signs are either present or not, whereas the symptoms of

alcohol intoxication are more likely perceived on a continuum. Self-perceived intoxication therefore has at least three dimensions, including the type, number, and intensity of symptoms experienced. Frequently reported symptoms of alcohol intoxication, in addition to the perception of 'being drunk', include dizziness, light headedness, nausea, feeling buzzed/high, concentration difficulties, feeling relaxed/sleepy, and lack of coordination (Williams & Burroughs 1994, Midanik 2003, Ray *et al.* 2009, Levitt *et al.* 2009, Reich *et al.* 2012).

While the observer assessment of alcohol intoxication is complicated, for example by lack of comparison to sober state, the assessment of self-perceived level of alcohol intoxication is complicated by alcohol intoxication itself. The conclusion from studies that have investigated the relation between perceived intoxication and actual BAC is that persons are generally inaccurate in their estimation of (in guessing) their actual BAC levels (Aston & Liguori 2013), and that the level of BAC affects the direction of bias in the estimation (e.g. Nicholson *et al.* 1992, McKnight *et al.* 1997, Brumback *et al.* 2007, Grant *et al.* 2012). Persons at low BAC levels tend to overestimate their actual BAC, whereas persons at higher BAC levels tend to underestimate their actual BAC (Grant *et al.* 2012). Perceived intoxication has been shown to correlate more strongly with psychomotor impairment than the actual BAC (Nicholson *et al.* 1992). The phase of the BAC curve including acute tolerance during the descending limb of the BAC curve, can therefore affect the assessment of perceived level of intoxication.

Alcohol intoxication and drunkenness

Alcohol intoxication (being intoxicated) and drunkenness (being drunk) are frequently used as synonyms. The concepts are, however, not fully equivalent. Alcohol intoxication refers to the presence of ethanol in the body, for which the objective indicator is BAC, whereas drunkenness is the subjective perception or interpretation of the state of being intoxicated by alcohol. Drunkenness can refer either to the subjective perception of an individual who has consumed alcohol, or to the subjective interpretation of an observer making assumptions of alcohol involvement in the other person's behaviour.

The assessment of drunkenness is made against various reference points, which include manifestations of alcohol intoxication (i.e. the signs and symptoms of intoxication), situational cues related to the context, expectations related to the effects of alcohol, and cultural norms and beliefs. As there are factors producing individual variability in the BAC levels at a given level of intake, there are also factors that produce individual variability in the level of perceived intoxication at a given level of BAC. As table 5 lists some of the main factors that have been commonly shown to affect the level of BAC, and thus the level of CNS exposure to the intoxicating effects of alcohol (Tabakoff *et al.* 1986, Eckardt *et al.* 1998), table 6 lists some of the main factors that have been commonly shown to affect the subjective perception of alcohol intoxication.

Table 6 Factors affecting the perception of alcohol intoxication.

Factor	Description
Phase of the BAC curve	Symptoms of intoxication vary by the phase of the BAC curve (Martin *et al.* 1993), and individual variability may exist in which symptoms are attributed to alcohol intoxication (Addicott *et al.* 2007, Corbin *et al.* 2008, Wetherill *et al.* 2012).
Tolerance	Functional tolerance reduces the perceived impairment of alcohol intoxication. Functional tolerance occurs when the brain functions adapt to compensate for the impairing effects of alcohol. Different types of functional tolerance include *acute tolerance*, which develops within a single drinking occasion during the descending limb of the BAC curve, *environmental tolerance* develops when drinking occurs frequently in the same context, and *learned tolerance* develops when a specific task is performed repeatedly under the influence of alcohol (Marczinski & Fillmore 2009, Fillmore & Weafer 2012).
Subjective response to alcohol	Differences in subjective response to alcohol potentially affect how intoxication is experienced (Holdstock *et al.* 2000), and how this experience affects drinking behaviours (Wetherill & Fromme 2009, Morean & Corbin 2010).
Alcohol expectancies	Drinkers' pre-drinking expectations of the effects of alcohol have been shown to predict the experienced effects of alcohol (Fillmore & Vogel-Sprott 1996) and drinking behaviour (Wall *et al.* 2003, Reich *et al.* 2012).
Situational cues	Previous drinking experiences and alcohol expectancies together with external situational cues (characteristics of a drinking occasion) may influence self-perceived intoxication (Sher 1985, Williams & Burroughs 1994).
Familial predisposition	Genetic predisposition and childhood family environment may be associated with differences in subjective response to alcohol (Viken *et al.* 2003, Quinn & Fromme 2011).
Drinking context	Drinking context may affect self-perceived intoxication through functional tolerance (Fillmore & Weafer 2012), alcohol expectations (Reich *et al.* 2012), situational cues (Williams & Burroughs 1994), and social setting (Sher 1985).
Fatigue	Fatigue/sleep deprivation may intensify the impairing effects of alcohol intoxication (Peeke *et al.* 1980).
Medications	Some medications may enhance the intoxicating effects of alcohol due to pharmacological interaction (Sands *et al.* 1993).

Culture and drunkenness

Culture affects the prevalence of drinking behaviours, including binge drinking patterns (Ahern *et al.* 2008, Song *et al.* 2012). The behavioural expression of a given level of intoxication and the interpretations of the behavioural expressions of intoxication are also likely influenced by personal and cultural expectations about the effects of alcohol (Room 2001). Cultural variability e.g. in the acceptability of drunkenness (Ahern *et al.* 2008, Müller *et al.* 2011) and the potential variability in definitions and manifestations of drunkenness i.e. subjectivity of drunkenness (Midanik 1999, Cameron *et al.* 2000, Midanik 2003) are seen as potential threats to the usefulness of measures of subjective drunkenness in epidemiological research as indicators of at-risk drinking patterns (e.g. Babor *et al.* 2010).

Babor *et al.* (2010, p.16), for example, refer to a study conducted in the U.S. as an indication of "change in the meaning of being drunk" within a culture. This U.S. study found that the number of alcoholic drinks needed to

'feel drunk' decreased significantly between the years 1979 and 2000 (Kerr *et al.* 2006). In male drinkers the average number of drinks needed to feel drunk fell from 9.8 drinks in 1979, to 7.4 drinks in 1995, and finally to 6.6 drinks in 2000 (one U.S. drink corresponding to 12 g of ethanol). A similar trend was also found in women. However, there is an alternative explanation to the above-mentioned finding, which is not related to change in the 'meaning of being drunk'. The prevalence of drunkenness increased markedly during the follow-up period, meaning that a much smaller proportion of drinkers contributed to the average number of drinks needed to feel drunk in 1979 than in 2000. It is therefore possible that increase in the prevalence of 'mild' drunkenness from 1979 to 2000 explained the relative reduction in the average number of drinks needed to feel drunk. Without information on changes in actual BAC levels reached per drinking occasion, it is impossible to establish whether the change in number of drinks needed to feel drunk reflected changes in drinking behaviours affecting the level of intoxication, such as drinking with meals versus drinking into empty stomach etc. For example, if drinking occasions in 1979 involved more food consumption than drinking occasions in 2000, the number of drinks needed to feel drunk may have been higher in 1979 due to differences in rate of absorption. All in all, in the absence of data on actual BAC levels reached per drinking occasion, studies on the number of drinks needed to feel drunk tell us very little about the validity of self-perceived drunkenness.

From an epidemiological perspective, self-perceived drunkenness i.e. subjective intoxication is a proxy to objective intoxication (i.e. high BAC), and not a proxy to number of drinks consumed on a drinking occasion, despite a correlation between these two. One of the main strengths of subjective intoxication in relation to quantity measures in approximating the effects of high BAC is that it is sensitive to various individual and contextual differences which determine the level of BAC (table 5).

2.4 ALCOHOL POISONING

At high BAC levels alcohol has acute toxic effects on the function of the CNS. The main signs of acute severe toxic effects of alcohol, i.e. alcohol poisoning are given in table 7 (Vonghia *et al.* 2008). Drinking large quantities of alcohol in a short period of time (binge drinking) is the main cause for alcohol poisoning. The BAC level can continue to rise a period of time after the last drink has been ingested, which can lead to unexpectedly high BAC levels, particularly if the rate of alcohol ingestion is high, e.g. due to gulping of drinks (Perry *et al.* 2006).

Signs and symptoms of alcohol poisoning range from mild to severe, and there are significant individual differences in the BAC levels at which the symptoms occur. In general, alcohol has marked depressant effects on the CNS when the BAC reaches 0.20%. These depressant effects manifest for example as disorientation, severe lack of coordination, and as overall sedation. In its mildest form, sedation leads to excessive involuntary

sleepiness, and in its more severe form, to loss of consciousness (pass-out) and coma.

Passing out (pass-out) is a popular language term used to describe loss of consciousness resulting from drinking too much alcohol. There is no formal definition for an alcohol-induced pass-out, and the term has been mainly used intuitively without a specific definition; other than that the term has been attributed to alcohol consumption either implicitly or explicitly (Kaprio *et al.* 1987, Järvenpää *et al.* 2005, Lewis *et al.* 2010). Some studies among college students in the U.S. have used an operational definition of 'involuntarily falling asleep after drinking' for pass-outs (Schuckit *et al.* 1997, Maggs *et al.* 2011).

There is currently no evidence on the actual BAC levels at which pass-outs occur in natural settings. Given the known average BAC levels at which sedative effects start to become apparent, the BAC levels associated with pass-outs likely start from 0.15%.

Due to correlation for example with alcohol poisoning, alcohol-induced pass-outs are potentially related to marked risk of severe adverse health outcomes. Alcohol poisoning can cause e.g. severe dehydration and hypothermia, lung damage and asphyxiation due to inhaling vomit, injury due to external causes, and death (Vonghia *et al.* 2008).

Table 7 Main signs of severe acute toxic effects of alcohol, i.e. signs of alcohol poisoning.

Signs of alcohol poisoning
Excessive involuntary sleepiness
Severe confusion/disorientation
Vomiting repeatedly and while unconscious
Slowed or irregular breathing
Cold clammy/pale/bluish skin (hypothermia)
Stupor/semi-consciousness (being conscious but unresponsive)
Unconsciousness (pass-out)
Seizures/convulsions
Coma
Death (lethal dose, LD_{50} generally at BACs >0.40%)

Vonghia *et al.* 2008.

2.5 POST-INTOXICATION EFFECTS OF ALCOHOL

The effects of alcohol intoxication do not end as soon as the BAC has reached zero and all alcohol and its metabolites have cleared from the body. Excessive drinking is associated with post-intoxication residual effects, typically experienced the morning after a heavy drinking occasion. Residual effects of alcohol intoxication refer to any physiological, cognitive, psychomotor, or other symptoms experienced when the BAC has returned to zero, or close to zero. Penning *et al.* (2012) identified 47 post-intoxication symptoms from the literature. Some of these symptoms frequently occur together, such as fatigue, thirst, headache, and nausea. This symptom constellation, in addition to self-perceived hangover state, is commonly used in defining alcohol hangover.

Alcohol hangover is probably the most frequently experienced adverse consequence of alcohol drinking. Apart from few early examples of biomedical studies on potential hangover mechanisms (e.g. Ylikahri *et al.* 1974, Ylikahri & Huttunen 1977), hangovers have received surprisingly little research attention until the very recent years (Swift *et al.* 1998, Wiese *et al.* 2000, Prat *et al.* 2009). The evidence that does exist is inconclusive due to heterogeneity in study methods, and due to methodological shortcomings (Verster *et al.* 2008, Verster *et al.* 2010).

As a consequence, there is no generally accepted definition for alcohol-induced hangover, other than that it is a constellation of unpleasant subjective symptoms, which occur after an excessive drinking session at intoxicating BAC levels. Some studies have included hangover symptoms, which occur when the BAC is still above zero, but it has been argued that for a symptom to qualify as a hangover symptom, it must be present when the BAC has reached zero (Verster *et al.* 2010). There is no agreement on which symptoms are the key symptoms of alcohol hangover, i.e. the symptoms which discriminate hangover as a separate syndrome from other post-intoxication symptoms. Table 8 lists symptoms frequently associated with alcohol-induced hangover in previous studies (Verster *et al.* 2010). None of these hangover symptoms are specific to hangover, that is, these symptoms can exist without alcohol exposure.

Table 8 Signs and symptoms frequently associated with hangover.

Signs and symptoms associated with hangover
Poor sense of overall well-being/discomfort
Fatigue/tiredness/drowsiness/weakness
Thirst/dry mouth
Headache
Nausea/stomach pain/vomiting
Dizziness/vertigo/confusion/disorientation
Tremors/sweating/shivering
Palpitations/heart pounding
Sensitivity to light/sound
Concentration problems/memory problems
Irritability/agitation/anger
Guilt/regret
Depression/anxiety/suicidal thoughts

Verster *et al.* 2010.

Also the epidemiology of hangovers is poorly understood; including lack of mechanism through which ethanol can produce hangover symptoms. It is unclear whether the symptoms most frequently associated with hangover, such as fatigue and thirst, are caused by hangover per se, or only result from correlates of heavy drinking occasions, such as poor sleep and dehydration. It has also been speculated that symptoms of hangover would, in fact, be those of acute alcohol withdrawal. Despite some symptom overlap with mild forms of acute alcohol withdrawal, alcohol hangover seems to be a distinct phenomenon (Prat *et al.* 2009).

Hangover symptom scales, such as the Acute Hangover Scale (AHS), the Hangover Symptoms Scale (HSS), and the Alcohol Hangover Severity Scale

(AHSS), have been developed to record hangover symptom number and severity (Slutske *et al.* 2003, Rohsenow *et al.* 2007, Penning *et al.* 2012). The AHS includes self-perceived hangover, and it is the best performing item in the scale in relation to item-total correlation (Rohsenow *et al.* 2007). The HSS has also been shown to correlate with self-perceived hangover state (Robertson *et al.* 2012). However, without a strong theoretical understanding of hangover mechanism, and without an objective criterion standard, the true validity of these scales remain unknown, because these scales can only be validated against each other (Penning *et al.* 2012), or against the subjective attribution by the study subjects (self-perceived hangover state). Therefore, the operationalizations of hangover state remain subjective, either from the side of researchers in terms of which symptoms to include, or from the side of study subjects in terms of symptom attribution to hangover.

In general, the likelihood of experiencing a hangover is proportional to BAC level. Hangovers are, however, shown to occur also among those who consume low quantities per drinking occasion (Wiese *et al.* 2000, Prat *et al.* 2009). In experimental settings alcohol doses between 1.0–1.5 g/kg of body mass have been frequently used to induce hangover (Wiese *et al.* 2000). For a person weighing 80 kg this would mean 80–120 g of ethanol (between 7 to 10 Finnish standard drinks). This is in line with a study among U.S. college students, which showed that drinking at least 10 drinks per occasion was the best predictor for hangovers (Jackson 2008). An 80 kg man consuming 10 standards drinks (120 g of ethanol) within two hours would, on average, have a BAC of 0.17%.

Few available studies, which have reported prevalence, suggest that hangover is commonly experienced across all consumption levels (light/moderate/heavy), but that the prevalence would be lower among alcohol dependent compared to non-dependent populations, and even some drinkers never report experiencing hangovers despite consuming large volumes of alcohol (Howland *et al.* 2008a). It is unknown why some drinkers, even among binge drinkers, seem to be resistant to hangover symptoms (Howland *et al.* 2008b).

The level of alcohol intoxication is the most important determinant of hangover incidence and symptom severity. The evidence of factors other than excessive drinking affecting hangover susceptibility is mostly inconclusive. Table 9 lists factors, which have been frequently linked to hangover susceptibility (Verster *et al.* 2010). The most consistent evidence on independent effects on hangover incidence and symptom severity comes from studies assessing the effect of congeners. Alcoholic beverages containing more congeners, such as whiskey and red wine, seem to induce hangover more likely and with more severe symptoms, than alcoholic beverages containing less congeners, such as vodka and beer (Rohsenow & Howland 2010, Rohsenow *et al.* 2010).

Table 9 Factors potentially associated with hangover susceptibility.

Factor	Description
Congener content	Higher beverage congener content may be associated with more severe hangover symptoms at constant BAC levels (Rohsenow *et al.* 2010, Rohsenow & Howland 2010).
Family history of alcoholism	Inconsistent findings. Some of the inconsistent findings could be explained by subjective response to alcohol, which is associated with family history of alcoholism.
Low subjective response to alcohol	Low response to alcohol has been found to be associated with decreased hangover susceptibility at a given level of intake, but with a higher overall frequency of hangovers due to higher total intake and higher peak BACs per drinking occasion (Piasecki *et al.* 2012).
Smoking	Heavy smoking may be associated with greater hangover susceptibility independently of intake level (Jackson *et al.* 2013).
Gender	Inconsistent findings. Some of the inconsistent findings could be explained by gender differences in the peak BACs per drinking occasions.
Dehydration/sleep quantity and quality	Excessive drinking causes dehydration and adversely affects sleep, but it is unclear whether these factors should be considered as a part of actual hangover mechanism or as contributing factors to hangover susceptibility.

2.6 ALCOHOL INTOXICATION AND BINGE DRINKING

Alcohol intoxication is an outcome of excessive alcohol intake. This pattern of drinking is frequently referred to as binge drinking. In alcohol epidemiology, 'binge' has been used either to refer to excessive drinking sessions lasting for several days (Herring *et al.* 2008), or more frequently, to a single heavy drinking occasion (Gmel *et al.* 2011). Binge drinking occasions typically lead to alcohol intoxication, as 'getting drunk' is often the main motivation for drinking among persons engaging in binge drinking (Wechsler *et al.* 1994, Engineer *et al.* 2003).

Operational definitions of binge drinking, however, vary internationally, and there is currently no consensus on how binge drinking should be operationalized and measured (Gmel *et al.* 2011). The NIAAA defines binge drinking as drinking occasions when the BAC reaches 0.08% (Courtney & Polich 2009). This BAC level is reached, for example when an average man of 75 kg body weight consumes at least 60 g of ethanol (5+ standard drinks) within two hours. Often, however, binge drinking is operationalized only through volume as 5+ drinking occasions without reference to time or the resulting BAC (Gmel *et al.* 2011).

Figure 3 shows how the number of standard drinks (one drink corresponding to 12 g of ethanol) consumed within a two-hour period is related to BAC in men and women. In women (65 kg), four to five drinks, and in men (80 kg), six to seven drinks consumed within two hours will likely produce a BAC of 0.10%; thus exceeding a BAC threshold after which alcohol intoxication starts to become apparent. In practise, however, there is

considerable variation in time used to consume a given number of drinks, and in the other contributing factors that determine the actual level of BAC.

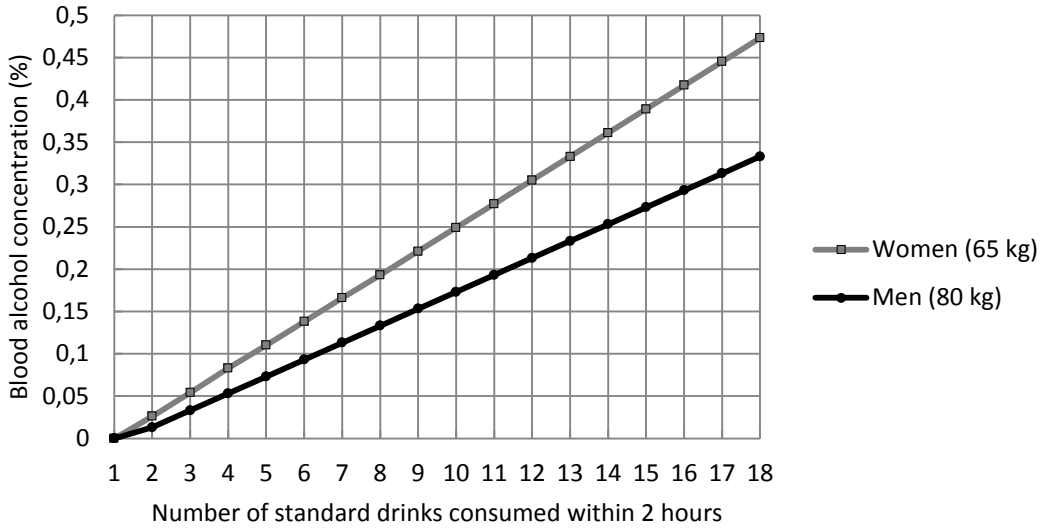

Figure 3 The relation between number of Finnish standard drinks (one standard drink corresponding to 12 g of ethanol) consumed within a two-hour period and the resulting BACs, separately for men and women. BACs were calculated using a modified Widmark formula (Andersson *et al.* 2009).

The 5+ drinks measure without explicit reference to length of time used to consume 60+ g of ethanol does not capture the behavioural intention to 'get drunk', which is often the main motivation of drinking among persons engaging in binge drinking, particularly in young adults (Engineer *et al.* 2003). Figure 4 shows how the length of time used to consume 60 g of ethanol in men (80 kg) and women (65 kg) affect the resulting BAC. The figure shows that male drinkers, weighing 80 kg, consuming exactly 60 g of ethanol should drink that amount of ethanol in less than 1.5 hours to reach a BAC close to the 0.08-0.1% threshold for alcohol intoxication/binge drinking. In female drinkers, weighing 65 kg, consuming the same amount of alcohol, the time window for reaching the 0.08-0.1% BAC threshold is three hours.

The above shows that in defining binge drinking it is important to consider what aspect of 'excessive' drinking is the key dimension; is it high peak BAC or is it a relatively large amount of alcohol consumed on a single drinking occasion (volume). The motivation to drink, such as whether it is to 'get drunk' or to drink sociably, is likely an important factor determining risk behaviours and type of adverse outcomes experienced as a result of drinking. The correlation between 5+ drinks measure and objective alcohol intoxication is implicit, whereas the correlation between self-perceived intoxication measure and objective alcohol intoxication is explicit. Neither of the measures is perfect in capturing the 'core' of binge drinking, which is (intentional) excessive drunkenness resulting from drinking large quantities of alcohol at a time. The 5+ drinks measure is a poor measure of intoxication (Lange & Voas 2001) due to variability in duration of drinking; and self-perceived intoxication is likely a poor measure of quantity e.g. due to

individual differences in perception of intoxication, but both capture one dimension of binge drinking.

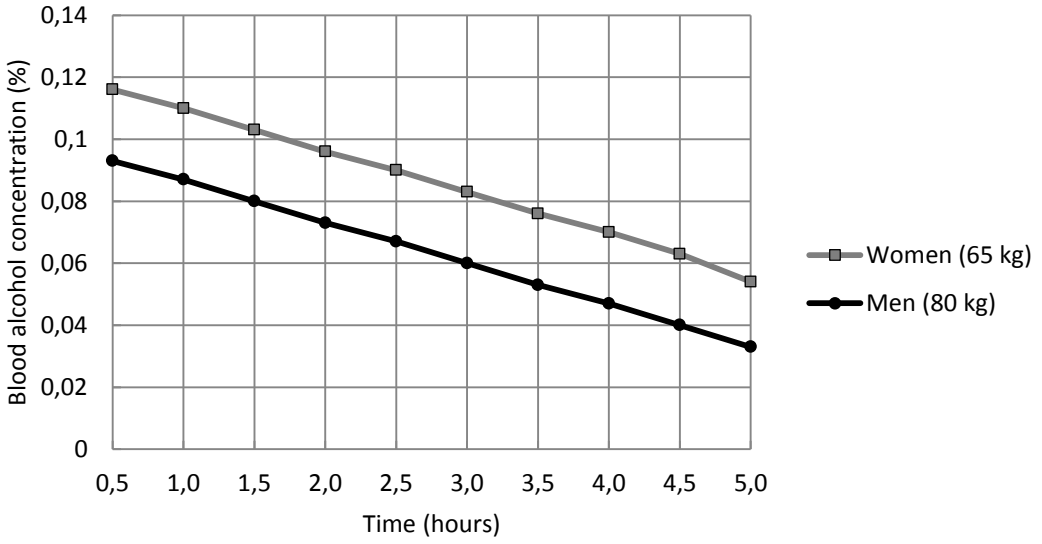

Figure 4 The relation between the time used to consume 60 g of ethanol and the resulting BAC, separately for men and women. BACs were calculated using a modified Widmark formula (Andersson *et al.* 2009).

Widmark formula (Andersson et al. 2009) for estimating peak BAC_{est} :

$$BAC_{est} = (0.806*SD*1.2)/(BW*Wt)-(0.017*DP)$$

0.806 is the constant for body water in the blood
SD is the number of Finnish standard drinks containing 12 g of ethanol
1.2 is a factor taking into account the size of the Finnish standard drink
BW is the body water constant (0.58 for men and 0.49 for women)
Wt is the body weight in kilograms
0.017 is the metabolism constant
DP is the drinking time in hours

Relation between binge drinking, alcohol intoxication, and 5+ drinks

The public and scientific debate and concerns expressed over binge drinking and its harmful effects (White *et al.* 2006, Read *et al.* 2008) suggest that binge drinking as a type of behaviour has trait-like characteristics (Measham & Brain 2005, Herring *et al.* 2008). This is particularly evident in relation to debate around binge drinking among young adults (Courtney & Polich 2009, Bonar *et al.* 2012).

Binge drinking as a construct, therefore, can be seen as a latent, unobserved trait, which can be assessed against observable indicators of binge drinking. A simplified theoretical presentation in figure 5 shows how different type of observable indicators could be associated with the latent binge drinking construct (circle). Indicators on the left side of the circle

define binge drinking (arrows are pointing to the latent structure). These causal indicators can include the number of drinks consumed on a drinking occasion (e.g. 5+ drinks), and other behavioural and motivational factors. Indicators such as intoxication/drunkenness, hangovers, and pass-outs are on the right side of the circle and these are the outcomes or effects of the latent binge drinking structure (arrows pointing out of the latent structure).

The above distinction between causal indicators and effect indicators has important implications to measurement of binge drinking, and to defining the relation between measures of subjective intoxication and X+ number of drinks per drinking occasion. First, X+ drinks measures and measures of subjective intoxication are not alternative to each other, because these are not the same kind of indicators of binge drinking. Second, and more importantly, it is likely that no single measure, neither the 5+ drinks nor subjective intoxication alone is sufficient for accurately measuring the latent binge drinking trait, but a set of indicators is needed (a binge drinking scale). As the X number of drinks measure can capture excessive drinking more accurately than subjective intoxication, it probably cannot accurately measure the intention to become intoxicated, for example, for which subjective intoxications can probably tap in on more accurately (Reich *et al.* 2012).

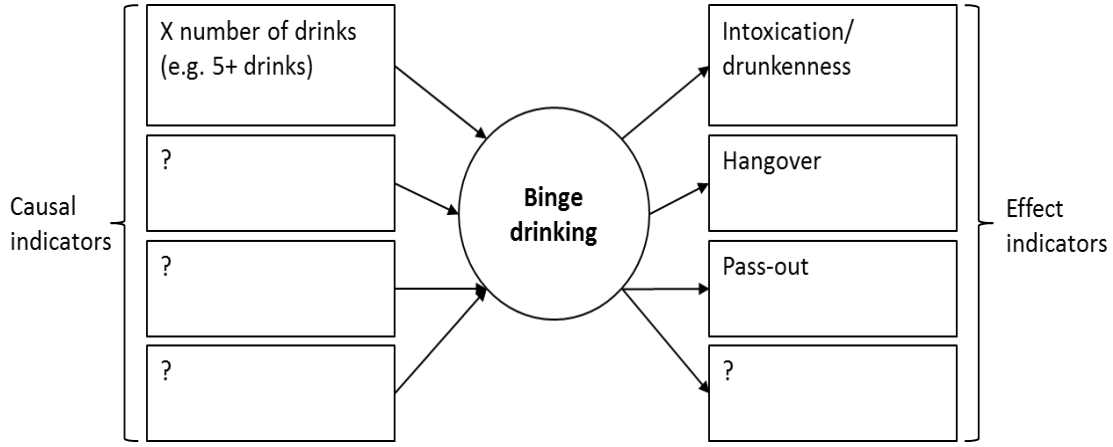

Figure 5 Theoretical presentation of the relations between latent binge drinking construct (circle), and causal indicators (left) and effect indicators (right).

2.7 CHARACTERISTICS OF BINGE DRINKERS

Socioeconomic factors are known to be important determinants of level of alcohol intake and drinking patterns, but the evidence on binge drinking is still scarce and partly inconclusive (Kuntsche *et al.* 2004). Furthermore, much of the evidence comes from studies conducted among U.S. college students, which limits the generalizability of the results to adult general populations. Table 10 lists the sociodemographic factors that have been commonly associated with adult binge drinking.

Table 10 Characteristics of binge drinkers.

Characteristics	Description
Age	Prevalence of binge drinking generally decreases with age. Binge drinking is typically seen as a problem of young adults, but drinking until intoxication is common also among middle-aged men (Naimi *et al.* 2003).
Gender	Binge drinking is more common among men than in women (Kuntsche *et al.* 2004).
Education	In many countries, low education in men is associated with binge drinking, but in women the evidence is inconsistent (Bloomfield *et al.* 2006). In some countries drinking until intoxication is more common among persons with a higher education (Van Oers *et al.* 1999).
Marital status	Married and persons cohabiting with a partner are less likely to binge drink compared to single and divorced persons (Helasoja *et al.* 2007).
Employment	Unemployment seems to be associated with binge drinking in men (Droomers *et al.* 1999), but the evidence in women is less clear. The direction of causality is also unclear (Claussen 1999).
Financial situation	There is a lack of studies assessing the relation between binge drinking and financial situation. Heavy drinking has been shown to be associated with financial difficulties (Joutsenniemi *et al.* 2007), but gender differences may exist (Droomers *et al.* 1999).

2.8 MEASUREMENT OF ALCOHOL EXPOSURE

Despite several decades of tradition and active research using various methods to assess alcohol consumption (Knupfer 1966, Room 1998, Feunekes *et al.* 1999, Dawson & Room 2000, Midanik 2005, Greenfield & Kerr 2008, Rossow & Norström 2012, Midanik *et al.* 2012), the field of alcohol epidemiology is underdeveloped methodologically compared to many other fields of epidemiology. This is exemplified by the lack of formal textbooks dedicated to methods of alcohol epidemiology; in contrast with several being available for other specific fields of epidemiology, such as cardiovascular, cancer and occupational epidemiology.

So far, alcohol epidemiologists have reached a consensus that average exposure alone (volume of intake) does not sufficiently describe alcohol use as a risk factor, because there is substantial variation in exposure intensity levels within a given average exposure level. The need to develop exposure measurement beyond volume has been frequently expressed through a concept of 'pattern of drinking' (Bondy 1996). Pattern of drinking as an epidemiological concept, however, is of very limited practical use, because it is used to refer to any aspect of alcohol use and drinking behaviour other than total volume of intake. Pattern of drinking as a concept therefore denotes merely that there is variability in alcohol exposure over time and context.

Problems with defining and operationalizing indicators of drinking patterns, such as binge drinking, may arise partly from lack of explicit attention to epidemiologically relevant dimensions of alcohol exposure. Due to practical limitations in epidemiological research, it is typically not feasible or even possible to measure true exposure (ethanol dose and the resulting BAC). Instead, exposure variables are used to approximate true exposure. Exposure variables are always, to some degree, imprecise representations of true exposure, i.e. exposure variables contain measurement error due to the

difference between true exposure and exposure variable. As the performance of a given exposure variable depends on its overall correlation with true exposure, it specifically depends on the dimension of true exposure for which it is supposed to be a proxy/surrogate.

There are at least four important dimensions of exposure, which potentially affect the risk of a given outcome, namely frequency of exposure episodes, duration of exposure over time, amount of exposure per exposure episode i.e. exposure intensity, and highest level of exposure per exposure episode i.e. peak exposure (White *et al.* 2008). The relative importance of these dimensions as determinants of risk of adverse outcomes depends on the type of outcome of interest. Different dimensions of exposure also classify subjects differently in at-risk groups, and therefore give different prevalence estimates. Therefore, in relation to operationalizing binge drinking as an exposure, it should be clearly defined whether the purpose is to approximate exposure intensity, peak exposure, or some other dimension of alcohol exposure.

In conclusion, alcohol exposure measurement must be sensitive to various dimensions of alcohol exposure, reflecting different time x dose combinations. In situations where the best representation of alcohol exposure is unknown, several types of exposure variables should be used to determine the best fitting statistical model for predicting the outcome of interest. Furthermore, consistent findings using multiple different exposure variables within a same study, reduces the risk of false conclusions due to bias resulting from exposure measurement error and exposure misclassification.

2.9 RATIONALE OF THE STUDY

Alcohol exposure measurement should not be fixed to any exposure variable without sound theoretical understanding of the causal process between exposure and outcome, and without empirical evidence supporting the choice of exposure variable and, in particular, the use of a specific threshold/cut-off value. There is substantial lack of evidence on the performance of other exposure variables than total volume and 5+ drinks per drinking occasion in predicting various adverse health outcomes.

Alcohol intoxication is an important mediator of alcohol-related harm, but in epidemiological research, alcohol intoxication is typically used either as an indication of negative outcome of drinking, or as a risk factor for injuries among accident and emergency department patients. Therefore, little is known about how drinking until intoxication is related to risk of adverse outcomes among adult general populations.

A commonly expressed critique towards using self-reported intoxications/drunkenness as a risk marker in epidemiological research is that subjective intoxication is 'too subjective' in relation to heavy drinking or number of drinks consumed (Dawson & Room 2000, Babor *et al.* 2010). This however is partly a misperception because self-perceived intoxication is not a measure of volume of intake per drinking occasion per se, but a measure of effects of volume and therefore an indicator of a certain type of drinking pattern leading to experiencing the intoxicating effects of alcohol. If supported by evidence, subjective intoxications could potentially serve as a simple, rapid, and low cost method to identify at-risk drinkers in epidemiological research and in clinical settings.

The intensity of alcohol intoxication is likely an important determinant of alcohol-related harm. Without objective information on BAC levels, it is difficult to subjectively assess the level of intoxication, as the perception of intoxication depends on various individual and situational factors. The assessment of severity of alcohol intoxication can be potentially captured by using outcomes of alcohol intoxication, which are, on average, related to specific intensity levels of intoxication, such as alcohol-induced hangovers and pass-outs.

Only a very small number of studies have used alcohol-induced hangovers in predicting adverse health outcomes. Evidence suggests that hangovers may be related to higher risk of developing alcohol use disorders (Piasecki *et al.* 2010), risk of cardiovascular deaths (Kauhanen *et al.* 1997), and ischemic stroke (Rantakömi *et al.* 2012). Alcohol-induced pass-outs have thus far been included infrequently in epidemiological studies as a risk factor for adverse health outcome, apart from few examples (Kaprio *et al.* 1987, Järvenpää *et al.* 2005).

3 AIMS OF THE STUDY

Given that there are no previous prospective studies that have assessed the relative performance of subjectively defined intoxications, hangovers, and alcohol-induced pass-outs in the same study, the purpose of this study is to validate these measures as indicators of at-risk drinking patterns in epidemiological research. Each of the sub-studies contributed to the overall purpose of the study by providing information on specific aspects of the relative performance of these measures, either in differentiating at-risk drinkers or in predicting adverse health outcomes.

The specific aims were:

1. To establish how subjective intoxications, hangovers, and pass-outs are related to measures of socioeconomic disadvantage (sub-study I).

2. To establish the relative performance of subjective intoxications, hangovers, and pass-outs in identifying drinkers at risk for current and future alcohol-specific harm (sub-study II).

3. To establish how subjective intoxications, hangovers, and alcohol-induced pass-outs predict selected adverse health outcomes, including alcohol-specific outcomes, symptoms of depression, and suboptimal subjective health (sub-studies II, III, and IV).

4 DATA AND METHODS

4.1 DATA SOURCES

This study utilizes data from three separate sources. Self-reported information on various aspects of psychosocial health, health behaviours, and related factors come from repeated postal surveys. Information on cause-specific hospitalizations were linked to the survey data from the national hospital discharge register of National Institute for Health and Welfare, and information on cause-specific deaths were linked to the survey data from the cause-of-death register of Statistics Finland.

4.2 HEALTH AND SOCIAL SUPPORT STUDY

The Health and Social Support Study (HeSSup Study) is a currently ongoing nation-wide prospective cohort study, which was originally launched to establish relations between social support and various health outcomes. The data consists of three repeated postal questionnaires: at baseline, after five years, and after 14 years. The third and final measurement point was originally scheduled to be conducted after 10 years, but due to financial constrictions, it was postponed until 2012. The baseline cohort will be monitored for morbidity and mortality for 15 years from the baseline i.e. until the end of 2013. For the present study, the two first measurement points were available.

For specific research purposes, the data collection included two oversamples; one from the City of Turku and its surroundings, and the other from the minority language group of Swedish-speaking Finns. These oversamples were collected with the same protocol as was used for the main sample, but only with a higher representation.

The HeSSup Study cohort and the oversamples were generated by drawing a random sample of individuals from the Finnish Population Register Centre database. The sample was stratified according to gender and four age groups (20–24, 30–34, 40–44, 50–54 years of age at baseline).

A pilot study was conducted in 1997 to test the performance of the survey questionnaire. Appendix 1 shows the structure of the HeSSup data and the study populations used in sub-studies I to IV.

4.3 REGISTER-BASED DATA ON HOSPITALIZATIONS AND DEATHS

Information from the national hospital discharge register of the National Institute for Health and Welfare, and information from the cause-of-death register of Statistics Finland were linked to the data using a personal identification number. The diagnostic classifications for causes of hospital

admissions and deaths were based on the ICD-10, Finnish modification codes (1999). For hospitalizations, primary and secondary diagnoses, and for causes of death, main and contributory causes were used to identify alcohol-specific hospitalizations and deaths. At the time when the sub-studies were conducted, the maximum length of register-based follow-up was seven years. The follow-up time was either 7.2 years, days until death, or days until the first hospital admission due to the selected end-point, whichever came first.

Alcohol-specific diagnoses by definition were identified using the following ICD-10, Finnish modification codes: F10, alcohol abuse, dependence and psychosis; G312 degeneration of the nervous system; G4051, epilepsy; G621, polyneuropathy; G721, myopathy; I421, cardiomyopathy; K929, gastritis; K70, diseases of the liver; K8600, pancreatitis; T510 and X45, poisoning. Hospitalizations due to depression were identified using codes F32, F33, and F341. The following ICD-10 codes were used to identify hospitalizations due to ischemic heart disease (IHD), I20–I25; and other cardiovascular diseases (OCVD), I00–I19, I26–I99.

4.4 ETHICAL ASPECTS OF DATA COLLECTION

According to the Turku University Central Hospital Ethics committee, the HeSSup Study did not require a formal ethics approval because the study used a general population sample and did not collect any biological specimens. The Population Register Centre of Finland granted permission for the use of the HeSSup Study sample drawn from its population database. A signed informed consent for linking information from pre-named health registers was obtained from study participants.

4.5 MEASUREMENT OF ALCOHOL USE

In the HeSSup questionnaire, a total of eight questions were asking about respondents' alcohol use. A list of these questions and their original format and order in the HeSSup questionnaire is given in English and in Finnish in the appendices 2a and 2b, respectively.

Age of drinking onset, i.e. when the respondent first had an alcoholic drink, was asked using an open-ended question. This question included a response option for lifetime abstainers. In sub-study II, age of drinking onset was categorized into three categories (<15; 15–17; >17 years of age). In sub-study III, a variable indicating number of years of alcohol exposure was calculated as age at T1 minus age of drinking onset (categorized as <10; 10–25; 26–35; 36+ years of alcohol exposure).

Alcohol drinking frequency was asked using an eight-point scale with response options ranging from 'I do not use alcohol' and 'once a year or less often' to 'daily or almost daily'. Drinking frequency was used in sub-study II as a variable indicating number of drinking occasions per year.

4.5.1 Beverage-specific intake

Average alcohol intake was asked separately for beer, wine and other mild alcoholic beverages, and spirits. The time frame of the questions varied so that for beer and wine and other mild alcoholic beverages the time frame asked was a week, and for spirits a month. When calculating total intake, the intake of spirits was converted to correspond to weekly intake. For beer and spirits consumption all response options were given as "bottles", whereas for consumption of wine and other mild alcoholic beverages the response options were given as "glasses" and "bottles". The volume of the "glass" for wine and other mild alcoholic beverages was not specified. The volumes of the "bottles" were specified for beer as 0.33l and for spirits as 0.5l. For wine and other mild alcoholic beverages, the volume of the "bottle" was not specified, but in calculating total intake it was assumed to be 0.75l.

Potential bias in questions on beverage-specific intake

For beer, another very common container volume is 0.5l, in particular for beer sold in cans, but this was not specified in the question. None of the beverage-specific questions differentiated between varying strengths of a given beverage. The question for wine consumption was formulated as how much do you consume on average "wine and other mild alcoholic beverages…". Given that consumption of such popular alcoholic beverages as ciders and so called long drinks (mild alcoholic factory pre-mixed drinks) were not included in the question of beer consumption, it is likely that this question therefore includes an unknown proportion of responses representing wine, cider, long drinks, and other mild alcoholic beverages. However, in calculating beverage-specific consumption of "wine and other mild alcoholic beverages" the consumption was assumed to be exclusively wine.

Therefore, it is likely that in addition to typical error found in alcohol measurement in population surveys (i.e. underestimation), the beverage-specific alcohol intake estimated in the HeSSup study is likely biased so that beer consumption is further underestimated due to omitting the 0.5l container volume from the question, and "wine and other mild alcoholic beverages" consumption is overestimated due to the fact that all consumption was assumed to be equivalent in strength to wine.

4.5.2 Average total intake

Estimated beverage-specific intake was converted to grams of absolute alcohol (ethanol) using the assumed alcohol content of each given beverage-portion combination. A "bottle" of beer of volume 0.33l was assumed to contain 12 g of ethanol, a "glass" of wine and other mild alcoholic beverages was assumed to contain 12 g of ethanol, a "bottle" of wine and other mild

alcoholic beverages was assumed to contain 72 g of ethanol, and a "bottle" of spirits of volume 0.5l was assumed to contain 156 g of ethanol. For response options which contained a range of values (e.g. "1 to 4 bottles" of beer) the mid-value of the range was used in calculating the corresponding quantity in grams of ethanol. Appendix 3 shows how beverage-specific consumption was converted to grams of ethanol. Total intake was calculated as a sum of beverage-specific weekly intake.

In sub-studies I to IV, various different categorizations of average intake were used either to ensure enough statistical power (e.g. depending on the joint distribution with the given dependent variable), or to answer specific research questions. Average intake was used either as a continuous variable, ordinal categorical variable, or as a dichotomous variable.

4.5.3 Hazardous weekly intake

Hazardous weekly intake was defined using the Finnish gender-specific guidelines (Halme *et al.* 2008) for men as weekly intake exceeding 287 g, and for women as weekly intake exceeding 191 g of ethanol (corresponding to ≥24 and ≥16 Finnish standard drinks, respectively). For the purpose of sensitivity analyses in sub-studies I and II, hazardous weekly intake was also defined according to the gender-specific UK guidelines (Department of Health 2007) for men as weekly intake exceeding 168 g, and for women as weekly intake exceeding 112 g of ethanol (corresponding to ≥14 and ≥9 Finnish standard drinks, respectively). In addition, in sub-study II, also for the purpose of sensitivity analysis, harmful weekly intake was defined using the UK guidelines for men as weekly intake exceeding 400 g, and for women as weekly intake exceeding 280 g of ethanol (corresponding to ≥34 and ≥24 Finnish standard drinks, respectively).

4.5.4 Binge drinking

Binge drinking pattern was estimated by asking the respondent to report how often they had experienced intoxications/drunkenness, hangovers, and alcohol-induced pass-outs during the past 12 months. The Finnish term used for 'passing out' (sammua) refers to alcohol-induced loss of consciousness, but without reference to loss of memory (blackout). For the frequency of intoxications and hangovers the response options on a nine-point scale ranged from 'never' to 'at least twice weekly'. For the frequency of alcohol-induced pass-outs the response options on a five-point scale ranged from 'never' to 'at least seven times a year'.

In sub-studies I to IV, various different categorizations of binge drinking measures were used either to ensure enough statistical power (e.g. depending on the joint distribution with the given dependent variable), or to answer specific research questions. Binge drinking measures were used either as

continuous variables, ordinal categorical variables, or as dichotomous variables. Appendix 4 shows the categorizations of binge drinking measures used in each sub-study.

4.6 MEASUREMENT OF OTHER STUDY VARIABLES

4.6.1 Background variables

All sub-studies included *gender* (man, woman) and age as covariates. *Age* retained its original categorization as derived from the Finnish population register (20–24; 30–34; 40–44; 50–54-years at T1). Also the respondents' *official mother tongue* (either Finnish or Swedish speaker) was derived from the Finnish population register. *Vocational education* (later referred to as 'educational level') was asked using a structured question with five response options ('no vocational education'; 'vocational course'; 'apprenticeship contract'; 'vocational school'; 'college'; 'polytechnic'; 'university'). *Employment status* was asked using a structured question with twelve response options describing different employment situations ('employed, full-time'; 'employed, part-time'; 'unemployed, on earnings-related allowance'; 'unemployed, on basic allowance'; 'laid-off'; 'student'; 'house mother or father'; 'retired, based on age'; 'on disability pension'; 'on early retirement pension'; 'part-time retirement pension'; 'something else, specify?'). *Living alone* was assessed by an open-ended question "How many persons are living in your household (including you)?" A number greater than one indicated that the respondent did not live alone. *Family history of alcohol problems* was assessed using a question "When you think about your childhood, did someone of your family members have problems because of alcohol?" The respondent chose from three response options ('no'; 'yes'; 'I do not know'). *Negative life-events* were asked using a 19-item list of various life-events with response options indicating the timing of the event ('never'; 'during the past six months'; 'during the past five years'; 'earlier'). In sub-study IV, information from the T2 measurement was used to identify respondents who *divorced* or *became unemployed after T1* (i.e. at T2 indicated that they had either divorced or became unemployed during the past five years). Using the same list of negative life-events, in sub-study I, *history of financial hardships* was indicated by responses to a statement 'significant hardships in financial situation'. A variable indicating *history of unemployment* among those currently employed in sub-study I, was constructed using information on current employment status, as described earlier, and a question asking about episodes of unemployment during the past three years "Have you been unemployed or laid-off during the past three years?". The respondents' chose from seven response options ('I have not been unemployed or laid-off during the past three years'; 'yes, once for a short period (less than 3 months)'; 'yes, several short periods'; 'yes, once for a longer time (over 3 months)'; 'yes, several longer periods'; 'I have not been

part of the workforce during the past three years'; 'I have never been part of the workforce').

4.6.2 Health behaviours

Daily smoking of cigarettes was asked with a question "How many cigarettes on average do you currently smoke daily?" The respondents chose from eight response options ('none'; 'less than 5 cigarettes'; '5–9 cigarettes'; '10–14 cigarettes'; '15–19 cigarettes'; 20–24 cigarettes'; '25–40 cigarettes'; 'over 40 cigarettes').

Physical activity was assessed using a question "How much you have had physical activity on your leisure time or while commuting to work (during the past year)? How would you assess the strenuousness of your physical activity? The respondents' were first provided with four examples of strenuousness of the physical activity ('walking or similar'; 'fast walking or similar'; 'jogging or similar'; 'fast running or similar') and then asked to estimate the average duration of each given example of physical activity during a typical week ('none'; 'less than half an hour per week'; 'about an hour per week'; '2–3 hours per week'; 4 hour or more per week').

4.6.3 Self-reported health and related factors

Subjective health was assessed with a single global question "How would you describe your health status?" Response options were given on a five-point scale ('good'; 'rather good'; 'fair'; 'rather poor'; 'poor').

Use of psychotropic medicines was asked as a part of list containing various different medicines and products "How often you have used the following medicines or products during the past year?" Psychotropic medicines in the list were 'depression medicines', 'sleeping pills', and 'sedatives'. The respondents were asked to give the frequency of use as days for each given medicine ('none'; 'less than 10 days'; '10–59 days'; '60–180 days (2–6 months)'; 'over 180 days (over 6 months)').

4.6.4 Psychosocial factors

Social support was measured using the Brief Social Support Questionnaire (Sarason *et al.* 1987). The sum score (range 0–36) was dichotomized using lowest decile of the distribution as an indication of low social support (Korkeila *et al.* 2005). *Hostile personality* was measured by expressed aggression (Koskenvuo *et al.* 1988). The summary measure (range 3–21) was dichotomized using highest decile to indicate hostile personality. *Subjective stress* was assessed with the four-item Reeder Stress Inventory measuring the stressfulness of daily activities (Reeder *et al.* 1973, Metcalfe *et al.* 2003). The

summary measure (range 4–20) was dichotomized using the highest quartile to indicate high level of subjective stress. *Symptoms of depression* were assessed with the 21-item Beck Depression Inventory (BDI) scale (Beck *et al.* 1988).

4.7 ELIGIBILITY AND HANDLING OF MISSING INFORMATION

Because the focus of this study was on binge drinking occasions, eligible participants were those men and women who reported consuming any alcohol at baseline measurement. Abstainers were therefore excluded from the sub-studies. Previous research has shown that reasons for abstaining are a probable source of unmeasured confounding. Reasons to abstain from alcohol are frequently related to poor health status and history of substance abuse (Fillmore *et al.* 1998, Green *et al.* 2001). Abstainers were those respondents who either reported that they had not consumed any alcohol in their lifetime, those who reported that they "do not use alcohol" or they drank alcohol "once a year or less often", or their average total intake was recorded as zero.

In each sub-study, those with missing information on some of the analysis variables were excluded from the analyses. The analyses were therefore based on complete case analyses. Excluding respondents with missing information was based on the fact that only a small proportion of respondents had missing information in the analysis variables. In sub-studies I, II, and IV, the proportion of respondents with missing information was 3.4%, and in sub-study III, 2.4%, of the total samples.

4.8 STATISTICAL PROCEDURES

Table 11 shows the main methodological characteristics of the sub-studies I–IV.

Table 11 Methodological characteristics of the sub-studies I to IV.

Sub-study	Participants	Design	Main statistical methods	Main dependent variables	Main independent variables	Covariates/confounders adjusted for
I	21 204 alcohol-drinking men and women aged 20 to 54 years at baseline.	Cross-sectional study using baseline data, linked with register-based follow-up data.	Multivariate binary logistic regression models. Results expressed as odds ratios and their 95% confidence intervals.	Risky drinking indicated by hazardous weekly intake according to Finnish guidelines, intoxications, hangovers, alcohol-induced pass-outs, and alcohol-specific diagnoses.	Socioeconomic disadvantage measured by low educational level, history of unemployment, current unemployment, being on disability pension, and history of financial difficulties.	Age. Models separately for men and women.
II	21 204 alcohol-drinking men and women aged 20 to 54 years at baseline.	Prospective cohort study using baseline measurement, linked with register-based follow-up data.	Receiver operating characteristics (ROC) curves, and Cox proportional hazard models. Results expressed as areas under the ROC curve, and hazard ratios and their 95% confidence intervals.	Hospitalizations and deaths related to alcohol by definition (ICD-10, Finnish modification codes), and intake exceeding the Finnish guidelines for hazardous weekly intake.	Drinking frequency, total intake, subjectively defined intoxications, hangovers, and alcohol-induced pass-outs.	Gender, age, educational level, living alone, unemployment, family history of alcohol problems, age of drinking onset, and cigarette smoking.
III	16 111 alcohol-drinking men and women aged 20 to 54 years at baseline.	Prospective two-wave cohort study with measurement points at baseline and after five years, linked with register-based follow-up data.	Multivariate binary logistic regression models. Results expressed as odds ratios and their 95% confidence intervals and as percentage reduction in odds ratios after adjusting for mediators and confounders.	Incident suboptimal subjective health.	Total intake, subjectively defined intoxications, hangovers, and alcohol-induced pass-outs.	Gender, age, educational level, living alone, unemployment, social support, physical activity, cigarette smoking, family history of alcohol problems, length of drinking history, beverage-specific intake separately for beer, wine, and spirits, depressive symptoms, use of psychotropic medicines, and hospitalizations due to alcohol-specific causes, depression, ischemic heart disease, or other cardiovascular disease.
IV	15 926 alcohol-drinking men and women aged 20 to 54 years at baseline	Prospective two-wave cohort study with measurement points at baseline and after five years, linked with register-based follow-up data.	Ordinal logistic regression models i.e. proportional odds models. Results expressed as odds ratios and their 95% confidence intervals.	Self-reported symptoms of depression measured with the Beck Depression Inventory.	Total intake, subjectively defined intoxications, hangovers, and alcohol-induced pass-outs.	Gender, age, language status, family history of alcohol problems, educational level, living alone, unemployment, social support, hostile personality, subjective stress, symptoms of depression at T1, duration of depression medication, divorced between T1 and T2, became unemployed between T1 and T2.

4.8.1 Sub-study I

In sub-study I, data was analysed from the baseline measurement and linked with information on alcohol-specific hospitalizations and deaths. The analysis sample consisted of 21 204 alcohol-drinking men and women.

The dependent variable was risky drinking. Risky drinking was operationalized using five different dichotomous indicators capturing different aspects of risky drinking: hazardous weekly intake, intoxications, hangovers, alcohol-induced pass-outs, and alcohol-specific diagnoses. The indicator of alcohol-specific diagnoses consisted of men and women who had either died, or were hospitalized at least once during the seven-year follow-up period after the baseline due to alcohol-specific causes by definition (according to the ICD-10, Finnish modification). The majority of these diagnoses were related to symptoms of alcohol dependence, or diseases of stomach, liver or pancreas. For the purpose of comparison, gender-specific prevalence of hazardous intake was used in determining the cut-off values for intoxications, hangovers, and alcohol-induced pass-outs (see Appendix 4 for the cut-off values used in dichotomizing frequency of intoxications, hangovers, and pass-outs). In addition, a composite variable was coded, which indicated whether the respondent had any of the five indicators of risky drinking.

The independent variables were educational level, employment history during the past three years, and history of experiencing financial hardships, all of which were considered to indicate different aspects of socioeconomic disadvantage. Educational level was dichotomized to indicate low educational level (no vocational education or vocational course or vocational school). Employment history was a composite variable with five categories (currently employed and no history of unemployment; currently employed and at least one previous episode of unemployment; currently unemployed; on disability pension; other). The category ‘other’ consisted of students, house mothers and fathers, those on other type of pension than disability pension, and those with undefined employment status. History of experiencing financial hardships was categorized into three categories (never; during the past five years or earlier; during the past six months).

The main method of analysis was binary logistic regression (Hosmer & Lemeshow 2000). Results from multivariate logistic regression models are expressed as odds ratios and their 95% confidence intervals. All models were stratified by gender and adjusted for age.

4.8.2 Sub-study II

In sub-study II, data was analysed from the baseline measurement and linked with information on alcohol-specific hospitalizations and deaths. The analysis sample consisted of 21 204 alcohol-drinking men and women.

Two separate criterion standards were used to assess the relative performance of the three binge drinking measures in identifying drinkers at risk for current and future alcohol-specific harm. First, hazardous intake was defined using the Finnish gender-specific guidelines for hazardous weekly intake. Second, the ICD-10, Finnish modification codes were used to identify hospitalizations and deaths due to alcohol-specific causes.

The main independent variables were frequency of intoxications, hangovers, and alcohol-induced pass-outs (see Appendix 4 for the cut-off values used in categorizing these variables). For the purpose of comparison with the above three binge drinking measures, frequency of drinking (converted to times per year and categorized as 3–4; 6; 12–52; 104; ~365 times i.e. daily or almost daily), and categorized total intake were also included. Average total intake was first categorized into gender-specific quartiles and the upper quartile was split into two, using the gender-specific limit for hazardous drinking (categories for women 1–26; 27–39; 40–78; 79–191; >191 g/week; for men 1–48; 49–78; 79–150; 151–287; >287). Total intake was also categorized into 10% equal intervals according to gender-specific intake distributions.

The effects of the following confounders were adjusted for in regression models: gender, age, educational level (university; polytechnic or college; vocational school or apprenticeship contract; vocational course or no vocational education), living alone (yes; no), unemployed (yes; no), family history of alcohol problems (yes; no; do not know), age of drinking onset (<15; 15–17; >17 years), and number of cigarettes smoked daily (0; 1–9; 10–19; >19).

The data were analysed using receiver operating characteristic curves (ROC), and Cox proportional hazard models (Cox & Oakes 1984). The results from the ROC analyses are expressed as areas under the ROC curves (AUC) and their 95% confidence intervals. AUCs were used to assess the overall performance of each binge drinking measure in differentiating at-risk drinkers. The results from the multivariate regression models are expressed as hazard ratios (HR) and their 95% confidence intervals. The assumptions for proportional hazard models were inspected visually, separately for each analysis variable, and no violations of assumptions were observed.

4.8.3 Sub-study III

In sub-study III, data was used from the baseline measurement and the repeated measurement after five years, then linked with information on alcohol-specific hospitalizations, hospitalizations due to depression, and hospitalizations due to ischemic heart disease and other cardiovascular diseases. The main analysis sample consisted of 13 213 alcohol-drinking men and women who did not report suboptimal subjective health at T1.

The main dependent variable was a dichotomous variable indicating incident suboptimal subjective health. Suboptimal health was defined as health status being reported either as 'fair', 'rather poor', or 'poor'. Incident suboptimal subjective health was defined as health status being 'rather good' or 'good' at T1, but below 'rather good' at T2.

The main independent variables were frequency of intoxications, hangovers, and alcohol-induced pass-outs (see Appendix 4 for the cut-off values used in categorizing these variables). Total intake was converted to number of standard drinks consumed, and then categorized into gender-specific quartiles and the upper quartile was further split into two, using the gender-specific limit for hazardous weekly intake according to the Finnish guidelines (the resulting categories in standard drinks for women 1–2; 3–4; 5–6; 7–15; >15; for men 1–4; 5–7; 8–12; 13–23; >23 drinks/week).

The effects of the following confounders were adjusted for in regression models: gender, age, educational level (university; polytechnic or college; vocational school or apprenticeship contract; vocational course or no vocational education), living alone (yes; no), unemployment (yes; no), social support (high; low), low physical activity (less than 1h of any type physical activity weekly; at least 1h weekly), number of cigarettes smoked daily (none; 1–9; 10–19; >19), family history of alcohol problems (yes; no; do not know), years of alcohol exposure (<10; 10–25; 26–35; >35), symptoms of depression (BDI scores categorized as 0–9; 10–19; >19), any use of psychotropic medicines during the past year measured from T2 (yes; no), hospitalizations after T1 due to alcohol-specific causes, depression, ischemic heart disease, or other cardiovascular diseases, and weekly intake of beer, wine and other mild alcoholic beverages, and spirits, converted to number of standard drinks. The following categories were used for beer: none; less than one; 1–4; 5–12; at least 13 standard drinks per week; for wine and other mild alcoholic beverages: none; less than one; 1–4; 6–15; at least 16 standard drinks per week; and for spirits: none; less than two; 2–5; 7–12; at least 13 standard drinks per week.

Binary logistic regression models were used to analyse the data. The results are expressed as odds ratios (OR) and their 95% confidence intervals.

4.8.4 Sub-study IV

In sub-study IV, data was used from the baseline measurement and repeated measurement after five years, then linked with information on hospitalizations due to depression and alcohol-specific causes. The analysis sample consisted of 15 926 alcohol-drinking men and women.

The main dependent variable was self-reported symptoms of depression assessed with the 21-item Beck Depression Inventory (BDI) scale (Beck *et al.* 1988). The sum score of responses was categorized into a variable with six categories (0; 1–4; 5–9; 10–14; 15–19; >19). A dichotomous variable was coded to indicate 'at least mild symptoms' (1=BDI score >9). A continuous variable indicating change in the BDI score between T1 and T2 was calculated by subtracting the T1 score from the T2 score (range -40 to 38).

The main independent variables were frequency of intoxications, hangovers, and alcohol-induced pass-outs (see Appendix 4 for the cut-off values used in categorizing these variables). Total intake was categorized separately for men and women according to quintiles of intake distributions (1–19; 20–48; 49–78; 79–138; >138 g/week for women, and 1–37; 38–110; 111–168; 169–255; >255 g/week for men). Heavy intake was defined as the highest quintile. Variables indicating change in alcohol consumption were calculated by subtracting the T1 value from the T2 value. For average intake the range of values indicating change over time was -864 to 900 g/week, for frequency of intoxications and hangovers from -104 to 104, and for frequency of pass-outs from -7 to 7 times per year.

The effects of the following confounders were adjusted for in regression models: gender, age, official mother tongue of the respondent (Finnish or Swedish speaker), family history of alcohol problems (yes; no; do not know), educational level (at least college vs. lower), whether the respondent lived alone (yes; no), unemployment (no; yes), social support (high; low), expressed hostility (no; yes), level of subjective stress (low; high), T1 depression scores (BDI) categorized into six levels, duration of depression medication (none; <3 months; 3–6 months; >6 months), whether the respondent had divorced between T1 and T2 (6 months ago; 5 years ago; earlier or never), and whether the respondent became unemployed between T1 and T2 (6 months ago; 5 years ago; earlier or never).

The main results are based on ordinal logistic regression models (Hosmer & Lemeshow 2000). The results of these proportional odds models are expressed as odds ratios (OR) with their 95% confidence intervals. The proportional odds assumption was tested with the score test. No violations of proportional odds assumption were detected. Multiple linear regression models were used to analyse the relations between continuous change measures.

5 RESULTS

5.1 BINGE DRINKING AND SOCIOECONOMIC DISADVANTAGE (SUB-STUDY I)

Of the men, 9.4% exceeded the Finnish guidelines for hazardous weekly intake (5.4% women), 14.5% reported at least weekly intoxications (4.4% women), 16.0% reported at least twice monthly hangovers (6.1% women), and 14.9% reported at least twice a year alcohol-induced pass-outs (4.3% women). During the seven-year follow-up, 2.5% of the men and 0.6% of the women died or were hospitalized at least once due to alcohol-specific causes. When information from all these five separate indicators was combined, 30% of the men and 13% of the women reported at least one type of risky drinking pattern or experienced the alcohol-specific outcome. Strong correlation between indicators of risky drinking was observed only for at least weekly intoxications and at least twice monthly hangovers (tetrachoric correlation in men, r=0.78; in women r=0.82), and for weekly hazardous intake and at least weekly intoxications in men (r=0.72). All other correlations were below 0.70, indicating only modest overlap between the indicators of risky drinking.

A socioeconomic gradient in binge drinking was consistently found across all indicators of binge drinking, but the magnitude of the gradient was somewhat larger in indicators reflecting higher intensity drinking occasions, such as frequent hangovers, and alcohol-induced pass-outs (figures 6 and 7). The results also show that the magnitude of the socioeconomic gradient varied by indicator of socioeconomic disadvantage.

The overall associations were, to a large extent, comparable in men and women. In both men and women, binge drinking was associated with low educational level, past episodes of unemployment among those currently unemployed, current unemployment, being on disability pension, and experiencing financial hardships. In men, current unemployment, and in women, being on disability pension, showed the largest socioeconomic gradients in binge drinking. Adjusting for weekly hazardous intake slightly attenuated the odds ratios, but weekly hazardous intake did not fully explain the associations between binge drinking and indicators of socioeconomic disadvantage.

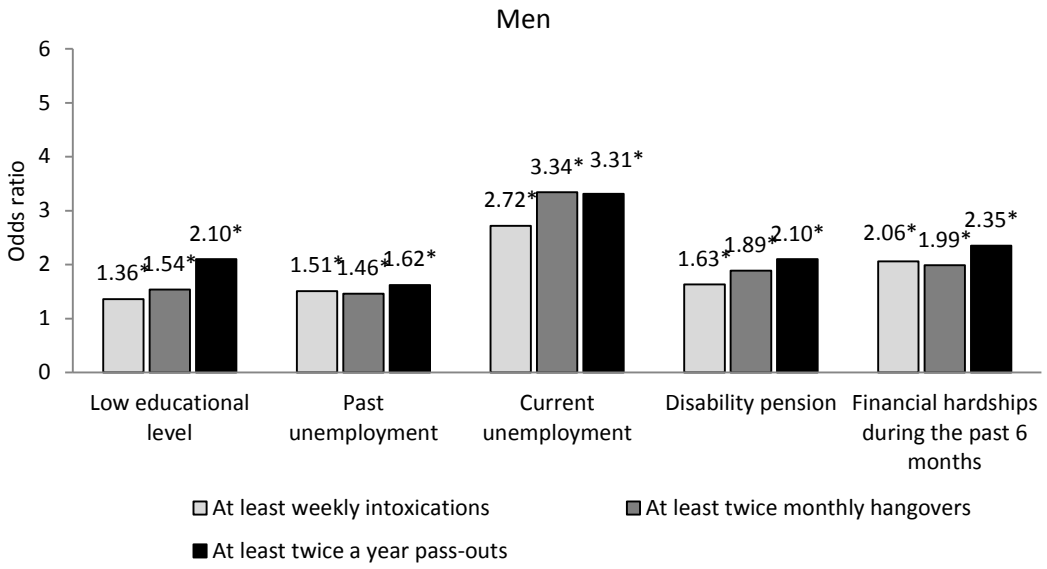

Figure 6 Age adjusted odds ratios for indicators of socioeconomic disadvantage and indicators of binge drinking in alcohol-drinking men. The reference category for low educational level was university or college. For financial hardships during the past 6 months the reference category was 'never'. The reference category for the other indicators was currently employed persons with no history of unemployment during the past three years. Statistically significant odds ratios at level $P<0.05$ are indicated by an asterisk.

Figure 7 Age adjusted odds ratios for indicators of socioeconomic disadvantage and indicators of binge drinking in alcohol-drinking women. The reference category for low educational level was university or college. For financial hardships during the past 6 months the reference category was 'never'. The reference category for the other indicators was currently employed persons with no history of unemployment during past three years. Statistically significant odds ratios at level $P<0.05$ are indicated by an asterisk.

5.2 PERFORMANCE OF BINGE DRINKING MEASURES IN IDENTIFYING AT-RISK DRINKERS (SUB-STUDY II)

Of the men, 91% experienced at least occasional intoxications (77% women), 79% at least occasional hangovers (64% women), and 26% at least occasional alcohol-induced pass-outs (12% women). The amount of average intake increased with the frequency of binge drinking. The frequency levels for hangovers reflected slightly higher intake throughout, than those of intoxications.

Of the men who experienced weekly intoxications, 50% had a weekly average intake of 22 drinks (median, 261 g/week), and of those men who experienced weekly hangovers, 50% had a weekly average intake of 24 drinks (median, 290 g/week). Mean intake in these frequency categories were 26 drinks and 30 drinks, respectively. Of the women who experienced weekly intoxications, 50% had a weekly average intake of 13 drinks (median, 150 g/week), and of those women who experienced weekly hangovers, 50% had a weekly average intake of 14 drinks. Mean intake in these categories were 18 drinks and 19 drinks, respectively. Of the men who experienced an alcohol-induced pass-out at least seven times, 50% had a weekly average intake of 24 drinks (median, 291 g/week), and of the women in the same category, 50% had a weekly average intake of 22 drinks (median, 267 g/week). (Unpublished results)

Frequency of intoxications and frequency of hangovers were strongly correlated (bivariate polychoric correlation 0.84).

Of the 21 204 eligible men and women, 310 persons (of which 77% were men) experienced an alcohol-related endpoint during the seven-year follow-up. Among these persons (Alc+ cases), the level of average intake was considerably higher in all binge drinking frequency categories. The median intake among Alc+ cases was two-fold among those experiencing weekly intoxications or weekly hangovers, compared to those not experiencing the alcohol-related endpoint (Alc- cases), but experiencing as frequent intoxications or hangovers. Among Alc+ cases, the frequency levels for hangovers reflected larger intake than those of intoxications. This difference was more profound among Alc+ cases, than among Alc- cases.

Of the Alc+ cases, 40% experienced weekly intoxications, and 27% experienced weekly hangovers, compared to 9% and 4% among Alc- cases, respectively (table 12). Similarly, of the Alc+ cases, 64% (about two-thirds) had experienced an alcohol-induced pass-out at least once during the past 12 months, compared to 18% (about one in five) among Alc- cases.

Figure 8 illustrates the relative performance and the cut-off point specific performance of each binge drinking measure in identifying hazardous drinkers. Alcohol-induced pass-outs performed poorest of all intensity measures, irrespective of cut-off point. In identifying hazardous drinkers, the performance of frequency of intoxications, and frequency of hangovers was similar, overall and across cut-off points (i.e. the ROC curves were parallel). (Unpublished results)

Table 12 Proportion of responders drinking at or above a given frequency category, and proportion of those exceeding weekly hazardous intake[a] by subjective measures of binge drinking.

Annual frequency	No alcohol-specific diagnosis (n=20 894)		Alcohol-specific diagnosis (n=310)	
	At or above the cut-off value (%)	Hazardous drinkers (%)	At or above the cut-off value (%)	Hazardous drinkers (%)
Intoxications				
None	100	1	100	0
1 to 5 times	83	2	97	27
6 to 11 times	45	3	84	5
12 to 23 times	35	5	77	13
24 to 51 times	22	12	62	34
52+ times	9	37	40	73
Hangovers				
None	100	2	100	36
1 to 5 times	71	4	91	34
6 to 11 times	28	8	68	11
12 to 23 times	21	9	59	19
24 to 51 times	10	18	44	35
52+ times	4	45	27	81
Pass-outs				
None	100	5	100	33
Once	18	8	64	19
2 to 3 times	9	18	52	42
4 to 6 times	3	27	29	45
7+ times	1	50	15	81

[a]Hazardous intake defined according to Finnish guidelines for men >287 g, and for women >191 g per week. Alcohol-drinking men and women aged 20 to 54 years at baseline.

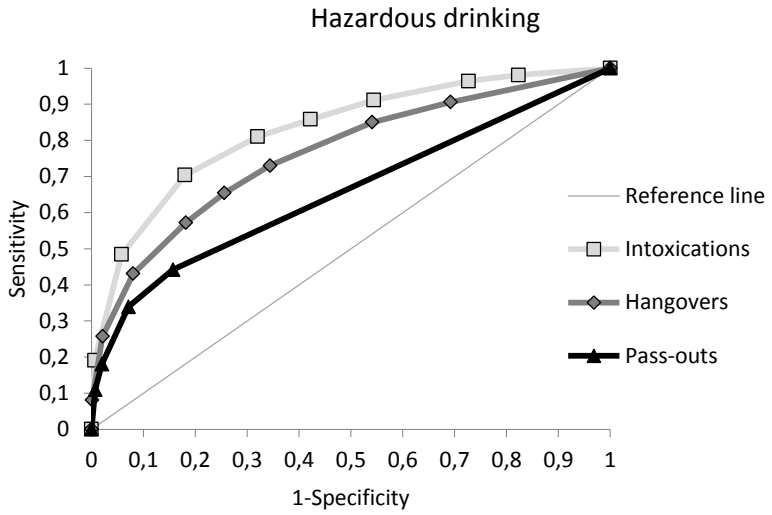

Figure 8 Receiver operating characteristic (ROC) curves for binge drinking measures in identifying hazardous drinking (for men >287 g, and for women >191 g per week). Unpublished results.

Figure 9 shows that there is very little difference in the relative cut-off point specific performance between the binge drinking measures in identifying drinkers at risk for future alcohol-related hospitalization or death. Frequency of alcohol-induced pass-outs showed somewhat better discriminatory power

at the lower frequency levels, compared to the other intensity measures, but due to lack of higher frequency levels in the original measure, the ROC curve converged towards the 0.5 diagonal line. (Unpublished results)

Table 13 shows that frequency of intoxications had significantly better overall performance in identifying hazardous drinkers compared to frequency of hangovers, and frequency of alcohol-induced pass-outs (i.e. the 95% confidence intervals did not overlap). The overall performance in identifying drinkers at risk for future alcohol-specific hospitalizations or death did not differ between the three intensity measures, and all three intensity measures had a comparable performance with average intake (table 13).

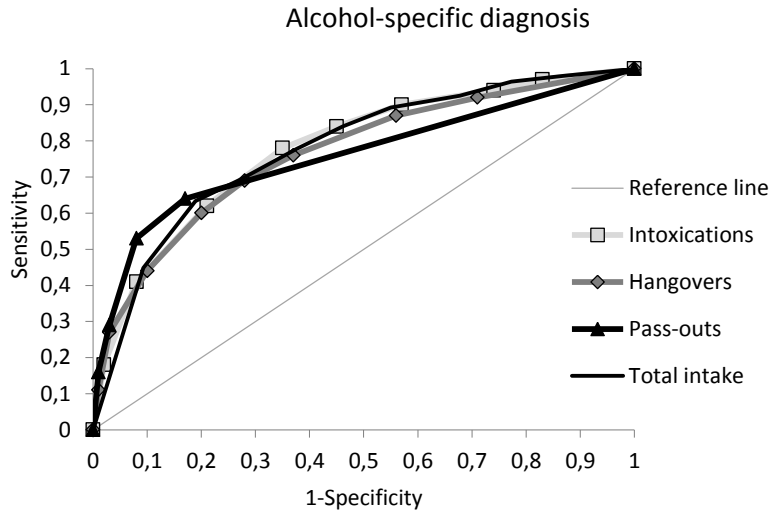

Figure 9 Receiver operating characteristic (ROC) curves for binge drinking measures and total intake in identifying drinkers at risk for future alcohol-related harm. Unpublished results.

Table 13 Overall performance of subjective measures of binge drinking in identifying at-risk drinkers. Areas under the receiver operating characteristics curve (AUC).

	Hazardous intake[a] (n=1519)	Future alcohol-specific diagnosis[b] (n=310)
	AUC (95%CI)	AUC (95%CI)
Intoxications	0.83 (0.82,0.84)	0.78 (0.75,0.81)
Hangovers	0.76 (0.75,0.78)	0.76 (0.73,0.79)
Pass-outs	0.66 (0.64,0.67)	0.76 (0.73,0.79)
Total intake[c]		0.78 (0.75,0.81)

[a]Hazardous intake at baseline according to Finnish guidelines for men >287 g and for women >191 g per week. [b]Alcohol-specific hospitalization or death by definition (ICD-10, Finnish modification) during seven years of follow-up. [c]Categorized into 10% equal intervals according to gender-specific intake distributions.

5.3 SUBJECTIVE MEASURES OF BINGE DRINKING AND ADVERSE HEALTH OUTCOMES

5.3.1 Binge drinking as a predictor of alcohol-specific hospitalization or death (Sub-study II)

All three measures of binge drinking showed strong graded relations with future alcohol-specific hospitalization or death (figures 10 and 11), when gender and age were adjusted for (P<0.001 for trend for each measure of binge drinking). Experiencing intoxications or hangovers weekly – compared to never experiencing them – both resulted in a nearly 30-fold risk for the combined alcohol-specific outcome.

When total average weekly intake (as a continuous variable) was additionally adjusted for, weekly intoxications were associated with almost 12-fold risk for the alcohol-related outcome (HR=11.89; 95%CI=5.99, 23.62), and weekly hangovers were associated with a 10-fold risk for experiencing the outcome (HR=10.42; 95%CI=6.47, 23.62). (Unpublished results)

The relative predictive power of the binge drinking measures was tested by adding all three measures of binge drinking simultaneously in the same model, together with gender, age, total intake, and overall drinking frequency. In this model, the hazard ratios attenuated markedly, but all three measures retained significant linear trend (P=0.001), and statistically significant hazard ratios. Thus, all three measures of binge drinking predicted future alcohol-specific hospitalization or death independent of each other, and of average total intake.

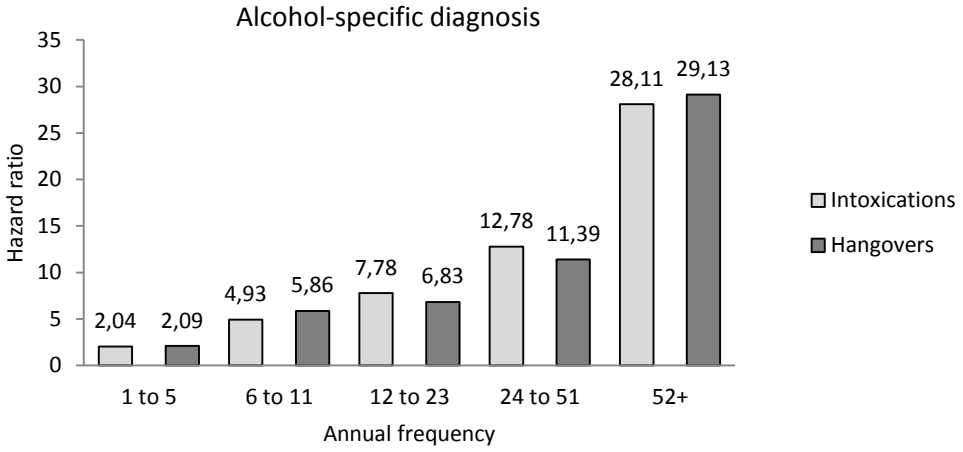

Figure 10 Annual frequencies of intoxications and hangovers at baseline predicting alcohol-specific hospitalizations or death during seven years of follow-up. Reference category 'None'. Hazard ratios adjusted for gender and age. All hazard ratios were statistically significant at level P<0.05. Alcohol-drinking men and women aged 20 to 54 years at baseline.

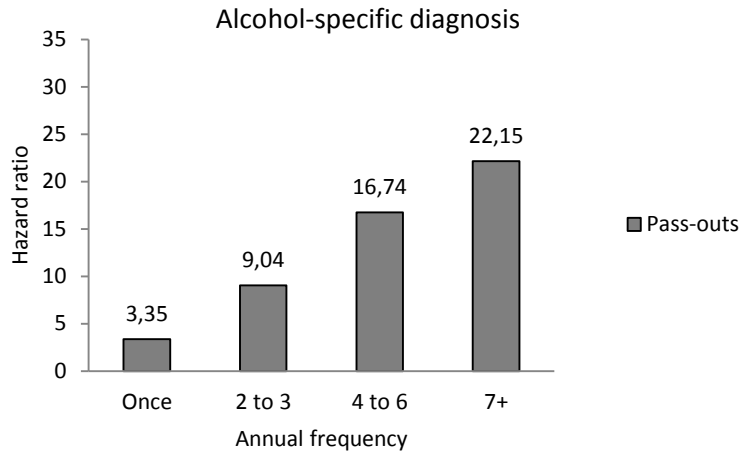

Figure 11 Annual frequency of alcohol-induced pass-outs at baseline predicting alcohol-specific hospitalizations or death during seven years of follow-up. Reference category 'None'. Hazard ratios adjusted for gender and age. All hazard ratios were statistically significant at level *P*<0.05. Alcohol-drinking men and women aged 20 to 54 years at baseline.

5.3.2 Binge drinking as a predictor of suboptimal subjective health (Sub-study III)

Of the eligible baseline current drinkers (n=13 213) who reported their subjective health as optimal (rather good or good) at T1, 12% (n=1606) rated their health as being suboptimal (fair or below fair) at T2 (i.e. T2 incident cases). Of these baseline drinkers, 82% reported at least once a year intoxications, 69% at least once a year hangovers, and 16% at least once a year alcohol-induced pass-outs.

All three measures of binge drinking showed significant graded relations with incident suboptimal subjective health after five years (figures 12 and 13), when gender and age were adjusted for (P<0.001 for trend for all three measures).

Further adjusting for beverage-specific total intake attenuated the odds ratios slightly, but all previously statistically significant odds ratios retained statistical significance. When the relative predictive power of the binge drinking measures was tested by adding all three measures of binge drinking simultaneously in the same model, together with total intake, only annual frequency of alcohol-induced pass-outs retained statistically significant linear trend in predicting incident suboptimal subjective health (*P*<0.001 for trend).

The effects of potential mediating factors, i.e. self-reported symptoms of depression at T2, use of psychotropic medicines at T2, and hospitalizations after T1 (depression, IHD, OCVD, and alcohol-specific causes), were tested separately for each binge drinking measure. These models showed that the effects of binge drinking on suboptimal subjective health were markedly, but not fully, mediated through depression and alcohol-specific health outcomes.

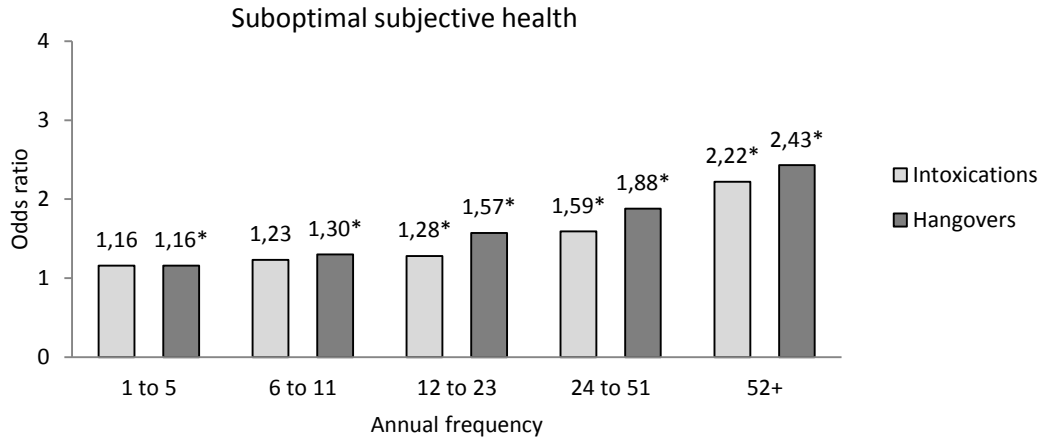

Figure 12 Annual frequencies of intoxications and hangovers predicting incident suboptimal subjective health after five years. Reference category 'None'. Odds ratios adjusted for gender and age. Statistically significant odds ratios at level *P*<0.05 are indicated by an asterisk. Alcohol-drinking men and women aged 20 to 54 years at baseline.

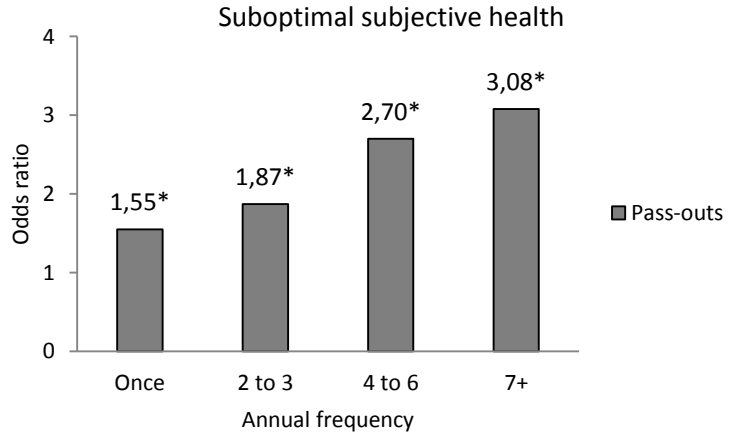

Figure 13 Annual frequency of alcohol-induced pass-outs predicting incident suboptimal subjective health after five years. Reference category 'None'. Odds ratios adjusted for gender and age. Statistically significant odds ratios at level *P*<0.05 are indicated by an asterisk. Alcohol-drinking men and women aged 20 to 54 years at baseline.

5.3.3 Binge drinking as a predictor of symptoms of depression (Sub-study IV)

The prevalence of at least mild depressive symptoms (BDI>9) at T2 was 20%. Of the eligible baseline current drinkers (n=15 926) whose total BDI score was below 10 (indicating no depression) at T1, 12% (n=1537) experienced an increase in their depressive symptoms at T2, such that their BDI total score was over 9 (indicating at least mild depression), i.e. these were T2 incident cases. For the majority of the incident cases, the symptoms were mild (BDI

10–18). Between T1 and T2, 63 persons were hospitalized due to depression. Of the baseline current drinkers, 81% reported at least once-a-year intoxications, 69% reported at least once-a-year hangovers, and 16% reported at least once-a-year alcohol-induced pass-outs.

A positive graded relation with a significant linear trend was found between all three baseline measures of binge drinking and symptoms of depression at T2 ($P<0.001$ for trend for each measure of binge drinking), when gender and age were adjusted for (figures 14 and 15).

The relative predictive power of binge drinking measures was tested by adding all three measures of binge drinking simultaneously in the same model, together with gender, age, and total intake. In this model, only frequency of hangovers retained statistically significant point estimates and a trend. Dichotomized baseline binge drinking measures also predicted hospitalizations due to depression between T1 and T2, when gender and age were adjusted for (table 14).

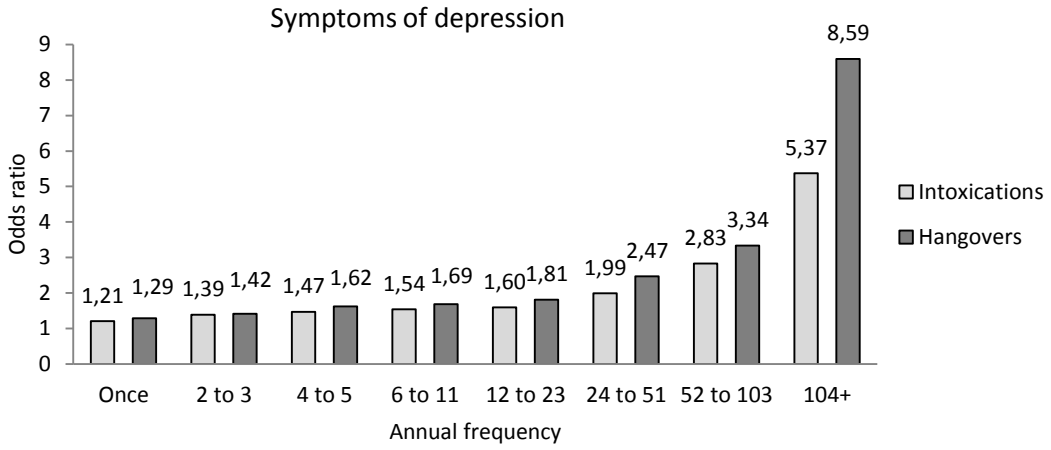

Figure 14 Annual frequencies of intoxications and hangovers at baseline predicting symptoms of depression after five years. Reference category 'None'. Odds ratios from ordinal logistic regression models adjusted for gender and age. All hazard ratios statistically significant at level $P<0.05$. Alcohol-drinking men and women aged 20 to 54 years at baseline.

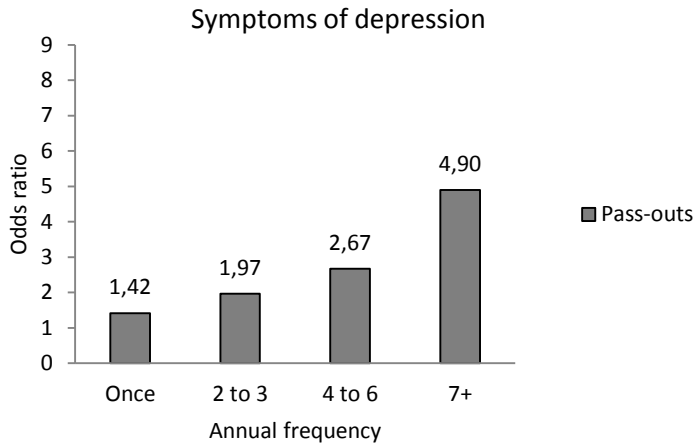

Figure 15 Annual frequency of alcohol-induced pass-outs at baseline predicting symptoms of depression after five years. Reference category 'None'. Odds ratios from ordinal logistic regression models adjusted for gender and age. All hazard ratios statistically significant at level *P*<0.05. Alcohol-drinking men and women aged 20 to 54 years at baseline.

Table 14 Measures of binge drinking at baseline predicting hospitalization due to depression[a] during seven years of follow-up. Binary logistic regression models adjusted for gender and age.

	Hospitalization due to depression (n=63)
	OR (95%CI)
Frequency of intoxications	
Less than monthly	1.00
At least once a month	2.65 (1.55,4.55)
Frequency of hangovers	
Less than monthly	1.00
At least once a month	4.42 (2.59,7.56)
Frequency of pass-outs	
None	1.00
At least once a year	2.97 (1.73,5.08)

[a]According to the ICD-10, Finnish modification codes F32, F33, F341.

6 DISCUSSION

The overall purpose of this study was to validate measures of subjectively defined intoxications, hangovers, and alcohol-induced pass-outs as indicators of at-risk drinking patterns in epidemiological research. In the following sections, the results of this study are discussed from the point of view of validity, which is here reflected against the level of confidence that can be placed on conclusions that the above three subjective measures of binge drinking are feasible measures of binge drinking patterns, and that the measures are able to reflect causal mechanisms determining the relation between alcohol exposure and adverse health outcomes.

6.1 VALIDITY OF SUBJECTIVE MEASURES OF BINGE DRINKING AS INDICATORS OF AT-RISK DRINKING PATTERNS

Of the alcohol-drinking men, nine out of ten, and of the women, three out of four, reported any intoxications during the past 12 months. Hangovers were also commonly reported; of the men, eight out of ten, and of the women, two out of three, reported any hangovers during the past 12 months. Alcohol-induced pass-outs were less commonly reported but still one out of four of the men, and one in ten of the women, reported experiencing any pass-outs during the past 12 months. In other words, of the alcohol-drinking men and women aged 20 to 54 years, the majority reported at least once a year binge drinking. In particular among men, frequent binge drinking was common; around 15% of the alcohol-drinking men reported at least weekly intoxications (around 5% of the women). These results are in line with previous Finnish studies that have consistently shown that drinking until intoxication is a common characteristic of Finnish drinking habits particularly in men, but also increasingly among women (Mäkelä *et al.* 2001, Huhtanen *et al.* 2011, p.22).

All the three binge drinking measures had high face validity, i.e. the meaning of each measure was most likely evident to the respondent. It can therefore be assumed that persons who reported intoxications, hangovers, and pass-outs also experienced these events, meaning that the prevalence of binge drinking in the data is not likely inflated. Measures with high face validity have some advantages over measures with lower face validity. Measures with high face validity reduce measurement error by improving ease of responding, by reducing misclassification of risk status, and by reducing number of missing information due to difficulties in understanding the question. In addition, results obtained using measures with high face validity are easier to interpret, and the implications of the results are easier to formulate into a format which is comprehensible and acceptable e.g. by decision-makers and the general public.

High face validity, however, may come with a cost if, for example, perceived social acceptability issues affect the likelihood of a certain type of

response. A weakness of measures with high face validity is that perceived social acceptability may bias responses in some population groups. This is a potential problem particularly in cross-cultural comparisons where population groups differ in cultural norms related to alcohol use in general and binge drinking in particular. In such situations it is necessary to adjust face validity, terminology used to refer to binge drinking, so that it is culturally sensitive to socially acceptable expressions and manifestations of alcohol intoxication.

Given the high prevalence of binge drinking in Finnish society in general, which reflects high acceptability of drinking until intoxication, it is unlikely that intentional misreporting of binge drinking would have considerably affected the results of this study. In other words, the high prevalence of binge drinking in Finland supports the feasibility of using measures with high face validity, such as those used in this study.

Given that no information was available on the intensity (degree of severity) of each of the individual binge drinking measures reported, it is possible that some of the persons reporting pass-outs were reporting the event more as 'falling asleep' rather than as losing consciousness due to severe alcohol poisoning. The mix of markedly different intensity levels captured by the given binge drinking measure could potentially affect the practical utility of the measure, which would indicate that the measures are 'too subjective' and contain too much variation to be epidemiologically useful. The question then is how confidently it can be said that persons reporting a given frequency level of alcohol-induced pass-outs are at risk for adverse health outcomes due to their drinking, i.e. that they are 'true risky drinkers'?

Evaluation of results against three validation hypotheses

The performance of the three binge drinking measures in coherently reflecting levels of at-risk drinking can be assessed against three validation hypotheses (White *et al.* 2008). *First*, subjects at higher frequency levels, within a given binge drinking measure, should be more likely heavier drinkers than subjects at lower frequency levels. *Second*, subjects at higher frequency levels, within a given binge drinking measure, should have higher risk of experiencing adverse health outcomes than subjects at lower frequency levels. *Third*, if all the three instruments (intoxications, hangovers, and pass-outs) measure the same underlying exposure, i.e. binge drinking, all three instruments should yield coherent and comparable results on the same outcomes. The third hypothesis also requires that the observed results for the three binge drinking measures are in line with previous research conducted on the relation between binge drinking and adverse health outcomes.

First hypothesis. The results consistently showed that subjects at higher frequency levels, within a given binge drinking measure, drank on average more than subjects at lower frequency levels. Hangover frequency levels were associated with slightly higher average intake than the corresponding

frequency levels of intoxication, suggesting that hangovers on average reflected somewhat heavier drinking than intoxications, despite the high correlation between the two measures. The proportion of hazardous drinkers, defined according to the Finnish guidelines (for men ≥24 drinks and for women ≥16 Finnish standard drinks per week), also increased with the frequency levels of all three binge drinking measures. However, the performance of the three binge drinking measures in discriminating between non-hazardous and hazardous drinkers was relatively modest, except perhaps for intoxications. As these results support the first validation hypothesis described above to be true, i.e. higher binge drinking frequency levels are associated with heavier drinking, they also indicate that different persons are captured by hazardous drinking guidelines based on total intake and by using cut-off values of these binge drinking measures, meaning that a cut-off value of at least weekly intoxications is not an alternative measure for weekly hazardous total intake.

The first validation hypothesis can also be assessed against outcomes of heavy drinking, such as hospitalizations and deaths due to alcohol-specific causes, from the perspective that receiving an alcohol-specific diagnosis is an indication of heavy drinking. Binge drinking should therefore be more common among persons who have an alcohol-specific diagnosis than among persons who do not have such a diagnosis (validation against an extreme group). The results showed that all three binge drinking measures were markedly more frequently reported by persons who were diagnosed with an alcohol-specific diagnosis than by persons who were not. The relative difference in the prevalence of binge drinking between those who received an alcohol-specific diagnosis and those who did not was higher at higher frequency levels for all three binge drinking measures, and furthermore, the relative differences were largest in binge drinking measures potentially capturing higher intensity binge drinking, i.e. in hangovers and pass-outs. For example, half (52%) of the persons who received an alcohol-specific diagnosis during the seven-year follow-up period reported experiencing an alcohol-induced pass-out at least twice during the past 12 months, whereas only one in every ten persons (9%) among those who did not receive an alcohol-specific diagnosis reported experiencing pass-outs as often. Similarly, of the persons who received an alcohol-specific diagnosis 15% reported experiencing pass-outs more frequently than every second month (7+ times a year), whereas only 1% of the persons who did not receive an alcohol-specific diagnosis reported experiencing pass-outs as often.

The performance of the three binge drinking measures in discriminating between persons receiving future alcohol-specific diagnosis (i.e. those who likely were current heavy/at-risk drinkers) and those who did not, showed that all three binge drinking measures performed equally well, and more importantly, their discriminatory power was as good as that of total weekly intake. The latter means that using the six frequency levels of experiencing alcohol-induced pass-outs during the past 12 months for screening persons at risk for alcohol-specific diagnoses performed equally

well as the total intake which required recoding average weekly consumption for beer, wine, and spirits separately, converting the consumption into grams of ethanol, and summing it up to total weekly consumption. This result has important implications as it shows that asking a simple and straightforward question about frequency of experiencing alcohol-induced pass-outs has high practical utility in identifying persons at-risk for future alcohol-specific morbidity and mortality.

To conclude, the results described above provide confirmation to the first validation hypothesis, that all the three binge drinking measures are able to coherently capture levels of alcohol exposure reflecting aspects of heavy drinking.

Second hypothesis. The results on the ability of each binge drinking measure to predict adverse health outcomes showed coherent and consistent relations. In predicting future alcohol-specific diagnoses, symptoms of depression after five years, and suboptimal subjective health after five years, all three binge drinking measures showed positive graded relations. In predicting future alcohol-specific diagnoses all three measures predicted the outcome independently of total intake, and of each other, meaning that all three measures had predictive power for the outcome, which was not captured by total intake or the other two binge drinking measures. This implicates that all three binge drinking measures contain additional information in relation to total intake and to each other of the risk profile of persons who later experience alcohol-specific adverse outcomes. As this finding suggests that the causal process leading to experiencing alcohol-specific outcomes involves multiple dimensions of alcohol exposure, including level of total intake, and frequencies of intoxications, hangovers, and pass-outs, it also further support the conclusion that these three measures must be seen as complementary to each other and not as alternatives.

All in all, also the second validation hypothesis described above is supported by the results of this study, i.e. higher frequency levels of the binge drinking measures are associated with higher relative risk of adverse outcomes compared to lower frequency levels.

Third hypothesis. The first requirement in the third validation hypothesis was that the three measures would have comparable relations with the same outcomes, which, if true, would serve as an indication of relative validity given that all the three indicators measure the same underlying construct (i.e. binge drinking). The results showed that a comparable socioeconomic gradient was found for all three measures of binge drinking; the overall performance in identifying drinkers at risk for alcohol-specific outcomes in a general population sample was adequately high in terms of discriminatory power (AUCs over 0.75) and the performance did not differ between the three measures; and that the shapes of the risk functions in predicting alcohol-specific outcomes, symptoms of depression, and suboptimal subjective health were comparable. The fact that the 'best' indicator for a given outcome varied, e.g. for suboptimal subjective health it

was the frequency of pass-outs, whereas for symptoms of depression it was the frequency of hangovers, likely reflect variation in causal mechanisms leading to adverse health outcomes, including differences in distributions of other relevant disease determinants captured by the different binge drinking measures. Again this finding highlights the complementary relative contribution of these measures to capture varying dimensions of alcohol exposure.

The second requirement in the third validation hypothesis was that the results observed in this study for the three binge drinking measures are in line with previous research. Comparable results with previous research using different measures of binge drinking or using same measures of binge drinking within a different population provide support to the findings of this study by providing support to a conclusion that the measures are able to tap in on a similar causal mechanism underlying the relation between measures of binge drinking and adverse health outcomes. However, dissimilar results with previous research would not necessarily invalidate the findings of this study, but would indicate a source of heterogeneity, either in causal mechanisms or in population characteristics, for example.

The evidence on the performance of subjective intoxications in predicting adverse health outcomes is probably strongest in relation to cardiovascular outcomes (Roerecke & Rehm 2010), but evidence on other outcomes, such as depression, alcohol use disorders, certain cancers, and injury, also support the utility of subjective intoxications and hangovers as risk markers of alcohol exposure (Poikolainen 1982, Poikolainen & Simpura 1983, Dawson 1998, Hämäläinen *et al.* 2005, Piasecki *et al.* 2005, O'Brien *et al.* 2006). The predictive utility of subjective intoxications and particularly the predictive utility of hangovers, have, however, received only very limited research attention internationally, and therefore direct comparisons between instruments and outcomes is difficult. Furthermore, evidence on the predictive utility of alcohol-induced pass-outs is almost non-existent. The only two available previous studies have shown that the frequency of alcohol-induced pass-outs predicts cognitive impairment (Virta *et al.* 2010) and dementia (Järvenpää *et al.* 2005). Although these two studies used the same Finnish dataset to analyse the relations between pass-outs and the outcomes of interest, these studies provide support to the utility of alcohol-induced pass-outs as a risk marker for adverse health outcomes by indicating that the predictive utility of alcohol-induced pass-outs is not confined to the population represented in the HeSSup dataset or to the selected outcomes analysed.

The few previous Finnish studies which have assessed the predictive utility of subjective intoxications and hangovers have linked intoxications (Poikolainen 1983) and hangovers (Poikolainen 1983, Kauhanen *et al.* 1997, Rantakömi *et al.* 2013) in particular to deaths from cardiovascular diseases. These studies used dichotomous indicators of intoxications and hangovers and therefore the shape of the risk function was not established, but similar results have also been found elsewhere by using different cut-off values for

subjective intoxications (Kozarevic *et al.* 1982, Hammar *et al.* 1997, Dorn *et al.* 2007).

It seems that only one previous study (Dawson 1998) has assessed the association between subjective intoxications and alcohol use disorders (AUD). Dawson showed that frequency of subjective intoxications had the strongest association with AUD diagnoses (according to the DSM-IV) of the other consumption indicators in the study, which were frequency of drinking 5+ drinks, morning drinking, and total intake. Only one previous study (Piasecki *et al.* 2005) has established the prognostic utility of hangovers in predicting future AUD. Piasecki *et al.* (2005) found that hangover frequency at T1 predicted diagnoses from AUDs (according to the DSM-III) after seven and 11 years, independent of gender, family history of alcohol use disorders and of several confounders.

It seems that only one previous study (Hämäläinen *et al.* 2005) has established the association between subjective intoxications and depression. This cross-sectional study showed that frequent intoxications were associated with depression assessed with the Short Form of the University of Michigan version of the Composite International Diagnostic Interview (UM-CIDI). It seems that no previous studies have assessed the utility of hangovers in predicting depression. However, decreased sense of general wellbeing, feelings of guilt, remorse, and even suicidal thoughts the morning after a heavy drinking session have been associated with hangover (McKinney 2010), and these symptoms may trigger or intensify depression among susceptible persons (Harburg *et al.* 1981). However, when results from studies using other measures of binge drinking, such as the X+ number of drinks per drinking occasion are taken into account, the association between binge drinking and depression has been established (Manninen *et al.* 2006, Levola *et al.* 2011), but not consistently across different populations (Wang & Patten 2002, Haynes *et al.* 2005). It has been suggested that aspects of alcohol exposure measurement would be more important in explaining inconsistent findings across studies than measurement of depression (Graham *et al.* 2007), suggesting that the risk of depression may be confined to a specific pattern or to a specific threshold of alcohol consumption. It should be also noted that the prevalence of binge drinking within a population under study is an important factor in determining the ability of binge drinking measures to capture risk of depression. If the prevalence of binge drinking is low within a population, it means that a relatively small proportion of the population level causal pathway explaining depression is accounted for binge drinking, and thus lack of statistical power to observe significant associations may also explain some of the inconsistent findings.

No previous prospective studies have assessed the utility of subjective intoxications or hangovers in predicting suboptimal subjective health, but some previous cross-sectional studies have assessed the relation between binge drinking and various indicators of subjective health. A previous Finnish study found that frequency of intoxications failed to show

statistically significant association with suboptimal subjective health after beverage-specific intake was adjusted for (Poikolainen & Vartiainen 1999), suggesting that beverage type, i.e. beer and spirits, or the factors correlating strongly with beverage type, would be a more important determinant of poor subjective health than intoxications. Another study found that frequency of intoxications together with spirits consumption was associated with poor health-related quality of life (Stranges *et al.* 2006). These results indicate that binge drinkers tend to prefer mainly beer and spirits and therefore beverage preference carries important information on the risk profile of drinkers at risk for suboptimal subjective health. Binge drinking measured by drinking X+ number of drinks per drinking occasion has been shown to be associated with poor health-related quality of life (Okoro *et al.* 2004, Wen *et al.* 2012), and with suboptimal subjective health (Valencia-Martin *et al.* 2009).

In conclusion, empirical evidence on the utility of binge drinking measures in general, and measures of subjective intoxications in particular, in predicting future adverse health outcomes is scarce. All in all, however, there is evidence that provides support to the findings of this study by showing that despite some inconsistencies, the results observed in this study are in line with previous research. This suggests that subjective intoxications, hangovers and alcohol-induced pass-outs are able to reflect underlying causal pathways similar to those established in other studies, conducted within different populations or by using different measures of binge drinking. Comparison with previous research, therefore, provides further support to the relative validity of the three binge drinking measures.

6.2 METHODOLOGICAL CONSIDERATIONS

Strengths of the study

This study had several strengths in terms of study design, sample size, and study variables. First, three of the four sub-studies utilized prospective design in studying the relations between subjective measures of binge drinking and adverse health outcomes. For some of the outcomes it was also possible to utilize prospective follow-up information derived from national health registers, meaning that this information was free from potential reporting bias. The two measurement points for recording alcohol consumption enabled some of the variability in alcohol consumption over time to be taken into account (sub-study IV). Second, the large sample size from a source population with a high prevalence of binge drinking ensured statistical power to detect differences, enabled providing detailed information on the shape of the risk functions due to fine categorizations of binge drinking frequency levels, and ensured that enough cases with the outcome of interest were captured by the study sample, particularly in

relation to relatively rare outcomes, such as alcohol-specific hospitalizations and deaths. Third, these sub-studies were the first general population studies that have been able to prospectively study the relative performance of subjective intoxications, hangovers, and alcohol-induced pass-outs against various adverse health outcomes in the same study. The three subjective measures of binge drinking had high face validity and did not require the potentially complex estimation of standard drinks (Gill *et al.* 2004, Kerr *et al.* 2005, Kraus *et al.* 2005). Fourth, measurement of health related factors other than alcohol consumption enabled conducting comprehensive statistical analyses taking into account various health outcomes, and enabled for adjustment of potential confounding factors.

Generalizability

The low baseline response proportion of 40% is likely to raise questions about generalizability and how possible bias may have affected the results. As Rothman (1998, p.133) points out, the scientific goal of the study should be kept in mind when discussing generalizability issues. The purpose of this study was to establish the overall shapes of the risk functions and the relative performance of subjective measures of binge drinking as proxies for at-risk drinking patterns, and not to establish the prevalence of binge drinking in the Finnish general population.

The key question therefore is whether the study data are biased so that the associations observed in this study between the three subjective measures of binge drinking and the selected adverse health outcomes would be markedly different from the (true) associations found in the general Finnish population? When studying disease aetiology based on biological mechanisms, it is possible to obtain unbiased and generalizable results from 'unrepresentative' cohort as long as the groups under comparison are equally biased and there is enough heterogeneity in the values of the study variables, and as long as all major subgroups of the target population are represented in the study population, even if under-represented, so that the effects of these subgroups can be controlled for in the statistical analyses (Rothman 1998, p.133).

It is clear that the HeSSup data is less heterogeneous than the actual Finnish general population because of the original sampling design with the specific age groups, non-response at T1 and T2, and due to the restriction criteria used in the sub-studies. This, however, does not bias the analyses on diagnostic and predictive utility and on the relative performance of the subjective measures of binge drinking presented here.

Under-reporting and measurement error

All alcohol exposure measures in this study were based on self-reports. It is well known that survey participants tend to under-report their consumption (Gmel & Rehm 2004). It has been suggested that heavy drinkers would

under-report their consumption more than other drinking groups (Poikolainen 1991). This could lead to bias in the rank order of the drinking groups in the data, which would then bias the shape of the risk functions describing the relationship between alcohol consumption and the health outcomes. If the relative difference in under-reporting alcohol consumption is systematic and large enough, the risk estimates for the heaviest drinking group would be diluted in comparison to the lower drinking groups, because the lower-risk groups would be contaminated with high-risk heavy drinkers. As a result, the shape of the risk function could deviate from positive linearity in the upper end of the drinking measures. However, the potential non-proportional under-reporting of alcohol consumption may more likely affect risk functions for total consumption levels (Poikolainen 1991), and affect less risk functions for the frequency levels of binge drinking, as there is no obvious reason for why respondents at higher (true) frequency levels would have greater difficulty to accurately recall binge drinking occasions than respondents at lower frequency levels.

Effects of non-response

The register-based non-response analysis (Korkeila *et al.* 2001) of the baseline study population showed that men, older age groups, less educated, divorced, unemployed, current smokers, and persons using anti-depressants were less likely to participate. A mortality analysis showed that non-respondents had around two-fold excess total mortality compared with those who responded (Suominen *et al.* 2012).

In their non-response analysis, Korkeila *et al.* (2001) used only heavy total intake to assess the potential bias related to alcohol consumption. Based on their analysis they concluded that there would not be marked selection in relation to heavy total intake. However, given that Korkeila *et al.* (2001) did not analyse non-response in relation to the three subjective measures of binge drinking, it is possible that binge drinkers participated less frequently than those who were not binge drinkers. Higher non-response among binge drinkers than among non-binge drinkers, however, does not invalidate the analyses of association, as stated in the previous section discussing generalizability.

In contrast, selection within the binge drinking group will potentially affect the effect estimates reported in this study. It is possible that non-response is more common among sicker binge drinkers than among binge drinkers with better health (Koskenvuo *et al.* 1987, Meiklejohn *et al.* 2012). If this is indeed the case here, it would dilute the effect estimates of binge drinking on the selected outcomes, and would therefore indicate poorer performance for binge drinking measures, because a smaller proportion of binge drinkers would develop the outcome of interest during follow-up. It is therefore likely that the associations and effect sizes observed here are conservative estimates rather than overestimates.

Limitations

The data had some limitations that need to be acknowledged. Despite the relatively large baseline sample size, some comparisons were still based on a small number of individuals. The data did not allow separate analysis by gender for alcohol-specific outcomes, due to a small number of alcohol-specific diagnoses among women during the follow-up period. It is unclear how these measures of binge drinking would perform in populations with a markedly different prevalence of binge drinking, e.g. due to different social acceptability of binge drinking. The data collection of the baseline study sample was restricted to persons aged 20 to 54 years, which means that the results do not necessarily apply to populations younger or older than that. The most important limitation perhaps was that the study did not include the 5+ drinks measure for direct comparison with subjective intoxications, hangovers, and alcohol-induced pass-outs.

7 CONCLUSIONS

The results of this study support the feasibility and utility of self-reported frequencies of intoxications/drunkenness, alcohol-induced hangovers, and alcohol-induced pass-outs as indicators of at-risk drinking patterns in epidemiological research. These three indicators show high potential, both theoretically and based on the results of this study in terms of empirical evidence, to be used as outcome indicators of binge drinking pattern.

The results showed that these three indicators were acceptable to respondents in a population where binge drinking is common. This was evidenced by the observed high overall prevalence of intoxications, hangovers and pass-outs, and by the distribution of responses at the high frequency levels of each indicator. The high face validity of these indicators combined with the high acceptability of the indicators in the Finnish general population support the feasibility and practical utility of these indicators in epidemiological research in particular, but also potentially in clinical settings and in public health practice as well.

The results demonstrated that in terms of methodological performance, the three indicators were complementary to each other, meaning that each measure contained additional information of the risk of adverse health outcomes that was not captured by the other two indicators. The relative performance of the indicators varied by the type of adverse health outcome potentially reflecting differences in underlying causal mechanisms. The results also showed that the three indicators were not alternatives to total intake.

Although not tested in this study, it is unlikely that these three indicators would be alternatives to any other quantity measure either, such as the 5+ drinks measure. The choice of alcohol exposure measures in a given study should be based on understanding of the underlying causal mechanism between alcohol exposure and the outcome of interest, or in the absence of this information, multiple exposure measures should be used to determine the best fitting statistical model. This is of paramount importance particularly in epidemiological studies attempting to establish effect sizes (level of risk) between levels of exposure and a given adverse health outcome. If the purpose is to merely rank respondents in relation to average exposure levels, e.g. for the purpose of adjusting for the effects of alcohol exposure alongside other confounders, cruder measurement of exposure levels can be used, but the effects of residual confounding due to inaccurate alcohol exposure measurement should still be kept in mind.

The results showed that self-reported intoxications, alcohol-induced hangovers, and alcohol-induced pass-outs had both diagnostic and prognostic utility in identifying harmful alcohol drinking patterns. Future studies should determine whether and how these three indicators could be used in developing a binge drinking scale, because these indicators can capture the motivation to drink alcohol, i.e. a drunkenness-prone drinking habit, and in particular frequent alcohol-induced hangovers and pass-outs

can capture the motivation to continue drinking until intoxication, despite of experienced negative consequences of one's alcohol use. Motivation to drink until intoxication, and lack of willingness or ability to change drinking behaviour despite negative consequences, are potentially important characteristics of drinkers, which on one hand define binge drinking, and on the other hand explain the relation between binge drinking and various adverse health outcomes. Quantity measures, such as the 5+ drinks measure, without information on outcome of drinking, cannot capture these motivational aspects of binge drinking behaviour, because quantity measures are not indicators of alcohol intoxication. This is an additional advantage of these three subjective indicators of intensity of alcohol exposure, which further supports the utility of self-reported intoxications, hangovers, and pass-outs as indicators of binge drinking pattern.

8 IMPLICATIONS TO PUBLIC HEALTH

Because asking about the number of drinking occasions leading to intoxication, experiencing a hangover, or passing out as a consequence of drinking is much simpler and quicker than asking about quantities of intake of various different beverage types and beverage ethanol strengths, these results have important implications to clinical and public health practice. Public health messages should be formulated to encourage avoiding/cutting-down drinking until intoxication in general, but highlighting the prognostic role of experiencing alcohol-induced hangovers and alcohol-induced pass-outs could potentially enhance that message further. In particular passing out as a consequence of drinking indicates that drinking is not likely under a full control of the drinker, and that the drinker is at significant risk of experiencing alcohol-related harm. Frequency of experiencing hangovers and alcohol-induced pass-outs could therefore be promoted to be used as face valid self-screening instruments of at-risk drinking patterns.

Future research should in particular test whether a dichotomous question about experiencing any pass-outs during the previous year could be used as a pragmatic screening instrument in clinical settings by comparing its performance against standard multi-item screening instruments, such as the Alcohol Use Disorders Identification Test (AUDIT). Future studies should also determine the prevalence of hangovers and in particular the prevalence of alcohol-induced pass-outs among Finnish male drinkers. Although this study was not well suited for assessing prevalence, the markedly high prevalence of around every one in four alcohol-drinking men aged 20–54-years experiencing an alcohol-induced pass-out at least once a year in this study population, is a worrying finding from a public health perspective. If the prevalence of alcohol-induced pass-outs is as high as this, it would mean that a significantly large proportion of Finnish working-aged men could be at risk of alcohol poisoning each year with potentially severe outcomes (Poikolainen *et al.* 2002).

The observed linear relations between the three indicators of binge drinking and the various adverse health outcomes suggest that preventive efforts should target the overall number of drinking occasions leading to intoxication. As the risk functions are linear, or close to linear, there is no obvious population level threshold value that could be used to separate 'low-risk' drinkers from 'high-risk' drinkers in relation to binge drinking frequency.

The high prevalence of binge drinking in the Finnish population combined with the fact that the risk of adverse health outcomes seems to increase linearly as a function of binge drinking frequency, suggests that the population level burden of harm related to binge drinking in Finland comes, to a considerable extent, from the majority of the alcohol-drinking population, i.e. the group of drinkers who are not necessarily defined as heavy drinkers based on their total intake, and are not necessarily alcohol dependent.

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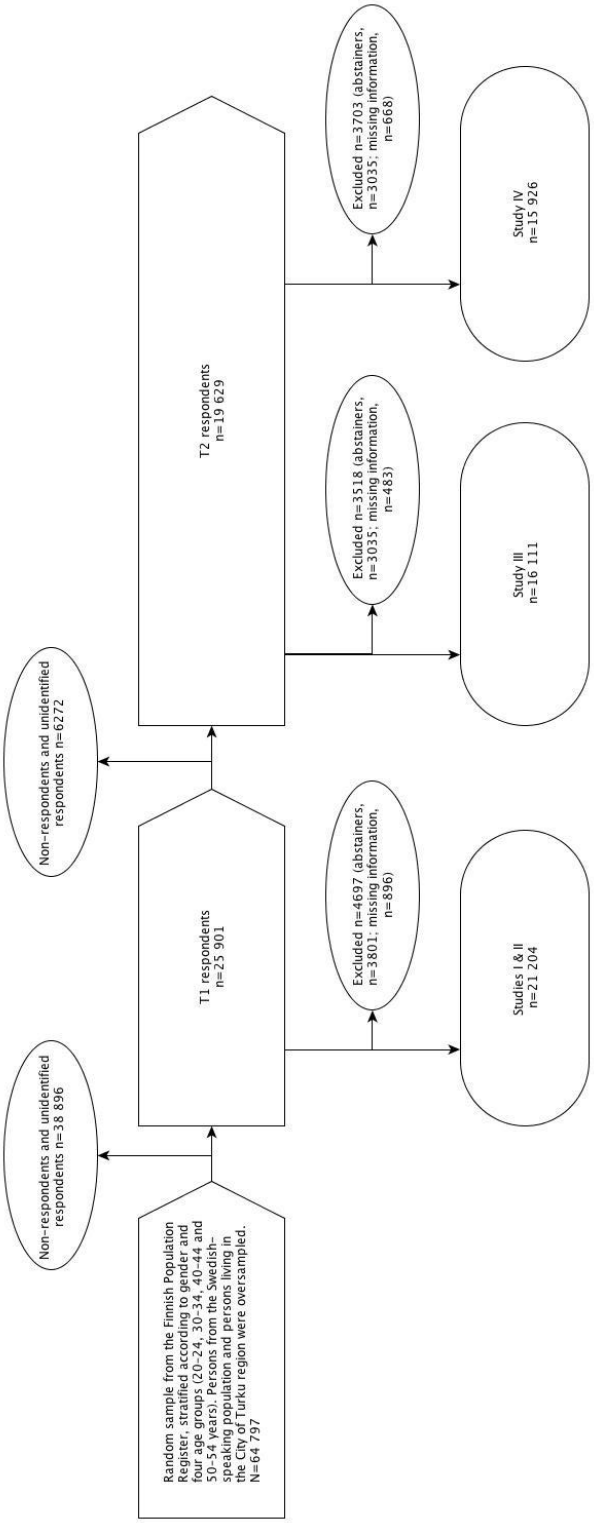
APPENDICES

Appendix 1 The structure of the HeSSup data and the sub-studies I–IV.



Appendix 2a The original format and order of the alcohol consumption questions in the HeSSup survey translated into English.

Age of drinking onset and lifetime abstaining was asked as

How old were you, when you first time drank at least one glass of any alcoholic beverages?

____ years old

____ I have never drank alcohol, I have been an abstiner all my life.

Drinking frequency was asked as

How often do you drink alcohol nowadays? Which one of the following alternatives best describes your consumption of beer, wine and spirits?

1) I don't use alcohol
2) Once a year or less
3) 3-4 times a year
4) About once in two months
5) About once – twice a month
6) Once a week
7) Couple of times a week
8) Daily or almost daily

Frequency of intoxications/drunkenness was asked as

How often during the past 12 months you have been drunk?

1) Never
2) Once
3) 2-3 times
4) 4-5 times
5) About once in two months
6) About once a month
7) 2-3 times a month
8) About once a week
9) Couple of times a week or more

Frequency of hangovers was asked as

How often during the past 12 months you have suffered a hangover?

1) Never
2) Once
3) 2-3 times
4) 4-5 times
5) About once in two months
6) About once a month
7) 2-3 times a month
8) About once a week
9) Couple of times a week or more

For the estimation of total quantity of alcohol intake, the respondent was asked to estimate one's beverage specific intake as

How much do you drink the following alcoholic beverages on average?

Beer in a WEEK

1) Not at all
2) Less than a bottle (0.33l)
3) 1-4 bottles
4) 5-12 bottles
5) 13-24 bottles
6) 25-47 bottles
7) Over 48 bottles

Wine or other mild alcoholic beverages in a WEEK

1) Not at all
2) Less than a glass
3) 1-4 glasses
4) 1-2.5 bottles
5) 3-4.5 bottles
6) 5-9 bottles
7) Over 10 bottles

Spirits in a MONTH

1) Not at all
2) Less than half a bottle (0.5l)
3) 0.5-1.5 bottles
4) 2-3.5 bottles
5) 4-9 bottles
6) 10-19 bottles
7) Over 20 bottles

Frequency of alcohol-induced pass-outs was asked as

”Have you ’passed out’ while drinking alcohol during the past year?

1) Never
2) Once
3) 2-3 times
4) 4-6 times
5) 7 times or more

Appendix 2b The original format and order of the alcohol consumption questions in the HeSSup survey in Finnish.

Juomisen aloitusikä ja elinikäinen raittius kysyttiin

Kuinka vanha olit, kun ensimmäisen kerran joit vähintään lasillisen jotain alkoholijuomaa?

____ -vuotias

____ en ole koskaan juonut alkoholia, olen ollut raitis koko elinikäni.

Juomistiheys kysyttiin

Kuinka usein nautit nykyään alkoholia? Mikä seuraavista vaihtoehdoista kuvaa parhaiten oluen, viinin ja väkevien alkoholijuomien käyttöäsi?

1) en käytä alkoholia
2) kerran vuodessa tai harvemmin
3) 3-4 kertaa vuodessa
4) noin kerran parissa kuukaudessa
5) noin kerran – pari kertaa kuukaudessa
6) kerran viikossa
7) pari kertaa viikossa
8) päivittäin tai lähes päivittäin

Humaltumistiheys kysyttiin

Kuinka usein olet ollut viimeksi kuluneiden 12 kuukauden aikana humalassa?

1) en kertaakaan
2) kerran
3) 2-3 kertaa
4) 4-5 kertaa
5) noin kerran kahdessa kuukaudessa
6) noin kerran kuukaudessa
7) 2-3 kertaa kuukaudessa
8) noin kerran viikossa
9) pari kertaa viikossa tai useammin

Krapulatiheys kysyttiin

Kuinka usein olet ollut viimeksi kuluneiden 12 kuukauden aikana krapulassa?

1) en kertaakaan
2) kerran
3) 2-3 kertaa
4) 4-5 kertaa
5) noin kerran kahdessa kuukaudessa
6) noin kerran kuukaudessa
7) 2-3 kertaa kuukaudessa
8) noin kerran viikossa
9) pari kertaa viikossa tai useammin

Kokonaiskulutuksen arvioimiseksi vastaajaa pyydettiin raportoimaan kulutus juomalajeittain

Miten paljon nautit seuraavia alkoholijuomia keskimäärin?

Olutta VIIKOSSA

1) en yhtään
2) vähemmän kuin pullollisen (0,33l)
3) 1-4 pulloa
4) 5-12 pulloa
5) 13-24 pulloa
6) 25-47 pulloa
7) yli 48 pulloa

Viiniä tai muita mietoja alkoholijuomia VIIKOSSA

1) en yhtään
2) vähemmän kuin lasillisen
3) 1-4 lasillista
4) 1-2.5 pullollista
5) 3-4.5 pullollista
6) 5-9 pullollista
7) yli 10 pullollista

Väkeviä KUUKAUDESSA

1) en yhtään
2) alle puoli pullollista (0,5l)
3) 0.5-1.5 pullollista
4) 2-3.5 pullollista
5) 4-9 pullollista
6) 10-19 pullollista
7) yli 20 pullollista

Sammumistiheys kysyttiin

Oletko "sammunut" alkoholinkäytön yhteydessä viimeksi kuluneen vuoden aikana?

1) en kertaakaan
2) kerran
3) 2-3 kertaa
4) 4-6 kertaa
5) 7 kertaa tai useammin

Appendix 3 Conversion of reported beverage-specific alcohol consumption to grams of ethanol

Original response options	Assumed alcohol content in grams of ethanol by container volume	Multiplying factor	Resulting grams of ethanol in a WEEK
Beer in a WEEK			
Not at all		0.0	0
Less than a bottle (0.33l)		0.75	9
1 to 4 bottles		2.5	30
5 to 12 bottles	12→	8.5	102
13 to 24 bottles		18.5	222
25 to 47 bottles		36.0	432
Over 48 bottles		48.0	576
Wine and other mild alcoholic beverages in a WEEK			
Not at all		0.0	0
Less than a glass	12→	0.75	9
1 to 4 glasses		2.5	30
1 to 2.5 bottles		1.75	126
3 to 4.5 bottles	72→	3.75	270
5 to 9 bottles		7.0	504
Over 10 bottles		10.0	720
Spirits in a MONTH*			
Not at all		0	0
Less than half a bottle (0.5l)		0.09	14
0.5 to 1.5 bottles		0.25	39
2 to 3.5 bottles	156→	0.68	106
4 to 9 bottles		1.62	253
10 to 19 bottles		3.62	565
Over 20 bottles		5.0	780

*Converted to consumption in a week.

Appendix 4 Categorizations of binge drinking measures in sub-studies I to IV.

Original response options and the corresponding annual frequency given in the parenthesis	Categorizations used in sub-studies			
	Sub-study I	Sub-study II	Sub-study III	Sub-study IV
Intoxications Never (0) Once (1) 2-3 times (2-3) 4-5 times (4-5) About once in two months (6) About once a month (12) 2-3 times a month (24-36) About once a week (52) Twice weekly or more often (≥104)	-Dichotomized as '1=at least weekly' vs. 0='less often'. Cut-off value based on the prevalence of hazardous weekly intake. -For the purpose of sensitivity analysis dichotomized as '1=at least once a year' vs. 0='never'.	-Converted to times per year and categorized as 0='never'; 1='1-5'; 2='6-12'; 3='24-36; 4='≥52 times'. -Original categorization used in estimating receiver operating characteristics curve.	-Converted to times per year and categorized as 0='never'; 1='1-5'; 2='6-11'; 3='12-23'; 4='24-51'; 5='≥52 times'. (NB. values in categories expressed as continuous, as opposed to the actual annual frequency represented in the original response options).	-Dichotomized as 1='≥12 times' vs. 0='up to 11 times'. -T2 variable dichotomized as 1='at least twice monthly' vs. 0='less often'. -Converted to times per year and categorized as 0='never'; 1='1-5'; 2='6'; 3='12'; 4='≥24 times'. -Continuous variable coded using the annual frequency of the original categorization. In case of range of values, the mid-point of the values was used.
Hangovers Never (0) Once (1) 2-3 times (2-3) 4-5 times (4-5) About once in two months (6) About once a month (12) 2-3 times a month (24-36) About once a week (52) Twice weekly or more often (≥104)	-Dichotomized as '1=at least twice monthly' vs. 0='less often'. Cut-off value based on the prevalence of hazardous weekly intake. -For the purpose of sensitivity analysis dichotomized as '1=at least once a year' vs. 0='never'.	-Converted to times per year and categorized as 0='never'; 1='1-5'; 2='6-12'; 3='24-36; 4='≥52 times'. -Original categorization used in estimating receiver operating characteristics curve.	-Converted to times per year and categorized as 0='never'; 1='1-5'; 2='6-11'; 3='12-23'; 4='24-51'; 5='≥52 times'. (NB. values in categories expressed as continuous, as opposed to the actual annual frequency represented in the original response options).	-Dichotomized as 1='≥12 times' vs. 0='up to 11 times'. -T2 variable dichotomized as 1='at least twice monthly' vs. 0='less often'. -Converted to times per year and categorized as 0='never'; 1='1-5'; 2='6'; 3='12'; 4='≥24 times'. -Continuous variable coded using the annual frequency of the original categorization. In case of range of values, the mid-point of the values was used.
Pass-outs Never (0) Once (1) 2-3 times (2-3) 4-6 times (4-6) 7 times or more often (≥7)	-Dichotomized as '1=at least twice a year' vs. 0='less often'. Cut-off value based on the prevalence of hazardous weekly intake. -For the purpose of sensitivity analysis dichotomized as '1=at least once a year' vs. 0='never'.	-Original categorization retained and converted to times per year.	-Original categorization retained and converted to times per year.	-Dichotomized as 1='at least once a year' vs. 0='never'. -Categorized as 0='never'; 1='once'; 2='at least 2 times'. -Original categorization retained and converted to times per year. -Continuous variable coded using the annual frequency of the original categorization. In case of range of values, the mid-point of the values was used.

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