

#### **MAURI AALTO**

## Prevalence and Brief Intervention of Heavy Drinkers in Primary Health Care

Lahti Project Study

#### **ACADEMIC DISSERTATION**

To be presented, with the permission of the Faculty of Medicine of the University of Tampere, for public discussion in the small auditorium of Building B, Medical School of the University of Tampere, Medisiinarinkatu 3, Tampere, on May 11th, 2001, at 13 o'clock.

University of Tampere Tampere 2001



#### **MAURI AALTO**

## Prevalence and Brief Intervention of Heavy Drinkers in Primary Health Care

Lahti Project Study

University of Tampere Tampere 2001

## Prevalence and Brief Intervention of Heavy Drinkers in Primary Health Care

#### ACADEMIC DISSERTATION

University of Tampere, Medical School, Department of General Practice National Public Health Institute, Department of Mental Health and Alcohol Research Tampere University Hospital, Department of Psychiatry Finland

#### Supervised by

Professor Kaija Seppä University of Tampere Docent Pekka Sillanaukee University of Tampere

#### Reviewed by

Docent Rauno Mäkelä University of Tampere Docent (Professor h.c.) Timo Pitkäjärvi University of Tampere

#### Distribution



University of Tampere Sales Office P.O. Box 617 33101 Tampere Finland

Cover design by Juha Siro

Printed dissertation Acta Universitatis Tamperensis 802 ISBN 951-44-5060-4 ISSN 1455-1616 Tel. +358 3 215 6055 Fax +358 3 215 7685 taju@uta.fi http://granum.uta.fi

Electronic dissertation
Acta Electronica Universitatis Tamperensis 93
ISBN 951-44-5061-2
ISSN 1456-954X
http://acta.uta.fi

Tampereen yliopistopaino Oy Juvenes Print Tampere 2001

## **CONTENTS**

LIS	ST OF	ORIGI	NAL PUI	BLICATIONS	7
ΑE	BREV	/IATIO	NS		8
ΑE	BSTRA	.CT			9
1	INTF	RODUC	TION		11
2	REV	IEW O	F THE LI	TERATURE	13
	2.1	The c	oncept of	alcohol problem	13
	2.2	Preve	ntion of a	alcohol problems	15
	2.3	Preva	lence of l	neavy drinking in primary health care and general	
		popul	ation		16
	2.4	Detec	tion of he	eavy drinking	18
		2.4.1	Self-rep	orted alcohol consumption	19
		2.4.2	Medical	history and clinical findings	20
		2.4.3	Structur	ed questionnaires	21
		2.4.4	Laborate	ory markers	23
	2.5	Brief	intervent	ion of heavy drinkers	24
		2.5.1	Descrip	tion of brief intervention	25
		2.5.2	Random	nized controlled brief intervention studies	27
			2.5.2.1	Primary health care: consultation based studies	28
			2.5.2.2	Primary health care: health screening based	
				studies and the WHO study	32
			2.5.2.3	Hospital based studies and studies with special	
				patient groups	32
			2.5.2.4	Considerations of brief intervention studies	33
3	AIM	S OF T	HE STUI	OY	35
4	SUB.	JECTS	AND ME	ETHODS	37
	4.1	Brief	intervent	ion study (II-V)	37
		4.1.1	Setting a	and screening of heavy drinking	37
		4.1.2	Recruitr	nent for brief intervention	39

		4.1.3 Study groups and content of brief intervention	40
		4.1.4 End point assessment	41
		4.1.5 Laboratory analyses	41
	4.2	Prevalence of heavy drinking and drinking habits study (I)	42
		4.2.1 Primary health care	42
		4.2.2 General population	43
	4.3	Statistical analyses	44
5	RESU	JLTS	45
	5.1	Prevalence of heavy drinking and drinking habits (I)	45
	5.2	Laboratory markers as indicators for brief intervention (II)	46
	5.3	Compliance rate and associated factors for entering brief	
		intervention (III)	48
	5.4	Effectiveness of brief intervention (IV,V)	49
6	DISC	USSION	53
	6.1	Subjects	53
	6.2	Methods	54
	6.3	Prevalence of heavy drinking and drinking habits (I)	55
	6.4	Laboratory markers as indicators for brief intervention (II)	57
	6.5	Compliance rate and associated factors for entering brief	
		intervention (III)	59
	6.6	Effectiveness of brief intervention (IV,V)	61
7	CON	CLUSIONS	65
8	SUM	MARY	67
9	ACK	NOWLEDGEMENTS	71
10	REFE	ERENCES	73
11	ORIC	GINAL PUBLICATIONS	83

#### LIST OF ORIGINAL PUBLICATIONS

This dissertation is based on the following original publications, which are referred to in the text by their Roman numerals. The original publications have been reproduced at the end of the dissertation with the kind permission of the copyright holders.

- I Aalto M, Seppä K, Kiianmaa K and Sillanaukee P (1999): Drinking habits and prevalence of heavy drinking among primary health care outpatients and general population. Addiction 94:1371-1379 (www.tandf.co.uk).
- II Sillanaukee P, Aalto M and Seppä K (1998): Carbohydrate-deficient transferrin and conventional alcohol markers as indicators for brief intervention among heavy drinkers in primary health care. Alcohol Clin Exp Res 22:892-896.
- III Aalto M and Sillanaukee P (2000): Compliance rate and associated factors for entering an alcohol brief intervention treatment programme. Alcohol Alcohol 35:372-376.
- IV Aalto M, Saksanen R, Laine P, Forsström R, Raikaa M, Kiviluoto M, Seppä K and Sillanaukee P (2000): Brief intervention for female heavy drinkers in routine general practice: a 3-year randomised, controlled study. Alcohol Clin Exp Res 24:1680-1686.
- V Aalto M, Seppä K, Mattila P, Mustonen H, Ruuth K, Hyvärinen H, Pulkkinen H, Alho H and Sillanaukee P: Brief intervention for male heavy drinkers in routine general practice: a three year randomized controlled study. Alcohol Alcohol, in press.

#### **ABBREVIATIONS**

ALAT Alanine aminotransferase

ASAT Aspartate aminotransferase

AUDIT Alcohol Use Disorders Identification Test

CAGE Acronym (Have you ever felt you ought to cut down on your

drinking? Have people annoyed you by criticising your

drinking? Have you ever felt guilty about your drinking? and

Have you ever had a morning eye-opener?); screening test for

heavy drinking

CDT Carbohydrate-deficient transferrin

CI Confidence interval

DSM Diagnostic and Statistical Manual of Mental Disorders

FRAMES Acronym (feedback, responsibility, advice, menu, empathy, self-

efficacy); recommended ingredients of brief intervention

GGT Gamma-glutamyltransferase

HMO Health Maintenance Organisation

ICD International Classification of Diseases

MAST Michigan Alcoholism Screening Test

MCV Erythrocyte mean corpuscular volume

Mm-MAST Malmö modified MAST

OR Odds ratio

SAAST Self-Administered Alcoholism Screening Test

SD Standard deviation

SRA Self-reported alcohol consumption

WHO World Health Organisation

#### **ABSTRACT**

The aim of brief intervention is to provide early intervention in heavy drinking, before or close to the onset of alcohol-related damage. It includes identifying of heavy drinking and short consultation sessions. The aims of this study were to estimate the prevalence of heavy drinking in primary health care and general population and among non-alcohol treatment-seeking early-phase heavy drinkers, to evaluate the usefulness of laboratory markers (CDT, MCV, ASAT, ALAT, GGT) in detection, a rate of compliance in entering brief intervention, and the effectiveness of a three-year long brief intervention carried out in the naturalistic environment of routine primary health care (effectiveness study).

Before the normal general practitioner's consultation time 14,548 consecutive patients were screened for heavy drinking. Of 658 males and 353 females identified as early-phase heavy drinkers 296 males and 118 females were randomised to one of the study groups: brief intervention group A (7 sessions), brief intervention group B (3 sessions), and control group C (minimal advice to reduce drinking). Brief intervention was given by a general practitioner, except for three sessions by a nurse in group A. Outcome measures were self-reported alcohol consumption and laboratory values. Subjects from the general population (n=544) were randomly selected by telephone.

Among men the prevalences of heavy drinking in the primary health care and general population were 17-20% and 16% (p≥0.05) and among women 6-9%, and 13% (p<0.05). The sensitivities of markers were low; not more than 40%. However, marker combinations reached a good sensitivity level of about 70%. Of the early-phase heavy drinkers 48% complied with a recommendation to participate in brief intervention. Men and older subjects complied to participate about 1.7 times more often than women and young adults. Depending on the outcome measure and the study group a clinically meaningful reduction of drinking was found in 23-53% of the male and 30-75% of female heavy drinkers

after three years. However, there was no statistically significant difference between the study groups.

The study indicates that heavy drinkers are commonly seen, even if not necessarily over-represented, in primary health care. Marker combinations could be considered to be part of the detection of heavy drinking, and half of early-phase heavy drinkers, women and young adults more than others, do not want to participate in brief intervention. The study also suggests that minimal advice may reduce drinking as much as the more extensive brief intervention and in the routine environment brief intervention may not be as effective as in special research conditions. There is a possible problem of engaging professionals in providing competent brief intervention. This justifies a need to evaluate methods of implementing brief intervention in the future.

## 1 INTRODUCTION

High alcohol consumption is one of the greatest health hazards and leads to social problems as well (Eckardt et al. 1981, Anderson et al. 1993, Lieber 1995, O'Connor and Schottenfeld 1998). Nowadays, non-dependent heavy drinking is recognised as highly prevalent (Saunders and Lee 2000), and as causing more harm among the general population than dependent drinking, even though problems of individual non-dependent heavy drinkers are generally less frequent and severe (Kreitman 1985, Rush 1989).

Physicians, general practitioners in particular, are in a favourable position to intervene in heavy drinking in its early stage before it causes irreversible damage and treatment becomes more demanding and complicated. General practitioners frequently meet most of the individuals in the community. In Finland, depending on the area, 60-75% of its inhabitants attend their primary health care clinic each year. Thus, at primary health care there are many opportunities for patient counselling about alcohol (Strecher et al. 1994). General practitioners are also documented as being a credible source of information in health issues by patients and information about alcohol given by general practitioners is also well received by patients (Wallace and Haines 1984, Wallace et al. 1987a, Richmond et al. 1996, Herbert and Bass 1997). Obviously, in primary health care the likelihood of stigmatisation of a heavy drinker is less than in services specially aimed at treatment of drinking problem.

Definitions of brief intervention vary and it should not be regarded as a homogenous entity (Heather 1995, Jönson et al. 1995). In primary health care brief intervention refers to any therapeutic or preventive consultation of short duration undertaken by a health care professional. The optimal target group for brief intervention is early-phase heavy drinkers without alcohol dependence or severe alcohol-related health hazards (Bien et al. 1993).

The evidence in favour of brief intervention treatment for heavy drinkers has been demonstrated in numerous studies, even if problems in carrying out trials and interpreting the results in this field have also been recognised (Saunders and Foulds 1992, Anderson 1993, Bien et al. 1993, Richmond and Anderson 1994a, Heather 1995, Kahan et al. 1995, Seppä 1996, Wilk et al. 1997, Poikolainen 1999, Watson 1999). Also, the cost of brief intervention is low and the benefit-cost ratio has been proven to be positive (Miller et al. 1995, Fleming et al. 2000). Recently greater emphasis has been placed on real-world effectiveness studies (Holder et al. 1999) and in spite of the evidence in favour of brief intervention, there is still the question of its effectiveness in a naturalistic environment and of putting research findings into practice in routine primary health care (Heather 1995, Richmond et al. 1995).

This study was a part of the multi-component collaboration community action project of the WHO Regional Office for Europe, called the Lahti Project (Holmila 1997). Beside brief intervention, the Lahti Project implemented a range of other preventive initiatives concerning alcohol problems: youth work, initiation of discussion on alcohol policy, information and education, cultural projects and mobilisation of organisations and citizens. The purpose was to throw light on two interlinked issues: the local community as a frame of reference in the prevention of alcohol problems and the practical planning and implementation of prevention projects in the community (Holmila 1997). This study focuses on a component of the Lahti Project dealing with brief intervention as a part of the naturalistic environment of routine primary health care (effectiveness study) (Sillanaukee 1997). The study protocol was approved by the Ethical Committee of Lahti Primary Health Care Clinics.

## 2 REVIEW OF THE LITERATURE

### 2.1 The concept of alcohol problem

There has been an expansion of the concept regarding what counts as an alcohol problem and the dichotomous model of alcoholism and moderate drinking has been replaced by a more complex spectrum dividing alcohol problem into more detailed subgroups (Saunders and Lee 2000). The argument for the necessity of this expansion was already made four decades ago by Jellinek (1960). The terminology for categorising alcohol problems is based on risks and effects. To some extent there are discrepancies and overlap in the terminology used in the literature.

Heavy drinking is much-used term to specify an individual's alcohol problem. It is defined as a quantity of alcohol consumption that exceeds an established threshold value (Reid et al. 1999). Heavy drinking and moderate drinking distinguish levels of alcohol consumption on the basis of health risks. Although there is variability in the level of consumption that is injurious to different individuals (Buchsbaum et al. 1995), for routine practice the recommendation of thresholds is substantial. In Finland widely accepted threshold values for men are 280 grams (24 standard drinks; standard drink = 12 grams of pure ethanol) and for women 190 grams (16 standard drinks) of absolute ethanol per week (Sillanaukee et al. 1992). Thresholds have also been set for one drinking occasion; 7 standard drinks for men and 5 for women (Sillanaukee et al. 1992). These thresholds are based on epidemiological data of alcohol health hazards. Thresholds are subject to debate and thus vary in different countries. Moreover, they are different in special populations, such as pregnant women.

It should be noted that the heavy drinking category encompasses a broad range of drinkers from those just above the threshold values to drinkers who get drinking is used to specify a subgroup of heavy drinkers with less advanced drinking problem. Early-phase heavy drinker usually refers to those heavy drinkers who consume alcohol at the risk level but who do not suffer from dependence or major alcohol-related health hazards. When accepting the concept that dependence exists on a continuum throughout the population of heavy drinkers (Edwards and Gross 1976), the early-phase heavy drinkers are considered those who do not at present show a significant degree of dependence.

Beside heavy drinking, hazardous drinking, harmful drinking and alcohol dependence categories are used to define the type of alcohol problems (Reid et al. 1999, Saunders and Lee 2000). Hazardous drinking, harmful drinking and alcohol dependence can be seen as different types of heavy drinking, because they usually exceed established heavy drinking thresholds. However, harmful drinking and alcohol dependence are diagnostic terms and the amount of drinking is not specified in their diagnostic criteria (World Health Organisation 1992, American Psychiatric Association 1994).

In hazardous drinking alcohol consumption places individuals at risk for adverse health events (Saunders and Lee 2000), whereas in harmful drinking alcohol consumption already results in significant adverse consequences in health (psychological or physical). In contrast to harmful drinking, hazardous drinking is not yet an ICD diagnosis (World Health Organisation 1992, Saunders et al. 1993a). In DSM alcohol abuse is a corresponding diagnosis to harmful use in ICD, even though due to differences in criteria they are not equivalent (World Health Organisation 1992, American Psychiatric Association 1994). In alcohol abuse social harm due to drinking is more directly among the criteria than in harmful use.

Alcohol dependence is both the ICD and DSM diagnosis (World Health Organisation 1992, American Psychiatric Association 1994). Important features of the diagnosis of alcohol dependence are the compulsion to drink and drinking despite adverse consequences. The dependent drinker devotes substantial time to

obtaining alcohol, drinking and recovering. A physiological dependence on alcohol, marked by tolerance or withdrawal symptoms, may or may not be present (World Health Organisation 1992, American Psychiatric Association 1994).

### 2.2 Prevention of alcohol problems

Many of the major causes of morbidity and mortality have their origins in the lifestyle of individuals. Prevention is based on the realisation that treatment of diseases is an incomplete answer and one should also go out into the community, and discover and tackle the origins of the diseases. Primary health care has often been seen as having the leading role in prevention at the level of individuals (Rose 1990, David 1994).

Alcohol problems are seen not only as a social but also as a health issue today (Bromley 1992, O'Brien and McLellan 1996, Weaver et al. 1999) and the role of physicians in the prevention and treatment of alcohol problems is growing in importance and magnitude (Dube 1999, Miller and Sheppard 1999). Just as patients can be assessed for risk of a medical condition, such as cardiovascular disease (Campbell et al. 1998), patients can also be assessed for risk of alcohol-related damage based on their consumption of alcohol. The physician's role in prevention may span all levels of following preventive services (Radouco-Thomas et al. 1979, Skinner 1990, Blondell et al. 1996, Dube 1999): (1) primary prevention (interventions aimed at preventing a problem from occurring); (2) secondary prevention (interventions aimed at early identification and treatment of a problem); and (3) tertiary prevention (interventions aimed at preventing further complications of a condition or problem).

Counselling moderate drinkers about alcohol to prevent them turning into heavy drinkers is primary prevention. Secondary prevention, such as brief intervention, means counselling heavy drinkers to reduce their drinking to avoid alcohol dependence and other alcohol-related hazards. Thus the natural target

group of brief intervention is early-phase heavy drinkers excluding alcohol dependent and heavy drinkers with major alcohol-related health defects. Tertiary prevention is treating those with alcohol dependence or alcohol-related health defects to avoid further complications.

# 2.3 Prevalence of heavy drinking in primary health care and general population

Heavy drinking is known to be common both among primary health care patients and general population. In previous studies the prevalence of heavy drinking reported has varied greatly. In primary health care the prevalence has been found in western countries to be 5-40% among men and 0.3-42% among women (Wallace and Haines 1985, Nicol and Ford 1986, Wiseman et al. 1986, Wallace et al. 1987b, Cherpitel 1991, Simon et al. 1991, Saunders et al. 1993a, Cherpitel 1994, Cherpitel 2000). In the general population the observed prevalences of heavy drinking have been 12-22% and 2-6% respectively (Hilton 1987, Simpura 1987, Smart et al. 1991, Alvarez and Del Rio 1994, Chan et al. 1994, Cherpitel 1994, Cherpitel 1995, Holmila 1995, Bongers et al. 1997, Cherpitel 2000). A common finding is that heavy drinking both in primary health care and general population is more prevalent among men than women.

Cultural factors in relation to alcohol use often vary from country to country. This may be instrumental in influencing the results of prevalence studies to a significant extent. In addition, the prevalences in different studies are seldom directly comparable, since the research methods and criteria of heavy drinking have been different between studies. One reason for the great variation is also different primary health care populations, which is partly due to differences in health care systems.

Heavy drinking is commonly believed to be over-represented in primary health care patients compared with the general population. However, this has been compared using the same method, criteria and geographical area in only few studies (Cherpitel 1991, Chan et al. 1994, Cherpitel 1994, Cherpitel 1995, Cherpitel 2000). Two of the studies suggest that heavy drinking is over-represented in primary health care (Cherpitel 1991, Chan et al. 1994) and three of them suggest it may not always be so (Cherpitel 1994, Cherpitel 1995, Cherpitel 2000).

In the study by Chan et al. (1994), where CAGE was used to detect heavy drinkers, prevalences in primary health care and general population among men were 23% and 15%, and among women 7% and 6% respectively. Cherpitel (1991, 1994, 1995, 2000) used a quantity-frequency scale in the detection of heavy drinkers in her studies. First she reported frequent heavy drinking as being more prevalent in primary health care both among men (29% vs. 19%) and women (10% vs. 4%) than in the general population (Cherpitel 1991). Prevalence was studied among drinkers and the difference between populations would be less if abstainers were also included. In further studies by Cherpitel (1994, 1995) results were partly the opposite. The Health Maintenance Organisation (HMO) primary health care showed a significantly lower prevalence than in the general population both among men (5% vs. 12%) and women (0.3 % vs. 2%) (Cherpitel 1994). Instead, in the same study, in county primary care proportions were higher than in the general population, 15% in men and 3% in women (Cherpitel 1994). In the another study Cherpitel (1995) reported HMO general population to have higher prevalence of heavy drinking than HMO patients visiting a clinic. In the latest study by Cherpitel (2000) no difference was found in prevalence between primary health care and general population: among current drinkers, 5% of the primary care sample reported heavy drinking compared to 4% of the general population.

### 2.4 Detection of heavy drinking

To be able to perform an effective brief intervention the recognition of heavy drinking in its early phase is considered to be important (Bien et al. 1993). However, in the majority of cases detection of heavy drinking, especially in its early-phase, is challenging. Even if nine tenths of general practitioners think that they have a legitimate role in working with patients with drinking problems (Anderson 1985), their rate of recognition of heavy drinking ranges from 35% to 55% in primary health care (Reid et al. 1986, Aasland et al. 1987, Woodall 1988, Seppä et al. 1996). This is probably due to the fact that often heavy drinkers do not seek treatment for their drinking problem and because there is no absolutely reliable way of detection (Poikolainen 1985, Sillanaukee 1996). The combination of interview, clinical findings, questionnaire and laboratory markers is often needed in the detection of heavy drinking.

One issue related to detection of heavy drinkers is whether it is applied to the entire population or only the population attending health care. In some brief intervention studies (Wallace et al. 1988, Anderson and Scott 1992) the first option has been partly used, but in most of the studies recruitment has been done only among patients attending health care. Another issue is whether the detection of heavy drinkers is in some way selective among the health care population. It can be applied only to some subgroups of the population with a higher prevalence of heavy drinking. This is where patients are pre-selected with factors that are known to be associated with heavy drinking. Such factors could be sociodemocraphic such as gender and age or health problems like high blood pressure or depression. The benefit of pre-selection is that the proportion of patients to be screened for alcohol use is reduced. When using health factors physicians are given a legitimate clinical reason to ask about alcohol consumption. Pre-selection would, however, cause the exclusion of some heavy drinkers. The screening all procedure has been used in most of the brief intervention studies and it has several benefits. It allows one to identify heavy drinking in its early phase before

any damage, it educates patients, and it motivates some patients by expressing interest in their drinking (Peters et al. 1996).

## 2.4.1 Self-reported alcohol consumption

Researchers and clinicians have commonly used self-report assessment to measure alcohol consumption. Hoyer et al. (1995) found that self-reported alcohol consumption accounted for approximately 40% of the sales volume. In spite of this and other similar findings, self-reported alcohol consumption is considered to be reasonably valid, especially if using properly designed questions (Fitzgerald and Mulford 1987, Embree and Whitehead 1993, Babor et al. 2000). Fallible memory or intentional underestimation is considered to cause inaccuracy in self-reports. However, it appears that generally underestimation, if it exists, is due to fallible memory rather than intentional underestimation (Babor at al. 2000). Validity of self-reports also seems to depend on whether the target population consists of moderate or heavy drinkers (Bongers et al. 1999). Heavy drinkers tend to underestimate their consumption more than moderate drinkers (Poikolainen 1985). Instead, different data collection methods by mail survey and personal interviews or time frames used in questions do not seem to lead to notable differences in validity (Bongers and van Oers 1998, Weisner et al. 1999).

The commonly used measure of self-reported alcohol consumption is quantity-frequency questions covering a certain period of time. It is called an aggregate or averaging method. In research it is usually structured and thus a person selects from a number of fixed quantities of how much is consumed on a usual drinking occasion and from a number of fixed frequencies of drinking occasions. Respondents are asked to generalise a drinking behaviour, which may lead to underestimation of alcohol consumption. This is especially the case if one's drinking is irregular. Beverage-specific quantity-frequency questions have

been shown to be more accurate than global quantity-frequency questions (Russell et al. 1991, Serdula et al. 1999).

Another way is to try measure actual consumption instead of averaging. This can be done through such methods as timeline follow-back (Sobell and Sobell 1992). This is a daily estimation method developed for retrospective collection of data up to some months prior to the date of interview. It seems to perform well as compared with any other method (Sobell and Sobell 1992, Grant et al. 1995, Carney et al. 1998). However, in some situations, employing detailed survey instruments such as the timeline follow-back method, may not be justified, as the increased respondent burden may result in decreased response rates (Cunningham et al. 1999).

Another method to estimate actual consumption is a prospective diary which seems to offer a higher validity than a quantity-frequency questions (Webb et al. 1990, Lemmens et al. 1992). However, the superiority of the diary in detecting heavy drinkers compared a quantity-frequency questions seem to decrease with increasing consumption (Webb et al. 1990) and using a diary requires well-motivated persons.

Continued direct observation is an alternative method to self-reports and it is sometimes useful for research purposes (Poikolainen 1985), but often it is too time-taking and expensive. Self-reported alcohol consumption can be supplemented with information from relatives.

## 2.4.2 Medical history and clinical findings

In some cases, heavy drinking is self-evident according to clinical findings and medical history, but rarely in the case of early-phase heavy drinkers (Saunders and Conigrave 1990). Regular heavy drinking is often associated with social and psychological problems, but physicians are more likely to recognise physical findings such as smelling of alcohol, hypertension, gastritis, anxiety, insomnia,

depression, accidents of all types, abnormal skin vascularization, hand and tongue tremor, and hepatomegaly (Saunders and Conigrave 1990). Frequent use of health services is also considered to be associated with heavy drinking (Ogborne and Gavin 1990). Based on clinical findings Skinner et al. (1986) constructed the Alcohol Clinical Index, which performed better than laboratory tests or medical history items in detection of heavy drinkers. However, there is no exact clinical finding, symptom or item in medical history that is sufficiently sensitive and specific to detect early-phase heavy drinking. Rather, the value of such things is to alert physicians to enquire about alcohol drinking.

### 2.4.3 Structured questionnaires

The prototype structured questionnaire is the Michigan Alcoholism Screening Test (MAST) with 25 questions (Selzer 1971). It has been used widely and has proven successful in detecting alcohol dependent patients in a clinical setting. Modifications of the original questionnaire include the brief MAST (Pokorny et al. 1972), the Self-Administered Alcoholism Screening Test (SAAST) (Swenson and Morse 1975) and the Malmö modified MAST (Mm-MAST) (Kristenson and Trell 1982). MAST and its modifications were developed to detect alcohol dependence and many of the questions focus on symptoms of advanced heavy drinking. Thus their sensitivity falls markedly among early-phase heavy drinkers (Saunders and Kershaw 1980).

The CAGE with four questions was also developed to screen for alcohol dependence (Mayfield et al. 1974). It has been found to be very useful and accurate among the screening instruments of alcohol dependence (Reid et al. 1999). Its brevity is an important advantage. Beside screening alcohol dependence, it has also been used in the detection of early-phase heavy drinking (Wallace and Haines 1985, Smart et al. 1991, Chan et al. 1994). The CAGE acronym is derived from its four questions: (1) Have you ever felt you ought to

cut down on your drinking? (2) Have people annoyed you by criticising your drinking? (3) Have you ever felt guilty about your drinking? and (4) Have you ever had a morning eye-opener?

In CAGE two affirmative answers detected 74% heavy drinkers and a specificity was 91% (Buchsbaum et al. 1991). These figures are in accordance with other studies (Mayfield et al. 1974, Bush et al. 1987). However, sensitivity seems to be lower when detecting early-phase heavy drinkers and depends on the population to which it is applied (Crowe et al. 1997). Usual cut-off levels have been two affirmative answers for both men and women. Because binge drinking, which accumulates the adverse effects tested in CAGE, is common in Finland, the cut-off level has been often three yes-answers for men in Finnish studies (Seppä and Mäkelä 1993, Seppä et al. 1995).

The Alcohol Use Disorders Identification Test (AUDIT) was designed to identify early-phase heavy drinkers before dependence and before major physical or psychosocial damage occurs and to meet the needs of primary health care. Its sensitivity was found to be 92% and specificity 94% in a cross-national study (Saunders et al. 1993b). These figures, however, are higher than in some other samples (Allen et al. 1997). It does not seem to be affected by ethnic or sex bias (Saunders et al. 1993b, Volk et al. 1997, Steinbauer et al. 1998). It includes ten questions and one of its advantages is that the first three questions provide an estimate of drinking amounts. For some purposes it has been found to be too long and shortened versions of AUDIT are under development (Seppä et al. 1998).

The MAST and its modifications, CAGE and AUDIT can be self-administered or administered by physicians or nurses. In order to make screening for the identification of heavy drinking less threatening, questions about alcohol use have sometimes been incorporated into questionnaires covering broader lifestyle problems, such as exercise, diet, tobacco use, sleep and sexual functioning (Wallace and Haines 1985, Fleming and Barry 1991).

### 2.4.4 Laboratory markers

There is a need for a laboratory marker to help to provide objective information in the detection of heavy drinking. A variety of laboratory tests to detect heavy drinking is available (Hoeksema and de Bock 1993, Conigrave et al. 1995, Sillanaukee 1996, Musshoff and Daldrup 1998, Salaspuro 1999).

Carbohydrate-deficient transferrin (CDT) is an abnormal form of the glycoprotein transferrin and is a relatively new marker of heavy drinking. Transferrin is involved in the delivery of iron to the body tissues. Heavy drinking alters the glycosylation process in transferrin formation, with the result that transferrin often miss carbohydrate terminal chains. Its advantage is a high specificity, which has varied between 82-100% depending on the study (Stibler 1991, Sillanaukee 1996, Musshoff and Daldrup 1998, Meerkerk et al. 1998). False-positives have been reported in patients with severe liver diseases, with genetic D-variant of transferrin and with inborn error of glycoprotein metabolism. It normalises after withdrawal in about two weeks (Stibler 1991, Sillanaukee 1996, Musshoff and Daldrup 1998). Sensitivity has been between 31-94% in different studies (Poupon et al. 1989, Stibler 1991, Sillanaukee 1996, Musshoff and Daldrup 1998, Meerkerk et al. 1999). Sensitivities vary depending on the target population. In primary health care based studies the sensitivity of CDT has been 31-45% (Poupon et al. 1989, Meerkerk et al. 1999).

Mean corpuscular volume (MCV), an index of red blood cell size, increases with heavy drinking, but is also widely used for purposes other than the detection of heavy drinking. In the detection of heavy drinking its specificity is 26-91% and it normalises slowly compared with other tests; in 1-3 months (Wu et al. 1974, Morgan et al. 1981, Sillanaukee 1996, Musshoff and Daldrup 1998). The reasons of false-positives include vitamin B12 and folic acid deficiency, reticulocytosis, severe haematological disorders, liver diseases, hypothyroidism and the use of antiepileptics. Sensitivity ranges from 17 to 96% (Morgan et al. 1981, Baxter et al. 1980, Nalpas et al. 1989, Sillanaukee 1996, Musshoff and Daldrup 1998,

Meerkerk et al. 1999). In a primary health care setting the sensitivity has been found to be 17-30% (Baxter et al. 1980, Nalpas et al. 1989, Meerkerk et al. 1999).

enzymes aspartate aminotransferase (ASAT), aminotransferase (ALAT), and gamma-glutamyltransferase (GGT) have also been widely used. Their specificities are also often found to be lower than with CDT; 30-50%, 20-45%, and 11-90% respectively (Rosalki and Rau 1972, Sillanaukee 1996, Musshoff and Daldrup 1998). Increased values are also found in non-alcohol related liver disease and in the case of GGT in obesity, diabetes mellitus, hypertriglyceridaemia, and the use of antiepileptics and anticoagulants. Transferases normalise after withdrawal in 1-5 weeks (Sillanaukee 1996, Musshoff and Daldrup 1998). ASAT/ALAT ratio 1.5 or higher is suggestive of alcohol-related liver damage (Cohen and Kaplan 1979). Sensitivities ASAT, ALAT, and GGT have been found to be 10-69%, 10-58%, and 31-90% respectively (Baxter et al. 1980, Nalpas et al. 1989, Sillanaukee 1996, Musshoff and Daldrup 1998, Meerkerk et al. 1999). In primary health care based studies the sensitivities have been 10%, 10%, and 31-50% respectively (Baxter et al. 1980, Nalpas et al. 1989, Meerkerk et al. 1999).

Due to the sensitivity problems an optimal laboratory marker for detecting heavy drinking, especially in its early phase, has not yet been found (Sillanaukee 1996). The parallel use of markers has been noted to improve the ability to identify heavy drinking (Yersin et al. 1995, Helander et al. 1996). Several other laboratory abnormalities are also associated with heavy drinking and some of them may yield better options in future (Sillanaukee 1996, Musshoff and Daldrup 1998).

## 2.5 Brief intervention of heavy drinkers

The common element of brief intervention is its shortness, either in time taken for one session or in number of sessions, or in both. However, there are two classes of brief intervention with heavy drinkers which must be differentiated (Heather 1996). The first refers to interventions among people who are not seeking help for an alcohol problem and who need to be identified by screening in settings where they have usually attended for some other reason than an alcohol problem. In this study this class of brief intervention is in focus. The second class includes treatments usually given in specialist alcohol treatment settings where people attend to seek help for an alcohol problem. To separate these two Heather (1996) proposed names of primary care brief intervention for earlier intervention and specialist brief intervention for the later type, but these terms are not widely used. Sometimes, brief intervention has also been seen as a way to provide preparation and motivation for further necessary treatment mainly for alcohol dependents in settings where they have attended for some other reason than an alcohol problem (Weaver et al. 1999).

## 2.5.1 Description of brief intervention

Brief intervention represents a new perspective on responding to drinking problems and is due to the expansion of the concept of what counts as an alcohol problem. It is intended to provide early intervention, before or close to the onset of alcohol-related damage. The term brief intervention and its synonyms were first used in the context of smoking cessation advice (Russell et al. 1979). Brief intervention for heavy drinking given in previous studies has varied and it is not a homogenous entity (Heather 1995, Jönson et al. 1995). However, in general brief intervention includes identifying heavy drinking and consultation of short duration about the health risks associated with heavy drinking. In previous studies brief interventions have usually included 1 to 5 sessions and one session taking 5-60 minutes. The usual target group has been early-phase heavy drinkers who are not alcohol-dependent and have not experienced severe alcohol-related harm.

Brief intervention is often within the scope of health care providers, such as primary health care physicians or nurses, who are not specialists in the treatment of alcohol problems. Because alcohol dependents are usually excluded, the treatment goal is usually moderate drinking rather than total abstinence. The evidence shows that moderation-oriented brief intervention and allowing individuals to set their goals is effective among early-phase heavy drinkers (Sanchez-Craig et al. 1984, Bien et al. 1993). This, at least partly, is due to the fact that those who have not experienced severe alcohol related harm are unlikely to respond to a total abstinence goal (Sanchez-Craig and Lei 1986). In brief intervention verbal advice is often supplemented with reading material.

Many people who consume alcohol at the risk level do not seek treatment or want to change their drinking behaviour. Thus, one aim of brief intervention is to motivate a change in drinking habits. It is possible that the primary impact of brief intervention is on motivation for change (Miller and Rollnick 1991, Rollnick et al. 1992), and that once such motivation has been achieved, early-phase heavy drinkers may proceed to change their behaviour with minimal assistance and relatively easily (Bien et al. 1993).

While there is no specific protocol for a brief intervention, the FRAMES acronym (feedback: review problems experienced because of alcohol; responsibility: changing alcohol use is the patient's responsibility; advice: advice to cut down or abstain; menu: provide options for changing behaviour; empathy: use an empathic approach; self-efficacy: encourage optimism about changing behaviour) summarises a counselling method often used (Miller and Rollnick 1991, Bien et al. 1993). However, Heather (1995) pointed out, that even if these elements have been often present in previous brief intervention studies, it does not mean the same as demonstrating that they represent the effective ingredients of brief interventions. Specific steps to reach the goal appears to be more effective than only general information on alcohol (Spivak et al. 1994). Thus, primary preventive activities are not to be expected to be effective in reducing heavy drinking. Rather, it seems that a goal-orientated approach is needed

(Davila et al. 2000). The question concerning what type of brief intervention is effective in different subgroups of heavy drinkers has not yet been profoundly addressed in research.

#### 2.5.2 Randomized controlled brief intervention studies

When assessing the applicability of brief intervention to health care, there are three levels of research questions according to Richmond and Anderson (1994b) which should be considered at separately: (1) does brief intervention work in health care under special research conditions? (efficacy); (2) does brief intervention work widely in a naturalistic environment of health care? (effectiveness); and (3) what is the rate of adoption of brief intervention in health care and how to promote it?

Brief intervention has mainly been studied in health care environment. Here most of the subjects has been recruited opportunistically; that is under normal conditions of health care where the opportunity is taken to detect heavy drinking among patients attending health care mainly for other reasons than alcohol use. However, it has to be noted that Wallace et al. (1988) and Anderson and Scott (1992) used partly another method for recruitment and mailed a questionnaire to a random sample of registered patients. There are also studies with self-recruited treatment-seeking heavy drinkers (Miller et al. 1980, Heather et al. 1986, Sanchez-Craig et al. 1989). In them subjects have been recruited by newspaper advertisements. In this review only randomly controlled health care studies with non-treatment-seeking populations are reviewed. The literature was gathered via the Medline data base using numerous search words. Additionally, the reference lists in the research reports and reviews found were used.

### 2.5.2.1 Primary health care: consultation based studies

There are several studies conducted at consultation based primary health care environment (Table 1). At least one of them could be considered to be an effectiveness study done in the naturalistic environment of routine primary health care (Richmond et al. 1995). The study was carried out in 40 group practices in Sydney, Australia. Inclusion criteria were more than 35 drinks per week for men and 21 for women. Patients with severe alcohol dependence, severe level of alcohol-related problems, a disease in which alcohol consumption is contraindicated, pregnancy, major psychiatric disturbance or previous treatment for alcohol problems were excluded. The heavy drinkers (216 males and 162 females) identified opportunistically were assigned to one of the four groups: (1) a five-session intervention by the general practitioner (the Alcoholscreen Program); (2) a single session of 5 minutes' advice by the general practitioner plus self-help manual (minimal intervention); (3) an alcohol-related assessment but not intervention; and (4) neither intervention nor assessment. Follow-up assessment was carried out at 6 and 12 months after entry. Minimal intervention or alcohol-related assessment were not effective in reducing alcohol consumption or problems. Patients undergoing the Alcoholscreen Program reduced their drinking more than controls, but this difference was not significant. However, there was significantly greater reduction in the number of alcohol-related problems at the 6 month follow-up reported by those in the Alcoholscreen Program. At 12 months no significant difference in the number of alcohol-related problems was present. Thus, in Richmond et al.'s (1995) study no clear positive treatment results were found. This study indicated that brief intervention may lose some of its effectiveness when translated from special research conditions to naturalistic environments in primary health care (Heather 1995).

In other earlier controlled studies in consultation based primary health care there are both positive findings, where brief intervention groups reduced drinking significantly more than control groups (Wallace et al. 1988, Anderson and Scott 1992, Fleming et al. 1997, Ockene et al. 1999) and negative treatment results (Heather et al. 1987, Seppä 1992, Senft et al. 1997) among male heavy drinkers (Table 1). Among female heavy drinkers there are also positive results (Wallace et al. 1988, Fleming et al. 1997, Ockene et al. 1999) and negative results (Heather et al. 1987, Scott and Anderson 1990, Seppä 1992, Senft et al. 1997). Follow-up times have been 6-18 months.

In two positive brief intervention studies some of the subjects were recruited from those registered in the primary health care clinics instead of from those attending clinics (Wallace et al. 1988, Anderson and Scott 1992). Screening for heavy drinking was done by mail. Those screened positive were further interviewed in person. Subjects recruited in this way cannot be considered as a genuine primary health care population (Heather 1995). This problem was avoided in the study by Ockene et al. (1999), who used a similar recruitment procedure and screening was done by telephone or mail by research assistants. Thus, the detection of heavy drinkers was done for the brief intervention providers, which is not the case in routine work. Subjects received brief intervention at their next regularly scheduled appointment with physicians and those who did not have an appointment within six months were excluded.

In two studies the physicians giving brief intervention were research-oriented; in the study by Wallace et al. (1988) all participating general practitioners were members of the Medical Research Council's research network and in the study by Fleming et al. (1997) not all but only those who were willing participated. Such study procedures raises questions about the generalizability of the results to the broader population of general practitioners (Drummond 1997). Senft et al. (1997) used trained health counsellors to supplement the primary care clinicians' advice.

Table 1. Randomised controlled brief intervention studies at consultation based primary health care (to be continued).

Conclusion based on statistically significant superiority of intervention group	No effect	Effect	No effect	Effect	No effect	No effect
Follow-up: months/ rate (%)	88/9	12/82	12/69	12/65	12/53	12/69
Self-report and laboratory values as outcome measures	SR, MCV, GGT	SR, MCV, ASAT, GGT	SR, MCV, GGT	SR, MCV, GGT	MCV	SR
Prior advice and dependence as an exclusion criterion	Alcohol dependence	Prior advice	Prior advice	Prior advice	None	Prior advice and alcohol dependence
Inclusion measure	SR or ARP	SR and CAGE	SR	SR	MCV and Mm-MAST or GGT or APR	SR
Agegroup (years)	18-65	17-69	17-69	17-69	17-	18-70
Sample size by gender	M: n=78 F: n=26	M: n=640 F: n=267	F: n=72	M: n=154	M: n=140 F: n=38	M: n=105 F: n=92
Study	Heather et al. 1987	Wallace et al. 1988	Scott and Anderson 1990	Anderson and Scott 1992	Seppä 1992	Richmond et al. 1995

*Table I (to be continued).* 

Study	Sample size by gender	Agegroup (years)	Inclusion measure	Prior advice and dependence as an exclusion criterion	Self-report and laboratory values as outcome measures	Follow-up: months/ rate (%)	Conclusion based on statistically significant superiority of intervention group
Burge et al. 1997	M+F: n=242	18-78	Alcohol abuse or dependence diagnose	Prior advice	SR, MCV, ASAT, ALAT	18/77	No effect
Fleming et al. 1997	M: n=482 F: n=292	18-65	SR	Prior advice	SR	12/93	Effect
Senft et al. 1997 M: n=359 F: n=157	M: n=359 F: n=157	21-	AUDIT	Alcohol dependence	SR	12/80	No effect*
Ockene et al. 1999	M: n=343 F: n=187	21-70	SR	Prior advice	SR	6/91	Effect

M=male, F=female SR=self-reported alcohol consumption, ARP=alcohol-related problems \*Positive effect was found among men at 6 months, but it disappeared at 12 months.

# 2.5.2.2 Primary health care: health screening based studies and the WHO study

In an original health care brief intervention study by Kristenson et al. (1983) 585 male heavy drinkers were identified in a health screening program. Over a five year follow-up period, those given advice had 80% fewer days of absenteeism from work, 60% fewer days in hospital and 50% fewer deaths when compared with the control group. The results of subsequent studies carried out as part of a health screening programs are also, on the whole, encouraging (Romelsjö et al. 1989, Nilssen 1991, Suokas 1992, Tomson et al. 1998). In the Hämeenlinna study (Suokas 1992) GGT levels were significantly lower than at the baseline in both treatment and control groups. Suokas (1992) concluded that physicians should take greater responsibility to intervene with their heavy drinking patients.

The WHO co-ordinated a large international multi-centre brief intervention study (WHO Brief Intervention Study Group 1996). It was conducted in a range of settings, but partly in primary health care. Subjects (1260 men, 299 women) with no prior history of alcohol dependence were selected by using self-reported alcohol consumption. It was found that males exposed to the brief intervention reported 17% lower average alcohol consumption than those in the control group after 9 months. Five minutes of simple advice was as effective as 20 minutes of brief counselling.

# 2.5.2.3 Hospital based studies and studies with special patient groups

Several controlled studies have been conducted in the hospital setting and/or among special patient groups (Chick et al. 1985, Antti-Poika et al. 1988, Elvy et al. 1988, Persson and Magnusson 1989, Maheswaran et al. 1992, Lang et al.

1995, Cushman et al. 1998, Chang et al. 1999, Fleming et al. 1999, Gentilello et al. 1999). In the first such study (Chick et al. 1985) the subjects were 156 male patients in different medical wards of a general hospital. The treatment consisted of one counselling session by the nurse. Both treatment and control groups reported a reduction in alcohol consumption after 12 months and the treatment group had a significantly better outcome than the control group. The results of subsequent studies have all shown brief intervention to be effective in reducing drinking (Antti-Poika et al. 1988, Elvy et al. 1988, Persson and Magnusson 1989, Maheswaran et al. 1992, Lang et al. 1995, Cushman et al. 1998, Chang et al. 1999, Fleming et al. 1999, Gentilello et al. 1999). In some of these special patient groups were studied: Antti-Poika et al. (1988) and Gentilello et al. (1999) studied heavy drinkers with trauma, Maheswaran et al. (1992), Lang et al. (1995) and Cushman et al. (1998) studied heavy drinkers with hypertension, Chang et al. (1999) studied heavily drinking pregnant women and Fleming et al. (1999) heavy drinkers aged 65 and older.

#### 2.5.2.4 Considerations of brief intervention studies

There are pitfalls in making direct comparisons of results of different brief intervention studies because of the differences between studies. First of all the brief interventions given in previous studies are not directly comparable (Heather 1995, Jönson et al. 1995). This is seen, for example, in the variation of time used in the studies with only one session: in the WHO study (WHO Brief Intervention Study Group 1996) in one group's advice took 5 minutes compared to Chick et al.'s (1985) 60 minutes. The number of sessions has usually varied between 1 and 5. In addition the content of brief intervention has varied. So far it can be concluded that precise description of essential parts of brief intervention is not possible.

Additionally, there is also variability in the means of identifying subjects, inclusion and exclusion criteria in different studies. Beside these differences the population from which the sample is drawn and cultural factors may be instrumental in influencing the results of brief intervention studies to a significant extent. The WHO study (WHO Brief Intervention Study Group 1996) produced powerful evidence of the efficacy of brief intervention in different sociocultural groups.

There is substantial evidence supporting the efficacy of brief intervention in special research conditions (Saunders and Foulds 1992, Anderson 1993, Bien et al. 1993, Richmond and Anderson 1994a, Heather 1995, Kahan et al. 1995, Seppä 1996, Wilk et al. 1997, Poikolainen 1999, Watson 1999). Recent meta-analysis of 12 controlled studies found that heavy drinkers who received brief intervention were twice as likely to moderate their drinking when compared to heavy drinkers who did not receive any intervention (Wilk et al. 1997). Because assessment of patient controls is unavoidable and yet is an important component of brief intervention which may alone produce reduction of alcohol consumption, the overall effectiveness may be underestimated.

However, there is still the question of the effectiveness of brief intervention and putting research findings into practice in routine primary health care (Heather 1995, Richmond et al. 1995). Defining differences between efficacy and effectiveness studies is difficult. Certainly naturalistic environments vary in different countries and settings. It would be beneficial for authors to estimate in their research reports if their study addresses either efficacy or effectiveness.

## 3 AIMS OF THE STUDY

The aims of the present study were:

- 1. to estimate the prevalence of heavy drinking and to identify the drinking habits among primary health care patients, and to compare the prevalences of two different primary health care populations and the general population in the same geographical area (I).
- 2. to evaluate how useful CDT and conventional laboratory markers (MCV, ASAT, ALAT, GGT) are in the detection of early-phase heavy drinkers for brief intervention as part of routine primary health care (II).
- 3. to estimate the rate of compliance among non-alcohol treatment-seeking early-phase heavy drinkers as a whole and among subgroups with recommendations to enter brief intervention (III).
- 4. to evaluate separately among male and female early-phase heavy drinkers the effectiveness of a three-year lasting brief intervention treatment carried out in the naturalistic environment of routine primary health care (IV,V).

### 4 SUBJECTS AND METHODS

### 4.1 Brief intervention study (II-V)

### 4.1.1 Setting and screening of heavy drinking

In Finland primary health care clinics and occupational health care clinics are the two main providers of primary health care services. Primary health care clinics provide equal access health care services to the unselected population of a certain area. Occupational health care clinics provide services for a selected population of employed persons. The differences between populations of primary health care clinics and occupational health care clinics are that in the former patients are not necessarily employed (either due to their health, age or unemployment) but in the latter patients are employed, and that in the former patients always live in a certain geographical health care district but in the latter they may live in many different places. In spite of the organised occupational health care system, it is also possible for employees to visit the primary health care clinic in their own geographical area.

This study was carried out in primary health care of the city of Lahti, which includes four primary health care clinics (Ahtiala-Mukkula, Jalkaranta-Metsäkangas, Keskusta, Laune) and one occupational health care clinic. All practices participated and thus were not selected in any way. Screening, detection and brief intervention were done by the local personnel; general practitioners and nurses were not selected and all of them participated. A total of 41 general practitioners and 15 nurses were involved and given two half-day training sessions about brief intervention. The Brief Intervention Study Group was responsible for the collection of data. It included among others one general practitioner and one nurse from each participating clinic. They were trained

before the study and met frequently in Brief Intervention Study Group meetings throughout the study.

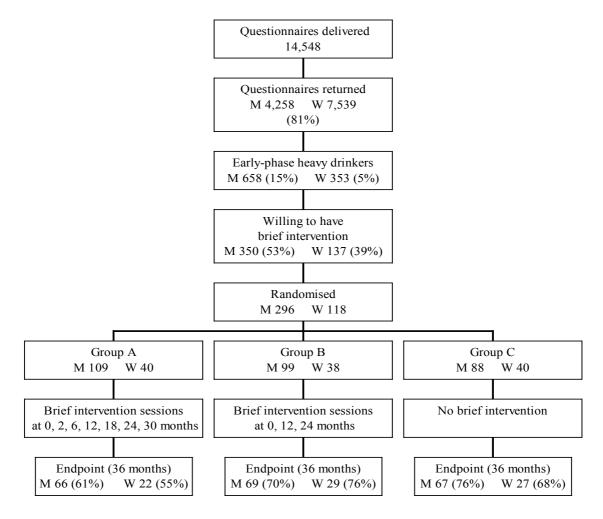


Figure 1. Trial profile (M=men, W=women).

When attending the clinic for the first time during the study period (February 1993 to May 1994), all patients aged 20-60 were given a health questionnaire by the receptionist to be completed before the normal general practitioner's consultation time (Figure 1). The response rate was 81% (11,797/14,548). This self-administered questionnaire contained the CAGE test and structured quantity-frequency alcohol consumption questions covering the last two months. The latter included 9 different fixed quantities, 6 different fixed

frequencies and 4 different beverages. The weekly consumption (grams of absolute ethanol per week) was calculated from these quantity and frequency numbers. The health questionnaire also contained structured questions related to the following socio-demographic and health factors: gender, age, education, employment, marital status, smoking, coffee drinking, exercise, weight, height, type of fat used on bread, sleeping time per night, and self-assessment of physical and mental health.

A male patient was suspected of being an early-phase heavy drinker if his self-reported alcohol consumption was at least 280 grams of absolute ethanol (24 standard drinks) per week and/or if he had at least three affirmative answers in CAGE (Seppä and Mäkelä 1993). For women the limits were 190 grams (16 standard drinks) and/or two affirmative answers (Seppä et al. 1992).

#### 4.1.2 Recruitment for brief intervention

After screening, based on the information from medical records and a face-to-face interview, general practitioners excluded from the suspected early-phase heavy drinkers: (1) those who had severe somatic or psychiatric disease; (2) those who had had at least one detoxification treatment; (3) those who were known to be alcohol dependent or had other severe alcohol-related diseases; and (4) those social drinkers who had a CAGE score above the screening limits because of earlier heavy drinking but who had stopped or reduced their drinking.

Altogether 658 male and 353 female early-phase heavy drinkers were identified (Figure 1). After detection, general practitioners informed patients about the risks inherent in their drinking and offered them the opportunity of participating in the brief intervention study. General practitioners also recorded the use of anxiolytics or sleeping pills of heavy drinkers. Altogether 350 out of 658 (53 %) among males and 137 out of 353 (39%) among females consented to participate in the brief intervention study and were randomised to one of the study

groups: brief intervention group A, brief intervention group B, and control group C (Figure 1). At this point, early-phase heavy drinkers who agreed to participate gave a blood sample for laboratory testing for CDT, MCV, ASAT, ALAT, and GGT and were given an appointment to return in 1-3 weeks for a feedback session with a general practitioner. Altogether 296 males and 118 females returned for the feedback session (Figure 1).

### 4.1.3 Study groups and content of brief intervention

During the feedback groups A and B had the first brief intervention session. The brief intervention session (10-20 minutes) consisted content of the FRAMES (Bien et al. 1993) according to the needs of each individual patient based on the general practitioner's judgement; for example, information about the adverse effects of alcohol, information on how the patient's alcohol consumption compared with recommended limits, feedback from the laboratory tests, information on the benefits of drinking less, and encouragement to reduce drinking. In brief intervention groups A and B advice was supplemented with a self-help booklet. The subsequent brief intervention sessions were carried out in the same manner. For each session new laboratory values were available and the patient's alcohol consumption level was ascertained.

Group A had seven brief intervention sessions (at the baseline and at 2, 6, 12, 18, 24 and 30 months) and group B three sessions (at the baseline and at 12 and 24 months). Brief intervention was given by a general practitioner, except in group A, where advice was given by a nurse at 6, 18, and 30 months. At the baseline control group C was advised to reduce drinking and contact their general practitioner in the event of any health problems. However, the controls were not told about an invitation to follow-up at 36 months.

### 4.1.4 End point assessment

End point assessment was carried out at 36 months. The subjects were invited in two rounds of letters and one phone call. Outcome measures were self-reported alcohol consumption, CDT, MCV, ASAT, ALAT and GGT.

The drop-out rates in the groups A, B, and C were 39% (43/109), 30% (30/99), and 24% (21/88) among males and 45% (18/40), 24% (9/38), and 32% (13/40) among females respectively (Figure 1). Differences between the groups were not statistically significant. Those who participated in the end point assessment attended brief intervention sessions on an average among males 6.0 (range 2-7) times out of 7 in group A and 2.7 (range 2-3) times out of 3 in group B and among females 5.9 times out of 7 in group A and 2.8 times out of 3 in group B.

### 4.1.5 Laboratory analyses

Serum for CDT, ASAT, ALAT, and GGT, and EDTA blood for MCV were collected in a routine way. MCV, ASAT, ALAT, and GGT were measured on the same day. Serum samples for CDT were stored at -70°C and were measured later. The CDT containing di-, mono-, and asialotransferrin (Stibler 1991) was separated by anion exchange chromatography and quantified by double antibody radioimmunoassay (CDTect, Pharmacia Upjohn, Diagnostics, Sweden). MCV was measured with a Coulter Counter Stacker hematological analyser (Coulter Electronics, Inc., Hialeah, FL, USA). Activities for serum ASAT, ALAT, and GGT were determined by Hitachi 717 Automatic Analyser (Hitachi Ltd., Tokyo, Japan). Cut-off points of CDT, MCV, ASAT, ALAT, and GGT were for men 20 u/l, 97 fl, 50 u/l, 50 u/l, and 80 u/l, and for women 26 u/l, 97 fl, 35 u/l, 35 u/l, and 50 u/l. Combinations of laboratory markers were considered to be positive if at

least one of the markers studied was elevated. The ASAT/ALAT ratio was positive when above 1.5 (Cohen and Kaplan 1979).

# 4.2 Prevalence of heavy drinking and drinking habits study (I)

There is a notable difference in methods between this prevalence and drinking habits study and the brief intervention study previously presented. In this prevalence and drinking habits study subjects were heavy drinkers and not early-phase heavy drinkers as in the brief intervention study. Thus, in this study there was no exclusion of other than early-phase heavy drinkers as in the brief intervention study. Samples were also only partly the same.

### 4.2.1 Primary health care

The sample of subjects from primary health care was partly the same as in the brief intervention study. Patients screened for alcohol consumption in the brief intervention study in the Laune primary health care clinic and the occupational health care clinic formed the sample (Figure 2). These clinics were chosen for comparison because of their obvious difference. During the study the area of Laune had the highest unemployment rates and use of health services in the town.

A male patient was defined as a heavy drinker if his self-reported alcohol consumption was at least 280 grams of absolute ethanol (24 standard drinks) per week and/or if he had at least three affirmative answers in CAGE (Seppä and Mäkelä 1993). For women the limits were 190 grams (16 standard drinks) and/or two affirmative answers (Seppä et al. 1992). The health questionnaire was distributed in a primary health care clinic and an occupational health care clinic to

2370 and 3268 patients respectively (Figure 2). The response rates were 79% (1861/2370) and 90% (2942/3268) respectively.

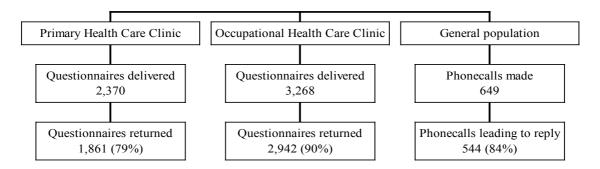


Figure 2. Study samples.

### 4.2.2 General population

In March 1994 a telephone survey was conducted by Gallup Finland Ltd among people aged 20-60 years in the town of Lahti. CAGE was included, but in contrast to the primary health care population, there was no questionnaire on self-reported alcohol consumption. Criteria for heavy drinking were the same as in the clinics: three or more affirmative answers in CAGE for males and two or more for females (Seppä et al. 1992, Seppä and Mäkelä 1993). The randomly collected sample size was 544 (Figure 2). First telephone numbers were randomly chosen by a computer. Then the numbers were called and structured questions about gender, age, education and occupation were asked to make sure that the sample was representative of the population of Lahti. During the collection of the sample 105 (16%) people refused to answer the questions (Figure 2).

### 4.3 Statistical analyses

Frequency of drinking per week, usual drinking amount per occasion and self-reported alcohol consumption per week were compared among all men and women between two primary health care settings (I). Distributions of affirmative answers to CAGE and prevalence of heavy drinking according to it were compared between primary health care clinic, occupational health care clinic and general populations.

Laboratory markers were compared separately in both genders divided into four agegroups and self-reported alcohol consumption was used as a covariate when studying the effect of gender, age, body mass index and smoking on the marker values in logistic regression model (II).

Compliant and non-compliant heavy drinkers were compared through odds ratios and their 95% confidence intervals (III). Odds ratios were considered to be significant if confidence intervals did not include the value 1.0, and adjustment for gender and age were made based on a logistic regression model.

The general idea of the brief intervention effectiveness study was to compare the outcome measures of different study groups, and also to test the changes within the groups (IV, V). In the intention to treat analysis it was assumed that patients who did not attend the end point assessment had no change in alcohol consumption or in other outcome measures.

In frequency comparisons chi-square test was used. When means were compared t-test for independent samples or one way analysis of variance was used for parametric variables and the Mann-Whitney test or Kruskal-Wallis one way analysis of variance for non-parametric variables. T-test for paired samples was used for parametric variables and the Wilcoxon test was used for non-parametric variables to test the change between two time points within the groups. Differences were considered statistically significant at p<0.05. SPSS statistical software was employed (Norušis 1993).

## 5 RESULTS

#### 5.1 Prevalence of heavy drinking and drinking habits (I)

The prevalences of heavy drinking according to CAGE among men in the primary health care clinic, occupational health care clinic and general population were 20% (145/744), 17% (148/856) and 16% (46/281) respectively (Table 2). Differences were not statistically significant. Among women the corresponding figures were 9% (95/1103), 6% (127/2062) and 13% (34/263) and the differences were found to be significant between all the populations. The general population had relatively more individuals giving one to three positive answers than in the clinics (Table 2). The proportion of those having four affirmative answers was highest in the primary health care clinic. In primary health care using self-reported alcohol consumption beside CAGE detected 1% more of male and equal numbers of female heavy drinkers than if using CAGE alone.

The primary health care clinic patients drank significantly (p<0.05) more per occasion than the patients of the occupational health care clinic (75 vs. 66 grams in men; 33 vs. 27 grams in women) and fewer times per week (0.8 vs. 0.9 in men; 0.5 vs. 0.6 in women). The male patients in the primary health care clinic and in the occupational health care clinic reported drinking 76 vs. 67 grams per week (p $\geq$ 0.05). Among females the corresponding figures were 23 vs. 19 grams (p<0.05). In spite of this there were significantly more patients reporting not drinking at all in the primary health care clinic than in the occupational health care clinic (17 vs. 11% in men; 34 vs. 29% in women).

Table 2. Affirmative answers to CAGE (%) among primary health care clinic (PHC), occupational health care clinic (OHC) and general population (GNP) subjects.

	Men			Women		
CAGE score distribution	PHC (n=744)	OHC (n=856)	GNP (n=281)	PHC (n=1103)	OHC (n=2062)	GNP (n=263)
0	47	51	42	90	05	71 &
0	47 21	51 20	42 22	80 12	85 9 *	71 ‡
1						16 ‡‡
2	12	12	19 ††‡‡	4	4	9 ††‡‡
3	8	9	9	2	1 *	4 ‡‡‡
4	12	8	7 †	2	0.6 **	0.0 †

Comparison within male and female groups: \*PHC vs. OHC, †PHC vs. GNP, ‡ OHC vs. GNP. One symbol p<0.05, two symbols p<0.01, three symbols p<0.001.

## 5.2 Laboratory markers as indicators for brief intervention (II)

An elevated value of at least one of the five markers was found in 75% of the male early-phase heavy drinkers and in 76% of the female early-phase heavy drinkers. The marker with the best sensitivity was CDT (39%) in men and MCV (40%) in women (Table 3). In the agegroup 20-40 years among men and 20-30 years among women CDT was more often increased than conventional laboratory markers (Table 3). Sensitivities of ASAT and GGT were rather poor in the youngest agegroup, but in the agegroup 41-50 years GGT was the most sensitive in both genders. In the oldest male group CDT was slightly better than GGT and MCV, but in the oldest female group MCV clearly had the highest sensitivity (68%).

Table 3. Sensitivities (%) of laboratory markers among early-phase heavy drinkers in different agegroups.

		Agegroup (years)				
	All patients	20-30	31-40	41-50	51-60	
Men	(n=329)	(n=55)	(n=79)	(n=123)	(n=72)	
CDT MCV ASAT ALAT GGT	39 28 12 28 33	47 11 7 22 13	44 28 13 33 37	30 29 11 29 37	41 39 15 25 40	
Women	(n=136)	(n=30)	(n=34)	(n=44)	(n=28)	
CDT MCV ASAT ALAT GGT	29 40 20 29 34	37 23 0 7 3	32 38 12 15 29	32 36 36 48 52	14 68 25 39 43	

The best combination of two laboratory markers among men (CDT or GGT) was increased in 62%, and among women (CDT or MCV) in 60% of the early-phase heavy drinkers. The best triple combination (CDT or MCV or GGT) was positive in 69% of the men and 70% of the women.

According to logistic regression MCV and GGT in both genders and ALAT in women were increased by age. High body mass index increased all three transaminases among men and GGT among women, but decreased CDT in both genders and MCV among women. Among male smokers MCV was higher and among female smokers ASAT was lower. Self-reported alcohol consumption had

only a slight effect among men and hardly any among women as regards laboratory values.

# 5.3 Compliance rate and associated factors for entering brief intervention (III)

In sum, 487 out of 1011 (48%) early-phase heavy drinkers agreed to enter brief intervention treatment. Men complied 1.7 (95% CI: 1.3-2.2) times more with treatment than women. Patients aged 40-60 years agreed to have it 1.6-1.7 (95% CI: 1.1-2.6) times more than the youngest ones. Patients aged 30-39 years did not differ from those aged 20-29 years.

All drinking factors had a marked effect on compliance in starting the treatment. The higher the weekly self-reported consumption, drinking frequency and usual drinking amount were, the larger the proportions of compliant patients. Those who reported drinking more than 200 grams of pure alcohol per week were 6.4-7.9 (95% CI: 4.3-13.1) times more likely to agree start a brief intervention treatment program than those who reported drinking less than 100 grams per week.

Patients who smoked more than twenty cigarettes per day were 1.6 (95% CI: 1.1-2.4) times more willing to begin treatment than non-smokers. Those who exercised only occasionally, were 1.8 (95% CI: 1.2-2.5) times more willing than those who exercised more than three times per week.

Education, employment, partner status, CAGE score, coffee drinking, body mass index, fat used on bread, use of anxiolytics or sleeping pills, and self-assessment of physical or mental health were not associated with compliance.

### 5.4 Effectiveness of brief intervention (IV,V)

Randomization of 296 males and 118 females into the three study groups was appropriate, because only the variables to show significant difference between three groups at baseline were education among males and MCV among females.

Table 4 shows the results based on analyses according to protocol. Analyses according to protocol and intention to treat did not differed in producing statistically significant figures. In mean changes between the baseline and end point there was no statistically significant difference between the study groups A, B, and C in outcome measures (Table 4). Instead, a significant reduction of MCV values was found within all groups after three years (Table 4). Among men a significant increase was found in the ASAT value of the control group C at three years.

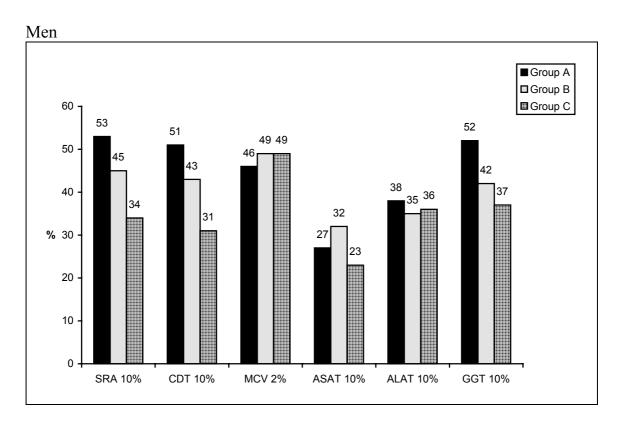
Mean changes in drinking variables and laboratory values were compared separately in the following male subgroups: Age groups (20-30, 31-40, 41-50, 51-60 years old); partner (having, not having), education (basic compulsory education, vocational school, college/university) and employment (working/studying, unemployed, retired). Significant differences between treatment and control groups were not found in any of the subgroups. Female subgroups were too small to be analysed.

Figure 3 shows the proportion of patients with clinically meaningfully decreased values of outcome measures indicating positive development during follow-up. Depending on the outcome measure and the study group clinically meaningful reduction of drinking (at least 10% in self-reported alcohol consumption, CDT, ASAT, ALAT and GGT, and 2% in MCV) was found in 23-53% of the male early-phase heavy drinkers. The corresponding figures for females were 30-75%. Among females heavy drinkers in group B the number of subjects having decreased self-reported alcohol consumption was statistically significantly lower than in the other two groups. There were no other significant differences between the study groups.

Table 4. Means (SD) of outcome measures at baseline and three-year follow-up according to protocol. There were no statistically significant difference between the study groups.

		Men		Women		
	Group	Baseline	3 years	Baseline	3 years	
SRA (gr/week)	A	237 (169)	240 (279)	216 (193)	131 (176)	
2-1-1 ( <b>B</b> ., 2 3-1)	В	269 (190)	278 (217)	180 (169)	279 (395)	
	C	267 (278)	320 (350)	154 (134)	146 (158)	
CDT (u/l)	A	21.2 (12.3)	19.0 (11.1)	22.2 (12.7)	20.8 (12.2)	
. ,	В	23.4 (13.2)	22.1 (13.4)	23.6 (13.8)	21.4 (13.4)	
	C	20.6 (16.1)	20.3 (12.2)	20.1 (6.9)	19.0 (6.3)	
MCV (fl)	A	94.5 (4.5)	93.1 (4.3)**	95.7 (3.6)	93.8 (5.1)*	
. ,	В	94.1 (4.0)	92.6 (3.8)**	96.8 (4.1)	95.4 (3.2)*	
	C	94.2 (3.7)	92.4 (3.2)**	94.2 (4.0)	93.0 (4.0)**	
ASAT (u/l)	A	31.9 (19.7)	32.8 (16.6)	31.8 (21.8)	33.7 (31.0)	
,	В	30.5 (11.0)	39.4 (60.0)	34.5 (33.0)	32.7 (30.8)	
	C	37.0 (32.5)	38.2 (28.5)*	25.4 (13.6)	27.6 (23.5)	
ALAT (u/l)	A	40.1 (31.7)	37.7 (24.1)	41.3 (38.6)	39.9 (53.5)	
( )	В	35.3 (19.3)	48.2 (93.6)	36.1 (24.8)	28.5 (18.0)	
	C	49.7 (49.3)	47.4 (43.7)	28.0 (21.5)	28.6 (25.6)	
GGT (u/l)	A	87.7 (83.0)	93.6 (113.6)	86.1 (122.1)	76.3 (96.7)	
<b>\</b>	В	77.2 (63.4)	89.1 (102.7)	90.0 (156.0)	55.6 (51.0)	
	C	96.4 (208.3)	77.3 (89.1)	35.8 (24.7)	40.3 (33.9)	

<sup>\*</sup> p<0.05, \*\* p<0.01, comparison with the baseline value within group SRA=Self-reported alcohol consumption



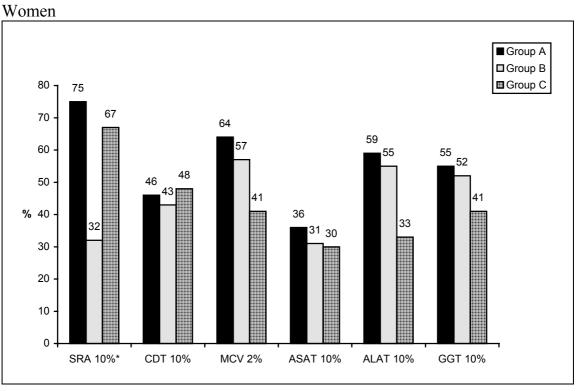


Figure 3. Proportion (%) of early-phase heavy drinkers with decreased outcome measure values. Variable percentage refers to minimum decrease from baseline to three years. \* p<0.05 between the groups. (SRA = self-reported alcohol consumption)

## 6 DISCUSSION

### 6.1 Subjects

There is a notable difference in subjects between the prevalence and drinking habits study (I) and the brief intervention study (II-V). In the prevalence and drinking habits study all heavy drinkers were included (also alcohol dependents and subjects who did not use primary health care services) and in the brief intervention study subjects were treatment-seeking early-phase heavy drinkers.

The early-phase heavy drinking subjects were consecutive patients attending a primary health care outpatient clinic for any reason (II-V). This type of non-alcohol treatment-seeking population is a natural target for brief intervention in routine primary health care work. Subjects represent early-phase heavy drinkers, since alcohol dependent patients or those having some other major alcohol-related disease were not included. This is also supported by the fact that the ASAT/ALAT ratio indicative of alcohol-related liver damage was greater than 1.5 in only 11-12% of the selected heavy drinkers (Cohen and Kaplan 1979).

The response rate to a health questionnaire was good (81%). Sample size was small among women (IV), but among men (V) a sample size calculation gives 81% power using the 5% level of significance.

The dropout rates were high (24-45% depending on the group) (IV,V). However, in an effectiveness study the dropout rate is not only a methodological problem but can also be considered as a result. This is an important issue because high dropout rates may cause a lack of credibility of brief intervention among busy general practitioners and impair the implementation process of brief intervention. Beside the naturalistic environment high dropout rates were partly due to the long three-year follow-up.

#### 6.2 Methods

The strengths of the present study were the use of the routine environment of primary health care (I-V), the use of several different and the most accurate laboratory markers (II,IV,V), and a sufficiently long three-year follow-up in evaluating the effectiveness of brief intervention (IV,V). Many outcome measures were used because there is no absolutely reliable way to monitor changes in drinking (IV,V) (Poikolainen 1985, Sillanaukee 1996).

Because this study was done in the naturalistic environment of primary health care, there are conceivable weaknesses which must be recognised. It is possible that self-reported alcohol consumption may not be as reliable as in a strict research setting. This might explain why self-reported alcohol consumption did not decrease in the same way as CDT and MCV among men or why self-reported alcohol consumption increased but CDT, MCV and GGT values decreased in group B among women (IV,V).

CAGE is shown to be a reasonably valid marker of heavy drinking in primary health care (Wallace and Haines 1985) and it has also shown its applicability in a population survey (Smart et al. 1991). However, it must be remembered that CAGE does not measure alcohol consumption itself, but can be used rather as marker of heavy drinking, The chosen CAGE cut-off, higher than in international studies, for men has earlier been found valid in Finland, where binge drinking is the most common type of alcohol abuse (Seppä et al. 1992, Seppä and Mäkelä 1993).

Beside the real difference in the prevalence of heavy drinking based on CAGE between primary health care and general population, there are other conceivable explanations (I). The collection of the CAGE data was done using different methods: the self-administered questionnaire was used among primary health care population and the telephone survey among general population. This may affect the validity of comparison of these populations, even though Aertgeerts et al. (2000) found no difference between the oral and the written

versions of CAGE. One may speculate that there was greater pressure to belittle problems caused by drinking in primary health care, where the patient returned the questionnaire to a general practitioner, than in a telephone survey (I). On the other hand one might say for the same reason and also because the general practitioner knows patients personally, that in primary health care patients underestimated their problems less. These explanations are not obvious, because a recent study indicated that patients' self-reports of alcohol consumption or problems were not affected by their knowledge that physicians would know their responses, and that interviews conducted in medical settings did not skew self-report data (Chan et al. 1996).

An important aim of the study was to evaluate brief intervention in a naturalistic environment, but the study protocol included some parts that can be considered artificial in a real context (IV,V). Heavy drinkers with severe somatic or psychiatric disease were excluded. This has been a common procedure in previous brief intervention studies and it is not known how these patients respond to brief intervention.

One study aim was to compare brief intervention programs with different frequencies, which were therefore structured beforehand, but in practice it could vary for different patients (IV,V). Also, a case-finding strategy would be an alternative procedure to the screening strategy which we used. It could be better accepted by the personnel and patients, and may have led to better treatment outcomes. Another important item is that the study procedure demanded effort from the personnel and thus reluctance on their part may be due to study procedure as much as brief intervention (IV,V).

### 6.3 Prevalence of heavy drinking and drinking habits (I)

According to CAGE among men the prevalences of heavy drinking in the primary health care clinic, occupational health care clinic and general population were 20%, 17% and 16% respectively. Among women the corresponding figures were 9%, 6% and 13%. These numbers are within the limits of the previous findings (Wallace and Haines 1985, Nicol and Ford 1986, Wiseman et al. 1986, Hilton 1987, Simpura 1987, Wallace et al. 1987b, Cherpitel 1991, Smart et al. 1991, Simon et al. 1991, Saunders et al. 1993a, Alvarez and Del Rio 1994, Chan et al. 1994, Cherpitel 1994, Cherpitel 1995, Holmila 1995, Bongers et al. 1997, Cherpitel 2000). The prevalences found in different studies are not directly comparable, because the research methods, criteria of heavy drinking and characteristics of populations are different. In the present study the number of heavy drinkers visiting and not the number of visits were compared in primary health care, and thus these data permit no conclusions about heavy drinkers' use of health services.

A common finding in previous studies is that heavy drinking both in primary health care and general population is more prevalent among men than women; in the present study the ratio was between 1.5 and 3 depending on the sample. According to self-reported alcohol consumption the primary health care clinic patients drank significantly more per occasion than the patients of the occupational health care clinic and fewer times per week. The female patients in the primary health care clinic also reported drinking more per week. These are natural findings, since the patients of the occupational health care clinic were all working.

The prevalence of heavy drinking in primary health care patients and the general population in the same geographical area has been compared in only few studies using the same method and criteria (Cherpitel 1991, Chan et al. 1994, Cherpitel 1994, Cherpitel 1995, Cherpitel 2000). However, it is advisable to use the same method and criteria before drawing any conclusions about prevalence being higher in either one of them. Three of the previous studies in addition to the present one suggest that heavy drinking is not necessarily over-represented in primary health care compared with the general population (Cherpitel 1994, Cherpitel 1995, Cherpitel 2000).

When considering the difference in prevalence between primary health care and general population, it is possible that in general women have recently increased alcohol consumption in the area studied, but health consequences have not yet occurred and thus the prevalence of heavy drinking is lower in primary health care than in the general population. The second possibility is that heavy drinkers visiting the clinics have reduced alcohol consumption already because of successful health advice from health personal or because of some illness. The third possibility is that female heavy drinkers might not dare to look for help for their heavy drinking or problems due to drinking. This could be particularly true with female heavy drinkers having fewer problems from drinking according to CAGE. The fourth possible explanation is that female heavy drinkers seek for help from other than primary health care services for their alcohol-related problems.

In the primary health care clinic there were significantly more subjects having four affirmative answers to the CAGE test than in the general population (Table 2). This is suggestive of an advanced alcohol problem. By contrast women with two or three affirmative answers, which refers to them having fewer problems, were significantly more prevalent in the general population. These results suggest that female heavy drinkers with advanced problems may be more common in primary health care than in the general population, but that female heavy drinkers with fewer problems may be more common in the general population.

## 6.4 Laboratory markers as indicators for brief intervention (II)

Even though in the present study the mean self-reported alcohol consumption was 280 grams per week in male and 170 grams per week in female early-phase heavy drinkers, none of the single markers exceeded a sensitivity of 40%. Taking into

account that in this study the limits for heavy drinking were lower than in earlier studies, the sensitivity problems are in accordance with previous studies on primary health care (Baxter et al. 1980, Nalpas et al. 1989, Poupon et al. 1989, Meerkerk et al. 1999). In these studies the sensitivities of CDT, MCV, ASAT, ALAT, and GGT were 31-45%, 17-30%, 10%, 10%, and 31-50% respectively. However, marker combinations including CDT seem to be a useful help in detecting early-phase heavy drinkers. The best triple combination (CDT or MCV or GGT) reached a good level of sensitivity (69% in men and 70% in women) among these early-phase heavy drinkers. Aithal et al. (1998) found this combination to produce sensitivity of 85% in a general medical setting. On the basis of the present data the specificities of the markers cannot be defined and one should keep in mind the decreasing effect of combination on specificity. In the case of CDT specificity is relatively good; up to 97% (Stibler 1991). The specificities of conventional laboratory markers are lower and have to be taken into account especially if using only laboratory markers for the detection of heavy drinkers. However, in clinical work specificity is not generally problematic, since usually use of laboratory markers is indicated only to assist in the detection of heavy drinking. Patient history, findings and questionnaires also usually play an important role.

Age and gender seemed to affect the markers considerably. MCV was more sensitive in women, and ageing seemed to increase it, especially among them. The probable reasons for this are biological changes caused by menopause (Chalmers et al. 1979, Morgan et al. 1981). The present study confirmed previous results that GGT is rarely elevated in young adults (Whitfield et al. 1978, Bliding et al. 1982, Nyström et al. 1993) but is contradictory to GGT being less sensitive in women than in men (Whitfield et al. 1978). Age did not have an effect on CDT. However, it was surprisingly rarely elevated among the oldest (51-60 year) female group. The reason for this is unknown, although it has recently been reported that after menopause women have lower levels of CDT than earlier in life (Stauber et al. 1996). Chan et al. (1989) reported that CDT is less likely to be

elevated in young adults, which is contradictory to our results; CDT was the best marker in the agegroup 20-30 years. This is consistent with the study of Yersin et al. (1995) who noted that among 20-40 year old men it was the most sensitive marker for heavy drinking.

In the present study body mass index had an effect on all the markers studied, at least in one gender. As expected, high body mass index elevated transaminases including GGT (Nilssen et al. 1990), and had negative correlation with MCV among women. A novel finding was that body mass index correlated negatively with CDT (Stibler 1991). The reason for this is not known, and the finding needs to be confirmed. In this study smoking clearly elevated only MCV values among men. This is in accordance with previous results (Chalmers et al. 1979, Morgan et al. 1981).

# 6.5 Compliance rate and associated factors for entering brief intervention (III)

As many as about half of the early-phase heavy drinkers complied with a recommendation for brief intervention. Gender, age, drinking variables, smoking and exercise were associated with compliance. Women and young adults were subgroups of early-phase heavy drinkers whose compliance was lower than others. There have been only few previous attempts to identify factors associated with early-phase heavy drinkers' willingness to enter brief intervention (Edwards and Rollnick 1997). The factors found here are associated with willingness to enter the treatment and they may differ from those associated with completing the treatment according to a plan or those factors associated with a good outcome.

Patients' motivation for treatment is not only intrinsic, it also depends on the interaction with the person trying to get them into treatment. However, in the present study general practitioners' characteristics were not ascertained. General practitioners were not selected and they mainly used skills that they had adapted before through practical work and professional training.

Men complied to participate brief intervention almost twice more frequently than women. This may indicate higher thresholds for women than men to overcome, if they are to enter treatment for their alcohol problems (Duckert 1987). In the study by Wallace et al. (1988) 60% of men and 64% of women screened as heavy drinkers, including alcohol dependents, attended the initial interview. In the present study the proportions were lower (54% for men and 39% for women) and men demonstrated higher compliance than women. The reason for the difference is probably partly due to the exclusion of alcohol dependents from the present study. In one study the attendance rate was as low as 29% (Heather et al. 1990). In many brief intervention studies no compliance rate for entering treatment comparable to the present study has been reported. Variation in study designs and in populations also makes comparison of compliance rates difficult.

Wallace et al. (1988) noted that compliance was greater among older patients with lower levels of alcohol consumption than in younger and heavier drinkers. The present study found the same phenomenon concerning age, but those who reported drinking more had higher compliance. Other self-reported drinking variables were also strongly associated with willingness to enter brief intervention in the present study. A higher refusal rate among young patients has also been found in earlier studies concerning the treatment of alcoholism (Rees et al. 1984, Noel et al. 1987).

In treating addiction, the most important factors associated with lack of treatment compliance have been found to be low socio-economic status, lack of family support, and comorbid psychiatric conditions (McLellan et al. 1980, Alterman and Cacciola 1991, Havassy et al. 1995). According to the present data, early-phase heavy drinkers' education, employment or partner status did not affect willingness to enter the treatment. Neither did the use of anxiolytics, which may indicate psychiatric disorder. Additionally, even if there was a trend suggesting that unhealthy lifestyle is mildly associated with greater compliance,

only in the groups of smoking more than a package per day or exercising only occasionally was the ratio significant.

It is slightly surprising that factors such as CAGE score, hours of sleep or self-assessment of health indicating consequences of drinking were not associated with compliance enough to reach significance. However, there was a trend in self-assessment suggesting poorer health being associated with higher compliance. CAGE score indicating mainly the social consequences of drinking did not show any association with compliance. This can probably be explained by the fact that high CAGE score was the most common inclusion criterion in the present study.

### 6.6 Effectiveness of brief intervention (IV,V)

A statistically significant decrease of MCV in the brief intervention and control groups was found (Table 4). However, brief intervention was not found to be superior in terms of statistical significance. A clinically meaningful reduction of drinking was found in 23-53% of the male and 30-75% of female early-phase heavy drinkers after three years (Figure 3).

To estimate the meaning of results, answers to the following questions must be attempted:

(1) Was drinking reduced among the subjects as a whole?

Based on a statistically significant decrease of MCV and tendencies in some other outcome measures justifies an affirmative answer to this question.

(2) If there was reduction as a whole, was it at least partly due to study action?

Based on the present data this cannot be answered with certainty. However, based on the high reduction rates found in this study it is unlikely that these numbers would have been reached only by natural development without the study activity. A recent study about the natural development of alcohol use supports

this improbability among men (Seppä et al. 1999). Another reason to think that reduction to some point was due to study activity is the evidence already existing in favour of brief intervention.

(3) Why did brief intervention groups A and B not differ from control group C?

There are three possible answers:

- (a) The minimal advice, as offered in group C, reduces drinking as much as the more extensive brief intervention. The control group patients were first screened by a health questionnaire including alcohol-related questions and then visited a general practitioner twice. Patients in the control group also received feedback from their laboratory tests and high drinking amounts even if they were not told that they were going to be asked to attend follow-up after three years. The forming of a 'true' control group would have been unethical, because of evidence already existing in favour of brief intervention.
- (b) Brief intervention in the routine environment is not as effective as in special research conditions. This was an effectiveness study. Thus, screening, detection and brief intervention were done by the local personnel, and general practitioners and nurses were not selected; all of them participated. In giving brief intervention they mainly used skills that they had adapted earlier through practical work and professional training.

Over a decade ago Heather (1989) already saw the main obstacle to the successful implementation of brief intervention to be the reluctance of professionals. One consequence of the routine environment may have been a problem of committing general practitioners and nurses to provide competent brief intervention (Thom and Tellez 1986). It has been noted in health care that giving only information about treatment recommendations does not change practices much (Greco and Eisenberg 1993, Glanville et al. 1998). In a routine environment there are possibly more negative attitudes to the treatment of heavy drinkers than in a strict research situation (Drummond 1997). Negative attitudes about patients' alcohol problems, scepticism about the effectiveness of brief

intervention treatment, and the perception that alcohol problems are not in the realm of primary health care providers may affect the treatment results in a naturalistic environment (Peters et al. 1996, O'Connor and Schottenfeld 1998).

Preventive work calls for quite a different battery of skills, with a non-authoritarian approach and shared responsibility with the patient. The counselling style of professionals and certain aspects of their behaviour probably predict patient outcomes. Probably there is variation in the general practitioners' and nurses' choice of delivery of brief intervention. However, allowing them to select what is the most appropriate brief intervention for themselves and their patients is thought to be a crucial factor in promoting brief intervention in practice (Richmond and Anderson 1994b). Allowing this is also rational, because we do not know what the exact ingredients for successful brief intervention are (Bien et al. 1993, Spivak et al. 1994, Heather 1995).

In a naturalistic environment study populations are often different from strict research conditions. One possible explanation why this study failed to demonstrate good effectiveness of brief intervention is the high proportion of unemployed people among subjects. There were about twice as many unemployed people among subjects than in the community at the time. Unemployment sometimes includes a complexity of problems and may thus have an impact in brief intervention results as a whole.

Richmond et al. (1995) conducted a controlled effectiveness study using naturalistic screening and brief intervention. In that study male patients receiving brief intervention reduced drinking more than controls, but this difference was not significant. However, there was a significantly greater reduction in the number of alcohol-related problems at the 6 months follow-up reported by those receiving brief intervention. Thus, these results are in accordance with the present study.

(c) Especially among women, lack of difference may be due to small sample size.

### 7 CONCLUSIONS

- 1. The high prevalence of heavy drinking found in this study confirms that the potential target group for brief intervention is abundant. About every fifth male and every fourteenth female outpatient of primary health care is a heavy drinker. The present study indicates that the prevalence of heavy drinking and drinking habits depend on the nature of the clinic and that heavy drinkers in general may not be over-represented in primary health care, as is usually believed. Female heavy drinkers may even be over-represented in the general population. This raises the question of how to reach and to provide health advice to those female heavy drinkers who do not visit primary health care.
- 2. The marker with the best sensitivity in men was CDT and in women MCV, but none of the single markers detected more than 40% of early-phase heavy drinkers. Thus, when laboratory markers are considered for use in the detection of early-phase heavy drinking, CDT combined with MCV and GGT rather than single markers should be considered. In the agegroup 20-30 years the use of CDT beside conventional markers is especially recommended.
- 3. For many early-phase heavy drinkers it is not easy to make the decision to participate in a brief intervention treatment program or then they are not sufficiently aware of their drinking problem. However, as many as about half of the early-phase heavy drinkers complied with a recommendation for brief intervention. Gender, age, drinking variables, smoking and exercise are associated with willingness to enter brief intervention. According to the present study, women and young adults are subgroups among early-phase heavy drinkers whose compliance is lower than others. The study raises the

question of how better to motivate women and young adult heavy drinkers to reduce their drinking.

4. The results indicate that drinking was reduced in all the study groups after three years. Depending on gender, outcome measure and intervention received, clinically meaningful reduction of drinking was found in 23-75% of the early-phase heavy drinkers. It is unlikely but unknown whether these numbers would have been reached only by natural development without the study actions. The present study suggests that the minimal advice, as offered in group C, is associated with reduced drinking as much as the more extensive brief intervention, and in the routine environment of primary health care the effectiveness of brief intervention may not be as good as in special research conditions. Different methods of implementing brief intervention need to be evaluated to find better ways to support primary health care personnel in their efforts to help heavy drinking patients to reduce drinking.

### 8 SUMMARY

Brief intervention represents a new perspective on responding to drinking problems. It is intended to provide early intervention, before or close to the onset of alcohol-related hazards. In general it includes identifying of heavy drinkers and short consultation sessions. There is the question of its effectiveness in a naturalistic environment of routine primary health care.

This study is divided into two parts: prevalence and brief intervention studies. The studies were carried out in primary health care and general population of the city of Lahti in Finland. The aim of the prevalence study was to estimate the prevalence of heavy drinking and to compare prevalences of two different primary health care populations and the general population. In brief intervention the study aims were to evaluate among non-alcohol treatment-seeking early-phase heavy drinkers the usefulness of certain laboratory markers in detection, rate of compliance to enter brief intervention, and the effectiveness of three-year long brief intervention carried out in the naturalistic environment of routine primary health care (effectiveness study).

Before the normal general practitioner's consultation time 14,548 consecutive patients aged 20-60 were screened for early-phase heavy drinking by quantity-frequency alcohol questions and CAGE test. The response rate was 81%. Screening criteria were 280 grams of absolute ethanol (24 standard drinks) per week and/or three affirmative answers in CAGE for men and 190 grams (16 standard drinks) and/or two affirmative answers for women. Of those positively screened, those who had severe somatic or psychiatric disease, who had had at least one detoxification treatment, who were alcohol dependent or had other severe alcohol-related disease, and who were social drinkers, were excluded.

Altogether 658 male and 353 female early-phase heavy drinkers were identified. Their CDT, MCV, ASAT, ALAT and GGT laboratory values were

tested. Of identified early-phase heavy drinkers 296 males and 118 females were randomised to one of the study groups: brief intervention group A (7 sessions), brief intervention group B (3 sessions), and control group C. Brief intervention was given by a general practitioner, except for three sessions by a nurse in group A. Group C was only advised briefly to reduce drinking. At end point assessment, which was at 36 months, the drop-out rates were 32% among males and 34% among females. Outcome measures were self-reported alcohol consumption and laboratory values.

The subjects of the prevalence study were partly the same as in the brief intervention study. Subjects were screened in two of the primary health care clinics (n=5638) and randomly drawn by telephone from the general population (n=544) formed a sample. The prevalence study concerned the whole population of heavy drinkers and not just early-phase heavy drinkers.

According to CAGE among men, the prevalences of heavy drinking in the primary health care clinic, occupational health care clinic and general populations were 20%, 17% and 16% respectively (p≥0.05). Among women the corresponding figures were 9%, 6% and 13% (p<0.05). However, the results suggest that female heavy drinkers with advanced problems are more common in primary health care than in the general population. Primary health care clinic and occupational health care clinic populations differed significantly in drinking variables. The high prevalence of heavy drinking found confirms that the potential target group for brief intervention is abundant. The study indicates that drinking habits depend on the nature of the clinic and heavy drinkers in general may not be over-represented in primary health care. Female heavy drinkers may even be over-represented in the general population, which raises the question of how to reach those female heavy drinkers who do not visit primary health care.

The sensitivities of CDT, MCV, ASAT, ALAT and GGT values were low; in men respectively 39%, 28%, 12%, 28% and 33%, and in women 29%, 40%, 20%, 29% and 34%. Age and gender seemed to affect the sensitivity of markers considerably. However, marker combinations including CDT reached a good

level of sensitivity; the best triple combination (CDT or MCV or GGT) was positive in 69% of the men and 70% of the women. It can be concluded that when laboratory markers are considered for use in detection, marker combinations including CDT rather than single markers should be considered. When only one marker is used gender and age should be taken into account.

As many as 48% of the early-phase heavy drinkers complied with a recommendation to enter brief intervention treatment. Men and older patients complied about 1.7 times more than women and young adults. All drinking variables had a significantly positive effect on compliance to start the treatment. Thus, for many early-phase heavy drinkers it is not easy to make the decision to participate in brief intervention. Women and young adults are subgroups of heavy drinkers whose compliance is lower than others and the study raises the question of how better to motivate them to reduce their drinking.

A statistically significant decrease of MCV indicates that drinking was reduced in all the study groups. However, in mean changes of the outcome measures there was no significant difference between the study groups. Especially among women, the lack of difference may be due to small sample size. Depending on the outcome measure and the study group a clinically meaningful reduction of drinking was found in 23-53% of the male and 30-75% of female early-phase heavy drinkers after three years. It is unlikely but unknown whether these numbers would have been reached only by natural development without the study actions. The results suggest that the minimal advice, as offered in group C, is associated with reduced drinking as much as the more extensive brief intervention, and that in the routine environment of primary health care brief intervention may not be as effective as in special research conditions. A possible reason for brief intervention not being as effective in routine environment as in special research conditions is the problem of committing professionals to provide competent brief intervention. Different methods of implementing brief intervention need to be evaluated to find better ways to support primary health care personnel.

## 9 ACKNOWLEDGEMENTS

This study was originated in 1993 by Docent Pekka Sillanaukee. I came along first to do my licentiate's thesis about prevalence of heavy drinking. As in my doctoral thesis, Docent Pekka Sillanaukee and Professor Kaija Seppä were my supervisors. Those were extremely exciting times when the scientific world was opening to me and a wish to go on with research slowly entered my mind. I am deeply grateful to Docent Pekka Sillanaukee and Professor Kaija Seppä for giving me encouragement and support of many kinds throughout these years. Beside scientific learning, they have given me valuable ingredients for personal growth, both of which I value equally.

The study began in the Biomedical Research Center of Alko Group Ltd and in later years was carried out in the Department of Mental Health and Alcohol Research of the National Public Health Institute. Many other organisations, such as Lahti City Primary Health Care, the Medical School of the University of Tampere, Tampere University Hospital and Pharmacia Upjohn, offered facilities.

Professor Timo Pitkäjärvi and Docent Rauno Mäkelä offered valuable advice as the official reviewers of this study, for which I am sincerely grateful.

My gratitude is also due to Professor Kalervo Kiianmaa for valuable advice, for providing facilities to perform the study and being a co-author. My sincere thanks to the members of the Lahti Project Group, especially Docent Marja Holmila and Kari Haavisto, M.A.

My sincere thanks are also due to all the personnel of Lahti City Primary Health Care and especially those who were members of the Brief Intervention Study Group: Raija Forsström, Margit Kainlauri, Markku Kiviluoto, Marja-Leena Kyllönen, Pirkko Laine, Reijo Saksanen, Pekka Mattila, Heikki Mustonen, Sirkka-Liisa Mäkelä, Hannu Pulkkinen, Jaakko Ripatti, Mia Raikaa, Kirsti Ruuth, Ritva Salminen, Marja-Leena Silkkari and Ritva Teräväinen.

I am very grateful to several other people: to Docent Hannu Alho for help in laboratory analyses and being a co-author; Hannu Koponen, M.A., and Jyrki Ollikainen, M.A., helping with the statistical analyses; Virginia Mattila, M.A., for her linguistic assistance; and Tuula Mäkelä for technical assistance.

I wish also to thank my parents, Raimo and Irene Aalto, for the support they have provided in many ways and for planting a seed of desire to learn in me. Finally, I owe my gratitude to my dear wife, Andrea, for the sharing joys of success and for her loving support in the moments of despair. My children, Sabiina and Daniel, has given me a different perspective on life, which has helped me when striving to possess a scientific mind.

Tampere, February 2001

Mauri Aalto

## 10 REFERENCES

- Aasland OG, Bruusgaard D and Rutle O (1987): Alcohol problems in general practice. Br J Addict 82:197-201.
- Aertgeerts B, Buntinx F, Fevery J and Ansoms S (2000): Is there a difference between CAGE interviews and written CAGE questionnaires? Alcohol Clin Exp Res 24:733-736.
- Aithal GP, Thornes H, Dwarakanath AD and Tanner AR (1998): Measurement of carbohydrate-deficient transferrin (CDT) in a general medical clinic: is this test useful in assessing alcohol consumption. Alcohol Alcohol 33:304-309.
- Allen JP, Litten RZ, Fertig JB and Babor T (1997): A review of research on the Alcohol Use Disorders Identification Test (AUDIT). Alcohol Clin Exp Res 21:613-619.
- Alterman AI and Cacciola JS (1991): The antisocial personality disorder in substance abusers: problems and issues. J Nerv Mental Dis 179:401-409.
- Alvarez FJ and Del Rio MC (1994): Screening for problem drinkers in general population survey in Spain by use of the CAGE scale. J Stud Alcohol 55:471-474.
- American Psychiatric Association (1994): Diagnostic and statistical manual of mental disorders, 4th edn. American Psychiatric Association, Washington DC.
- Anderson P (1985): Managing alcohol problems in general practice. Br Med J 290:1873-1875.
- Anderson P (1993): Effectiveness of general practice interventions for patients with harmful alcohol consumption. Br J Gen Pract 43:386-389.
- Anderson P and Scott E (1992): The effect of general practitioners' advice to heavy drinking men. Br J Addict 87:891-900.
- Anderson P, Cremona A, Paton A, Turner C and Wallace P (1993): The risk of alcohol. Addiction 88:1519-1534.
- Antti-Poika I, Karaharju E, Roine R and Salaspuro M (1988): Intervention of heavy drinking--a prospective and controlled study of 438 consecutive injured male patients. Alcohol Alcohol 23:115-121.
- Babor TF, Steinberg K, Anton R and Del Boca F (2000): Talk is cheap: measuring drinking outcomes in clinical trials. J Stud Alcohol 61:55-63.
- Baxter S, Fink R, Leader AR and Rosalki SB (1980): Laboratory tests for excessive alcohol consumption evaluated in general practice. Alcohol Alcohol 15:164-166.
- Bien TH, Miller WR and Tonigan JS (1993): Brief interventions for alcohol problems: a review. Addiction 88:315-335.
- Bliding G, Bliding A, Fex G and Tornqvist C (1982): The appropriateness of laboratory tests in tracing young heavy drinkers. Drug Alcohol Depend 10:153-158.
- Blondell RD, Frierson RL and Lippmann SB (1996): Alcoholism. Taking a preventive, public health approach. Postgrad Med 100:69-72,78-80.
- Bongers IM and van Oers HA (1998): Mode effects on self-reported alcohol use and problem drinking: mail questionnaires and personal interviewing compared. J Stud Alcohol 59:280-285.

- Bongers IM, van Oers HA, van de Goor IA and Garretsen HF (1997): Alcohol use and problem drinking: prevalences in the general Rotterdam population. Subst Use Misuse 32:1491-1512.
- Bongers IM, van de Goor IA, Garretsen HF and van Oers HA (1999): Aggregate comparisons of self-reported versus nonself-reported drinking in a general population survey. Subst Use Misuse 34:421-441.
- Bromley JW (1992): Our Society's response to addictions. Clin Chem 38: 1530-1531.
- Buchsbaum DG, Buchanan RG, Centor RM, Schnoll SH and Lawton MJ (1991). Screening for alcohol abuse using CAGE scores and likelihood ratios. Ann Intern Med 115:774-777.
- Buchsbaum DG, Welsh J, Buchanan RG and Elswick RK Jr (1995): Screening for drinking problems by patient self-report: even 'safe' levels may indicate a problem. Arch Intern Med 155:104-108.
- Burge SK, Amodei N, Elkin B, Catala S, Andrew SR, Lane PA and Seale JP (1997): An evaluation of two primary care interventions for alcohol abuse among Mexican-American patients. Addiction 92:1705-1716.
- Bush B, Shaw S, Cleary P, Delbanco TL and Aronson MD (1987): Screening for alcohol abuse using the CAGE questionnaire. Am J Med 82:231-235.
- Campbell NC, Thain J, Deans HG, Ritchie LD, Rawles JM and Squair JL (1998): Secondary prevention clinics for coronary heart disease: randomised trial of effect on health. BMJ 316:1434-1437.
- Carney MA, Tennen H, Affleck G, Del Boca FK and Kranzler HR (1998): Levels and patterns of alcohol consumption using timeline follow-back, daily diaries and real-time "electronic interviews". J Stud Alcohol 59:447-454.
- Chalmers DM, Levi AJ, Chanarin I, North WR and Meade TW (1979): Mean cell volume in a working population: the effects of age, smoking, alcohol and oral contraception. Br J Haematol 43:631-636.
- Chan AW, Leong FW, Schanley DL, Welte JW, Wieczorek W, Rej R and Whitney RB (1989): Transferrin and mitochondrial aspartate aminotransferase in young adult alcoholics. Drug Alcohol Depend 23:13-18.
- Chan AW, Pristach EA and Welte JW (1994): Detection by the CAGE of alcoholism or heavy drinking in primary care outpatients and the general population. J Subst Abuse 6:123-135.
- Chan AW, Welte JW and Pristach EA (1996): Detection of alcohol problems in primary care outpatients under different conditions. Drug Alcohol Depend 41:151-155.
- Chang G, Wilkins-Haug L, Berman S and Goetz MA (1999): Brief intervention for alcohol use in pregnancy: a randomized trial. Addiction 94:1499-1508.
- Cherpitel CJ (1991): Drinking patterns and problems among primary care patients: a comparison with the general population. Alcohol Alcohol 26:627-633.
- Cherpitel CJ (1994): Alcohol use among primary care patients: comparing an HMO with county clinics and the general population. Drug Alcohol Depend 36:167-173.
- Cherpitel CJ (1995): Alcohol use among HMO patients in the emergency room, primary care and the general population. J Stud Alcohol 56:272-276.
- Cherpitel CJ (2000): Drinking patterns and alcohol dependence: a comparison of primary care patients in a southern county with the regional general population. J Stud Alcohol 61:130-133.

- Chick J, Lloyd G and Crombie E (1985): Counselling problem drinkers in medical wards: a controlled study. Br Med J 290:965-967.
- Cohen JA and Kaplan MM (1979): The SGOT/SGPT ratio an indicator of alcoholic liver disease. Dig Dis 24:835-838.
- Conigrave KM, Saunders JB and Whitfield JB (1995): Diagnostic tests for alcohol consumption. Alcohol Alcohol 30:13-26.
- Crowe RR, Kramer JR, Hesselbrock V, Manos G and Bucholz KK (1997): The utility of the Brief MAST' and the CAGE' in identifying alcohol problems: results from national highrisk and community samples. Arch Fam Med 6:477-483.
- Cunningham JA, Ansara D, Wild TC, Toneatto T and Koski-Jännes A (1999): What is the price of perfection? The hidden costs of using detailed assessment instruments to measure alcohol consumption. J Stud Alcohol 60:756-758.
- Cushman WC, Cutler JA, Hanna E, Bingham SF, Follmann D, Harford T, Dubbert P, Allender PS, Dufour M, Collins JF, Walsh SM, Kirk GF, Burg M, Felicetta JV, Hamilton BP, Katz LA, Perry HM Jr, Willenbring ML, Lakshman R and Hamburger RJ (1998): Prevention and Treatment of Hypertension Study (PATHS): effects of an alcohol treatment program on blood pressure. Arch Intern Med 158:1197-1207.
- David AK (1994): Challenges in personal and public health promotion: the primary care physician perspective. Am J Prev Med 10 (3 Suppl):36-38.
- Davila R, Sanchez-Craig M and Wilkinson DA (2000): Effects of using recommended coping strategies on drinking outcome following a brief intervention. Addiction 95:115-122.
- Drummond DC (1997): Alcohol interventions: do the best things come in the small packages? Addiction 92:375-379.
- Dube C (1999): The physician's role in preventing alcohol and drug abuse. Med Health R I 82:95-98.
- Duckert F (1987): Recruitment into treatment and effects of treatment for female problem drinkers. Addict Behav 12:137-150.
- Eckardt MJ, Harford TC, Kaelber CT, Parker ES, Rosenthal LS, Ryback RS, Salmoiraghi GC, Vanderveen E and Warren KR (1981): Health hazards associated with alcohol consumption. JAMA 246:648-666.
- Edwards G and Gross M (1976): Alcohol dependence: provisional description of a clinical syndrome. BMJ 281:1058-1061.
- Edwards AG and Rollnick S (1997): Outcome studies of brief intervention in general practice: the problem of lost subjects. Addiction 92:1699-1704.
- Elvy GA, Wells JE and Baird KA (1988): Attempted referral as intervention for problem drinking in the general hospital. Br J Addict 83:83-89.
- Embree BG and Whitehead PC (1993): Validity and reliability of self-reported drinking behaviour: dealing with the problem of response bias. J Stud Alcohol 54:334-344.
- Fitzgerald JL and Mulford HA (1987): Self-report validity issues. J Stud Alcohol 48:207-211.
- Fleming MF and Barry KL (1991): A three-sample test of a masked alcohol screening questionnaire. Alcohol Alcohol 26:81-91.
- Fleming MF, Barry KL, Manwell LB, Johnson K and London R (1997): Brief physician advice for problem alcohol drinkers: A randomized controlled trial in community-based primary care practices. JAMA 277:1039-1045.

- Fleming MF, Manwell LB, Barry KL, Adams W and Stauffacher EA (1999): Brief physician advice for alcohol problems in older adults: a randomized community-based trial. J Fam Pract 48:378-384.
- Fleming MF, Mundt MP, French MT, Manwell LB, Stauffacher EA and Barry KL (2000): Benefit-cost analysis of brief physician advice with problem drinkers in primary care settings. Med Care 38:7-18.
- Gentilello LM, Rivara FP, Donovan DM, Jurkovich GJ, Daranciang E, Dunn CW, Villaveces A, Copass M and Ries RR (1999): Alcohol interventions in a trauma center as a means of reducing the risk of injury recurrence. Ann Surg 230:473-480.
- Glanville J, Haines M and Auston I (1998): Getting research findings into practice: Finding information on clinical effectiveness. BMJ 317:200-203.
- Grant KA, Tonigan JS and Miller WR (1995): Comparison of three alcohol consumption measures: a concurrent validity study. J Stud Alcohol 56:168-172.
- Greco PJ and Eisenberg JM (1993): Changing physicians' practices. N Engl J Med 329:1271-1274.
- Havassy BE, Wasserman D and Hall SM (1995): Social relationships and cocaine use in an American treatment sample. Addiction 90:699-710.
- Heather N (1989): Psychology and brief interventions. Br J Addict 84:357-370.
- Heather N (1995): Interpreting the evidence on brief interventions for excessive drinkers: the need for caution. Alcohol Alcohol 30:287-296.
- Heather N (1996): The public health and brief interventions for excessive alcohol consumption: the British experience. Addict Behav 21:857-868.
- Heather N, Whitton B and Robertson I (1986): Evaluation of a self-help manual for media-recruited problem drinkers: six-month follow-up results. Br J Clin Psychol 25:19-34.
- Heather N, Campion PD, Neville RG and Maccabe D (1987): Evaluation of a controlled drinking minimal intervention for problem drinkers in general practice (the DRAMS scheme). J R Coll Gen Pract 37:358-363.
- Heather N, Kissoon-Singh J and Fenton GW (1990): Assisted natural recovery from alcohol problems: effects of a self-help manual with and without supplementary telephone contact. Br J Addict 85:1177-1185.
- Helander A, Carlsson AV and Borg S (1996): Longitudinal comparison of carbohydrate-deficient transferrin and gamma-glutamyl transferase: complementary markers of excessive alcohol consumption. Alcohol Alcohol 31:101-107.
- Herbert C and Bass F (1997): Early at-risk alcohol intake: definitions and physicians' role in modifying behaviour. Can Fam Physician 43:639-644.
- Hilton ME (1987): Drinking patterns and drinking problems 1984: results from a general population survey. Alcohol Clin Exp Res 11:167-175.
- Hoeksema HL and de Bock MA (1993): The value of laboratory tests for the screening and recognition of alcohol abuse in primary care patients. J Fam Pract 37:268-276.
- Holder H, Flay B, Howard J, Boyd G, Voas R and Grossman M (1999): Phases of alcohol problem prevention research. Alcohol Clin Exp Res 23:183-194.
- Holmila M (1995): Intoxication and hazardous use of alcohol: results from the 1992 Finnish Drinking Habits Study. Addiction 90:785-792.
- Holmila M (1997): Community prevention of alcohol problems. Macmillan Education, Basingstoke.

- Hoyer G, Nilssen O, Brenn T and Schirmer H (1995): The Svalbard study 1988-89: a unique setting for validation of self-reported alcohol consumption. Addiction 90:539-544.
- Jellinek EM (1960): The disease concept of alcoholism. Hillhouse Press, New Haven.
- Jönson H, Hermansson U, Rönnberg S, Gyllenhammar C and Forsberg L (1995): Comments on brief intervention of alcohol problems: a review of a review. Addiction 90:1118-1120.
- Kahan M, Wilson L and Becker L (1995): Effectiveness of physicians-based interventions with problem drinkers: a review. Can Med Assoc J 152:851-859.
- Kreitman N (1985): Alcohol consumption and the prevention paradox. Br J Addict 81:353-363.
- Kristenson H and Trell E (1982): Indicators of alcohol consumption: comparison between a questionnaire (mm-MAST), interviews and serum gamma glutamyl transferase (GGT) in a health survey of middle aged males. Br J Addict 77:297-304.
- Kristenson H, Öhlin H, Hulten-Nosslin MB, Trell E and Hood B (1983): Identification and intervention of heavy drinking in middle-aged men: results and follow-up of 24-60 months of long term study with randomized controls. Alcohol Clin Exp Res 7:203-209.
- Lang T, Nicaud V, Darne B and Rueff B (1995): Improving hypertension control among excessive alcohol drinkers: a randomised controlled trial in France. J Epidemiol Community Health 49:610-616.
- Lemmens P, Tan ES and Knibbe RA (1992): Measuring quantity and frequency of drinking in a general population survey: a comparison of five indices. J Stud Alcohol 53:476-486.
- Lieber CS (1995): Medical disorders of alcoholism. N Engl J Med 333:1058-1065.
- Maheswaran R, Beevers M and Beevers DG (1992). Effectiveness of advice to reduce alcohol consumption in hypertensive patients. Hypertension 19:79-84.
- Mayfield D, McLeod G and Hall P (1974): The CAGE questionnaire: validation of a new alcoholism screening instrument. Am J Psychiatry 131:1121-1123.
- McLellan AT, Druley KA, O'Brien CP and Kron R (1980): Matching substance abuse patients to appropriate treatments. A conceptual and methodological approach. Drug Alcohol Depend 5:189-193.
- Meerkerk GJ, Njoo KH, Bongers IM, Trienekens P and van Oers JA (1998): The specificity of the CDT assay in general practice: the influence of common chronic diseases and medication on the serum CDT concentration. Alcohol Clin Exp Res 22:908-913.
- Meerkerk GJ, Njoo KH, Bongers IM, Trienekens P and van Oers JA (1999): Comparing the diagnostic accuracy of carbohydrate-deficient transferrin, gamma-glutamyltransferase, and mean cell volume in a general practice population. Alcohol Clin Exp Res 23:1052-1059.
- Miller NS and Sheppard LM (1999): The role of the physician in addiction prevention and treatment. Psychiatr Clin North Am 22:489-505.
- Miller WR and Rollnick S (1991): Motivational interviewing: preparing people to change addictive behaviour. Guilford Press, New York.
- Miller WR, Taylor CA and West JC (1980): Focused versus broad-spectrum behaviour therapy for problem drinkers. J Consult Clin Psychol 48:590-601.
- Miller WR, Brown JM, Simpson TL, Handmaker NS, Bien TH, Luckie LF, Montgomery HA, Hester RK and Tonigan JS (1995): What works? A methodological analysis of the alcohol treatment outcome literature. In: Handbook of alcoholism treatment approaches: Effective alternatives, pp. 12-44. Eds. Hester RK and Miller WR, Ally and Bacon, Massachusetts.
- Morgan MY, Camilo ME, Luck W, Sherlock S and Hoffbrand AV (1981): Macrocytosis in alcohol-related liver disease: its value for screening. Clin Lab Haematol 3:35-44.

- Musshoff F and Daldrup TH (1998): Determination of biological markers for alcohol abuse. J Chromatgr B 713:245-264.
- Nalpas B, Poupon RE, Vassault A, Hauzanneau P, Sage Y, Schellenberg F, Lacour B and Berthelot P (1989): Evaluation of mAST/tAST ratio as a marker of alcohol misuse in a non-selected population. Alcohol Alcohol 24:415-419.
- Nicol EF and Ford MJ (1986): Use of the Michigan alcoholism screening test in general practice. J R Coll Gen Pract 36:409-410.
- Nilssen O (1991): The Tromsö Study: identification of and a controlled intervention on a population of early-stage risk drinkers. Prev Med 20:518-528.
- Nilssen O, Forde OH and Brenn T (1990): The Tromsö Study. Distribution and population determinants of gamma-glutamyltransferase. Am J Epidemiol 132:318-326.
- Noel NE, McCrady BS, Stout RL and Fisher-Nelson H (1987): Predictors of attrition from an outpatient alcoholism treatment program for couples. J Stud Alcohol 48:229-235.
- Norušis MJ (1993): SPSS for Windows: base system user's guide, release 6.0. SPPS Inc., Chicago IL.
- Nyström M, Peräsalo J, Pikkarainen J and Salaspuro M (1993): Conventional laboratory tests as indicators of heavy drinking in young university students. Scand J Prim Health Care 11:44-49.
- O'Brien CP and McLellan AT (1996): Myths about the treatment of addiction. Lancet 347:237-240
- O'Connor PG and Schottenfeld RS (1998): Patients with alcohol problems. N Engl J Med 338:592-602.
- Ockene JK, Adams A, Hurley TG, Wheeler EV and Hebert JR (1999): Brief physician- and nurse practitioner-delivered counseling for high-risk drinkers: does it work? Arch Intern Med 159:2198-2205.
- Ogborne AC and Gavin MT (1990): Identifying and helping alcohol abusers attending general health care services. Can J Public Health 81:307-309.
- Persson J and Magnusson PH (1989): Early intervention in patients with excessive consumption of alcohol: a controlled study. Alcohol 6:403-408.
- Peters C, Wilson D, Bruneau A, Butt P, Hart S and Mayhew J (1996): Alcohol risk assessment and intervention for family physicians: project of the college of family physicians of Canada. Can Fam Physician 42:681-689.
- Poikolainen K (1985): Underestimation of recalled alcohol intake in relation to actual consumption. Br J Addict 80:215-216.
- Poikolainen K (1999): Effectiveness of brief interventions to reduce alcohol intake in primary health care populations: a meta-analysis: Prev Med 28:503-509.
- Pokorny AD, Miller BA and Kaplan HB (1972): The brief MAST: a shortened version of The Michigan Alcoholism Screening Test. Am J Psychiatry 129:118-121.
- Poupon RE, Schellenberg F, Nalpas B and Weill J (1989): Assessment of the transferrin index in screening heavy drinkers from general practice. Alcohol Clin Exp Res 13:549-553.
- Radouco-Thomas S, Garcin F, Radouco-Thomas C, Marquis PA, Lambert J, Laforge H, Denver D, Laperriere A, Lacroix D and Gaudreault V (1979). Primary and secondary prevention of alcoholism: emerging trends and research strategy. Prog Neuropsychopharmacol 3:579-600.

- Rees DW, Beech HR and Hore BD (1984): Some factors associated with compliance in the treatment of alcoholism. Alcohol Alcohol 19:303-307.
- Reid AL, Webb GR, Hennrikus D, Faney PP and Sanson Fisher RW (1986): Detection of patients with high alcohol intake by general practitioners. Br Med J 293:735-737.
- Reid MC, Fiellin DA and O'Connor PG (1999): Hazardous and harmful alcohol consumption in primary care. Arch Intern Med 159:1681-1689.
- Richmond RL and Anderson P (1994a): Research in general practice for smokers and excessive drinkers in Australia and the UK. I. Interpretation of results. Addiction 89:35-40.
- Richmond RL and Anderson P (1994b): Research in general practice for smokers and excessive drinkers in Australia and the UK. II. Representativeness of the results. Addiction 89:41-47.
- Richmond R, Heather N, Wodak A, Kehoe L and Webster I (1995): Controlled evaluation of a general practice-based brief intervention for excessive drinking. Addiction 90:119-132.
- Richmond R, Kehoe L, Heather N, Wodak A and Webster I (1996): General practitioners' promotion of healthy life styles: what patients think. Aust N Z J Public Health 20:195-200.
- Rollnick S, Heather N and Bell A (1992): Negotiating behaviour change in medical settings: The development of brief motivational interviewing. J Ment Health 1:25-37.
- Romelsjö A, Andersson L, Barrner H, Borg S, Granstrand C, Hultman O, Hässler A, Källqvist A, Magnusson P, Morgell R, Nyman K, Olofsson A, Olsson E, Rhedin A and Wikblad O (1989): A randomized study of secondary prevention of early stage problem drinkers in primary health care. Br J Addict 84:1319-1327.
- Rosalki SB and Rau D (1972). Serum-glutamyl transpeptidase activity in alcoholism. Clin Chim Acta 39:41-47.
- Rose G (1990): Doctors and the nation's health. Ann Med 22:297-301.
- Rush BR (1989): The use of family medical practices by patients with drinking problems. Can Med Assoc J 140:35-39.
- Russel MAH, Wilson C, Taylor C and Baker CD (1979): Effect of general practitioners' advice against smoking. Br Med J 288:231-235.
- Russell M, Welte JW and Barnes GM (1991): Quantity-frequency measures of alcohol consumption: beverage-specific vs global questions. Br J Addict 86:409-417.
- Salaspuro M (1999): Carbohydrate-deficient transferrin as compared to other markers of alcoholism: a systematic review. Alcohol 19:261-271.
- Sanchez-Craig M and Lei H (1986): Disadvantages of imposing the goal of abstinence on problem drinkers: an empirical study. Br J Addict 81:505-512.
- Sanchez-Craig M, Annis HM, Bornet AR and MacDonald KR (1984): Random assignment to abstinence and controlled drinking: evaluation of a cognitive behavioral program for problem drinkers. J Consult Clin Psychol 52:390-403.
- Sanchez-Craig M, Leigh G, Spivak K and Lei H (1989): Superior outcome of females over males after brief treatment for the reduction of heavy drinking. Br J Addict 84:395-404.
- Saunders JB and Conigrave KM (1990): Early identification of alcohol problems. Can Med Assoc J 143: 1060-1069.
- Saunders JB and Foulds K (1992): Brief and early intervention: experience from studies of harmful drinking. Aust NZ J Med 22:224-230.

- Saunders JB and Lee NK (2000): Hazardous alcohol use: its delineation as a subthreshold disorder, and approaches to its diagnosis and management. Compr Psychiatry 41(2 Suppl 1):95-103.
- Saunders W and Kershaw P (1980): Screening tests for alcoholism: findings from a community study. Br J Addict 75:35-41.
- Saunders JB, Aasland OG, Amundsen A and Grant M (1993a): Alcohol consumption and related problems among primary health care patients: WHO collaborative project on early detection of persons with harmful alcohol consumption-I. Addiction 88:349-362.
- Saunders JB, Aasland OG, Babor TF, De La Fuente JR and Grant M (1993b): Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption-II. Addiction 88:791-804.
- Scott E and Anderson P (1990): Randomised controlled trial of general practitioner intervention in women with excessive alcohol consumption. Drug Alcohol Review 10:313-321.
- Selzer ML (1971): The Michigan Alcoholism Screening Test: the quest for a new diagnostic instrument. Am J Psychiatry 127:89-94.
- Senft RA, Polen MR, Freeborn DK and Hollis JF (1997): Brief intervention in a primary care setting for hazardous drinkers. Am J Prev Med 13:464-470.
- Seppä K (1992): Intervention in alcohol abuse among macrocytic patients in general practice. Scand J Prim Health Care 10:217-222.
- Seppä K (1996): Mini-interventiohoidon teho alkoholihaittojen ehkäisyssä (in Finnish). Suom Lääkäril 51:1431-1439.
- Seppä K and Mäkelä R (1993): Heavy drinking in hospital patients. Addiction 88:1377-1382.
- Seppä K, Koivula T and Sillanaukee P (1992): Drinking habits and detection of heavy drinking among middle aged women. Br J Addict 87:1703-1709.
- Seppä K, Mäkelä R and Sillanaukee P (1995): Effectiveness of the Alcohol Use Disorders Identification Test in occupational health screenings. Alcohol Clin Exp Res 19:999-1003.
- Seppä K, Heinilä K, Sillanaukee P and Saarni M (1996): Evaluation of macrocytosis by general practitioner. J Stud Alcohol 57:97-100.
- Seppä K, Lepistö J and Sillanaukee P (1998): Five-shot questionnaire on heavy drinking. Alcohol Clin Exp Res 22:1788-91.
- Seppä K, Pitkäjärvi T and Sillanaukee P (1999): Alcohol consumption profile by time in middle-aged men A longitudinal study based on three different diagnostic instruments. Alcohol Alcohol 34:65-70.
- Serdula MK, Mokdad AH, Byers T and Siegel PZ (1999): Assessing alcohol consumption: beverage-specific versus grouped-beverage questions. J Stud Alcohol 60:99-102.
- Sillanaukee P (1996): Laboratory markers of alcohol abuse. Alcohol Alcohol 31:613-616.
- Sillanaukee P (1997): Brief intervention in primary health care. In: Community prevention of alcohol problems, pp. 108-122. Ed. Holmila M, Macmillan Education, Basingstoke.
- Sillanaukee P, Kiianmaa K, Roine R and Seppä K (1992): Alkoholin suurkulutuksen kriteerit (in Finnish). Suom lääkäril 47:2919-2921.
- Simon DG, Eley JW, Greenberg RS, Newman N, Gillespie T and Moore M (1991): A survey of alcohol use in an inner-city ambulatory care setting. J Gen Intern Med 6:295-298.
- Simpura J (1987): Finland's annual alcohol consumption and its distribution. In: Finnish drinking habits, pp. 55-77. Ed Simpura J, Gummerus, Jyväskylä.

- Skinner HA (1990): Spectrum of drinkers and intervention opportunities. Can Med Assoc J 143:1054-1059.
- Skinner HA, Holt S, Sheu WJ and Israel Y (1986): Clinical versus laboratory detection of alcohol abuse: the alcohol clinical index. Br Med J 292:1703-1708.
- Smart RG, Adlaf EM and Knoke D (1991): Use of the CAGE scale in a population survey of drinking. J Stud Alcohol 52:593-596.
- Sobell LC and Sobell MB (1992): Timeline follow-back. In: Measuring alcohol consumption: psychosocial and biochemical methods, pp. 41-72. Eds. Litten RZ and Allen JP, Humana Press, Totowa NJ.
- Spivak K, Sanchez-Craig M and Daivila R (1994): Assisting problem drinkers to change on their own: effect of specific and non-specific advice. Addiction 89:35-42.
- Stauber RE, Vollmann H, Pesserl I, Jauk B, Lipp R, Halwachs G and Wilders-Truschnig M (1996): Carbohydrate-deficient transferrin in healthy women: relation to estrogens and iron status. Alcohol Clin Exp Res 20:1114-1117.
- Steinbauer JR, Cantor SB, Holzer CE 3<sup>rd</sup> and Volk RJ (1998): Ethnic and sex bias in primary care screening tests for alcohol use disorders. Ann Intern Med 129:353-362.
- Stibler H (1991): Carbohydrate-deficient transferrin in serum: a new marker for potentially harmful alcohol consumption reviewed. Clin Chem 37:2029-2037.
- Strecher VJ, Kobrin SC, Kreuter MW, Roodhouse K and Farrell D (1994): Opportunities for alcohol screening and counseling in primary care. J Fam Pract 39:26-32.
- Suokas A (1992): Brief intervention of heavy drinking in primary health care: Hämeenlinna study. Academic dissertation. University Printing House, Helsinki.
- Swenson WM and Morse RM (1975): The use of a self-administered alcoholism screening test (SAAST) in a medical center. Mayo Clin Proc 50:204-208.
- Thom B and Tellez C (1986): A difficult business: detecting and managing alcohol problems in general practice. Br J Addict 81:405-418.
- Tomson Y, Romelsjö A and Aberg H (1998): Excessive drinking brief intervention by a primary health care nurse. A randomized controlled trial. Scand J Prim Health Care 16:188-192.
- Volk RJ, Steinbauer JR, Cantor SB and Holzer CE 3<sup>rd</sup> (1997): The Alcohol Use Disorders Identification Test (AUDIT) as a screen for at-risk drinking in primary care patients of different racial/ethnic backgrounds. Addiction 92:197-206.
- Wallace PG and Haines AP (1984): General practitioner and health promotion: what patients think. Br Med J 289:534-536.
- Wallace PG and Haines AP (1985): Use of a questionnaire in general practice to increase the recognition of patients with excessive alcohol consumption. Br Med J 290:1949-1953.
- Wallace PG, Brennan PJ and Haines AP (1987a): Are general practitioners doing enough to promote healthy lifestyle? Findings of the Medical Research Council's general practice research framework study on lifestyle and health. Br Med J 294:940-942.
- Wallace PG, Brennan PJ and Haines AP (1987b): Drinking patterns in general practice patients. J R Coll Gen Pract 37:354-357.
- Wallace P, Cutler S and Haines A (1988): Randomised controlled trial of general practitioner intervention in patients with excessive alcohol consumption. Br Med J 297:663-668.
- Watson HE (1999): Minimal interventions for problem drinkers: a review of the literature. J Adv Nurs 30:513-519.

- Weaver MF, Jarvis MAE and Schnoll SH (1999): Role of the primary care physician in problems of substance abuse. Arch Intern Med 159:913-924.
- Webb GR, Redman S, Sanson-Fisher RW and Gibberd RW (1990): Comparison of a quantity-frequency method and a diary method of measuring alcohol consumption. J Stud Alcohol 51:271-277.
- Weisner C, Kaskutas LA, Hilton ME and Barile AL (1999): 'When you were drinking' vs. 'in the past 12 months': the impact of using different time frames in clinical and general populations. Addiction 94:731-736.
- Whitfield JB, Hensley WJ, Bryden D and Gallagher H (1978): Effects of age and sex on biochemical responses to drinking habits. Med J Aust 2:629-632.
- WHO Brief Intervention Study Group (1996): A cross-national trial of brief interventions with heavy drinkers. Am J Public Health 86:948-955.
- Wilk AI, Jensen NM and Havighurst TC (1997): Meta-analysis of randomized control trials addressing brief interventions in heavy alcohol drinkers. J Gen Intern Med 12:274-283.
- Wiseman SM, McCarthy SN and Mitcheson MC (1986): Assessment of drinking patterns in general practice. J R Coll Gen Pract 36:407-408.
- Woodall HE (1988): Alcoholics remaining anonymous: resident diagnosis of alcoholism in a family practice center. J Fam Pract 26:293-296.
- World Health Organisation (1992): The ICD-10 Classification of Mental And Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. World Health Organisation, Geneva.
- Wu A, Chanarin I and Levi JA (1974): Macrocytosis of chronic alcoholism. Lancet 1(7862):829-831.
- Yersin B, Nicolet JF, Dercrey H, Burnier M, van Melle G and Pecoud A (1995): Screening for excessive alcohol drinking. Comparative value of carbohydrate-deficient transferrin, gamma-glutamyltransferase, and mean corpuscular volume. Arch Intern Med 155:1907-1911.

## 11 ORIGINAL PUBLICATIONS