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Community Control of Hypertension

A Study of Trends in Finland with Special Emphasis on Lifestyle Modification

Doctoral dissertation

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ABSTRACT

The objective of this study was to assess hypertension care in eastern and southwestern Finland during 1982-1997, in the Helsinki-Vantaa region during 1992-1997 and in the Oulu region in 1997. The data were derived from four independent cross-sectional national FINRISK population surveys conducted in 1982, 1987, 1992 and 1997. For each survey, a random sample of the population aged 25-64 years were chosen from the national population register. Altogether 29036 men and women participated in these surveys. The efficacy of non-pharmacological treatment of hypertension in primary care setting was assessed in a two-year randomised controlled trial conducted in nine health care centres in eastern Finland with 715 hypertensive men and women aged 25-74 years. The intervention was based mainly on intensified lifestyle counselling provided by public health nurses.

During 1982-1997, the mean systolic blood pressure (BP) and the prevalence of hypertension decreased significantly in both genders and in all areas except in men in Helsinki-Vantaa region during 1992-1997. The mean diastolic BP decreased significantly only in men and women in eastern Finland. The rates for awareness, drug treatment and control of hypertension improved significantly in all areas except in men in Helsinki-Vantaa region. Mean total cholesterol decreased significantly in both normotensive and hypertensive populations. Mean high density lipoprotein cholesterol increased in all subjects except in men unaware of their hypertension, and the mean value remained significantly higher in the drug-treated hypertensive subjects compared to the rest of the population. The prevalence of smoking decreased significantly in normotensive and in drug-treated hypertensive men, but increased significantly in drug-treated hypertensive women. The mean body mass index and alcohol consumption increased in the whole population, but especially in the hypertensive subjects. The proportion of subjects engaging in recommended levels of self-reported leisure-time physical activity increased significantly in all BP groups, except in women unaware of their hypertension. In the separate trial of non-pharmacological treatment of hypertension in primary health care, the net reductions in systolic and diastolic BP at two years were significantly greater in the intervention group compared to subjects assigned to usual care among the participants with no antihypertensive drug treatment, but not among the drug-treated subjects.

In conclusion, hypertension care has improved significantly in Finland during 1982-1997. In the future, the observed trends in mean body mass index and in alcohol consumption of the whole population should be reversed to maintain these trends. The health behaviour of newly detected hypertensive individuals should be monitored and intervened in primary health care in a more systematic and efficient way than currently. In addition, effective antihypertensive drug treatment should be initiated in persons with moderate or high cardiovascular risk early enough if lifestyle modification does not give satisfactory results.

To Anniina and Juhana

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ABBREVIATIONS

ACE	Angiotensin-converting enzyme
BMI	Body mass index
BP	Blood pressure
CHD	Coronary heart disease
CI	Confidence interval
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
HDL	High density lipoprotein
LDL	Low density lipoprotein
LIFE	Losartan Intervention For Endpoint reduction
LIHEF	Lifestyle Intervention against Hypertension in Eastern Finland
LVH	Left ventricular hypertophy
MONICA	Monitoring of Trends and Determinants in Cardiovascular Disease
MRFIT	Multiple Risk Factor Intervention Trial
SBP	Systolic blood pressure
VO_2max	Maximal oxygen uptake
WHO	World Health Organization

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following original articles. In the text, STUDY 1 refers to the first article, STUDY 2 to the articles II, III and IV and STUDY 3 to the article V.

I   Kastarinen MJ, Salomaa VV, Vartiainen EA, Jousilahti PJ, Tuomilehto JO, Puska PM, Nissinen AM. Trends in blood pressure levels and control of hypertension in Finland from 1982 to 1997. J Hypertens 1998; 16:1379-87.

II   Kastarinen M, Tuomilehto J, Vartiainen E, Jousilahti P, Sundvall J, Puska P, Nissinen A. Trends in lipid levels and hypercholesterolemia in hypertensive and normotensive Finnish adults from 1982 to 1997. J Intern Med 2000; 247:53-62.

III   Kastarinen MJ, Nissinen AM, Vartiainen EA, Jousilahti PJ, Korhonen HJ, Puska PM, Tuomilehto JO. Blood pressure levels and obesity trends in hypertensive and normotensive Finnish population from 1982 to 1997. J Hypertens 2000; 18:255-62.

IV   Kastarinen M, Tuomilehto J, Vartiainen E, Jousilahti P, Nissinen A, Puska P. Smoking trends in hypertensive and normotensive Finns during 1982-1997. J Hum Hypertens 2002; 16:299-303.

V   Kastarinen MJ, Puska PM, Korhonen MH, Mustonen JN, Salomaa VV, Sundvall JE, Tuomilehto JO, Uusitupa MI, Nissinen AM, for the LIHEF Study Group. Nonpharmacological treatment of hypertension in primary health care. A 2-year open randomised controlled trial of Lifestyle Intervention against Hypertension in Eastern Finland. Submitted.

This work includes also some previously unpublished data.

CONTENTS

1 INTRODUCTION

Many long-term epidemiological studies have shown that elevated blood pressure (BP) is an independent and strong predictor for cardiovascular diseases (CVD) (1, 2). This evidence is further supported by numerous antihypertensive drug trials, which have demonstrated the favourable effect of BP reduction on the incidence of these diseases (3).

In Finnish men the mortality rate from coronary heart disease (CHD) was the highest in the world in the 60's (4). Thereafter, the age-adjusted death rate from CHD in men aged 35-64 years has decreased by 65 % (5). Also the rates for stroke mortality in both sexes and for CHD mortality in women have greatly declined. More than half of this reduction is estimated to have occurred due to reductions in the levels of the three major cardiovascular risk factors: smoking, serum cholesterol and BP (6, 7). Despite the favourable development detected in community control of hypertension in Finland since the beginning of the 70's (8), the BP levels in Finland were still among the highest in the world in the mid-80's (9). Finland took part of the multinational MONICA (Monitoring of Trends and Determinants in Cardiovascular Disease) project which was initiated by the World Health Organization (WHO) in 1982 (10). This international collaboration with highly standardized field survey methods enabled the follow-up of the community control of hypertension in Finland that originally started in 1972 when the North Karelia Project was launched (11).

Evidence from prospective observational studies has established that the risk for CVD in hypertensive subjects depends highly on coexistence of other cardiovascular risk factors (12-14). This fact has also been taken into account in the latest national and international hypertension guidelines which emphasize the subject's absolute risk estimated from the levels of the main CVD risk factors as the key for treatment decisions (15-17). Despite the importance of the topic, there are virtually no data available of the trends in other cardiovascular risk factors of the hypertensive subjects at the population level, although some cross-sectional data exists (18, 19). The WHO MONICA project provided an opportunity to investigate also this issue.

From the public health point of view, the main determinants for the changes in BP levels are the changes in lifestyle factors affecting BP. The efficacy of lifestyle modification in prevention and treatment of high BP has been shown in many randomised, clinical trials (20-22). These trials with rather intensive intervention have been mainly performed in

academic study centres with expert personnel trained for the trial. So far, the intervention methods used in these trials have not been tested in a larger-scale controlled clinical trial in every-day clinical practice. Therefore, a 2-year open randomised, controlled trial of Lifestyle Intervention against Hypertension in Eastern Finland (LIHEF) was conducted during 1996-1999 to assess the feasibility and efficacy of moderately low intensity patient-counselling programme planned for hypertensive subjects in primary health care.

2 REVIEW OF THE LITERATURE

2.1 Physiology and measurement of blood pressure

The circulatory system consists of the heart and blood vessels. Blood is ejected from the left ventricle of the heart to the aortic arch during systole. Thereby the blood is transported through smaller arteries and arterioles to capillaries which are responsible for the exchange of nutrients, electrolytes, hormones and other active substances between the blood and tissue interstitial fluid. The veins transport blood back to the heart. BP means the force exerted by the blood against the vessel wall (23). Systolic BP (SBP) is defined as the peak BP measured during the heart systole and diastolic BP (DBP) as the lowest BP measured during heart diastole, respectively. The subject's BP level is determined from the equation: BP = cardiac output x peripheral resistance. Hypertension is preceded by the increase in either or both of the components in the equation. SBP is dependent of the stroke volume of the left ventricle, of elasticity of the aorta and other large arteries, and of the peripheral resistance which is determined by the diameter of the arterioles. DBP is determined mainly by the peripheral resistance and also to some extent by the elasticity of the large arteries. In western countries, the average SBP level increases progressively along with the increasing age due to the stiffening of the arteries. Conversely, the age-related increase in DBP levels off at around the age of 50 years and tends to decline thereafter (24). However, in some acculturated populations the BP level does not increase along with age (25).

A subject's BP level is conventionally measured indirectly by devices using an inflatable cuff to occlude the artery of an extremity - usually the right brachial artery (26). SBP and DBP values are determined either oscillometrically or by detection of pulse sounds. The classical mercury sphygmomanometer, introduced by Riva-Rocci already in 1896 and modified by Korotkoff in 1905 using the auscultatory method, is the most commonly used apparatus for BP measurement (27). It is still kept as the reference in comparisons with the other BP measurement devices, since it carries the main epidemiological evidence of the long-term risks associated with the elevated BP. With this technique, SBP is determined as the pressure where the occluded artery opens and pulse sounds are heard at each heart beat (phase I of the Korotkoff sounds). Respectively, DBP is usually determined as the point where all the pulse sounds completely disappear (phase V of the Korotkoff sounds).

The accuracy of BP measurement using this method is vulnerable to many sources of error, of which the observer error is the most important one. However, this type of error can be diminished by careful and standardized observer training, which is of major importance in the follow-up of hypertensive patients and especially in hypertension research (28).

2.2 Definition of hypertension

The relationship between BP and adverse health effects is graded but continuous, with no actual threshold value below which there would not be any reduction in risk for the diseases associated with the increase in BP (1). Therefore, in theory, the classification of subjects into categories of "normotensive" and "hypertensive" is to some extent artificial. It has been suggested that the best operational definition for hypertension would be the level at which the benefits associated with reduction of BP would exceed the possible disadvantages of treatment (29). However, to be able to identify high-risk individuals and to provide guidelines for management of high BP, classification of BP is mandatory (30).

Due to the increasing knowledge from the benefits of BP lowering derived from the drug trials, the definition of high BP has undergone many changes towards lower and lower threshold values during the last 40 years. Usually this threshold has been set to the level where the long-term risk for CVD events is doubled (31). Although there has been quite marked variation in classification of BP between the hypertension guidelines proposed by different institutions during these years, the latest of the most recognized guidelines are quite uniform with this respect (15-17). The classification of BP levels by the latest Finnish Hypertension Society guidelines are presented in Table 1.

In addition to the observer's performance, the accuracy of BP measurement can be affected by several other factors (32-34). An individual's BP tends to vary markedly even in highly standardized conditions. Therefore the clinical diagnosis of hypertension should be based on multiple BP measurements, taken on several separate occasions. In the current Finnish Hypertension guidelines the diagnosis and classification of hypertension is recommended to be based on a mean value of BP measurements taken on at least four separate consecutive occasions with two measurements at each visit, and with the patient in a sitting position (35).

Table 1. Classification of systolic and diastolic blood pressure levels according to the Finnish Hypertension Society Guidelines. Modified from (35).

Category	SBP, mmHg		DBP, mmHg
Optimal	< 120	and	< 80
Normal	< 130	and	< 85
Satisfactory	130-139	and	85-89
Hypertension			
Mild	140-159	or	90-99
Moderate	160-179	or	100-109
Severe	$\geq$ 180	or	$\geq$ 110

2.3 Aetiology of hypertension

2.3.1 Overview

Roughly 90-95 % of hypertensive subjects have no definite reason for their elevated BP, i.e. they have primary or, in other words, essential hypertension. In the rest of the cases, some specific disease or condition causing BP elevation is present (36, 37). The most common reasons for the secondary hypertension are renal parenchymal diseases, obliterative renal artery disease, primary aldosteronism and oral contraceptive use (31). From the public health point of view, of these two main forms of hypertension, primary hypertension is of much more importance and is therefore the main topic of this review.

Although the exact origin of the primary hypertension is still unknown, many hypotheses exist (Figure 1). It has been argued that renal dysfunction, too subtle to be detected and leading to increased retention of salt and water by many different mechanisms, may be the leading cause for primary hypertension (38, 39). It has also been suggested that some defects in cell ion transport could increase the movement of sodium into the cell and thereby to the

increase in intracellular calcium concentration and in vascular tone (40). The other main hypotheses include vascular hypertrophy caused by multiple vasoactive substances, sympathetic nervous hyperactivity, hyperinsulinemia and endothelial cell dysfunction (41-44).

From a population perspective, it can be concluded that the primary hypertension develops from the complex interaction between the inherited genes and the environmental factors. It has been estimated that 30-40 % of BP variation is determined by genetic factors and the rest by the environment. It has been proposed that the mean value of BP in the population is determined by environmental factors, whereas the subject's BP rank or range of possible variation is determined by genes (45).
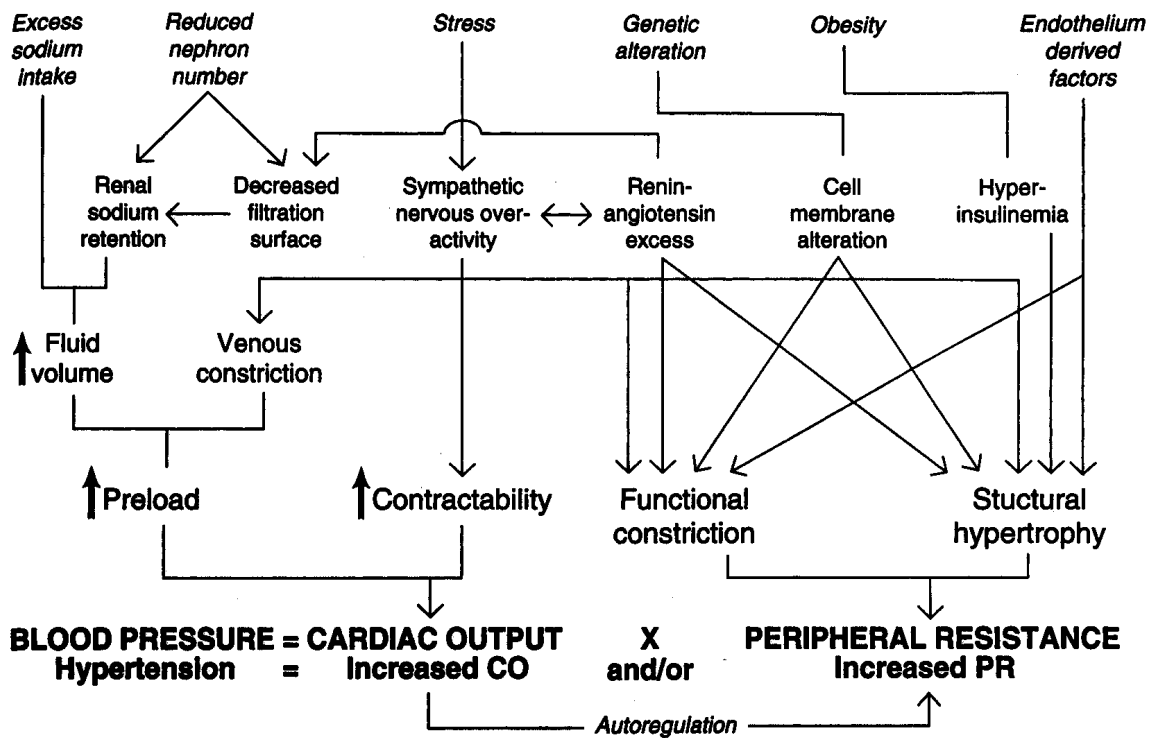
Figure 1. Some of the factors involved in the pathogenesis of hypertension. Reprinted with permission of Williams & Wilkins from (46) .

2.3.2 Genetic factors

Numerous studies in various parts of the world show that the levels of both SBP and DBP correlate significantly within families (47, 48). So far, no definite causally related genetic marker for primary hypertension has been established, although some polymorphisms have been found to be associated with hypertension in some populations (49, 50). Genetically, primary hypertension is currently believed to be of polygenic origin, although some rare monogenic forms of hypertension have been established (51-53). These genes will hopefully work as a tool for better understanding of the pathophysiology of primary hypertension and simultaneously lead to possible new proceedings in antihypertensive drug therapy (54). Hopefully, in the future along with possible progress in the genetic epidemiology of hypertension we will be able to distinguish susceptible subjects who would benefit most from environmental manipulation already during childhood (55).

2.3.3 Environmental factors - the evidence from the observational studies and clinical trials

2.3.3.1 Body weight

Epidemiological studies

The positive, independent association between either overweight (body mass index, BMI above 25 kg/m^2) or obesity (BMI above 30 kg/m^2) and elevated BP has been verified in numerous cross-sectional population-based studies. Depending of the magnitude of overweight, the prevalence of hypertension has been documented as 1.5-6 times higher in overweight or obese subjects compared to subjects with normal weight (56, 57). In the international INTERSALT study of 52 populations worldwide, a 10 kg increase in body weight was associated with a 3.0 mmHg increase in SBP and a 2.2 mmHg increase in DBP, respectively (58). In prospective epidemiological studies, obesity and weight gain have been associated with the increased risk of hypertension (59). This risk has been shown to be especially high in subjects with abdominal adiposity (60-62). Also the risk for antihypertensive drug treatment has been proposed to increase along with increasing BMI (63).

Clinical trials

It was shown in a recent review of the randomised trials of weight reduction in overweight hypertensive subjects that a weight loss of from three to nine percent was associated with a decrease of 3 mmHg in both SBP and DBP (64). The efficacy of even modest weight reduction in the prevention of hypertension has also been documented in overweight subjects with high normal BP (21, 65, 66). In one study, however, a weight loss of 20 kg following gastric surgery did not have any effect on the 8-year incidence of hypertension (67).

It has been shown in both middle-aged and elderly subjects that weight reduction may substitute antihypertensive drug treatment in a sizable part of the hypertensive patients (68, 69). In addition, some studies have demonstrated that weight loss combined to the antihypertensive drug treatment is significantly more effective in control of hypertension compared to drug treatment alone (70, 71).

The mechanisms of obesity-induced hypertension

Obesity and especially abdominal obesity is suggested to increase BP by several mechanisms (72, 73). These mechanisms include increased sympathetic activity caused by increased caloric intake and hyperinsulinemia, increased renal sodium reabsorbtion due to hyperinsulinemia, impaired peripheral vasodilatation due to the peripheral insulin resistance and possibly reduced endothelium-dependent vasodilatation caused by obesity-induced dyslipidaemia. Interestingly, it has also been shown that in a subset of hypertensive population high BP precedes the gain of weight (60). Based partly on this finding, it has been proposed that both the BP elevation and weight gain may reflect the primary increase in sympathetic tone (74). According to this theory, the decrease in β-adrenergic responsiveness established in hypertensive subjects with increased sympathetic activity could lead to diminished energy expenditure and thereby to inevitable weight gain.

2.3.3.2 Sodium intake

Sodium is a mineral found all around in nature. In industrialised countries, over 80 % of the sodium intake originates from the sodium chloride added to food. The association between sodium intake and BP has been recognised for a long time although the strength and importance of the association is still widely debated (75).

The measurement of sodium intake in epidemiological studies

For research purposes, the best method for assessment of sodium intake is the measurement of sodium excretion from a single 24-hour urine sample (76). It has been estimated that 77-86 % of the ingested sodium is excreted to urine (77). Due to relatively large day-to-day variation in sodium output, multiple collections are needed for assessment of the sodium intake of an individual person (78). However, single 24-hour urine collections are reliable in estimating the mean or median sodium excretion of the population (79).

The preliminary epidemiological studies

The first epidemiological studies plotting the data of salt intake against hypertension prevalence in various populations demonstrated the linear positive association between these two variables (80-82). In these studies, it was found that a 100 mmol extra daily intake of sodium (~5.8 g sodium chloride) was associated with an 8-9 mmHg rise in SBP and with a 4-5 mmHg rise in DBP. Primarily the same data used in these studies was analysed further in a meta-analysis by Law et al. in 1991 (83). Their analysis yielded principally the same results, but in addition, demonstrated that the impact of sodium intake on BP in subjects aged 60-69 years was twice of that than in subjects at age 15-19 years. Similarly, they showed that the predicted change in BP was greatest in the upper end of the BP distribution. However, these studies were objected to major criticism because of the varied methodology in assessment of sodium intake and BP, as well as for not controlling the possible confounding variables. These serious limitations resulted in a launching of a major international collaboration, the INTERSALT study in the mid 80's (84).

The INTERSALT study

The INTERSALT study was conducted in altogether 52 study centres, in 32 countries worldwide with a sample of 10 079 men and women aged 20-59 years. Data collection methods were highly standardized and the investigators went through careful training before the fieldwork was started. It was found in pre-defined within-population analyses of the study that there was an independent association between 24-h urinary sodium excretion and SBP (25). In further analyses with multivariate correction for regression dilution bias SBP was estimated to be on average 3.1-6.0 mmHg and DBP 0.1-2.5 mmHg lower with 100 mmol/day smaller sodium intake depending whether BMI was included or not into the multivariate

analysis (85). The association was more pronounced at age-group 40-59 years compared to the younger age group. In between populations-analyses, 100 mmol higher sample median 24-hour urinary sodium excretion was associated with on average by 5-7/2-4 mmHg higher SBP/DBP and with 6.2 % higher prevalence of hypertension. The estimated mean difference in SBP/DBP with this difference of sodium excretion at age 55 compared with age 25 was greater by 10-11/6 mmHg demonstrating the impact of sodium in age-related rise in BP level found in all western societies. The four INTERSALT populations with very low sodium excretion had low median blood pressures, low prevalence of hypertension, and no significant increase of blood pressure with age – the finding shown also by many other previous ecological studies of isolated populations still following a more or less traditional hunter-gatherer lifestyle (86, 87).

Clinical trials

The most compelling evidence of the causal relationship between the salt intake and hypertension originates from experimental studies in animals and from randomised trials of sodium supplementation and restriction in humans. In a controlled study by Denton et al. in the normotensive chimpanzees with a low-sodium diet rich in fruits and vegetables, the increase in salt intake to 5 grams/day caused a 12 mmHg rise in SBP by 19 weeks (88). The further increase of salt intake to 15 grams/day to 62 weeks caused a rise of 33 mmHg in SBP and of 10 mmHg in DBP. The BP of the experimental group reverted to the baseline level 20 weeks after reinstitution of the original diet. Salt supplementation studies done in humans have been of shorter duration. In a randomised trial assessing the impact of salt intake on BP during the first 6 months of life in infants, SBP at 6 months was 2.1 mmHg higher in the group assigned to higher salt intake compared to control group (89). Fifteen years later, the group fed with more salt had still 3.6 mmHg higher SBP than the control group, indicating the possibility of long-term effects of salt intake during infancy (90). In a meta-analysis of randomised controlled salt supplementation trials in hypertensive adults, a high salt diet produced on average an increase of 5.6 mmHg in SBP and an increase of 3.5 mmHg in DBP, respectively (91).

The most recognized meta-analyses of clinical trials of salt restriction show a reduction of 3.7-5.8 mmHg in SBP and of 0.1-2.3 mmHg in DBP of hypertensive subjects for a 100 mmol reduction in 24-hour urinary sodium excretion – the results depending of the inclusion criteria

of the trials (20, 92-94). In these meta-analyses, the effect of sodium reduction in BP was larger in elderly subjects compared to younger subjects and somewhat smaller in normotensive subjects compared to hypertensive population. After publishing of these meta-analyses, two landmark studies of sodium restriction have been reported. The first one, called TONE (Trial of Nonpharmacologic Interventions in the Elderly) including 681 patients aged 60-80 years showed that a 40 mmol/day reduction in 24-hour urinary sodium excretion for a mean follow-up time of 28 months was accompanied by a net decrease of 4.3 mmHg in SBP and of 2.0 mmHg in DBP, respectively (95). Along with the observed reduction in DBP, also the need for antihypertensive drug therapy could be significantly reduced. In the "DASH II" study (Dietary Approaches to Stop Hypertension) 412 subjects with or without hypertension were randomised to a diet typical in the United States or the DASH diet, which is rich in vegetables, fruits and low-fat dairy products (96). Within the assigned diet, the participants consumed foods with high, intermediate and low sodium content for 30 days each, in a random order. The results showed that both the DASH diet and the reduced sodium intake reduced significantly and independently both SBP and DBP. The effect of sodium reduction of 100 mmol/day in the control diet was 6.7 mmHg in SBP and 3.5 mmHg in DBP in hypertensive participants. The reductions in BP were even larger in black hypertensive subjects, and somewhat smaller but still significant in normotensive subjects.

The effect of reduced sodium intake on BP has also been studied in many clinical trials assessing the independent and combined effects of sodium restriction and antihypertensive drug treatment in hypertensive subjects. The evidence from these studies show that the restriction of sodium intake enhances significantly the BP-lowering effect of beta-blockers, diuretics and angiotensin-converting enzyme (ACE) inhibitors (97-99).

The data from the studies aiming to reduce salt intake in the general population show that the long-term compliance to a low-salt diet is difficult to achieve (100). The North Karelia Salt Project was started in 1979 in eastern Finland to assess the feasibility and effects of salt reduction in the population of North Karelia (101). The results of the programme were compared with the neighbouring county, Kuopio. The intervention programme aiming to increase the common knowledge of the adverse health effects of excess salt intake lasted for three years. The local health care personnel and home economics teachers who were trained by the dieticians provided health education. The local press and radio was also used. After three years of intervention, the population mean salt intake, assessed at the baseline and at

three years by 24-hour urine samples, did not change significantly except in normotensive women. Similar results were also reported in a community survey in Belgium (102).

Salt sensitivity

As demonstrated in many studies, there is quite a marked individual variation in BP response to salt restriction (103). In studies of drastic salt restriction, BP falls in a proportion of subjects, increases in others and remains unchanged in the rest of the population. On the other hand, BP rises in virtually everyone, if large amount of salt is supplemented even for a short time (104). It has been proposed that this "salt sensitivity", defined usually as an arbitrary cut-off point of 10 mmHg change in mean BP after salt loading or depletion, is more prevalent in hypertensive than in the normotensive population (50-70 % vs. 26-36 %) (103), in blacks compared to other races (104), in elderly than in the young (105) and in the obese compared to subjects with normal weight (106). The suggested pathophysiologic mechanisms accounting for salt sensitivity include low plasma renin activity (107), increased sensitivity of the sympathetic nervous system (108) and insulin resistance, especially in obese subjects (109). So far, no clinical test with good reproducibility has been invented for salt sensitivity. From a population perspective, however, it has been claimed that the vast majority of the population are more or less sodium sensitive (84).

Pathophysiology of salt-induced hypertension

The exact mechanisms by which excess sodium intake induces BP to rise are still somewhat unclear. The main hypotheses include the volume expansion associated with the defect in the excretory function of the kidneys, increased activity of the sympathetic nervous system and the increase in intracellular calcium concentration (110).

Other health-related effects of excessive sodium intake

Independent of its effect on BP, high salt intake has been shown to be a predictor for left ventricular hypertrophy (LVH) and dysfunction, renal disease, decreased vascular compliance, stroke, osteoporosis and stomach cancer (111-114). In addition, in a recent Finnish prospective study with 2436 men and women, a positive association between a high 24-hour urinary sodium excretion and the incidence of CHD was demonstrated for the first time (115). The finding of this study was in a strong discordance with two previous studies

published by Alderman et al. (116, 117), which suggested an increased risk of myocardial infarction among subjects with low sodium intake. However, these two American studies have been an object of a great deal of criticism because of serious flaws in the methodology used in the assessment of salt intake (118).

2.3.3.3 Alcohol consumption

Observational studies

The independent positive association between alcohol intake and BP has been found in many cross-sectional population-based studies (119). It has been suggested in these studies that both SBP and DBP rise steadily when alcohol intake increases beyond two drinks (26 g of pure alcohol) per day, and that there is no further increase in BP when alcohol intake exceeds six drinks per day (120). This association has been documented as more linear in men than in women, in whom the relationship has been found to be more or less "J-shaped" (121, 122). The prevalence of hypertension ($\geq$160/95 mmHg or antihypertensive drug treatment) has been approximately twofold in subjects consuming six or more drinks per day compared to subjects with 0-2 drinks per day. It was shown in the second Kaiser Permanente study that the alcohol-BP relationship was stronger in men than in women, in whites than in blacks and in subjects aged 60 or more (121). It was also found that this relationship existed only in subjects consuming alcohol daily. In addition, the choice of alcohol beverage did not have a significant impact on this relationship. In the multinational INTERSALT study, SBP was 3-4 mmHg and DBP 2-3 mmHg higher in subjects consuming 240 g of alcohol (21 standard drinks) per week compared with subjects consuming less than that or with abstainers (123).

The role of alcohol intake as a predictor of elevated BP, independent of other well-known risk factors for hypertension, has been established in many prospective epidemiological studies (124-128). Some studies suggest that the alcohol-induced increase in BP has been stronger in SBP than in DBP (129) and in black than in white subjects (128). The suggested threshold value for the association between alcohol intake and hypertension in these studies has varied between two and three standard drinks of alcohol per day.

Clinical trials

The effect of changes in alcohol intake on BP has been shown in many crossover and randomised, controlled trials (32, 130-132). These trials have demonstrated the acute pressor effect of alcohol intake on BP at the level of three to eight drinks per day, as well as the short-term decrease in BP following reduction of alcohol ingestion by three drinks per day. These effects have been demonstrated in both normotensive and hypertensive subjects, and they have been independent of weight loss, sodium restriction or exercise (133-135). In a recent meta-analysis, the restriction of alcohol consumption was associated with a decrease of 3.31 mmHg in SBP and of 2.04 mmHg decrease in DBP, respectively (136). In this study, a clear dose-response relationship between alcohol restriction and BP reduction was observed. The observed reductions in BP were greatest in those with the highest baseline BP. The same effects of alcohol abstinence on BP have been also demonstrated using 24-hour ambulatory BP monitoring (137). So far, the results from studies assessing the long-term effects of alcohol restriction on BP have been negative (138).

According to some studies, the regular alcohol consumers seem to respond less well to antihypertensive drug treatment (139). This finding is possibly a consequence of diminished compliance with the treatment regimens found in this patient-group (140).

Possible mechanisms for alcohol-induced hypertension

There are many hypothetical mechanisms by which alcohol intake could increase BP. The suggested mechanisms include the increase in plasma catecholamine, renin, cortisol and intracellular calcium levels causing vasoconstriction, tachycardia and increased heart rate variability (32, 141-144). Some studies suggest that the observed effect of alcohol intake on BP could be due to a physiological withdrawal reaction related to acute alcohol abstinence just before the medical examinations (120, 145). However, also opposite findings have been reported (146).

The evidence from both observational and interventional studies suggests that the alcohol-induced pressor effect on BP is rapidly reversible (147, 148). Similarly, in the studies comparing the effects of binge and daily drinking on BP, it has been shown that the effects of regular drinking are more sustained than that of "binging" (149, 150). However, also the BP rise related to regular drinking is found to be reversible.

Other health-related effects of excess alcohol use

According to many large-scale studies, moderate drinking (1-2 drinks per day) has a slight protective effect against CHD (151). In contrast, more severe drinking has been shown to be an independent risk factor for cardiomyopathy, haemorrhagic stroke (152) and all-cause mortality (151). The increased risk of ischaemic stroke in young adults has been suggested to be related especially to binge drinking (153) during the weekend and holiday times (154), possibly due to rapid changes in BP associated with this type of alcohol intake (155).

2.3.3.4 Physical activity and fitness

Observational studies

The results of the several large cross-sectional studies examining the relationship BP and either physical activity or physical fitness are somewhat inconsistent. Many population-based studies have, after adjusting with age and other confounders, reported of the inverse relationship between these variables (156-160). In these studies, the adjusted difference in both SBP and DBP between the most and least physically active has averaged 5 mmHg (161). According to some studies, however, the observed differences in BP have become insignificant after adjusting with the other lifestyle variables (162, 163).

It has been shown in some prospective studies that physical activity and fitness are inversely and independently related to later development of hypertension (164-166). In these studies, the relative risk for elevated BP has been reported as 1.5-1.9 times higher in the least fit compared to the fittest subjects (165, 166). In addition, a low physical fitness has been documented as an independent risk factor for all-cause mortality in hypertensive men (167). Some studies have suggested that the changes in physical activity or fitness have been inversely related with the changes in SBP in women (168, 169).

Clinical trials

The independent BP-lowering effect of aerobic training has been documented by several reviews (161, 170, 171) and meta-analyses of clinical trials (22, 172). In a meta-analysis including 29 randomised controlled trials lasting 4 weeks or longer (mean 18.9 weeks, range 4-52 weeks), it was reported that aerobic exercise training reduced resting SBP by 4.7 mmHg (95% confidence interval, CI 4.4 to 5.0 mmHg) and DBP by 3.1 mmHg (95 % CI 3.0 to

3.3 mmHg) (22). Additionally, the results of this meta-analysis suggested that observed BP reduction was independent of the intensity of exercise (mean 62 % of the maximal oxygen uptake, VO_2 max, range 30-87 % VO_2 max) and of the number of exercise sessions per week (mean 3.2 sessions). The authors concluded that increasing exercise intensity above 70 % VO_2 max or increasing exercise frequency to more than three sessions per week did not any further impact on BP. The results of a meta-analysis of 54 randomised controlled trials published just recently by Whelton et al. were in accordance with these findings (173). The effect of exercise on BP has been reported to be equally great in both hypertensive and normotensive subjects in all but one review that also included non-randomised trials (161).

The evidence of the impact of progressive resistance exercise on resting BP is still inconclusive. In a recent meta-analysis of the randomised controlled trials lasting four weeks or more, a pooled decrease of 3 mmHg (95 % CI -4 to -1) could be detected in both SBP and DBP (174). However, as mentioned by the authors, the low methodological quality of many studies did not justify for making very firm conclusions about the importance of this kind of training in non-pharmacological treatment of hypertension

The antihypertensive mechanisms of exercise

The decrease in BP induced by endurance training may be explained by decreased stroke volume and contractility of the heart after exercise (175) combined with the decreased systemic vascular resistance (176) - both phenomena caused possibly by decreased sympathetic activity. The other suggested mechanisms include reduced levels of plasma renin activity and catecholamines (177), as well as increased urinary sodium excretion and insulin sensitivity (178). It has been shown in the studies using ambulatory BP measurement that these acute haemodynamic effects caused by aerobic exercise exist only in hypertensive subjects and that they are of limited duration (179). This finding may explain the need for continuous regular exercise to maintain the favourable effects achieved on BP level in hypertensive persons.

2.3.3.5 Potassium intake

Observational studies

Potassium intake, assessed by 24-hour urinary potassium excretion or by 24-hour dietary recall, has been shown to be inversely related with BP in many cross-sectional within population-studies (25, 180-183). In the INTERSALT study, after adjustment for potential confounders, an increase in potassium excretion of 50 mmol/day was associated with the decreases of 2 mmHg in SBP and of 1.5 mmHg in DBP (25). These relationships between either SBP or DBP and potassium excretion were stronger than those with sodium excretion. However, as documented also in some other observational studies, the ratio of urinary sodium to potassium correlated even more closely to BP than either electrolyte excretion individually (184). It has been speculated that these measured associations between urinary electrolyte excretions and BP within population-studies are underestimations of the true relationships because of the great intraindividual day-to-day variation in the urinary output of electrolytes (78).

Clinical trials

There are so far two published meta-analyses of the trials assessing the effects of potassium supplementation on BP (185, 186). It was estimated in the latter one of these studies, including 33 randomised controlled trials in both normotensive and hypertensive subjects, that a 53 mmol/day increase in potassium intake was associated with a mean decrease of 3.11 mmHg in SBP (95 % CI 1.91 to 4.31 mmHg) and of 1.97 mmHg decrease in DBP (95 % CI 0.52 to 3.42 mmHg), respectively (186). It was shown in this meta-analysis, that the treatment related-reductions in both SBP and DBD were significantly higher in the studies including subjects with mean 24-hour urinary sodium excretion greater than 165 mmol per day compared with the subjects with sodium excretion less than that. Based on this finding, the authors concluded that increased potassium intake should be considered for prevention and treatment of hypertension especially in subjects unable to reduce their high intake of sodium. The controlled studies of the effects dietary intake of potassium on BP are rare, but the results of these studies are in accord with those of the supplementation studies (187, 188).

The suggested mechanisms by which a lack of potassium could elevate BP include vasoconstriction induced by the increases in intracellular calcium concentration (189),

increase in sympathetic activity (190), increased release of renin (191) and the retention of sodium (192).

2.3.3.6 Dietary fat intake

Observational studies

The association between BP and different types of dietary fat has been investigated in several cross-sectional studies in various populations. Most of these studies have found no relationship between BP and intake of saturated, monounsaturated, polyunsaturated or trans fatty acids. However, some population-based studies in Finland and United States have reported of positive correlations between BP and the intake of saturated fats, even after adjustment for possible confounders (193, 194). Correspondingly, some studies have suggested an inverse relationship between the intake of polyunsaturated fats and BP or between the ratio of polyunsaturated to saturated fat intake and BP (194-196). The prospective studies assessing the incidence of hypertension in relation to intake of any type of fat intake have failed to show any association (126, 197).

Clinical trials of the effects of dietary fat manipulation on BP

The effect of manipulation of dietary fat intake on BP has been investigated in numerous intervention studies. The impact of dietary fat modification was assessed in three separate Finnish studies with crossover design in 1981-1983 (198-200). During the intervention period of these studies, the total fat intake was reduced from 39 % to 24 % of the total energy intake and the ratio of polyunsaturated to saturated fat intake was increased from 0.2 to 0.4-1.2. Both SBP and DBP decreased significantly during the intervention periods, and the BP values returned to the initial levels during the switchback period. The observed decrease in SBP/DBP in the intervention groups of these studies was 7-8/3-5 mmHg in normotensive subjects and 4-10/4-6 mmHg in hypertensive subjects. When the data of these studies were pooled, the multiple regression analyses including weight and other dietary variables suggested that the increase in polyunsaturated fatty acid intake was the strongest predictor of BP change (201). However, all the other trials except one Finnish study (202) reported since then have failed to repeat this finding (203-205). It has been criticized that the interpretation of the results of these Finnish and also many other studies with manipulation of dietary fat is difficult, because

the changes in fat intake were accompanied by other dietary changes possibly affecting BP (206). For this reason, few studies have used a basal diet supplemented with n-6 polyunsaturated fatty acids (207, 208). These studies have also not detected any significant association between changes in BP and type of fat intake. It has been suggested that this inconsistency between the studies could be related to the baseline ratio of polyunsaturated to saturated fat intake. This hypothesis originates from the finding that in all the studies with positive results the baseline ratio was less than 0.3 whereas the ratio was more than that in all the studies with negative results (209). According to the evidence, the changes in the intake of monounsaturated or trans fatty acid have no significant influence on BP (210), although the increased intake of trans fatty acids is recently suggested to contribute to some extent to the risk of CHD (211).

Clinical trials of fatty acid supplementation and BP

The effects of dietary supplements of n-3 fatty acids, eicosapentanoic and docosahexanoic acid - found especially in fish, on BP have been summarized in two meta-analyses including 17 (212) and 31 (213) placebo-controlled trials, respectively. In the former study, the pooled effect on SBP/DBP was -1.0/0 mmHg in normotensive subjects and -5.5/-3.5 mmHg in hypertensive subjects, respectively. The average dose of n-3 fatty acid supplementation in this review was 1 g/day. In the latter study, there was no significant change in BP of the normotensive subjects, but the reduction in SBP/DBP in hypertensive subjects with the supplement intake of on average 5.6 g/day was 3.4/2.0 mmHg. In this study, a significant dose-response relationship between fish oil supplementation and BP was observed. In one controlled study comparing the effects of daily fish meal (3.4 g n-3 fatty acids) to either 5 or 10 g fish oil supplements on BP, the decrease in BP was similar in all groups with increased n-3 fatty acid intake (214). Accordingly, it was shown in double-blind placebo-controlled Norwegian study that fish oil supplementation of 6 g per day did not have any influence on BP among the subjects with at least three fish meals per week (215). It has been suggested that of the two n-3 fatty acids derived from fish, docosahexanoic acid may be more effective in 24-hour BP reduction compared to eicosapentanoic acid (216). The BP-lowering effects of n-3 fatty acids are possibly amplified by weight reduction (217). In addition to the effect on BP, it has been suggested that the n-3 fatty acids may decrease the risk for CHD even at moderate level of fish consumption (218).

Antihypertensive mechanisms of fatty acids

The possible antihypertensive mechanisms of the increased ratio of the polyunsaturated to saturated fats include an increase in vasodilator prostaglandin synthesis and improved endothelial dilator function due to reduced serum Low density lipoprotein (LDL) cholesterol levels (219, 220). The suggested antihypertensive effects of the n-3 fatty acids are likely due to increased endothelial vasodilatation, reduced vascular smooth muscle contractility and possibly also to a decrease in heart rate (215, 221).

2.3.3.7 Other environmental factors

In addition to lifestyle factors listed above, there is also some evidence of the association between a few other environmental factors and BP. These factors include birth weight, smoking, coffee ingestion, intake of some other nutrients than already mentioned in this review, socio-economic status, migration and psychological stress.

Birth weight

The independent inverse association between the birth weight and SBP during both childhood and adult life has been verified in many epidemiological studies. In these studies, a 1 kg increase in birth weight has been associated with decrease of 1-4 mmHg in SBP in children, adolescents and adults (222, 223). It is hypothesized that fetal undernutrition caused by maternal undernutrition would play a crucial role in the development of this association. According to the "fetal origins" hypothesis, this would lead to intrauterine "programming" causing structural, physiological and metabolic changes in the fetus affecting the levels of BP and other cardiovascular risk factors in later life (224). In contrast, the results from twin studies emphasize that placental dysfunction could be the major cause for retarded intrauterine growth leading to the elevated SBP (225, 226). The impact of retarded intrauterine growth on incidence of hypertension is reported to be even stronger in the subjects with accelerated postnatal growth (227). The suggested mechanisms for the association between low birth weight and elevated BP include the programming of the fetal hypothalamic-pituitary axis leading to higher fasting cortisol levels in adults (228), increased sympathetic activity (229) and impaired renal development (230). The data from some studies show that the effect of low birth weight on BP is strongest in those with the highest BMI as

adults (231). This observation suggests that the prevention of obesity is especially important among the children and adults with low birth weight.

Smoking

It has been shown in several clinical studies that smokers present higher 24-hour BP levels than their non-smoking counterparts (232, 233). This association is mediated probably by nicotine - the most detrimental element of the tobacco smoke for the cardiovascular system. The acute nicotine-induced effects of smoking are 1) the rise in sympathetic activity leading to increase in heart rate, cardiac out-put and peripheral vasoconstriction (234); and 2) the increase in plasma cortisol and aldosterone levels (235). In contrast to the results of these clinical studies, the most epidemiological surveys have demonstrated equal or even lower BP levels in smokers compared to non-smokers, even after adjustments for BMI and other risk factors for hypertension (236, 237). This paradoxical finding has been attributed to the fact that in large epidemiological studies BP is measured casually and the participants are not permitted to smoke within a certain period before the measurements. Therefore, the possible acute rise in BP during smoking could not be observed (238). Surprisingly, it was reported in a recent large 4-year follow-up study including 8170 healthy men that smoking cessation was associated with increased risk of hypertension (239). This association was independent of the changes in body weight and the risk was attenuated with the increased length of the period of cessation. In short, taking account the current evidence from epidemiological studies, the chronic effect of smoking on BP is likely to be small. Still, the effect of smoking on cardiovascular risk among hypertensive subjects is of major importance and will be discussed later in this review.

Coffee drinking

The effect of coffee consumption on BP was assessed in a meta-analysis comprising 11 controlled clinical trials with a median duration of 56 days (240). According to this study, SBP/DBP increased by 2.4 /1.2 mmHg more in the group consuming on the average 5 cups of coffee/day compared to the control group. Accordingly, a significant coffee-induced increase in both ambulatory SBP and DBP was reported in a recent trial in older subjects with hypertension, but not in normotensive subjects (241). In addition, in one case-control study assessing the relationship of coffee consumption and smoking on ambulatory BP, the

ambulatory SBP was reported to especially high in smokers consuming at least four cups of coffee per day, suggesting an additive interaction between these two variables (242). The results of these short-term studies are not in accord with the findings of a recent American prospective study with a median follow-up of 33 years (243). In this study, consumption of one cup of coffee a day raised SBP by 0.19 mmHg (95 % CI 0.02 to 0.35 mmHg) and DBP by 0.27 mmHg mmHg (95 % CI 0.15 to 0.39 mmHg). The relative risk for the development of hypertension was not significant in subjects drinking coffee at least five cups a day compared to coffee abstainers. Therefore, it can be concluded that according to the current evidence the long-term effects of coffee drinking on BP are relatively small.

Intake of calcium, protein, magnesium and fibre

The data from the observational studies show no consistent association between dietary calcium and BP (244). However, the results of the two meta-analyses of the intervention studies assessing the effect of calcium supplementation on BP show that 1150-1300 mg dose of calcium regimen reduced SBP in hypertensive subjects by 1.7-4.4 mmHg (245, 246). According to the limited evidence, also the increase in dietary intake of protein, magnesium and fibre may lower BP (126, 247, 248).

Sosioeconomic status and mental stress

In developed countries, there have been studies reporting of the association of a lower socio-economic status with high BP (249, 250) In contrast, in developing countries this association is documented to be vice versa, i.e., mean BP is highest in the subjects with higher socio-economic status (251). These associations are explained mainly by the differences in well-established lifestyle factors affecting BP across the socio-economic groups (252). The same explanation seems to account for the rise in BP level demonstrated in migration studies with the subjects moving from the rural areas to areas with more "westernised" societies (253). In the migration studies, the environmental stress is hypothesised to be one of the key factors in the initiation of the BP rise, although the evidence of the efficacy of stress management in treatment of hypertension is lacking (254, 255)

2.3.3.8 Trials of the effects of lifestyle intervention on blood pressure in primary health care

As reviewed above, there is sufficient evidence to suggest that certain changes in nutrition and physical activity can decrease BP in subjects with hypertension. This evidence comes from the intervention studies organised in carefully controlled clinical conditions in academic study centres. What is less clear, however, is how to achieve these changes in lifestyle in primary health care as a part of routine management of hypertension (256). So far there are a limited number of randomised, primary prevention trials assessing the effects of lifestyle intervention in primary health care with BP as one of the outcome variables. The majority of these trials have been targeted subjects with increased cardiovascular risk (257-259), the population as a whole (260, 261) or families (262, 263). In an analysis using pooled data of these studies, the net difference in SBP/DBP reduction between intervention groups and usual care was 2.3/1.3 mmHg (264). In this analysis, studies with antihypertensive drug treatment were excluded. The randomised controlled trials assessing the impact of lifestyle changes on BP solely among subjects with hypertension in a primary care setting are rare. These studies are listed in Table 2. In three of these trials, the intervention was based on individual lifestyle counselling (265-267) and in one on group sessions (268). The three studies based on individual counselling could be characterized as pilot studies with a relatively small number of patients and short duration of follow-up. Therefore, the results of these studies are difficult to apply to every-day clinical practice. In contrast, it was demonstrated in a Japanese study (268) that community-based health education given in a group setting can effectively reduce SBP in patients with hypertension. In this study, the reduction in SBP was attributed mainly to the reduction in sodium and alcohol intake.

2.4 Hypertension and cardiovascular risk

2.4.1 The evidence from the epidemiological studies

Several large-scale epidemiological studies in various parts of the world have demonstrated the strong positive association between elevated BP and the incidence of atherosclerotic cardiovascular diseases (1, 2, 269, 270). It was summarized in a review of these studies that

Table 2. Randomised controlled trials of efficacy of non-pharmacological treatment of hypertension in primary health care.

Reference, country	Participants	Inclusion criteria	Number of participants	Intervention	Duration of follow-up	Net difference in BP (mmHg) between intervention and control groups
(265), Netherlands	Men and women, screened in one general practice, mean age 45 years	DBP 90-109 mmHg, no history of CHD, diabetes and antihypertensive drug treatment, BMI $\leq$ 27	35	3 individual counselling sessions by nutritionist	3 months	SBP: -2.8 (p=0.17) DBP: -2.0 (p=0.15)
(266), USA	Men and women, screened in one health care centre, mean age 60 years	SBP $\geq$140 mmHg or DBP $\geq$ 90 mmHg and BMI $\geq$ 27.8 in males and $\geq$ 27.3 in females	30	Monthly counselling sessions by GP	12 months	MAP: 3.7 (p>0.1); SBP and DBP: NA
(267), Australia	Men and women, screened from 13 general practices, mean age 58 years	Drug treatment for hypertension	166	Low intervention group: one appointment with a nurse and five 15 min telephone counselling sessions; High intervention group: Six appointments with a nurse	4.5 months	SBP: -6 (p<0.05); DBP: -5 (p<0.05)
(268), Japan	Men and women, screened from community-based program for stroke prevention; mean age 59 years	SBP 140-179 mmHg and/or DBP 90-109 mmHg, no antihypertensive drug treatment, no target-organ disease	111	7 group meetings conducted by physician, nutritionist and public health nurse.	18 months	SBP: -5.8 (p=0.04); DBP: 0.4 (p=0.41)

MAP, mean arterial pressure; NA, not applicable

a long-term difference of 5-6 mmHg in casual DBP was associated with reductions of 35-40 % and 20-25 % in the incidences of stroke and CHD, respectively (269). In the 36-year follow-up data of Framingham Study, the risk ratios in hypertensive men (SBP $\geq$ 140 mmHg or DBP $\geq$ 90 mmHg) aged 35-64 years were 2.0 for CHD, 3.8 for stroke, 2.0 for peripheral artery disease and 4.0 for cardiac failure compared to their normotensive counterparts (2). The corresponding risk ratios in women were 2.2, 2.6, 3.7 and 3.0, respectively. In addition, elevated BP is documented as one of the main predictors of LVH, a strong independent risk factor for cardiovascular events (271, 272). Elevated BP is also consistently documented as an important precursor for end-stage renal disease (273). The relationship between BP and these disease outcomes has been documented in both men and women and in all age-groups as graded, i.e. the higher the BP level the higher the risk, and as continuous with no actual threshold value below which there would be no risk (1). This continuum of risk was just recently clearly demonstrated by the Framingham Study investigators, who showed that the risk ratio for major CVD events in the subjects with even high normal BP (130-139/85-89 mmHg) was 2.5 in women and 1.6 in men compared to subjects with optimal BP (<120/80 mmHg) (274).

According to many observational studies, SBP is more closely related to cardiovascular risk than DBP (275, 276). In the Framingham study, the incidence of CVD events was substantially greater in subjects with isolated systolic hypertension compared to subjects with isolated diastolic hypertension and more or less the same than in subjects with combined systolic and diastolic hypertension. Therefore, it has even been suggested that in persons with SBP elevation, knowledge of the level of DBP is of limited use in cardiovascular risk assessment (2). This strong, positive association between isolated systolic hypertension and CVD events has been verified especially in studies of elderly subjects (277, 278), but it applies also to the middle-aged population (279, 280). Studies comparing the pulse pressure (the difference between SBP and DBP) and SBP as independent variables in predicting CVD events in middle-aged subjects have yielded inconsistent results (281, 282). On the contrary, the respective studies in the elderly have found pulse pressure to be a better predictor of CVD than SBP (283).

The pathophysiology of accelerated atherosclerosis associated with hypertension

The exact mechanism by which elevated BP enhances the development of atherosclerotic diseases is not yet well defined. However, there is some evidence that hypertension predisposes to and accelerates atherosclerosis in co-operation with other atherogenic risk factors by exerting oxidative stress on arterial wall (284). This oxidative stress may activate endothelial genes which are involved in generating an inflammatory response that, especially in presence of hyperlipidaemia, leads to the formation of atheroscletoric plaques.

2.4.2 Antihypertensive drug trials

The benefits of antihypertensive drug treatment in prevention of cardiovascular events associated with malignant hypertension were recognized in the early 60's. The Veterans Administration Trial was the first trial to demonstrate the efficacy of antihypertensive drugs in prevention of cardiovascular events among middle-aged subjects with less severe hypertension (285). The results of this trial comparing the hydrochlorthiazide/ reserpine/hydralazine-based treatment to placebo in subjects with baseline DBP 115-129 mmHg were published in 1967. In this study, active treatment was associated with significant reduction in the incidence of stroke and total cardiovascular events, but not in the incidence of myocardial infarction. Since then, several large trials comparing usually diuretic- or beta-blocker-based treatment with placebo have been conducted in middle-aged subjects and also in elderly subjects with a DBP of 90-115 mmHg. In a systematic review of these trials, including 37 000 patients with mean treatment duration of 5 years, it was concluded that a 5 mmHg difference in DBP reduced stroke incidence by 42 % and CHD incidence by 14 %, respectively (3). In this review, the relative risk reduction associated with antihypertensive drug treatment was of the same magnitude in all individuals, irrespective of the age of the participants.

The increasing evidence of the hazards associated with elevated isolated systolic hypertension, the most common type of hypertension among the elderly, resulted in a launching of studies assessing the effects of antihypertensive drugs in this subgroup of hypertensive subjects older that 60 years (286-288). In a recent meta-analysis the data from these studies were combined with the data of the subgroup of elderly subjects with isolated systolic hypertension enrolled in five other trials primarily of systolic-diastolic hypertension

(289). In this review, active treatment leading to a fall of 10.4 mmHg in SBP and of 4.1 mmHg in DBP reduced total mortality by 13 %, cardiovascular mortality by 18 %, all cardiovascular events by 26 %, the incidence of stroke by 30 % and all coronary events by 23 %.

Some studies suggest that there could be a J-shaped relationship between mortality and on-treatment DBP in hypertensive patients with evidence of CHD, i.e. those with the highest and lowest on-treatment DBP have the highest mortality risk. This increased risk in the subjects with low DBP has been speculated to be due to decreased coronary perfusion associated with overaggressive reduction of DBP (290). However, according to accumulated evidence from randomised trials and observational studies, the lowering of BP to a level of 140/85 mmHg and even lower will produce the greatest reduction in cardiovascular complications (291, 292). In these studies, the CVD risk reduction was greatest in subjects with greatest BP reduction irrespective of the baseline BP level. It has been suggested that the possible explanation for increased mortality in the patients with the lowest DBP observed in some studies could be related with deterioration of the general health independent of antihypertensive drug treatment or that the low DBP is a consequence of underlying CHD (293, 294).

The studies assessing the association between the BP lowering and the reduction of cardiovascular events before 90's were mainly based on treatment with beta-blockers or diuretics - "the older" type of antihypertensive drugs. Since then the newer classes of antihypertensive drugs, i.e. calcium-channel blockers and ACE inhibitors, have been investigated and compared with the older classes of antihypertensive drugs in different aspects of hypertension management. Based on these studies, it has been concluded that there are on average no significant differences between the antihypertensive drug classes in terms safety or efficacy in terms of BP reduction or CVD prevention (71, 295, 296). However, this conclusion was just recently challenged by the results of the LIFE (Losartan Intervention For Endpoint reduction in hypertension) study (297). In this randomised trial with 9193 participants having both hypertension and LVH, the CVD risk reduction associated with BP reduction induced by losartan, an angiotensin-II type 1-receptor antagonist, was compared to the risk reduction induced by atenolol, a well-known β-blocker from the previous large-scale studies. The results of the study showed that the number of CVD events and CVD deaths was significantly smaller in the losartan group compared with the atenolol group. This finding did

not change significantly when the small difference in BP reduction between the groups was taken into account in the analyses. Based on these findings, the authors concluded that, at least in this high-risk group of hypertensive subjects, the treatment of high BP with losartan can offer benefits that are beyond the BP reduction.

2.4.3 The effects of other risk factors on cardiovascular risk in subjects with hypertension

The relative cardiovascular risk reduction associated with antihypertensive drug treatment, as reviewed in the previous paragraph, is found to be relatively constant regardless of other cardiovascular risk factors or characteristics of the subject. In contrast, the effect of antihypertensive drug treatment on absolute cardiovascular risk is more dependent of the level of other cardiovascular risk factors, age of the subject and of the presence or absence of the target-organ damage than on the absolute BP level of the subject (298, 299). It has been even argued, that treatment of mild hypertension in subjects with no other cardiovascular risk factors could do more harm than good (300). Therefore, the treatment decisions in latest guidelines for hypertension management are based on estimated absolute cardiovascular risk for the individual patient instead of pure BP levels (15, 16). In the following, the most important factors affecting the CVD risk in subjects with high BP will be reviewed.

2.4.3.1 Age and gender

In the 36-year follow-up data of the Framingham study, the cardiovascular disease risk ratio among hypertensive men and women aged 65-94 years compared to normotensive subjects of the same age group was 1.8 (14). This risk ratio was somewhat smaller than the corresponding ratio in hypertensive subjects aged 35-64 years. This decrease in relative risk for CVD events along with the increasing age is offset by the striking increase in the CVD incidence in the elderly. This makes the absolute cardiovascular risk associated with hypertension greater in this age group compared to the younger age groups with the same BP level. Accordingly, the relative CVD risk reduction observed in antihypertensive drug trials including only elderly subjects with systolic or diastolic hypertension has been of similar size to those seen in trials with younger subjects. However, the absolute benefits observed in the

elderly subjects have been more than twice as great as those observed with the younger subjects (301). So far, the evidence of the benefits of antihypertensive drug treatment is limited to subjects aged up to 80 years. Currently, a new trial is recruiting hypertensive subjects aged 80 years or more to investigate the effects of BP-lowering therapy in this patient-group (302).

According to the Framingham data, the relative risk for CVD events is very similar in both genders (14). However, the absolute risk in men up to 64 years was almost twofold compared to that of women. This difference in absolute CVD risk between the sexes was halved in subjects older than that.

2.4.3.2 Smoking

The data of the large observational studies show that cigarette and cigar smoking are powerful predictors of CHD and ischaemic stroke in the general population (303, 304). These studies have also indicated that this risk decreases sharply in those who quit, especially in the middle-aged and younger population (303). In hypertensive subjects, cigarette smoking increases the CVD risk for any level of BP. The Framingham data suggest that the risk for any CVD event is almost twofold in a hypertensive 50-year-old male patient who smokes compared to his non-smoking counterpart (305). In a study among the drug-treated hypertensive patients, the total 5-year mortality was 2.3 times higher in smokers compared to non-smoking patients (306). Correspondingly, in both middle-aged hypertensive men and women who smoke 20 cigarettes per day, quitting smoking will reduce the CVD risk by 35-40 % during the next two years (305). It has been estimated that 70-80 % of the expected benefit in terms of CVD risk reduction from simultaneous treatment of hypertension and smoking cessation can be attributed to smoking cessation (307). The additive effects of smoking as a CVD risk factor is mediated by the increase in formation of atherosclerotic lesions (308), as well as by increased thrombus formation and detrimental effects on the haemostatic system (232). In addition, smoking can reduce the BP-lowering effect of some antihypertensive drugs, especially non-selective β-blockers (309, 310). Smoking also probably worsens the lipid profile especially among those with drug treatment for hypertension (311, 312).

2.4.3.3 Dyslipidaemia

A large body of evidence derived from observational studies shows that high serum concentrations of total and LDL cholesterol, as well as the low levels of serum High density lipoprotein (HDL) cholesterol are associated with increased CHD risk (313, 314). In these studies, a 0.6 mmol/l decrease in total cholesterol was associated with 54 % reduction in CHD risk in men aged 40 years, whereas the similar fall in cholesterol in men aged 70 years could produce a CHD risk reduction of 20 %, respectively. Similarly, a 0.03 mmol/l increase in HDL-cholesterol was associated with at least a 3% reduction in CHD risk at all ages. Some epidemiological studies suggest that the elevated ratio of total to HDL cholesterol is a stronger predictor of CHD incidence than either of these variables alone (315). The benefits of total and LDL cholesterol reduction by statin treatment in the primary and secondary prevention of CHD have been demonstrated in several trials (316-319). In these trials, the net reduction in CHD events has varied between a fifth and a third.

In the hypertensive screenees (DBP $\geq$ 90 mmHg) of the large Multiple Risk Factor Intervention Trial (MRFIT) study, the CHD death rate was 5.14 times higher in hypertensive subjects with total cholesterol $\geq$ 6.34 mmol/l compared to normotensive subjects with a cholesterol value of less than 4.71 mmol/l (320). In the pooled data of the treated hypertensive men of the Gothenburg Primary Prevention study, the 8-year risk for all CVD events were approximately fourfold in subjects with no change in SBP or in total cholesterol during the follow-up compared to subjects with 20 % reduction in SBP and 11 % reduction in total cholesterol (321). In this study, the effect of SBP reduction on CVD and CHD events was very small if serum cholesterol levels remained unchanged. The subgroup analyses of the statin trials demonstrate the similar relative benefits of treatment both in normotensive and hypertensive subjects in CHD prevention (318). In a few years, the data of two large on-going trials will be available to demonstrate the possible absolute benefits of statin treatment in drug-treated hypertensive patients without CHD (322, 323).

2.4.3.4 Type 2 diabetes

Type 2 diabetes is a well-established independent risk factor for CHD, stroke and peripheral vascular disease (324, 325). It has even been reported that diabetic patients without previous

history of CHD have as high a risk for myocardial infarction as non-diabetic subjects with previous myocardial infarction (325). The risk for CVD events is already significantly higher in subjects with pre-diabetic levels of hyperglycaemia compared to normoglycaemic subjects (324, 326). In subjects with type 2 diabetes, the increase in CVD risk associated with co-existing hypertension is significantly greater than that observed in non-diabetic subjects, suggesting an effect more than additive (327). It has been proposed that the risk for CVD events is approximately fourfold in subject with both type 2 diabetes and hypertension compared to non-diabetic normotensive subjects (328).

The effects of antihypertensive drug treatment on CVD morbidity and mortality in hypertensive patients with type 2 diabetes have been studied in many randomised clinical trials. Based on the studies with a pre-specified DBP target level, it has been concluded that the benefits of tight BP control in reduction of CVD risk and total mortality in this patient-group are even greater than in hypertensive subjects in general (291, 329, 330). These findings have been taken into account in the latest guidelines for management of hypertension, which recommend somewhat lower target BP in diabetic hypertensive patients than in hypertensive subjects without diabetes (15-17, 35). The potential of BP reduction especially in this patient-group has also been shown in a subgroup analyses of three separate placebo-controlled trial assessing the effects of antihypertensive drug treatment on isolated systolic hypertension (331-333). The benefits of different antihypertensive drug classes in hypertensive diabetic patients have been compared in subgroup analyses of many recent trials (330, 334-338). In most of these trials, there were no differences in the CVD risk reduction between these different drug classes (330, 334, 336, 337). However, the results of the CAPPP (the Captopril Prevention Project) and just recently published LIFE studies suggest that the ACE inhibitor- or angiotensin-II type 1-receptor antagonist-based treatment could offer more efficient cardiovascular protection than the conventional treatment with β-blockers and diuretics in hypertensive patients with type 2 diabetes (335, 338).

2.4.3.5 Obesity

The positive independent association between obesity and the incidence of CHD has been shown in many epidemiological studies (339, 340). This association has been demonstrated as linear, starting already within the normal BMI range, i.e. in subjects considered to have

a normal weight. Also the weight gain during adulthood, even within the normal weight range, has been found to be a strong predictor for CHD (341, 342). In contrast, in most of the studies including only hypertensive subjects the risk for CHD and CVD mortality has been significantly higher among lean subjects compared to their obese counterparts (343-346), although also some opposite findings exist (347). It has been suggested that this excess in CHD mortality among lean hypertensive subjects could be explained by different and "more severe" pathophysiology and haemodynamics of hypertension in these subjects compared to the obese hypertensives (346). However, in addition to the importance of obesity as a predictor of hypertension, it has been shown that elevated BP is an important risk factor for CVD and all-cause mortality also in obese subjects (346, 348). Therefore, the concomitant treatment of hypertension and obesity in overweight subjects with high BP is important.

2.5 Community control of hypertension

2.5.1 Rationale

The effective prevention of the diseases preceded by high BP at the population level requires a two-tailed approach. The first approach aims to identify those subjects in the population who have their BP already on hypertensive level and to control their BP by non-pharmacological means and also by drug treatment if warranted (15, 16). This approach is called "the individual approach" and reaches only the minority of the population.

In populations, the BP values are distributed more or less in the normal manner with a slight dominance of higher values (349). In the western populations, this distribution curve and mean BP are shifted to the right at older ages. The steeper this rise along increasing age is, the higher is the population mean BP. Due to the continuous nature of the BP distribution the prevalence of hypertension increases in conjunction with the increase in the population mean BP. This increase in BP along with the age is apparent in most populations with a westernised lifestyle, but virtually absent in some remote populations with healthier lifestyle patterns. Therefore, it has been suggested that the main reason for these large differences between the populations in the position of BP distribution curve and so, in the mean BP and prevalence of hypertension are mainly due to the large differences in the environmental factors affecting BP (85).

In the western populations, the main proportion of the BP readings is located within the normal or high normal range (120-129/80-84 mmHg or 130-139/85-89 mmHg). Although the risk for CVD associated with elevated BP is continuous and progressive along with the increasing BP values, the largest number of CVD events in the population occurs in this category due to the large number of subjects with their BP at this level. According to the hypertension guidelines, the vast majority of these patients should not be treated with antihypertensive drugs, at least partly because it would not be by no means cost-effective. Therefore the only possibility to lessen the CVD burden in this BP category and at the same time in the majority of the population is to shift the entire BP distribution of the population to the left towards lower BP values by detecting and modifying the environmental factors affecting BP. This strategy is called the "population approach" because in this strategy the target for intervention is the whole population.

Both strategies mentioned above are important and complementary. However, the "population approach" carries a larger potential for decreasing the sequeale of hypertension in community, and at the same time it offers the possibility for primary prevention of hypertension (2). For instance, according to just recently published findings of the Framingham study, 37 % of the subjects with high normal BP aged 65 years or less became hypertensive over 4 years of follow-up (350). In this study, one of the main predictors for the development of hypertension was weight gain of 5 % or more. The results of the study emphasise the importance of adequate follow-up and modification of unfavourable lifestyle factors in these subjects. It has been estimated that in most of the western populations only a 2-3 mmHg decrease in population mean SBP could reduce the prevalence of hypertension by one fifth and the annual mortality rate from stroke and CHD by 6 % and 4 %, respectively (351, 352). To investigate the situation and the trends with respect to both of these strategies in the population, the monitoring of independent random samples of the target population is a feasible approach.

2.5.2 Prevalence, awareness, treatment and control of hypertension in the community

In 1972, Wilber and Barrow published their classic paper of a community control of hypertension in which the term "rule of halves" was introduced for the first time (353). According to this rule, only half of the hypertensive subjects are detected, and half of those

who are detected are under antihypertensive drug treatment, of whom only half have their BP controlled adequately. These results demonstrating the poor situation of hypertension control at the population level were soon confirmed in population surveys also in other parts of the world (354, 355). These findings were adopted as the basis for the many population-based hypertension control programmes starting in the early 70´s. The main targets of these programmes were the early detection and effective drug treatment of hypertension. Since the implementation of these population-based programmes, some improvement in these various aspects of hypertension control have taken place.

In a review by Marques-Vidal and Tuomilehto 24 population surveys of hypertension awareness, treatment and control published since 1983 were assessed (356). In men, the rates for hypertension awareness, antihypertensive drug treatment among the detected hypertensives and control of BP among drug-treated hypertensive subjects varied from 23 % to 93 %, from 5 % to 89 % and from 5 % to 97 %, respectively. The corresponding figures in women were from 28 % to 97 %, from 6 % to 97 % and from 0 % to 97 %. On the average, in the industrialized countries the vast majority of the hypertensive subjects were aware of their condition, two thirds of those aware of their high BP were treated with antihypertensive drugs and half of those treated had their BP at a normotensive level. The rates for awareness, treatment and control were somewhat better in women than in men. Conversely, in the developing countries, as confirmed also by another recent review (357), the situation was more or less the same as in the industrialised countries at the time the "rule of halves" was invented. Also in these countries, the rates for different aspects of hypertension management were higher in women than in men.

In contrast to the relatively high number of published reports of single cross-sectional samples assessing the situation in hypertension management at the population level, there are relatively few studies assessing the evolution of hypertension care in the same population. Such studies published in English-language journals are listed in Table 3. These studies, if using similar field methods in each survey, are suitable for the assessment of trends in hypertension care in the same population.

In Finland, as in most other western countries, a favourable development in hypertension care has been reported (8, 358). This development started along with the establishing of the hypertension programme of the North Karelia Project in 1971 (359). The specific aims of the programme were to detect as many of the hypertensive subjects as possible, to control BP as

efficiently as possible in these subjects, to create uniform and appropriate methods in hypertension management among the physicians and to gather data on hypertension epidemiology (359). During 1972-1977, a significant improvement in detection and management of hypertension was observed. In next five years, the situation in hypertension care was maintained, but no further reduction in population BP levels was seen (8). During 1982-1987, a significant reduction in population SBP levels and to some extent also in hypertension care especially among men took place (358). However, the situation in 1987 was reported as far from optimal.

The variability of the cut-off points chosen for the definition of hypertension affects strongly the epidemiological estimates of hypertension (367). This fact can be easily seen also in table 3 where the different cut-off points are used between and within the studies. Also the different methodology used in BP measurements makes the international comparisons difficult. These aspects were taken account in the WHO MONICA project with highly standardised methodology in BP measurements and with a uniform definition for hypertension (10). When 41 MONICA study populations were ranked by descending levels of age-adjusted SBP measured between 1982 and 1987, the Kuopio province in Eastern Finland was ranked first in both sexes (9). In men, the difference between the Kuopio province and Catalonia of Spain was 24 mmHg (148 mmHg-124 mmHg). In women, the SBP of women in Kuopio was 27 mmHg higher than in women in Halifax, Canada (145 mmHg-118 mmHg), who had the lowest mean SBP of the WHO MONICA populations. With the WHO MONICA criteria for hypertension (SBP $\geq$ 160 mmHg and/or DBP $\geq$ 95 mmHg or antihypertensive drug treatment) the rates for prevalence of hypertension in those aged 35-64 years in Kuopio were approximately fivefold in men and threefold in women compared to the survey participants in Catalonia (368)

2.5.3 The prevalence of other cardiovascular risk factors in hypertensive subjects

The data from the studies reviewed here which assess the levels of one or several other cardiovascular risk factors in hypertensive subjects originate from random samples of the target population (18, 369, 370), from all the available subjects or subsample of subjects in a defined geographical area (19, 371) or from the hypertensive screenees in the primary health

Table 3. Population-based studies of trends in community control of hypertension.

Country, reference	Criteria for hypertension*	Age-range, years	Gender	Study years	Prevalence of hypertension (%)	Awareness of hypertension (%)	Drug-treated (%)	Drug-treated of aware (%)	Controlled (%)	Controlled of drug-treated (%)
Australia, (360)	1		Combined	1980	31	67	33	49	17	52
				1983	30	77	33	43	19	58
Belgium, (361)	1	25-64	Men	1980-84	20	49	26	53	15	58
				1985-92	13	67	47	71	31	65
			Women	1980-84	19	66	48	73	28	60
				1985-92	13	88	74	83	62	84
England, (362)	1	≥ 16	Men	1994	19	60	45	75	27	60
				1998	20	68	54	79	37	68
			Women	1994	20	66	54	83	32	58
				1998	20	74	64	86	40	63
	2		Men	1994	41	33	20	60	5	23
				1998	42	40	26	64	8	31
			Women	1994	35	46	32	69	7	23
				1998	33	52	38	73	11	28
Finland[1], (8)	3	30-59	Men	1972	30	39	13	33	4	31
				1982	26	67	45	66	23	51
			Women	1972	35	66	28	42	6	27
				1982	21	82	57	67	27	47
Finland, (358)	3	25-64	Men	1982	18-24[2]	70	42	60	23	55
				1987	14-22[2]	79	51	65	29	57
			Women	1982	12-19[2]	85	61	72	39	64
				1987	14-17[2]	87	65	75	41	63

	*	Age	Sex	Period						
France, (363)	1	35-64	Men	1985-87	28	47	38	81	16	41
				1994-97	21	71	57	80	33	58
			Women	1985-87	19	67	57	85	25	44
				1994-97	19	87	76	87	52	68
Germany, (364)	1	25-64	Men	1984-85	19	66	32	48	17	55
				1994-95	20	75	46	61	28	61
			Women	1984-85	14	83	56	67	34	61
				1994-95	15	82	60	73	42	69
	2		Men	1984-85	38	48	16	33	5	30
				1994-95	39	55	24	44	7	29
			Women	1984-85	25	66	32	48	10	31
				1994-95	25	66	38	58	15	39
Taiwan, (365)		≥ 18	Combined	1976	14	32	26	81	5	19
				1982	15	74	42	57	5	12
USA, (366)	1	18-74	Men	1976-80	21	59	37	NA	18	49
				1988-91	15	85	72	NA	57	80
			Women	1976-80	19	78	62	NA	40	63
				1988-91	14	93	86	NA	72	84
	2		Men	1976-80	37	42	21	NA	5	24
				1988-91	23	66	46	NA	22	50
			Women	1976-80	27	63	43	NA	15	36
				1988-91	18	81	65	NA	38	58

*1=SBP ≥ 160 mmHg or DBP ≥ 95 mmHg or antihypertensive drug treatment, 2=SBP ≥ 140 mmHg or DBP ≥ 90 mmHg or antihypertensive drug treatment, 3= SBP ≥ 175 mmHg or DBP ≥ 100 mmHg or antihypertensive drug treatment; [1] North Karelia province; [2]Variation between the study areas; NA, not applicable

care or occupational health clinics (13, 372-375). In only two of these studies were the time trends in these risk factors assessed (369, 370).

The common features of the studies comparing the lipid levels or prevalence of lipid abnormalities between hypertensive and normotensive subjects have been a significantly higher prevalence of hypercholesterolaemia amongst hypertensive persons and significantly lower HDL cholesterol among the drug-treated hypertensive patients compared to normotensive subjects. For instance, in a large population-based random sample of men and women aged 25-64 years in Australia, the prevalence of hypercholesterolaemia (total cholesterol $\geq$ 6.5 mmol/l) in untreated hypertensive men and women were 57 % and 94 % greater compared to their normotensive counterparts (28.5 % vs. 18.1 % in men and 37.0 vs. 19.1 in women, p-values<0.001) (18). The level of HDL cholesterol in drug-treated hypertensive men and women was significantly lower compared either to normotensive or to the untreated hypertensive group. Furthermore, the ratio of total to HDL cholesterol was significantly higher in the drug-treated hypertensive patients compared to the other groups in men, but not in women. At least part of the observed low levels of HDL cholesterol among the treated hypertensive patients participating the population-based studies is suggested to be due to the adverse effects on lipid metabolism caused by antihypertensive drug treatment - especially treatment with diuretics and β-blockers (370). However, these findings have not been confirmed in long-term clinical trials comparing the effects of different antihypertensive drug regimens on lipid profile (376).

In contrast to other cardiovascular risk factors reviewed, the prevalence of smoking in most of the hypertensive populations is not significantly different from that of general population. For example, in the screenees of the MRFIT study, the prevalence of smoking was 37.7 % in hypertensives and 34.5 % in normotensives (372). In the Tromssr Heart study the prevalence of smoking in men and women with antihypertensive drug treatment was 28 % and 9 %, whereas the corresponding figures in normotensive men and women were 35 % and 13 %, respectively (19). In contrast to these findings, there were significantly fewer smokers among the drug-treated hypertensive subjects in both sexes compared to normotensive population in a large Finnish population-based sample among those aged 35-64 years in 1982 (24.9 % vs. 38.7 % in men, 8.1 % vs. 16.4 % in women) (369).

The mean BMI, and the prevalence of obesity and type 2 diabetes are consistently reported to be significantly higher in the hypertensive subjects attending the primary care clinics

compared to their background population (373-375). In the hypertensive population of Gubbio study, the prevalence of obesity was approximately twofold in both sexes up to age of 64 years compared to the normotensive subjects (371).

The changes in levels of cardiovascular risk factors in Finnish hypertensive subjects aged 35-64 years during 1982-1987 were assessed in two random population-based samples as a part of the FINMONICA study (369). During the five-year period, the mean serum cholesterol decreased in treated hypertensive men and women by 2 % and 4.7 %, respectively. The mean serum HDL-cholesterol increased by 4.5 % and 9.9 % in these same groups. In contrast to these favourable findings, the prevalence of smoking tended to increase and mean BMI increased significantly, especially in men with antihypertensive drug treatment.

3 AIMS OF THE STUDY

3.1 General aim

The purpose of this study was to assess the trends in community control of hypertension in Finnish population samples aged 25-64 years, with special interest in cardiovascular risk factors of hypertensive subjects. Another aim was to examine in a randomised, controlled trial if BP and other cardiovascular risk factors of hypertensive subjects could be affected in primary health care setting by non-pharmacological means.

3.2 Specific aims

1.   To describe the trends in blood pressure levels and in prevalence, awareness and control of hypertension in various parts of Finland during 1982-1997 (STUDY 1).

2.   To compare the trends in serum lipids, BP, smoking, diabetes, BMI and obesity, waist circumfererence, alcohol consumption and leisure-time physical activity in hypertensive population during 1982-1997 with those of the normotensive population (STUDY 2).

3.   To assess the efficacy of a lifestyle-counselling programme planned for hypertensive subjects in a randomised controlled clinical trial conducted in ten health care centres in eastern Finland (STUDY 3).

4 METHODS

4.1 Community control of hypertension (STUDIES 1 and 2)

4.1.1 Study populations

A multinational MONICA project was initiated by the WHO in 1982 (10). The FINMONICA study was the Finnish part of this project. The FINMONICA survey areas since 1982 were the provinces of North Karelia and Kuopio in eastern Finland and the Turku-Loimaa region in southwestern Finland. In 1992, the Helsinki-Vantaa region was included in the study areas and since that the surveys have been carried out under the name of the National FINRISK Study to indicate their role in national cardiovascular risk factor monitoring. In 1997, the monitoring was started also in the Oulu region (Figure 2).

Four independent cross-sectional population surveys were carried out in 1982, 1987, 1992 and in 1997. The survey methods followed the WHO MONICA protocol each year (377). The random samples aged 25-64 years were chosen each year from the national population register. In 1982, the sample was stratified so that 500 persons for each sex and 10-year age group were chosen in the areas. In 1987, the procedure was similar, but the number of subjects in Kuopio and Turku-Loimaa region was halved. Since 1992, the number of subjects was halved also in North Karelia province so that the samples were of equal size in each area.

4.1.2 Data collection

Questionnaire

Information on awareness of hypertension and hypercholesterolaemia, use of antihypertensive drugs, smoking behaviour, disease history, alcohol use and leisure-time physical activity were obtained with a standardised, self-administered questionnaire. The question about diagnosed diabetes was analysed in the present study since 1987. Correspondingly, the use of lipid-lowering drugs was asked since the 1992 survey. The participants were classified to following categories according to their smoking behaviour: (I) current smokers (those who had smoked regularly cigarettes, cigars or pipe for at least one year and had been smoking during the preceding month), (II) ex-smokers (those who had
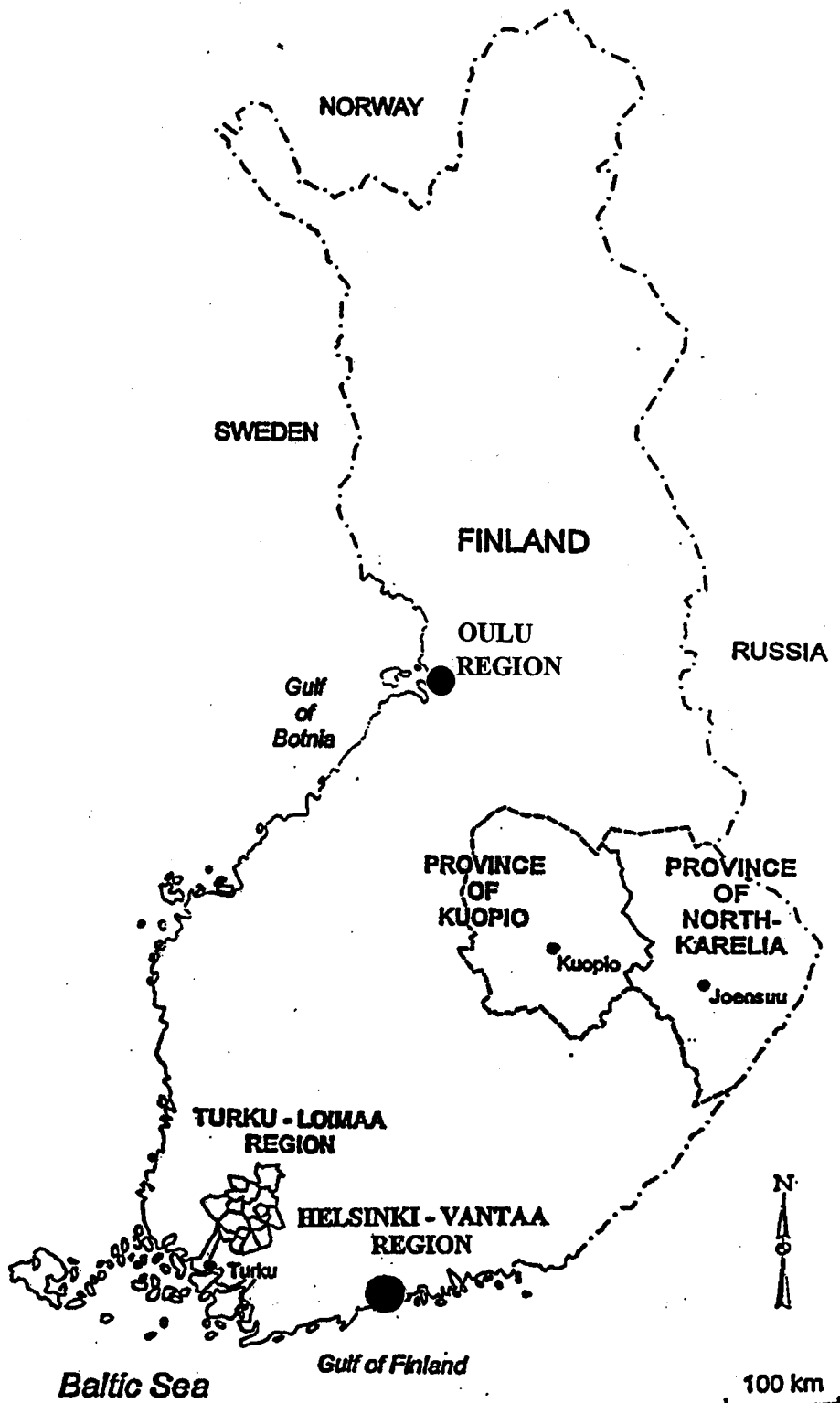
Figure 2. Survey areas in studies 1 and 2. Modified from (378).

smoked regularly in the past but had stopped smoking no later than a month before the survey) and (III) never smokers (those who had never smoked regularly).

BP measurement and criteria for hypertension

Specially trained nurses measured BP in each survey. These nurses were circulated between the study areas to eliminate the possible observer bias in the between-areas comparisons. BP was measured twice from the right arm of the subject, who was seated for five minutes before the measurement. A standard mercury sphygmomanometer with a cuff bladder 13 cm wide and 42 cm long was used. The fifth phase of the Korotkoff sounds was used as the diastolic pressure, and the values were recorded to the nearest 2 mmHg. The mean of these two measurements was used in the analyses. In Study 1, two different cut-off points for hypertension were used: SBP/DBP $\geq$ 160/95 mmHg and SBP/DBP $\geq$ 140/90 mmHg. With both these criteria, the subject was considered hypertensive if he or she reported having taken antihypertensive drugs during the preceding seven days. In Study 2, only the higher cut-off point was used.

Anthropometrical measurements and classification of overweight

Weight was measured with light clothing and height was measured without shoes. Waist circumference was measured in the surveys since 1987. It was measured from the midway between the inferior margin of the last rib and the crest of the ileum, as recommended by WHO (379). BMI was used as a measure of relative body weight. Participants were divided into four classes according to their BMI following the classification by WHO: BMI < 25 kg/m^2 (normal weight), BMI 25-29.99 kg/m^2 (grade 1 overweight), BMI 30-39.99 kg/m^2 (grade 2 overweight) and BMI $\geq$ 40 kg/m^2 (grade 3 overweight) (379).

Lipoprotein determinations and criteria for hypercholesterolaemia

Non-fasting serum total and HDL cholesterol concentrations after the precipitation of b-lipoproteins with dextran sulphate and magnesium chloride were determined using an enzymatic method (CHOD-PAP, Boehringer Mannheim, Germany) (380). A new batch of Dextran Sulphate Sodium Salt (Pharmacia, Sweden, Lot No MM 97012) for precipitation of ApoB containing lipoproteins was introduced in the laboratory on May 1987. However, the HDL cholesterol values with the new precipitant were approximately 4.4 % lower than those

measured with the old precipitant. Therefore the results measured before May 1987 were corrected using the following formula: $HDL_{corrected} = ((HDL_{old} - 1.2621)/0.3592) * 0.3230) + 1.1969$. After this correction, the average and standard deviation of the sample results were the same as those measured using the new precipitant. All lipoprotein determinations were made in the same central laboratory, and the laboratory data were standardized against the WHO reference laboratory in Prague. Hypercholesterolaemia was defined as the serum total cholesterol $\geq$ 6.5 mmol/L or if having drug treatment for hypercholesterolaemia. The ratio of total to HDL cholesterol was considered as high when the ratio was greater or equal to five.

4.1.3 Study designs

The designs of Studies 1 and 2 are presented in Table 4. In trend analysis of the community control of hypertension (Study 1), the data were analysed in all five study areas separately. The total number of participants during 1982-1997 was 29,036 (Table 5). In Study 2, all three original FINMONICA study areas (the North Karelia and Kuopio provinces and the region of Turku-Loimaa) were pooled together, and the Helsinki-Vantaa and Oulu region were left out from the analyses. The study population was classified into four groups according to their BP status: Unaware and untreated hypertensive subjects, aware but untreated hypertensive subjects, hypertensive patients treated with antihypertensive drugs and normotensive subjects. The total number of participants was 24,083, with participation rates varying from 69 % to 75 % in men and from 76 % to 82 % in women, respectively. The number and mean age of subjects in each BP group are shown in Table 6.

4.1.4 Statistical methods

Statistical analyses were conducted with the SPSS/PC+ in Study 1 and SPSS for Windows version 7.5 in Study 2. In Study 1, analysis of variance was used as a statistical method to test the differences between the BP means in each gender separately, with SBP and DBP as dependent variables, area and year as independent variables and age as a covariate. Differences between the proportions were assessed by hierarchical log-linear model with year and area together with the variable to be tested within the model.

Table 4. Designs of studies 1 and 2.

	Study years	Study areas	Subjects	Number of subjects	Explanatory variables	Outcome variables	Type of study
Study 1	1982-1997	North Karelia, Kuopio, Turku-Loimaa	Men and women aged 25-64 years	29,036	Study year, area	SBP, DBP; prevalence, awareness, treatment and control of hypertension; prevalence of antihypertensive drug treatment	Cross-sectional trend analysis
	1992-1997	Helsinki-Vantaa					
	1997	Oulu					
Study 2	1982-1997	North Karelia, Kuopio, Turku-Loimaa	Men and women aged 25-64 years	24,083	Study year, blood pressure group	Total and HDL cholesterol, SBP, DBP, BMI, waist circumference; prevalences of hypercholesterolaemia, smoking, obesity and diabetes; alcohol use, leisure-time physical activity	Cross-sectional trend analysis

Table 5. Number of participants (N) and participation rates (%) by gender, year and area in Study 1.

Study area and year	Men		Women	
	N	%	N	%
North Karelia province				
1982	1538	76	1681	83
1987	1561	79	1689	85
1992	673	68	803	81
1997	712	71	751	75
Kuopio province				
1982	1475	80	1349	86
1987	793	80	857	86
1992	752	76	830	84
1997	707	71	799	80
Southwestern Finland				
1982	1602	81	1702	86
1987	755	76	824	83
1992	749	75	832	84
1997	683	68	747	75
Helsinki-Vantaa region				
1992	675	68	737	74
1997	631	63	716	72
Oulu region				
1997	663	66	750	75

Table 6. The number (N, %) and mean age of the participants according to gender, year and the BP group in Study 2.

| | Hypertensive | | | | | | Normotensive | | All | |
| | Untreated and unaware | | Aware but untreated | | Treated with drugs | | | | | |
	N (%)	Age (years)	N (%)	Age (years)	N (%)	Age (years)	N (%)	Age (years)	N (%)	Age (years)
Men										
1982	688 (15.3)	48.1	440 (9.8)	46.1	411 (9.1)	52.8	2960 (65.8)	41.9	4499 (100)	44.3
1987	373 (13.0)	47.1	290 (10.0)	48.3	314 (10.9)	53.1	1901 (66.1)	42.8	2878 (100)	45.2
1992	199 (9.2)	50.3	198 (9.2)	50.1	240 (11.1)	53.6	1525 (70.5)	42.8	2162 (100)	45.3
1997	140 (6.8)	47.9	194 (9.4)	49.6	254 (12.3)	54.6	1472 (71.5)	43.2	2060 (100)	45.6
Women										
1982	329 (7.1)	53.7	403 (8.7)	50.1	507 (11.0)	55.6	3373 (73.1)	42.0	4612 (100)	45.2
1987	207 (6.6)	53.4	238 (7.6)	49.2	366 (11.6)	55.0	2336 (74.2)	42.0	3147 (100)	44.9
1992	108 (4.4)	53.3	175 (7.1)	51.5	239 (9.7)	55.1	1934 (78.8)	42.7	2456 (100)	45.0
1997	65 (2.9)	53.3	132 (5.8)	49.8	230 (10.1)	55.3	1842 (81.2)	43.0	2269 (100)	45.0

In Study 2, analysis of variance was used to test the differences between the total cholesterol and HDL cholesterol means for each sex separately, with total and HDL cholesterol as dependent variables, BP group and study year as independent variables and age, body mass index and alcohol use as covariates. Correspondingly, the differences between the BP and BMI means for each sex separately were tested with SBP, DBP and BMI as dependent variables, BP group and study year as independent variables and age as a covariate. Differences between the proportions were assessed by a hierarchical log-linear model with year, BP group and 10-year age group together with the variable to be tested within the model. Confidence intervals for the change between the years in means of continuous variables and in proportions for each gender and BP group separately were calculated using a special software package (381).

4.2 Non-pharmacological treatment of hypertension in primary health care (STUDY 3)

4.2.1 Screening and randomisation of the participants

The LIHEF study (Lifestyle Intervention against Hypertension in eastern Finland) was conducted in ten primary health centres in eastern Finland. Eight of the health centres were located in rural municipalities with 3000-12,000 inhabitants (the health centres of Eno, Kiihtelysvaara, Kitee, Kontiolahti, Lieksa, Liperi, Nurmes and Pyhäselkä). The remaining two health centres were located in the cities of Joensuu and Kuopio which have 50,000 and 90,000 inhabitants, respectively (51 % of all participants). The study protocol was approved by the Ethics Committee of the Kuopio University Hospital. The study participants were enrolled between February 1996 and May 1997. Vast majority of the participants were recruited by newspaper advertisements. Eligible subjects were men and women aged from 25 to 74 years with systolic BP 140-179 mmHg or diastolic BP 90-109 mmHg or patients on antihypertensive drug therapy. Exclusion criteria included secondary hypertension, mental or physical illness serious enough to prevent compliance with the study procedures, alcoholism, type 1 diabetes mellitus, current or planned pregnancy and history of myocardial infarction or stroke within the preceding 3 months.

Three screening visits in one-week intervals were organised to assess the BP level of the subjects not using any antihypertensive medication. During each screening visit BP was measured twice from the right arm of the subject in a sitting position according to the WHO MONICA protocol using a standard mercury sphygmomanometer with a cuff bladder 12 cm wide and 36 cm long (382). The mean of the BP measurements performed in the second and third visit (a total of four readings) was used as the screening BP. The randomisation visit was organised within 30 days after the third screening visit. A written informed consent was obtained from every eligible subject agreeing to participate after which they were randomised to intervention or usual care by the same study physician using a dice (odd numbers-intervention group, even numbers-control group). Of the 813 subjects originally eligible for the study, 715 were eventually assigned to intervention or usual care.

4.2.2 Data collection

The design of the Study 3 is presented in Figure 3. BP, weight and waist and hip circumferences were measured from every participant during the randomisation visit, the 1-year visit and at the final study visit 2 years after randomisation. During these visits, BP was measured twice using the same method as during the screening and the mean was used in the analyses. Weight was measured with the subjects in light clothing using the same digital scale. Height was measured only at the baseline. BMI (kg/m²) was calculated. Waist circumference was measured with the same method as in Study 2. The circumference of hip was measured from the maximum extension of the buttocks.

Most of the BP and anthropometrical measurements during the screening and follow-up period were performed by one study nurse trained for the trial and blinded to the treatment assignment. However, in 176 participants of one health centre, the second study nurse did the measurements during the screening and randomisation visits. During the training period, the mean BP of ten volunteers did not differ significantly between the nurses when a double stethoscope method was used.

The venous blood samples were collected after 12 hours of fasting in each health centre for determination of serum total and HDL-cholesterol, triglycerides and insulin. All laboratory analyses were performed in the Department of Biochemistry, National Public Health Institute, Helsinki, Finland. Before April 1 in 1998, total cholesterol, HDL cholesterol and triglycerides
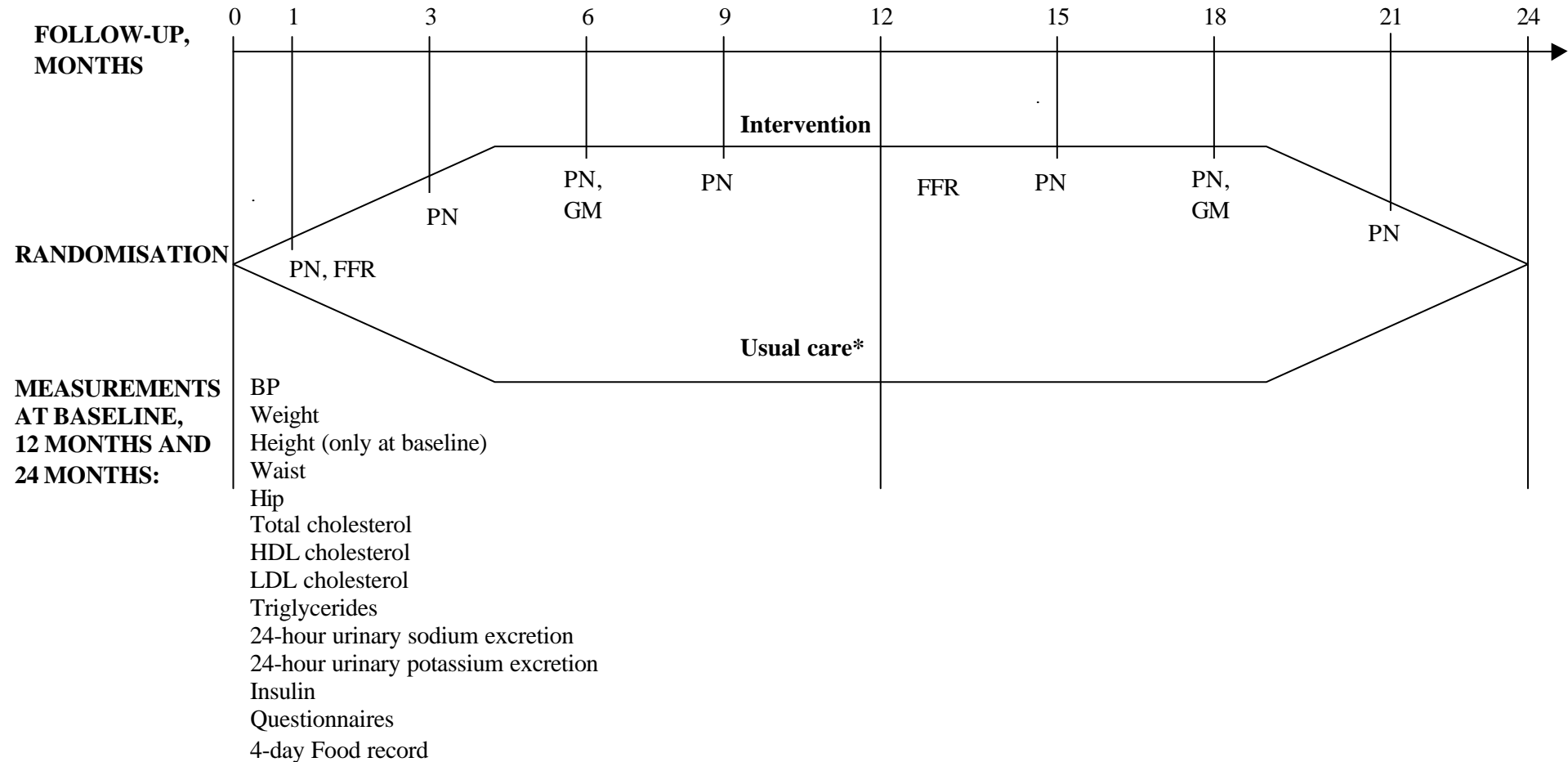
Figure 3. The design of the study 3. PN= public health nurse, FFR=feedback from the food record, GM=group meeting, other abbreviations in page 9. *Usual care group visited their own public health nurses as usual.

were determined using the same commercial kit (Boehringer Mannheim GmbH, Germany) and Olli C analyser (Kone Ltd, Espoo, Finland). Total cholesterol was determined by an enzymatic GPO-CHOD-PAP method and triglycerides by a GPO-PAP method, respectively. HDL cholesterol was determined by an enzymatic CHOD-PAP method after the precipitation of β-lipoproteins with dextran sulphate and magnesium chloride. After April 1 in 1998, total cholesterol and triglycerides concentrations were determined using the same enzymatic method of another company (Konelab Corporation, Espoo, Finland). The HDL cholesterol concentration was determined using a direct method of this same company. There were no significant differences between the lipid values given by the two different laboratory methods and analysers. LDL cholesterol concentrations were calculated by Friedewald's formula (383). Twenty-four-hour urine samples were collected for determination of 24-hour potassium and sodium excretion. The urine was collected in plastic containers or in throwaway containers. The containers were returned at the health centre to the study nurse, who ascertained the completeness of the collection. Urinary sodium and potassium concentrations were determined potentiometrically using the direct ISE method (Ion-Selective Electrodes).

Information on medical history, smoking, alcohol use, physical activity and daily medication were collected annually using separate questionnaires with standard questions used also in Studies 1 and 2. A four-day food record was collected for the annual visits. The detailed information of the dietary methods and results are published elsewhere (384).

4.2.3 Intervention goals and methods

The goals for the intervention were 1) to achieve normal weight (BMI < 25 kg/m²) if overweight, 2) to reduce a 24-hour sodium intake to less than 85 mmol (< 5 g sodium chloride), 3) to modify alcohol consumption to no more than two drinks per day if using more, 4) to exercise at moderate intensity at least three times per week and at least to 30 minutes and 5) to stop smoking if a smoker.

Before the launching of the study, the study physician and a dietitian carried out a teaching session to the local public health nurses in each health care centre separately. The training session dealt with simple counselling and behaviour modification methods targeting weight reduction, reduction in salt, alcohol and saturated fat consumption, and increasing leisure time physical activity.

The core of the actual intervention consisted of four visits by the participants to local public health nurses during the first year of the follow-up, and of three visits during the second year (Figure 3). At these visits, the participants were instructed to change their health behaviour primarily based on their individual situation. At every visit, BP and weight were measured and the values were written down using a special follow-up card. A written feedback of the four-day food record was sent to the public health nurse to support the intervention. In addition, six and 18 months after the randomisation, a two-hour group session was organized in every health care centre for the intervention group by a dietitian and the study physician. During the two-year follow-up, the participants in the usual care group were instructed to visit the public health nurses and their own physicians according to usual practices.

4.2.4 Statistical analyses

Statistical analyses were conducted with SPSS for Windows version 10.0. For continuous variables, t-test was used to test the differences and changes in mean values between the groups. Confidence intervals for the differences in proportions were calculated using a special software package (381). An intention to treat-analysis was used, i.e. all subjects assigned to intervention or usual care were included in the analysis. In case of missing responses, the last observed response was used when calculating the one- and two-year changes in continuous variables (the carry forward-method). The same method was used with dichotomous variables. In a separate analysis of BP changes in subjects without previous antihypertensive drug treatment, the last BP measurement without antihypertensive drug treatment was used if drug treatment was initiated during the trial. Accordingly, in subjects already on antihypertensive medication, the last BP measurement with antihypertensive drug treatment was used if the treatment was discontinued during the trial. In the calculations of BP changes, the changes in doses of antihypertensive medication were not taken into account. Multiple linear regression analysis was used to examine the associations of changes in body weight, sodium and potassium excretion, alcohol intake and leisure-time physical activity (times/week) with the changes in BP, controlling for the baseline BP levels. This analysis was done only in subjects without antihypertensive drug treatment.

The original target sample size was 800 subjects, which was not reached due to numerous dropouts before the randomisation among the subjects already recruited. It was estimated that

this sample size would enable to detect a 3.2 mmHg difference in change of SBP and a 1.6 mmHg difference in change of DBP between the intervention and usual care groups with 80 % power at the 5 % significance level.

5 RESULTS

5.1 Trends in community control of hypertension (STUDY 1)

5.1.1 Systolic and diastolic blood pressure levels

The changes in mean SBP and DBP during 1982 to 1997 stratified by gender, survey year and study area are shown in Figure 4. During 1982-1987, the mean SBP in men decreased significantly in Kuopio province and in southwestern Finland, but remained unchanged in North Karelia. During 1987 to 1997, a downward trend was seen in all three areas. In Helsinki-Vantaa region, however, the mean SBP of the men did not fall from 1992 to 1997. In 1997, the mean SBP was significantly lower in southwestern Finland compared to the other areas. During the entire 15-year period, the mean SBP fell 6 mmHg, 7 mmHg and 7 mmHg in men in North Karelia, Kuopio and southwestern Finland, respectively.

In women, the mean SBP decreased in Kuopio and in North Karelia during 1982 to 1987, whereas in southwestern Finland no significant change was observed. A further decrease was seen in all areas during 1987 to 1997. In 1997, the mean SBP was significantly lower in southwestern Finland and in Helsinki-Vantaa region compared to the women in Eastern Finland. During the entire 15-year period, the mean SBP fell 7 mmHg, 10 mmHg and 7 mmHg in women in North Karelia, Kuopio and southwestern Finland, respectively.

The mean DBP in men remained essentially unchanged in all areas from 1982 to 1987. There was a significant downward trend in DBP in men during 1987 to 1992, which was steeper in eastern than in southwestern Finland. During 1982-1992, the mean DBP decreased by 3, 4 and 1 mmHg in North Karelia, Kuopio and southwestern Finland, respectively. During next five years, however, the mean values increased slightly but significantly in all areas except North Karelia.

There were no significant changes mean DBP among women during 1982-1987. During the next five years, the mean DBP fell significantly in all areas, but especially in eastern Finland. During 1992-1997, however, the mean value increased slightly in all areas together. In 1997, the mean DBP in women was similar in all areas.

SBP, men

SBP, women

DBP, men

DBP, women

Legend: North Karelia, Kuopio, Turku-Loimaa, Helsinki-Vantaa, Oulu
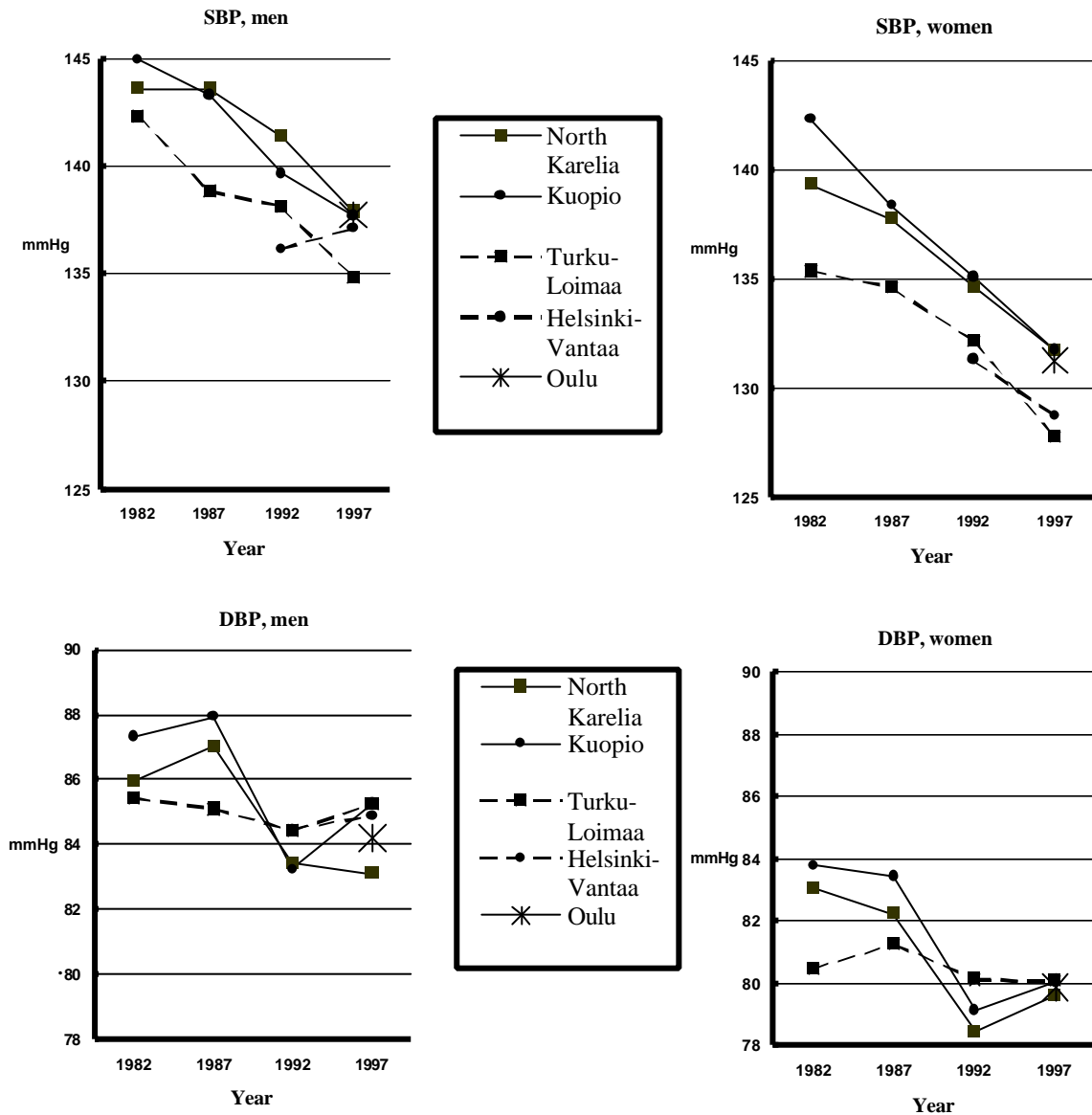
P for analysis of variance, adjusted for age

	North Karelia-Kuopio-Turku-Loimaa 1982-1992		All areas except Oulu 1992-1997		All areas 1997	
	Men	**Women**	**Men**	**Women**	**Men**	**Women**
Systolic BP						
Area	< 0.001	< 0.001	< 0.001	< 0.001	0.008	< 0.001
Year	< 0.001	< 0.001	< 0.001	< 0.001		
Area x year	0.003	0.015	0.004	0.590		
Diastolic BP						
Area	0.001	< 0.001	0.002	0.024	0.001	0.907
Year	< 0.001	< 0.001	0.020	0.070		
Area x year	< 0.001	< 0.001	0.051	0.264		

Figure 4. Systolic and diastolic blood pressure by gender, year and area.

5.1.2 Prevalence of antihypertensive drug treatment

The prevalence of antihypertensive drug treatment in men increased steadily in all areas during the entire study period (Figure 5). In 1997, this proportion was highest, almost 14 %, in Oulu area. In contrast to men, the proportion of women with antihypertensive drug treatment decreased slightly in all study areas except Kuopio during 1982-1997. In 1997, the proportion of female subjects with antihypertensive drug treatment was significantly smaller in southwestern Finland compared especially to Kuopio.
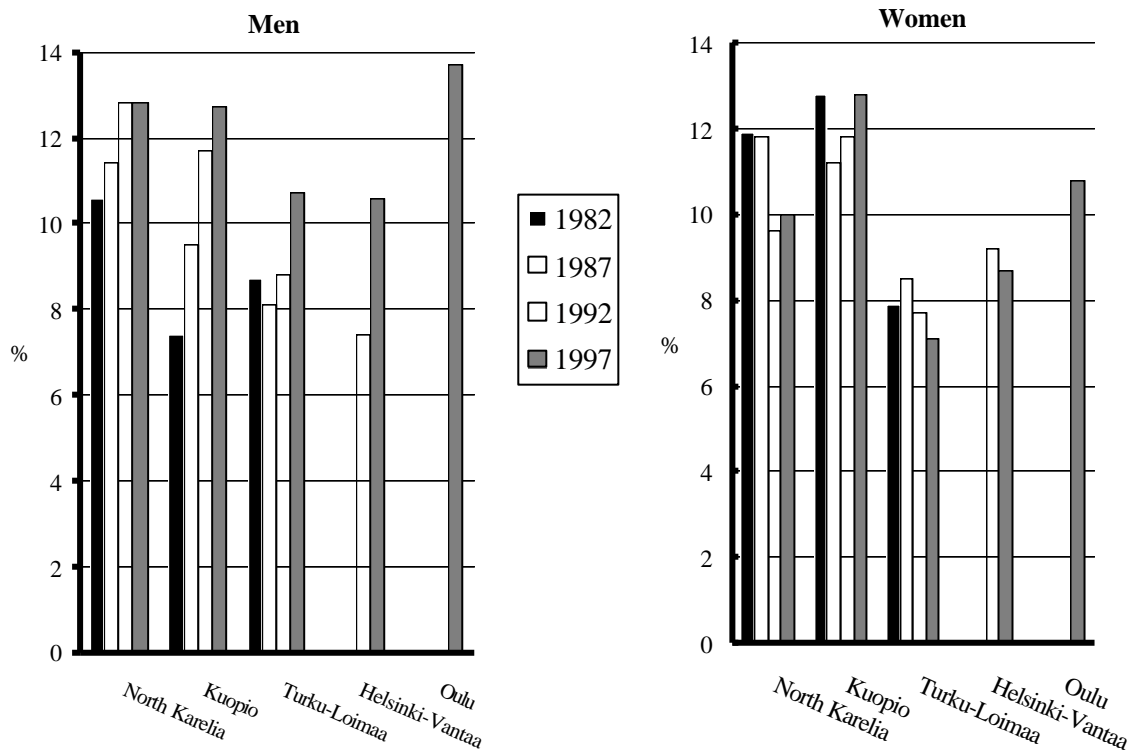
P by saturated log-linear model (10-year age group included):

	North Karelia-Kuopio-Turku-Loimaa 1982-1992		All areas except Oulu 1992-1997		All areas 1997	
	Men	**Women**	**Men**	**Women**	**Men**	**Women**
Drug treatment x area	< 0.001	< 0.001	0.002	< 0.001	0.306	0.003
Drug treatment x year	0.018	0.316	0.072	0.930		
Drug treatment x area x year	0.213	0.592	0.442	0.860		

Figure 5. Prevalence of antihypertensive drug treatment (%) by gender, year and area

5.1.3 Prevalence, awareness, treatment and control of hypertension

The trends in the prevalence, awareness, treatment and control of hypertension according the two different hypertension criteria are shown in Tables 7 (men) and 8 (women). In men, the prevalence of hypertension remained at the same level in Eastern Finland, but decreased to a small extent in southwestern Finland during 1982-1987. During the next five years, vice versa happened. During 1992-1997, there were no significant changes in the prevalence of hypertension in any of the areas. In 1997, there was no difference in the prevalence of hypertension among the areas, irrespective of the hypertension criteria used. In women, the proportion of hypertensive subjects fell significantly in Kuopio during 1982-1987, but not in the other areas. During 1987-1997, the proportion of hypertensive women decreased significantly in all areas. In 1997, this proportion was significantly smaller in southwestern Finland compared to other study areas.

In men, awareness of hypertension increased significantly in eastern Finland but not in southwestern Finland during 1982-1987. During next ten years a continuing upward trend was seen in all areas, except in Helsinki-Vantaa during 1992-1997 when the upper threshold for hypertension was used. However, with the lower threshold values, the proportion of aware hypertensive men increased also in this area. In women, the awareness of hypertension increased significantly in all areas during 1982-1997. The main part of this increase was observed during 1992-1997 in all areas but Kuopio. With the higher of the two different hypertension criteria, at least of 82 % of female hypertensive subjects in each area were aware of their condition in 1997.

During 1982-1992, the prevalence of antihypertensive drug treatment among the hypertensive men increased significantly in all study areas, but especially in eastern Finland. This increase continued in all areas during 1992-1997. However, even with the higher threshold for hypertension, at least 55 % of the male hypertensive subjects and 40 % of the aware hypertensive men in every area were still not receiving antihypertensive drug treatment in 1997. Also in women, these corresponding proportions increased steadily in all areas during the entire study period. In 1997, the proportion of hypertensive women with antihypertensive drug treatment was somewhat higher than in men in all areas.

Table 7. Prevalence, awareness, treatment and control of hypertension by area and year according to different criteria for hypertension in men.

Study area	Hypertension criteria*	Survey year	Prevalence of hypertension (%)	Awareness of hypertension (%)	On drug-treatment of those with hypertension (%)	On drug-treatment (%) of those aware of hypertension	Controlled of those with hypertension (%)	Controlled of those treated with drugs (%)
North Karelia	1	1982	35	60	30	51	10	35
		1987	36	66	33	52	13	39
		1992	31	73	41	57	17	42
		1997	29	81	44	56	24	54
	2	1982	63	44	17	39	2	14
		1987	67	47	18	40	2	14
		1992	54	54	24	44	4	15
		1997	50	62	25	42	7	26
Kuopio	1	1982	37	51	20	41	5	26
		1987	37	59	27	47	7	29
		1992	30	71	39	55	18	47
		1997	30	75	42	56	24	58
	2	1982	67	36	11	31	1	12
		1987	66	45	15	34	1	9
		1992	52	53	23	42	5	21
		1997	53	59	24	41	5	21
Turku-Loimaa	1	1982	32	56	27	50	10	36
		1987	28	56	29	54	15	54
		1992	28	62	32	52	16	49
		1997	27	73	40	56	19	47
	2	1982	59	38	15	40	2	15
		1987	52	38	16	43	3	18
		1992	54	43	16	38	2	14
		1997	48	55	22	41	3	14
Helsinki-	1	1992	26	71	28	40	13	46

Vantaa								
		1997	29	71	36	52	12	33
	2	1992	50	49	15	31	3	20
		1997	51	59	21	36	3	15
Oulu	1	1997	31	77	45	60	29	64
	2	1997	54	57	25	46	7	29

* 1=SBP$\geq$160 mmHg or DBP$\geq$ 95 mmHg or antihypertensive drug treatment, 2=SBP$\geq$140 mmHg or DBP$\geq$ 90 mmHg or antihypertensive drug treatment

P by saturated log-linear model:

	North Karelia-Kuopio-Turku-Loimaa 1982-1992		All areas except Oulu 1992-1997		All areas 1997	
	Hypertension criteria 1	Hypertension criteria 2	Hypertension criteria 1	Hypertension criteria 2	Hypertension criteria 1	Hypertension criteria 2
Prevalence x area	< 0.001		0.200	0.716	0.461	0.237
Prevalence x year	< 0.001		0.972	0.139		
Prevalence x area x year	0.283	< 0.001	0.420	0.172		
Awareness x area	< 0.001		0.023	0.002	0.173	0.419
Awareness x year	< 0.001		0.008	< 0.001		
Awareness x area x year	0.088	0.045	0.403	0.719		
Treatment x area	< 0.001		0.112	0.011	0.409	0.550
Treatment x year	< 0.001		0.028	0.004		
Treatment x area x year	0.065	0.026	0.720	0.452		
Control x area		0.401	0.004	0.024	< 0.001	0.025
Control x year		0.016	0.047	0.092		
Control x area x year	0.032	0.085	0.600	0.623		

Table 8. Prevalence, awareness, treatment and control of hypertension by area and year according to different criteria for hypertension in women.

Study area	Hypertension criteria*	Survey year	Prevalence of hypertension (%)	Awareness of hypertension (%)	On drug-treatment of those with hypertension (%)	On drug-treatment of those aware of hypertension (%)	Controlled of those with hypertension (%)	Controlled of those treated with drugs (%)
North Karelia	1	1982	28	77	42	55	14	33
		1987	28	74	44	61	20	46
		1992	21	81	46	57	25	55
		1997	20	88	51	60	28	56
	2	1982	50	56	24	43	2	10
		1987	47	58	26	47	4	15
		1992	39	60	24	40	5	20
		1997	37	72	27	39	6	21
Kuopio	1	1982	33	74	39	53	16	41
		1987	27	80	43	56	18	43
		1992	24	85	49	58	26	53
		1997	21	84	61	72	43	71
	2	1982	55	57	23	41	2	10
		1987	49	58	24	43	2	6
		1992	41	66	29	44	6	19
		1997	39	69	33	48	10	30
Turku-Loimaa	1	1982	21	69	37	55	17	45
		1987	22	70	40	59	20	49
		1992	19	70	41	58	25	61
		1997	16	82	45	55	30	68
	2	1982	40	51	20	40	3	15
		1987	38	54	23	45	6	25
		1992	35	53	22	41	5	23
		1997	31	63	23	37	7	32

Helsinki-Vantaa	1	1992	21	79	45	57	27	59
		1997	18	85	48	58	31	63
	2	1992	35	62	26	43	5	21
		1997	31	70	28	41	7	24
Oulu	1	1997	22	85	50	58	34	68
	2	1997	37	73	29	40	8	27

1=SBP$\geq$160 mmHg or DBP$\geq$95 mmHg or antihypertensive drug treatment, 2=SBP$\geq$140 mmHg or DBP$\geq$90 mmHg or antihypertensive drug treatment

P by saturated log-linear model:

	North Karelia-Kuopio-Turku-Loimaa 1982-1992		All areas except Oulu 1992-1997		All areas 1997	
	Hypertension criteria 1	Hypertension criteria 2	Hypertension criteria 1	Hypertension criteria 2	Hypertension criteria 1	Hypertension criteria 2
Prevalence x area	< 0.001	< 0.001	0.004	< 0.001	0.029	0.001
Prevalence x year	< 0.001	< 0.001	0.015	0.005		
Prevalence x area x year	0.062	0.072	0.864	0.870		
Awareness x area	< 0.001	< 0.001	0.014	0.004	0.827	0.110
Awareness x year	0.027	0.031	0.013	< 0.001		
Awareness x area x year	0.136	0.624	0.371	0.435		
Treatment x area	0.147	0.028	0.018	0.013	0.055	0.138
Treatment x year	0.057	0.193	0.022	0.127		
Treatment x area x year	0.829	0.617	0.635	0.958		
Control x area	0.768	0.221	0.148	0.357	0.049	0.409
Control x year	< 0.001	0.002	0.002	0.019		
Control x area x year	0.796	0.120	0.226	0.792		

The hypertensive subjects of the 1997 survey were categorized according to their BP level, other CVD risk factors and CVD history (Table 9 A-B). Based on this categorization, 46 % of the men and 57 % of the women with untreated hypertension had mild hypertension with no or one additional CVD risk factor, i.e. a combination with relatively low CVD risk usually not requiring institution of antihypertensive drug therapy.

In hypertensive men, the proportion of subjects with normal BP increased steadily especially in eastern areas but also in southwestern Finland during the entire study period. In contrast, this proportion tended to fall in Helsinki-Vantaa region during 1992-1997. Accordingly, the corresponding proportion in hypertensive women increased in all areas, with the greatest changes in Kuopio, throughout the study period. In 1997, the proportion of controlled hypertensive men in Helsinki-Vantaa region was significantly smaller than in other areas independent of the hypertension criteria used. In women, this proportion was significantly higher in Kuopio than in other areas in 1997 if using the higher hypertension criteria, but not if using the lower threshold. The trends in control of hypertension in subjects with antihypertensive drug treatment were otherwise similar as described above, but in men a downward trend in control rates were seen since 1987 in southwestern Finland and since 1992 in Helsinki-Vantaa region. In 1997, only 33 % of the treated hypertensive men in Helsinki had their BP below 160/95 mmHg. In contrast, the corresponding proportion in men in Oulu was 64 %. With the lower cut-off point for hypertension the control rates were 2-3 times lower depending on the area. Among the inadequately controlled drug-treated hypertensive patients, 95 % the men and 100 % of the women had undergone a BP measurement during the previous year (data not shown).

Table 9 A-B. Distribution (%) of untreated hypertensive subjects by BP level and associated cardiovascular risk factors or clinical conditions in the pooled data of the all survey areas of the FINRISK study in 1997. Table structure modified from (16). The subjects in the categories within bold frames do not usually require antihypertensive drug treatment based on their low absolute CVD risk.

A

	Men (n=1126)		
	Grade 1 (mild hypertension) SBP 140-159 mmHg or DBP 90-99 mmHg	Grade 2 (moderate hypertension) SBP 160-179 mmHg or DBP 100-109 mmHg	Grade 3 (severe hypertension) SBP $\geq$ 180 mmHg or DBP $\geq$ 110 mmHg
No other CVD risk factors[1]	18	4	1
1 risk factor	28	8	2
2 risk factors	15	6	1
3 or more risk factors or diabetes	5	2	1
Associated clinical condition[2]	5	3	1

[1] Smoking, serum total cholesterol $\geq$ 6.5 mmol/l, family history of myocardial infarction under the age of 60 years, age $\geq$ 55 years.
[2] Myocardial infarction, stroke, heart failure or angina pectoris diagnosed by a physician.

B

	Women (n=779)		
	Grade 1 (mild hypertension) SBP 140-159 mmHg or DBP 90-99 mmHg	Grade 2 (moderate hypertension) SBP 160-179 mmHg or DBP 100-109 mmHg	Grade 3 (severe hypertension) SBP $\geq$ 180 mmHg or DBP $\geq$ 110 mmHg
No other CVD risk factors[1]	29	8	1
1 risk factor	28	10	2
2 risk factors	8	3	1
3 or more risk factors or diabetes	2	0	0
Associated clinical condition[2]	6	2	0

[1] Smoking, serum total cholesterol $\geq$ 6.5 mmol/l, family history of myocardial infarction under the age of 60 years.
[2] Myocardial infarction, stroke, heart failure or angina pectoris diagnosed by a physician.

5.2 Trends in cardiovascular risk factors in hypertensive and normotensive populations (STUDY 2)

5.2.1 Lipid levels and hypercholesterolaemia

The changes in mean total and HDL cholesterol concentrations are shown in Figure 6. The mean total cholesterol concentration remained higher in hypertensive groups compared to the normotensive population during 1982-1997. However, this difference between the hypertensive and normotensive population decreased throughout the study period. The mean total cholesterol decreased markedly in both sexes and in every subgroup, but the fall was most prominent in drug-treated hypertensive patients - 0.86 mmol/l in men and 0.94 mmol/l in women, respectively.

The mean HDL cholesterol concentration increased significantly in both sexes and in every BP group, except in unaware hypertensive men during 1982-1997. In both men and women, the mean HDL cholesterol remained significantly lower in drug-treated hypertensive patients compared to the other BP groups during the entire study period. The increase in all BP groups combined was 0.09 mmol/l in men and 0.17 mmol/l in women, respectively.

During 1982-1997, the prevalence of hypercholesterolaemia fell significantly in all BP groups and in both sexes (II, Table 4). The main decline in the prevalence occurred since 1987. In both sexes throughout the study, the proportion of subjects with elevated total cholesterol remained higher in the hypertensive BP groups compared to the normotensive population. The prevalence of elevated total to HDL cholesterol ratio decreased significantly and similarly in every BP group during the study (II, Table 5). However, despite this favourable development seen also among the drug-treated hypertensive patients, 50 % of men and 24 % women in this subgroup still had a high ratio in 1997. The corresponding ratios in 1997 in the normotensive men and women were 31 % and 10 %, respectively.

The awareness of hypercholesterolaemia increased significantly in all BP groups and in both sexes during 1982-1997 (II, Table 6). During the entire study period, the awareness was significantly higher in drug-treated hypertensive group compared to other BP groups (p<0.001). In 1997, 87 % of the drug-treated men and 86 % of the women in the same subgroup were aware of their high total cholesterol concentration. Among the subjects with

Total cholesterol, men

Total cholesterol, women

HDL cholesterol, men

HDL cholesterol, women
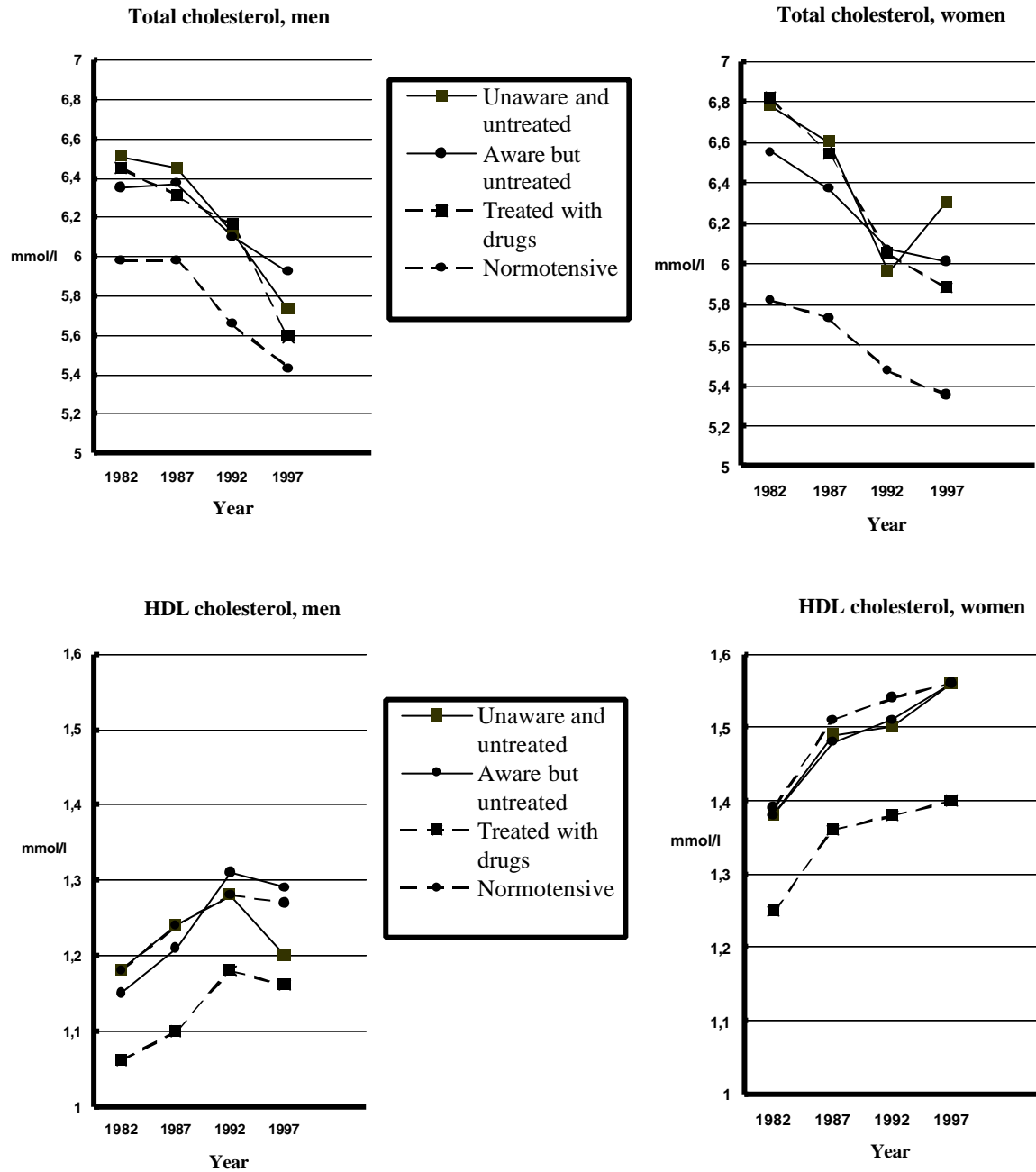
P for analysis of variance, adjusted for age, BMI and alcohol consumption:

	Men	**Women**
Total cholesterol		
Study year	< 0.001	< 0.001
Blood pressure group	< 0.001	< 0.001
Study year x blood pressure group	0.012	0.003
HDL cholesterol		
Study year	< 0.001	< 0.001
Blood pressure group	< 0.001	< 0.001
Study year x blood pressure group	0.002	0.742

Figure 6. Mean serum total and HDL cholesterol by gender, year and BP group

hypercholesterolaemia, cholesterol measurements were done more frequently within the previous year in drug-treated hypertensive patients compared to the other BP groups during the entire study period. In 1997, 72 % of the men and 67 % of the women in this subgroup had their cholesterol measured during the previous year. Also the use lipid-lowering drugs was most common in this BP group. In 1997, 18 % of the men in this subgroup were using lipid-lowering agents, whereas the corresponding proportions in the other male BP groups were 3-5 %. In women, 11 % of the subjects with antihypertensive drug treatment were using these agents in 1997. The corresponding proportions in other BP groups were 0-1 %. When the subjects with lipid-lowering drug treatment in 1992 and 1997 were omitted from the analyses, the observed reductions in mean total cholesterol or increments in HDL-cholesterol did not change significantly.

5.2.2 Systolic and diastolic blood pressure

  The changes in mean SBP and DBP are shown in Figure 7. During 1982-1997, the mean SBP decreased significantly in both sexes and in all BP groups. In men, the reduction in SBP was slightly but significantly greater in hypertensive groups compared to normotensive subjects. Over the entire 15-year period, the mean SBP decreased by 15 mmHg in women with antihypertensive drug treatment, which was significantly more than in the other BP groups.

  In both sexes, the mean DBP decreased significantly only in the group with antihypertensive drug treatment. Also a small but statistically significant reduction was observed in normotensive women. The mean DBP in other BP groups remained unchanged.

5.2.3 Smoking

  In men, proportion of current smokers decreased significantly in both normotensive subjects and in subjects with antihypertensive drug treatment, whereas in other BP groups no change was detected during 1982-1997 (Figure 8). In normotensive women, the prevalence of smoking remained unchanged during the study period. In contrast, the proportion of current

SBP, men

SBP, women

DBP, men

DBP, women
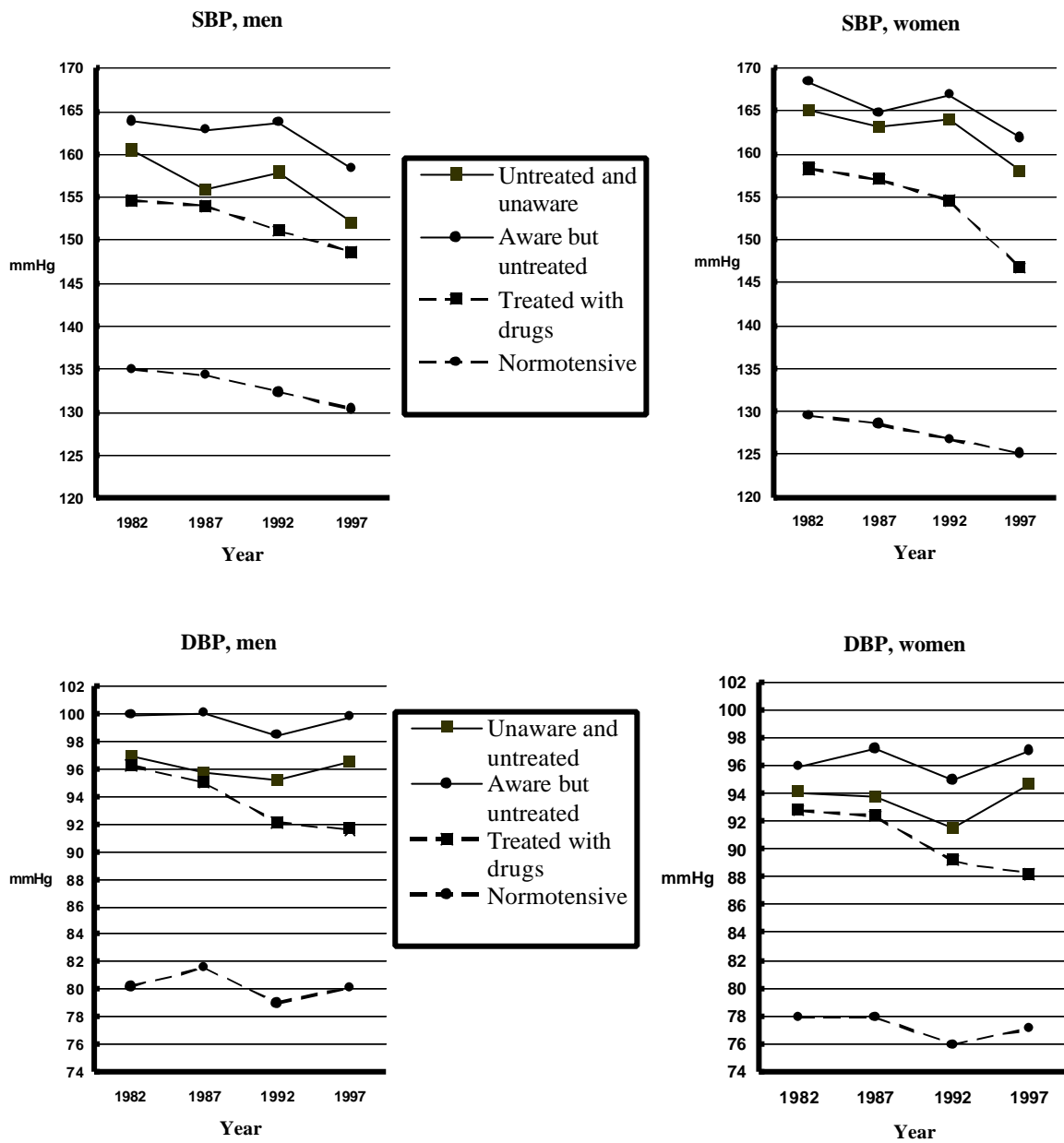
P for analysis of variance, adjusted for age:

	Men	**Women**
Systolic BP		
BP group	< 0.001	< 0.001
Year	< 0.001	< 0.001
BP group x year	0.004	< 0.001
Diastolic BP		
BP group	< 0.001	< 0.001
Year	< 0.001	< 0.001
BP group x year	< 0.001	< 0.001

Figure 7. Systolic and diastolic blood pressure by gender, year and BP group.
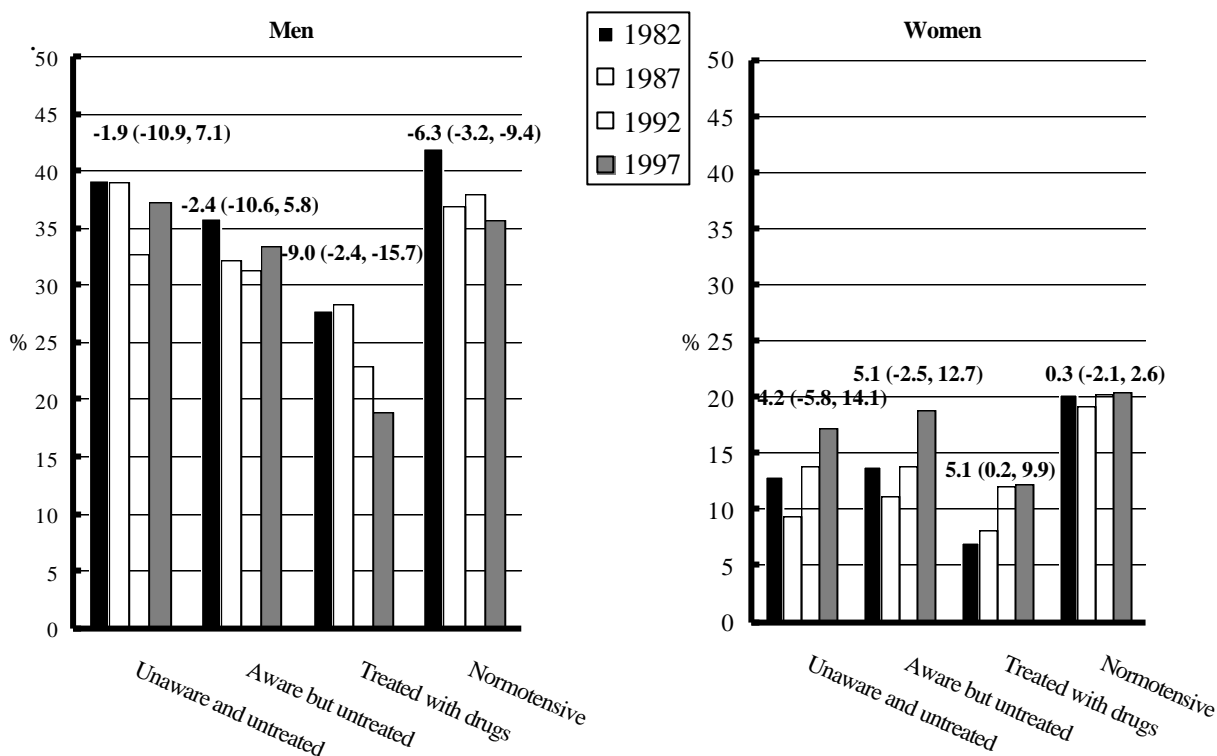
P by saturated log-linear model (10-year age group included):

	Men	Women
Smoking x BP group	< 0.001	0.004
Smoking x study year		
Smoking x BP group x study year	0.409	0.421

Figure 8. The prevalence of smoking and the changes in the prevalence ($\pm$ 95 % CI) by gender, year and BP group.

smokers tended to increase in every female hypertensive subgroup, although the change was significant only in women with antihypertensive drug treatment. In both sexes, the proportion of smokers was smallest in subjects with antihypertensive drug treatment and greatest in normotensive subjects throughout the study period. The prevalence of smoking among the hypertensive groups with no antihypertensive drug treatment was almost at same level as with the normotensive population.

During 1982-1997, the proportion of ex-smokers remained unchanged in every male BP group (IV, Table 2). In women, this proportion increased significantly in normotensive and in the aware but untreated group. In men, the proportion of never smokers increased significantly in the normotensive and in the aware but untreated hypertensive group. Contrary to men, this proportion decreased significantly in all female BP groups except in unaware

hypertensive subjects. The proportion of current smokers who had tried to quit during the past year did not change significantly in any of the BP groups in men (IV, Table 3). In women, the corresponding proportion tended to decrease in all BP groups (interaction between attempt to quit and survey year, p=0.004). Within the separate subgroups, the decrease was significant only in the aware but untreated hypertensive subjects. The proportion of male smokers who reported that they had received advice from their physician during the preceding year to stop smoking remained unchanged in every BP group during 1982-1997 (IV, Table 4). This proportion was highest in each survey in drug-treated hypertensive men (interaction between received advice and BP group, p<0.001). In 1997, 63 % of men in this BP group had received such advice, which was more than twice that in the normotensive group. In female smokers, the corresponding proportion tended to increase in every BP group during the study period, but the increase was significant only in the normotensive group. In 1997, the proportion of smokers who had received advice to quit was 46-55 % in the hypertensive groups compared to 29 % in normotensive subjects.

5.2.4 Diabetes

During 1987-1997, the prevalence of self-reported diabetes increased significantly in men with antihypertensive drug treatment, but remained unchanged in other BP groups (Table 10). In women, this proportion did not change significantly in any of the BP groups. In both sexes, the proportion of diabetics was significantly greater in drug-treated hypertensive patients compared to the other BP groups. In 1997, 12 % of the men and 7 % of women in this BP group reported to have diabetes. In 1997, 60 % of the men and 53 % of the women with antihypertensive drug treatment had their blood sugar concentration determined during the previous year, whereas the corresponding proportion in every other male or female BP groups was less than 22 % (data not shown).

Table 10. The prevalence (%) of self-reported diabetes by gender, year and BP group.

	Hypertensive			Normotensive
	Untreated and unaware	Aware but untreated	Treated with drugs	
Men				
1987	1	2	7	2
1992	2	2	6	1
1997	3	2	12	2
Change	2	0	5	0
(95 % CI)	(-1, 5)	(-3, 3)	(0, 10)	(-1, 1)
Women				
1987	3	1	9	1
1992	2	2	6	1
1997	0	2	7	1
Change	-3	1	-2	0
(95 % CI)	(-5, 0)	(-2, 3)	(-7, 2)	(0, -1)

P for log-linear analysis (10-year age-group included)

	Men	**Women**
Prevalence x BP group	< 0.001	
Prevalence x study year	0.026	
Prevalence x BP group x study year	0.794	0.318

5.3 Trends in lifestyle factors affecting blood pressure in hypertensive and normotensive populations (STUDY 2)

5.3.1 Body mass index, obesity and waist circumference

The mean BMI in men increased significantly in all BP groups during the 15-year period (Figure 9). This increase in BMI was significantly greater in the hypertensive groups compared to normotensive subjects. In women, the mean BMI increased significantly in all BP groups except in the unaware but untreated hypertensive subjects. During 1982-1997, the
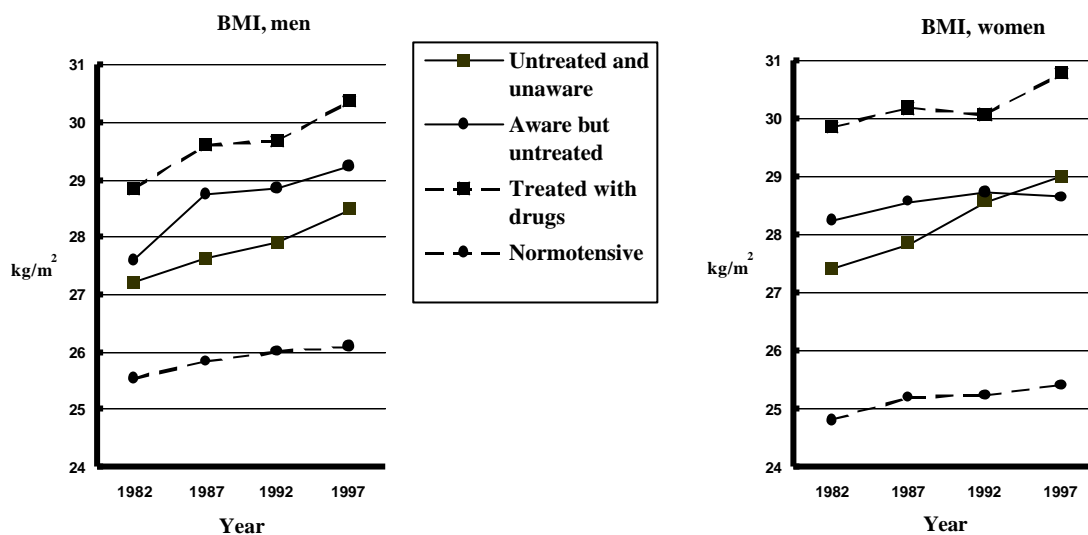
P for analysis of variance, adjusted for age:

	Men	Women
Study year	< 0.001	< 0.001
BP group	< 0.001	< 0.001
Study year x BP group	0.01	0.486

Figure 9. Mean body mass index by gender, year and BP group.
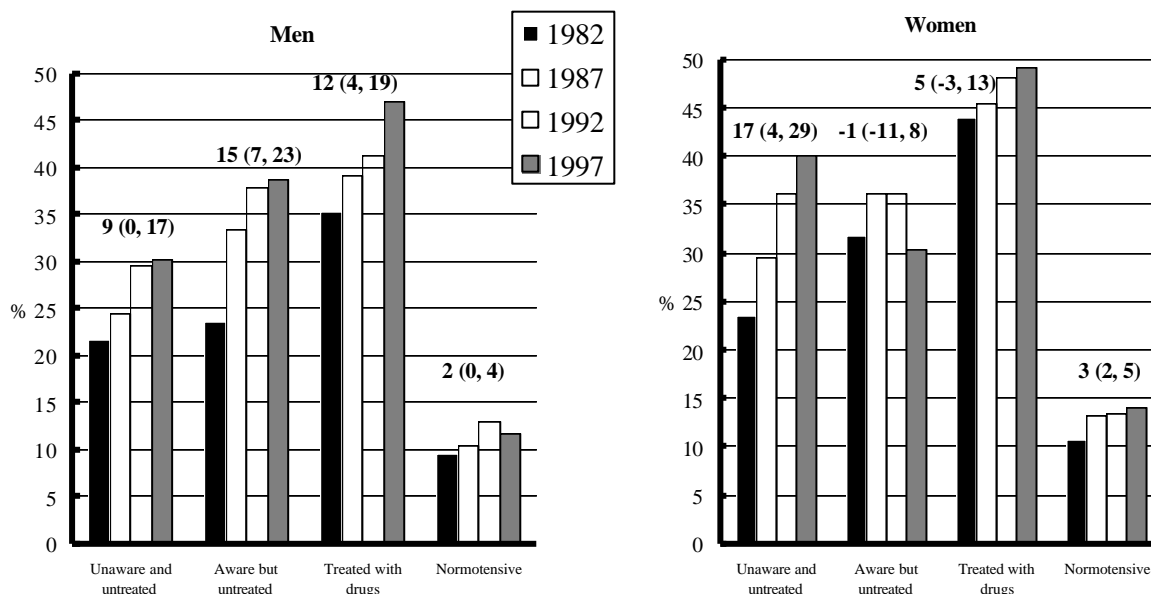
P for log-linear analysis (10-year age-group included):

	Men	Women
Obesity x BP group		
Obesity x study year	< 0.001	< 0.001
Obesity x BP group x study year	0.324	0.348

Figure 10. Prevalence of obesity (BMI $\geq$ 30 kg/m^2) and the changes in prevalence ($\pm$95 CI) by gender, year and BP group.

mean BMI remained significantly lower in the normotensive subjects compared to the hypertensive groups in both sexes. In both men and women, the mean BMI was highest in the drug-treated hypertensive group in every survey.

The prevalence of obesity increased significantly in every male BP group during 1982-1997 (Figure 10). In women, this increase was seen only in normotensive and unaware hypertensive subjects. In 1997, 47 % of the drug-treated hypertensive men and 49 % of the women in this same BP group were obese. The corresponding proportions in the normotensive men and women were 12 % and 14 %, respectively.

The changes in the mean waist circumference in different BP groups followed the same pattern as the changes in BMI: The mean waist circumference increased significantly in every BP group of both sexes during 1987-1997 (Table 11). This increase tended to be greater in hypertensive groups compared to normotensive subjects. In every survey, the waist circumference was highest in the group with antihypertensive drug treatment

5.3.2 Alcohol consumption

The mean alcohol consumption increased significantly in all BP groups of both sexes during 1982-1997 (Table 12). In men, this increase was significantly greater in hypertensive groups compared to the normotensive subjects. In women, the increase was greater in the two untreated hypertensive groups compared to the drug-treated hypertensive or to the normotensive subjects. In 1997, the mean alcohol consumption was highest in the two untreated hypertensive groups in both sexes.

5.3.2 Leisure-time physical activity

During 1982-1997, the proportion of subjects with leisure-time physical activity at usually recommended level (at least three times per week for at least 30 minute per session) increased significantly in all BP groups and in both sexes, except in unaware hypertensive women (Table 13). This increase was of the same magnitude in every male BP group. In women, the increase was most prominent the drug-treated hypertensive patients and in normotensive subjects. In 1997, these two BP groups were the two most physically active groups in both sexes.

Table 11. Mean waist circumference (cm $\pm$ SD) by gender, study year and BP group.

	Hypertensive			Normotensive
	Untreated and unaware	Aware but untreated	Treated with drugs	
Men				
1987	94.7 $\pm$ 10.3	98.0 $\pm$ 11.2	100.9 $\pm$ 11.2	90.0 $\pm$ 9.6
1992	97.1 $\pm$ 11.5	100.8 $\pm$ 11.1	103.0 $\pm$ 12.2	92.0 $\pm$ 10.1
1997	99.7 $\pm$ 12.5	101.1 $\pm$ 10.9	103.6 $\pm$ 12.6	91.9 $\pm$ 10.1
Change	5.0	3.1	2.7	1.9
(95 % CI)	(2.9, 7.1)	(1.0, 5.1)	(0.7, 4.7)	(1.2, 2.6)
Women				
1987	83.7 $\pm$ 11.0	84.8 $\pm$ 11.4	88.8 $\pm$ 12.7	77.5 $\pm$ 10.2
1992	86.9 $\pm$ 12.8	86.9 $\pm$ 12.8	90.4 $\pm$ 12.0	79.0 $\pm$ 10.8
1997	89.8 $\pm$ 13.2	87.6 $\pm$ 15.2	92.1 $\pm$ 13.4	79.4 $\pm$ 11.1
Change	6.1	2.8	3.3	1.9
(95 % CI)	(2.9, 9.4)	(0.1, 5.6)	(1.2, 5.5)	(1.3, 2.6)

P for analysis of variance, adjusted for age:

	Men	**Women**
Study year	< 0.001	< 0.001
BP group	< 0.001	< 0.001
Study year x BP group	0.087	0.067

.

Table 12. Mean alcohol consumption (g/week $\pm$ SD) by gender, study year and BP group.

	Hypertensive			Normotensive
	Untreated and unaware	Aware but untreated	Treated with drugs	
Men				
1982	65 $\pm$ 102	81 $\pm$ 149	42 $\pm$ 75	63 $\pm$ 104
1987	84 $\pm$ 112	83 $\pm$ 125	66 $\pm$ 104	69 $\pm$ 114
1992	102 $\pm$ 133	117 $\pm$ 152	94 $\pm$ 112	87 $\pm$ 118
1997	137 $\pm$ 159	136 $\pm$ 147	107 $\pm$ 158	91 $\pm$ 128
Change	72	55	65	28
(95 % CI)	(51, 94)	(29, 82)	(47, 84)	(21, 36)
Women				
1982	12 $\pm$ 52	10 $\pm$ 29	7 $\pm$ 26	16 $\pm$ 36
1987	19 $\pm$ 29	23 $\pm$ 41	16 $\pm$ 30	24 $\pm$ 39
1992	50 $\pm$ 72	29 $\pm$ 56	29 $\pm$ 64	30 $\pm$ 47
1997	42 $\pm$ 65	40 $\pm$ 57	28 $\pm$ 49	33 $\pm$ 45
Change	30	30	21	17
(95 % CI)	(14, 47)	(23, 38)	(16, 27)	(15, 20)

P for analysis of variance, adjusted for age:

	Men	**Women**
Study year	< 0.001	< 0.001
BP group	< 0.001	< 0.001
Study year x BP group	< 0.001	< 0.001

Table 13. The proportion of subjects (%) with leisure-time physical activity at least three times per week and at least to 30 minutes by gender, year and BP group.

	Hypertensive			Normotensive
	Untreated and unaware	Aware but untreated	Treated with drugs	
Men				
1982	20	17	20	23
1987	21	21	24	26
1992	28	24	36	33
1997	33	30	36	36
Change	13	13	16	13
(95 % CI)	(5, 22)	(5, 20)	(9, 24)	(11, 16)
Women				
1982	20	17	18	18
1987	21	29	23	20
1992	26	30	32	32
1997	28	31	37	39
Change	8	14	19	21
(95 % CI)	(-3, 20)	(5, 23)	(11, 26)	(18, 23)

P for log-linear analysis (10-year age-group included)

	Men	**Women**
Physical activity x BP group	< 0.001	
Physical activity x study year	< 0.001	
Physical activity x BP group x study year	0.957	0.043

5.4 Non-pharmacological treatment of hypertension in primary health care (STUDY 3)

5.4.1 Baseline characteristics and adherence to treatment

The mean age of the 715 participants was 54.3 years. Of them, 52 % were on antihypertensive drug treatment in the beginning of the trial (V, Table 1). There were no statistically significant differences between the groups in any of the baseline variables analysed. Attendance rates at the one-year and two-year study visits were satisfactory (V, Figure 1). The attendance rate to both group meetings organised for the intervention group after six and 18 months of intervention was 50 %. At baseline, the dropouts were significantly younger (50 vs. 55 years) and heavier (83.1 kg vs. 80.1 kg) compared with the completers of the study (data not shown). Also alcohol use (73 g/week vs. 42 g/week) and proportion of smokers (13 % vs. 7 %) were significantly higher among the dropouts.

5.4.2 Changes in blood pressure and related lifestyle factors

Without taking into account the effect of antihypertensive drug treatment, the reduction in DBP during the first study year was significantly greater in the intervention group compared to the usual care group (V, Table 2). The reductions in SBP at the one-year and two-year follow-ups and in DBP from baseline to two years tended to be greater in the intervention group, although they did not reach the level of statistical significance. In the subgroup with no antihypertensive drug treatment, the reductions in both SBP and DBP were significantly greater in the intervention group compared with the usual care group during both the first and the second year of follow-up (Figure 11). In subjects with antihypertensive drug treatment at baseline, the BP reductions were of the same magnitude in both groups. Among the subjects with antihypertensive drug treatment, the self-reported frequency of BP measurements during the previous year decreased significantly more in the intervention group during the first year (Table 14). Otherwise the number of BP measurements did not differ significantly between the groups during any phase of the study.

SBP, no antihypertensive drug treatment

DBP, no antihypertensive drug treatment

SBP, antihypertensive drug treatment

DBP, antihypertensive drug treatment
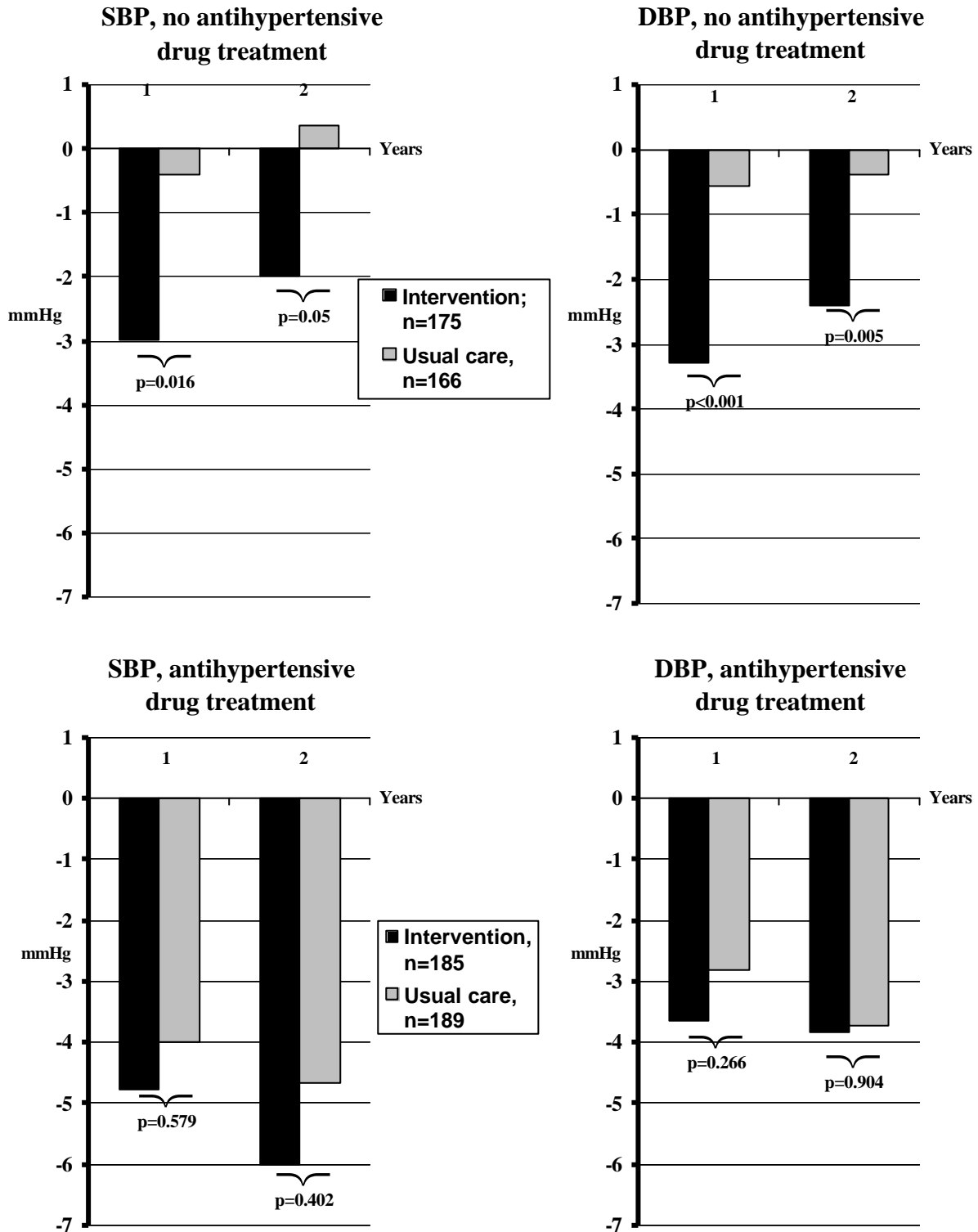
Figure 11. Changes in SBP and DBP from baseline to 1- and 2-year visits stratified by antihypertensive drug treatment status.

Table 14. Changes in number of self-reported BP measurements (95 % CI in parentheses) done during previous year.

	No antihypertensive drug treatment		Antihypertensive drug treatment		All	
	Intervention	Usual care	Intervention	Usual care	Intervention	Usual care
Baseline	4.6	5.4	8.6	8.9	6.7	7.3
Change 0-1 year	1.1	0.1	-1.7	0.7	-0.3	0.4
Change 0-2 years	1.2	-0.1	-2.5	-1.4	-0.7	-0.8
Net change 0-1 year	1.0 (-0.3, 2.3)		-2.3 (-4.3, -0.3)		-0.7 (-1.9, 0.5)	
Net change 0-2 years	1.3 (-0.2, 2.8)		-1.0 (-2.7, 0.6)		0.1 (-1.0, 1.3)	

The net reductions (intervention vs. usual care) in weight at one and two years of follow-up were significant. Eight percent of the initially overweight participants (BMI ≥ 25 kg/m^2) assigned to intervention had achieved normal weight at the end of the trial, which was significantly more than that in the usual care group (V, Table 4). Also the waist and hip circumferences decreased significantly more in the intervention group than in usual care throughout the study. The changes in 24-hour urinary sodium and potassium excretion were small, with no significant differences between the groups. Self-reported alcohol consumption fell significantly more during the first study year in the intervention group, but this difference disappeared during the second year. Compared to the usual care group, a significantly larger proportion of the participants in the intervention group had increased their physical activity to the target level by both one-year and two-year visits.

The net reduction in weight between the randomised groups was significantly greater in the group with no antihypertensive drug treatment during the first year compared to the group with antihypertensive drug treatment (-1.5 kg vs. -0.8 kg, p for the interaction term 0.021), but such a difference was not detected in the analysis from baseline to two years. Similarly, the net reductions in alcohol consumption from baseline to one-year and two-year visits were significantly greater in this group compared to the group with antihypertensive drug treatment (from baseline to 1-year visit -17 g/week vs. 1 g/week, p for the interaction term 0.025; from baseline to two-year visit -9 g/week vs. 5g /week, p for the interaction term 0.029).

The response for the intervention in terms of lifestyle changes did not differ significantly between the sexes or according to the baseline age. In a multiple linear regression analysis including only the subjects without antihypertensive drug treatment, a positive relation with two-year SBP and DBP change was found for weight change (SBP, p=0.003; DBP, p<0.001), but not for the changes in other lifestyle variables. In a separate analysis, adjusting for both BP and weight at baseline, the estimated effect of the 1kg weight lost at two years was a reduction of 0.55 mmHg in SBP and 0.50 mmHg in DBP.

5.4.3 Changes in other cardiovascular risk factors

After two years of intervention, the net changes in total (-0.10 mmol/l) and in LDL cholesterol (-0.15 mmol/l) were significant in favour of the intervention group (V,Table 2). Also in persons without lipid-lowering drug treatment during the study the reductions in total cholesterol (-0.11 mmol/l; 95 % confidence interval –0.20 to -0.02) and in LDL cholesterol (-0.13 mmol/l; 95 % confidence interval –0.22 to -0.03) were larger in the intervention group than in the control group (data not shown). Smoking was rare already at baseline, and no significant changes in that habit were observed during the study. The serum insulin concentration decreased more among the persons assigned to intervention, but the net change was not statistically significant.

6 DISCUSSION

6.1 Methodological issues

6.1.1 Study populations

In Studies 1 and 2, the subjects of each population survey originated from independent random samples drawn from the population register of the study areas. In addition, the samples were stratified according to sex and 10-year age group. Therefore, the samples can be considered to be representative of the target population, justifying the comparisons between the areas in cross-sectional setting and between the surveys in time trend analysis. The participation rates of the surveys declined over time especially in men, but were still quite satisfactory in the last survey in 1997. In 1992, a special telephone survey was organised for the non-participants (385). In this survey, 50 % of the non-participants could be contacted. Among the non-participants the smoking prevalence was 53 %, which was significantly greater than that of participants. Otherwise, there were no significant differences between the participants and non-participants of the survey. Hence, a minor part of the decrease in smoking prevalence in men during 1982-1997 could be related to decline in participation rates.

In the primary health care trial (Study 3) the participants were recruited mostly by the newspaper announcements. As usual in volunteer-based intervention studies, the participants were probably more likely to accept the recommended lifestyle advice than the hypertensive population at large. On the other hand, many volunteers in lifestyle intervention studies are more likely to have previously changed their lifestyle, which could reduce the power of intervention. The participants of the study 3 had lower levels of total cholesterol, BMI and alcohol consumption compared to the aware hypertensive subjects in the FINRISK study in 1997 (see Study 2). In addition, the prevalence of smoking was lower and the proportion of subjects with recommended levels of leisure-time physical activity was greater than in the subjects in Study 2. Among the subjects without antihypertensive drug treatment, the levels of SBP and DBP were lower compared to the FINRISK population. Surprisingly, the BP levels were similar in both studies among the drug-treated hypertensive subjects. In addition, the participants of the primary health care trial came from a geographical area with a long history

of cardiovascular prevention activities, and thus many of them already had a good knowledge of the lifestyle factors affecting BP (11).

6.1.2 Risk factor measurements

The accuracy of BP measurements in epidemiological surveys is of paramount importance. The technique employed must be capable of detecting small changes and differences in BP levels within and between populations that are trivial at the individual level, but very important from the public health point of view (386). The main sources of systematic error in BP measurement in these population surveys are differences in equipment and differences between the observers in the technique used. In Studies 1 and 2, the BP measurements were taken in each survey by a small number of well-trained study nurses, who were circulated between the survey areas. The nurses spent approximately same length of time in each study area and the BP values and last digit frequencies of each measurer were monitored during the surveys. A standard mercury sphygmomanometer with the same cuff size was used in each survey. In the analysis of the BP measurement data of WHO MONICA baseline surveys, the quality of BP measurements in the three FINMONICA areas was considered high (387).

The diagnosis of hypertension in the WHO MONICA surveys, as usual in epidemiological studies, was based on casual BP, i.e. the BP was measured on only one occasion. According to a Canadian study, this can lead to the overestimation of the prevalence of hypertension and to the underestimation in rates for awareness, treatment and control of high BP (388). In addition to the number of BP measurements used, also the chosen cut-off point for elevated BP strongly affects the epidemiological estimates of hypertension (367), and also the observed trends in them as seen in the present study. Hence, the upper cut-off point for hypertension used in this study (160/95 mmHg) could probably correspond quite well to the recommended clinical diagnosis of hypertension with follow-up measurements and a lower cut-off point for hypertension (140/90 mmHg). On the other hand, as shown in many large-scale studies, also the subjects with casual BP $\geq$140/90 mmHg are at increased risk for cardiovascular events related to hypertension (276). Therefore, this lower threshold for elevated BP is justified and is also nowadays more widely used than before in studies of the community control of hypertension in different parts of the world.

In Study 3, all the BP measurements were performed by the same study nurse except in one health care centre, where another trained study nurse did the baseline measurements. There was only a 0.2/0.5 mmHg difference in mean SBP/DBP measured by these two nurses when ten volunteer subjects had their BP measured twice with a double-headed stethoscope method. The accuracy of BP measurements by the principal study nurse was assessed annually with a double-headed stethoscope. All the BP measurements were done with a standard mercury sphygmomanometer using the same technique as in the population surveys (Studies 1 and 2).

The reliability of self-reported smoking tested against biomarker measurements related to smoking has been reported as satisfactory in most study types (389). In the present study, serum cotinine levels were measured in the risk factor survey conducted in 1992. In this survey, the self-reporting of smoking was in good agreement with these biomarker measurements (390). On the other hand, it can be speculated that the hypertensive population could be more likely to deny their smoking habit, since they have been advised to quit smoking more often than normotensive subjects. However, there are no data to confirm this suggestion, nor should this aspect affect the trends observed. The smoking habits were assessed with exactly the same standard set of questions in both Studies 2 and 3.

The estimation of the prevalence of diabetes (Study 2) was based on self-reporting, which could have led in theory to misclassification of subjects. When the prevalence of diabetes based on 2-hour glucose tolerance tests was determined in the same survey population aged 45-64 years in 1987, the proportion of diabetic patients was 5.7 % in men and 4.6 % in women, respectively (391). The corresponding proportions of self-reported diabetes (dietary or drug treatment) in this same population in 1987 were 4.0 % in men and 3.1 % in women (data not shown). Hence, the self-reporting could have led to a slight underestimation of the prevalence of diabetes. Similarly, the self-reporting of alcohol consumption and leisure-time physical activity (Studies 2 and 3) could have had led to underestimation and overestimation of these variables, respectively. However, there are no better or more feasible methods to assess these variables in epidemiological studies. Again, the observed trends and changes in these variables should not be affected by missestimation, because same set of questions were used in each survey.

All the laboratory analyses in Studies 2 and 3 were performed in the same central laboratory. In both studies, the commercial kits for cholesterol determinations were changed

during the study, and this was also taken account in the HDL cholesterol analyses of Study 2. The change of methods did not affect the corresponding analyses in Study 3.

24-hour urinary collection can be a very demanding procedure for some study subjects. Usually the 24-hour urinary creatinine is determined to ascertain the completeness of the collection. In the primary health care intervention trial, the urinary creatinine was determined only at 1- and 2-year visits due to a misunderstanding. However, there were no statistically significant differences in the mean 24-hour urinary creatinine values between the randomised groups at either of these visits or between the visits within the groups (data not shown). In addition, the completeness of collection was checked and registered at each annual visit by a trained study nurse.

6.2 Results

6.2.1 Trends in community control of hypertension (STUDY 1)

The results of Study 1 showed that the SBP levels and the prevalence of hypertension decreased significantly in all three FINMONICA areas during 1982-1992 in both sexes. In contrast, the levels of DBP in both men and women decreased only in eastern Finland. During the next five years in men, the mean SBP decreased further in all areas except in Helsinki-Vantaa. The mean DBP showed a slight upward trend, however, and the prevalence of hypertension remained unchanged in all areas. In women, the mean SBP and the prevalence of hypertension decreased significantly in all areas, whereas the mean DBP did not change. Significant progress took place in awareness, treatment and control of hypertension throughout the 15-year study period in both men and women of all areas. In 1997, there were statistically significant differences in rates for control between the study areas in both sexes, but the rates for awareness and treatment were pretty much the same. The previous differences between eastern and southwestern Finland in the prevalence of hypertension had disappeared in men and had also diminished in women.

It has been estimated that antihypertensive drug therapy explained no more than 10-15 % of the observed decreases in mortality from stroke and ischaemic heart disease in Finland during 1972-1992 (392). Approximately 10 % of the population were using antihypertensive drugs during 1982-1997. In these subjects, as demonstrated in Study 2, the change in mean SBP in

men during the same time period was of the same magnitude as in the rest of the male population. On the contrary, in women the decrease in SBP was greatest in the group with antihypertensive drug treatment. It can therefore be proposed that less than 10 % of the observed decrease in SBP of the entire population could be attributed to the more efficient use of antihypertensive drugs. Hence, the observed trends in the BP level of the population are largely explained by changes in lifestyle.

The dietary intake of sodium and saturated fat has decreased markedly in Finland during 1982-1997, contributing to the observed decline in BP (393, 394). In addition, as demonstrated in Study 2, the proportion of subjects with recommended level of physical activity has increased. Unfortunately, the mean BMI and alcohol consumption of the population has increased continuously, counterbalancing the situation in lifestyle factors affecting BP. It could be speculated that one of the possible reasons for the continuing downward trend in mean SBP could be the steady decrease in mean serum cholesterol levels. The development of atherosclerosis and stiffening of the arteries, which can lead to elevation of SBP, may thus be delayed (395). It has also been proposed that a fall in serum LDL cholesterol could improve the endothelial vasodilatation capacity and thereby decreases BP (284).

The main part of the detected improvement in different aspects of hypertension care in Finland during the study period can be attributed to the reorganizing of the hypertension care system and to intensified health education in the community (396). Compared to the recent population surveys in some other European countries using the same criteria for hypertension (see Table 3), the prevalence of hypertension in Finnish men in 1997 was approximately one third higher than in these countries. In contrast, the rates for prevalence in women were of the same magnitude across the populations. The awareness of hypertension in Finland in 1997 was at least at the same level as in these countries. However, the rates for treatment were somewhat lower in Finland compared to other countries. Correspondingly, the proportion of drug-treated subjects with normal BP was smaller in Finnish men, but not in women. Interestingly, the rates for awareness, treatment and control of hypertension were significantly higher in the third National Health and Nutrition Examination Survey (NHANES III) in U.S.A. compared to any of the European populations (366). The reasons for these differences among populations are not clear, but they could at least partly be explained by the differences among the national hypertension guidelines, especially in recommendations for the initiation

of antihypertensive drug treatment. At least previously, guidelines in the U.S.A. have used a lower threshold for treatment than the guidelines published in other countries (352).

In Finland the biggest problem in hypertension care has shifted from detection to the adequate treatment of high blood pressure. Among the Finnish drug-treated hypertensive patients of this study, 33-64 % of the men and 56-71 % of the women had their BP inadequately controlled in 1997. Practically all of them had had their BP measured during the previous year. Thus, this finding suggests that one of the possible reasons for poor BP control among this patient-group could be the lack of aggressiveness in treating the patients. The other well-known reason for not achieving the goal pressure is poor patient compliance. According to some studies, only 50-60 % of the patients adhere well to the prescribed antihypertensive medication (397-399). In addition, the hypertension guidelines published in the early 90's have been criticized due to inconsistency, complexity and inability to clarify the absolute benefits of treatment, thus increasing the burden for physicians in achieving normotension or cardiovascular risk reduction in their hypertensive patients (400). At least partly for this reason, in the most recent hypertension guidelines the treatment decisions are based on the estimated absolute cardiovascular risk of the patient (15-17, 35). This approach, using a risk chart as tool for better management for hypertension, has already demonstrated to carry a larger potential for hypertension control than the treatment policy based on crude BP values (401).

The threshold for the initiation of antihypertensive drug treatment in low-risk patients (subjects with mild hypertension, i.e. 140-159/90-99 mmHg, and no other CVD risk factors) or medium-risk patients (subjects with mild hypertension and 1-2 other CVD risk factors or subjects with moderate hypertension, i.e.160-179/100-109 mmHg, and 0-2 other CVD risk factors) is somewhat different among the current hypertension guidelines. In the WHO hypertension guidelines, antihypertensive drug therapy should be initiated in the low-risk group within 6-12 months if SBP/DBP remains at the level of $\geq$150/95 mmHg, and in the medium-risk group within 3-6 months at the BP level of 140/90 mmHg, respectively (16). In contrast, the 1997 Joint National Committee (JNCVI) hypertension guidelines recommend the initiation of antihypertensive drug treatment for all subjects with ascertained moderate hypertension immediately, and for all subjects with sustained mild hypertension within 6-12 months (15). The just recently published Finnish guidelines are in accordance with the US guidelines in treatment of subjects with moderate hypertension (35). However, they are more

conservative than the US guidelines in respect of the treatment schedule in patients with mild hypertension. According to the Finnish guidelines, the antihypertensive drug therapy should be added to lifestyle modification in this patient-group, only if the absolute 10-year risk for CVD events exceeds 20 %. If this recommendation is applied to the FINRISK population, in most men and in almost all women with mild hypertension and 0-1 additional CVD risk factor antihypertensive drug therapy is not necessarily warranted.

In the future, the criteria used for evaluation of hypertension care in and between the populations could also be based on estimated absolute cardiovascular risk instead of BP values alone, at least when calculating the rates for antihypertensive drug treatment among the hypertensive subjects. This kind of approach was recently used in a Swedish population-based study, which applied the latest WHO hypertension guidelines to a WHO MONICA sample of 6000 subjects in Northern Sweden (402). In this study, the untreated hypertensive subjects were stratified into groups of different levels of absolute cardiovascular risk, i.e. to the groups justified or not justified to receive antihypertensive drug treatment according to the current evidence. The distribution of untreated hypertensive subjects across the low-, medium-, high- and very high-risk groups in the present study (Table 9A-B) was very much similar to this Swedish study. In both studies, the vast majority of these subjects belonged to the low- or medium-risk group.

6.2.2 Trends in cardiovascular risk factors and in lifestyle factors affecting blood pressure (STUDY 2)

6.2.2.1 Lipid levels and hypercholesterolaemia

The mean total cholesterol levels of both the normotensive and hypertensive population of both sexes fell continuously during the entire 15-year study period. A significant increase in mean HDL cholesterol was observed in every BP subgroup except in men unaware of their hypertension. Similarly, the prevalence of hypercholesterolaemia decreased significantly across the BP groups. The awareness of hypercholesterolaemia increased markedly, and thus in 1997 more than 80 % of the drug-treated hypertensive subjects were aware of their high cholesterol level.

The main reasons for the observed favourable trends in total and HDL cholesterol trends are the dietary changes observed in the Finnish diet since 1972. During 1972-1992, the changes in fat intake included the decrease in total fat content of the diet from 38 % of total energy intake to 34 %, the decrease in saturated fat intake from 21 % to 16 % and the increase in the polyunsaturated fat intake from 3 % to 5% of total energy intake (393). Simultaneously, the majority of the population changed from boiled to filtered coffee, which may also have contributed to the decrease in mean total cholesterol of the population. One of the factors behind these dietary changes include launching of the North Karelia Project and other population-based cardiovascular disease prevention programmes since the 1970's, which have increased the public awareness of the health risks connected to elevated cholesterol. In addition, at least a part of the observed trends are due to changes in the legislation concerning dietary fats and their manufacture. In 1987, the Finnish Cardiac Society and Internists' Association published their recommendations on screening for hypercholesterolaemia in the general population. According to these recommendations, every adult aged 20 years or more should have his or her cholesterol level determined every 5 years. This is one of the obvious reasons for rapid rise in awareness of hypercholesterolaemia that has taken place especially since 1987.

The mean decline in total cholesterol among men was of the same magnitude in all BP groups between 1982 and 1992. During the next five years, the steepest fall was seen in the group with antihypertensive drug treatment (0.6 mmol/L). It could be proposed that a change of such a magnitude could not have been achieved without the reported increase in the use of lipid-lowering medication during the same time period (from 9 % to 18 %). However, when the subjects using these agents were left out from the analyses, the observed fall in mean total cholesterol remained equally large. This finding suggests that the main reason for the change was related to dietary changes, induced possibly by the dietary counselling given by health personnel. In women, the total cholesterol fell more in drug-treated hypertensive patients compared to the normotensive subjects already during 1982-1992. The decrease was similar in all BP groups during 1992-1997 except for the unaware hypertensive subjects, where a small sample size during the two last surveys could have affected the trends observed.

Despite the proven benefits of a multifactorial treatment approach in hypertensive subjects (403), the prevalence of lipid-lowering drug therapy in Finnish hypertensive subjects in 1997 was still unexpectedly low. Similar results have been reported also in other studies (404).

It has been reported that one of the reasons for such an apparent undertreatment of hypercholesterolaemia in this high-risk patient group is the inconsistency between the official guidelines for treatment for hypercholesterolaemia and an inappropriate dissemination of these guidelines to practising physicians (405, 406).

The results of the present study demonstrating significantly lower levels of HDL cholesterol in drug-treated hypertensive subjects compared to the other three BP groups are in accord with the findings of other population-based studies (18, 19, 370). The consistency of the findings suggests that the antihypertensive drug treatment can cause reductions in HDL cholesterol that are important at the public health level. During the study period, beta-blockers and diuretics, which are both known to have the ability to lower HDL cholesterol (407), still remained as the most frequently prescribed antihypertensive drugs in Finland (408). The increasing trend in prescribing metabolically more neutral beta-blockers, low-dose diuretics, calcium channel blockers and ACE-inhibitors during the study period in Finland did not affect this difference between the BP groups in mean HDL cholesterol. The low level of HDL cholesterol among the drug-treated hypertensive patients was also the most important contributing factor for the high prevalence of the elevated ratio of total to HDL cholesterol detected in both sexes of this BP group.

6.2.2.2 Smoking

According to the results of the present study the prevalence of smoking in normotensive men as well as in drug-treated hypertensive men decreased significantly in Finland during 1982-1997. An increasing trend in the proportion of smokers was observed in all female BP groups, but the change was significant only in the drug-treated hypertensive group. The proportion of current smokers who had been advised to quit by their doctor during the last year increased slightly but significantly in normotensive women, but not in any other female or male BP group.

In Finland, the prevalence of smoking in both men and women is nowadays among the lowest in Europe. Since the early 1960's, the proportion of smokers has decreased by one half in men. Among women, smoking was fairly rare until the 1970's, but since then a significant increase has occurred. During 1972-1982, the decrease in smoking prevalence in men was mainly explained by the increased smoking cessation, but since 1982 the decrease in the

numbers starting to smoke has been the main reason for the continuing trend (409). The contributing factors for the observed decrease in smoking include several preventive activities targeted against smoking and the passing of the first tobacco control legislation in 1977, which was updated in 1995. In women, the observed increase in smoking prevalence among the middle-aged women was mainly due to an augmented rate of smoking initiation among young women in the 1960's and the 1970's, suggesting a cohort effect. Since then the initiation rate among the youngest age groups has remained rather stable. In contrast to men, smoking cessation has increased steadily among women also since 1982, though not sufficient to prevent the moderate upward trend in female smoking.

According to many prospective studies, continued smoking is one of the main determinants for excess mortality among treated hypertensive subjects (12, 292). Therefore, activities targeting smoking cessation are of major importance especially in this patient-group. In the present study, the proportion of ex-smokers was significantly higher in treated hypertensive patients throughout the study period compared with other BP groups. However, this proportion remained rather stable also in this BP group, indicating that the decrease in smoking prevalence was mainly due to decreased smoking initiation. In fact, that the proportion of smokers remained unchanged and was of the same magnitude in the two untreated hypertensive groups as in the normotensive subjects in 1997 was alarming. In women, the observed increase in smoking in the drug-treated hypertensive group was mainly caused by an increased initiation rate.

Patient education for smoking cessation is one of the cornerstones in the treatment of hypertension as recommended by the most recent Finnish as well as international hypertension guidelines (15-17, 35). In this study, the proportion of current smokers being recently advised by their physician to quit was significantly greater in the drug-treated hypertensive men in every survey compared with three other male BP groups. In women, the situation was somewhat similar until 1997, when the proportion of smokers who had been recently encouraged to quit increased in the two untreated hypertensive groups to the same level as in the drug-treated group. Despite this observed difference in health counselling between the BP groups, there were no differences between the groups in self-reported attempts to quit smoking among the current smokers. Paradoxically, at the same time as the proportion of normotensive smoking women being advised to quit during 1982-1997 increased, the rate of quitting attempts tended to decrease. In both genders, the small number

of ex-smokers who had managed to quit smoking during the preceding year did not allow to make any comparison between them and current smokers in terms of provision of anti-smoking advice.

Individual behavioural counselling alone or combined with nicotine-replacement therapy or antidepressants are strategies used in clinical trials that have proven efficacy in smoking cessation (410-412). In the future, to increase the efficacy of advice offered by physicians against smoking, these strategies should be used more routinely as a part of multifactorial cardiovascular risk approach in the treatment of hypertensive patients. One barrier for achieving this goal is the somewhat limited knowledge among physicians on how to implement these strategies in practice. One of the key elements to overcome this barrier could be the creation of national smoking cessation guidelines such as those already developed for the treatment of hypertension and dissemination of these guidelines to all practicing physicians. More routine involvement of nurses in anti-smoking counselling in co-operation with physicians could also represent one solution to this problem (413).

6.2.2.3 Diabetes, obesity, alcohol use and physical activity

The results of the present study showed that mean BMI increased significantly in every BP group during the 15-year study period except in aware but untreated hypertensive women. The proportion of obese women increased especially in aware hypertensive men and in unaware hypertensive women. The prevalence of self-reported diabetes increased significantly in drug-treated hypertensive men, but not in any other male or female BP groups.

Obesity results from the imbalance between energy intake and energy expenditure. In Finland, the mean total energy intake decreased significantly during 1972-1992 (393). Unfortunately, according to another Finnish study, the energy expenditure during work and during moving to and from work decreased even more (414). The reported simultaneous increase in leisure-time physical activity was not enough to counterbalance the situation. It was concluded in this same report that in the future the promotion of daily, moderate-intensity activities could be the most feasible method to increase the energy increase and thereby decrease the burden of obesity at the population level.

Obesity, especially abdominal obesity, is a strong predictor of type 2 diabetes (415). On the other hand, as recently shown in a Finnish landmark study, type 2 diabetes can be prevented in subjects with impaired glucose tolerance by weight reduction and other changes in lifestyle similar to the ones to be used in treatment of high BP (416). In the present study, the increasing trends in both obesity and in waist circumference in men with antihypertensive drug treatment may have contributed to the observed increase in self-reported diabetes during the study. However, such an increase in the prevalence of diabetes was not seen in any other of the male or female BP group despite the similar trends in BMI and waist circumference across the BP groups. Other explanations are therefore possible. Drug-treated hypertensive subjects are usually under regular follow-up and have their blood sugar determined more often than the subjects in the other BP groups, as reported also in this study. The diagnosis of symptom-free diabetes is thus more evident in this BP group compared to the other groups. Diuretics and especially beta-blockers have the ability to increase insulin resistance (417, 418). The wide use of these drug classes during the study period may also at least partially explain the higher prevalence of diabetes in both men and women with antihypertensive drug treatment (408).

In Finland the hypertensive subjects who are aware of their elevated BP are usually under regular follow-up, which is carried mainly by primary health care nurses and doctors. This follow-up includes monitoring of the efficacy of drug treatment and health counselling about adverse lifestyles, including obesity, excess intake of salt and alcohol, physical inactivity and smoking. According to the results of this study, the mean BMI and weekly alcohol consumption increased especially in this patient-group. In addition, only one third of these subjects in both sexes reported as having practised leisure-time physical activity at the recommended level in 1997. Therefore, as also shown in some previous studies (419), there is an urgent need for more effective measures in lifestyle counselling of hypertensive patients in Finnish primary health care.

6.2.3 Non-pharmacological treatment of hypertension in primary health care (STUDY 3)

The Study 3 is probably the first large-scale controlled trial reporting the effects of lifestyle intervention on BP and other cardiovascular risk factors in hypertensive persons in primary care setting. The small reductions in BP and lipid levels achieved in this study are in accord with the changes detected in trials of multiple risk factor intervention or dietary intervention with people at high risk but not necessarily hypertensive (259, 264, 420). In contrast, the BP reduction observed in the subjects without antihypertensive drug treatment was smaller compared to some clinical trials of non-pharmacological treatment of hypertension (69, 96). However, this BP reduction can be considered as important from the public health point of view. A small number of current smokers among the participants made it at least partly difficult to achieve any significant reduction in proportion of smokers during the study.

The achieved weight reduction in our study was of the same magnitude than in some trials with much more intensive intervention (21). The intervention program could not bring about any significant reductions in salt intake. Despite the fact that in 95 % of the participants the weekly alcohol consumption was already at the recommended level at baseline, a small but significant reduction in alcohol intake occurred in the intervention group during the first year. Self-reported leisure-time physical activity increased significantly more in the intervention group throughout the study.

According to the separate analysis of the dietary data of this study, the proportion of fat, especially saturated fats, from total energy intake (E%) decreased significantly more in the intervention group compared to usual care (the net reductions at two years; total fat intake -2.7 % E% and saturated fat intake -1.7 E%) (384). Also the total energy intake tended to decrease more in the intervention group, although not reaching the level of statistical significance. In addition to the increase in physical activity, these changes in diet may have contributed to the observed differences in changes of body weight, lipid levels and BP between the randomised groups. The dietary data were in accordance with the results of the 24-hour urinary sodium excretion showing no significant changes in sodium intake. These results repeat the findings of the many other studies that have demonstrated the difficulties in achieving the recommended level of salt intake in free-living subjects (101, 421). It has been suggested that the main reason for this difficulty in salt restriction seen in all western

countries is the still relatively high concentration of salt in processed foods (422). Therefore, in the future, one of the cornerstones in the reduction of salt intake in the whole population is the close collaboration with the food industry to increase the production of low-salt food items.

The differences in BP reduction observed between the groups could not be explained by accustomisation with BP measurement, because there were no differences in self-reported frequency of BP measurements between the groups during the study. One explanation for the greater fall in blood pressure among the participants who continued antihypertensive drug treatment compared with the participants without antihypertensive drugs could be a more regular use of antihypertensive drugs during the trial than before.

In addition to the factors related with the volunteering of the participants, also the "contamination" of the control group due to the fact their follow-up visits were done by the same nurses as with the intervention group might have reduced the difference in the lifestyle changes between the groups. Also the fact that they were under systematic observation in an interesting study likely influenced them. It is also worth noticing that most of the study subjects were under regular follow-up provided by the health centres already before the study. Therefore, the favourable changes observed in the lifestyle factors of the intervention group were based mostly on the change in the way how lifestyle counselling was provided, not on the initiation of it. Thus, our observed effects of the intervention, as usual in this kind of study, are likely to be conservative.

The principal aim of Study 3 was to find out the extent to which lifestyle intervention will work in the usual primary health care setting. From this point of view, the results of the study were quite satisfactory, considering the limited requirement for the use of health care resources. The potential of the intervention shown in this study can certainly be much improved by further development and systematic dissemination, especially concerning newly detected hypertensive persons. Non-pharmacological treatment of hypertension has been advocated for a long time, but so far only limited evidence and experience has been available as to its effective implementation within the primary care. The task is not easy due to the limited time and resources that the public health service can allocate for such preventive services. However, the present study demonstrates that also this approach works.

7   SUMMARY AND CONCLUSIONS

This doctoral thesis consisted of three separate studies that assessed different aspects of community control of hypertension in Finland. In the first study, the trends in BP levels and in the prevalence, awareness and control of hypertension were assessed in cross-sectional surveys of the representative samples of the population aged 25-64 years in eastern and southwestern Finland during 1982-1997 and in Helsinki-Vantaa area during 1992-1997. In 1997, also the Oulu region was included in the study areas. The second study examined the trends in cardiovascular risk factors and in lifestyle factors affecting BP in aware and unaware hypertensive subjects of the southwestern and eastern Finland during 1982-1997 and compared the observed trends with those seen in the normotensive population. In the third study, the efficacy of a lifestyle counselling programme targeting BP reduction in hypertensive subjects was assessed in a two-year randomised controlled trial organised in ten primary health centres in eastern Finland.

The results of the three studies can be summarized as follows:

1.   The mean SBP levels and the prevalence of hypertension decreased significantly in both sexes in eastern and southwestern Finland during 1982-1992. The mean DBP decreased only in eastern Finland. During next five years in men, the mean SBP decreased in all areas except in the Helsinki-Vantaa area, and the mean DBP and the prevalence of hypertension remained stable in all areas. In women the mean SBP and the prevalence of hypertension decreased further in all study areas, but also in women the mean DBP remained unchanged. The rates for awareness, treatment and control of hypertension increased significantly in both sexes and in all areas throughout the study period, except in men in Helsinki-Vantaa during 1992-1997.

2.   The mean total cholesterol and prevalence of hypercholesterolaemia decreased significantly in both hypertensive and normotensive subjects of both sexes during 1982-1997. The mean HDL cholesterol increased markedly in all BP groups except in men unaware of their hypertension, but the mean value remained at significantly lower level in drug-treated hypertensive patients compared to subjects with no

antihypertensive drug treatment. The prevalence of smoking decreased significantly in normotensive men and in men with antihypertensive drug treatment, whereas an upward trend in smoking was seen in drug-treated hypertensive women. The prevalence of self-reported diabetes increased significantly in men with antihypertensive drug treatment, but not in the rest of the population. The mean BMI and waist circumference increased significantly in the whole population, but especially in hypertensive subjects. Alcohol consumption increased more in the hypertensive subjects of the both sexes compared to the normotensive population. Self-reported leisure-time physical activity increased in all BP groups except in unaware hypertensive women.

3. The two-year lifestyle intervention programme conducted in primary health care produced significantly greater reductions in BP levels of the subjects with no antihypertensive drug treatment assigned to intervention compared to subjects receiving usual care. This difference in BP reduction was mainly attributed to the decrease in mean body weight and to the increase in leisure-time physical activity, which were significantly greater in the intervention group during the study. The differences in BP reduction between the randomised groups were not statistically significant among the subjects with antihypertensive drug treatment.

It can be concluded that the control of hypertension has improved markedly in Finland during 1982-1997. Despite this favourable development, intensified efforts for both "the individual approach"- and "the population approach"-strategies are needed in the future to improve the situation further. Firstly, the unfavourable trends in BMI and in alcohol consumption of the whole population should be reversed. In addition, the observed increase in leisure-time physical activity and the decrease in salt intake should be maintained to shift the distribution of the population BP further to the left. Secondly, the health behaviours of newly diagnosed hypertensive subjects should be carefully monitored and modified in primary health care in a more systematic and efficient way than presently. Lastly, effective antihypertensive drug treatment should be initiated in subjects with moderate or high cardiovascular risk early enough if lifestyle modification does not achieve satisfactory results.

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ORIGINAL PUBLICATIONS

I-V

I

Kastarinen MJ, Salomaa VV, Vartiainen EA, Jousilahti PJ,
Tuomilehto JO, Puska PM, Nissinen AM.
Trends in blood pressure levels and control of hypertension in Finland
from 1982 to 1997. J Hypertens 1998; 16:1379-87.

II

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III

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V

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