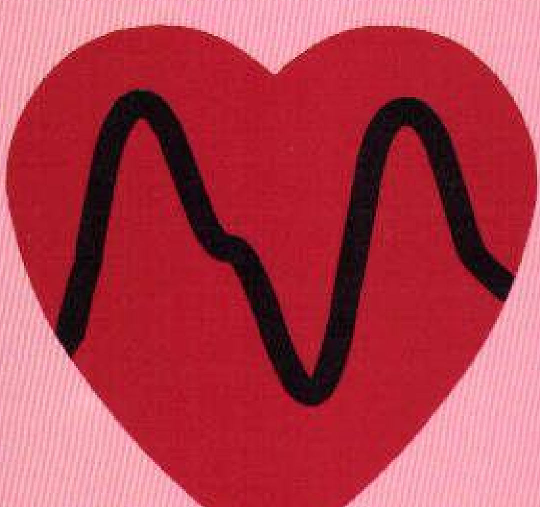
BLOOD PRESSURE

TRENDS
DETERMINANTS
AND
CONSEQUENCES



Edith van Leer

Stellingen

1. De seizoensinvloed op de bloeddruk is onmiskenbaar. In de zomer is de bloeddruk lager dan in de winter.
Dit proefschrift

2. Aangezien de bloeddrukverlagende effecten van medicamenteuze en niet-medicamenteuze behandelingen vergelijkbaar zijn, verdient de niet-medicamenteuze behandeling meer aandacht vooral met het oog op kosten en neveneffecten.
Dit proefschrift

3. In observationeel onderzoek kunnen de afzonderlijke associaties van de inname van kalium, magnesium en calcium met de bloeddruk niet betrouwbaar bepaald worden vanwege sterke onderlinge correlaties. Gebruik van bijvoorbeeld de residu methode kan wel leiden tot andere correlaties, maar de betrouwbaarheid van de associaties verandert daardoor niet.

4. Het eten van groente en fruit heeft behalve een beschermend effect op kanker ook een bloeddrukverlagende werking.
NRC Handelsblad, 5 oktober 1994; dit proefschrift

5. Een uitspraak over lange-termijn trends in bloeddruk kan alleen worden gebaseerd op continue bloeddrukmetingen over een zeer lange periode en niet op incidentele bloeddrukmetingen met intervallen van 5 tot 10 jaar.

6. Het drinken van een paar glazen alcoholische drank per dag heeft een positief effect op hart- en vaatziekten. Het negatieve effect op de bloeddruk dient hierbij in ogenschouw te worden genomen, met name voor rokers.

7. Meer gedegen onderzoek is nodig voordat lichamelijke inactiviteit als determinant van hoge bloeddruk erkend kan worden.
World Hypertension League, Physical exercise in the management of hypertension, Bull WHO 1991;69:149-153.

8. Naarmate rapporten zijn opgesteld door meer gerenommeerde personen of instanties verdient het sterker aanbeveling de literatuur waarop deze uitspraken gebaseerd zijn, kritisch te evalueren.
Joint National Committee on Detection, Evaluation, and treatment of high blood pressure, The fifth report of the Joint National Committee on Detection, Evaluation, and Treatment of high blood pressure (JNC V), Arch Intern Med 1993;153:154-183.

9. De vanzelfsprekendheid waarmee het overleven van de mens centraal staat in toekomstscenario's staat in schril contrast met de massale uitstervingsgolf in planten- en dierenwereld die de mens veroorzaakt heeft.

10. Het ageren tegen vriendjespolitiek klinkt vreemd in het licht van de huidige tendens om 'networking' te stimuleren.

Stellingen behorend bij het proefschrift "Blood pressure: trends, determinants and consequences" van Edith van Leer

Wageningen, 14 juni 1995

BLOOD PRESSURE:
TRENDS, DETERMINANTS AND CONSEQUENCES

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BLOOD PRESSURE:
TRENDS, DETERMINANTS AND CONSEQUENCES

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in de landbouw- en milieuwetenschappen
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in het openbaar te verdedigen
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ABSTRACT

BLOOD PRESSURE: TRENDS, DETERMINANTS AND CONSEQUENCES

PhD Thesis.
Agricultural University, Wageningen, The Netherlands and the National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands.
Edith M. van Leer

Trends in blood pressure, prevalence and treatment of hypertension were studied in 30,000 men and women aged 37-43 years during the period 1974-1980, in 80,000 men aged 33-37 years during the period 1981-1986 and 36,000 in men and women aged 20-59 years during the period 1987-1991. Between 1974 and 1991 changes in systolic and diastolic blood pressure were minor with the exception of an increase in the prevalence of hypertension in men between 1974-1980. Between 1981 and 1991 the prevalence of hypertension remained stable in men and in women between 1987 and 1991. More women than men were treated for hypertension; this did not change between 1974 and 1991. An increase in the percentage of treated hypertensive men between 1974 and 1986 was followed by a decrease in the period between 1987 and 1991 when a decrease in the treatment of hypertension in women was also seen.

In a cross-sectional analysis in about 30,000 men and women aged 20-59 years a linear relation between alcohol consumption and blood pressure was observed in men. The results in women suggest a threshold of two glasses per day. In this study it was observed that gender, age and smoking were important effect modifiers of the alcohol-blood pressure association. An inverse association was observed between blood pressure and the intake of potassium and magnesium in both men and women. Dietary calcium was inversely related to systolic blood pressure in women and to systolic and diastolic blood pressure in both men and women. Men and women consuming a diet high in potassium, magnesium and calcium had about 2 mmHg lower blood pressure than their counterparts consuming a diet low in these minerals.

In a 12-year follow-up study in 50,000 men and women aged 30-54 at baseline, elevated blood pressure was strongly related to cardiovascular and total mortality in both sexes. However, in men the mortality rates and relative risks were higher than in women. It was estimated that a reduction of 6 mmHg in diastolic blood pressure results in a 41% reduction in cardiovascular mortality and 28% reduction in total mortality for men and 29% and 12%, respectively, for women. Evidence from observational studies and intervention trials suggest that such a reduction may be achieved through preventive measures such as weight control, alcohol and salt restriction, and increased potassium intake.

Contents

1

GENERAL INTRODUCTION

GENERAL INTRODUCTION

Coronary heart disease (CHD) and cerebrovascular accidents (CVA) are the main causes of death in the Netherlands (1). Of the 129,000 people who died in 1990, 17% were victems of coronary heart disease and 10% of cerebrovascular accident. High blood pressure, together with smoking and elevated serum cholesterol is one of the major risk factors for cardiovascular diseases (CVD) and the most important one for cerebrovascular accidents (2). It has been calculated that 25% of the coronary heart disease and cerebrovascular accident mortality in the Netherlands can be attributed to high blood pressure (3).

The risk associated with raised blood pressure increases progressively through the entire range of blood pressure levels and the dividing line between 'normotension' and 'hypertension' is arbitrary. The most commonly used definition of hypertension is the one proposed by the WHO: i.e. persons with a systolic blood pressure of ≥160 mmHg and/or a diastolic blood pressure of ≥95 mmHg and/or use of antihypertensive medication are called hypertensive (4). Because this also includes persons who actually are hypertensive but whose blood pressure is controlled by medication, this is a practical definition to estimate the prevalence of hypertension in a population. Hypertension is divided in primary and secondary hypertension (5). Essential hypertensives are defined as individuals who may have generalized or functional abnormalities causing their hypertension. Individuals with a specific organ defect responsible for hypertension are called secondary hypertensives. Of all patients with hypertension, 90-95% have essential hypertension (6).

The measurement of intra-arterial blood pressure is the 'gold standard'. For practical purposes blood pressure is measured with a mercury sphygmomanometer using the Korotkoff sound technique (7). In practice, the difference between the intra-arterial blood pressure measurement and the measurement with the sphygmomanometer is small unless the arm circumferences are smaller or larger than appropriate for the standard cuff-size (8). Under standardized conditions the reproducibility of the blood pressure measurement is reasonably good. The correlation coefficients for repeated systolic and diastolic blood pressure measurements are generally in the order of 0.7 (9,10).

Blood pressure can be influenced by several factors such as age, diabetes mellitus; alcohol consumption; intake of sodium, potassium, calcium and magnesium; obesity and physical activity (11,12). The modifiable lifestyle factors such as alcohol consumption, mineral intake and obesity are of great importance for primary prevention and form a part of the treatment of hypertension.

High blood pressure is one of the major risk factor for cardiovascular diseases. The level of blood pressure in the population is directly related to the burden of cardiovascular diseases in the society. From a public health perspective data are needed on levels and trends in blood pressure, and on the prevalence and treatment of hypertension in the population. For primary prevention purposes information is needed about the relationship between lifestyle-related risk factors and blood pressure.

The studies described in this thesis are given in Table 1. The first screening project (the Consultation Bureau Heart Project or CB Heart Project) was carried out between 1974 and 1980. In this period about 30,000 men and women with an average age of 40 years were examined. The second screening project (the Coronary Heart Disease Risk Factor Project or RIFOH Project) was carried out between 1981 and 1986. This study included about 80,000 men with an average age of 35 years. The aim of these studies was both to screen a large number of people and to give persons in a high-risk category advice about risk factor reduction. In Chapter 2 the baseline data from the CB Heart and RIFOH Projects were used to study the trends in systolic and diastolic blood pressure, as well as the prevalence and treatment of hypertension.

The Cardiovascular Risk Factors Monitoring Project (CRFM Project) was carried out between 1987 and 1991. In that period about 36,000 men and women aged 20-59 years were examined. In Chapter 3 data from the CRFM Project were used to study levels and trends in systolic and diastolic blood pressure and prevalence, and treatment of hypertension in men and women. In this chapter we also described seasonal variation in blood pressure.

Data of the CRFM Project were used in Chapter 4 to describe the form of association between alcohol consumption and blood pressure. Furthermore, effect modification and confounding of this association by age, smoking, degree of obesity, coffee consumption, physical activity during leisure time and educational level were studied. Data from this project were also used to investigate the association between blood pressure and the intake of dietary potassium, magnesium and calcium (Chapter 5). High correlations between the different dietary minerals called for assessment of the combined effect of potassium, magnesium and calcium intake on blood pressure.

Table 1. Description of the three studies used in this thesis

Project	Period	Number	Gender	Age	Aim of the study
Consultation Bureau Heart Project (CB Heart)	1974-1980	30,000	men women	37-43	trends in blood pressure, and prevalence and treatment of hypertension (chapter 2)
Coronary Heart Disease Risk Factor Project (RIFOH)	1981-1986	80,000	men	33-37	trends in blood pressure, and prevalence and treatment of hypertension (chapter 2)
Cardiovascular Risk Factors Monitoring Project (CRFM)	1987-1991	36,000	men women	20-59	1 trends in blood pressure, and prevalence and treatment of hypertension (chapter 3) 2 association between alcohol consumption and blood pressure (chapter 4)[1] 3 association between the intake of potassium, magnesium and calcium, and blood pressure (chapter 5)
Consultation Bureau Heart Project (CB Heart)[2]	1974-1980	50,000	men women	30-54	association between blood pressure and mortality from coronary heart disease, cerebrovascular disease, cardiovascular disease and all causes (chapter 6)

[1] This association was studied in 30,000 men and women and the data was collected between 1987-1990.
[2] This is the same project as used for the trend analysis, but instead of only subjects aged 37-43 years the total study population was used.

In Chapter 6 we used the data from the Consultation Bureau Heart Project carried out between 1974 and 1980. In this period about 50,000 men and women aged 30-54 years were screened. Between 1987 and 1993 the vital status of all these persons was verified; of those who died the underlying causes of death were established. The association between blood pressure, hypertension and mortality from coronary heart disease, cerebrovascular accident, cardiovascular diseases and all causes was studied. Particularly investigated were possible differences in the form and strength of the association between men and women, as well as effect modification by smoking status and obesity. Further to this, the population-attributable risks were calculated for different degrees of hypertension.

In Chapter 7 we discussed the methodological problems in trend studies and investigated whether these problems were specific for our studies or could also be observed in those conducted in other countries. The results on the life-style-related determinants of blood pressure are discussed in the context of those of other important observational studies and intervention trials. Also, the importance of modifiable lifestyle factors not investigated in this thesis is discussed. Finally, primary prevention and non-pharmacological treatment of hypertension are discussed in the context of guidelines for management of hypertension.

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2

TRENDS IN BLOOD PRESSURE AND PREVALENCE AND TREATMENT OF HYPERTENSION IN YOUNG ADULTS IN THE NETHERLANDS, 1974-1986

ABSTRACT

Data from two screening projects on cardiovascular risk factors were used to investigate trends in blood pressure and the prevalence and treatment of hypertension in the Netherlands between 1974 and 1986. Between 1974 and 1980 about 30,000 men and women aged 37-43 were screened. Between 1981-1986 about 80,000 men aged 33-37 were examined. An increase of 2 mmHg in average systolic blood pressure in men in the period 1974-1980 was followed by an insignificant change during the period 1981-1986. Average diastolic blood pressure increased by 4 mmHg between 1974 and 1980, but decreased by the same amount between 1981 and 1986. The prevalence of hypertension in 40-year-old men increased from 12.7% in 1974 to 17.8% in 1980. The prevalence of hypertension in 35-year-old men did not change between 1981 and 1986 and amounted to 9.6%. Treatment of 40-year-old hypertensive men increased from 8% in 1974 to 21% in 1980 and from 9% in 1981 to 13% in 1986 among 35-year-old men. Average systolic blood pressure did not change in 40-year-old women between 1974-1980 but average diastolic blood pressure increased by 2 mmHg during that period. The percentage of hypertensive women was 8.5% and did not change between 1974 and 1980. Also, the percentage of treated hypertensive women did not change and amounted to 28%. It can be concluded that the prevalence of hypertension did not change in 40-year-old women while in 40-year-old men it increased between 1974-1980. In 35-year-old men the prevalence of hypertension did not change between 1981-1986. Treatment of hypertension was more common in young adult women than in young adult men. However, an increase in treatment of hypertension in young adult men was observed in both periods.

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INTRODUCTION

Blood pressure is considered a major risk factor for cardiovascular diseases (CVD) (1-3). In the Netherlands no information is available about trends in blood pressure. From a public health point of view it is of interest to investigate changes in systolic and diastolic blood pressure levels as well as the prevalence and treatment of hypertension. Between 1974 and 1986 two screening projects on cardiovascular risk factors were carried out in The Netherlands. During the total study period blood pressure was measured in a standardized way. With data from these two projects, the trends in blood pressure as well as the prevalence and treatment of hypertension in 40-year-old men and women during the period 1974-1980 and in 35-year-old men during the period 1981-1986 were studied.

METHODS

The Consultation Bureau Heart Project (CB Heart Project; 1974-1980) and the Coronary Heart Disease Risk Factor Project (the RIFOH Project; 1981-1986) were carried out by tuberculosis clinics or 'Consultation Bureaus' in Amsterdam, Doetinchem, Maastricht, Tilburg and Leiden. These towns are located in different parts of The Netherlands: Amsterdam, the capital city (700,000 inhabitants) and Leiden (100,000 inhabitants) are situated in the west; Doetinchem (40,000) is a small town in a rural area in the east; Maastricht (100,000) lies in the south, and Tilburg (150,000) is a middle-sized industrial town in the southwest.

The CB Heart Project was initiated in October 1974 in Tilburg and Doetinchem. In 1976 consultation bureaus in Amsterdam, Maastricht and Leiden joined the study. For the CB Heart Project different birth cohorts were selected in different towns. All persons born in certain years were invited for the study. Names and addresses of the participants were obtained from the municipal registry. The response rate, about 80% at the beginning of the study, dropped to about 70% at the end of the study (4). During the period 1974-1980 a total of about 50,000 men and women, who varied in age between 30 and 54 years, were examined. The age range differed from town to town. Therefore, a subsample with a narrower age range (37-43 years) was selected for the trend analyses. The mean age of those 30,000 persons was 40 years. In Leiden, the age range of the subjects examined in the period 1974-1980 deviated and therefore data from Leiden were excluded from the trend analyses for this period.

In 1981 the CB Heart Project was followed by the RIFOH Project. This project covered only men aged 33-37 years (about 80,000 in total) in the 5 towns. Potential respondents were identified from the civil registry and invited to participate. For each 2-year period, certain birth cohorts were invited to participate: from 1981 to 1982, all men born in 1946 and 1947; from 1983 to 1984, all men born in 1948 and 1949; and from 1985 to 1986, all men born in 1950 and 1951. This ensured a narrow age range across the entire study period, and no respondents had to be excluded in the trend analyses. The response rate was on the average about 55% for Amsterdam and about 70% for the other towns. The mean age of the subjects participating in the RIFOH Project was 35 years during the whole study period (1981-1986).

In both the CB Heart Project and the RIFOH Project, information was obtained on risk factors for coronary heart disease using standardized methods (4). The participants filled out a questionnaire in which information was obtained about smoking habits, current use of medication for high blood pressure, history of hypertension, diabetes and complaints of cardiovascular disease. Blood was taken for total cholesterol determination. Height, weight and blood pressure were measured. Blood pressure was measured once in the sitting position with a random zero sphygmomanometer. The measurements were carried out by the same trained technicians in both projects. The technicians had received detailed instructions on use of the sphygmomanometer (5). The cuff (size 12 x 23 cm) was applied to the left upper arm. Systolic blood pressure was recorded at the appearance of sounds (first-phase Korotkoff) and the diastolic blood pressure was recorded at the disappearance of sounds (fifth-phase Korotkoff). Hypertension was defined according to the criteria of a WHO expert committee as a systolic blood pressure ≥160 mmHg and/or a diastolic blood pressure ≥95 mmHg and/or use of antihypertensive medication (1).

For statistical analyses the SPSS/PC+ package program was used (6). Multiple linear regression analysis was performed for trend analyses using blood pressure or percentage hypertensives or percentage on medication as the dependent variable and time (months) as the independent variable. Adjustment for age differences was made by calculating the regression coefficients for the relation between age and the dependent variables. Subsequently, the dependent variable for each individual was extrapolated to a value for a subject 40 years of age (CB Heart Project) or 35 years of age (RIFOH Project). The age-adjusted blood pressure or percentage hypertensives or percentage on medication was then used as the dependent variable in the regression analysis. Age-adjustments for hypertension and treatment of hypertensives were made by analysis of covariance. Analysis of variance was used to investigate regional differences in blood pressure level. Contrasts were tested for statistical significance using the Scheffé test.

During the study period the number of persons per town differed. An increasing number of persons from a town with a high (or low) blood pressure could cause an artificial time trend. Therefore, dummy variables for the different towns were added to the regression model, using Amsterdam as a reference. As a rule the overall regression coefficients are presented. Only in case of a difference in the trends in mean blood pressure between the various towns, are these differences specified.

In the RIFOH Project the average systolic blood pressure first increased and then decreased. Therefore two regression lines were fitted. This was accomplished by comparing the explained variance of the two regression lines with that of a straight line. The two lines significantly increased the explained variance. The explained variance of the model based on two regression lines was also slightly higher than the explained variance of a model including a quadratic term. The 'breakpoint' in the line was determined by optimizing the explained variance. The analysis was performed with two time variables: one for the total period (B_1) and one for the period after the breakpoint (B_2). The change in systolic blood pressure and percentage hypertensives over the first period (until the breakpoint) is given by B_1, the change over the second period (after the breakpoint) is given by $B_1 + B_2$. The interpretations of the results from both the CB Heart Project and the RIFOH Project are based on the age and town adjusted regression coefficients.

RESULTS

CB Heart Project (1974-1980)

Table 1 shows the regional differences in blood pressure and body mass index in both men and women. For men mean systolic blood pressure in Doetinchem and Tilburg was significantly higher when compared with the other towns. Diastolic blood pressure in Amsterdam was significantly higher than in Tilburg and Maastricht. For women systolic blood pressure in Doetinchem was significantly higher than in the other towns and diastolic blood pressure in Doetinchem was significantly higher than in Maastricht and Tilburg. For both men and women the mean body mass index was significantly higher in Doetinchem when compared with the other towns.

Table 1. Mean blood pressure (mmHg) and body mass index (kg/m^2) adjusted for age in men and women aged 37-43 years in the period 1974-1980, by town (CB Heart Project) (between brackets standard deviation)

	Systolic blood pressure	Diastolic blood pressure	Body mass index	Number
Men				
Amsterdam	132.1 (15.9)	82.0 (11.0)	24.8 (3.1)	3,481
Doetinchem	134.7 (16.2)	80.0 (10.7)	25.4 (2.8)	1,818
Maastricht	132.8 (17.0)	81.6 (11.9)	25.0 (3.1)	3,678
Tilburg	134.2 (15.2)	80.5 (10.2)	24.9 (3.1)	5,165
Women				
Amsterdam	125.4 (16.9)	77.8 (11.1)	24.1 (3.7)	4,185
Doetinchem	130.6 (17.1)	78.5 (10.8)	25.4 (3.6)	1,999
Maastricht	124.8 (16.1)	77.3 (10.9)	24.1 (3.5)	3,810
Tilburg	129.0 (15.9)	77.4 (10.1)	24.3 (3.7)	5,387

Tables 2 and 3 show the mean systolic and diastolic blood pressure, the prevalence of hypertension and the percentage treated hypertensives for men and women in the period 1974-1980. For men, a significant overall increase in mean systolic blood pressure was observed after adjustment for age and town between

1974 and 1980 (Table 4). This was due to a significant increase of 1.56 mmHg per year in Doetinchem. A significant increase in mean diastolic blood pressure was observed after adjustment for age and town. This increase was significant in all towns except Tilburg. Both the percentage hypertensive men and the percentage treated hypertensive men increased significantly.

For women, no significant changes in mean systolic blood pressure was observed; this was consistent in all towns. The mean diastolic blood pressure increased significantly after adjustment for age and town. This increase was due to an increase in the mean diastolic blood pressure of 0.55 mmHg per year in Amsterdam and 0.97 mmHg per year in Maastricht. Both the percentage hypertensive women and the percentage treated hypertensive women did not change. The percentage of hypertensives was lower among women compared with men. Hypertensive women were, however, more frequently treated than hypertensive men.

Table 2. Mean blood pressure, prevalence of hypertension and percentage treated hypertensives, men aged 37-43 years in the period 1974-1980 (CB Heart Project)[1]

	1974[2]	1975[2]	1976	1977	1978	1979	1980[3]
N	452	1,070	3,370	2,972	2,805	1,738	1,735
Systolic blood pressure							
Mean (mmHg)	130.8	130.9	133.9	133.9	133.0	134.1	131.9
(SD)	13.6	13.1	16.7	16.8	16.3	16.2	14.9
Diastolic blood pressure							
Mean (mmHg)	79.6	78.3	80.6	81.1	81.3	82.9	82.1
(SD)	10.3	10.0	10.9	11.4	11.1	11.3	10.1
Hypertension (%)[4]	8.6	7.8	13.5	15.9	15.9	17.4	12.7
Treated for hypertensives (%)	12.8	20.9	13.2	14.3	16.6	16.3	23.1

[1] data adjusted for age
[2] data from Amsterdam and Doetinchem were not available
[3] data from Doetinchem were not available
[4] systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥95 mmHg and/or use of antihypertensive medication

Table 3. Mean blood pressure, prevalence of hypertension and percentage treated hypertensives, women aged 37-43 years in the period 1974-1980 (CB Heart Project)[1]

	1974[2]	1975[2]	1976	1977	1978	1979	1980[3]
N	511	1,175	3,462	3,368	2,991	1,949	1,925
Systolic blood pressure							
Mean (mmHg)	127.8	127.6	128.5	126.8	126.4	127.3	126.2
(SD)	15.2	16.0	16.9	17.1	16.8	16.6	14.5
Diastolic blood pressure							
Mean (mmHg)	78.3	76.6	77.3	77.3	77.6	78.4	78.6
(SD)	10.3	10.5	10.8	10.8	10.5	10.9	10.3
Hypertension (%)[4]	7.8	8.4	10.4	10.7	11.2	11.0	10.1
Treated for hypertension (%)	56.1	45.7	33.9	31.5	40.3	31.0	34.9

[1] data adjusted for age
[2] data from Amsterdam and Doetinchem were not available
[3] data from Doetinchem were not available
[4] systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥95 mmHg and/or use of antihypertensive medication

RIFOH Project (1981-1986)

Table 5 shows that systolic blood pressure in Doetinchem and Tilburg was higher when compared to the other towns. Diastolic blood pressure in Doetinchem was significantly higher than in Leiden, Maastricht and Tilburg. Body mass index in Doetinchem and Maastricht was significantly higher when compared with the other towns.

Table 6 shows the mean systolic and diastolic blood pressure, the prevalence of hypertension and the percentage treated hypertensives for men in the period 1981-1986. After adjustment for age and town a significant increase in mean systolic blood pressure was observed from July 1981 until December 1983 (Table 7). This increase was due to an increase in all towns except Tilburg. Between January 1984 and September 1986 a significant decrease was observed, due to decreases in Amsterdam, Leiden and Maastricht. The 'net' change in mean systolic blood pressure over the total study period was insignificant (< 1 mmHg). The mean diastolic blood pressure decreased significantly after adjustment of age and town between 1981 and 1986. This was due to a decrease in mean diastolic blood pressure in Amsterdam, Leiden and Maastricht while in Doetinchem and Tilburg no changes were observed. The percentage hypertensive men did not change significantly between July 1981 and December 1983. From January 1984 until September 1986 the percentage hypertensives decreased significantly. The 'net' change in the prevalence of hypertensives between 1981 and 1986 was insignificant. The percentage treated hypertensives increased significantly between 1981 and 1986.

Table 4. Regression coefficients (B) and intercepts for the relation between blood pressure or percentage hypertensives or percentage treated hypertensives and time for men and women aged 37-43 years in the period 1974-1980 (CB Heart project).

	Men (n=14,142)		Women (n=15,381)	
	Crude	Adjusted[1]	Crude	Adjusted[1]
Mean systolic blood pressure				
intercept	133.1	130.9	129.2	125.6
B (mmHg/year)	0.06	0.33*	-0.55**	-0.07
Mean diastolic blood pressure				
intercept	78.9	79.9	77.2	76.7
B (mmHg/year)	0.67***	0.58***	0.19	0.29***
Hypertension %[2]				
intercept	11.4	12.7	10.5	8.5
B (%/year)	0.95***	0.81**	0.08	0.39
Treated hypertensives %				
intercept	12.9	8.3	42.1	28.0
B (%/year)	1.49*	2.04**	-1.48	0.05

[1] data adjusted for age and town
[2] systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥95 mmHg and/or use of antihypertensive medication
* $p<0.05$; ** $p<0.01$; *** $p<0.001$

Table 5. Mean blood pressure (mmHg) and body mass index (kg/m^2) adjusted for age in men aged 33-37 years in the period 1981-1980, by town (RIFOH Project) (between brackets standard deviation)

	Systolic blood pressure	Diastolic blood pressure	body mass index	Number
Amsterdam	128.7 (15.0)	79.4 (10.1)	24.4 (3.2)	21,645
Doetinchem	132.8 (15.0)	79.5 (10.6)	25.0 (3.0)	13,425
Leiden	125.9 (14.4)	78.7 (10.0)	24.4 (2.9)	14,158
Maastricht	130.5 (15.5)	79.0 (10.4)	25.0 (3.1)	16,349
Tilburg	132.3 (15.1)	77.8 (9.3)	24.7 (3.1)	15,147

Table 6. Mean blood pressure, prevalence of hypertension and percentage under treatment for men aged 33-37 years in the period 1981-1986 (RIFOH Project)[1]

	1981	1982	1983	1984	1985	1986
N	8,083	12,252	17,633	14,870	15,882	12,004
Systolic blood pressure						
Mean (mmHg)	127.9	129.6	130.8	131.1	129.9	129.1
(SD)	14.7	15.5	15.5	14.8	15.2	15.2
Diastolic blood pressure						
Mean (mmHg)	80.4	80.5	79.6	79.0	77.1	77.5
(SD)	9.9	10.5	10.2	8.9	7.6	7.8
Hypertension (%)[2]	9.2	10.5	10.2	8.99	7.6	7.8
Treated for hypertension (%)	13.0	8.8	11.2	10.3	13.3	13.0

[1] data adjusted for age
[2] systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥95 mmHg and/or use of antihypertensive medication

Table 7. Regression coefficients (B) and intercepts for the relation between blood pressure or percentage hypertensives or percentage treated hypertensives and time, and the 'net' change[1] over the total study period for men (n=80,724) aged 37-43 years in the period 1981-1986 (RIFOH Project).

	Crude	Adjusted[2]
Mean systolic blood pressure		
intercept	127.8	126.4
B (mmHg from July 1981-December 1983)	1.51***	1.58***
B (mmHg from January 1984-September 1986)	-1.13***	-1.21***
'Net' July 1981-September 1986	0.66	0.64
Mean diastolic blood pressure		
intercept	81.0	81.3
B (mmHg/year)	-0.75***	-0.73***
Hypertensives (%)[3]		
intercept	10.0	9.6
B (% from July 1981-December 1983)	-0.10	-0.06
B (% from January 1984-September 1986)	-1.01***	-1.00***
'Net' July 1981-September 1986)	-0.53	-0.42
% Treated hypertensives		
intercept	10.0	9.1
B (%/year)	0.73*	0.74*

[1] calculated as the predicted value in the first month minus the predicted value in the last month, based on the regression equation
[2] data adjusted for age and town
[3] systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥95 mmHg and/or use of antihypertensive medication.
* p<0.05; *** p<0.001

DISCUSSION

The prevalence of hypertension increased from 12.7% in 1974 to 17.8% in 1980 for 40-year-old men but remained stable at 9.6% in 35-year-old men between 1981 and 1986. For 40-year-old women the prevalence of hypertension was 8.5% in 1974 and did not change between 1974-1980. Due to lack of information it was not possible to divide hypertension into primary and secondary hypertension. The advantage of the present study was that blood pressure was measured in a standardized way in both periods. A disadvantage of the present study was that only one cuff size was used, which can bias the blood pressure measurement (7). However, from the Monitoring Risk Factor Project, an ongoing screening project carried out in The Netherlands, it was shown that in only 1.5% of the subjects another cuff size was used (8) because young adults in the Netherlands are relatively lean (9).

In the periods 1974-1980 and 1981-1986, response rates between 70-80% were observed in 4 of the 5 Dutch towns participating in the present study. In Amsterdam the response rate amounted to 55% in the period 1981-1986. In the nationwide Health Surveys carried out by the Central Bureau of Statistics in the Netherlands the lowest response rate was also observed in Amsterdam (10). In the present study we are primarily interested in the trend in blood pressure. It is unlikely that this trend is influenced by the relatively low response rate in Amsterdam because the response rate in Amsterdam was fairly constant between 1981 and 1986.

In the present study the prevalence of hypertension might be overestimated since the blood pressure of each subject was only measured once. To obtain an indication of the order of magnitude of the overestimation on the prevalence of hypertension due to a single blood pressure measurement, data from the Monitoring Risk Factor Project, an ongoing screening project carried out in the Netherlands, were used (8). In this study blood pressure is measured twice with a random zero sphygmomanometer by trained technicians. These data were used to estimate the influence of the use of one measurement instead of the average of two measurements on the prevalence of hypertension among men and women of the same age range. The results of these analyses suggest that the prevalence of hypertension may be overestimated by 9% for men aged 37-43 years, 10% for women aged 37-43 years and 7% for men aged 33-37 years. This means that the average prevalence of hypertension would have been 11.6%

instead of 12.7% for men and 7.7% instead of 8.5% for women in the CB-project and for men in the RIFOH project it would have been 8.9% instead of 9.6%.

Other studies on trends in blood pressure in subjects of the same age range are not available. However, trends in blood pressure can be compared between studies because the trends within studies are of primary interest and not the level of blood pressure itself, which is highly dependent on age. In Italy the mean systolic and diastolic blood pressure of men and women aged 20-59 years in 1978/1979 were compared with those of individuals examined in 1983/1984 (11). Systolic blood pressure was lower (1.3 mmHg for men and 4.0 mmHg for women) in 1983/1984 compared to 1978/1979. Diastolic blood pressure decreased by 1.8 mmHg in men and 3.3 mmHg in women in this period. In the Minnesota Heart Survey systolic and diastolic blood pressure values for men and women aged 25-59 years in 1973/1974 were compared with the values in 1985/1987 (12). Age-adjusted systolic blood pressure levels declined by 1.2 mmHg for men and 2 mmHg for women between 1973 and 1987. Mean age-adjusted diastolic blood pressure levels decreased significantly in both men and women by 2.6 and 1.5 mmHg, respectively. In Japan trends in blood pressure were studied in men and women aged 40-49 years in the period 1956-1980 (13). No changes in blood pressure were observed for Japanese men between 1964-1980 while blood pressure decreased in Japanese women in the same period. Both men and women in Italy and The United States and women in Japan exhibited a decrease in systolic and diastolic blood pressure whereas the present study did not show a decrease during the period 1974-1986.

The prevalence of hypertension is highly dependent on the definition used and the age distribution of the population studied. Results from comparable studies were not available. However, the trend in the prevalence of hypertension can be compared between studies using different definitions of hypertension and different age ranges. In the Minnesota Heart Survey the prevalence of hypertension (diastolic blood pressure $\geq$90 mmHg and/or use of antihypertensive medication) in 1973/74 was compared with values in 1980/82 (14). For both men and women aged 25-59 years no change in the prevalence of hypertension was observed. Also in the present study no change in the prevalence in 40-year-old women was observed in the same period. However, the prevalence of hypertension increased in 40-year-old Dutch men during that period.

Between 1974 and 1980 the percentage treated hypertensives in The

Netherlands increased from 8% to 21% of the 40-year-old men and from 9% to 13% of the 35-year-old men between 1981 and 1986. The percentage treated hypertensive 40-year-old women was around 28% in 1974 and remained stable between 1974-1980. In Italy the proportion treated hypertensive men increased from 15.5% in 1978/1979 to 27.7% in 1983/1984 (11). Between 1978/1979 and 1983/1984 the proportion treated hypertensive women increased from 26.9% to 40.2%. In the Minnesota Heart Survey the age-adjusted use of antihypertensive medication increased from 1973/74 (4.5% of the men, 5.1% of the women) to 1980/82 (8.6% of the men, 7.9% of the women) (14). The prevalence of hypertension in 1973/74 was 17% for men and 11.8% for women. In 1980/82 the prevalence for men was 17.7% and for women 12.9%. As in both cases the use of antihypertensive medication as a fraction of the total population was similar for men and women, the fraction of treated hypertensive women was higher than that of men. The results from these studies show that in The Netherlands, Italy and the United States more women were treated for hypertension than men.

An increase in average systolic blood pressure in men between 1974-1980 was followed by an insignificant change between 1981-1986. Average diastolic blood pressure increased between 1974-1980 but decreased with the same amount between 1981-1986. Between 1974-1980 average systolic blood pressure did not change in women while average diastolic blood pressure decreased during that period. An increase in the prevalence of hypertension in young adult men was observed in the period 1974-1980. This increase can be partly due to better reporting or more public awareness because in the CB Heart Project, between 1974-1980 the use of antihypertensive medication increased by 2.3%. On the other hand the increase in average body mass index of 0.5 kg/m^2 between 1974-1980 could also have played a role in the average increase in hypertension (9).

The observed trends in blood pressure in The Netherlands are in contrast with the trends in Italy, the United States and Japan. In those countries a decrease in blood pressure was observed with the exception of Japanese men, who did not show a change in blood pressure level. Possible reasons for this discrepancy are that important determinants of blood pressure such as sodium intake, alcohol intake and body mass index did not decrease between 1974-1986 in The Netherlands (9,15). We also did not have a National High Blood Pressure Education Program as in the United States (16). This program resulted in a change in attitude of American physicians in relation to treatment of hypertension. Also the American public became more aware that hypertension is an important risk factor for cardiovascular diseases. In spite of the lack of such a program in The Netherlands, the percentage treated hypertensive men increased while no change in the percentage treated hypertensive women was observed between 1974-1980. However, women were treated more frequently than men and the prevalence of hypertension was much higher in 40-year-old Dutch men than in 40-year-old Dutch women.

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3

LEVELS AND TRENDS IN BLOOD PRESSURE AND PREVALENCE, AND TREATMENT OF HYPERTENSION IN THE NETHERLANDS, 1987-1991

ABSTRACT

Levels and trends in blood pressure, as well as prevalence and treatment of hypertension, were studied in the Netherlands between 1987 and 1991. Blood pressure was measured continuously using a standardized method in 36,273 men and women 20-59 years of age. The data were weighted for the age distribution of the general Dutch population in 1990 and adjusted for each technician who measured the blood pressure. In summer in both men and women, systolic blood pressure was about 1.5-2.0 mmHg lower than in the other seasons, and diastolic blood pressure was 0.5-1.0 mmHg lower. In 1987 systolic blood pressure was 124 mmHg in men and 117 mmHg in women. Diastolic blood pressure was 78 mmHg in men and 75 mmHg in women. The prevalence of hypertension was 8% in both men and women. Between 1987 and 1991, systolic blood pressure decreased slightly while diastolic blood pressure increased slightly. The prevalence of hypertension did not change in this period. The percentage of treated hypertensive men decreased significantly from 44% in 1987 to 34% in 1991 and from 60% to 49% in women. We conclude that the prevalence of hypertension did not change between 1987 and 1991, yet the treatment of hypertension decreased, possibly due to a change in the pattern of treatment by Dutch physicians.

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INTRODUCTION

Increased blood pressure is one of the major risk factors for cardiovascular diseases (1-3). From a public health point of view it is important to get insight in the levels and trends in blood pressure, as well as on the prevalence and the treatment of hypertension. We have previously described trends in blood pressure and in the prevalence and treatment of hypertension, during the period 1974 to 1980 for both sexes 37-43 years of age and during the period 1981 to 1986 for men 33-37 years of age (4). In 1987 we started the Monitoring Project on Cardiovascular Risk Factors, in which random samples of individuals aged 20-59 years of age are investigated yearly (5). The aim of this project was to study the levels and trends in major risk factors for cardiovascular diseases. For this study we used data collected between 1987 and 1991 to study levels and trends in blood pressure, prevalence, and treatment of hypertension in both men and women. In addition, we investigated seasonal variation in blood pressure.

METHODS

The Monitoring Project on Cardiovascular Risk Factors is an ongoing screening project that started in 1987. The project is carried out in basic health services in Amsterdam, Doetinchem, and Maastricht, located in different parts of the Netherlands: Amsterdam, the capital city in the west; Doetinchem, a small town in the east; and Maastricht a town in the south. Each year we selected a new random sample of men and women 20-59 years of age in each city. The random sample was selected from the civil registry in each town. To obtain equal numbers in each age category, we stratified the sample according to gender and five-year age classes. In Doetinchem and Maastricht, 400 persons were selected per stratum; in Amsterdam, 500 because of the lower response there. The overall response rate was about 50% for men and 57% for women. From 1987 until 1991 we examined about 36,000 men and women.

In this study, we measured blood pressure, height, and weight were measured and draw blood for total and high density lipoprotein cholesterol determination. Using a random zero sphygmomanometer, we measured blood pressure with the subject in a sitting position. Trained technicians who were all instructed by the same physician conducted the measurements. The cuff (size 12 x 23 cm) was applied to the left upper arm. A larger (15 x 33 cm) or a smaller (9 x 18 cm) cuff was used when appropriate. In about 1.1% of the subjects, a larger cuff was used, and in about 0.4% of the subjects a smaller cuff was used. Systolic blood pressure, was recorded at the appearance of sounds (first-phase Korotkoff), and the diastolic blood pressure was recorded at the disappearance of sounds (fifth-phase Korotkoff). After the first measurement, the heart rate was measured for 30 seconds followed by a second blood pressure measurement. For the analyses, we used the average of the two blood pressure measurements. We asked the subjects to fill out a questionnaire from which information was obtained about demographic variables, presence and family history of cardiovascular diseases, presence of a number of other chronic diseases, current medication use, a prescribed diet status, use of alcohol, smoking habits, physical activity, psychosocial factors, selected dietary habits, and, for women, reproductive history. We exclude pregnant women (n = 306) from the analyses.

We divided age groups in the following 10-year age categories: 20-29, 30-39, 40-49 and 50-59 years. The seasons were defined to coincide with quarters: winter (January, February, March), spring (April, May, June), summer (July, August, September) and fall (October, November, December). Education was divided into three levels: low, intermediate and high. Hypertension was defined according to the criteria of a World Health Organization (WHO) expert committee as a systolic blood pressure ≥160 mmHg and/or a diastolic blood pressure ≥95 mmHg and/or use of antihypertensive medication (2).

A nonresponse study has been performed among 1,620 subjects who had been invited for the first time between august and December 1991 (5). In April/May 1992 they were approached for a second time by telephone (75%) or by mail for those who did not have a telephone (25%). The response was 61%, 23% could not be reached and 16% refused to participate. Information was obtained on demographic variables including educational level, use of alcohol, smoking habits, weight, and height.

Statistical analyses

Analysis of variance was used to estimate mean blood pressure, prevalence of hypertension and percentage of treated hypertensives per year or per season. The percentage of treated hypertensives represents of those with hypertension who received treatment. Blood pressure was analyzed as a continuous variable and the presence and treatment of hypertension, as dichotomous variables. The data were weighted to the age distribution of the general Dutch population in 1990 because in the study population the age distribution was shifted toward older age. About 9% of the studied subjects were 20-29 years compared to about 15% in the Dutch population in 1990 while about 14% of the studied subjects were 50-59 years compared to 9% in the Dutch population. The data, were also adjusted for the technicians who measured the blood pressure. We adjusted for technician because analyses showed some differences in average blood pressure measured by different technicians.

We used regression analysis to examine the relation between blood pressure, prevalence and treatment of hypertension and time (months). We adjusted for technician by adding dummy variables for different technicians to the model. One of the technicians served as the reference. We also used regression analysis to test whether average blood pressure in winter, summer, and fall differed from blood pressure in spring. Three dummy variables for season were entered in the model.

To test whether the trends in mean blood pressure differed among the three towns, the various 10-years age categories, and the various educational levels, we entered cross-product terms (town*month), (age group*month) or (educational level*month) in the regression model. In general, we present regression coefficients of the pooled towns in our tables. We specified trends in mean blood pressure that differed significantly among the three towns, or the different age groups or the different levels of education. We also studied trends by quartiles of blood pressure to indicate whether these changes are differential across blood pressure levels. The cutoff points were based on quartiles of systolic and diastolic blood pressure for both men and women. The interpretations of the results are based on the regression coefficients, weighted to the age distribution of the general Dutch population in 1990 and adjusted for technicians.

RESULTS

Table 1 presents mean blood pressure, the prevalence of hypertension, and the percentage of those with hypertension who received treatment for both men and women per 10-year age category. Both for men and women, systolic and diastolic blood pressure increased with age. In all 10-year age categories, mean systolic and diastolic blood pressure were higher in men than in women. The prevalence of hypertension also increased with age. The prevalence of hypertension was higher for men than for women except in the oldest age category, where the prevalence in both sexes was about 19%. In all age categories, a higher percentage of women was treated for hypertension than men.

Table 1. Mean blood pressure, prevalence of hypertension[1] and percentage of treated hypertensive[2] men and women per 10-year age category in the period 1987-1991

	20-29	30-39	40-49	50-59
Men				
Number	3103	4483	4908	4646
Systolic blood pressure (mmHg)	121.4	121.3	123.7	129.1
Standard deviation	11.6	12.3	14.0	16.9
Diastolic blood pressure (mmHg)	73.4	76.3	79.8	81.3
Standard deviation	8.7	9.5	10.0	10.2
Prevalence of hypertension (%)	1.8	4.4	10.5	18.9
Treated hypertension (%)	10.9	21.3	35.8	52.0
Women				
Number	3615	4986	5254	5278
Systolic blood pressure (mmHg)	111.2	111.3	116.8	125.1
Standard deviation	10.6	11.7	15.1	17.3
Diastolic blood pressure (mmHg)	70.1	71.6	75.3	78.8
Standard deviation	8.5	9.0	9.9	10.3
Prevalence of hypertension (%)	1.0	2.1	7.3	18.8
Percentage treated for hypertension (%)	27.8	49.5	52.6	66.1

[1] systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥95 mmHg and/or use of antihypertensive medication

[2] the percentage of those with hypertension who received treatment

Table 2 indicates mean blood pressure, the prevalence of hypertension, and the percentage of those with hypertension who received treatment per year for both men and women. Table 3 shows the intercepts, which give an estimation of mean blood pressure, the prevalence of hypertension, and the percentage of treated hypertensive patients in 1987 measured by the technician who served as reference category. The intercepts are not the same as the mean values in 1987, which appear in Table 2. In Table 3 also shows the regression coefficients indicating the average change per month in blood pressure, prevalence, and treatment of hypertension. Systolic blood pressure showed a small but significant decrease between 1987 and 1991, whereas diastolic blood pressure showed a small but significant increase. Figures 1 and 2 show that the changes in systolic and diastolic blood pressure in both men and women were minor between 1987 and 1991. When subjects with hypertension were excluded from the analyses, the decrease in systolic blood pressure in both men and women was slightly stronger, whereas the increase in diastolic blood pressure was slightly weaker. The results for the trends remained the same.

The prevalence of hypertension did not change in the period from 1987 to 1991. The percentage of treated hypertensives, however, decreased significantly by 12% in men and 18% in women. When hypertension was defined as a systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or use of antihypertensive medication, the trend for the prevalence of hypertension was similar to the trend for the prevalence of hypertension defined according to the WHO criteria. When hypertension was defined as a systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or use of antihypertensive medication the percentage of treated hypertensive men did not change, but the percentage of treated hypertensive women decreased. When dietary treatment for hypertension was included in the definition of hypertension (systolic blood pressure ≥160 and/or diastolic blood pressure ≥95 and/or use of antihypertensive medication and/or dietary treatment), the percentage of hypertensive men treated with diet did not change, but treatment with medication or with both medication and diet decreased by 11% and 9%, respectively. In women, the percentage of dietary treatment, treatment with medication or with both medication, and a diet decreased by 14%, 10%, 15%, respectively.

Crude trends in mean blood pressure differed significantly among the towns, but after adjustment for technician the differences were negligible.

Table 2. Mean blood pressure, prevalence and percentage treated hypertensive[1,2] in men and women aged 20-59 years in the period 1987-1991[3]

	1987	1988	1989	1990	1991
Men					
Number of subjects	3,006	3,853	3,495	3,258	3,525
Mean SBP (mmHg)	124.2	124.0	123.1	122.0	123.0
Mean diastolic blood pressure (mmHg)	78.2	77.8	78.7	78.3	79.0
Prevalence of hypertension (%)	8.1	7.7	8.8	7.6	9.2
Percentage treated for hypertension (%)	43.8	40.0	31.8	29.4	33.5
Women					
Number of subjects	3,283	4,302	3,975	3,627	3,942
Mean Systolic blood pressure (mmHg)	116.6	116.5	115.8	114.5	116.1
Mean Diastolic blood pressure (mmHg)	74.7	74.0	74.9	74.3	75.2
Prevalence of hypertension (%)	7.6	7.1	7.1	5.3	7.6
Percentage treated for hypertension (%)	60.0	63.5	51.5	49.5	48.7

[1] systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥95 mmHg and/or use of antihypertensive medication
[2] the percentage of those with hypertension who received treatment.
[3] weighted for the age distribution of the general Dutch population in 1990 and adjusted for technician

Therefore, we show only overall regression coefficients. The trends in mean systolic blood pressure level did not differ between the 10-year age categories, and, for women also, the trend in mean diastolic blood pressure did not differ between the 10-year age categories. Diastolic blood pressure increased 0.034 mmHg/month in men 20-29 years, whereas in men 30-59 years, blood pressure did not change. In men systolic and diastolic blood pressure decreased in the lowest quartile, but, in the other quartiles did not change. In women, systolic and diastolic blood pressure did not change in any quartile. In both men and women, trends in mean systolic and diastolic blood pressure did not differ among groups with different levels of education.

Table 3. Intercepts and regression coefficients (B) for the relation between blood pressure, prevalence and percentage treated for hypertensives[1,2] and time (months) for men and women 20-59 years of age, 1987-1991[3]

	MEN	WOMEN
Systolic blood pressure		
intercept (mmHg)	123.6	115.1
B (mmHg/month)	-0.040	-0.026
95 % confidence interval	(-0.054, -0.027)	(-0.039, -0.013)
Diastolic blood pressure		
intercept (mmHg)	77.8	73.7
B (mmHg/month)	0.018	0.011
95 % confidence interval	(0.009, 0.027)	(0.003, 0.020)
Prevalence of hypertension		
intercept (%)	7.9	5.8
B (%/month)	0.017	-0.010
95 % confidence interval	(-0.009, 0.044)	(-0.032, 0.013)
Percentage treated for hypertension		
intercept (%)	53.8	69.8
B (%/month)	-0.203	-0.298
95 % confidence interval	(-0.348, -0.059)	(-0.450, -0.146)

[1] systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥95 mmHg and/or use of antihypertensive medication
[2] the percentage of those with hypertension who received treatment
[3] data are weighted for the age distribution of the general Dutch population in 1990 and adjusted for technician

Table 4 shows mean systolic and diastolic blood pressure per season for both men and women. Systolic and diastolic blood pressure were significantly lower in summer than in spring for both men and women. In men, systolic blood pressure was significantly higher in winter than in spring, and in women, systolic blood pressure was significantly higher in fall than in spring. Diastolic blood pressure was significantly higher in fall than in spring in men. In women, diastolic blood pressure was significantly higher in fall and winter than in spring.

Table 4. Mean systolic and diastolic blood pressure[1] per season in men and women in the period 1987-1991

	Men	Women
Systolic blood pressure		
Spring	123.6	116.1
Summer	122.1***	114.6***
Fall	123.7	116.8*
Winter	124.3*	116.7
F-value[2]	34.8***	22.4***
Diastolic blood pressure		
Spring	78.4	74.6
Summer	77.8***	73.9***
Fall	78.8*	75.1**
Winter	78.7	75.0*
F-value[2]	65.4***	66.5***

[1] weighted to the age distribution of the Dutch population in 1990 and adjusted for technician
[2] F-value was obtained from variance analysis.
* $p < 0.05$ (significantly different from spring = reference category).
** $p < 0.01$ (significantly different from blood pressure in spring).
*** $p < 0.001$ (significantly different from blood pressure in spring).

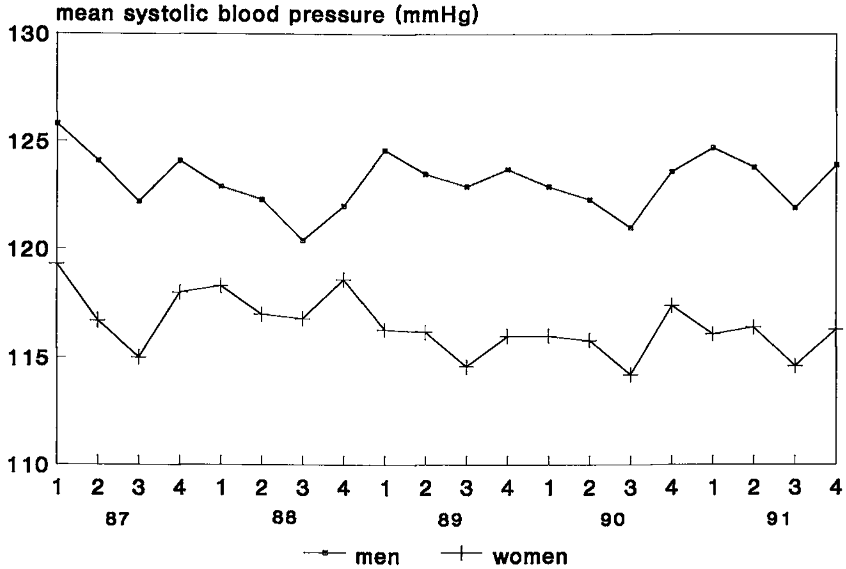

Figure 1. Mean systolic blood pressure weighted for the age distribution of the general Dutch population in 1990 and adjusted for technician per quarter for men and women 20-59 years of age, 1987-1991.

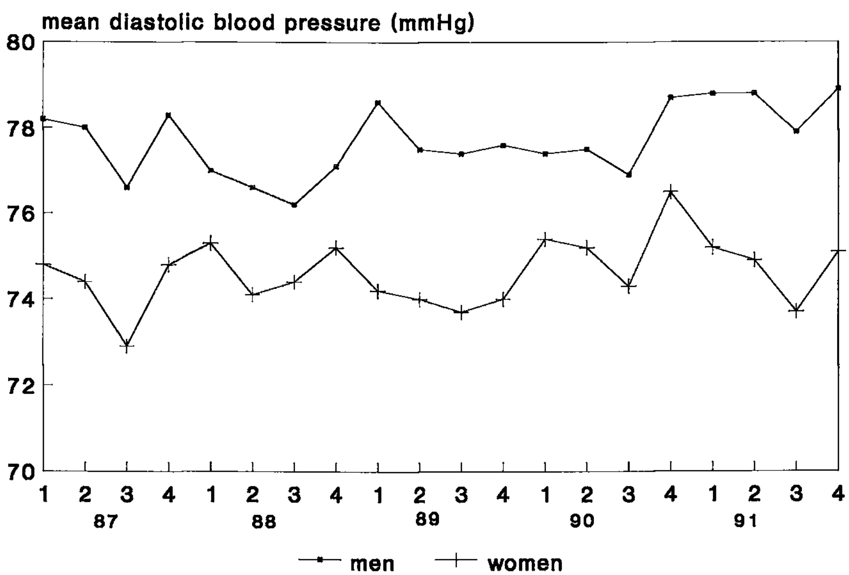

Figure 2. Mean diastolic blood pressure weighted for the age distribution of the general Dutch population in 1990 and adjusted for technician per quarter for men and women 20-59 years of age, 1987-1991.

DISCUSSION

The advantage of this study was that blood pressure was measured continuously in a standardized method in a large number of men and women with a wide age range. Continuous measurements over a long period are desirable to establish reliable trends. The trends of this study were based on a five-year period. Trends in blood pressure and hypertension and their cardiovascular sequelae are of great public health importance because of the insights provided about their determinants and continuing contribution to national morbidity and mortality (6). In the future, it may be possible to present trends over a longer period because continuation of the measurements is being planned.

This study, the overall response rate was 54%, which could have been a source of bias. Obviously, in the nonresponders, blood pressure could not be measured (5). Instead, we used educational level, alcohol consumption, and smoking to estimate potential bias. Education, a known determinant of nonresponse, is associated with blood pressure and hypertension. From the non-response study, it appeared that the calculated distribution of educational level among responders and nonresponders was similar. In both men and women, the percentage of alcohol users was higher among the responders than among the nonresponders. In men, the percentage of smokers was higher among the non-responders than among the responders. In women, the percentage of smokers was similar among responders and nonresponders. It appeared that the average blood pressure level was similar to the blood pressure level weighted for the distribution drinkers and nondrinkers in the nonresponse survey. In men, average systolic and diastolic blood pressure was about 1 mmHg lower than the blood pressure level weighted for the distribution smokers and nonsmokers. These results suggest that the low response rate probably did not affected blood pressure levels.

This study the, response rate decreased from 57% in 1987 to 51% in 1991. Possible changes in educational level, alcohol and coffee consumption, body mass index (BMI) and smoking among the nonresponders also could have biased the results of the trend analysis. Therefore, we adjusted the data for educational level, alcohol and coffee consumption, BMI, and smoking. The changes in the regression coefficients for systolic and diastolic blood pressure, the prevalence, and the treatment for hypertension were negligible after adjustment for these potential confounders.

The percentage of subjects in this study who required a larger cuff was low because adults in The Netherlands are rather lean. The average BMI in this study was about 25 kg/m^2. The percentage of subjects who required a larger cuff decreased steadily from 2.1% in 1987 to 0.7% in 1991. The decrease in the use of a larger cuff could bias the results of the trend analysis. The use of too small a cuff size results in an overestimation of the blood pressure (7). By using too smaller a cuff technicians can overestimate blood pressure by about 6 mmHg in men and by about 4 mmHg in women. Therefore, the blood pressure levels of obese subjects (BMI greater than 30 kg/m^2) were corrected for the use of an inappropriate cuff size by subtracting 6 mmHg for men and 4 mmHg for women in an additional analysis. The changes in the regression coefficient for systolic and diastolic blood pressure, prevalence, and treatment of hypertension were, however, negligible after correcting blood pressure for this measurement error.

We observed seasonal variation in blood pressure in this study in both men and women. Seasonal variation in blood pressure has been studied in some other studies. One study observed that diastolic blood pressure in 22 subjects in the high-to-mild hypertension range was significantly higher in the cold season than in the warm season (8). Systolic blood pressure was also higher in the cold season but did not reach statistical significance. Giaconi et al. observed in their study that, in adults, both systolic and diastolic blood pressure were significantly higher in the cold than in the warm season (9). In Finland in 801 men 50 years of age and older, systolic and diastolic blood pressure revealed significant seasonal patterns with peaks in spring and late autumn and troughs in mid-winter and summer (10). The results of these studies and of this study support the importance of considering seasonal variation in epidemiological studies, particularly when changes in blood pressure over time are evaluated.

Mean levels of blood pressure, prevalence, and treatment of hypertension cannot be compared between different studies or different study periods because of the differences in blood pressure measurements, age ranges, and the definitions used for hypertension. However, trends in the prevalence and treatment of hypertension from different studies can be compared. The Netherlands trends in prevalence and treatment of hypertension in men and women 37-43 years of age have been studied over the period 1974-1980, and in men 33-37 years of age, over the period 1981-1986 (4). The prevalence of hypertension hardly changed in adults from 1974 to 1986, with the exception of a slight increase in men from 1974 to 1980. From 1974 to 1986, the percentage of treated hypertensive men increased but from 1987 to 1991 the percentage of treated hypertensive men decreased. The percentage of treated hypertensive women did not change over the period 1974-1980, yet over the period 1987-1991 the percentage of hypertensive women decreased.

Other countries' trends in the prevalence and treatment of hypertension until 1987 are available in the literature (11-15). In Israel and in the Minnesota Heart Study the prevalence of hypertension did not change during the previous 10 to 15 years, although in Japan the prevalence of hypertension decreased between 1964 and 1980. The treatment of hypertension increased in Israel, Japan and Italy during the seventies and early eighties, but in the Minnesota Heart Study the treatment of hypertension did not change during that period. In The Netherlands, a decrease in treatment of hypertension has been observed, but such a decrease has not been observed in other countries. In the United States, the National High Blood Pressure Education Program was started already in 1972 (16). From that time onward, physicians were trained to diagnose and treat hypertension according to specific guidelines. Such efforts to increase the awareness of the importance of the diagnosis and treatment of hypertension were not undertaken in The Netherlands.

The decrease in treatment of hypertension was stronger in this study in women than in men. However, the percentage of treated hypertensive women was still higher than the percentage of treated hypertensive men. Perhaps because women consult a physician more often than men (17). The decrease in treatment of hypertension in both men and women could result from the debate in the mid-eighties among general practitioners in The Netherlands about the usefulness of drug treatment for mild hypertensives (18). Afterward physicians started to base the hypertension diagnosis on more blood pressure measurements instead of a single measurement (19). This resulted in a reduction of the number of patients treated for hypertension because only "real" hypertensives were treated. However, even with hypertension defined as systolic blood pressure ≥140 or diastolic blood pressure ≥90 or use of medication, the percentage of treated hypertensive men did not change between 1987 and 1991, perhaps that physicians treated persons with only high blood pressure less frequently than persons with high blood pressure in combination with other risk factors for cardiovascular diseases.

In the period 1987-1991, changes in blood pressure were minor in both men and women. Because none of the adjustments for possible confounding or methodological aspects affected appreciably the trends in blood pressure, we conclude that the observed changes in blood pressure are probably real. The importance of the minor changes in systolic and diastolic blood pressure is unknown. Further research is needed to monitor future changes in blood pressure to see if the apparent divergent pattern of a decrease in systolic blood pressure and an increase in diastolic blood pressure are persistent and real. In 1987 the prevalence of hypertension based on an average of two blood pressure measurements was 8% in both men and women, and the prevalence of hypertension did not change between 1987 and 1991 in both sexes. This suggested a need for greater efforts at primary prevention by salt and alcohol restriction, weight control, and exercise. However, the percentage of treated hypertensive men and women decreased significantly in this period, probably because of a change in physicians' attitude toward treatment of hypertension.

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4

DIFFERENCES IN THE ASSOCIATION BETWEEN ALCOHOL CONSUMPTION AND BLOOD PRESSURE BY AGE, GENDER AND SMOKING

ABSTRACT

The positive association between alcohol consumption and blood pressure is well-known. Little is known, however, about effect modification by age, gender, and smoking on the alcohol-blood pressure association. We used data of a cross-sectional study conducted in the Netherlands to investigate the association between alcohol consumption and blood pressure. Between 1987 and 1990, we examined about 30,000 men and women age 20-59 years. After adjustment for age, body mass index and smoking, we found that in men systolic and diastolic blood pressure increased by 0.9 and 0.6 mmHg, respectively, per daily drink. In women systolic and diastolic blood pressure were 2 mmHg and 1 mmHg higher in those who consumed 2 or more glasses per day, respectively, compared with nondrinkers. We observed a stronger association between alcohol and blood pressure in older men compared with younger men and in male and female smokers compared with nonsmokers. These data show that gender, age and smoking all are important effect modifiers of the alcohol-blood pressure relation.

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INTRODUCTION

Many epidemiologic studies have observed a positive association between alcohol consumption and blood pressure in both men and women (1-8). These studies have reported both linear and nonlinear associations (J-shaped, U-shaped, or threshold). For both men and women it is not yet clear at which level of alcohol consumption blood pressure starts to increase. Furthermore, a difference in the relation between alcohol consumption and blood pressure among smokers and nonsmokers has been observed in three cross-sectional studies in Germany (9,10). Using data from a cross-sectional study conducted in the Netherlands among about 30,000 persons age 20-59 years (11), we investigated the shape of the association and the level of alcohol consumption at which systolic and diastolic blood pressure begin to increase in men and women. We also assessed effect modification and confounding of this association by age, smoking, degree of obesity, coffee consumption, physical activity during leisure time, and educational level.

METHODS

The Monitoring Risk Factor Project is an ongoing screening project that started in 1987. The project is carried out as part of the basic health services in Amsterdam, Doetinchem, and Maastricht. These towns are located in different parts of the Netherlands: Amsterdam, the capital city in the west; Doetinchem, a small town in the east; and Maastricht, a city in the south. Each year, a new random sample of men and women age 20-59 years was selected from the civil registry in each town. To obtain equal numbers in each age category, the sampling was stratified by gender and 5-year age classes. In Doetinchem and Maastricht, 400 persons were selected per stratum; in Amsterdam, 500 persons per stratum were selected because of the expected lower response rate. The overall response rate was about 54%, ranging from 46% in Amsterdam to 63% in Doetinchem. The response rate of women was higher than that of men (58% versus 51%). From 1987 through 1990, we examined about 30,000 men and women.

In this study, blood pressure, height, and weight were measured, and blood samples were taken for total and high density lipoprotein cholesterol determination. Blood pressure, with the subjects sitting, was measured using a random zero sphygmomanometer. Trained technicians, all of whom were instructed by one physician, carried out the measurements. The cuff (size 12 x 23 cm) was applied to the left upper arm. A larger (15 x 33 cm) or a smaller (9 x 18 cm) cuff was used when appropriate. The average body mass index in this population was relatively low (25 kg per m^2); a larger cuff was needed in only 1.1 % of the subjects, and a smaller cuff was needed in 0.4 %. Systolic blood pressure was recorded at the appearance of sounds (first-phase Korotkoff), and diastolic blood pressure was recorded at the disappearance of sounds (fifth-phase Korotkoff). After the first measurement, the heart rate was measured for 30 seconds, followed by a second blood pressure measurement. For these analyses, we used the average of the two blood pressure measurements. Weight was measured in subjects without shoes and wearing indoor clothing, after they emptied their pockets. Weight was recorded to the nearest 0.1 kg and height to the nearest 0.5 cm. The subject stood upright against the wall with the feet at a 45° angle. Body mass index was calculated as weight per $height^2$ (kg per m^2). The subjects were asked to fill out a questionnaire from which information was obtained about demographic variables, presence and family history of cardiovascular diseases, presence of a number of other chronic diseases, current medication use, being on a prescribed diet, use of alcohol, smoking habits, physical activity, psychosocial factors, and, for women, reproductive history.

We have estimated alcohol consumption from the following question: "Do you use alcohol?" with possible answers "never," "not anymore," "once in a while, but less than 1 glass a week," and "yes". We obtained the current consumption by asking for the number of glasses of beer, wine, port wine and liquor per week. For each alcoholic beverage, we assumed that one drink contains the same amount of alcohol (10 gm). We added the number of glasses of alcoholic beverages and divided by 7 to get the number of drinks per day. For men we divided alcohol consumption into 7 categories and, for women, into 5 categories, because for men the range of alcohol consumption was larger than for women. We combined the group "once in a while, but less than 1 glass per week" with the category "less than 1 glass of alcohol intake per day" for both men and women. Average blood pressure was essentially the same in these categories. We excluded the group who responded "not anymore" from the analyses (276 men and 179 women) because they may have stopped drinking because of health problems (12). Subjects were also asked whether they were treated for hypertension either by medication or prescribed diet. We excluded these men (n = 693) and women (n = 949) from the analyses. We also excluded pregnant women (n = 246) from the analyses.

We divided age into 10-year age classes. We dichotomized cigarette smoking into smokers and nonsmokers, and physical activity during leisure time into inactive and active. Active was defined as exercise for at least 4 hours per week. For coffee consumption we used 4 categories: non-coffee drinkers and drinkers of regular coffee, decaffeinated coffee and other types of coffee. For education, we used categories of low, medium and high. For body mass index, we used two categories: ≤25 kg per m^2 and >25 kg per m^2.

Reproducibility study

In 1990, a subsample of about 450 men and 470 women age 20-60 years who also participated in 1989 was examined for a second time. The response rate in the second survey was 64%. This subpopulation did not differ from the total population with respect to age, blood pressure, and alcohol consumption. The purpose of this second examination was to estimate the within-person variation and the reproducibility of the blood pressure measurements and level of alcohol consumption. We used the within-person variation to estimate the unattenuated correlation coefficient of the relation between alcohol consumption and blood pressure.

Nonresponse study

In 1992, a nonresponse survey was carried out among 1,620 subjects who had been approached between August and December 1991 to assess possible selection bias (11). Responders and nonresponders were similar with respect to educational level, but the percentage of alcohol users was about 10% higher among responders than among nonresponders. In men, but not in women, the percentage of smokers was 15% higher among the nonresponders than among the responders.

Statistical analyses

We used linear regression analysis, with indicator variables for categories of alcohol consumption. We used two indicator variables for the different towns and three indicator variables for the different survey years, because mean blood pressure differed by town and survey year. We used indicator variables for decade of age, and an indicator for smoking. The reference categories were for town, Amsterdam; survey year, 1987; age, 20-29 years; and nonsmoking. We entered body mass index in the model as a continuous variable.

We analyzed the data by stratum of town and survey year to investigate whether the relation differed by these variables. We considered age, smoking, body mass index, education, coffee consumption, and physical activity during leisure time as potential effect-modifiers, using a linear regression model in which alcohol consumption was entered as a continuous variable.

We calculated Pearson correlation coefficients to obtain an indicator for the reproducibility of the blood pressure measurements and alcohol consumption assessed in 1989 and 1990 in about 900 subjects. To estimate the effect of the two replicate measurements on the observed correlation between alcohol consumption and blood pressure, we calculated the unattenuated correlation coefficient (13). The observed correlation coefficient is lower than the unattenuated one because of within-person variability. The attenuation can only calculated for a Pearson correlation coefficient, relating variables with a normal distribution. Because alcohol consumption showed a skewed distribution, we applied a square root transformation. The correlation coefficients are adjusted for age, town, survey year, smoking, and body mass index.

RESULTS

About 92% of the men and about 73% of the women consumed alcoholic beverages. In men, we observed higher blood pressure levels in all six alcohol consumption categories compared with blood pressure in nondrinkers (Figure 1). We estimated that men who drank less than 1 drink per day had systolic pressures 2 mmHg (95% CI: 1.3-3.1) greater and diastolic pressures 0.6 mmHg (95% CI: -0.05 - 1.19) greater than nondrinkers. Men who drank more than 5 drinks per day had systolic pressures 8 mmHg (95% CI: 6.7 - 9.2) greater and diastolic pressures 4 mmHg (95% CI: 3.4 - 5.2) greater than nondrinkers. Women who drank 2 or more drinks per day had higher systolic 2 mmHg (95% CI: 1.0 - 3.2) and diastolic blood pressures 1 mmHg (95% CI: 0.4 - 1.9) than nondrinkers (Figure 2).

In every town and survey year, we observed a positive relation between alcohol consumption and blood pressure in both men and women. The relation

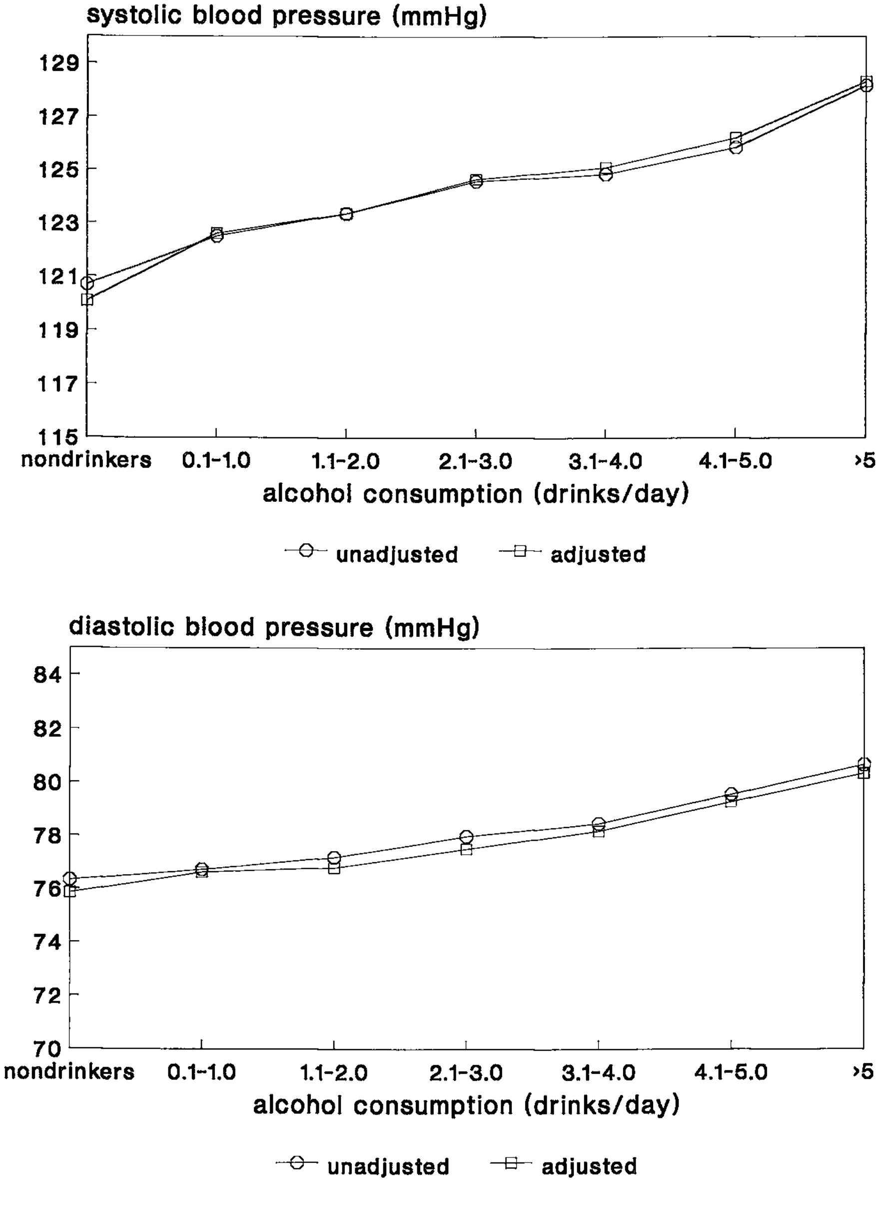

Figure 1. Mean systolic and diastolic blood pressure unadjusted and adjusted for town (three categories), year (four categories), age (four categories), smoking (two categories), and body mass index (continuous) by categories of alcohol consumption for men (n=12,609) age 20-59 in the Monitoring Project on Cardiovascular risk Factors, 1987-1990.

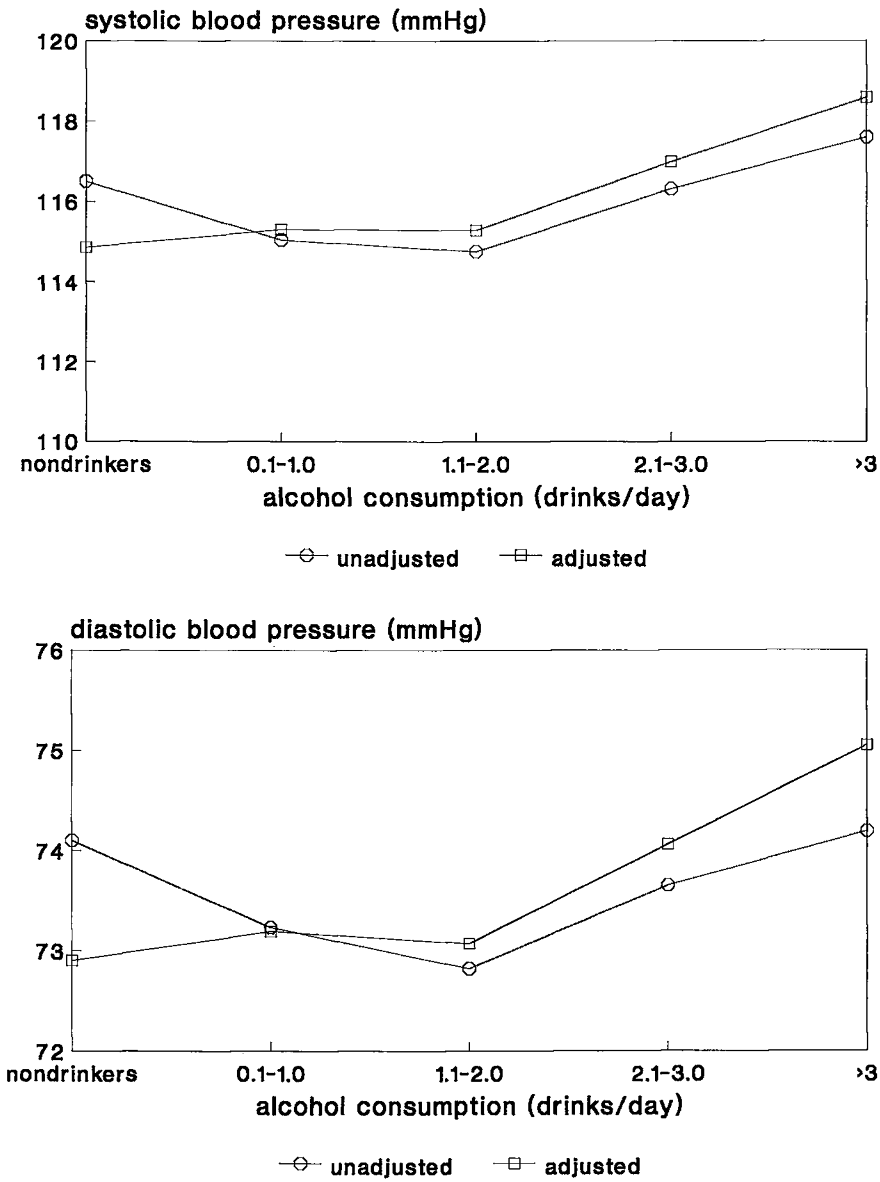

Figure 2. Mean systolic and diastolic blood pressure unadjusted and adjusted for town (three categories), year (four categories), age (four categories), smoking (two categories), and body mass index (continuous) by categories of alcohol consumption for women (n=14,010) aged 20-59 in the Monitoring Project on Cardiovascular Risk Factors, 1987-1990.

between alcohol consumption and blood pressure did not differ much between the categories of body mass index and physical activity during leisure time (Table 1). In the different categories of educational level, the increase in blood pressure per glass of alcoholic drink was of the same order of magnitude. In women, however, we observed a somewhat weaker relation between alcohol consumption and diastolic blood pressure in the middle category of education than in the other categories. Among coffee drinkers, the relation between alcohol consumption and blood pressure was only consistent for drinkers of regular coffee. In the other categories of coffee consumption, the relation was less clear, possibly owing to small numbers. In both men and women, physical activity during leisure time, education, or coffee intake did not confound the relation between alcohol consumption and blood pressure.

We observed a stronger relation between alcohol consumption and systolic blood pressure in older than in younger men (Tables 2 and 3). This pattern did not hold for women. The relation between alcohol consumption and diastolic blood pressure did not differ much by age category for men or for women. In both men and women, we observed a stronger relation between alcohol consumption and blood pressure in smokers than in nonsmokers (Tables 4 and 5).

The correlation coefficients for reproducibility were 0.87 for alcohol consumption, 0.73 for systolic blood pressure, and 0.63 for diastolic blood pressure for both men and women. For men, the adjusted observed correlation between alcohol consumption and systolic blood pressure was 0.12, and the unattenuated correlation was 0.13. For women, these correlations were 0.045 and 0.051, respectively. For diastolic blood pressure, these correlations were 0.11 and 0.12 in men and 0.027 and 0.032 in women, respectively.

DISCUSSION

The results of the present study were based on self-reported information about alcohol consumption and on the average of two blood pressure measurements measured at one occasion. Therefore, we estimated the unattenuated correlation between alcohol intake and blood pressure. The unattenuated correlations did not increase very much after taking the within-person variation into account because the correlations between the first and second measurements were high.

Table 1. Regression coefficients (B) and standard deviation (SD) of the relation between alcohol consumption (drinks/day) and blood pressure (mmHg) by strata of body mass index, education, physical activity and coffee consumption and the overall regression coefficient and standard deviation.

variable	men				women			
	Systolic blood pressure		Diastolic blood pressure		Systolic blood pressure		Diastolic blood pressure	
	B	SD	B	SD	B	SD	B	SD
Body mass index[1]								
≤ 25 kg/m[2]	0.95	0.09	0.54	0.06	0.64	0.13	0.30	0.09
> 25 kg/m[2]	0.90	0.09	0.60	0.06	0.52	0.21	0.28	0.13
Education[2]								
low	0.93	0.08	0.61	0.05	0.80	0.14	0.49	0.09
medium	0.97	0.14	0.53	0.10	0.40	0.25	0.06	0.17
high	0.80	0.15	0.47	0.10	1.01	0.25	0.32	0.17
Physical activity[2]								
inactive	0.88	0.10	0.59	0.07	0.60	0.17	0.34	0.12
active	0.92	0.08	0.53	0.06	0.70	0.14	0.32	0.09
Coffee consumption[2]								
no coffee	0.35	0.27	0.27	0.18	1.73	0.49	0.65	0.36
regular	0.90	0.07	0.56	0.05	0.58	0.12	0.32	0.08
decaffeinated	0.91	0.33	0.40	0.23	0.20	0.44	0.05	0.30
other types	1.26	0.46	0.99	0.31	1.22	0.59	0.60	0.39
Overall[2]	0.90	0.06	0.55	0.04	0.67	0.11	0.33	0.07
Overall[4]	0.89	0.06	0.56	0.04	0.70	0.11	0.38	0.07

[1] adjusted for age, town, survey year, smoking
[2] adjusted for age, town, survey year, smoking, body mass index.
[3] adjusted for age, town, survey year, smoking, body mass index, coffee consumption, physical activity, education.

Table 2. Difference in mean blood pressure (mmHg)[1] (and standard error) between each category of alcohol consumption (drinks/day) and nondrinkers by 10-year age group for men (the average blood pressure[1] in nondrinkers in each age stratum is given in bold type)

	0	0.1-1.0	1.1-2.0	2.1-3.0	3.1-4.0	4.1-5.0	>5
Age (years)							
Number	919	4,860	2,824	1,891	807	607	697
SBP							
20-29	**117.3**	3.3 (0.8)	4.2 (0.9)	5.1 (1.0)	6.3 (1.3)	3.4 (1.4)	5.3 (1.5)
30-39	**118.2**	1.8 (0.9)	1.9 (0.9)	3.1 (1.0)	4.5 (1.1)	5.8 (1.2)	5.9 (1.2)
40-49	**118.4**	3.3 (0.9)	3.7 (0.9)	6.1 (1.0)	5.3 (1.1)	7.1 (1.2)	9.8 (1.1)
50-59	**125.3**	0.9 (1.0)	2.8 (1.1)	3.2 (1.2)	3.5 (1.5)	5.9 (1.7)	8.9 (1.5)
DBP							
20-29	**72.1**	0.6 (0.6)	0.2 (0.7)	1.0 (0.7)	3.2 (1.0)	1.1 (1.1)	2.7 (1.1)
30-39	**74.7**	0.1 (0.7)	0.4 (0.7)	1.1 (0.7)	2.0 (0.9)	4.1 (0.9)	3.5 (0.9)
40-49	**76.9**	1.4 (0.6)	1.2 (0.7)	2.5 (0.7)	2.5 (0.8)	3.3 (0.9)	5.3 (0.8)
50-59	**79.2**	0.3 (0.6)	1.3 (0.7)	1.2 (0.7)	1.4 (0.9)	3.5 (1.0)	4.7 (0.9)

SBP = systolic blood pressure
DBP = diastolic blood pressure
[1] adjusted for town, survey year, smoking, body mass index.

In the literature, there is no agreement on the shape of the association between alcohol consumption and blood pressure (14-16). Specifically, at the lower end of alcohol consumption it is not clear whether or not a linear relation exists. Most studies have reported elevated blood pressure in subjects consuming 3 or more glasses per day, in comparison with nondrinkers. Adjustment for age, smoking, and body mass index has been found to affect the shape of the association between alcohol consumption and blood pressure (17).

Women in this population drank more wine and less beer and spirits, which could explain the different findings for men and women. Some studies have suggested that the blood pressure elevating effect of wine is lower than the

Table 3. Difference in mean blood pressure (mmHg)[1] (and standard error) between each category of alcohol consumption (drinks/day) and nondrinkers by 10-year age group for women (the average blood pressure[1] in nondrinkers in each age stratum is given in bold type)

	0	0.1-1.0	1.1-2.0	2.1-3.0	> 3
AGE (years)					
number	2,638	8,390	1,879	684	417
SBP					
20-29	**110.7**	0.7 (0.5)	0.9 (0.5)	1.9 (0.8)	-0.7 (1.4)
30-39	**110.3**	0.6 (0.5)	0.8 (0.6)	1.0 (0.9)	3.4 (1.1)
40-49	**115.6**	-0.03 (0.6)	0.3 (0.8)	2.5 (1.0)	4.6 (1.2)
50-59	**112.5**	0.4 (0.7)	-0.3 (0.9)	3.4 (1.4)	3.9 (1.7)
DBP					
20-29	**69.3**	0.5 (0.4)	0.6 (0.6)	1.1 (1.1)	1.1 (1.4)
30-39	**70.8**	0.2 (0.4)	0.02 (0.5)	0.4 (0.7)	2.8 (0.8)
40-49	**74.2**	0.2 (0.4)	0.2 (0.5)	1.2 (0.7)	2.1 (0.8)
50-59	**77.0**	0.3 (0.4)	0.0 (0.5)	2.1 (0.8)	1.6 (1.0)

SBP = systolic blood pressure
DBP = diastolic blood pressure
[1] adjusted for town, survey year, smoking, body mass index.

effect of beer and spirits (2,3). Two randomized controlled studies have shown a direct effect of alcohol consumption on blood pressure (17). The mechanisms by which alcohol consumption may lead to elevated blood pressure are still uncertain, however.

Many studies have reported conflicting results on the association between alcohol intake and blood pressure in different age categories. Some studies have reported stronger associations between alcohol consumption and blood pressure in younger subjects, (10,18-20) and other studies have observed these associations in older subjects (2,3,9,21-23).

To our knowledge, very few studies have investigated the possibility of a modifying effect of smoking on the blood pressure-alcohol association. In the

Table 4. Difference in mean blood pressure (mmHg)[1] (and standard error) between each category of alcohol consumption (drinks/day) and nondrinkers for smoking and nonsmoking men (the average blood pressure[1] in nondrinkers in each stratum of smoking is given in bold type)

	0	0.1-1.0	1.1-2.0	2.1-3.0	3.1-4.0	4.1-5.0	> 5
Smoking							
number	326	1,652	1,104	900	408	330	425
SBP	**118.0**	3.5 (0.8)	4.9 (0.8)	6.5 (0.8)	7.2 (1.0)	7.7 (1.0)	10.2 (1.0)
DBP	**74.2**	1.5 (0.5)	1.8 (0.6)	2.6 (0.6)	3.8 (0.7)	4.9 (0.7)	5.6 (0.7)
Nonsmoking							
number	593	3210	1720	991	399	279	272
SBP	**121.2**	1.6 (0.6)	2.1 (0.6)	3.1 (0.7)	3.1 (0.8)	4.9 (0.9)	6.0 (0.9)
DBP	**77.0**	0.1 (0.4)	0.2 (0.4)	0.9 (0.5)	1.0 (0.6)	2.0 (0.7)	3.3 (0.7)

SBP = systolic blood pressure
DBP = diastolic blood pressure
[1] adjusted for age, town, survey year, body mass index.

Framingham Study lower blood pressure levels were observed in smokers compared with nonsmokers, but this seemed to be due to the lower body weights (6).In an Australian study of men, mean diastolic blood pressure was lower in smokers compared with nonsmokers even after adjustment for age and body mass index (24). In the Nurses' Health Study, risks for hypertension did not differ between smokers and nonsmokers (18). The observed interaction between alcohol consumption and smoking in the present study for both men and women has also been found in the MONICA Augsburg Survey (10). In this study, it was observed that effect modification by smoking was stronger in men than in women. A possible explanation for the interaction of smoking on the association between alcohol intake and blood pressure may be that smoking is associated with a change in pattern of body fat distribution, which results in a higher waist-to-hip circumference ratio in smokers compared with nonsmokers (25). A higher waist-to-hip circumference ratio is correlated with hyperinsulinemia and hypertension (26). It is possible that smoking influences blood pressure by changing the body fat distribution (27).

Table 5. Difference in mean blood pressure (mmHg)[1] (and standard error) between each category of alcohol consumption (drinks/day) and nondrinkers for smoking and nonsmoking women (the average blood pressure[1] in nondrinkers in each stratum of smoking is given in bold type)

	0	0.1-1.0	1.1-2.0	2.1-3.0	>3
Smoking					
number	900	3,092	952	394	297
SBP	**114.0**	0.8 (0.5)	1.0 (0.6)	3.1 (0.8)	4.3 (0.9)
DBP	**71.9**	0.7 (0.3)	0.7 (0.4)	1.6 (0.5)	2.8 (0.6)
Nonsmoking					
number	1,738	5,300	927	290	120
SBP	**115.4**	0.3 (0.4)	0.1 (0.5)	1.2 (0.8)	3.1 (1.2)
DBP	**73.6**	0.1 (0.2)	-0.2 (0.4)	0.9 (0.6)	1.2 (0.8)

SBP = systolic blood pressure
DBP = diastolic blood pressure
[1] adjusted for age, town, survey year, body mass index.

Several studies investigated the influence of body mass index on the alcohol-blood pressure association but did not draw clear conclusions (1,24). In the present study, we did not observe an interaction between alcohol consumption and body mass index. This finding differs from those of the Nurses' Health Study, (18) in which a stronger association between the risk for hypertension and alcohol consumption was observed for women with a body mass index <29 kg per m^2 compared with women with a body mass index ≥29 kg per m^2.

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DIETARY CALCIUM, POTASSIUM, MAGNESIUM AND BLOOD PRESSURE IN 20,921 MEN AND WOMEN AGED 20-59 YEARS IN THE NETHERLANDS

ABSTRACT

The relation between blood pressure and dietary calcium, potassium and magnesium and the combined effect of these minerals on blood pressure was studied in 20,921 Dutch men and women aged 20-59 years. Food intake was measured by a food frequency questionnaire. After adjustment for age, body mass index, alcohol and energy intake an inverse association was observed between blood pressure and dietary potassium, and magnesium, in both men and women. Dietary calcium was inversely related to systolic blood pressure in women and with diastolic blood pressure in both men and women. The relation between magnesium intake and blood pressure was stronger than those between blood pressure and intakes of potassium and calcium. Men and women who consumed a diet with intakes in the upper tertiles of all three minerals had a lower systolic and diastolic blood pressure compared to those who had intakes in the lower tertiles (men: SBP: -1.7 ± 0.7 mmHg, DBP: -2.1 ± 0.4 mmHg, women: SBP: -2.0 ± 0.7 mmHg, DBP: -1.7 ± 0.4 mmHg). These results suggest that diets rich in calcium, potassium and magnesium are associated with lower blood pressure.

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Submitted

INTRODUCTION

In most cross-sectional studies an inverse association between dietary calcium and blood pressure has been reported (1,2). However, the results of prospective studies were inconsistent (3,4) and the majority of intervention studies have not supported the inverse association between calcium supplementation and blood pressure (1,5). Some observational studies have observed an inverse association between blood pressure and dietary potassium (6-11) while others have not observed such an association (4,12-15). Intervention studies have suggested that potassium supplementation may be an effective therapy for producing a modest decrease in blood pressure (16), particularly in patients who consume large quantities of sodium (17). In most observational studies an inverse relation between dietary magnesium and blood pressure has been observed (4,8,14,15,18). However, the results of intervention studies were inconsistent (1). In observational studies the intake of calcium, potassium and magnesium are highly correlated. Therefore, in the present cross-sectional study besides the relation between blood pressure and dietary calcium, potassium and magnesium also the combined effect of the intake of the three minerals on blood pressure has been investigated in more than 20,000 men and women aged 20-59 years in The Netherlands.

METHODS

The Monitoring Project on Cardiovascular Risk Factors is a screening project which has been performed between 1987 and 1991. The project is carried out in basic health services in Amsterdam, Doetinchem and Maastricht. These towns are located in different parts of the Netherlands: Amsterdam, the capital city in the west; Doetinchem, a small town in the east and Maastricht a town in the south. Each year a new random sample of men and women aged 20-59 years was selected in each city. The random sample was selected from the civil registry in each town. To obtain equal numbers in each age category, the sample was stratified according to gender and five year age classes. In Doetinchem and Maastricht 400 persons were selected per stratum, in Amsterdam 500 because of the lower response in Amsterdam. The overall response rate was about 50 per cent for men and 57 per cent for women. From 1987 till 1991 about 36.000 men and women were examined.

In this study blood pressure, height and weight were measured and blood was taken for total and high density lipoprotein cholesterol determination. Blood pressure was measured with the subject in sitting position using a random zero sphygmomanometer. The measurements were carried out by trained technicians who were all instructed by the same physician. The cuff (size 12 x 23 cm) was applied to the left upper arm. In about 1.5 per cent of the subjects a larger (15 x 33 cm) or a smaller (9 x 18 cm) cuff was used when appropriate. Systolic blood pressure was recorded at the appearance of sounds (first-phase Korotkoff) and the diastolic blood pressure was recorded at the disappearance of sounds (fifth-phase Korotkoff). After the first measurement heart rate was measured for 30 seconds followed by a second blood pressure measurement. For the analyses the average of the two blood pressure measurements was used. Weight was measured in subjects without shoes and wearing indoor clothing and after subjects emptied their pockets. Weight was recorded to the nearest 0.1 kg and height to the nearest 0.5 cm. The subjects stood upright against the wall with the feet at a 45° angle. Body Mass Index (BMI) was calculated as weight/height^2 (kg/m^2). The subjects were asked to fill out a questionnaire from which information was obtained about educational level, current medication use, being on a prescribed diet, use of alcohol and of calcium supplements.

The usual dietary intake was assessed by using a short (70 food items) self-administered semi-quantitative food frequency questionnaire (19). The questionnaire was constructed to be able to assess the intake of energy and nutrients of interest in cardiovascular disease epidemiology. The food frequency questionnaire was validated in a subsample of 203 subjects. In this sample the food and nutrient intake was assessed both by the food frequency questionnaire and a cross-check dietary history in which information about the food intake was obtained from the last 14 days. The cross-check dietary history was carried out in 1989 by two experienced dieticians. The nutrient content of the diet was calculated using the computerized version of the Netherlands (NEVO) food table, containing about 1300 foods (20). The magnesium content of the diet was collected from different sources (21). The reproducibility of the food frequency questionnaire was assessed by repeating the administration of this questionnaire with a one-year interval in 925 subjects.

Subjects (n=2601) treated for hypertension either by medication or prescribed diet were excluded from the analyses. Pregnant women (n=306) were also excluded from the analyses. Subjects who were vegetarian (n=1046), macrobiotic (n=127), antroposophic (n=57) or seventh-Day adventists (n=48) were also excluded from the analyses. This was done because the food items (such as potatoes, rice and legumes) used by these subjects were not included in the food frequency list. Subjects who have 1 or more missing food items in the food frequency list were excluded from the analysis (n=3,266) because it was not possible to estimate their nutrient intake accurately. In order to be able to exclude subjects who overreport or underreport their energy intake the basal metabolic rate (BMR) was estimated from WHO equations (22). In the present study subjects with an energy intake of less than 1 times BMR (n=1570) or an energy intake of more than 2.1 times BMR for men or 1.82 times for women (n=7652) were excluded from the analyses. These limits were chosen because it is unlikely that an energy intake below the lower limit and above the upper limit are real. After excluding these subjects 11,679 men and 9,224 women were left for analysis. In the reproducibility study pregnant women and subjects treated for hypertension either by medication or prescribed diet were excluded from the analyses. In the reproducibility study 834 subjects were left for analysis.

Age was divided in 10-year age classes. Alcohol consumption was divided into three categories: 0 g/day, >0-≤20 g/day and >20 g/day. Calcium supplementation was divided in users and non-users. The cut-off points for low and high mineral intake were based on tertiles. For men: tertile cut-off points were 1023 and 1393 mg/day for calcium, 3923 and 4673 mg/day for potassium and 384 and 469 mg/day for magnesium. For women: tertile cut-off points were 899 and 1229 mg/day for calcium, 3417 and 4070 mg/day for potassium and 327 and 390 mg/day for magnesium. Mineral intake was divided in 8 categories which were made of all combinations of tertiles of the three elements.

A non-response study was performed among 1620 subjects who had been invited for the first time between august and december 1991 (23). In april/may 1992 they were approached for a second time by telephone (75 per cent) or those who did not have a telephone by mail (25 per cent). Information of 61 % of the non-participants could be obtained, 23 % could not be reached and 16 % refused to participate. Information included educational level, use of alcohol, smoking habits, weight and height.

Statistical analysis

Pearson correlation coefficients between the nutrients were calculated to diagnose potential problems with collinearity. The food frequency questionnaire was compared with a dietary history. Pearson correlation coefficients were used to compare the intake of calcium, potassium and magnesium from the food frequency questionnaire with the intake from the dietary history in 203 subjects. Pearson correlation coefficients were also calculated as indicators for the reproducibility of the intake of calcium, potassium, magnesium and the blood pressure measurement assessed in 1989 and 1991.

Regression analysis was used to examine the association between blood pressure and dietary calcium, potassium and magnesium. The minerals were entered separately in the model because of multi-collinearity. The analyses were adjusted for age, town, survey year, body mass index, alcohol and energy intake. Because dietary magnesium and fiber were strongly correlated, the effect of dietary fiber on the association between blood pressure and magnesium was also studied. Body mass index and energy intake were entered in the model as continuous variables. Dummy variables for the categories of age, town, survey year and alcohol intake were entered to the model. This was done because mean blood pressure was different between the towns and survey years. The relation between blood pressure and age was not linear and alcohol intake showed a skewed distribution. These categories were chosen because previously we observed that blood pressure increased at an intake of about 20 g/day in both men and women (24). The reference categories were for age: 20-29 years, town: Amsterdam, survey year: 1987, alcohol consumption: non-drinkers.

Dietary calcium, potassium and magnesium were strongly correlated with each other. Therefore, the combined effect of these three minerals on blood pressure was studied. To estimate the difference in systolic and diastolic blood pressure between persons consuming a diet high in calcium, potassium and magnesium compared to persons consuming a diet low in these minerals regression analysis was also used. Seven dummy variables for the combination of tertiles of the high mineral intake were entered in the regression model and compared to the combination of the lower tertiles. Regression analysis was also used to estimate the difference in systolic and diastolic blood pressure in the category calcium supplementation users compared with the category never users.

RESULTS

Table 1 shows mean blood pressure, body mass index, age, energy, alcohol and mineral intake in men and women aged 20-59 years. Average body mass index was about the same for both men and women. Blood pressure and energy, alcohol and mineral intake were higher in men than in women.

Table 1. Blood pressure, body mass index, age, energy, alcohol and mineral intake among men and women aged 20-59 years in the Monitoring Project on Cardiovascular Disease Risk Factors.

Variable	Men	Women
	Mean (sd)	Mean (sd)
N	11,697	9,224
systolic blood pressure (mmHg)	123.7 (13.4)	116.5 (14.7)
diastolic blood pressure (mmHg)	77.9 (9.8)	74.3 (9.8)
body mass index(kg/m^2)	25.3 (3.2)	25.2 (4.1)
age (years)	41.4 (10.7)	41.5 (11.2)
energy (Kcal/day)	2793 (508)	2088 (317)
alcohol (g/day)[1]	20 (17)	14 (11)
calcium (mg/day)	1237 (441)	1082 (374)
potassium (mg/day)	4332 (892)	3761 (746)
magnesium (mg/day)	429 (99)	359 (74)

[1] mean alcohol intake among alcohol users.

The correlation coefficients between calcium and potassium intake were 0.64 in men and 0.65 in women, 0.53 in men and 0.54 in women for calcium and magnesium intake and 0.84 in both men and women for potassium and magnesium intake. The correlation coefficient between the food frequency questionnaire and the dietary history data varied in men between 0.47 for potassium and 0.64 for magnesium. In women the coefficients varied between 0.55 for calcium and 0.72 for magnesium. The correlation coefficient between the two replicate measurements varied in men and women between 0.63 and 0.76 for calcium, potassium, magnesium, systolic and diastolic blood pressure. All these coefficients were significant.

For both men and women an inverse significant association was observed between blood pressure and dietary potassium and magnesium (table 2). In men, the association between systolic blood pressure and dietary calcium was not significant while in women systolic blood pressure was significantly inversely associated with dietary calcium. In both men and women the association between diastolic blood pressure and dietary calcium was significant.

Table 2. Regression coefficients[1] (95% confidence intervals between brackets) for the relation between blood pressure (mmHg) and calcium, potassium and magnesium (mg/day) in 20,921 men and women aged 20-59 years.

	Men	Women
Systolic blood pressure		
Calcium	-0.0003 (-0.0009, 0.0003)	-0.0010 (-0.0018, 0.0002)
Potassium	-0.0008 (-0.0011, -0.0005)	-0.0006 (-0.0010, -0.0002)
Magnesium	-0.0081 (-0.0011, -0.0050)	-0.0095 (-0.0140, -0.0050)
Diastolic blood pressure		
Calcium	-0.0007 (-0.0011, -0.0003)	-0.0006 (-0.0011, -0.0001)
Potassium	-0.0007 (-0.0008, -0.0004)	-0.0005 (-0.0008, -0.0002)
Magnesium	-0.0069 (-0.0090, -0.0048)	-0.0068 (-0.0098, -0.0038)

[1] adjusted for age, town, survey year, body mass index, alcohol and energy intake.

The association between blood pressure and dietary potassium and magnesium was stronger than the association between blood pressure and dietary calcium. Both systolic and diastolic blood pressure were inversely related with dietary fiber but after adjustment for dietary magnesium this association disappeared. When subjects who overreported or underreported their energy intake were not excluded from the analyses the associations between blood pressure and dietary calcium, potassium and magnesium were weaker except for the relation between systolic blood pressure and dietary calcium in men (regression coefficient = -0.0005; 95% CI = -0.0010, 0).

In both men and women mean systolic and diastolic blood pressure were significantly lower in the upper tertiles of calcium, potassium and magnesium intake compared to those in the lower tertiles (figure 1 and 2). The difference in both systolic and diastolic blood pressure between the two categories was about 2 mmHg. In the category with high mineral intake the average intake per

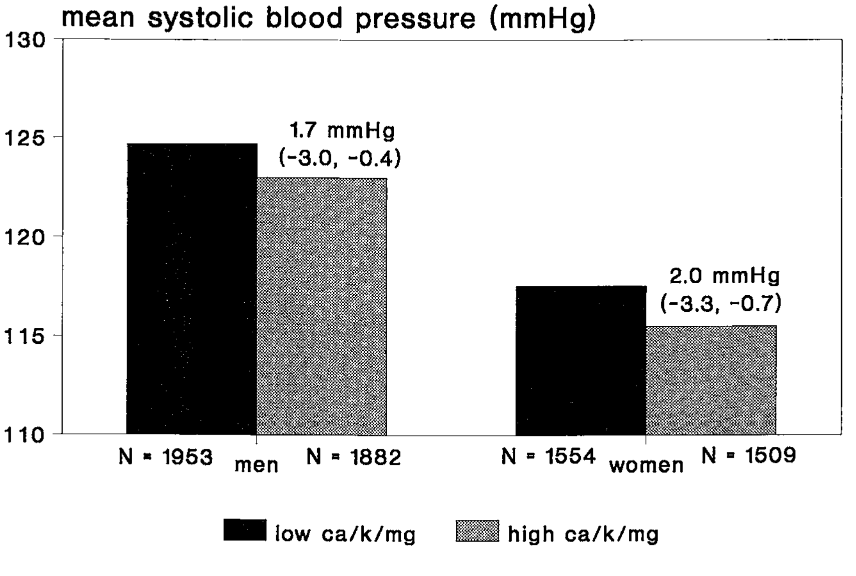

Figure 1. Mean systolic blood pressure adjusted for age, town, survey year, body mass index, alcohol and energy intake in persons with respectively low and high intakes of calcium, potassium and magnesium. Difference in systolic blood pressure between the two categories (mean and between the brackets 95% confidence interval of the regression coefficient between brackets).

day was 1800 mg calcium, 5500 mg potassium and 550 mg magnesium in men and 1600 mg calcium, 4800 mg potassium and 450 mg magnesium in women. The average intake per day in the reference category was 740 mg calcium, 3200 mg potassium and 300 mg magnesium in men and 650 mg calcium, 2800 mg potassium and 265 mg magnesium in women. Mean blood pressure in the other combinations of tertiles did not differ significantly from the reference category, except diastolic blood pressure in the category low calcium, low potassium and high magnesium in women. For most combinations the number of subjects was relatively small.

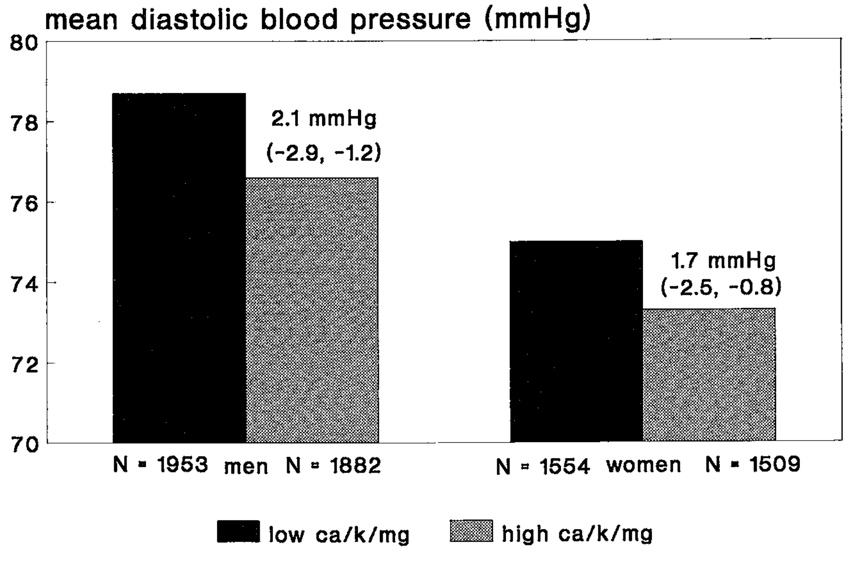

Figure 2. Mean diastolic blood pressure adjusted for age, town, survey year, body mass Index, alcohol and energy intake in persons with respectively low and high intakes of calcium, potassium and magnesium. Difference in diastolic blood pressure between the two categories (mean and between brackets 95% confidence interval of the regression coefficient).

The percentage of subjects using calcium supplementation was 2.6 % in men and 9.5 % in women. Only in women who used calcium supplements systolic blood pressure was significantly lower compared to women who never used supplements (table 3). In both men and women diastolic blood pressure did not differ significantly between users and non-users of calcium supplements.

Table 3. Differences in mean blood pressure[1] (95% confidence interval between brackets) between calcium supplementation users (299 men and 872 women) and never users (11,395 men and 8,351 women)

	Men	Women
	Mean difference	mean difference
systolic blood pressure (mmHg)	-0.77 (-2.28, 0.74)	-1.40 (-2.38, -0.51)
diastolic blood pressure (mmHg)	-0.05 (-1.08, 1.00)	-0.26 (-0.76, 0.49)

[1] adjusted for age, town, survey year, body mass index, dietary calcium, alcohol and energy intake

DISCUSSION

In the present study inverse associations were observed between blood pressure and dietary potassium and magnesium with the exception of calcium. The strongest association was observed for dietary magnesium. Also the combined effect of these minerals was studied because it was not possible to study the independent linear associations between dietary potassium, magnesium and calcium and blood pressure because of problems with multi-collinearity. Mean systolic and diastolic blood pressure in the upper tertiles of calcium, potassium and magnesium was about 2 mmHg lower than in the lower tertiles of these minerals in both men and women.

In the present study the response was about 54 %. Educational level is a potential confounder of the relation between mineral intake and blood pressure. However, among responders, adjustment for educational level did not affect the observed relations. Also responders and non-responders were similar with respect to educational level (23). Subjects who were on a prescribed diet or used medication for high blood pressure were excluded because these could have affected the observed associations. Subjects who over or underreported their energy intake were excluded because these biases weakened the associations.

In the present study food intake was measured by a short semi-quantitative food frequency questionnaire because in this large study it was not possible to measure food intake by an extensive dietary survey method. The calcium, potassium and magnesium intake calculated from the food frequency questionnaire were compared with the intake of these minerals estimated with the dietary history method. The correlation coefficients between calcium, potassium and magnesium intake from the food frequency method and the dietary history varied between 0.5 and 0.7. These correlation coefficients are in the same order of magnitude as those observed in other studies in which a food-frequency questionnaire is compared with other dietary assessment methods such as dietary history, food records, 24-hour-recall (25-28). Ideally dietary survey methods with independent error structures should be compared. In all these validation studies this prerequisite is not fulfilled because the usually food intake is estimated by or with the same person. Also the reproducibility of the food frequency questionnaire was assessed. The correlation coefficients varied between 0.6 and 0.8. In other reproducibility studies similar coefficients were obtained (28). These results suggest that the reproducibility and validity of the dietary minerals estimated with the food frequency questionnaire was comparable with those observed by other investigators.

Many cross-sectional studies suggested that calcium intake is inversely associated with blood pressure (1,2). In the present study calcium was inversely related to diastolic blood pressure in men and to both systolic and diastolic blood pressure in women. However, the effect of dietary calcium on blood pressure was small. Blood pressure did not differ between users of calcium supplements and never users with the exception of systolic blood pressure in women, that was lower in users compared with never users. In randomized controlled trials no effect of oral calcium supplementation on blood pressure was observed (5). These results suggest that dietary calcium is not independently associated with blood pressure.

An inverse association between potassium intake and blood pressure has been observed in both men and women in the present study. This association was found in several other observational studies (6-11), however, in some studies such a relationship has not been observed (4, 12-15). A meta-analysis of 19 clinical trials indicated that oral potassium supplementation significantly lowered systolic and diastolic blood pressure (16). The results of both observational studies and clinical trials suggest that potassium supplementation can play a role in blood pressure lowering.

In most observational studies an inverse relation between magnesium intake and blood pressure has been observed (4,8,14,15,18). The results of the present study are in agreement with the results of these studies. The effect of magnesium on blood pressure has also been investigated in clinical trials (1). These trials do not unanimously support a contributing role for magnesium in the regulation of blood pressure. The relation between dietary magnesium and blood pressure needs further study.

In the present study the relation between blood pressure and dietary fiber disappeared after adjustment for dietary magnesium. Also in the Nurses Health Study no association between hypertension and dietary fiber has been observed after adjustment for dietary magnesium (14) while in the US male health professionals follow-up study an inverse association has been observed between hypertension and dietary fiber after adjustment for dietary magnesium (4). In a cross-sectional study in normotensive males an inverse association has been observed between blood pressure and only fruit fiber after adjustment for magnesium (12). A definite statement about the independent effects of dietary fiber and magnesium on blood pressure can therefore not be made.

The results of the present study suggest that men and women consuming a diet high in calcium, potassium and magnesium had 2 mmHg lower systolic and diastolic blood pressure levels compared to men and women consuming a diet low in calcium, potassium and magnesium. A reduction in diastolic blood pressure of 2 mmHg may lead to about 15 % less stroke and about 5 % less coronary heart disease (29). The evidence of observational and supplementation studies suggests that a high intake of potassium and magnesium may be of importance for the prevention of major public health issues such as coronary heart disease and stroke. The intake of calcium seems to be less important because hardly no effect of calcium supplementation on blood pressure was observed. Magnesium intake can be increased by increasing the intake of whole wheat bread, brown rice, legumes, potatoes and nuts. Potassium intake can be increased by increasing the intake of vegetables and fruit. Changes in blood pressure by using this type of a diet are small but can have important health benefits if applied to the population as a whole (30).

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6

BLOOD PRESSURE AND MORTALITY IN 50,000 MEN AND WOMEN IN THE NETHERLANDS DURING A 12-YEAR FOLLOW-UP. THE NETHERLANDS CONSULTATION BUREAU PROJECT ON CARDIOVASCULAR DISEASES.

ABSTRACT

Objective: To study the association between blood pressure and mortality from coronary heart disease (CHD), cerebrovascular accidents (CVA), cardiovascular diseases (CVD) and all causes in the Netherlands. Interaction with obesity and smoking was analyzed as well.
Method: A single blood pressure measurement was obtained in 50,000 men and women aged 30-54 years at baseline. Average follow-up time was 12 years.
Results: Systolic blood pressure levels of 140 mmHg or higher, or diastolic blood pressure levels of 90 mmHg or higher, were strongly associated with total and cardiovascular mortality in both sexes. In men both the absolute and relative risks were higher than in women. In men the population attributable risks were 18% for total mortality, 28% for CHD and 58% for CVA mortality. For women these percentages were 7%, 19% and 27%, respectively. No significant interactions were observed with obesity and smoking. It was estimated that a 6-mmHg decrease in diastolic blood pressure would result in a mortality reduction of about 41% for CVD and 28% for all causes in men, and 29% and 12% in women.
Conclusion: high blood pressure is strongly related to CVD and all cause mortality in both men and women, but the public health impact of blood pressure reduction is higher in men than in women.

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Submitted

INTRODUCTION

In prospective studies blood pressure has been shown to be a strong predictor of mortality from coronary heart disease (CHD), cerebrovascular diseases (CVA), cardiovascular diseases (CVD) and all causes (1-7). Only a few prospective studies included both sexes and analyzed possible differences in the association between blood pressure and mortality in men and women (5,8,9).

In addition to the effect of gender on the association between blood pressure and mortality we also investigated potential effect modification of smoking and obesity on this association. Several prospective studies have reported a more pronounced risk of dying from CHD, CVD and all causes when hypertension was associated with leanness rather than obesity (10-13) while others did not (14-16). In the MRFIT Study and British Regional Heart Survey the risk of CHD was higher among hypertensive men who were smokers compared to nonsmokers (17-18). These results suggest that the relation between hypertension and mortality from all causes, CHD, CVA and CVD may be different between hypertensive smokers and nonsmokers.

This is the first prospective study in The Netherlands in which the relation between blood pressure and cause-specific mortality has been studied in about 50,000 Dutch men and women aged 30-54 years. In this paper the associations between systolic and diastolic blood pressure and mortality from CHD, CVA, CVD and all causes will be reported. Special attention was paid to whether the shape and strength of the association differ between men and women. In addition to the relative risks, the population-attributable risks were calculated for different degrees of hypertension. Also effect modification by obesity and smoking was assessed.

METHODS

The Consultation Bureau Project on Cardiovascular Diseases was carried out in five towns in the Netherlands: Amsterdam, Doetinchem, Maastricht, Leiden and Tilburg. The examinations were carried out between 1974 and 1980. Different birth cohorts were selected in different towns. Names and addresses of the participants were obtained from the municipal registries. The response rate ranged from 70% to 80% (19) The study was aimed at the age group of around 40 years. The age range was 30 to 54 years, about two-third of the respondents was between 35 and 45 years. In this period about 50,000 men and women were examined.

In the present study blood pressure, height and weight were measured and non-fasting blood samples were taken for total cholesterol determination (20). Blood pressure was measured once while subjects were seated with a random zero sphygmomanometer. The measurements were carried out by trained technicians who had received detailed instructions on the use the of the sphygmomanometer. The cuff (size 12 x 23 cm) was applied to the right upper arm. Systolic blood pressure was recorded at the appearance of sounds (first-phase Korotkoff) and the diastolic blood pressure was recorded at the disappearance of sounds (fifth-phase Korotkoff). Weight was measured in subjects without shoes and wearing indoor clothing, after they emptied their pockets. Body mass index was calculated as weight/height (kg/m^2). Serum total cholesterol was determined according to the Huang method (21). The participants filled out a questionnaire in which information was obtained about current smoking habits, current use of medication for high blood pressure, history of hypertension, diabetes mellitus and cardiovascular diseases.

The mortality follow-up was started in 1986 and completed in 1993. The names and addresses of all participants were retrieved from the archives, and entered into the computer. The vital status was obtained from the municipal registry in the town of residence at the time of examination. The follow-up was considered completed when the respondent was identified at his/her present address or if the date of death of the respondent was known. Censor date was the date at which the information was obtained from the municipal registry (for the living) or the date of death. If a person had moved with unknown destination, the date at which the person was not living anymore in the town was used as censor date. From 49,202 of the 50,887 persons examined, the names and addresses were still present in the archives. For 49,018 of these 49,202 persons mortality follow-up was successfully completed. A total of 1319 persons had died during the follow-up. From 1288 the primary cause of death was obtained from the Central Bureau of Statistics, while from 31 persons who died outside the Netherlands, such information could not be obtained. The underlying causes of death were coded according to the 9th Revision of the International Classification of Diseases (ICD). For deaths that had occurred before January 1st 1979 (n=89), the 8th Revision was used. All codes from ICD-8 remained in the same category when defined according to ICD-9. For the present analyses the following subgroups were used CHD ICD-codes 410-414, CVA ICD-codes 430-438, CVD ICD-codes 401-448.

Systolic and diastolic blood pressure were divided in categories of 10 mmHg. Participants were also classified into categories of hypertension according to the WHO guidelines (1). To study effect modification participants were classified into the category normotensive and hypertensive defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or use of antihypertensive medication. The cut-off points for body mass index was 25 kg/m^2. Smoking was dichotomized into smokers and current nonsmokers. Interaction was studied for CHD and CVA mortality and not for combinations of different causes of death.

Statistical analyses

Statistical analysis was carried out using the SAS program (version 6.1). All analyses were carried out separately for men and women. Mortality rates were calculated per category of 10 mmHg systolic and diastolic blood pressure and according to the WHO guidelines and for the normotensives and hypertensives per strata of body mass index and smoking (1). The relative risks were estimated by using the Cox proportional hazards models (22). The results were adjusted for age, serum cholesterol, body mass index and smoking. The Chi-square test for trend was used to test linearity. Age, serum cholesterol and body mass index were entered as continuous variables in the model. Current smoking was dichotomized into smoking and nonsmoking. Nonsmoking was the reference category. Population-attributable risks (PAR) were calculated for the categories of hypertension using normotension as the reference category (23).

RESULTS

Average follow-up time of the persons enrolled in the study was 12 years (Table 1). Average age was 39 years in both men and women. Blood pressure was higher in men than in women. Average body mass index was similar in both sexes. About two-third of the men and about half of the women were smokers. Twice as much women were treated for hypertension than men.

Figure 1 and 2 show that both systolic and diastolic blood pressure were associated with mortality from CHD, CVA, CVD and all causes in both men and women. In men the test for linear trend was significant for both systolic and diastolic blood pressure for all endpoints. In women the test for trend was not significant for the association between systolic blood pressure and CVA mortality and for diastolic blood pressure and CHD mortality. The curves for CVA mortality flatten what may be due to the small number of cases in the systolic blood pressure category ≥170 mmHg. The absolute and relative risks for CHD, CVA, CVD and total mortality were higher in men than in women.

In men mild as well as severe hypertension as defined by the WHO were

Table 1. Average age, follow-up time, blood pressure, body mass index, percentage of cigarette smokers and percentage of users of medication for high blood pressure.

Variable	Men mean (sd)	Women mean (sd)
N	23,389	25,629
age (years)	39.2 (4.3)	39.4 (4.4)
follow-up (years)	11.8 (2.3)	12.0 (2.2)
systolic blood pressure (mmHg)	132.8 (16.2)	126.7 (17.6)
diastolic blood pressure (mmHg)	81.1 (11.2)	77.8 (11.0)
body mass index (kg/m^2)	24.9 (3.0)	24.3 (3.7)
smokers (%)	65.6	47.0
hypertensive (%)*	33.1	23.7
treated hypertensive (%)	6.7	17.2

* hypertension: systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or use of antihypertensive medication

associated with CHD, CVA, CVD and total mortality (Table 2). Also, isolated systolic hypertension was significantly associated with CVA and CVD mortality. In men 28% of CHD mortality, 58% of CVA mortality, 31% of CVD mortality and 18% of total mortality were attributable to elevated blood pressure. In women mild hypertension was related to CVA, CVD and total mortality (Table 3). For severe hypertension increased relative risks were observed for all endpoints but these were only significant for CHD. Isolated systolic hypertension was only related to CHD mortality in women. In women the percent of cause-specific death attributable to elevated blood pressure ranged from 7% (total mortality) to 27% (CVA).

After excluding persons with a history of angina pectoris (n=1205), myocardial infarction (n=26), stroke (n=116) and diabetes mellitus (n=420) at baseline the results remained virtually identical in men. The association between mild hypertension and CVA mortality became weaker in women but remained significant (RR of 3.8 versus RR of 2.6 (95% CI 1.09-6.16)). After excluding

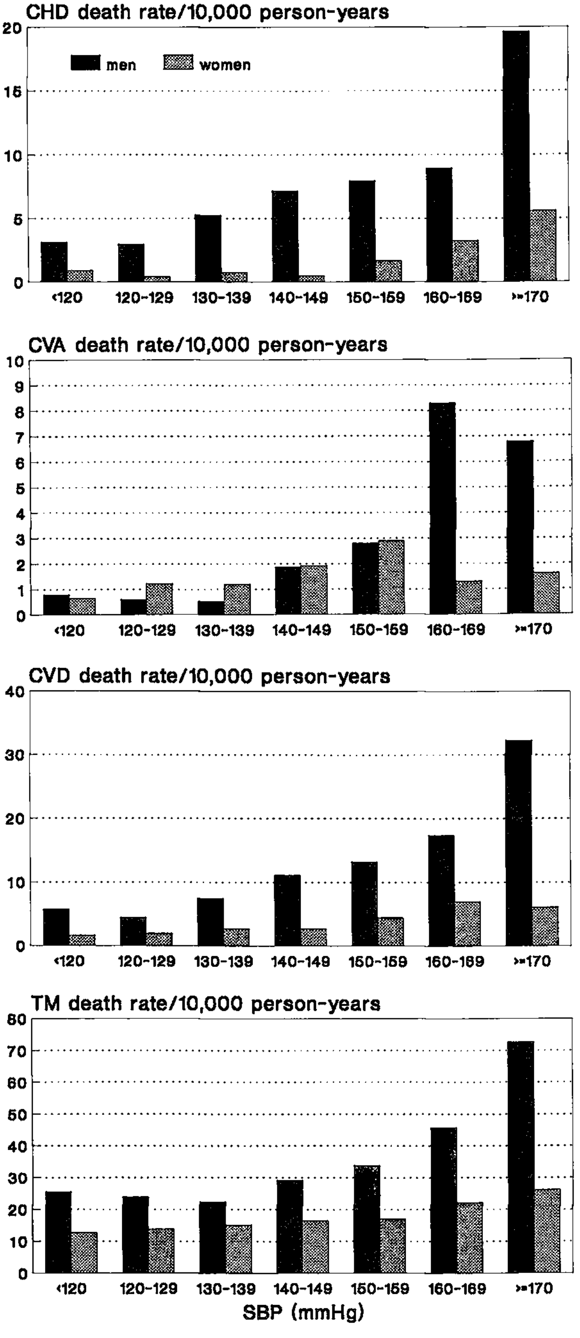

Figure 1. CHD, CVA, CVD and TM (total mortality) death rates per 10,000 person-years by level of systolic blood pressure (SBP) for men and women aged 30-55 years. Adjusted for age, serum cholesterol, body mass index and smoking.

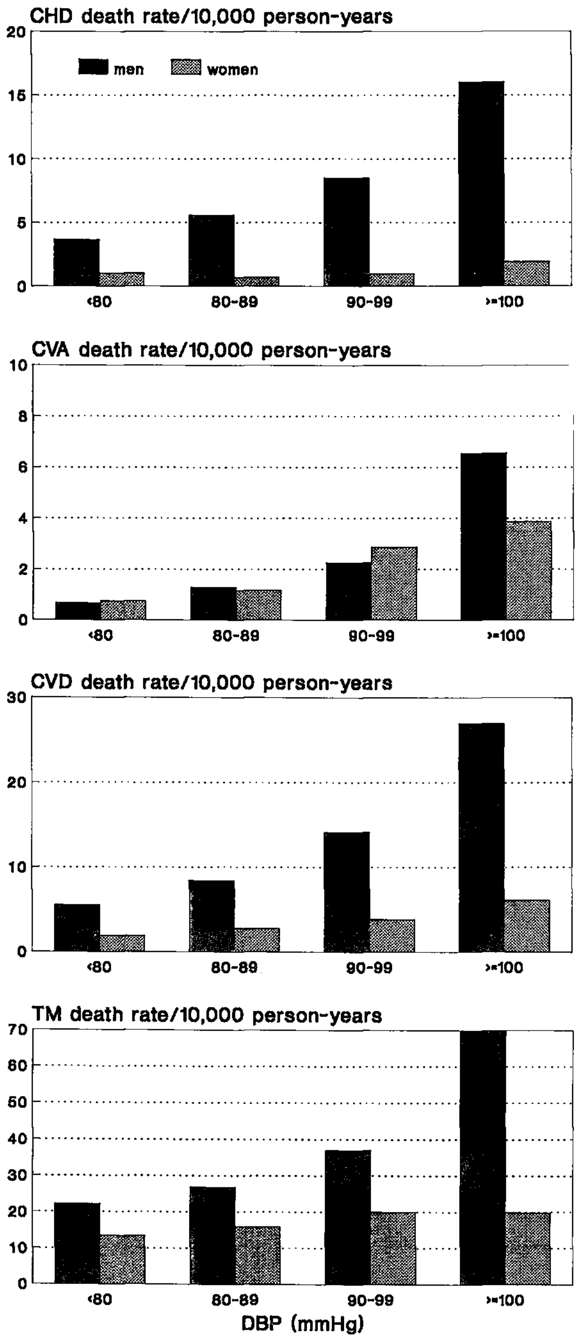

Figure 2. CHD, CVA, CVD and TM (total mortality) death rates per 10,000 person-years by level of diastolic blood pressure (DBP) for men and women aged 30-55 years. Adjusted for age, serum cholesterol, body mass index and smoking.

subjects who were on antihypertensive medication (n=1562) the results remained the same except that in women the association between blood pressure and CVA mortality became weaker. Adjustment for diabetes mellitus, history of angina pectoris, myocardial infarction, stroke and antihypertensive medications did not influence the results appreciably.

The association between hypertension and CHD mortality did not differ between lean and obese men (Figure 3). There was some indication that the relative risk for CHD mortality was higher in lean hypertensive women than in obese hypertensive women. The relative risk for CVA mortality was higher in hypertensive obese men than in hypertensive lean men while the relative risk did not differ between lean and obese hypertensive women. The relative risk for CHD and CVA mortality was somewhat higher in hypertensive nonsmokers than smokers, particularly in women (Figure 4). For both hypertensive men and women the death rates were higher for smokers than for nonsmokers.

DISCUSSION

The results of the present study indicate that both elevated systolic and diastolic blood pressure were related to CHD, CVA, CVD and total mortality in men and women. In women the relative risks were not always significant due to the small number of cases. For total and cause-specific mortality the absolute rate, relative and attributable risks were higher in men than in women. Significant interactions with BMI and smoking were not observed.

In the present study age varied between 30-54 years. However, most men and women were between 35 and 45 years old (n=32,631). Because of this rather homogeneous age distribution it is less meaningful to stratify the analyses by age. In the present study blood pressure values were based on a single measurement. Analysis based on one measurement is likely to lead to an underestimation of the true strength of the relationship between blood pressure and mortality risk. This implies that the true effects are stronger than those observed in the present study (2). It is estimated that the true association between diastolic blood pressure and stroke and CHD risk was about 60% stronger than the association based on a single reading or the average of two consecutive readings at one visit (2,24).

Table 2. Total, CHD, CVA and CVD mortality death rates (per 10,000 person-years) and relative risk(RR) estimates by classification of hypertension by blood pressure level for men.

classification of hypertension[1]	number	#death	Rate	RR[2]	95% CI	PAR
coronary heart disease						
normotension	15,664	82	4.42	1.00		0.28
mild hypertension	4,007	57	11.99	2.18	1.54 - 3.09	
severe hypertension	687	27	33.16	4.74	2.98 - 7.52	
isolated systolic hypertension	2,816	28	8.23	1.52	0.98 - 2.34	
cerebrovascular disease						
normotension	15,735	11	0.59	1.00		0.58
mild hypertension	4,049	15	3.16	5.66	2.54 - 12.63	
severe hypertension	711	3	3.69	6.42	1.73 - 23.87	
isolated systolic hypertension	2,835	9	2.65	4.30	1.76 - 10.48	
cardiovascular disease						
normotension	15,626	120	6.46	1.00		0.31
mild hypertension	3,974	90	18.93	2.53	1.91 - 3.35	
severe hypertension	680	34	41.76	4.69	3.14 - 7.01	
isolated systolic hypertension	2,804	40	11.76	1.54	1.07 - 2.21	
total mortality						
normotension	15,320	441	23,74	1.00		0.18
mild hypertension	3,865	201	42.26	1.70	1.43 - 2.02	
severe hypertension	639	75	92.12	3.47	2.69 - 4.47	
isolated systolic hypertension	2,747	101	29.66	1.14	0.92 - 1.42	

[1] normotension: SBP <140 and DBP <90 mmHg, mild hypertension: SBP 140-180 and/or DBP 90-105 mmHg, severe hypertension: SBP ≥180 and/or DBP ≥105 mmHg, isolated systolic hypertension: SBP ≥140 and DBP <90 mmHg.

[2] adjusted for age, serum cholesterol, body mass index and smoking.

Table 3. Total, CHD, CVA and CVD mortality death rates (per 10,000 person-years) and relative risk(RR) estimates by classification of hypertension by blood pressure level for women.

classification of hypertension[1]	number	#death	Rate	RR[2]	95% CI	PAR
coronary heart disease						
normotension	19,883	19	0.80	1.00		
mild hypertension	2,898	8	2.26	1.59	0.65 - 3.89	0.19
severe hypertension	503	3	4.91	3.15	0.87 - 11.42	
isolated systolic hypertension	2,297	8	2.82	2.41	1.03 - 5.66	
cerebrovascular disease						
normotension	19,882	20	0.84	1.00		
mild hypertension	2,895	11	3.11	3.79	1.74 - 8.24	0.27
severe hypertension	505	1	1.64	2.22	0.29 - 17.10	
isolated systolic hypertension	2,302	3	1.06	1.27	0.37 - 4.35	
cardiovascular disease						
normotension	19,853	49	2.06	1.00		
mild hypertension	2,884	22	6.23	2.21	1.29 - 3.79	0.19
severe hypertension	502	4	6.55	2.33	0.81 - 6.65	
isolated systolic hypertension	2,292	13	4.58	1.76	0.94 - 3.31	
total mortality						
normotension	19,573	337	14.13	1.00		0.07
mild hypertension	2,823	83	23.92	1.36	1.06 - 1.76	
severe hypertension	487	20	32.74	1.78	1.11 - 2.83	
isolated systolic hypertension	2,245	61	21.50	1.24	0.93 - 1.64	

[1] normotension: SBP <140 and DBP <90 mmHg, mild hypertension: SBP 140-180 and/or DBP 90-105 mmHg, severe hypertension: SBP ≥180 and/or DBP ≥105 mmHg, isolated systolic hypertension: SBP ≥140 and DBP <90 mmHg.

[2] adjusted for age, serum cholesterol, body mass index and smoking.

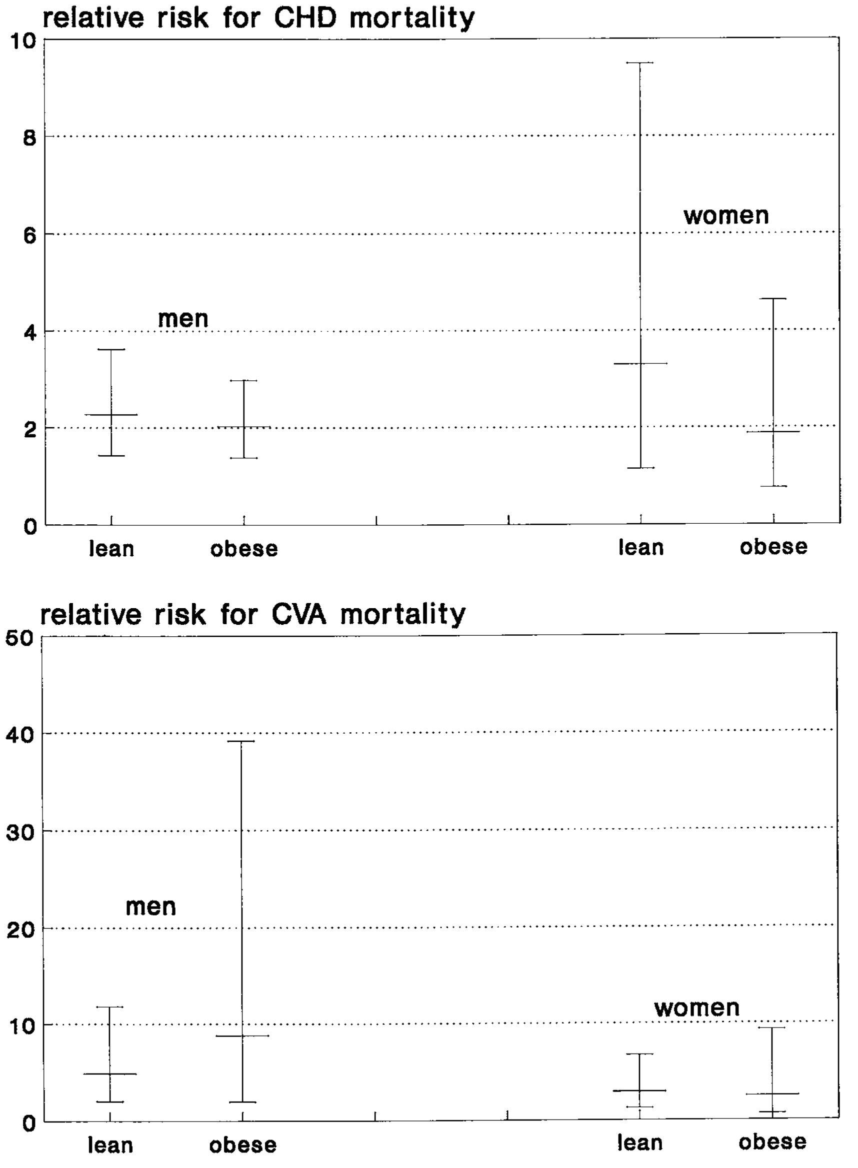

Figure 3. Number of cases and relative risk (RR) for CHD and CVA mortality by degree of obesity (BMI >25 kg/m^2) for hypertensive men and women (between brackets 95% confidence interval). RR adjusted for age, serum cholesterol, body mass index and smoking. Hypertension defined as SPB ≥140 mmHg and/or DBP ≥90 mmHg and/or use of antihypertensive medication.

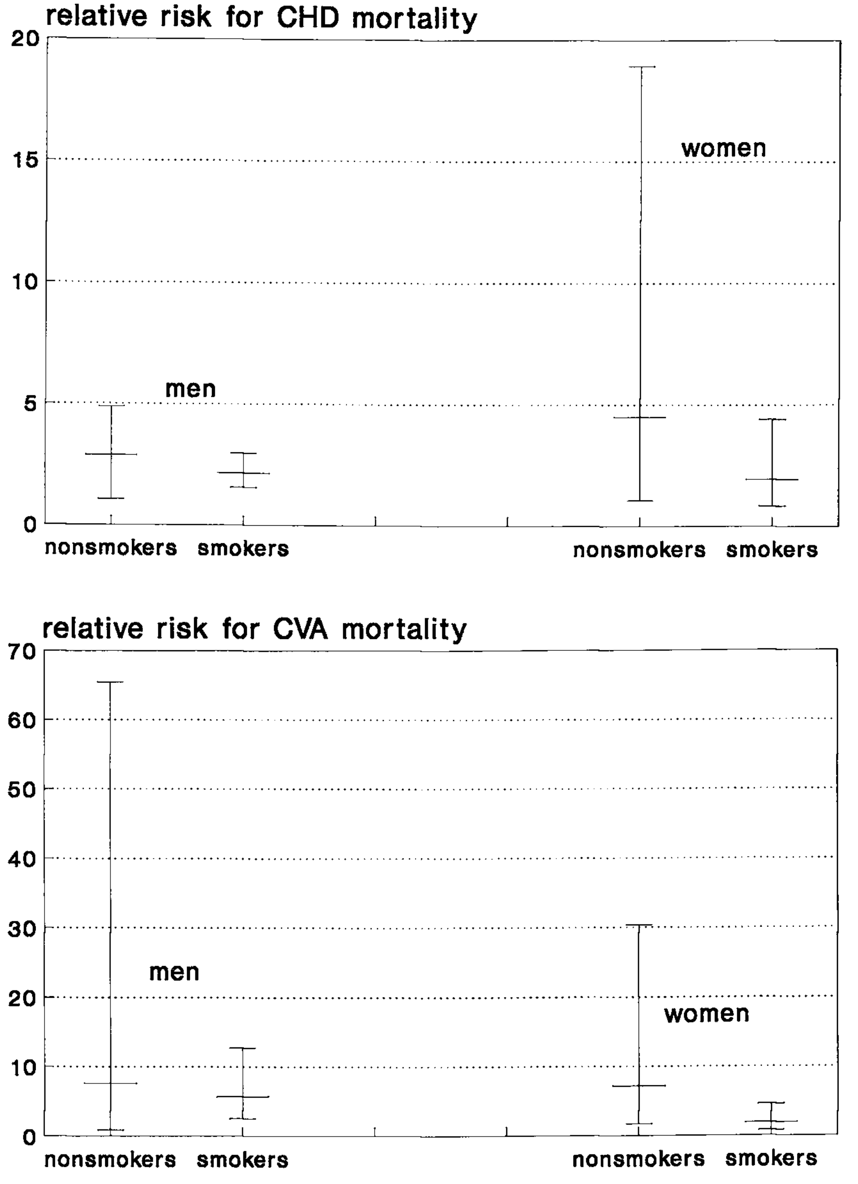

Figure 4. Number of cases and relative risk (RR) for CHD and CVA mortality by smoking status for hypertensive men and women (between brackets 95% confidence interval). RR adjusted for age, serum cholesterol and body mass index. Hypertension defined as SPB ≥140 mmHg and/or DBP ≥90 mmHg and/or use of antihypertensive medication.

From a recent review of US population data, it was concluded that systolic and diastolic blood pressure have a continuous and graded relationship with mortality from CHD, CVA and CVD in both men and women (5). Also in the Copenhagen Heart Study the risk for CHD and CVA mortality increased with increasing quintiles of systolic and diastolic blood pressure in both men and women (9). The Bergen Study from Norway showed exponentional relations. The findings of the present study and those from other studies suggest that the relation between blood pressure and mortality is linear in both sexes.

In the present study both the absolute rate and relative risks were higher in men than in women. Also in other studies the absolute rates were higher in men than in women but in most of these studies the relative risks were about the same for men and women (5,8,9,25). Based on the evidence available it can be concluded that the strength of the association between blood pressure and mortality is similar in men and women.

Isolated systolic hypertension has been mainly evaluated in the elderly (26). However, a few studies have investigated the association been isolated systolic hypertension in subjects less than 60 years (27,28). In the MRFIT study isolated systolic blood pressure was related to CHD, CVA and total mortality. Van den Ban et al. observed a relation between isolated systolic blood pressure and total mortality in both men and women. Because of the differences in definitions of isolated systolic hypertension the absolute and relative risks in different studies can not be compared. However, the present study confirms the association between isolated systolic hypertension and CHD, CVA and total mortality for middle aged men and shows for the first time that isolated hypertension is associated with CHD mortality in women.

The present study indicates that the relative risk for CHD and CVA mortality did not differ between lean and obese hypertensive men and women. However, there was an indication that the association between hypertension and CHD mortality was slightly stronger in lean women than in obese women. Because of the small number of cases the importance of the interaction with obesity is unclear. Some studies observed an excess mortality risk in lean hypertensive men and women (10-13) but others did not (14-16,29). This can partly be due to the fact that the definition of 'lean and obese' and 'hypertension' varies between the different studies and to different age groups studied.

In the MRFIT study and the British Regional Heart Survey it was observed that the risk of CHD mortality was higher in hypertensive smokers than in hypertensive nonsmokers (17,18). However, in the present study there was a tendency that the association was stronger in hypertensive nonsmokers than in hypertensive smokers. The confidence intervals for hypertensive smokers and hypertensive nonsmokers were overlapping and rather wide. Also no plausible mechanism is known why the relationship will be stronger in hypertensive nonsmokers than in hypertensive smokers. Therefore, no conclusion can be drawn whether smoking is an effect modifier or not.

From a public health point of view it is important to know what the effect will be of blood pressure reduction. The potential effect of a diastolic blood pressure reduction of 6 mmHg on CHD and CVA mortality based on a meta-analysis of a large number of prospective studies was for CHD 20-25% and for CVA 35-40% (Table 4) (2,30). Similar results were observed for men in the present study. For women, however, no results from other studies were available. The reduction in CHD mortality was not significant while a significant reduction was observed for CVA, CVD and total mortality. However, the public health impact of blood pressure seems to be lower in women compared with men except for CVA mortality.

Table 4. CHD, CVA, CVD and total mortality reduction as a result of a 6 mmHg reduction in diastolic blood pressure in the present study and the meta-analysis of Collins et al. and MacMahon et al.(2,30).

Cause of death	Collins/MacMahon	Present study	
	men and women[1]	men	women
coronary heart disease	20-25%	39% (28-50%)	7% (0-36%)
cerebrovascular disease	35-40%	49% (26-72%)	46% (20-72%)
cardiovascular disease		41% (32-50%)	29% (11-47%)
total mortality		28% (22-34%)	12% (4-20%)

[1] 96% of the population was men.

The results of the present study suggests that systolic blood pressure above 140 mmHg and diastolic blood pressure above 90 mmHg is associated with CHD, CVA, CVD and total mortality. In men reduction in blood pressure results in a larger reduction in mortality risk than in women. Because the prevalence of hypertension is higher in men than in women and middle aged men are more likely to develop CVD than women, more attention should be paid to treatment of hypertension in men. This is in contrast to current medical practice in the Netherlands in which treatment of hypertension is more common in women than in men.

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7

GENERAL DISCUSSION

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High blood pressure is associated with cardiovascular morbidity and mortality, as well as total mortality, is a major public health problem. From a public health perspective it is firstly, of interest to monitor blood pressure levels and to find out what percentage of mortality from coronary heart disease, cerebrovascular disease, cardiovascular diseases and all causes can be attributed to elevated blood pressure. Secondly, it is interesting to find out what the potential effect of lowering blood pressure on cause-specific and total mortality could be in the population. For primary prevention of hypertension and non-pharmacological treatment, it is important to determine the modifiable factors which influence systolic and diastolic blood pressure. These questions have been studied in the research behind this thesis. The results described are based on data from the following three projects: the Consultation Bureau Heart Project (CB Heart Project), the Coronary Heart Disease Risk Factor Project (RIFOH Project) and the Cardiovascular Risk Factors Monitoring Project (CRFM Project). The investigations presented deal with:

1 trends in blood pressure
2 lifestyle factors and blood pressure
3 blood pressure as a determinant of cause-specific and total mortality.

Trends in blood pressure

Between 1974 and 1986 two screening projects on cardiovascular risk factors were carried out in the Netherlands (Table 1). The first screening project 'Consultation Bureau Heart Project' (CB Heart Project) was carried out between 1974 and 1980. In this period about 30,000 men and women aged 37-43 years were examined. The second screening project the 'Coronary Heart Disease Risk Factor Project' (RIFOH Project) was carried out between 1980-1986. In this period about 80,000 men aged 33-37 years were examined. The aim of these two projects was to identify high-risk persons and to advise them on changes in lifestyle or if necessary start treatment. Between 1987 and 1991 the 'Monitoring Project on Cardiovascular Risk Factors' (CRFM Project) was carried out. The aim of this project was to study levels and trends in major risk factors for cardiovascular diseases. In this period about 36,000 men and women aged 20-59 years were examined. An advantage of these three studies was that blood pressure was measured continuously using standardized methodology. The trends in these three projects are based on average monthly blood pressure measurements. Between 1974 and 1980 an increase in systolic blood pressure of 2 mmHg in men was followed by an insignificant change during the period 1981-1986. Average diastolic blood pressure increased by 4 mmHg between 1974 and 1980, but decreased by the same amount between 1981-1986. Average systolic blood pressure did not change in women aged 37-43 years between 1974-1980, but average diastolic blood pressure increased by 2 mmHg during that period. Between 1987 and 1991, systolic blood pressure decreased by 2 mmHg and diastolic blood pressure increased by 1 mmHg in both men and women.

Table 1. Main trends in systolic and diastolic blood pressure (SBP, DBP), and prevalence and treatment of hypertension in men and women

Project	Survey year	Age (years)	SBP (mmHg)	DBP (mmHg)	Hypertension[1] (% change)	Treatment[2] (% change)
Men						
CB	1974-1980	37-43	+ 2	+ 4	+ 5	+ 13
RIFOH	1981-1986	33-37	0	- 4	0	+ 4
CRFM	1987-1991	20-59	- 2	+ 1	0	- 10
Women						
CB	1974-1980	37-43	0	+ 2	0	0
CRFM	1987-1991	20-59	- 2	+ 1	0	-11

[1] Hypertension= SBP ≥160 mmHg and/or DBP ≥95 mmHg and/or use of antihypertensive medication.
[2] Treatment=proportion of hypertensive subjects who were treated for hypertension.

In all three studies several measures were taken to standardize the blood pressure measurements. A random zero sphygmomanometer was used to reduce observer bias in blood pressure measurement. The random zero sphygmomanometers were regularly calibrated. The same technicians did the blood pressure measurements in the different study periods. They received detailed instructions on how to use the random zero sphygmomanometer (1). They were all instructed by the same physician in same study period. In the CB Heart Project blood pressure was measured after an electrocardiogram was made. The subjects had rested for about 10 minutes. In the RIFOH and CRFM Projects no electrocardiogram was made. In these two projects blood pressure was measured after the technician had checked the questionnaire with the participants. Thus blood pressure was also measured after 5 to 10 minutes rest.

In the CB Heart Project and the RIFOH Project one cuff-size was available, while in the CRFM project three cuff-sizes were used. In the CRFM Project a larger cuff was used for about 1.1% of the subjects and a smaller cuff was used for about 0.4% of the subjects (Chapter 3). The percentage of subjects in which a larger cuff was used was low because adults in the Netherlands are rather thin compared to their counterparts in the USA and Canada (2). In all the three projects the average BMI was 25 kg/m^2. When using too small a cuff technicians can overestimate blood pressure (3). Based on the experience in the CRFM project, it can be assumed that also in the CB Heart and RIFOH Projects probably a small percentage of subjects required a larger or smaller cuff. Differences in average blood pressure between the study periods cannot be explained by using an inappropriate cuff size because of the small number of persons for which a cuff size other than the standard was used.

In the CB Heart and RIFOH Projects blood pressure was measured once, while in the CRFM Project it was measured twice. To compare the average blood pressure levels from the three studies with each other, the first blood pressure measurement was taken from the CRFM project. When the CRFM Project age ranges comparable with the age ranges in the CB Heart and RIFOH Project were taken, it appeared that blood pressure in the CRFM Project was lower than in the other two projects (Tables 2 and 3). The average blood pressure in the RIFOH project was also lower than in the CB Heart Project. With each study the standard deviations also became smaller.

In spite of the standardization of the blood pressure measurement, we observed considerable differences between the average blood pressure levels during different study periods. Within a study period changes in blood pressure were minor. To gain insight into whether this phenomenon was specific for this project or universal, trend studies carried out in other countries were considered. Included are study in Japan, with almost yearly measurements over a long

Table 2. Mean systolic and diastolic blood pressure[1] (mmHg) in men in 1976 and 1979 (CB Project)[2], 1981, 1986 (RIFOH Project), and 1987 and 1991 (CRFM project)

Project	Year	Age	Number	SBP (SD)	DBP (SD)
CB Heart	1976	37-43	2195	132.2 (16.7)	80.3 (11.0)
CB Heart	1979	37-43	2204	133.4 (16.6)	83.7 (11.6)
RIFOH	1981	33-37	5068	128.1 (14.4)	81.0 (10.4)
RIFOH	1986	33-37	7149	128.9 (14.4)	77.1 (10.3)
CRFM[3]	1987	33-37	275	123.3 (12.3)	76.0 (9.7)
CRFM	1991	33-37	346	121.2 (12.6)	76.8 (9.5)

[1] Average based on data from Amsterdam, Doetinchem and Maastricht.
[2] Data from Amsterdam, Doetinchem and Maastricht were only available for the years 1976, 1977, 1978 and 1979.
[3] Only the first blood pressure measurement is used.

Table 3. Mean systolic and diastolic blood pressure[1] (mmHg) in women in 1976 and 1979 (CB Heart Project)[2], and 1987 and 1991 (CRFM project)

Project	Year	Age	Number	SBP (SD)	DBP (SD)
CB Heart	1976	37-43	2290	126.8 (16.9)	77.0 (10.9)
CB Heart	1979	37-43	1551	126.2 (16.7)	78.7 (11.2)
CRFM[3]	1987	37-43	562	115.3 (13.6)	73.6 (9.8)
CRFM	1991	37-43	669	114.2 (14.1)	74.1 (10.3)

[1] Average based on data of Amsterdam, Doetinchem and Maastricht.
[2] Data from Amsterdam, Doetinchem and Maastricht were only available for the years 1976, 1977, 1978 and 1979.
[3] Only the first blood pressure measurement is used.

period of time (4,5), and some studies in Finland and the USA with only a few measurements over long periods (Table 4, Figures 1 and 2) (6,7). These studies were selected because several measurements were done during a long time period and the studies were conducted in about the same time frame as

Table 4. Mean systolic and diastolic blood pressure (SBP, DBP, mmHg) in different countries

Country/area			Men			Women		
(references)	Year	Age	Number	Mean SBP	Mean DBP	Number	Mean SBP	Mean DBP
Finland/Kuopio Province (6)[1]								
	1972	30-59	2520	146.0	93.3	2621	147.2	91.3
	1977		2607	145.7	92.6	2747	142.9	88.4
	1982		1207	146.5	88.9	999	143.3	84.8
	1987		599	144.4	89.1	631	138.9	83.9
	1992		582	140.1	83.8	624	135.5	79.8
Japan (4,5)								
	1975	40-49		137.0	85.0		133.0	80.0
	1980			135.0	84.0		130.0	80.0
	1985			132.5	83.0		129.0	79.0
	1990			131.0	83.0		126.5	78.0
USA, Minnesota (7)[3]								
	1973	25-59	1724	122.8	77.4	1890	115.6	71.9
	1980/82		1375	122.2	75.6	1533	115.1	71.0
	1985/87		1881	121.6	74.8	2006	113.6	70.4

[1] In 1972/77 shorter cuff was used than in 1982/87. Shorter cuff reading 4 mmHg higher than with larger cuff. [2] Numbers for the age category 40-49 years were not available. [3] In 1973 mercury spygmomanometer and later random zero spygmomanometer used. Mean blood pressure adjusted for difference in method.

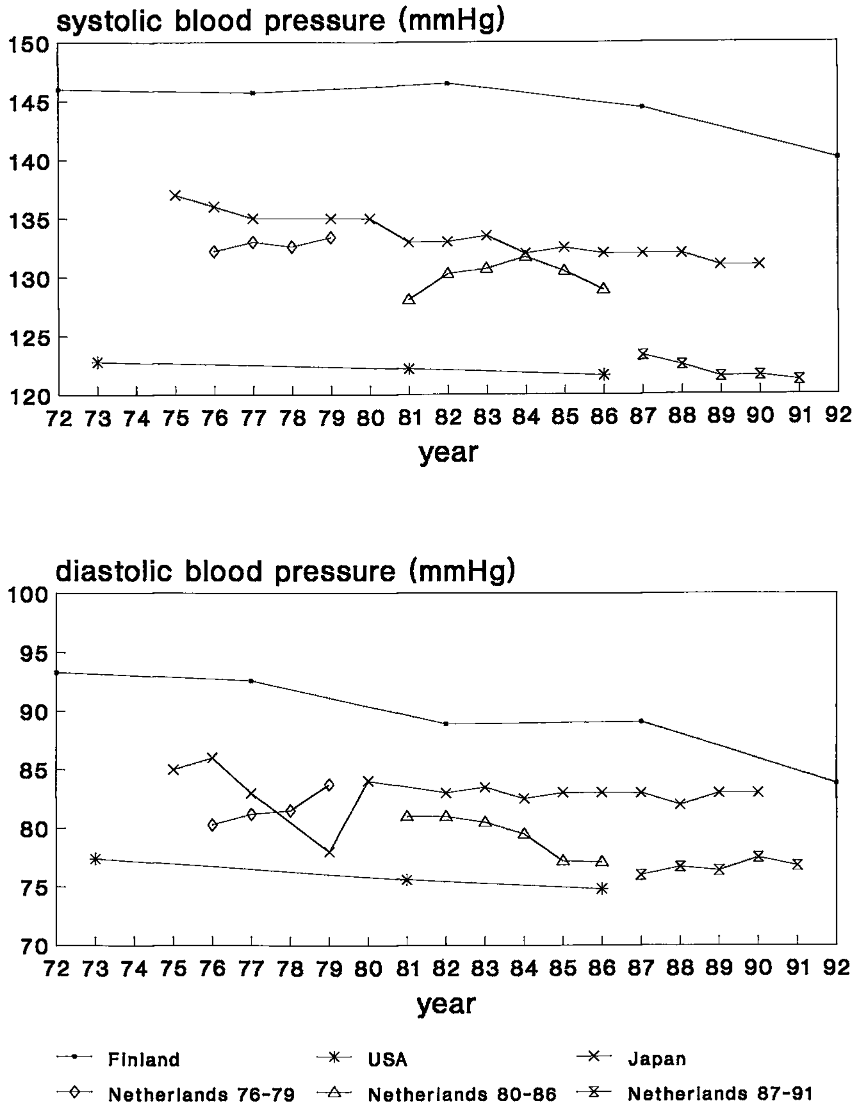

Figure 1. Trends in systolic and diastolic blood pressure in men in different countries.

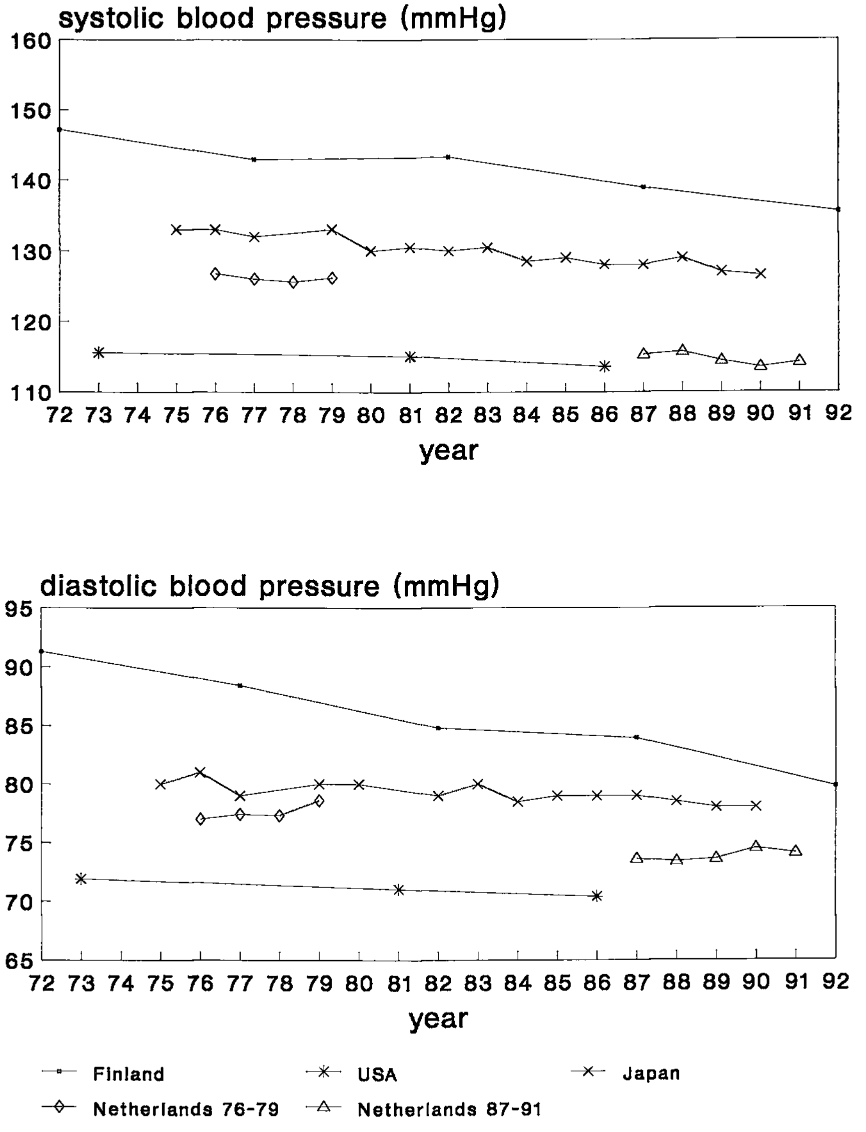

Figure 2. Trends in systolic and diastolic blood pressure in women in different countries.

ours. Our results cover a long period but come from three different projects. Generally, all studies showed a decreasing trend in time. The Japanese study confirms the fact that conclusions on trends in blood pressure should be made with caution and based on measurements which are five years apart. Continuous well-controlled series of measurements are needed to obtain reliable information about trends. Conclusions based on measurements taken with 5 to 10 year intervals like in Finland and the USA may not be justifiable (6,7).

A possible reason for the difference in average blood pressure and the standard deviation between different study periods is that patient-related factors may result in errors which are, for instance, larger than those made by the use of an inappropriate cuff-size (8). The anxiety caused by the physician measuring the blood pressure may in itself produce a substantial increase which is often referred to as white-coat effect (8,9). The CB Heart and RIFOH Projects were both screening projects aimed at identifying high-risk persons, which means that when increased risk factors or electrocardiographic changes were observed, advice on hygiene and/or treatment could be started. The differences in average blood pressure could result from the type of project, i.e.a. screening versus a monitoring project. In a screening project the white-coat effect is probably larger than in a monitoring project.

We observed differences in average blood pressure measurements among the 15 technicians in the CRFM Project. The systolic blood pressure averages varied between 114.5 and 124.1 mmHg, with a mean of 120.2 mmHg and a standard deviation of 2.5 mmHg. The diastolic blood pressure averages varied between 72.6 and 81.1 mmHg, with a mean of 76.6 mmHg and a standard deviation of 2.3 mmHg. The observed variation in blood pressure averages among different technicians is not surprising for a method that depends on the ability to detect sounds produced in the artery. It was not possible to differentiate between the technicians from the other two projects. It seems unlikely that differences in blood pressure measurements among the technicians in the other projects was very different. Therefore the differences in average blood pressure seen between the projects probably cannot be explained by the differences in blood pressure measured by different technicians.

Prevalence and treatment of hypertension

Between 1974 and 1980 an increase in the prevalence of hypertension was observed in men but not in women (Table 1). Between 1981 and 1986 the prevalence of hypertension remained stable in men. Between 1987 and 1991 the prevalence of hypertension remained stable in both men and women. An increase in the percentage of treated hypertensive men between 1974 and 1986 was followed by a decrease in the period 1987 and 1991. When a decrease in the treatment of hypertension was in women also seen.

As far as we know, no other studies are available in which trends in hypertension using the same definition as in our study were evaluated. We compared the prevalence of hypertension observed in the CRFM Project with the prevalence of hypertension in the MONICA Study (10). Thirty-nine collaborative centres in 26 countries participated in the MONICA Study. They used almost the same method for the blood pressure measurement as in our study except that in 29 centres the mercury sphygmomanometer was used instead of the random zero sphygmomanometer. Blood pressure was measured in the right arm instead of the left. In the MONICA Study the same definition for hypertension was used as the one we used. The age range in the MONICA Study was 35-64 years (estimated average standardized age of about 46 years) versus 20-59 years (average standardized age of 38 years) in the CRFM Project. In the CRFM Project the prevalence of hypertension increased with age at about 1% per year in both men and women aged 40-59 years. This age range was taken because the relation between age and hypertension was not linear until after the age of 40 when the increase was more or less linear (11). The prevalence in our study was 8% (weighted for age distribution and corrected for the technician who measured the blood pressure) (Chapter 3). Between 38 and 46 years hypertension increases by about 8%. When we adjust for the age difference, the estimated prevalence of hypertension at the age of about 46 would be about 16%. We have to be very careful when comparing our results with those of the MONICA Study because we used an estimate of the average age and prevalence of hypertension.

The Netherlands seems to have a low to intermediate position compared to other West European countries participating in the MONICA Study. In the INTERSALT Study 200 men and women aged 20-59 from 52 populations and 32 countries were examined. The method of blood pressure measurement in this study was standardized very well. The prevalence of hypertension was difficult to estimate because of the relatively small number of persons examined. Taking these limitations into account, the Netherlands in comparison with other countries was shown to have an intermediate position (12).

In the CB Project more women were treated for hypertension than men. Between 1974 and 1980 the percentage of treated hypertensive women remained stable, while during 1974 and 1986 the percentage of treated hypertensive men increased. In the CRFM Project it was observed that pharmacological treatment in both hypertensive men and women decreased between 1987 and 1991. In hypertensive women, also non-pharmacological treatment or a combination of non-pharmacological and pharmacological treatment decreased. In hypertensive men, non-pharmacological treatment remained stable, while the combination of non-pharmacological and pharmacological treatment decreased. This means that a decrease in hypertensive treatment with medication was not replaced with an increase in non-pharmacological treatment, while the prevalence of hypertension in both men and women did not change during that period. The decrease in pharmacological treatment can be due to the debate in the mid-eighties among general practitioners in the Netherlands about the usefulness of pharmacological treatment for mild hypertension (13). The Dutch guidelines for hypertension advise general practitioners to pay more attention to non-pharmacological treatment, and that the start of pharmacological treatment should also depend on the presence of other risk factors (14). Physicians increasingly based the diagnosis of hypertension on multiple blood pressure measurements rather than a single measurement. This resulted in a smaller number of subjects treated for hypertension because only the 'real' hypertensives were treated. The prevalence of hypertension in persons above ages 40-59 amounted to 15% in men and 13% in women in 1987 and remained stable in the period 1987-1991. In view of this sustained high prevalence more attention will need to be paid to primary and secondary prevention of high blood pressure through health education programmes in weight control, alcohol and salt restriction and increasing potassium intake.

Lifestyle factors and blood pressure

Overweight, high sodium and alcohol intake are presently considered the most important determinants of high blood pressure (15,16). Potentially protective effects have been suggested for high intakes of potassium, magnesium and calcium. The effect of physical activity on blood pressure is less clear (17). In this thesis only the associations between blood pressure and alcohol consumption, potassium, magnesium and calcium intake have been investigated. The relation between sodium intake and blood pressure has not been studied because in the present study no information was available about the amount of salt added during preparation of the meals and at the table. The relation between weight, body mass index, physical activity and blood pressure in the population studied is currently or will be investigated in the near future. The relation between blood pressure and alcohol consumption was studied because the nature of the relation is still unclear and little is known about effect modification of the relation between alcohol and blood pressure by other determinants such as smoking. The relations between dietary minerals and blood pressure were studied because little is known about the combined effect of dietary potassium, magnesium and calcium on blood pressure. The results from this thesis will be compared with those from other observational and experimental studies, and possible mechanisms on how lifestyle factors may influence blood pressure will be discussed. Conclusions will be drawn about the importance of lifestyle factors in prevention and treatment of hypertension.

Alcohol

In most cross-sectional studies a positive relationship between blood pressure and alcohol consumption has been observed (15, 18). This relationship persisted even after adjustment for body mass index, cigarette smoking, age, total serum cholesterol and heart rate. Both linear and non-linear relationships have been reported. U- or J-shaped relationships, or a threshold level, have been observed. Most studies have indicated elevated blood pressure levels in persons drinking three or more glasses per day in comparison with non-drinkers. In the CRFM project we observed a linear relationship for men and a threshold at two glasses per day for women. The U- or J-shaped relationship observed in other studies can be due to the fact that the category non-drinkers includes subjects who may have stopped drinking because of health problems or subjects using antihypertensive medication or a prescribed diet (19).

Prospective studies also provide consistent evidence of a strong relationship between baseline alcohol intake and the incidence of hypertension (15,20,21). A change in alcohol intake has also been associated with a change in blood pressure. In a randomized controlled trial in normotensive males a reduction in alcohol intake of 70 ml/week resulted in a reduction of about 3 mmHg in systolic blood pressure (18,20). The reduction in diastolic blood pressure was smaller and not statistically significant. In another randomized controlled trial a weekly alcohol reduction from 452 to 64 ml was associated with a fall in systolic and diastolic blood pressure of 5 and 3 mmHg, respectively, in three weeks in hypertensive men (17). The results of the trials and observational studies suggest that a reduction in alcohol intake is effective in lowering blood pressure in both hypertensive and normotensive individuals and may help to prevent hypertension. Still, there is no agreement about the acceptable level of alcohol consumption in relation to blood pressure. In most studies blood pressure was elevated in persons consuming three or more glasses per day in comparison with non-drinkers. Based on our results and those from other studies it is not possible to make a statement about acceptable alcohol consumption levels in relation to blood pressure.

The effect of alcohol on blood pressure can be explained by its influence on both the cardiac output and/or the peripheral vascular resistance, as these two haemodynamic characteristics determine the arterial blood pressure (18). This influence may be due to: an increase in sympathetic nervous system activity, as indicated by elevated concentrations of circulating catecholamines; activation of the renin angiotensin system; an increase in circulating vasopressin and aldosterone; elevation of plasma cortisol level; a rise in cardiac output and the cardiac index, or enlargement of the circulating volume due to water and salt retention (17,18).

Minerals

Potassium

In the CFRM Project an inverse association between potassium intake and blood pressure was observed in both men and women. Both epidemiologic studies and clinical trials have suggested that an increase in potassium intake lowers blood pressure (22). However, some clinical trials have clearly shown the beneficial effect of oral potassium supplements on blood pressure; other studies have failed to confirm this. There may be a number of possible explanations for the discrepancy between the studies. This can be due partly to insufficient sample size, heterogeneity of blood pressure response and absence of placebo-controlled studies. Therefore, a meta-analysis was carried out (22). The results of this meta-analysis indicate that an average potassium supplement of 86 mmol per day produced a significant reduction on supine systolic and diastolic blood pressure of 5.9 and 3.4 mmHg, respectively, in normotensive subjects and an even greater reduction in systolic and diastolic blood pressure of 8.2 and 4.5 mmHg, respectively, in hypertensive subjects. The effect of oral potassium on standing blood pressure was greater than for supine blood pressure. Based on the results of these studies, an increase in potassium intake should be included in the recommendations for a non-pharmacological treatment of hypertension.

Various mechanisms have been proposed to explain the possible effect of potassium on blood pressure (15). These include a direct natriuretic effect, suppression of the renin-angiotensin and sympathetic nervous systems, improvement of the baroreceptor function, and the reduction of peripheral vascular resistance by direct arterial vasodilation.

Magnesium

In our study and most other observational studies an inverse association between magnesium intake and blood pressure was observed (15). In the uncontrolled trials a significant fall in systolic and diastolic blood pressure was noticed (23). However, in most of the double-blind placebo controlled trials on magnesium supplementation and blood pressure, no significant fall in blood pressure was observed (23,24). It is possible that the placebo-controlled trials did not have enough power to detect an effect on blood pressure. These trials were also of short duration. In one double-blind randomized trial of six months the effect of magnesium supplementation on blood pressure was studied among 91 women with mild to moderate hypertension (25). Only in diastolic blood pressure was a significant fall observed. In the Trial Of Hypertension Prevention (TOHP) a group of 227 patients with diastolic blood pressure between 80 and 89 mmHg was randomized to a period of magnesium supplementation and their blood pressure response was compared to a group of 234 patients given placebo for six months (26). No blood pressure-lowering effect due to magnesium supplementation was detected. The available data provide insufficient evidence to recommend magnesium supplementation for the prevention of hypertension.

Magnesium is a regulator of the parathyroid hormone, which has a direct effect on blood pressure (23). Magnesium is known to be important co-factor for activation of the Na^+-K^+-ATPase activity, which plays an important role in the regulation of the vascular tone and reactivity. Magnesium is also a laxans which also increases the excretion of sodium.

Calcium

In the CRFM Project calcium intake was inversely related to diastolic blood pressure in men, and to systolic and diastolic blood pressure in women. Blood pressure hardly differed between users of calcium supplements and non-users. The majority of the observational studies provides evidence for an inverse relationship between calcium intake and blood pressure (15). This relationship could have been influenced by confounding variables, especially sodium, which was either measured not or not well in these studies. Over the past few years, several trials on the effect of oral calcium supplementation on blood pressure have been undertaken, both in normotensive and hypertensive subjects (15). The results of these trials are inconsistent and the effect of calcium supplementation on blood pressure remains a subject of controversy (27). Therefore a meta-analysis was carried out. Results of this meta-analysis indicate that the overall effect of calcium supplementation on blood pressure, if any, is very small and confined to standing blood pressure. Based on the evidence available it seemed prudent to consider the role of calcium in prevention and treatment of hypertension as unproven.

Calcium intake could theoretically lead to changes in blood pressure by inducing changes in the parathyroid hormone, which has a direct effect on blood pressure (28). Calcium also plays a role in the regulation of the vascular tone and increased calcium intake has also a natriuretic effect (29).

The combined effect of dietary potassium, magnesium and calcium

Dietary potassium, magnesium and calcium are highly intercorrelated. Therefore, it was not possible to enter the three minerals at the simultaneously in a regression model in order to estimate the independent association between blood pressure and potassium, magnesium and calcium. The combined effect of the three minerals on blood pressure was investigated as an alternative. As far as we know there are no other studies in which the combined effect of potassium, magnesium and calcium were studied. We observed that men and women consuming a diet high in calcium, potassium and magnesium had 2 mmHg lower systolic and diastolic blood pressure levels than men and women consuming a diet low in these minerals (Chapter 5). These results were based on a study in which the food intake was measured through a food frequency questionnaire. Food intake estimated by a food frequency method results in an underestimation of the true association. The results of our study suggest that an increase in mineral intake can be an important contributing factor for a reduction in blood pressure of at least 2 mmHg. A reduction of 2 mmHg in diastolic blood pressure can result in a reduction in cardiovascular diseases of about 14% in men and about 10% in women (Chapter 6).

Sodium
Excess sodium intake has been associated with increased systolic and diastolic blood pressure in both men and women. The evidence for this association is provided by both observational and experimental studies (15). From a meta-analysis it appeared that a reduction in sodium chloride consumption of 3-6 grams per day can result in an average reduction in systolic and diastolic blood pressure in hypertensive subjects of approximately 5 and 3 mmHg, respectively, and in normotensive subjects of 2 and 1 mmHg, respectively (30). This suggests that a reduction in salt intake can be an important contributing factor to a reduction in blood pressure.

The mechanism whereby sodium affects blood pressure reflects its place in the sodium-renin-aldosterone-angiotensin control system that maintains blood pressure and flow through the balance of volume and vasoconstriction (17).

Other lifestyle factors
Body weight
Both cross-sectional and prospective studies have shown a positive relation between body weight, body mass index and blood pressure (15). This relationship has been observed in both men and women. From the Intersalt Study the association between blood pressure and body mass index appeared somewhat stronger in men than in women (31). Two meta-analyses were conducted in which the effect of weight reduction on blood pressure was analyzed (32,33). It was calculated from 4 and 5 well-controlled studies that a weight reduction of 1 kg in obese hypertensive men and women resulted in a respective reduction in systolic blood pressure between 1.2 and 1.6 mmHg and in diastolic blood pressure between 1.0 and 1.3 mmHg. Subjects with a higher waist-to-hip ratio are even more likely to have a raised blood pressure and also have a greater risk of cardiovascular mortality (17). In general, men have higher waist-to-hip ratios than women. This can result in higher blood pressure levels in men than in women.

Obesity may increase blood pressure by its effects on the sympathetic nervous system, activation of the plasma renin/aldosterone system, expansion of plasma volume and insulin resistance accompanied by hyperinsulinaemia (17).

Physical activity

Most observational studies have suggested that individuals who have a more physically active lifestyle have lower blood pressure than less physically active individuals (17,34). In a recent review the results of 22 trials in which the effect of physical activity on blood pressure was studied were evaluated (35). Of the 22 trials, including a control group, only 13 analyzed habitual physical activity. Of these studies only 1 did not have a major design fault. In this particular study 30 men aged 39 years exercised one hour three times a week for a period of 16 weeks. The type of exercise was cycling, callisthenics and jogging with an intensity of 75% VO_2. A fall in both systolic and diastolic blood pressure of 5 and 4 mmHg, respectively, was observed. However, a reduction in weight of about 2 kg was also observed. Taking the weight reduction into account, the reduction through physical activity can be estimated to be in the order of about 1 to 2 mmHg. In spite of all the design problems in the other studies (such as failure to randomize, absence of a blind blood pressure measurement, the use of a before-and-after design, no detailed information on the intensity, weight change not reported) there was a consistent finding that physical activity lowered blood pressure in both normotensive and hypertensive persons. Most of the studies included only men. When both sexes were included women were in the minority. The frequency of the exercise was, in most studies, at least three times a week. In most studies the intensity was between 60-70% VO_2. The frequency and the intensity in most of these studies is high, so that for practical purposes such an intensive physical activity programme cannot be used in the prevention and treatment of hypertension.

In a recent randomized trial of adequate power in 99 non-obese men and women with mild hypertension, no reduction in blood pressure was observed after the subjects had spent 30-60 minutes in supervised jogging or walking at 70% of maximum initial oxygen consumption during three sessions per week (36). The body weight remained constant during this period. The available data provide some evidence for recommending physical activity in non-pharmacological treatment and in the prevention of hypertension. Although, the effect on blood pressure is not known, it can reduce body weight, which then results in a decrease in blood pressure.

The mechanism for an exercise-induced reduction of blood pressure is uncertain, but it is possible that decreased sympathetic nerve activity plays a role (17). Physical activity may increase cardiac output and decrease peripheral vascular resistance (35).

Cigarette smoking

Smoking does not seem to be a determinant of blood pressure (16). However, in the CRFM Project it was an important effect modifier of the alcohol-blood pressure relation in both men and women (Chapter 4). The relation between alcohol and blood pressure was stronger in male and female smokers than in male and female non-smokers. Only in a few studies was this interaction investigated (21,37,38). Arkwright and co-workers observed that diastolic blood pressure was lower in male smokers than in non-smokers even after adjustment for age and body mass index (38). In the Nurses Health Study no interaction was observed with smoking (37). However, in the MONICA Augsburg Studies an interaction with smoking was observed in both men and women (21). A possible explanation for the interaction with smoking may be that smoking is associated with a change in pattern of body fat distribution, which results in a higher waist-to-hip circumference ratio in smokers compared with nonsmokers (39). A higher waist-to-hip circumference ratio is correlated with hyperinsulinemia and hypertension (40). It is possible that smoking influences blood pressure by changing the body fat distribution (41). Based on the available data and a plausible mechanism we concluded that the prevalence of hypertension may be positively influenced by intervention in both alcohol and tobacco consumption.

Combination of lifestyle factors

A 5-year trial involving 201 men and women with high normal blood pressure at baseline (with a second-screen diastolic value of 85 to 89 mmHg) demonstrated the ability to reduce the incidence of hypertension in participants randomized to nutritional-hygienic intervention compared with a control group (42). Mean trial blood pressure was lower in the intervention group compared with the control group (-2.0 mmHg for systolic blood pressure and -1.9 mmHg for diastolic blood pressure). During the trial in the intervention group weight loss amounted to 2.2 kg, alcohol intake decreased by 10 g and salt intake by 2.3 g. The majority of the participants in the intervention group reported an increase in physical activity. Effect on blood pressure was strongly related to degree of weight loss.

In the Trial Of Hypertension Prevention (TOHP) three lifestyle groups (weight reduction, sodium reduction and stress management) were each compared with non-intervention controls over 18 months (26). In addition, four nutritional supplement groups (calcium, magnesium, potassium and fish oil) were each compared singly, in a double-blind fashion, with placebo controls over six months. They concluded weight reduction to be the most effective strategy tested for reducing blood pressure in normotensive persons. However, a reduced body weight is notoriously difficult to sustain. Sodium reduction is also effective but less effective than weight reduction.

Based on the results of our study and those of others it can be concluded that a reduction in body weight, and in alcohol and sodium intake, and an increase in potassium intake can result in a considerable reduction in blood pressure. When simply adding up the effects of these four modifiable factors a reduction of about 5-6 mmHg can be expected in hypertensive subjects. A reduction in diastolic blood pressure of 2 mmHg can be realized by an increase in potassium of about 2.5 grams per day, a decrease in salt intake of 2-4 grams per day or a reduction in body weight of about 2 kg. Furthermore, a reduction in alcohol consumption of one glass per day results in a diastolic blood pressure reduction of about 0.5 mmHg. The reduction in diastolic blood pressure due to the combined effect of these minor changes in lifestyle factors is in the same order of blood pressure reduction as can be obtained by pharmacological treatment (43).

Stamler et al. observed a reduction in blood pressure of as little as 2 mmHg through combined lifestyle interventions (42). The effect of these interventions on blood pressure were lower than could be expected on the basis of changes in salt intake, alcohol intake and body weight. This means that changes in blood pressure resulting from each of the separate determinants are not independent. Generally, the reduction in blood pressure is greater in hypertensive subjects than in normotensive subjects. This means that the effects of these measures cannot be added up or the observed small reduction in blood pressure observed by Stamler et al. is due to the fact that the intervention was done in subjects with a high normal blood pressure and not in real hypertensives (42). If all known preventive measures are applied in hypertensive subjects, it is theoretically possible to reduce diastolic blood pressure by 5-6 mmHg.

A reduction in diastolic blood pressure of about 6 mmHg can result in a mortality reduction of about 41% for cardiovascular diseases and 28% for all causes in men, and 29% and 12% in women, respectively (Chapter 6). This shows the large potential for a combined nutritional intervention, in hypertensive subjects at least.

Mortality and blood pressure

In this thesis and in most observational studies that both systolic and diastolic blood pressure are found to be strongly related to mortality from coronary heart disease, cerebrovascular disease, cardiovascular diseases and all causes (44,45). The mortality risk increases progressively throughout the entire blood pressure range. The type and strength of the association is about the same in men and women. However, the absolute mortality rate is higher in men than in women. Blood pressure also seems to be an important and independent risk factor in renal insufficiency and consequence (45). However, because of insufficient cases of renal diseases in the CB Project this association could not be studied. Cerebrovascular accident can be divided in cerebral infarction and hemorrhagic stroke. Cerebral infarction is the most common form of cerebrovascular accident in the Netherlands (about 80% of the cases) (46). Because of the small number of stroke cases it was not possible to study the association separately for these two types of cerebrovascular accidents.

High blood pressure may lead to smooth muscle cell proliferation with medial thickening and an increase in the arterial wall content of elastin, collagen and glycosaminoglycans (47). They all contribute to the growth of the atherosclerotic plaque. There is suggestive evidence that a key role played by hypertension might be the triggering of acute plaque disruption caused by effect of shear stress on the arterial wall. The narrowing of the arteries can result in coronary heart disease and cerebral infarction. Cerebral haemorrhage is caused by a rupture of an artery (46). This rupture can be a result of high blood pressure.

In this thesis and in a meta-analysis it was estimated that blood pressure reduction could lead to a considerable reduction in cause-specific and total mortality (43). We observed that the reduction in cause-specific and total mortality is expected to be larger in men than in women. In both men and women it is important to prevent and treat high blood pressure. Changes in lifestyle factors are recommended as a first step in the management of hypertensive persons and also as a way to prevent hypertension (45). The following modifications in lifestyle factors are recommended: weight reduction if overweight, moderation of alcohol intake, reduction in salt consumption, increased intake of potassium, cessation of smoking as smoking amplifies the effect of alcohol on blood pressure and overall cardiovascular health (14-16,48). The effect of physical activity on blood pressure is less clear but is also recommended because it improves cardiovascular health (14). Physical activity is also important in treating obesity (34). All these measures take several months to become effective.

Hypertension can also be treated by medication in which several classes of drugs can be recommended (48). In order of proven benefit, based on mortality and morbidity studies, they are: (1) diuretics, (2) beta-blockers, (3) angiotensin-concerting enzyme inhibitors, (4) calcium antagonists. Diuretic and beta-blocker-based therapy have been shown to reduce cardiovascular mortality and morbidity. Angiotensin-converting enzyme inhibitors and calcium antagonists are effective in lowering blood pressure, but the ability of these drugs to reduce cardiovascular events in hypertensive patients has not yet been proven in controlled clinical trials. If a decision is made to start pharmacological treatment, non-pharmacological treatment remains an important component of the overall therapeutic programme. Drug dosages and associated costs may be reduced when accompanied by appropriate patient education/counseling in diet and weight control (16). Stopping with smoking may also be important because otherwise subjects may not receive the full degree of protection against cardiovascular diseases from the drugs (49).

Long-term and large clinical trials using antihypertensive treatment have included both men and women, but have not clearly demonstrated gender differences in blood pressure response and outcomes (16). Because the rate of cardiovascular events is much lower in middle-aged women than in men, these trials had a limited ability to distinguish the degree of benefit from treatments between men and women. At the moment data are insufficient to support a different approach to the management of hypertension in women. Because of the higher death rate in men than in women, more women than men need to be treated to achieve the same result with blood-pressure-lowering medication.

In the CB Heart Project the mortality risk had already increased in persons with mild hypertension. These persons need to be followed to monitor their blood pressure levels because they are at an increased risk, compared with normotensive persons of developing definite high blood pressure and of experiencing non-fatal and fatal cardiovascular events (48). In persons with initial high blood pressure repeated blood pressure measurements will show whether or not initial elevations persist and require close attention, or whether they have returned to normal and need only periodic remeasurement.

The goal of treating persons with high blood pressure is to prevent cardiovascular morbidity and mortality. This should be accomplished by reaching and maintaining a systolic blood pressure below 140 mmHg and a diastolic blood pressure below 90 mmHg (48). In addition to blood pressure measurement, the presence of other cardiovascular risk factors should be evaluated because the risk of high blood pressure is substantially modified by the presence of other risk factors. These risk factors can be divided in non-modifiable and modifiable risk factors. The non-modifiable factors are: gender (men), family history of premature cardiovascular diseases, previous cardiovascular events and diabetes mellitus. The modifiable factors are: smoking, hypercholesterolemia (6.5 mmol/l or higher), reduced high-density lipoprotein cholesterol (<0.9 mmol/l) and a Quetelet index of 30 kg/m^2 or higher. Besides blood pressure also the other modifiable cardiovascular risk factors should be controlled.

The current practice for the treatment of hypertension in the Netherlands is as follows:

- Blood pressure must be measured at least three times over a period of 1 to 3 months to establish increased diastolic blood pressure of 105 mmHg or above and must be measured twice each time (14).
- Blood pressure must be measured at least five times over a period of 3 to 6 months to establish increased diastolic blood pressure between 95 to 104 mmHg. and must be measured twice each time.
- If diastolic blood pressure is 105 mmHg or above, both pharmacological and non-pharmacological treatment is needed.
- If diastolic blood pressure is between 100-104 mmHg, non-pharmacological treatment is needed.
- Pharmacological treatment should be considered when two or more other cardiovascular risk factors are present.
- If diastolic blood pressure is between 95 to 99 mmHg, only non-pharmacological treatment is needed.

In the CB Heart Project it was observed that pharmacological treatment was more common in women than in men. This may simply be a consequence of the fact that women more often consult a physician for various reasons and therefore may have their blood pressure checked more often (50). Also, in other countries it was observed that more women were treated for hypertension than men (51,52). In men the mortality rate and the population-attributable risks are high; a reduction in blood pressure results in a considerable mortality reduction. Therefore treatment of high blood pressure is of great importance for men. Men do not consult a physician very often and therefore means need to be explored to trace men with high blood pressure. Occupational health services providing (periodic) physical examinations or physicians who do check-ups at centres for blood donation offer possibilities. An advantage of these periodic checks is that the blood pressure levels can be monitored.

Conclusion

In our study it was shown that within a study period in which blood pressure measurements were taken continuously the levels remained about the same, while the average blood pressure level decreased in every following study period. This indicates that reliable trends in blood pressure can only be established when continuous standardized blood pressure measurements over a long time period are available.

Weight reduction, salt and alcohol restriction, and increased potassium intake, are the most effective approaches to the primary prevention of hypertension. These measures also lower blood pressure in patients with mild hypertension. These dietary recommendations are in agreement with the Guidelines for a Healthy Diet of the Netherlands Nutrition Council. The evidence for dietary magnesium is less convincing. Because the available data are insufficient more placebo-controlled studies should be conducted to estimate the effect of magnesium on blood pressure. Calcium does not seem to have a to have a blood-pressure-lowering effect. The effect of physical activity on blood pressure is less clear and requires more well-designed studies before it can be confidently recommended for prevention and treatment of hypertension.

Blood pressure is strongly associated with cardiovascular and total mortality in both men and women. It was estimated that a downward shift in blood pressure will result in a considerable reduction in cardiovascular and total mortality in both men and women, greater in men than in women. These potential benefits make primary prevention of hypertension an important goal.

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SUMMARY

SAMENVATTING

SUMMARY

High blood pressure along with smoking and elevated serum cholesterol is one of the major risk factors for cardiovascular diseases and the most important risk factor for cerebrovascular accidents. The level of blood pressure in the population is directly related to the burden of cardiovascular diseases in the society. From a public-health point of view data are needed on levels and trends in systolic and diastolic blood pressure, and on the prevalence and treatment of hypertension, in the population. It is also important to know what percentage of mortality from coronary heart disease, cerebrovascular accident, cardiovascular diseases and all causes is due to elevated blood pressure and what the potential effect of blood pressure lowering on cause-specific and total mortality could be in the population. For primary prevention of hypertension and non-pharmacological treatment it is important to determine the factors which influence blood pressure.

Using data of the Consultation Bureau Project (CB Heart Project) and the Coronary Heart Disease Risk Factor Project (RIFOH Project), the trends in blood pressure, as well as the prevalence and treatment of hypertension, were studied in about 30,000 men and women aged 37-43 years during the period 1974-1980 and in about 80,000 men aged 33-37 years during the period 1981-1986 (Chapter 2). An increase in this average systolic blood pressure of 2 mmHg in men between 1974-1980 was followed by an insignificant change between 1981-1986. Average diastolic blood pressure increased by 4 mmHg between 1974-1980 but decreased by the same amount between 1981-1986. Between 1974-1980 average systolic blood pressure did not change in women while average diastolic blood pressure increased by 2 mmHg during that period. The prevalence of hypertension in men aged 37-43 years increased from 13% in 1974 to 18% in 1980; the percentage of hypertensive women aged 37-43 years was 9% in 1974 and did not change between 1974-1980. In 1981 the prevalence of hypertension was 10% in men aged 33-37 years and did not change between 1981-1986.Treatment of hypertensive men increased from 8% in 1974 to 21% in 1980, and from 9% in 1981 to 13% in 1986. The percentage of treated hypertensive women was 28% and did not change between 1974 and 1980.

Data from the Cardiovascular Risk Factors Monitoring Project (CRFM Project) collected between 1987 and 1991 were used to study levels and trends

in systolic and diastolic blood pressure, and prevalence and treatment of hypertension in about 36,000 men and women aged 20-59 years (Chapter 3). Seasonal variation in blood pressure was also studied. In summer blood pressure in both men and women was about 1 to 2 mmHg lower than in the other seasons. In 1987 systolic blood pressure was 124 mmHg in men and 117 mmHg in women. Diastolic blood pressure was 78 mmHg in men and 75 mmHg in women. The prevalence of hypertension was 8% in both men and women. Between 1987 and 1991 systolic blood pressure decreased slightly while diastolic blood pressure increased slightly. The prevalence of hypertension did not change in this period. The percentage of hypertensive men treated decreased from 44% in 1987 to 34% in 1991, and that of hypertensive women treated from 60% to 49%.

Data from the Cardiovascular Risk Factors Monitoring Project were used to investigate the association between alcohol consumption and blood pressure, and the level at which blood pressure starts to increase (Chapter 4). We also assessed effect modification and confounding of this association by age, smoking, degree of obesity, coffee consumption, physical activity during leisure time and educational level. After adjustment for age, body mass index and smoking, we found that in men systolic and diastolic blood pressure increased by 0.9 and 0.6 mmHg per drink per day, respectively. In women, systolic and diastolic blood pressure were 2 and 1 mmHg, respectively, higher in those who consumed two or more glasses/day compared with non-drinkers. We observed a stronger association between alcohol and blood pressure in older men compared with younger men, and in male and female smokers compared with non-smokers.

The data from the Cardiovascular Risk Factors Monitoring Project were also used to study the relation between blood pressure and dietary potassium, magnesium and calcium, and the combined effect of these minerals on blood pressure (Chapter 5). After adjustment for age, body mass index, alcohol and energy intake an inverse association was observed between blood pressure and dietary potassium and magnesium in both men and women. Dietary calcium was inversely related to systolic blood pressure in women and with diastolic blood pressure in both men and women. Men and women consuming a diet high in potassium, magnesium and calcium had about 2 mmHg lower systolic and diastolic blood pressure levels compared to men and women consuming a diet low in these minerals.

In the CB Heart Project the association between blood pressure and mortality from all causes, coronary heart disease, cerebrovascular accident and cardiovascular diseases was studied in 50,000 men and women aged 30-54 years at baseline (Chapter 6). Average follow-up time was 12 years. Interaction by obesity and smoking was analyzed as well. Systolic blood pressure levels of ≥140 mmHg or diastolic blood pressure levels of ≥90 mmHg were associated with increased cardiovascular and total mortality in both sexes. In men both the absolute and relative risks were higher than in women. In men the population-attributable risks were 18% for total mortality, 28% for coronary heart disease and 58% for cerebrovascular accident mortality. For women these percentages were 7%, 19% and 27%, respectively. No significant interactions were observed for obesity and smoking. It was estimated that a 6-mmHg decrease in diastolic blood pressure would result in a mortality reduction of about 41% for CVD and 28% for all causes in men, and 29% and 12%, respectively, in women.

We concluded that within a study period in which daily blood pressure measurements were available, the levels remained about the same while the average blood pressure level decreased in every following study period (Chapter 7). This indicates that reliable trends in blood pressure can only be established when continuous standardized blood pressure measurements over a long time period are available. Weight reduction, salt and alcohol restriction, and increased potassium intake, are the most effective approaches to the primary prevention of hypertension. The evidence for dietary magnesium is less convincing. Calcium does not seem to have a blood-pressure-lowering effect. Also the effect of physical activity on blood pressure is not yet clear. Blood pressure is strongly associated with cardiovascular and total mortality in both men and women. It was estimated that a downward shift in blood pressure through preventive measures results in a considerable reduction in cardiovascular and total mortality in both men and women. This reduction was greater in men than in women.

SAMENVATTING

Verhoogde bloeddruk is samen met roken en een verhoogd cholesterolgehalte een van de belangrijkste risicofactoren voor hart- en vaatziekten. De sterkste relatie wordt gevonden voor cerebrovasculaire ziekten. Het niveau van de bloeddruk is gerelateerd aan het voorkomen van hart- en vaatziekten in de bevolking. Vanuit het oogpunt van de volksgezondheid zijn gegevens nodig over de niveaus en trends in bloeddruk en over de prevalentie en behandeling van hypertensie. Het is van belang om te weten welk percentage van de sterfte aan coronaire hartziekten, cerebrovasculaire ziekten, cardiovasculaire ziekten en totale sterfte het gevolg is van een te hoge bloeddruk en wat het mogelijke effect is van bloeddrukverlaging in de bevolking op de totale en oorzaak-specifieke sterfte. Voor preventie en voor niet-medicamenteuze behandeling van hypertensie is informatie gewenst over factoren die de bloeddruk beïnvloeden.

In dit proefschrift worden trends in bloeddruk, prevalentie en behandeling van hypertensie beschreven aan de hand van gegevens van een drietal langlopende projecten. Van circa 30,000 mannen en vrouwen van 37-43 jaar zijn gegevens verzameld in het kader van het Consultatiebureau Project Hart- en Vaatziekten tussen 1974-1980. Circa 80,000 mannen van 33-37 jaar zijn onderzocht in het kader van het Risicofactoren Onderzoek Hart- en Vaatziekten tussen 1981-1986 (Hoofdstuk 2). Tussen 1974-1980 steeg bij mannen de gemiddelde systolische bloeddruk met 2 mmHg en werd dit gevolgd door een niet-significante verandering tussen 1981 en 1986. De gemiddelde diastolische bloeddruk steeg 4 mmHg tussen 1974 en 1980 en daalde met 4 mmHg tussen 1981 en 1986. Tussen 1974 en 1980 veranderde de gemiddelde systolische bloeddruk niet maar de diastolische bloeddruk steeg met 2 mmHg in die periode. Het percentage hypertensieve mannen steeg van 13% in 1974 tot 18% in 1980 en het percentage hypertensieve vrouwen was 9% en bleef constant tussen 1974 en 1980. Het percentage hypertensieve mannen bedroeg 10% tussen 1981 en 1986. Behandeling van hypertensieve mannen steeg van 8% in 1974 tot 21% in 1980 en van 9% in 1981 tot 13% in 1986. Van de hypertensieve vrouwen werd tussen 1974 en 1980 28% behandeld.

Tussen 1987 en 1991 zijn ongeveer 36,000 mannen en vrouwen van 20-59 jaar onderzocht in het kader van het Peilstationsproject Hart- en Vaatziekten. Gegevens van dit project werden gebruikt om de trends in bloeddruk, prevalentie en behandeling van hypertensie en de invloed van het seizoen op de bloeddruk te bestuderen (Hoofdstuk 3). In de zomer was de bloeddruk 1 à 2 mmHg lager dan in de andere seizoenen. In 1987 was de gemiddelde systolische en diastolische bloeddruk bij mannen 124 en 78 mmHg en bij vrouwen 117 en 75 mmHg. De prevalentie van hypertensie was in 1987 bij mannen en vrouwen 8%. Bij zowel mannen als vrouwen werd er een geringe daling van de systolische bloeddruk waargenomen en een geringe stijging van de diastolische bloeddruk. Het percentage hypertensieve mannen en vrouwen veranderde niet tussen 1987 en 1991. Het percentage behandelde hypertensieven daalde in de periode 1987-1991 van 44% tot 34% bij mannen en van 60 tot 49% bij vrouwen.

De gegevens van het Peilstationsproject Hart- en Vaatziekten werden ook gebruikt om de associatie tussen alcoholconsumptie en bloeddruk te bestuderen en na te gaan bij welk niveau van de alcoholconsumptie de bloeddruk begint te stijgen (Hoofdstuk 4). Daarnaast is de invloed van leeftijd, roken, Quetelet Index, koffieconsumptie, lichamelijke activiteit en opleiding op de associatie bestudeerd. Na correctie voor leeftijd, Quetelet Index en roken werd bij mannen een stijging van de systolische en diastolische bloeddruk van 0.9 en 0.6 mmHg per glas per dag waargenomen. Bij vrouwen was de systolische en diastolische bloeddruk respectievelijk 2 en 1 mmHg hoger bij een alcoholconsumptie van 2 of meer glazen per dag ten opzichte van de niet-drinkers. Verder werd waargenomen dat de relatie tussen alcoholconsumptie en systolische bloeddruk sterker is bij oudere vergeleken met jongere mannen. Voor zowel mannen als vrouwen werd waargenomen dat de relatie tussen alcoholconsumptie en systolische en diastolische bloeddruk sterker is bij rokers dan niet-rokers.

Het verband tussen de inname van kalium, magnesium en calcium en bloeddruk en het gecombineerde effect van deze drie mineralen op de bloeddruk werd eveneens bestudeerd in het Peilstationsproject Hart- en Vaatziekten (Hoofdstuk 5). Na correctie voor leeftijd, Quetelet index, inname van alcohol en energie werd bij zowel mannen als vrouwen een invers verband waargenomen tussen bloeddruk en de inname van kalium en magnesium. De inname van calcium was negatief geassocieerd met de systolische bloeddruk bij vrouwen en met de systolische en diastolische bloeddruk bij zowel mannen als vrouwen. Mannen en vrouwen die een voeding gebruiken die rijk is aan kalium, magnesium en calcium hebben een systolische en diastolische bloeddruk die 2 mmHg lager is dan bij personen die een voeding gebruiken die arm is aan deze mineralen.

In het Consultatiebureauproject Hart- en Vaatziekten werd de associatie tussen bloeddruk en sterfte aan coronaire hartziekten, cerebrovasculaire ziekten, cardiovasculaire ziekten en totale sterfte bestudeerd bij 50,000 mannen en vrouwen van 30-54 jaar (Hoofdstuk 6). De gemiddelde follow-up was 12 jaar. Ook werd de invloed van Quetelet index en roken op deze relaties bestudeerd. Een systolische bloeddruk ≥140 mmHg en/of een diastolische bloeddruk ≥90 mmHg waren geassocieerd met de totale en cardiovasculaire sterfte bij zowel mannen als vrouwen. Bij mannen was 18% van de totale sterfte, 28% van de sterfte aan coronaire hartziekten en 58% van de sterfte aan cerebrovasculaire ziekten het gevolg van een te hoge bloeddruk. Bij vrouwen waren deze percentages 7%, 19% en 27%. Roken en Quetelet index hadden geen invloed op deze associaties. Een daling van de diastolische bloeddruk met 6 mmHg kan resulteren in een daling van 41% in cardiovasculaire sterfte en 28% in totale sterfte bij mannen en van 29% in cardiovasculaire sterfte en 12% in totale sterfte bij vrouwen.

Wij concludeerden dat de gemiddelde bloeddruk nauwelijks is veranderd in elk van de drie studie periodes terwijl het bloeddruk niveau lager was in elke volgende studie periode (Hoofdstuk 7). Dit geeft aan dat betrouwbare trends alleen gebaseerd kunnen worden op continue gestandaardiseerde bloeddrukmetingen over een lange periode. Gewichtsvermindering, beperking van alcohol- en zoutinname en een verhoogde inname van kalium zijn de belangrijkste maatregelen die genomen kunnen worden om hypertensie te voorkomen. Het blijkt dat calcium geen bloeddrukverlagende werking heeft en dat het effect van magnesium op de bloeddruk nog onduidelijk is. Definitieve uitspraken over het effect van lichamelijke activiteit op de bloeddruk kunnen nog niet gedaan worden. Bloeddruk is sterk gerelateerd aan zowel totale en cardiovasculaire sterfte bij mannen en vrouwen. Een verlaging van de bloeddruk door preventieve maatregelen resulteert in een daling in totale en cardiovasculaire sterfte bij mannen en vrouwen. Deze daling is bij mannen groter dan bij vrouwen.

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