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Published in:
Journal of Internal Medicine

DOI:
[10.1046/j.1365-2796.2002.00996.x](https://doi.org/10.1046/j.1365-2796.2002.00996.x)

2002

[Link to publication](#)

Citation for published version (APA):
Henriksson, K. M., Lindblad, U., Gullberg, B., Agren, B., Nilsson-Ehle, P., & Råstam, L. (2002). Development of hypertension over 6 years in a birth cohort of young middle-aged men: the Cardiovascular Risk Factor Study in southern Sweden (CRISS). *Journal of Internal Medicine*, 252(1), 21-26. <https://doi.org/10.1046/j.1365-2796.2002.00996.x>

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6

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Development of hypertension over 6 years in a birth cohort of young middle-aged men: the Cardiovascular Risk Factor Study in southern Sweden (CRISS)

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Abstract. Henriksson KM, Lindblad U, Gullberg B, Ågren B, Nilsson-Ehle P, Råstam L (Lund University, Skaraborg Institute and Helsingborg County Hospital, Sweden). Development of hypertension over 6 years in a birth cohort of young middle-aged men: the Cardiovascular Risk Factor Study in southern Sweden (CRISS). *J Intern Med* 2002; **252**: 21–26.

Objectives. To explore the development of hypertension (HT) in a cohort of young middle-aged men.

Design. Prospective birth-cohort study of men surveyed over 6 years.

Setting. Helsingborg County Hospital, Sweden, 1990–97.

Subjects. A total of 628 men born in 1953–54, all surveyed at 37, 40 and 43 years of age.

Main outcome measures. Systolic blood pressure (SBP), diastolic blood pressure (DBP), S-cholesterol, body mass index (BMI), alcohol consumption, ethnicity. HT was defined as SBP $\geq$ 140 mmHg and/or DBP $\geq$ 90 mmHg, or ongoing treatment. Using SBP < 130 mmHg and DBP < 85 mmHg as reference, the odds of conversion to HT in men with high normal blood pressure (BP) (SBP

130–139 mmHg and DBP 85–89 mmHg) was investigated.

Results. At age 37, 243 men (39%) had reference BP, 167 (26%) had high normal BP and 218 (35%) were hypertensive. Corresponding numbers at age 40 were 265 (42%), 166 (27%) and 197 (31%); and at age 43, 180 (29%), 142 (22%) and 306 (49%), respectively. High normal BP at baseline was associated with the development of HT both at age 40 (odds ratio (OR) = 2.45 confidence interval (CI): 1.42–4.22) and at age 43 (OR = 2.46, CI: 1.59–3.80), independent of other cardiovascular disease risk factors and ethnicity. The progression to HT was predicted also by S-cholesterol, alcohol consumption, BMI and weight gain.

Conclusions. Over a short-term period, a substantial proportion of young middle-aged men with high normal BP develop HT with overweight and alcohol consumption as important determinants. These findings have implications for the prevention, screening and medical care of HT in this target population.

Keywords: alcohol consumption, high normal blood pressure, hypertension, overweight.

Introduction

High blood pressure (BP) is one of the most important risk factors for cardiovascular disease (CVD) [1], and determinants of high BP are major targets in the primary prevention of hypertension (HT) aiming at reduced morbidity and mortality from CVD [2, 3].

The Coronary Risk Factor Study in southern Sweden (CRISS) was designed to investigate the development of cardiovascular risk factors in young middle-aged men. We have previously found overweight, alcohol consumption and ethnicity to be significantly associated with increasing BP. The aim of this paper was to explore the development of

HT over 3 and 6 years' follow-up in men in the CRISS Study.

Materials and methods

Subjects

Two complete birth year cohorts of men born in 1953–54 and residing in Helsingborg, Sweden, were invited to a survey of CVD risk factors at age 37 starting in 1990. Of the 1460 summoned, 442 men (30%) did not come, 27 (2%) were excluded and 991 (68%) fulfilled the criteria for participation. The exclusion of 27 men at baseline were because of failure to participate or to understand the meaning of the requirements of the study protocol because of languages ($n = 4$), mental retardation ($n = 1$), abuse of alcohol and/or other drugs ($n = 5$). Further exclusions were because of medical disorders requiring immediate treatment; hypercholesterolemia ($n = 2$) and diabetes mellitus ($n = 1$), previous coronary event ($n = 1$), or to chronic disease or medical treatment that would interfere with the study results ($n = 13$). The recruitment has been described in detail previously [4]. The same birth cohorts were invited for follow-up 3 and 6 years after inclusion. Of the 991 participants included at baseline, 770 (78%) were examined at 40 years of age and 702 (71%) at age 43. The current study comprised those 628 men in the CRISS cohort that participated, and had their systolic blood pressure (SBP) and diastolic blood pressure (DBP) recorded, at all three surveys.

Methods

A physical examination was performed, blood samples were collected and a questionnaire covering socio-economic and behavioural factors that relate to cardiovascular risks was completed at each survey.

All three examinations took place at the hospital in Helsingborg at the same time of year to avoid seasonal variation [5], and were performed by a nurse specially trained for this project. SBP and DBP were read to the nearest 2 mmHg in a sitting position following at least 5 min rest. Weight was measured on the same calibrated electronic scale at all occasions (participants in pants and no shoes). Height was measured to the nearest centimetre with

a calibrated measuring rod, the subject standing without shoes. Body mass index (BMI) was calculated by the formula $\text{weight (kg)}/\text{height}^2 \text{ (m)}$.

Blood pressure was categorized into four categories: optimal BP (SBP < 120 mmHg and DBP < 80 mmHg), normal BP (SBP 120–129 mmHg and DBP 80–84 mmHg), high normal BP (SBP 130–139 mmHg and DBP 85–89 mmHg) and HT (SBP $\geq$ 140 mmHg and/or DBP $\geq$ 90 mmHg) [6, 7]. When a participant's SBP and DBP matched different categories, the higher category was applied. Subjects with optimal or normal BP at baseline were merged into one category (SBP < 130 mmHg and DBP < 85 mmHg) and were used as reference group. Regardless of BP levels registered, all men with ongoing BP lowering medication were categorized as hypertensive.

S-cholesterol was analysed using enzymatic methods, with reagents from Boehringer-Ingelheim, Germany, and calibrated using internationally recognized standards.

The participants completed the questionnaire on lifestyle variables without supervision by the staff, and information on ethnicity and smoking habits were gathered at all three visits. Subjects who confirmed daily smoking were defined as 'smokers'; those who did not were defined as 'nonsmokers'. Information based on ethnicity was answered by the question 'were you born in Sweden', with yes or no as only option.

Questions on alcohol consumption were included in the questionnaire only at the two last surveys. Alcohol intake was estimated by an adjusted quantity–frequency method, which assessed consumption of beer, wine and distilled spirits during the last 30 days [8]. The total alcohol consumption in grams of alcohol per month was calculated and then transformed into weekly consumption.

Statistical methods

Hypertension was defined as SBP $\geq$ 140 mmHg and/or DBP $\geq$ 90 mmHg, or ongoing treatment. Using SBP < 130 mmHg and DBP < 85 mmHg as reference group, the odds of conversion to HT in men with high normal BP (SBP 130–139 mmHg or DBP 85–89 mmHg) was investigated with logistic regression and expressed as odds ratio (OR) with 95% confidence interval (CI). Multivariate logistic regression was used when independent covariates

were entered in the model. All models were adjusted for baseline BP categories. For alcohol consumption with a very skewed distribution, one unit was added to all values and the logarithm was used in analyses with alcohol as a continuous variable. All tests were two-sided, and differences were considered statistically significant for $P \leq 0.05$.

Results

Table 1 presents descriptive data on CVD risk factors by categories of BP at 37, 40 and 43 years of age. CVD risk factor levels showed a consistent, statistically significant, increase by each higher BP category at all three surveys, except for the prevalence of smoking. At baseline, 167 men had high normal BP, of these 24% ($n = 40$) converted to HT after 3 years and 46% ($n = 77$) after 6 years follow-up (Table 2). Of the 218 men who were hypertensive at baseline, 60% remained in this category at age 40 and 77% correspondingly at age 43.

At baseline, the diagnosis of HT was based on an elevated SBP alone in 31%, on increased DBP alone in 32% and on elevation of both SBP and DBP in 37% of the cases. Corresponding percentages at age 40 were 37, 22 and 41%; and at age 43, 29, 23 and 48%, respectively. Very few men ($n = 1, 3, 11$ in the three surveys, respectively) were on BP lowering medication. The distributions of BP categories are shown in Fig. 1.

Having a high normal BP at baseline was associated with a consistent risk of developing HT both after 3 years, and after 6 years follow-up. When BMI, S-cholesterol and ethnicity were entered successively in the models, the estimated risks remained virtually unchanged (Table 3).

One (1.0) unit difference in baseline BMI, and weight change at follow-up, were associated with a significantly increased risk of being hypertensive after 3 and 6 years follow-up, respectively. Baseline S-cholesterol at age 37 and alcohol consumption at age 40, were both associated with progression to HT at age 43.

Levels of SBP and DBP at each survey showed a similar pattern in different strata of BMI, S-cholesterol and alcohol consumption. No significant differences were seen among the 628 men that comprised the study base in this paper, as compared with cross-sectional analyses of the 991, 770 and 702 participants at each survey, respectively.

Table 1 Cardiovascular disease (CVD) risk factors by categories of blood pressure in the 628 men participating in all three surveys in the CRISS Study

CVD risk factors	Baseline survey, age 37				Three-year follow-up, age 40				Six-year follow-up, age 43			
	I $n = 59$	II $n = 184$	III $n = 167$	IV $n = 218$	I $n = 92$	II $n = 173$	III $n = 166$	IV $n = 197$	I $n = 47$	II $n = 133$	III $n = 142$	IV $n = 306$
SBP	113 (5)	122 (4)	130 (5)	140 (8)	115 (5)	123 (3)	133 (5)	143 (9)	113 (5)	122 (4)	131 (5)	144 (11)
DBP	72 (5)	78 (5)	83 (5)	89 (6)	72 (5)	78 (5)	82 (5)	90 (8)	72 (5)	79 (4)	82 (5)	91 (7)
BMI	23 (3)	24 (3)	24 (3)	25 (3)	23 (3)	24 (3)	25 (3)	26 (4)	24 (3)	25 (3)	25 (2)	26 (3)
S-Cholesterol	5.1(0.9)	5.2 (1.0)	5.2 (1.0)	5.5 (0.9)	5.1 (1.0)	5.1 (0.9)	5.4 (1.1)	5.6 (1.0)	5.0 (0.8)	5.3 (1.0)	5.4 (1.0)	5.7 (1.0)
Weight	75 (11)	78 (12)	78 (11)	82 (11)	75 (11)	79 (10)	81 (10)	85 (13)	77 (11)	80 (12)	80 (10)	84 (12)
Smoker (%)	20 (34)	64 (35)	61 (37)	64 (29)	32 (35)	47 (29)	48 (29)	48 (24)	14 (30)	30 (23)	43 (30)	73 (24)

Data are mean (SD) or n (%)

I: Optimal BP: SBP < 120 mmHg and DBP < 80 mmHg

II: Normal BP: SBP 120–129 mmHg and DBP 80–84 mmHg

III: High normal BP: SBP 130–139 mmHg and DBP 85–89 mmHg

IV: Hypertension: SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg or ongoing BP medication

When a participant's SBP and DBP matched different categories, the higher category was applied.

BP, blood pressure; SBP, systolic blood pressure (mmHg); DBP, diastolic blood pressure (mmHg);

MI, body mass index (kg m^{-2}); S-cholesterol: serum cholesterol (mmol L^{-1}). Weight: kg. Smoker: smoking daily (%).

Table 2 Distributions of blood pressure (BP) categories at 3- and 6-year follow-up, according to baseline BP category in 628 men in the CRISS Study

BP category at baseline, age 37		BP category at 3-year follow-up, age 40				BP category at 6-year follow-up, age 43			
		Optimal <i>n</i> = 92	Normal <i>n</i> = 173	High normal <i>n</i> = 166	Hypertensive <i>n</i> = 197	Optimal <i>n</i> = 47	Normal <i>n</i> = 133	High normal <i>n</i> = 142	Hypertensive <i>n</i> = 306
Optimal <i>n</i> (%)	59	26 (44)	21 (35)	11 (19)	1 (2)	19 (32)	19 (32)	13 (22)	8 (14)
Normal <i>n</i> (%)	184	38 (21)	71 (39)	49 (26)	26 (14)	20 (11)	65 (35)	45 (25)	54 (29)
High normal <i>n</i> (%)	167	20 (12)	56 (34)	51 (30)	40 (24)	7 (4)	33 (20)	50 (30)	77 (46)
Hypertensive <i>n</i> (%)	218	8 (4)	25 (11)	55 (25)	130 (60)	1 (1)	16 (7)	34 (15)	167 (77)

I: Optimal BP: SBP < 120 mmHg and DBP < 80 mmHg

II: Normal BP: SBP 120–129 mmHg and DBP 80–84 mmHg

III: High normal BP: SBP 130–139 mmHg and DBP 85–89 mmHg

IV: Hypertension: SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg or ongoing BP medication

When a participant's SBP and DBP matched different categories, the higher category was applied.

BP, blood pressure; SBP, systolic blood pressure (mmHg); DBP, diastolic blood pressure (mmHg).

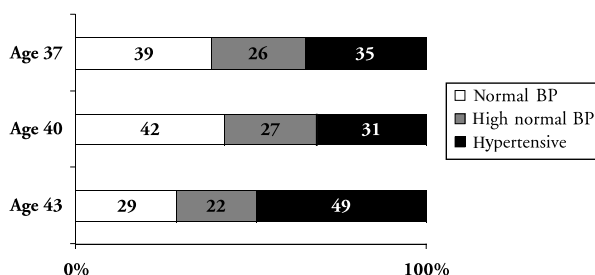


Fig. 1 The distribution of blood pressure (BP) categories at the baseline survey (age 37), and at 3- and 6-year follow-up (age 40 and 43 years, respectively). Normal BP (SBP 120–129 mmHg and DBP 80–84 mmHg), high normal BP (SBP 130–139 mmHg and DBP 85–89 mmHg), hypertension: (SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg). When a participant's SBP and DBP matched different categories, the higher category was applied.

The risk of development of HT remained at the same levels (OR = 3.05 CI: 1.61; 5.77) in the 47 men who had a high normal BP at baseline and were hypertensive at both age 40 and age 43 as compared to corresponding ORs for the main study group at 3 and 6 years follow-up.

Discussion

This study showed that young middle-aged men with high normal BP, as compared with men with optimal or normal BP, had a substantial risk of developing HT even over a short time period. Overweight and alcohol consumption were two important determinants. These findings are in accordance with previous studies [9–13]; however, our data were based on a birth cohort of young

middle-aged Swedish men and thus unconfounded by age and gender.

Short-term development of HT in nonhypertensive men and women was recently investigated in the Framingham Heart Study [13]. Over a 4-year study period, the risk of developing HT showed a step-wise increase across optimal, normal and high normal BP, especially in older adults. The results support the recommendation to monitor BP in nonhypertensive individuals regularly [6, 7]. The authors also confirm the importance of weight control, as a means of primary prevention of HT, which is well known from several earlier studies [14–17]. Another report showed that subjects with high normal BP have an increased risk of CVD, further emphasizing the relevance of recognizing this condition [18].

The Framingham Study included men and women in the age span of 35–94 years [13]. Subjects in this study were stratified into subjects between 35 and 64 and 65–94 years of age, respectively. There was a stepwise increase in the risk of conversion to HT across all baseline categories of BP in both age groups, a pattern that was strongest in the older subjects, and considerably weaker in the youngest subjects. Findings in the Framingham Study emphasize overweight and weight gain as some of the most important determinants for the development of HT.

In the Framingham Study, participants provided BP recordings several times as independent cases, as long as they were not diagnosed with HT. Even though there were important differences in

Table 3 Odds ratios of developing hypertension during 3- and 6-year follow-up according to baseline blood pressure category

Regression models	Hypertension at age 40			Hypertension at age 43		
	OR	CI	P	OR	CI	P
Reference group	1.0			1.0		
High normal BP	2.52	1.48–4.30	0.001	2.50	1.64–3.80	<0.001
Adjusted for BMI	2.48	1.44–4.26	0.001	2.48	1.61–3.80	<0.001
Adjusted for BMI and S-cholesterol	2.48	1.44–4.26	0.001	2.51	1.63–3.87	<0.001
Adjusted for BMI, S-cholesterol and ethnicity	2.45	1.42–4.22	0.001	2.46	1.59–3.80	<0.001
Independent contributions from covariates in the full model						
BMI	1.17	1.06–1.29	0.001	1.16	1.07–1.26	<0.001
S-cholesterol	1.15	0.87–1.53	0.330	1.39	1.11–1.76	0.005
Ethnicity	0.46	0.17–1.28	0.137	0.47	0.22–1.01	0.054

Reference group: SBP < 130 mmHg and DBP < 85 mmHg

High normal BP: SBP 130–139 mmHg and DBP 85–89 mmHg

Hypertension: SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg or ongoing BP medication

When a participant's SBP and DBP matched different categories, the higher category was applied.

BP, blood pressure; SBP, systolic blood pressure (mmHg); DBP, diastolic blood pressure (mmHg); BMI, body mass index (kg m^{-2});

S-cholesterol, serum cholesterol (mmol L^{-1}); ethnicity, men born abroad versus men born in Sweden.

Associations were estimated using logistic regression and expressed as odds ratios with 95% confidence interval.

development of HT in older versus younger participants conclusions were drawn for an age-span of 29 years.

Because of few cases with optimal BP developing HT in the CRISS cohort, optimal and normal BP had to be merged into a joint reference category. Consequently, even though the reference group in the CRISS cohort comprised higher BP categories than in the Framingham Study, men with a high normal BP at age 37 had a more than two-fold increased risk of having HT both at age 40 and at age 43, an association that was not explained by other CVD risk factors. The CRISS Study was planned with the assumption that there are important changes in CVD risk factors in early middle age. The present paper verified that the development of HT is substantial already in these young men. The importance of overweight was confirmed for young middle-age men, as BMI and weight change predicted the development of HT. Alcohol consumption was another significant contributor to this progression. Results from the CRISS Study further support the WHO recommendations of frequent follow-up of subjects with high normal BP, as young individuals at risk might benefit from intervention and from an earlier detection of HT [6, 19].

Blood pressure levels in northern Europe are higher than those seen in USA or in southern Europe [20]. This is one plausible explanation both to the high rates of HT and to the high conversion

rates to HT during follow-up seen in this study. Another explanation might be an overestimation of the frequency of HT because of the fact that BP was measured only once at each survey. The random within-subject variability in BP might lead to overestimation of the two tails in categorized variables. However, when analyses were performed on the men who were hypertensive both at age 40 and age 43, the results were consistent with that of the complete study population.

The risk of developing HT even over a short period of time is high also in young middle-aged men. Results in this report support the findings and the conclusions in the study from Framingham that BP monitoring should include individuals with moderately elevated BP. Primary prevention strategies in society should also focus on determinants of increasing BP, such as overweight and alcohol consumption, as they exert a strong influence on the progression of HT.

Acknowledgements

This work was supported by grants from Gorthon's and Zoega's foundations, Helsingborg, Lund and Malmö University Hospitals, the Physiographic Society of Lund, the Lund Medical Society, the National Institute of Public Health, Pålsson's Foundation, and the Swedish Medical Research Council (Project no. 04966).

References

- 1 Kannel WB. Blood pressure as a cardiovascular risk factor. *JAMA* 1996; **275**: 1571–6.
- 2 Luepker RV, Murray DM, Jacobs DR *et al.* Community education for cardiovascular disease prevention: risk factor changes in the Minnesota Heart Health Program. *Am J Public Health* 1994; **84**: 1383–93.
- 3 Tunstall-Pedoe H, Vanuzzo D, Hobbs M *et al.* Estimation of contribution of changes in coronary care to improving survival, event rates, and coronary heart disease mortality across the WHO MONICA project populations. *Lancet* 2000; **355**: 688–700.
- 4 Henriksson KM, Lindblad U, Ågren B, Nilsson-Ehle P, Råstam L. Associations between body height, body composition and cholesterol levels in middle-aged men. *Euro J Epidemiol* 2002; **17**: 521–6.
- 5 Råstam L, Hannan PJ, Luepker R, Mittelmark MB, Murray DM, Slater JS. Seasonal variation in plasma cholesterol distributions: implications for screening and referral. *Am J Prev Med* 1992; **8**: 360–6.
- 6 WHO. 1999 World Health Organization–International Society of Hypertension Guidelines for the Management of Hypertension. Guidelines Subcommittee. *J Hypertens* 1999; **17**: 151–83.
- 7 The Sixth Report of the Joint National Committee on Prevention, Evaluation and Treatment of High Blood Pressure. *Arch Intern Med* 1997; **157**: 2413–46.
- 8 Göransson M, Hanson BS. How much can data on days with heavy drinking decrease the underestimation of true alcohol consumption? *J Stud Alcohol* 1994; **55**: 695–700.
- 9 Echeverria RF, Carbajal HA, Salazar MR, Riondet B, Rechifort V, Quaini M. Prevalence of high normal blood pressure and progression to hypertension in a population sample of La Plata. *Medecina* 1992; **52**: 145–9.
- 10 Dyer AR, Liu K, Walsh M, Kiefe C, Jacobs DR, Bild DE. Ten-year incidence of elevated blood pressure and its predictors: the Cardia Study. *J Hum Hypertens* 1999; **13**: 13–21.
- 11 Nakanishi N, Nakamura K, Ichikawa S, Suzuki K, Kawashimo H, Tatara K. Risk factors for the development of hypertension: a 6-year longitudinal study of middle-aged Japanese men. *J Hypertens* 1998; **16**: 753–9.
- 12 Leitschuh M, Cupples LA, Kannel W, Gagnon D, Chobanian A. High-normal blood pressure progression to hypertension in the Framingham Heart Study. *Hypertension* 1991; **17**: 22–7.
- 13 Vasan RS, Larson MG, Leip EP, Kannel WB, Levy D. Development of hypertension among non-hypertensive subjects in the Framingham Heart Study. *Lancet* 2001; **358**: 1682–6.
- 14 National High Blood Pressure Education Program Working Group Report on Prevention of Hypertension. *Arch Intern Med* 1993; **153**: 186–208.
- 15 Stamler J. Epidemiologic findings on body mass and blood pressure in adults. *Ann Epidemiol* 1991; **1**: 347–62.
- 16 Wood D, Backer GD, Faergeman O *et al.* Prevention of coronary heart disease in clinical practice. recommendations of the second joint task force of European and other societies on coronary prevention. *Eur Heart J* 1998; **19**: 1434–503.
- 17 Ramsay L, Williams B, Johnston G. British Hypertension Society Guidelines for hypertension management 1999; summary. *BMJ* 1999; **319**: 630–5.
- 18 Vasan RS, Larson MG, Leip EP *et al.* Impact of high-normal blood pressure on the risk of cardiovascular disease. *N Engl J Med* 2001; **345**: 1291–7.
- 19 Lindblad U, Isacson SO. Development of hypertension: implications for primary prevention. *Lancet* 2001; **358**: 1659.
- 20 van den Hoogen PCW, Feskens EJM, Nagelkerke ND, Menotti A, Nissinen A, Kromhout D. The relation between blood pressure and mortality due to coronary heart disease among men in different parts of the world. *N Engl J Med* 2000; **342**: 1–8.

Received 15 February 2001; revision received 16 April 2002; accepted 16 April 2002.

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