A general practice-based study examining the absolute risk of cardiovascular disease in treated hypertensive patients

T P FAHEY

T J PETERS

SUMMARY

Background. *When managing hypertension, the assessment of the absolute risk of a cardiovascular' event is now advocated as the most accurate way in which the risks and benefits of anti-hypertensive therapy should be judged. Most studies that have examined control of hypertension have relied solely on the blood pressure level attained after treatment, with no measurement of the likely absolute risk in individual patients.*

Aim. *To assess control of hypertension by quantifying the 10-year absolute risk of cardiovascular disease in patients treated by their general practitioners, and to assess which risk factors are associated with uncontrolled hypertension in this group of patients.*

Method. *A cross-sectional sludy was made of patients on drug treatment for hypertension in 18 Oxfordshire general practices subscribing to the VAMP (value-added medical products) computer system. The absolute risk of suffering a cardiovascular event in the following 10 years was measured according to each individual's risk factor profile. Factors associated with uncontrolled hypertension were ascertained using multiple logistic regression analysis.*

Results. *Overall, 40.9% (37.6% to 44.1%) of the hypertensive population had an absolute risk exceeding 20% of having a cardiovascular event in the following 10 years. The distribution of risk factors varies throughout the population. A higher blood pressure reading was strongly associated with an increased likelihood of high absolute risk, but high blood pressure readings in individual patients did not necessarily equate to a high absolute risk. The factors independently associated with uncontrolled hypertension were age, sex, past history of stroke, ischaemic heart disease and transient ischaemic attack, a body mass index greater than 30, diabetes, and current smoking.*

Conclusions. *Absolute risk assessment maximizes the risk–benefit ratio in treated hypertensive patients. Individual control and management requires multifactorial assessment and management. Treatment of hypertension according to blood pressure reading alone is not a reliable way of reducing the absolute risk of cardiovascular disease.*

Keywords: cardiovascular disease; hypertension; risk factors.

Introduction

HIGH blood pressure is an independent risk factor in the development of cardiovascular disease.[1] The absolute risk of cardiovascular disease in each individual is substantially modified by the presence of other risk factors, most notably age, sex and the presence of coexisting cardiovascular disease.[1-3] Clinical guidelines, most recently those from New Zealand, make explicit the relationship between blood pressure, age, sex, and the presence of cardiovascular risk factors in terms of producing different levels of absolute risk for cardiovascular disease.[4] Thus, two people with identical blood pressure readings may have substantially different absolute risks for a cardiovascular event, mediated by the presence or absence of additional risk factors.[3,4]

Previous population studies of hypertension have focused primarily on blood pressure threshold as a measurement of controlled or uncontrolled hypertension.[5-8] Concern persists that treatment goals in terms of target blood pressure readings are not being achieved in many individuals diagnosed and treated for hypertension.[1] Little attention has been paid to the constellation of risk factors and the subsequent absolute risk of a cardiovascular event in individuals or in a population. Measuring control of hypertension by blood pressure attainment alone does not give a true estimate of the absolute risk of cardiovascular disease in either an individual patient or a population. It follows that, for each individual, quantification of overall cardiovascular disease risk has important implications for clinical management — the risk–benefit ratio of treatment being more favourable in those with higher absolute risk.[1,2] For example, fewer elderly than middle-aged people need to be treated to prevent a cardiovascular event.[9,10]

The purpose of the present study was to ascertain the proportions of individuals in various strata (defined in terms of absolute risk of a cardiovascular event), and the relationship between blood pressure level and absolute risk status. For this reason, the standard used to assess risk was not blood pressure reading alone but an estimate based on age, sex, blood pressure attained, and the presence of minor or major risk factors (Table 1). The second objective of the study was to assess which of the risk factors that determine absolute risk were also associated with inadequate control.

Methods

Individual patient-based morbidity data was collected from October 1994 to February 1995 in 18 of the 20 Oxfordshire practices that subscribe to the VAMP (value-added medical products) computer system. A systematic sample of 50 patients was obtained by taking every tenth person from the practice hypertension register. To be defined as hypertensive for the purposes of this study a patient had to be clearly diagnosed as hypertensive in their records in the computer database, and, at the time of the study, be taking medication to lower their blood pressure.

Morbidity data were collected according to the recommendations in the New Zealand guidelines, in order to provide explicit absolute risks of cardiovascular disease and to stratify individuals according to their absolute risk.[4] These guidelines were developed using longitudinal data on cardiovascular outcome from the Framingham cohort.[11,12] The information required was age, sex, blood pressure reading (averaged over the three most recent readings, when available), and the presence of major and minor risk factors (Table 1).[4] In addition, information on alcohol consumption was obtained from the VAMP database. Using the

T P Fahey, lecturer in primary care; and T J Peters, senior lecturer in medical statistics, Department of Social Medicine, University of Bristol.
Submitted: submitted: 22 January 1996: accepted: 23 July 1996.

Table 1. Major and minor risk factors according to New Zealand criteria.

Major risk factors	Minor risk factors
Present or previous history of:	*Presence of:*
Symptomatic CVS disease	Current smoking
Myocardinal infarction	Diabetes
Stroke	Body mass index (BMI) > 30
Transient ischaemic attack	HDL†:total cholesterol > 6.1*
Peripheral vascular disease	Family history of premature cardiovascular disease
Coronary artery bybass graft	
Coronary angioplasty	
Left ventricular hypertrophy	
Familial hypercholesterolaemia	

* Modified 10 UK recommendations of cholestrol > 7.8 mmol/l. †high-density lipoprotein cholesterol.

(cross-sectional) data collected in this way, each individual was thus stratified into one of five categories according to the New Zealand guidelines:

- Blood pressure ≤ 150/90 mmHg (below the range at which absolute risk is calculated according to New Zealand guidelines)
- Absolute risk < 10%
- Absolute risk between 10% and 19%
- Absolute risk between 20% and 40%, or
- Absolute risk > 40%.

The New Zealand guidelines contain no explicit statement about the reduction in absolute risk over the following 10 years that is required to achieve control; they do suggest that treatment should be commenced at levels greater than or equal to 20%.[4] Hence, for the purposes of this study, an absolute risk of 20% or higher indicated uncontrolled hypertension, while an absolute risk below 20% indicated controlled hypertension. This level of risk means that 150 people would need to be treated for one year to prevent a single cardiovascular event.[4] Although the New Zealand guidelines deal principally with pre-treatment absolute risk levels, these could not be ascertained reliably in the present study. Hence, the analyses relate to current blood pressure and risk factor levels, and thus to current cardiovascular risk status.

Statistical analysis

The first step was to calculate the percentages in the various risk strata that produced the proportions classified as controlled and uncontrolled. The key proportion of uncontrolled hypertensives and its 95% confidence interval (CI) were estimated, with and without the sampling method being taken into account. This involved adjustment for unequal sampling fractions[13] and the clustering effects of sampling individuals through the practices; the second of these corrections required the calculation of an intra-practice correlation coefficient.[14,15] The latter represents the inefficiency of the cluster sampling method compared with the simple random sampling approach (which is logistically much more difficult).

Potential risk factors according to New Zealand guidelines were coded as dichotomous variables, calculated in 2x2 tables and tested with the use of the chi-square statistic or Fisher's exact test when necessary. To identify independent risk factors for uncontrolled hypertension, unadjusted risk factors that were significantly associated with uncontrolled hypertension at the 5% level were entered into a multiple logistic regression model. Final adjusted estimates of the (independent) relationships of the risk factors with uncontrolled hypertension are presented as odds ratios with their 95% confidence intervals. All calculations were performed on Microsoft Excel, Minitab for Windows and SPSS for Windows.

Results

Absolute risk

Eighteen (90%) of the practices permitted data collection and provided a hypertension register. From these, morbidity data on a systematic sample of 895 patients were collected. Nineteen (2.1%) of these patients had no blood pressure record on the database and were excluded from further analysis. Overall, 40.9% (95% CI 37.6–44.1%) of the population had uncontrolled hypertension according to the New Zealand guideline criteria, including 11.6% (95% CI 9.5–13.8%) who had an absolute risk that exceeded 40% over the following 10 years (Table 2). After adjusting for the sampling method (the intra-practice correlation coefficient was 0.0551), the estimated proportion uncontrolled was 39.8% (95% CI 33.3–46.3%). As can be seen, the complex adjustments to this estimate and its standard error that were necessitated by the sampling method led to little change in the figures (as would be expected, the confidence interval became slightly wider). Consequently, such adjustments were not performed for the remaining analyses.

Distribution of risk factors

Overall, the prevalence of a major risk factor in this sample of 876 hypertensives with known absolute risk was 19.4% (95% CI 95% CI 16.8–22%), while the prevalence of a minor risk factor was 42.7% (95% CI 39.4–46%). Nearly half, or 46.1% (95% CI 42.8–49.4%), were male, and 37.7% (95% CI 34.5–40%) were taking two or more anti-hypertensive agents. The combination of major and minor risk factors in individuals varied throughout the sample, with just under half having no major or minor risk factors at all (Table 3).

Relationship between blood pressure and absolute risk

As blood pressure level increased (across the four categories: ≤ 150/90 mmHg, 150–159/90–94 mmHg, 160–169/95–99 mmHg, and ≥170/100 mmHg), so did the likelihood of having an absolute risk of a cardiovascular event that exceeded 20% (chi-square test for trend 247.5, 1 degree of freedom, $P<0.001$). Blood pressure level alone did not necessarily equate to controlled or uncontrolled hypertension. For example, for the 19% of the sample who had a blood pressure in the range 160–169/95–99 mmHg, just under half, or 46.7% (95% CI CI 39.2–54.3%), had an absolute risk greater than 20%. In addition, of the 27% in the range 150–159/90–94 mmHg, over one-third, or 39.4% (95% CI 33.2–45.6%), were uncontrolled.

Lastly, the New Zealand guidelines recommend that treatment

Table 2. Percentages (95% CI) of 876 individuals in various strata of absolute risk of a cardiovascular event according to the New Zealand guidelines in a hypertensive population.*

Absolute risk	Percentage of individuals	95% CI
BP < 150/90	33.0	29.9-36.1
<10%	5.4	3.9-6.9
10–20%	29.2	26.2-32.2
>40%	11.6	9.5-13.8

* Excluding 19 individuals without any blood pressure (BP) reading in whom absolute risk could not be calculated.

Table 3. Distribution of the major and minor risk factors in hypertensive individuals for whom absolute risk was known (figures given are the percentages out of 876).

Major risk factors*	Minor risk factors† 0	1	2	3
0	45.5	29.1	5.7	0.5
1	5.7	3.5	1.0	0.1
2	4.9	1.9	0.3	0
3	1.0	0.3	0.2	0
4	0.2	0.1	0	0

*Major risk factors include: symptomatic cardiovascular disease, past history of myocardial infarction, cerebro vascular accident, transient ischaemic attack, peripheral vascular disease, coronary artery bypass graft, percutaneous coronary angioplasty, left ventricular hypertropy, and hypercholesterolaemia. †Minor risk factor include: current smoking, diabetes, BMI > 30,Chol > 7.8 mmol/l, and positive family history of cardiovascolar disease.

is commenced in individuals with a blood pressure greater than or equal to either 170 mmHg systolic or 100 mmHg diastolic, even if the absolute risk is less than 20%. In this sample, 21% had a blood pressure reading that exceeded this level. When absolute risk was calculated in this group of individuals, 30.1% (95% CI 23.5–36.7%) had an absolute risk below 20%.

Risk factors and uncontrolled hypertension

Again defining uncontrolled hypertension in terms of a 20% or higher absolute risk of having a cardiovascular event within 10 years, age was significantly associated with uncontrolled hypertension ($\chi^2 = 71.3$, df = 1, $P<0.001$), while males were less likely to be controlled than females (the difference in proportions was 9.6%; 95% CI 3.1–16.1%) (Table 4). Both of these factors remained significantly associated with uncontrolled hypertension after adjustment for other risk factors (Table 5).

The presence of a major risk factor (difference in proportions 34.5%; 95% CI 26.5–42.5%) or minor risk factor (difference in proportions 13.1%; 95% CI 6.6–19.7%) was also associated with an increased chance of uncontrolled hypertension (Table 4). Furthermore, as the number of major risk factors ($\chi^2 = 9.0$, df = 1, $P<0.001$), minor risk factors ($\chi^2 = 15.8$, df = 1, $P<0.001$), or combined risk factors ($\chi^2 = 44.1$, df = 1, $P<0.001$) increased in individuals, so did the likelihood of having uncontrolled hypertension. Consumption of 30 or more units of alcohol a week was not associated with an increased absolute risk (unadjusted $\chi^2 = 0.18$, df = 1, $P = 0.89$).

When adjusted for potential confounding factors, the risk factors significantly associated with poor control were a past history of coronary heart disease (CHD) or transient ischaemic attacks (TIA), a body mass index greater than 30, the presence of diabetes, and a current smoking history (Table 5). The other risk factors, together with the number of anti-hypertensive drugs taken and the length of time diagnosed as being hypertensive, were not associated with poor control after adjusting for age, sex, and the other variables in Table 5.

Discussion

This study has shown that about 40% of these patients had an absolute risk exceeding 20% of suffering a cardiovascular event in the following ten years. By New Zealand guideline standards such patients remain uncontrolled and require additional therapeutic adjustment to reduce their absolute risk.[4] In addition, individuals displayed widely different combinations of major and minor risk factors that determined their absolute risk (Table 3). Quantification of overall risk in individual patients appears to be poorly understood or improperly managed in those individuals with uncontrolled hypertension. Notwithstanding the differences in classification for individuals, the overall estimated population level of uncontrolled hypertension is similar when blood pressure alone is used as the standard of management.[7]

This study confirms that blood pressure level alone may be a poor guide to each individual's absolute risk. Thus, treating solely on the basis of blood pressure level would appear to be a suboptimal management strategy[2]. Other risk factors associated with poor control further emphasize that reducing absolute risk requires a multifactorial approach to prevention. For example, smoking cessation is a realistic and feasible goal in individuals with hypertension.[16] Lowering blood pressure by drug treatment is only one of several methods by which the individual patient's absolute risk of cardiovascular disease may be reduced.

A shortcoming of the use of risk stratification according to the New Zealand guidelines as applied in this study, or indeed of any risk-scoring system, including blood pressure measurement alone, is the reliance on risk factors rather than actual cardiovascular outcome. This use of a proxy outcome measure (inevitable in a cross-sectional study of this nature) will lead to misclassification errors in either direction. Confirmation of these findings is needed from longitudinal studies where the initial (pre-treatment) level of absolute risk is known and cardiovascular mortality data is obtained.

Taking absolute risk as the standard against which management is to be judged may maximize the risk–benefit ratio but does not address the philosophical problem of which should be valued more highly: prevention of a cardiovascular event in an elderly person, or in a middle-aged person.[2] Similarly, though some individuals may not reach a treatment goal, whether by lowering of blood pressure or by modification of risk factors, they may have made substantial progress in terms of reduced absolute risk compared with their initial level of risk.[17] Such risk reductions are not apparent when simply measuring the proportion 'uncontrolled', and only become clear when examining individual response to treatment over time.

Previous studies have examined predisposing factors associated with poor control of hypertension in populations, most particularly in the US.[18,19] These studies have highlighted that failure to comply with medication, lack of medical insurance, and restricted access to a primary care physician were all associated with poor control when measured by attained blood pressure threshold. In the present study, poor control was not significantly associated with the number of drugs prescribed, the length of time a person had been diagnosed as being hypertensive, or increased alcohol consumption (≥30 units/week).

Explanations for the particular profile of factors associated with uncontrolled hypertension in the present study (age, sex, past history of stroke, ischaemic heart disease and transient

Table 4. Statistical significance of associations for reported risk factors with uncontrolled hypertension.

	df	Unadjusted χ^2	P
Age (40–49, 50–59, 60–69, 70–79)	3	78.1	<0.001
Sex	1	8.3	0.004
Major			
Symptomatic CHD	1	10.4	0.001
Past history of CHD	1	17.6	<0.001
Past history of CVA	1	5.4	0.02
Past history of TIA	1	13.4	<0.001
Past history of PVD	1	1.5	0.33*
Past history of CABG	1	0.06	0.81
Past history of PTCA	1	5.4	0.07*
Past history of LVH	1	0.55	0.46
Family history of hyperlipidaemia	1	0.07	1*
Minor			
Body mass index >30	1	9	0.003
Diabetes	1	7.6	0.006
Current smoker	1	4.4	0.04
Family history of CVD	1	0.9	0.34
Cholesterol >7.8	1	0.12	0.91
Number of anti-hypertensive agents taken (1, 2, 3 or more)	2	8.3	0.02
Length of time in years diagnosed as being hypertensive (0-5, 6 or more)	1	1.49	0.22

* Fisher's exact test.

Table 5. Adjusted odds ratios, 95% confidence intervals and *P* values for associations of various risk factors with uncontrolled hypertension.

Risk factor	Odds ratio	95% CI	P
Age (per year)	1.08	1.06–1.10	<0.0001
Sex			
Female*	1.0		
Male	1.85	1.36–2.50	0.0001
Major risk factors			
Past history of CHD			
No*	1.0		
Yes	2.13	1.34–3.37	0.0012
Past history of TIA			
No*	1.0		
Yes	4.10	1.70–9.91	0.0008
Minor risk factors			
Body mass index >30			
No*	1.0		
Yes	2.68	1.85–3.89	<0.0001
Diabetes			
No*	1.0		
Yes	1.77	1.05–2.98	0.030
Current smoker			
No*	1.0		
Yes	1.82	1.20–2.75	0.005

* Reference category.

ischaemic attack, body mass index, diabetes, and current smoking) are likely to be a combination of unavoidable risk factors (for example, increased age), lack of appreciation of the cumulative role of risk factors, and chance findings. Consequently, some of these findings would require replication in other studies.

What is clear is that a large proportion of hypertensive individuals remained at high absolute risk of a cardiovascular event despite drug treatment of their hypertension. Such a situation has most likely arisen for three reasons. First, doctors continue to treat according to blood pressure threshold alone and do not consider each person's absolute risk. Secondly, if absolute risk is considered in individual patient management, risk assessment may be too complex a task to be performed accurately — general practitioners have been shown to be inconsistent in their assessment of risk factors and estimation of absolute risk in coronary heart disease.[20,21] Lastly, doctors fail to understand the various methods by which clinical trials are presented, and tend to overestimate the benefits of relative risk measurements in comparison to absolute risk measurements when prescribing drugs.[22] Taken together, these reasons are likely to explain why so many individuals at high absolute risk of cardiovascular disease remained undertreated in this population.

New Zealand guidelines are not unique in attempting risk stratification for cardiovascular disease. Various scoring systems are now advocated for use by general practitioners in attempting to quantify absolute risk of coronary heart disease[23,24] and stroke.[25] At the same time, it has been shown that Canadian general practitioners overestimate the absolute risk of coronary heart disease,[21] while general practitioners in the United Kingdom appear to ignore relevant risk factors when the estimation of risk becomes too complex.[20]

Computer-based decision support systems (CDSSs) have been shown to improve clinician performance and patient outcome in hypertension and other diseases.[26,27] Facilitating accurate risk assessment for cardiovascular disease with CDSSs by the use of guidelines[4] or risk scores[23-25] should allow an accurate risk profile for each individual to be calculated. A CDSS will also enable the clinician to ascertain the relevance of results from particular randomized controlled trials in hypertension for the individual patient potentially requiring treatment. This relevance could be considered in terms of how easily the trial as a whole can be generalized, and specifically in terms of the absolute risk profile of patients included in the trial.[28] Therapeutic or lifestyle modification can then be based on a more accurate risk–benefit ratio for each individual.

References

1. Whelton P. Epidemiology of hypertension. *Lancet* 1994; **344:** 101-106.
2. Jackson R. Which hypertensive patients should be treated? *Lancet* 1994: **343:** 496-497.
3. Alderman MH. Blood pressure management: individualized treatment based on absolute risk and the potential for benefit. *Ann Intern Med* 1993; **119:** 329-335.
4. Jackson R. Barham P, Bills J, *et al.* Management of raised blood pressure in New Zealand: a discussion document. *BMJ* 1993; **307:** 107-110.
5. Smith WCS, Lee AJ, Crombie IK, Tunstall-Pedoe H. Control of blood pressure in Scotland: the rule of halves. *BMJ* 1990; **300:** 981-983.
6. Fahey T, Lancaster T. The detection and management of hypertension in the elderly of Northamptonshire. *J Publ Hlth Med* 1995; **17:** 57-62.
7. Whelton P, Brancati F. Hypertension management in populations. *Clin Exp Hypertens* 1993; **15:** 1147-1156.
8. Straesser T, Wilhelmsen L (eds). *Assessing hypertension control and management.* (vol. 23.) Geneva: World Health Organization, 1993.
9. Mulrow CD, Cornell JA, Herrera CR, *et al.* Hypertension in the elderly: implications and generalizability of randomised trials. *JAMA* 1994; **272:** 1932-1938.
10. Bennet N. Hypertension iu the elderly. *Lancet* 1994: **344:** 447-449.
11. Anderson KM, Wilson PW, Odell P, Kannel WB. An updated coronary risk profile. A statement for health professionals. *Circulation* 1991; **83:** 356-362.
12. Wolf PA, D'Agosino RB, Belanger AJ, Kannel WB. Probability of stroke: a risk profile from the Framingham study. *Stroke* 1991; **22:** 312-318.
13. Armitage P, Berry G. *Statistical methods in medical research.* 2nd edn. Oxford: Blackwell Scientific Publications, 1987.
14. Donner A, Birkett N, Buck C. Randomization by cluster. *Am J Epidemiol* 1981; **114:** 906-914.
15. Donner A, Klar N. Methods for comparing event rates in intervention studies when the unit of allocation is a cluster. *Am J Epidemiol* 1994; **140:** 279-289.
16. Silagy C, Mant D, Fowler G, Lodge M. Meta-analysis on efficacy of nicotene replacement therapies iu smoking cessation. *Lancet* 1994; **343:** 139-142.
17. Swales J. Guidelines for treating hypertension. In: Swales J (ed). *Textbook of hypertension.* 1st edn. Oxford: Blackwell Scientific Publications. 1994.
18. Shea S, Misra D, Ehrlich M, *et al.* Predisposing factors for severe, uncontrolled hypertension in an inner-city minority population. *N Eng J Med* 1992; **327:** 776-781.
19. Winickoff R, Murphy P. The persistent problem of poor blood pressure control. *JAMA* 1987; **147:** 1393-1396.
20. Evans JS, Hatties C, Dennis I, Dean J. General practitioners' tacit and stated policies in the prescription of lipid lowering agents. *Br J Gen Pract* 1995; **45:** 15-18.
21. Grover S, Lowensteyn I, Esrey K, *et al.* Do doctors accurately assess coronary risk in their patients? Preliminary results of the coronary health assessment stndy. *BMJ* 1995; **310:** 975-978.
22. Sackett D, Cook R. Understanding clinical trials. *BMJ* 1994; **309:** 755-756.
23. Shaper A, Pocock S, Phillips A, Walker M. Identifying men at high risk of heart attacks: strategy for use in general practice. *BMJ* 1986; **293:** 474-479.
24. Tunstall-Pedoe H. The Dundee coronary risk-disc for management of change in risk factors. *BMJ* 1991; **303:** 744-747.
25. Coppola W, Whincup P, Papacosta O, *et al.* Scoring system to identify men at high risk of stroke: a strategy for general practice. *Br J Gen Pract* 1995; **45:** 185-189.
26. McAlister N. Covvey H, Tong C, Lee A, Wigle E. Randomised controlled trial of computer assisted management of hypertension in primary care. *BMJ* 1986; **293:** 670-674.
27. Johnson M, Langton K, Haynes R, Mathieu A. Effects of computer-based clinical decision support systems on clinician performance and patients ontcome. *Ann Intern Med* 1994; **120:** 135-142.
28. Menard J, Chatellier G. Mild hypertension: the mysterious viability of a faulty concept. *J Hypertens* 1995; **13:** 1071-1077.

Acknowledgement

We thank Professor Deborah Sharp and Dr Yoav Ben Schlomo, University of Bristol, and Professor Rod Jackson, University of Auckland, for constructive criticisms on earlier drafts of this paper, and all Oxfordshire general practices who permitted data collection in their practices.

Address for correspondence

Dr T P Fahey, Department of Social Medicine, University of Bristol, Canynge Hall, Whiteladies Road, Bristol BS8 2PR.