PRACTICE OBSERVED

Practice Research

Randomised trial of treatment of hypertension in elderly patients in primary care

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Abstract

A randomised trial of the treatment of hypertension in 884 patients aged 60 to 79 years at the onset showed a reduction of 11.1 mm Hg in blood pressure over a mean follow up period of 4.1 years. The principal antihypertensive agents were atenolol and bendrofluazide. There was a reduction in the rate of fatal stroke in the treatment group to 30% of that in the control group (95% confidence interval 11-84%, $p < 0.025$). The rate of all strokes (fatal and non-fatal) in the treatment group was 58% of that in the control group (95% confidence interval 35-96%, $p < 0.03$). The incidence of myocardial infarction and total mortality was unaffected by treatment. Questionnaires completed by the patients and their relatives failed to identify any differences in symptoms that were likely to be due to treatment.

Introduction

This trial was designed in 1975 with the main aim of finding out whether the treatment of hypertension in patients between the ages of 60 and 79 years reduced the incidence of stroke or coronary disease or affected cardiovascular or overall mortality. At that date, although validation of the treatment of younger patients with hypertension of moderate to severe grade had been achieved by the Veterans Administration studies, there was no evidence on the efficacy of treating elderly patients.

The existence of fixed patient lists in the National Health Service

in Britain made it possible to recruit patients from a known population base for a multicentre study. The pilot stage was completed in 1977 and most of the participating centres were recruited between 1978 and 1981.

In the early 1970s there was no ethical committee for studies in general practice. After the pilot stage a pilot committee was invited to review the study before it was continued and to advise on continuing problems. This consisted of an expert on hypertension, a general physician, a cardiologist, and a statistician.

Subsidiary aims of the trial were: to estimate the "cost" of such treatment in side effects and unwanted morbidity; and, in follow up patients who had normal blood pressures on screening and to compare mortality and morbidity in this group with that in the hypertensive patients.

This paper reports the main outcomes of the trial in terms of cardiovascular disease in the treatment and control groups and also the incidence of side effects.

Patients and methods

PATIENT SELECTION

The study population consisted of patients aged 60 to 79 years who were registered in 15 general practices in England and Wales. A data card was inserted in the medical records of all the patients in this age range; who were identified from age-sex registers. Patients with the following conditions were excluded from participating in the trial: atrial fibrillation, A-V heart block, ventricular failure, bronchial asthma, diabetes mellitus, need for pharmacological treatment, or any serious concomitant disease limiting the prospect of fruitful living. Untreated hypertension with levels persistently above 200 mm Hg systolic or 120 mm Hg diastolic or patients already being treated for hypertension within three months were further reasons for exclusion. If any of these exclusion factors were known they were marked on the data cards, and these patients were not screened. In some cases causes for exclusion were only discovered later during screening, and these patients were withdrawn before randomisation.

Patients were invited to attend special screening clinics run by trial nurses. Blood pressures were measured after a short rest using the arm with the patient seated. They were returned to the nearest 2 mm Hg Cuffs with range

In August 1985, at nearly 4000 patient-years had been achieved in the combined treatment and control groups, the pilot committee examined the principal recordable events and decided that it was a good time to terminate the trial because prolonging the study would be unlikely to add appreciably to the conclusions.

Results

Altogether 10718 patients aged 60 to 79 years, men 4731, women 5987 were screened. This constituted 78% of the total age range on the practice lists. Excluded were 1871 patients because of medical conditions and 1165 because they were on treatment for hypertension, 30% were hypertensive but unwilling to participate in the study. A total of 884 patients were included in the treatment trial, 419 in the treatment group and 465 in the control group. Table 1 gives the characteristics of these patients. The groups were well

TABLE 1—Comparison between the treatment and control groups at the start of the trial

	Treatment group	Control group
No. of patients	419	465
No. of patients seen	1847	2051
No. of men	1227	1314
No. of women	1920	2137
Mean SD age years	68.2 7.2	68.3 7.3
Mean SD weight kg	70.2 12.1	70.4 12.1
Smokers		
Mean SD systolic blood pressure mm Hg	186.1 15.6	186.1 15.6
Mean SD diastolic blood pressure mm Hg	109.1 11.8	109.1 11.8
Mean SD blood pressure mm Hg	147.6 14.7	147.6 14.7
Mean SD serum creatinine mmol/l	18.9 8.9	18.9 8.9
Mean SD fasting blood glucose mmol/l	4.7 1.0	4.7 1.0
Mean SD serum uric acid mmol/l	404.4 2.4	404.4 2.4
Mean SD serum potassium mmol/l	4.3 0.6	4.3 0.6
Left ventricular hypertrophy on electrocardiogram	8	11
Left atrial enlargement on chest X-ray examination	22	21

Conversion: 1 mmol/l to mEq/l: Blood urea (mmol/l) $\times 10$ to mg/100 ml; Serum creatinine (mmol/l) $\times 1.13$ to mg/100 ml; Blood glucose (mmol/l) $\times 18$ to mg/100 ml; Serum uric acid (mmol/l) $\times 2.8$ to mg/100 ml.

balanced apart from a non-significant excess of smokers in the treatment group (28% v 21%) and a non-significant excess of left ventricular hypertrophy on electrocardiogram in the control group (8% v 11%). The mean period of follow up was 4.1 years, range 1-10 years. The distribution of the 884 patients by age and sex at entry to the trial was: age 60-64, 77 men and 156 women; age 65-69, 58 men and 152; age 70-74, 62 men and 157; age 75-79, 45 men and 99.

TREATMENT

Seventy per cent of the patients in the treatment group were on atenolol and 66% on bendrofluazide. 7% were on bendrofluazide only, 4% were on treatment throughout most of the study. In the control group 2% were put on hypertensive agents because of a rise in blood pressure above 280/120, 7% were put on diuretics because of ventricular failure. Figure 1 shows a life table analysis of the various treatments used in the study.

Compliance with the treatment regimen was tested once in the pilot stage of the trial by selecting the patients with a mean fall of 10 mm Hg or less in systolic pressure and taking a venous sample of blood at their next attendance. This group of 12 patients was on a regimen that included atenolol. Estimation of blood atenolol concentrations in the samples indicated that 10 had levels that suggested recent ingestion of the drug, and one of the remainder had probably had the drug in the previous few days. No further formal tests of compliance were made, but the trial nurses were instructed to watch for non-compliant patients, especially among those who showed little response to treatment or those on atenolol who showed no fall in pulse rate. When compliance was in doubt tablets were counted.

REDUCTION OF BLOOD PRESSURE

Figure 2 shows the level of blood pressure in the control and treatment group throughout the trial. There is a consistent difference of about 18 mm Hg in systolic pressure and 11 mm Hg in diastolic pressure between the two groups. The control group shows a reduction of about 16 mm Hg from their initial systolic pressure and about 10 mm Hg in diastolic pressure. The mean blood pressure in the treatment group conceals a great variation of response.

Since patients were not randomised to treatment groups it is impossible to compare response to the β -blocker and the diuretic. About two thirds of the patients who were put on atenolol, however, had to have bendrofluazide in addition to achieve a satisfactory blood pressure response.

In the first year of treatment only 36% of the treatment group were at or below 170 mm Hg systolic against 20% of the control group. This slowly increased until in the eighth year of treatment 62% were at goal pressure against 31% of the control group.

About a quarter of the patients were unable to tolerate atenolol because of side effects. The most common of these were general fatigue, muscular weakness, and breathlessness on exertion.

SYMPTOM QUESTIONNAIRES

Eighty three per cent of the treatment group and 81% of the control group were given self administered symptom questionnaires. Patients were encouraged to fill in the questionnaire on their own. A few, however, had to

FIG. 1—Percentage of patients on various treatment regimens

FIG. 2—Mean blood pressure in the treatment and control groups

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finders were used and large cuffs used as necessary. A few of the first screening pressures were obtained by the general practitioner when patients attended for other reasons. If the systolic pressure was 170 mm Hg or above, or the diastolic pressure 105 mm Hg or above, phase 1, they were asked to attend on another day when a further blood pressure reading was taken with a Hawksley random zero sphygmomanometer. If either the systolic or the diastolic pressure was at the same level the patient was asked to attend a third time. If the systolic or diastolic blood pressure was raised on this occasion the patient was considered eligible for the trial. At this stage the trial was explained and informed consent for participation obtained.

Before randomisation all patients had a general medical examination and the following measurements were made: height, weight, 12 lead electrocardiogram, the urine was tested for albumin and sugar and sent for microscopy and culture. A venous blood sample was taken after a 12 hour fast for full blood count and urea, sodium, potassium, creatinine, uric acid, cholesterol, and blood sugar concentrations. A standard postprandial test (fasting) was taken and peak excretion of glucose measured. A 10 question mental test modified from that used by Quereux and Hodkinson was used to exclude dementia. A score of less than 10 excluded patients from further participation.

RANDOMISATION AND STUDY DESIGN

The results of the tests were examined for exclusion factors. If these were absent the patient was randomised into the treatment or control group on a 50:50 basis without stratification. Randomisation was achieved by opening an opaque envelope supplied in sequence from the trial administrative centre that gave instructions for allocation to the treatment or control group. These had been prepared from random number tables.

An observation controlled study design was chosen without placebo. A double blind protocol, which would have ensured objectivity in the evaluation of side effects and compliance, was not possible because of the long period of follow up in an elderly population that was subject to many intercurrent illnesses, some of whom were taking multiple medications. Moreover, the doctor conducting the study was also the patient's sole medical adviser, and there was a possibility of conflicts arising between the needs of the trial and the medical needs of the patient, particularly if the doctor was blinded to the treatment the patient was receiving. There is no evidence that placebo reduces blood pressure over a long period or affect the incidence of heart attack or strokes. Their use might, however, have allowed a more objective measurement of side effects.

To increase objectivity in the identification of endpoints the following precautions were taken. Both the treatment and the control groups were followed up at the same intervals throughout the study with the exception of the first few months when patients in the treatment group were reviewed more often during the induction of treatment. The medical records of all patients in the treatment and control groups were reviewed by the trial nurses continuously throughout the trial, and every six months they were examined by two investigators from the trial administrative centre. All deaths and major recordable events were entered with full details on special forms which were submitted to the administrative centre. They were reviewed by the pilot committee who advised on the status of these events while being unaware of the treatment the patient was receiving. Standard definitions of major events were used by the committee (see appendix 1). All electrocardiograms were classified by an experienced coder using the Minnesota Code. He was also blinded to the treatment that the patients were receiving.

TRIAL SIZE

From the incidence of strokes and coronary events in the pilot stage of the trial a target of 4000 patient-years in the combined treatment and control groups was set. It was estimated that this would give the completed trial a 90% power of detecting a one third reduction in either event from an estimated 15% incidence over a five year period at the 5% level of significance.

NURSE RECRUITMENT AND TRAINING

The nurses who were recruited to this study were selected by their ability to supervise the complex protocol in busy general practices. They were trained in the technique of taking blood pressures and tested by the use of training tapes and double stethoscopes. Each nurse received a manual of instructions giving detailed advice on the implementation of the trial design. They were in constant communication with the trial administrative centre and attended trial meetings every six months.

TREATMENT REGIMEN

The principal antihypertensive agents used were atenolol and bendrofluazide, and these were introduced stepwise in that order.

Step 1—Atenolol 100 mg each morning. This was continued for three months. If at the end of three months the systolic blood pressure was still above 170 mm Hg or the diastolic pressure above 105 mm Hg the nurse proceeded to step 2.

Step 2—Bendrofluazide 5 mg daily was added to the atenolol.

Patients who could not tolerate 100 mg atenolol were given 50 mg atenolol or treated with bendrofluazide alone.

Step 3—If bendrofluazide and atenolol failed to lower the pressure alpha-methyldopa 500 mg was added as a single dose in the evening.

Patients who could not be effectively treated with any of the above regimens or who developed unacceptable side effects could be treated with any recognised therapy rather than remain untreated. In the last two years of the trial several of these patients were treated with nifedipine, usually as nifedipine retard 20 mg morning and night.

After they had been in the trial a year both groups of patients were given the same examination and tests as at the beginning. They were also given a self administered questionnaire to assess the level of side effects. Since no validated questionnaire that was suitable for assessing side effects in elderly patients taking antihypertensive treatment was available a specially designed questionnaire was produced (see appendix 2). Graded responses were elicited to questions regarding headaches, breathlessness, fatigue, worries about health, depression, dizziness, and general well being. The responses were added to tick one of three boxes in each question indicating that their level of complaint since entering the trial was usual, moderately worse, or much worse.

A questionnaire as described by Jackman et al. was also given to relatives to determine whether any change had been noticed in the patient's behaviour. If a near relative was not available a close neighbour or friend was asked to complete it.

After the patients had been in the trial for two years the biochemical tests and electrocardiograms were repeated, but no medical examinations were performed.

Patients in the control group who developed sustained blood pressures above 280/120 or who had stroke were treated. They were followed up in the trial, however, and further recordable events included in the final analysis. Cardiac complications such as ventricular failure were treated in the usual way. Patients who could not attend the medical centre were followed up at home.

RECORDABLE EVENTS

The following recordable events were entered on the trial cards from the medical notes: myocardial infarction, major stroke, minor stroke, transient ischaemic attack, congestive heart failure, atrial fibrillation, clinical gout, diabetes, non-fatal cancer, vertigo, dizzy spells, and death. Major recordable events: myocardial infarction, strokes including transient ischaemic attacks, and death, were referred to the trial administrative centre on special forms.

The data from the cards were transferred yearly to computer forms. These were transmitted to a central computer held by one of the practices. These data were processed by a computer secretary and access to the data was restricted to the trial organisers. The accuracy of transfer of data at all stages was audited and was satisfactory.

Analysis has been on the "intention to treat" basis. The treatment and control groups were kept intact for analysis irrespective of their actual treatment. Once patients reached the age of 80 and had been in the study for five years they were excluded from further analysis. Patients who left the practices were excluded at that time, but all events recorded until they were included. They were registered with the National Health Service Central Registry at Southampton so that in the event of their dying the cause of death could be ascertained. For this paper, however, no events that occurred to the patients after leaving the practices were included in the analysis.

The records of all patients dying in the practices were retained for examination. Where possible a necropsy report was obtained. This was achieved in all the "sudden deaths" in the trial. In three cases this led to a reclassification of the cause of death from one to a cerebral haemorrhage and in two to ruptured aortic aneurysms. Full reports of deaths were submitted by the doctors and, where necessary, hospitals were contacted for further details.

Patients suffering a number of events of the same type were counted as having only one event. A fatal event cancelled out non-fatal events of the same kind. A fatal myocardial infarction or "sudden death," for instance, took precedence over a non-fatal myocardial infarction. In the case of stroke the most serious, major, minor, or transient ischaemic attack was counted. For further details of the trial protocol the previous report should be consulted.¹

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have help from the nurse. There were no significant differences between the percentages of patients in the control and treatment groups who complained of any severe symptoms (table 1).

The relative questionnaire was filled in by either a close relative or a friend of the patient in 89% and 90% of the treatment and control groups respectively. This questionnaire was more difficult to complete. The question on sexual activity was excluded as it caused too much embarrassment. The questionnaire in scored for each question and a global score was calculated for the patient on a range of 0-35. High scores indicate increasing disability. The mean score of the treatment group was 3.73 and the control group was 4.20 was identical, 3.03. Therefore, no difference emerged in the response to the relative questionnaire.

There were 11 patients in the treatment group who reported clinical gout compared with two in the control group. Six patients in each group developed diabetes during the trial.

TABLE 1—Percentage of patients in the treatment and control groups complaining of moderate or severe side effects

	Treatment group n=419	Control group n=465
Side effect	Moderate	Severe
Headaches	18	4
Tiredness	35	46
Breathlessness	31	32
Dizziness	26	26
Depression	14	12
Indigestion	2	0
Worries	4	36
General illness	24	19

BIOCHEMICAL RESPONSE TO TREATMENT

Table III shows the biochemical values in the treatment and control groups at the first and second examinations during the trial. There was a significant increase in blood urea, creatinine, sugar, and urate concentrations in the treatment group. The increase in blood urea was modestly distributed. It occurred very soon after the onset of treatment and did not seem to get worse as the trial progressed. The mean serum potassium concentration was almost unaltered, being 0.07 mmol (mEq.) lower in the treatment group at the first examination and 0.08 mmol (mEq.) lower on the second.

TABLE III—Haematological measurements at the first and second trial visits trial examination at one year and two years

	Treatment group n=419	Control group n=465	p value	Fisher's test
Ha. g/dl	14.14 1.41	14.27 1.41	NS	-1.32
Urea (mmol/l)	6.15 1.17	5.78 1.14	$p < 0.001$	-1.42
Urea (mg/100 ml)	69.16 12.79	63.76 12.79	$p < 0.001$	-1.49
Blood glucose	5.13 1.15	5.18 1.15	NS	-0.05
Urea and creatinine	0.18 0.09	0.17 0.09	$p < 0.001$	0.25
Serum potassium	119.82 2.54	119.99 2.52	$p < 0.005$	-1.98
Serum creatinine	4.23 0.57	4.30 0.58	$p < 0.005$	-1.96
Cholesterol (mmol/l)	6.63 1.18	6.60 1.17	NS	-0.80
Packed cell volume	0.42 0.04	0.43 0.04	NS	-0.39

Conversion: 1 g/dl to mmol/l: Blood urea (mmol/l) $\times 10$ to mg/100 ml; Serum creatinine (mmol/l) $\times 1.13$ to mg/100 ml; Blood glucose (mmol/l) $\times 18$ to mg/100 ml; Serum potassium (mmol/l) $\times 10$ to mEq/l; Cholesterol (mmol/l) $\times 38.67$ to mg/100 ml; Packed cell volume (mmol/l) $\times 100$ to mmol/l.

MORTALITY AND MORBIDITY

Table IV gives the incidence rates of fatal and major non-fatal events in the treatment and control groups with the 95% confidence limits. There was no significant difference in the total mortality in the two groups. The rate of fatal stroke in the treatment group was 0.30 of that in the control group (confidence interval 0.11-0.84, $\chi^2 = 5.25$, 1 d.f., $p < 0.025$). The rate of all stroke in the treatment group was 0.58 of that in the control group (confidence interval 0.35-0.96, $\chi^2 = 4.53$, $p < 0.03$). Figure 3 shows a life table analysis of the proportion of patients who had a stroke of any kind by the interval since entry to the trial in the treatment and control groups.

TABLE IV—Major recordable events rates per 1000 patient-years: number of events in parentheses

	Treatment group rate	Control group rate	p value	95% confidence interval
Stroke				
Fatal	2.2	7.1	0.06	<0.025 0.11-0.84
Major	2.1	4.9	0.70	NS 0.21-2.12
All strokes	4.3	12.0	0.07	NS 0.35-0.96
Transient ischaemic attacks	1.8	3.5	0.77	NS 0.62-1.77
All strokes	12.5	21.4	0.14	<0.01 0.51-0.96
Stroke after attack				
Fatal	13.6	23.6	0.08	NS 0.41-1.71
Non-fatal	1.5	4.9	0.10	NS 0.11-0.84
All strokes after attack	15.1	28.5	0.03	NS 0.41-1.71
Unilateral weakness	2.2	4.9	0.11	NS 0.28-0.45
Non-fatal	2.8	15.6	0.33	NS 0.35-0.96
Unilateral sensory deficit	1.1	2.0	1.11	NS 0.16-1.90
Death from hypertension	0	0.48	1	NS 0.11-0.20
Death from myocardial infarction	0	0.48	1	NS 0.11-0.20
Death from stroke	14.0	24.3	0.10	NS 0.41-1.71
Death from cancer	4.2	4.9	0.89	NS 0.41-1.71
Death from all causes	11.7	11.2	0.90	NS 0.41-1.71
All deaths	12.5	23.6	0.07	NS 0.35-0.96
All patients	419	465		
Patients seen	1847	2051

FIG. 3—Proportion of patients who had a stroke (transient ischaemic attack, minor, major, or fatal) by the interval since entry to the trial.

Analysis of subsets of patients by age at first admission to the study: 60-69 years, 70-79 years, and by sex: men and women. There was a similar reduction in stroke for all these groups. The study, however, was not large enough for these differences to be significant.

Deaths from myocardial infarction and sudden deaths were combined as coronary artery deaths. In the treatment group there were 25 coronary artery deaths (sudden death, myocardial infarction 16) and in the control group 28 sudden death, myocardial infarction 20. The incidence per 1000 patient-years of coronary artery deaths was 13.6 in both the treatment group and the control group. Non-fatal coronary attacks were similar in both groups: treatment 10, control 10. This treatment had no effect on the incidence or mortality of coronary artery deaths. Overall cardiovascular

TABLE 1—The rate of all strokes in the treatment and control groups per 1000 patients years according to the site of the initial screening and the sex of the patients (numbers of strokes in parentheses)

	Treatment group	Control group	Significance χ^2
Age, years			
Men	74.9	74.3	NS
Women	74.9	74.3	NS
All ages	74.9	74.3	NS
Sex			
Men	74.9	74.3	NS
Women	74.9	74.3	NS
Both sexes	74.9	74.3	NS

TABLE 2—Types of cancer in the treatment and control groups

Treatment group	Control group
Female n=17	Female n=12
Breast	Breast
Stomach	Stomach
Colon	Colon
Liver	Liver
Bladder	Bladder
Thyroid	Thyroid
Uterine body	Uterine body
Prostate	Prostate
Testis	Testis
Lymphatic leukemia	Lymphatic leukemia
Male n=12	Male n=12
Colon	Colon
Stomach	Stomach
Bladder	Bladder
Uterine body	Uterine body
Prostate	Prostate
Testis	Testis
Lymphatic leukemia	Lymphatic leukemia
Basal cell carcinoma	Basal cell carcinoma

mortality due to stroke, coronary artery disease, ventricular failure, ruptured aneurysm, and hypertensive nephropathy showed a non-significant difference in the treatment group. Non-fatal ventricular failure was more common in the control group, but this difference was not significant.

SMOKING IN RELATION TO STROKE AND MYOCARDIAL INFARCTION

As most of the treatment group than the control group smoked (28% v 21%), the incidence of smoking in those who had strokes and myocardial infarctions was examined in the two groups. Of those who had strokes, 39% in the treatment group smoked against 23% in the control group. With myocardial infarction, however, this was reversed, with 38% in the treatment group smoking and 46% in the control group.

The incidence of all strokes (per 1000 patient-years) in smokers and non-smokers was: treatment group—smokers 17.4 (nine patients), non-smokers 10.5 (14 patients); control group—smokers 21.1 (10 patients), non-smokers 20.9 (34 patients). A significant reduction is seen only for non-smokers—a 50% reduction of stroke ($p < 0.05$).

The hypothesis has been suggested from the results of two recent trials that smoking in men may nullify the protective effect of β -blockade on heart attacks.^{1,2} We therefore looked at the rate of coronary artery attacks in the treatment and control groups by sex and according to smoking state at the onset of the study (treatment group—male smokers 4 (11 attacks), male non-smokers 2 (4 attacks); female smokers 8 (0 attacks), female non-smokers 15 (16 attacks); control group—male smokers 4 (8 attacks), male non-smokers 2 (0 attacks); female smokers 4 (8 attacks), female non-smokers 6 (8 attacks). There is a trend towards a reduction in the rate of attacks in men smoking or not and in women smokers, but this trend is reversed in non-smoking women. The numbers in this subanalysis are small, however, and the differences not significant.

Patients were admitted to this study with either systolic or diastolic hypertension: 23% had mean diastolic pressures of less than 90 mm Hg phase 5 at randomisation. The cardiovascular death rate in the treatment and control groups according to the diastolic blood pressure at the onset of the trial was: diastolic pressure ≥ 90 mm Hg—treatment group 15 (9 deaths), control group 23 (9 deaths); diastolic pressure < 90 mm Hg—treatment group 9 (2 deaths), control group 20 (11 deaths); not significant. There is a trend for a reduction in cardiovascular death rate for those with diastolic pressures ≥ 90 mm Hg, but an increase in death rate for treatment for those with low diastolic pressures before the trial.

There was a non-significant excess of fatal cancers in the treatment group table VI. The excess was entirely in cancers of the bronchus treatment group, control group.

Before randomisation 1165 patients were excluded because they were already being treated for hypertension. The mortality of these excluded patients was compared for comparison with patients in the treatment group. The rates, per 1000 patient-years, were: total mortality 39.6, stroke 7.3, coronary artery disease 11.7, and all cardiovascular disease 23.9. These are closely similar to those in the treatment trial, see table IV.

Discussion

In this population of elderly patients with hypertension blood pressure was reduced by 18.11 mm Hg for an average follow up period of 4.4 years. There was no effect on overall mortality or on the incidence of fatal or non-fatal heart attacks, but there was a reduction of 42% in the incidence of stroke, mainly apparent in fatal and major strokes. There was a 22% reduction in cardiovascular deaths, but this was not significant.

The absence of an effect on overall mortality was partly due to a non-significant increase in the death rate from cancer in the treatment group. These were mainly cancers of the bronchus. No reason can be given for this, and it is probably a fortuitous cluster.

The reduction in stroke rate was similar in men and women and in the two age groups 60-69 years and 70-79 years at randomisation. It was more evident in non-smokers, however, who showed a 50% reduction in overall stroke rate to treatment. The small number of reported transient ischaemic attacks is due to the fact that most of the patients who had such attacks later had serious strokes and were included in the enumeration of these events. The definition of transient ischaemic attacks also strictly excluded patients who had residual symptoms or signs after 24 hours. These were classified as minor strokes.

The lack of any effect of treatment on the incidence or mortality of myocardial infarction or on the incidence of sudden death was disappointing. There is evidence from the Medical Research Council trial of mild hypertension and from the International Prospective Primary Prevention Study in Hypertension that β -blockade may reduce the incidence of myocardial infarction in male non-smokers.^{3,4} There was no evidence for such a trend in this study. Indeed, female non-smokers showed an increased incidence of heart attack on treatment. As 58% of patients in the study fell into this latter category this may have contributed to the lack of overall effect on treatment of coronary events. No conclusions, however, can be drawn from the non-significant trends shown and this subanalysis is given only for comparison with other studies. As more patients in the treatment group than the control group smoked (28% v 21%), the possibility that smoking increased the rate of heart attacks in the treatment group must be considered. The proportion of smokers among the patients who suffered a coronary artery attack in the treatment group, however, was less than in the control group (38% v 44%), so this is unlikely to be the case.

The inclusion of patients with low diastolic pressures (systolic only hypertension) might have combined different responses to treatment in subgroups with high and low systolic pressures. In the Oslo study, which also included patients with low diastolic pressures, an improvement in the incidence of cardiovascular events with treatment was seen only in those with initial diastolic pressure of > 100 mm Hg.

Comparing the patients admitted to the trial with high and low diastolic blood pressure (≥ 90 mm Hg or < 90 mm Hg) showed a trend for a reduction in cardiovascular death rate in patients with low diastolic pressures. Patients with diastolic pressures below 90 mm Hg at the onset had an increased death rate from cardiovascular disease on treatment, although this difference was not significant. This was accounted for by deaths from stroke or cardiac failure, but not from those due to coronary artery disease.

The selection of patients in the trial was based on an attempt to screen all those in the age group on the practice lists. Seventy eight percent were in the treatment group; 1165 patients had to be excluded, however, because they were already being treated for hypertension.

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Appendix 1

Definition of events

These were used by the pilot committee in judging trial endpoints.

Myocardial infarction

Non-fatal: a) Typical pain with either electrocardiographic evidence of a myocardial infarction or raised cardiac enzymes or both. b) Alteration to the electrocardiogram indicative of a myocardial infarction, whether or not accompanied by typical pain.

Fatal: c) Death occurring as a result of infarct as defined in (a) or (b). d) Sudden fatality in which a postmortem examination showed a myocardial infarction or complete occlusion of a coronary artery.

Sudden death: Sudden fatality in which a postmortem examination showed no other cause of death than coronary infarction.

Common artery death: Deaths classified as due to myocardial infarction or sudden death.

Myocardial infarction: Death as a consequence of ventricular failure in which there was no evidence either clinically or at postmortem examination of a myocardial infarction.

100 YEARS AGO

The Bishop of Bedford is quoted as having come among the people, and knows them in sickness and in health. He gives some curious examples of the still prevalent superstitions as to charms against sickness, which are worth preserving among the records of medical folklore. For many years he laboured as a country parson in Shipbourne, and the remedies believed to be efficacious in various complaints absolutely surprised him. In cases of whooping cough, for instance, a woman would send children suffering from it about the town of a pig to a certain particular barn, the reason being that the barn was the house of a pig which had been killed by a severe cold, and it was thought, do you know? Another popular remedy was to pass children over and under a bean seven times. Another horrible thing was to draw three or four black ribbons from a bundle of five, and wear it round the neck, and another thing was to make a child breathe into a frog's mouth. It was supposed, too, that anybody riding on a pebbled horse could cure rheumatic pains. He had seen a woman pretending to charm away a tumour on the lips of another woman with elder-pith which was got at night under a full moon, and by the use of some words which, the charmer said, were the Bible, but he being told that they were not, she said she was sure they were the Prayer-book, and this was equally ridiculous. A farmer, who had the toothache, had given to him some gander's teeth to put in his waistcoat pocket. These were only a few of the superstitions which he had seen in his Northamptonshire, and perhaps none of our readers can do so this curious budget of surviving superstitions. (*British Medical Journal* 1886; 2: 409.)

The mortality from all causes and from principal cardiovascular endpoints in these treated patients was nearly the same as that for patients who were included in the control group of the treatment trial. Therefore the patients in the study were representative of those who are customarily accepted for antihypertensive treatment in this age range.

The trial was observation controlled without placebo. The degree to which lack of blinding of observers might have led to bias in the identification of events must therefore be considered. The biggest difference between the groups was in the incidence of strokes, and as this was mainly apparent in fatal and major non-fatal strokes it is unlikely to be affected by observer bias. The fact that all records were regularly scrutinised by observers from outside the medical centres and that all events were referred to a pilot committee that was independent of the treatment groups, however, receiving must reduce this source of bias further. With regard to coronary events in which no difference was found between the groups, observer bias is less likely.

As both patients and doctors knew what treatment was being given this could theoretically have affected the standard of care or the lifestyle of the patients. Both control and treatment groups, however, attended at similar intervals throughout the study, and apart from their antihypertensive treatment they received medical care from the same doctors. No difference in lifestyle or activities between the two groups was identified in the questionnaires that were completed by relatives. Random zero sphygmomanometers were used to reduce bias in the measurement of blood pressure.

The absence of placebo tablets also makes it more difficult to take account of the side effects of treatment. We were unable to detect any difference in the level of complaint of perceived symptoms from the questionnaires. The background level of symptoms, however, was high, and perhaps the self-administered questionnaire is too unresponsive an instrument for elderly patients, who are prone to forget, not understand, or even want to please the doctor. In younger patients both diuretics and β -blockers have caused symptoms when compared with a placebo. Perhaps direct interviews by trained observers who are unaware of the treatment might have shown a difference. There was an excess of goitres in the treatment group, which was presumably due to the diuretic treatment.

TABLE 3—Comparison of the number of deaths in the combined treatment and control groups in the European Working Party on High Blood Pressure in the Elderly study and in this study

	European Working Party study	This study
No. of patients	840	884
Mean age, years	72	74
Mean systolic blood pressure at entry	160	160
Diastolic blood pressure at entry	95	95
Cardiovascular deaths	162 (10)	169 (9)
Stroke deaths	100	100
Coronary artery deaths	62	69
Non-cardiovascular deaths	178	171

The other major trial in elderly patients was that organised by the European Working Party for Hypertension in the Elderly (EWPEH).⁵ The mean age in the European trial was 72 against 69 in our study. Both trials had similar numbers of men and women and patient-years. The treatment regimens were different because EWPEH did not use a β -blocker. The mean blood pressure at onset at our study was 166/95 compared with 160/101 in the EWPEH study, which had a diastolic requirement for entry, thus excluding "systolic only hypertension." The European protocol was double blind.

Both studies produced a similar reduction in the incidence of stroke by treatment, but EWPEH also showed a reduction in coronary mortality. Table VII gives the numbers of deaths from all

causes and for major endpoints in the two studies. Mortality from most causes in the European study was at least double that in the trial reported here. About a third of the increase can be accounted for by the difference in mean age between the trials. The remainder of the difference, however, suggests a population with much more pathology than the patients in our study and may reflect the fact that the European patients were drawn from clinic attendances, whereas our patients were identified by population screening. Thirty five percent of the EWPEH patients had a cardiovascular complication at entry. The difference in coronary mortality may be due to the prevalence in the control patients in the European study of mild or ventricular decompensation, and thus they would have been vulnerable at the time of myocardial infarction. The different treatment regimens might have affected coronary mortality, but this seems less likely.

Only one of the other published reports of trials of antihypertensive treatment directly addressed the problem in elderly patients. The patients were older than ours and were in residential homes. Only overall mortality was reported, and this was not altered by treatment.

The results in the Medical Research Council trial of elderly patients are closely similar to those shown here in treatment of hypertension. Both used β -blockers and diuretics as the main agents, and both showed a reduction in blood pressure and both showed no effect on the incidence or fatality of heart attacks but a reduction in strokes. The ratio, however, of patient-years of treatment to strokes prevented is different. In the younger patients it needs 850 patient-years of treatment to prevent one stroke. In this trial it needs 100 patient-years to prevent a stroke and 150 patient-years of treatment to prevent a major or fatal stroke. The initial blood pressure in our study is higher than that in the MRC trial, and strokes at any level of blood pressure are more frequent in older patients.

Against this benefit must be set the cost of medical care and possible adverse effects. The considerable effort that was required by dedicated trial nurses to treat hypertension effectively in the elderly—such as sending out many reminders to attend and, where necessary, visiting the patients in their homes—might be difficult to reproduce in everyday practice.

The disability and suffering caused by severe stroke in elderly patients, however, is considerable, and if a reduction of 42% can be achieved in these hypertensive patients by acceptable treatment this may make a systematic attempt to screen the elderly worth while. If 150 patient-years of treatment to prevent a major stroke is too big a task this might be reduced by adopting a higher level of pressure at which to start treatment than the 170 mm Hg used in this trial. Analysis of subsets suggests that women as well as men should benefit and that response is well maintained up to age 80. Those whose diastolic pressures are below 90 mm Hg should probably not be treated. The trial, however, was not large enough to yield significant results on these groups, and our main aim was to test the conclusion of larger trials such as the Medical Research Council's trial in Britain and the Systolic Hypertension in the Elderly study in the United States.⁶

The participating practices were: Drs T S Warrander, J Lushman, Nurse P Thredgold, March; Cambridge; Dr L A Pike, M G Clarkson, I G Cox, Nurse P Eggleston, Handsworth, Birmingham; Dr P H Dawson, P C Brown, M C Donaghy, J M Miller, A Mather, A Loner, Chesham; Hulme Health Centre, Cheshire; Dr J Tudor Hart, Dr G Watt, Mrs M Hart, Nurse W Dove, The Health Centre, Gillingham, Gillingham; Dr N Gostick, Nurse M Roddall, Rugby; Dr M Amali, Dr G Atrial, Nurse D Brown, Tumpers, Cheshire; Dr S L Barber, P G Brown, S Burgevine, J McGorran, W Vennell, Nurse M Walker, Sheffield; Dr M McBride, J High, P Brindley, Nurse T Connolly, Lache Health Centre, Chester; Dr S Bailey and J D Menzies, Nurse M Hui, Block Lane Clinic, Chadderton; Dr C A H Marr, R Orr, K Worrell, Nurse E Carter, Chadderton South Health Centre, Chadderton; Dr E Hughes, S H Street, O R Loner, Chesham; Dr H Watson, Nurse G Kibbey, Gillingham Health Centre, Oxford; Dr J R Cooper, J K M Cooper, G Cooper, K Goadge, K Handley, Nurse M Hanly, Bellingham Medical Centre, Cheshire; Dr J Casandra and T Heller, Nurses C McGuire and C Green, Sheffield.

The management and drug therapy was carried out by Mrs M D Hanly and data processing and computing by Dr T S Warrander and Dr J Lushman, secretary, Mrs M Brighly. The pilot committee of the study who adjudicated

Good Practice

What is a good GP?

NICHOLAS L BISHOP

The government's consultation document on primary health care, published last April, put forward suggestions for encouraging good practice among family doctors. One suggestion was that a good practice allowance might be linked to factors such as personal availability, the range of services provided, and attendance at postgraduate education. One of the purposes of this paper is to define and measure what others, for example, what is a good GP from a patient's point of view, or that of these hospital colleagues—are less easy to define. With this in mind the "BMP" has single the names of a range of people whose work brings them into close contact with GPs and asked them to give us their views of what constitutes a good GP. The article below is the first of a series.

Many of my patient referrals are direct from GPs, and so there is ample opportunity to assess the various styles of practice. I carefully avoid the use of the word "quality" at this early stage, though this is the essence of the whole article. If one is to accept that there are different qualities of GP, and the title presupposes that there are, how does one distinguish the good from the not so good? By what standards are we to measure and from whose point of view? The tweedy old buffer who is always available and good for a chat and a bottle of the usual may not be the doctor you would most desire in attendance when you present with a difficult clinical problem. Similarly, the keen young chap, his walls hung with newly framed diplomas, will undoubtedly handle your brittle diabetes with great aplomb but may not be the one to turn to for support when recently bereaved. Fortunately I do not have to crack this chestnut—but simply address the issue from my viewpoint as a radiologist.

Perhaps the most striking and unexplained element of the relationship between the radiologist and the GP is the wide variation in the usage of imaging facilities by practitioners. This can range from one or two patients a month by one GP to several patients a day by another. Clearly there is something amiss here, though the underuser of the department is probably as open to criticism as the overuser. Both may vigorously defend their practice, claiming that their methods are in the patient's best interest and that they have no desire to change. Such an attitude is commendable if only because it proves that something has been given to the matter and that the individual has a referral policy. My daily contact with requests suggests that many referrals are made without consideration of the patient's subsequent management. This is true of hospital radiology staff as of GPs, but hospital staff are generally more readily contacted.

Think aloud

So my first requirement of a good GP is prior consideration of the usefulness of the examination that the GP is requesting. In many instances this necessitates a depth of radiological knowledge beyond

that normally acquired by a trainee GP. How specific is a barium meal when diagnosing benign gastric ulcer? How good is ultrasound at excluding carcinoma of the pancreas? What is the importance of "clear lungs" on the chest x ray film when the patient has haemiparesis? If the referring doctor is not fully aware of the limitations of the test requested, then the doctor cannot make maximum use of the result. To acquire this knowledge it may be necessary for the doctor to encourage local radiologists to issue guidelines on the use of their department and press them to organise postgraduate meetings or workshops so that each can benefit. There is a tendency to believe that radiology is about interpretation of images only, and therefore GPs will gain little by attending tutorials or lectures. In practice the increasing number of imaging modalities now available means that instruction is needed in their appropriate use. Only if GPs remain aware of these developments and their advantages, their pitfalls, and their relative costs can they fairly expect these services to be available to them.

All this takes time, and many GPs are not sufficiently interested to learn new techniques, or they think that they already know enough about the old ones. Though few radiologists will sympathise with this attitude, most will remain happy provided sufficient information is given on the request form to enable the radiologist to make a decision about the best investigation. A good GP may even write a letter if the problem is particularly difficult or contact the radiologist by telephone so that questions can be answered. If the request is likely to be interpreted as inappropriate or unreasonable I would expect an explanation to be provided to justify it. This especially applies to requests for repeat studies where further documentation of a slowly progressive and essentially incurable condition is of little practical benefit to the patient. Indeed, it may do the patient a disservice if the examination is uncomfortable and falsely raises hopes of a cure.

Perhaps more than any other consultants radiologists lack feedback on their patients. We don't see them in outpatients departments, so the only opportunity we have to follow their progress is when they are re-examined. If a radiologist has had a lot of dealings with a patient in a therapeutic relationship, it is referred to the patient for subsequent examinations. Mentioning this on the request form will simplify the booking procedure and save the time of several radiologists becoming concerned in a complex case, or perhaps the radiologist with a chance to see where he or she previously went wrong.

Thus from the radiologist's point of view a good GP gives prior thought to the subsequent management of the patient and how this will be influenced by the results of the examination. The GP will communicate these thoughts to the radiologist through a concise, legible request form and will be aware of the nature of the procedure requested, its approximate cost related to other forms of management, and its value to the patient in relation to any suffering it may cause. By attending postgraduate meetings the GP's knowledge will remain up to date. In an especially difficult case the GP will contact the radiologist personally to seek advice and when possible will provide feedback on the patient's progress.

Having learned and adhered to all these commandments the GP may still have time for halo polishing.

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Transverse aortic aneurysm: Focal central nervous system symptoms or signs occurring suddenly and disappearing within 24 hours. Aneurysm rupture was included but not so-called "posterior fossa" attacks such as drop attacks.

Minor strokes: Focal central nervous system symptoms and signs occurring suddenly and leaving only a small deficit after a month. The patient could walk out of the house.

Major strokes: Focal central nervous system symptoms and signs occurring suddenly and leaving a substantial deficit after a month. The patient could not walk out of the house.

Cause of death: The definition of cause of death took account of the principal cause of death rather than the mode of death. Patients dying for instance as a result of pneumonia consequent on a stroke were classified as having died from stroke.

Appendix 2

Self-administered symptom questionnaire

Please tick (in the appropriate box).

1. Are you troubled with headaches?
rarely
occasionally
a lot
2. Do you feel more tired than usual?
no
sometimes
most of the time
all the time
3. Have you been getting short of breath lately?
no
occasionally
a lot
4. Have you been getting dizzy or light headed?
no
occasionally
a lot
5. Have you been feeling reasonably happy, all things considered?
yes
not very
very unhappy
6. Do you have more indignation than usual?
no
occasionally
a lot
7. Do you worry about your health?
no
sometimes
a lot
8. Do you feel well?
yes
not very
moderately
not at all