Strategies for Hypertension and Multiple Risk Factor Follow-up Care

by

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Declaration

I declare that this thesis has been composed by myself and is a record of work performed by myself. It has not been submitted previously for a higher degree.

The work described in this thesis was carried out under the supervision of Professor J L Reid, in the then Department of Materia Medica, later Department of Medicine and Therapeutics, when it was based at Stobhill General Hospital.

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Summary

Even though hypertension had been long identified as a major cardiovascular risk factor affecting up to 20-25% of the Scottish adult population (Hawthorne et al 1974), follow-up care had continually been shown to be inadequate (Hawthorne et al 1974, Miall & Chinn 1974, Heller & Rose 1977a,b). By 1981, nurse practitioner care, which had been established in the United States, had been judged to be at least equivalent to physician follow-up care in the ambulatory care setting (Sox 1979). In addition, microcomputer systems were being developed to facilitate data collection, standardisation, retrieval and information analysis (Lilford & Chard 1981). Therefore, a project was initiated to evaluate the effectiveness of a nurse practitioner hypertension follow-up clinic with a microcomputer patient information system. Additional research projects were generated directly from the patient problems revealed with long-term follow-up, and carried out within this alternative care setting.

Over 8 years, 1091 patients were admitted to the clinic with 705 (65%) continuing to attend at the end of Year 8 and only 11% of the population were lost due to non-attendance (Chapter 3). Blood pressure control was achieved in a substantial percentage of the population from the first year and was maintained throughout (Chapter 3), with slight improvements between Year 6 and Year 8 for those attending both years, concurrent with a change in emphasis of care from hypertension to multiple risk factor intervention (Chapter 7). There was greater blood pressure control in the nurse practitioner clinic patients compared with age/sex matched controls attending conventional hypertension clinics (Chapter 4).

The identification of increasing lipids in a population attending continuously for 4 years, and the high incidence of other risk factors, lead to the Cholesterol/Diet Study (Chapter 5) and the Guar Gum Study (Chapter 6). The effect of intensive lipid lowering dietary advice by dietitians over a 6 month period, in hyperlipidemic hypertensive patients, was shown to be limited with only a 2% greater reduction in mean cholesterol in the Advice Group compared to the No Advice Group. At the end

of the study 56% of the Advice Group and 57% of the No Advice Group continued to have a total cholesterol > 6.5 mmol/l (Chapter 5).

The soluble fibre guar gum was shown to have no effect on weight or blood pressure. A 6% reduction in total cholesterol in the lipid sub-group was non-significant in comparison with no change in the bran control. In addition, there was a high incidence of socially unacceptable side effects (Chapter 6).

Levels of reported smoking decreased over time in the clinic and were less than the Scottish population averages. The average weight in the clinic did not change, but clinically modest, but statistically significant reductions, were observed in those with Body Mass Index > 30. There were no changes in reported levels of alcohol intake (Chapter 3 and Chapter 7).

In conclusion, nurse practitioner care is as good as conventional hypertension care for the long term follow-up of hypertensive patients and may be more effective in terms of maintaining follow-up and adherence to management protocols. A microcomputer patient information system can facilitate the every day management of an outpatient clinic as well as providing data for research and audit. This system is capable of responding to and integrating the developments in knowledge and understanding which demand change in the provision of care. Finally, the success of current strategies for decreasing overall cardiovascular risk by decreasing levels of established risk factors, such as increased total cholesterol, smoking, excess weight and excessive alcohol consumption is limited.

Chapter 1. Introduction and Background

1.0 Introduction

Hypertension has been estimated to affect up to 20%-25% of the Scottish adult population (Hawthorne et al 1974, Smith et al 1990) and is a well established risk factor for cardiovascular mortality (Pooling Project 1978, MacMahon et al 1990). Cardiovascular disease, particularly coronary heart disease (CHD), is a leading cause of death in adults, and the rates in Scotland are amongst the highest in the world (Tunstall-Pedoe et al 1986). In addition, the north Glasgow centre of the World Health Organisation's (WHO) international Monitoring of Trends and Determinants in Cardiovascular Disease study (MONICA) had the highest coronary mortality rate in women of all the centres in the 1983-1984 survey (Principal Investigators 1987).

Treatment trials have shown significant decreases in cerebrovascular mortality and morbidity with the lowering of blood pressure (Collins et al 1990). These positive effects have also been seen in the elderly (SHEP 1991, Dahlöf 1991, MRC Working Party 1992)

Unfortunately, conventional hypertension care has been repeatedly shown to be inadequate in terms of follow-up, even up to the present day (Hawthorne et al 1974, Ritchie & Currie 1983, Smith et al 1990). Less than half of the women and only a quarter of the men identified as being hypertensive in the Scottish Heart Health Survey were found to have satisfactorily controlled diastolic blood pressure of 85-90 mmHg (Smith et al 1990). Thus, alternative, more effective forms of care are needed.

Nurse practitioners have been operating successfully in a number of settings in the United States since the 1960's. When compared with medical follow-up in ambulatory care settings, nurse practitioner follow-up has been judged to be at least equivalent (Sox 1979). However, this alternative was not widely publicised in the United Kingdom until Stilwell's work was described in 1982 in the Nursing Times, the year after this project was initiated (Stilwell 1982).

Computerised patient information systems have been shown to facilitate data

collection, standardisation, retrieval and information analysis (Slack et al 1966, Whiting-O'Keefe et al 1985, McDonald & Tierney 1988). The advent of small and relatively cheap desk top personal microcomputers, provided the opportunity for further exploration of the usefulness of such systems (Lilford & Chard 1981).

Thus these elements were brought together in an innovative approach to the long term follow-up care of hypertensive patients. The basis of this thesis is the description, assessment, comparison and evaluation of this approach. In addition, several research projects were generated directly from the patient problems revealed with long-term follow-up, and were carried out within this alternative care setting, and these are also presented.

1.1. Epidemiology of hypertension

During the first half of this century, interest in the measurement of blood pressure and its importance, grew with the establishment in 1905 by Korotkov of a method of auscultation using the device invented by Riva Rocci in 1898 (Korotkov 1905). It was also advanced with the identification of 'essential hypertension' by Allbutt (Allbutt 1915). Thereafter followed a series of reports with increasing scientific rigour as the century progressed. Anecdotal summaries of clinical experience lead to population surveys and comparisons of hypertensive and normotensive populations. The early studies are important for their identification of the link between hypertension and increased mortality, frequently due to a cardiovascular event.

In 1913, Janeway reported anecdotally on 458 patients with elevated blood pressure whom he had treated over a nine year period. By the end of nine years, 53.1% of the men and 32.5% of the women had died. Despite this apparent high level of mortality, he felt that blood pressure did not predict life expectancy (Janeway 1913).

Paullin reported on a series of 39 men and 37 women with elevated blood pressures whom he followed for up to 17 years. At analysis, 48.7% of the men and

9.2% of the women had died. Of the 54 survivors, 16 (30%) had experienced a cardiovascular event (heart failure, myocardial infarction, stroke, transitory ischaemic attack, angina or renal failure) (Paullin 1926).

Using a population approach, Blackford and Wilkinson in 1932 reported on the ten year mortality of 202 hypertensives with blood pressure > 170/100 mmHg. These patients were identified from a review of 10,000 consecutive patients examined in their clinic for a problem that necessitated a general examination, but who had not been referred for care of their hypertension. Approximately two-thirds of the sample was women and the overall mortality was 60%, with female mortality of 50% and 82% for men (Blackford & Wilkinson 1932).

Much effort went into classifying or grading levels of blood pressure and related physical findings. In 1939 Keith, Wagener and Barker from the Mayo Clinic published a retrospective analysis of 219 hypertensives whom they had followed for 5-9 years or until death. Patients were classified by blood pressure and physical findings, particularly retinal changes, and it was found that mortality increased with increasing severity of grading. Only 9% of their patients were alive at the end of the study period (Keith et al 1939).

Interest in the course of hypertensive disease, as described in the above American reviews, was also present in Europe. Frant and Groen followed 418 outpatients with initial blood pressures > 155/100 mmHg for nine years. Female total mortality was 25% compared with the male of 40%, with the median age range of death being 50-59 years for men and 60-69 years for women. Mortality was directly related to blood pressure and also to retinal changes. Finally, these mortality rates were more than twice the rates for the Dutch population at that time (Frant & Groen 1950).

Bechgaard, Kopp and Neilsen reported on a series of 1,038 Danish patients, followed for 16-22 years, who were first referred to a general medical clinic, and most of whom were previously unknown moderate hypertensives (>160/100 mmHg or systolic blood pressure > 180 mmHg). Again the differences between men and

women were apparent. Women with systolic blood pressure < 200 mmHg experienced a normal mortality rate while the men's rate was twice that of the women for an equivalent entry blood pressure. The mortality rate in the men with systolic blood pressure > 200 mmHg was also twice that of the women. These mortality rates are higher than in Frant and Groen's study and this may well have been due to the higher entry blood pressures in this population (Bechgaard et al 1956).

The above sample of reports from the first half of this century indicates that the clinical course of untreated hypertension was repeatedly noted to be associated with high morbidity and mortality, particularly in men. Unfortunately, such retrospective assessment and reporting of clinical data has limitations in that the patients described may well have been referred selectively to these specialist centres and would, therefore, not be representative of the 'true' hypertensive population. These studies do provide a basis and justification for the prospective epidemiological surveys that followed which attempted to assess the occurrence of hypertension in a variety of cultures and countries, and the impact that increasing blood pressure has on cardiovascular morbidity and mortality.

By the mid-1970's, prospective epidemiological studies had identified and confirmed the relationship between elevated blood pressure and increased mortality. From the United States came the large Society of Actuaries' Build and Blood Pressure Study in 1959 (Society of Actuaries 1959) and the Metropolitan Life Insurance Company's study published in 1961 (Metropolitan Life Insurance Company 1961).

The first major 'meta-analysis' (pooling of results) of prospective epidemiological surveys, which had a great impact on the clinical understanding of hypertension and other cardiovascular risk factors was the Pooling Project. It was undertaken by the Council on Epidemiology of the American Heart Association and pooled data from 8,422 white men aged 40-64 from 5 prospective studies. Data were

used from the Albany Cardiovascular Health Center, Chicago Peoples Gas Co, Chicago Western Electric Co, Framingham Heart Disease Epidemiology and Tecumseh Community Health Studies. This was the first time that the cardiovascular risk from blood pressure was identified as consistent, graded, and independent as well as predictive (Pooling Project Research Group 1978).

The Seven Countries Study's importance stems from its multi-cultural population and longevity. Over 15 years, 11,579 men aged 40-59 years from 7 countries were followed. Variability in mortality in the total cohort and amongst the countries was analysed in relation to a number of known cardiovascular risk factors (blood pressure, cholesterol, and smoking). Blood pressure was the only factor which helped to explain the variance in 'all cause' mortality amongst all the countries (Keys et al 1984).

The Whitehall study screened 18,403 male British civil servants aged 40-64 years. The 10 year coronary heart disease mortality correlated with blood pressure, but was more strongly associated with systolic than diastolic blood pressure, thus corroborating the impact of blood pressure in a British population (Lichtenstein et al 1985).

The ongoing Framingham Heart Study is the most important cardiovascular epidemiological study ever conducted. Not only has it continued to collect mortality data on a screened population of both sexes, but the health information has been updated on a regular basis for more than 30 years. Between 1949 and 1953, 5,209 men and women residents of Framingham, Massachusetts, USA, aged 35 to 65 years were recruited (McGee 1973), and surviving participants have been examined bi-annually since recruitment. After 16 years of follow-up, 6 year mortality rates were calculated, and systolic blood pressure was shown to be associated with an increase risk of developing cardiovascular disease (Wilson et al 1987). This was true also for those over the age of 65 years, particularly when the systolic blood pressure was > 160 mmHg at previous examinations (Harris et al 1985).

The largest single population prospectively studied was the Multiple Risk

Factor Intervention Trial (MRFIT) screenees. Unfortunately, they were all the same sex. The 325,348 middle-aged white men were followed-up for 6 years, and there were 2,426 deaths attributed to coronary heart disease from a total of 6,968 deaths. In this population, blood pressure was found to independently contribute to coronary risk (Kannel et al 1986).

Smaller and less well known surveys have shown that the prognostic value of casual blood pressure recordings in regards to cardiovascular complications is greater in men than in women (Miall & Chinn 1974), and increasing blood pressure is associated with an increased death rate from cardiovascular disease (Paul 1971, Tverdah 1987).

In the largest meta-analysis to date, the impact of diastolic blood pressure on incidence of stroke and coronary heart disease was evaluated by MacMahon et al. Data were pooled for 418,343 people from 9 prospective epidemiological studies, 90% of which were from men. The studies used were the MRFIT Screenees, Chicago Heart Association, Whitehall, Puerto Rico, Honolulu, Lipid Research Clinic Prevalence, Framingham, Western Electric, and People's Gas studies. Each study did not make an equal contribution, and the MRFIT screenees were the largest group by a factor of 10. An important aspect was that the analysis included a correction of the 'regression dilution' bias inherent in such data. The authors concluded that prolonged differences in diastolic blood pressure of 5, 7.5 and 10 mmHg were associated with at least a 34%, 46% and 56% difference in the risk of stroke and 21%, 29% and 37% in the risk of coronary heart disease (MacMahon et al 1990).

The Renfrew and Paisley survey is one of the most relevant for this study. It was conducted in the West of Scotland and is one of the few studies which included women as well as men. More than 15,000 men and women were followed for 15 years to study the impact of a number of cardiovascular risk factors as well differences between the sexes. The sexes had similar blood pressures and relative risk associated with increased diastolic blood pressure. Women's absolute risk

associated with rising blood pressure was less than the men's (Isles et al 1992). This result supports the concept that cardiovascular risk from hypertension is present in both sexes, albeit to different degrees.

The epidemiological role which hypertension plays as a risk factor for cardiovascular disease has been outlined. The conclusions drawn from these surveys must be evaluated in the light of several limitations. Most studies have been of middle-aged, middle class white men with only a comparatively small number of women and men of other ethnic origins. When women have been included, as in the Paisley-Renfrew study, a difference in the relative risk of cardiovascular mortality was revealed (Isles et al 1992). Results are based on one-off datasets, except in the Framingham study, which does not allow for the natural variability of results, including regression to the mean (although this had been addressed in MacMahon et al's 1990 meta-analysis), seasonal variations and changes in lifestyle which may have been instituted since the initial survey. The meta-analyses frequently contain the same datasets, with the Framingham study not only appearing in Paul's report in 1971, but in the Pooling Project of 1978 and MacMahon et al's reviews in 1986 and 1990.

Finally, hypertension is only one of a number of cardiovascular risk factors (Hopkins & Williams 1981). It's relationship to the other known cardiovascular risk factors is presented and discussed in section 1.3.

1.2. Impact of anti-hypertensive treatment

1.2.1. Clinical review of anti-hypertensive care

A number of reports of long term clinical follow-up of treating hypertensive populations have yielded data indicating that lowering blood pressure improves survival, with decreases particularly in cerebrovascular and cardiovascular mortality. Hodge et al reported on up to 8 years of follow-up of 497 treated and 156 untreated New Zealand hypertensives who had refused treatment during the 1950's. The groups were sub-divided by sex and the aforementioned retinal grading system of Keith, Wagener and Barker. Mortality was significantly greater in all untreated

controls for each sex/retinal sub-group (Hodge et al 1961).

Hamilton et al cared for 30 treated and 31 untreated hypertensives with diastolic blood pressure greater than 110 mmHg but without symptoms of arterial disease at entry. After 2-6 years of follow-up, there were significantly fewer events in those of the treated group who had blood pressure lowered (Hamilton et al 1964).

In Scandinavia, Berglund et al reported on improved overall mortality, but not coronary heart disease, after 4.3 years of follow-up in a group of 635 treated hypertensive men aged 47-54 years compared with a control group of 391. Both groups had blood pressures > 175/115 mmHg and were part of the intervention and control groups of the larger primary prevention trial (Berglund et al 1978).

The DHSS Hypertension Care Computing Project, in a follow-up report of 6,216 patients, identified that the relative hazard rate for death from ischaemic heart disease increased with diastolic blood pressure in men and women under the age of 60 years. It was noted that a positive relationship for systolic blood pressure continued into old age (Bulpitt et al 1992). The Glasgow Blood Pressure Clinic reported that 'all cause' and stroke 6-year mortality were reduced by treatment since those with the greatest reductions in blood pressure had the least mortality (Isles et al 1986).

Community based studies have also shown the relationship between anti-hypertensive treatment and decreased mortality. Tuomilehto et al studied the mortality from stroke in two areas of Finland from 1972-1977 and 1977-1982. Rates declined for men and women in relation to anti-hypertensive drug treatment, and, where drug treatment declined and blood pressure increased, stroke rates increased (Tuomilehto et al 1985). Lindholm and his colleagues have been following up a community based hypertensive population in Sweden since 1972 (Lindholm et al 1984) and, after 15 years of follow-up, they found a relative risk of myocardial infarction in male hypertensives of 3.8 in comparison to a normotensive population from the same community (Lindholm 1991). Al-Roomi et al conducted a case control

study in Western Australia comparing pre-myocardial infarction and pre-stroke blood pressures with blood pressures of other treated hypertensives who had not yet suffered an event. Blood pressure was higher for those experiencing an event than for those who had not (Al-Roomi et al 1990).

Hart et al analysed the screening and follow-up data over a 21 year period of 25 men and 16 women under the age of 40 who were hypertensive, in his general practice in Wales. Each was matched retrospectively with a normotensive age/sex control. The hypertensive group experienced greater cardiovascular mortality and morbidity than the control group, with hypertensive men having higher rates than hypertensive women (Hart et al 1993).

1.2.2. Controlled clinical trials of anti-hypertensive drug treatment

Despite the positive reports of clinical experience as indicated above, it is the accepted standard to look to prospective, randomised controlled clinical trials for definitive evidence. It was well established by 1980 that lowering blood pressure improved cardiovascular mortality, particularly cerebrovascular mortality. The United States Veterans Administration Study showed improved morbidity and mortality in treated hypertensives over placebo treated controls with diastolic blood pressures between 90-129 mmHg. The first report studied a sub-group of 143 men who had diastolic pressures between 115-129 mmHg (VA Cooperative Study Group 1967). The second presented the results from 380 men with levels between 90-114 mmHg (VA Cooperative Study Group 1970).

However, subsequent trials produced somewhat mixed results. One of the major negative studies of anti-hypertensive treatment was conducted in 452 stroke survivors, 80% of whom were black and 60% were male. Half were randomised to a deserpidine/methyclothiazide combination tablet or placebo after the first 6 weeks of the study when all participants received active drug treatment. There was no difference in stroke recurrence after 3 years of follow-up despite blood pressure reductions of 25/12 mmHg in the drug treatment group. These poor results may well be due to racial differences, the high risk nature of the population, the long effect of

6 weeks of active drug treatment in the placebo group at the beginning of the study, poor compliance with drug treatment or some other detrimental physiological effect of drug treatment, such as increased lipid levels (Hypertension-Stroke Cooperative Study Group (HSCSG) 1974).

Another negative study was the International Prospective Primary Prevention Study in Hypertension (IPPPSH) involving 288 centres in 6 countries and 6,357 men and women randomised to oxprenolol or placebo. Entry diastolic blood pressures were between 100-125 mmHg. Diuretic treatment was added to 67% in the oxprenolol group and 82% in the placebo group. Despite a statistically significant difference in the reduction in achieved mean blood pressure between the groups, this was clinically minimal at 3.8 mmHg/1.2 mmHg. The minimal blood pressure reductions, which were one third to one half the reductions achieved in following studies, and the fact that both groups were treated with active treatment, including the same agent, may well have contributed to there being no difference in any of the standard measures of mortality in this study. Non-smoking men on oxprenolol had the lowest mortality (IPPPSH 1985).

The more positive studies included the American Hypertension and Detection Follow-up Program (HDFP), which studied 5,901 hypertensive men and 5,039 women with diastolic blood pressures of 90-115 mmHg who received either specialist 'stepped care' treatment or were referred to their usual source of care. Diastolic blood pressure reduction in the specialist stepped care group was 5 mmHg lower than in the referred care group 5 years after entry. They also experienced fewer 'all cause' deaths in this time (HDFP Cooperative Group 1979).

The Oslo study randomised 785 men 40-49 years of age to treatment with a diuretic with or without methyldopa, or propranolol and to a control group. The control group did not receive a placebo. Entry systolic pressures were 150-179 mmHg with diastolic blood pressure $<$ 110 mmHg. Despite blood pressure reductions of 17/10 mmHg, only the incidence of cerebrovascular mortality was

reduced in the treatment group. There was no difference in 'overall', cardiovascular or coronary mortality (Helgeland 1980).

The Australian National Blood Pressure Study (ANBPS), a therapeutic trial in mild hypertension, reported a significant reduction in cardiovascular mortality over 4 years, in a group of 3,527 male and female hypertensives, without overt vascular disease, and aged 30-69 years and who were randomised to treatment or placebo. There was no significant difference in ischaemic heart disease rates. Entry diastolic blood pressures were 95-110 mmHg and systolic blood pressure < 200 mmHg, and the average decrease in diastolic blood pressure was 6 mmHg greater in the active treatment group compared with the placebo group (Management Committee 1980).

The Medical Research Council (MRC) trial of treatment of mild hypertension used propranolol or bendrofluazide in 17,354 men and women aged 35-64 years of age. Entry diastolic blood pressures were between 90-109 mmHg. At 5 years, blood pressure was reduced on average by 15/6 mmHg more in the bendrofluazide group, and 10/4 mmHg more in the propranolol group than in the control group. After 85,572 patient years of observation, there were significant reductions in stroke rates and cardiovascular events in the treatment versus placebo group. 'All cause' mortality and coronary events were not significantly reduced. There was no significant reduction in coronary event or cardiovascular rates for those taking bendrofluazide or for smokers taking propranolol. However, non-smokers taking propranolol did experience a significant reduction in coronary and cardiovascular events (MRC Working Party 1985).

More recently, treatment of hypertension in the elderly has been demonstrated to be clinically important, whereas earlier work had indicated that treatment had little effect in this age group (Spackling et al 1981). The European Working Party on High blood pressure in the Elderly Trial (EWPHE) randomised 840 men and women over the age of 60 to either diuretic treatment or placebo. Entry diastolic blood pressures were 90-119 mmHg and systolic blood pressures 160-239 mmHg. After 5 Years, the average blood pressure in the active treatment group was 19/5 mmHg less than in the

placebo group. There was a significant reduction in cardiovascular mortality but not 'all cause' mortality. This was due to a significant reduction in cardiac mortality while cerebrovascular mortality reductions were not significant (Amery et al 1985). The lack of effect on cerebrovascular mortality is at variance with the following studies' results.

Coope and Warrender's open study of 884 men and women between the ages of 60-79 years in primary care, compared treatment with atenolol and/or bendrofluazide and/or additional therapy to control blood pressure with untreated controls. Entry blood pressures were systolic > 170 mmHg and/or diastolic > 105 mmHg. After 4.4 years of follow-up, the average blood pressure in the treatment group was 18/11 mmHg less than in the untreated control group. The treatment group demonstrated a significant reduction in stroke rate, but not in the incidence of myocardial infarction or 'overall' mortality (Coope & Warrender 1986).

The Systolic Hypertension in the Elderly Program (SHEP) randomised 4736 men and women over the age of 60 years to diuretic with or without beta blocker treatment, or to placebo. Entry systolic blood pressures were between 160-219 mmHg and diastolic blood pressure < 90 mmHg. The average blood pressure reduction in the treatment group was 12/4 mmHg greater than in the placebo group. The occurrence of stroke after 5 years was significantly reduced in the treatment group compared to the placebo group, as was cardiovascular morbidity and mortality, but there was no significant reduction in 'all cause' mortality (SHEP 1991).

In another smaller placebo controlled study, the Swedish trial in old patients with hypertension (STOP-Hypertension), followed 1627 patients between the ages of 70-84 years for an average of 25 months. Entry systolic blood pressure was between 180-230 mmHg and diastolic blood pressure < 90 mmHg. Patients in the active treatment group received a beta blocker or diuretic or combination of the two. The average blood pressure in the treatment group was 29/8 mmHg less than in the

placebo group at the end of the study. There was a significant reduction in stroke morbidity and mortality and 'all cause' mortality in the treatment group (Dahlöf et al 1991). This is one of the few mortality studies showing a significant effect on 'all cause' mortality.

The MRC trial of hypertension in the elderly followed nearly 5,000 older adult men and women aged 65-74 years. Entry systolic blood pressures were between 160-209 mmHg and diastolic blood pressure < 115 mmHg. The difference in blood pressure reduction between the drug treatment and placebo groups, was approximately 15/5 mmHg. There were significant reductions in stroke, coronary events and all cardiovascular events. This was confined to non-smokers and those taking the diuretic. There was no difference in 'all cause' mortality (MRC Working Party 1992).

Finally, in a companion paper to MacMahon et al (MacMahon et al 1990), Collins et al evaluated the short-term reductions in blood pressure obtained in 14 unconfounded randomised trials of anti-hypertensive drug treatment (mostly diuretic and/or beta blocker). These included the 2 VA studies, USPHS, HSCSG, HDFP, Oslo, ANBPS, MRC (mild hypertension), EWPHE, and studies by Coope, Carter and Wolff. Thus information from 36,908 patients, who had an average reduction of 6 mmHg in diastolic blood pressure in the active treatment groups compared with placebo or control groups, was pooled. The stroke rate in the treatment group was reduced by 42%, which is in keeping with the potential predicted by the observational studies quoted above. Coronary Heart Disease mortality was reduced by 14% in the pooled treatment groups, less than predicted. The authors point out that most of these studies were of relatively short duration (2-3 years of treatment), and it is unknown whether this is a small, large or full portion of the effect to be expected from the blood pressure lowering under study (Collins et al 1990).

Further aspects of these studies will be discussed in the impact of treatment summary section (1.2.4.). In this way, these results can be considered with the results from clinical reports and the non-pharmacological treatment trials.

1.2.3. Controlled clinical trials of non-pharmacological anti-hypertensive treatment

A number of studies have evaluated the effectiveness of a variety of non-pharmacological or nutritional-hygienic advice on blood pressure, including salt restriction. Such advice has been compared with controls receiving no intervention or drug treatment or in addition to drug treatment as well as after withdrawal of drug treatment.

Most of these studies have involved relatively small groups and have lasted from a few months to a number of years. Reisin et al evaluated weight reduction with dietary advice given bi-weekly by a dietitian over 6 months. There were significant reductions of blood pressure in two weight reduction groups, one of which was normotensive (n=24) and the other treated hypertensives (n=57), compared with a 'drug treatment only' group (n=25), and this correlated with weight reduction in these groups (Reisin et al 1978).

A report from an Australian hypertension clinic in which patients were allocated to one of 5 groups, where blood pressure was monitored and either:
(a) no other treatment received (n=31),
(b) a low sodium diet advised (70-100 mmol/day) (n=31),
(c) received treatment with chlorothiazide with or without methyldopa (n=31) or
(d) treated with propranolol and a diuretic (n=31),
demonstrated that those on a low salt diet had less blood pressure reduction than the drug treatment groups, but had a greater reduction than those on no treatment. Almost a third of the diet group had diastolic blood pressures < 90 mmHg after 2 years of diet, despite minimal differences in measured sodium excretion for those who provided data. Only 16% of the monitored group had diastolic blood pressures < 90 mmHg at the end of 2 years (Morgan et al 1978).

Morisky et al reported on a complicated sequential randomised evaluation of three regimens with sub-groups of a 400 patient population attending their clinics,

91% of whom were black and 70% female. They identified 8 groups of 50 who received either none, one or a combination of interventions: exit interview, instructional family support session with a 'significant other' person, and a series of 3 one hour group sessions with a social worker. Blood pressure, weight and appointment keeping were all improved in the intervention groups compared with the controls. There were 18% more people in the interventions groups with diastolic blood pressure < 90 mmHg than in the controls at the end of 5 years, but absolute changes in blood pressure were not reported. 'All cause' mortality and 'hypertension related' mortality was significantly reduced in the intervention groups compared to the control group (Morisky et al 1983).

Wright et al measured the blood pressure of individuals who were identified in a dietary survey, in which participants weighed all food consumed for three days, to have high (n=49) or low fibre (n=45) intakes. The fibre consumed and used in subsequent interventions were wholemeal bread and added bran, non-water soluble fibres. Those habitually consuming a high fibre diet had significantly lower blood pressures. In follow-up studies, a high fibre group (n=11) significantly increased their blood pressure after consuming a low fibre diet for 4 weeks, and a low fibre group (n=17) statistically significantly lowered their blood pressure after 4 weeks on a high fibre diet. However, a group of 12 treated hypertensives with a habitually low fibre diet, who consumed a high fibre diet for 4 weeks, did not significantly decrease their blood pressures, which, unfortunately, had a wide degree of variability (Wright et al 1979).

Silman reported briefly on a study of 112 middle-aged men which correlated the reported fibre intake and blood pressure and concluded that there was no association between blood pressure and fibre intake (Silman 1980).

Stamler et al have reported on a number of larger and longer studies carried out in the Chicago area. They first reported on two groups of men who participated in the Chicago Coronary Prevention Evaluation Program (CPEP) over 10 years. There were 115 with baseline diastolic blood pressure > 90 mmHg, and 101 with

levels between 80-89 mmHg. In those who continued for 5 years with the program of weight reduction, moderation of salt intake and rhythmic exercise, there were significant reductions in weight and blood pressure compared to baseline (Stamler et al 1980).

The second study was a four year assessment of withdrawal of drug treatment and substitution of nutritional interventions (weight, sodium, saturated fat and alcohol intake reduction) called the Hypertension Control Program. A group of 97 patients who had controlled blood pressure on drug treatment, and were receiving non-pharmacological treatment, was compared with a group taken off drug treatment (n=44) and another continuing on drug treatment (n=48). Approximately 65% of each group was male. Almost 90% of the participants in this study were part of the HDFP study. After 4 years, 39% of the intervention group had controlled blood pressure and were not receiving drug treatment. Weight and sodium intake also decreased (Stamler et al 1987).

In a further study, Stamler et al assessed the effect of lowering weight, salt and alcohol intake and increasing physical activity on the development of hypertension. They identified 201 individuals (86% men) aged 30-44 years with diastolic blood pressures 85-89 mmHg after a second work site screening. Over 5 years, a significantly higher percentage of control group participants became hypertensive and required drug treatment (19.2% vs 8.8%). The intervention group lost weight (2.7 kg) on average and decreased their sodium ($p<0.001$) and alcohol intake (n.s.) compared with changes in control group. More smokers stopped smoking in the control group, which was their only intervention in addition to being monitored (Stamler et al 1989).

Anderson et al compared blood pressure and glycaemic control in a group of 12 diabetic men when taking their usual low fibre diet, and then taking one high in carbohydrates and fibre. Blood pressures were significantly lower by 10%, cholesterol by 26% and average insulin doses were 73% less when the men were on

the high carbohydrate/high fibre diet (Anderson 1983).

Pacy et al randomised 50 untreated mildly hypertensive diabetics (25 men and 25 women) to either a high fibre (30-45g/day), low fat (15% of daily calories), low sodium (40-50 mmol/day) diet or treatment with bendrofluazide 10 mg, to compare the hypotensive and metabolic effects of each treatment. Blood pressure was reduced significantly in both groups by 16/9 and 21/6 mmHg and weight by 2.9 and 1.5 Kg respectively. Glycosylated haemoglobin significantly decreased in the diet group and significantly increased in the bendrofluazide group. In a sub-group analysis of those with hyperlipidaemia, total cholesterol significantly decreased, by 1.1 mmol/l on average, in the diet group and increased, but non-significantly, by 0.5 mmol/l in the bendrofluazide group (Pacy et al 1984).

In a 4 year follow-up of an 8 week relaxation programme in 60 men and 39 women compared with 58 male and 35 female controls aged 35-64 years, Patel et al showed greater reductions in blood pressure in the relaxation group compared with the control group. There were significantly fewer morbid vascular events (electrocardiogram changes, reported angina, myocardial infarction, etc) in those followed up at 4 years (Patel et al 1985).

Langford et al randomised 496 middle aged men and women from the Hypertension Detection and Follow-up Program to continued therapy (obese patients), continued therapy (not overweight patients), drug withdrawal alone (obese patients), drug withdrawal alone (not overweight patients) or with weight reducing diet (obese patients), sodium restriction (obese patients), sodium restriction (not overweight patients). The nutritional interventions were conducted in weekly, then monthly group sessions, and after a year there were significantly more patients normotensive on no drug therapy in the weight reduction and the normal weight sodium restriction groups (Langford et al 1985).

An Australian 14 week parallel group study investigated the effects of diet on blood pressure in 58 untreated mild hypertensive men and women randomised to 3 groups. In the first 2 weeks, all groups took their usual diet. Group 1 acted as

control consuming their normal diet for the next 12 weeks, while group 2 consumed a ovo-lacto-vegetarian (OLV) diet for the next 6 weeks, then their usual diet for the last 6 weeks alternating with group 3 which took the OLV diet for the last 6 weeks of the study. Mean systolic blood pressure fell on average by 5 mmHg while subjects were on the OLV diet (Margetts et al 1985).

In a follow-up study this group carried out a randomised, controlled, cross-over study with 88 (51 men, 37 women) healthy normotensive omnivores changing from their usual diet to a high fibre diet or vice versa for 6 week periods. Blood pressure and lipids did not change over the course of the study (Margetts et al 1987).

Two Danish studies were undertaken with 60 and 45 obese females placed on weight reducing diets with fibre or placebo supplementation taken with 300 ml of water 30 minutes before each meal. The first study lasted for 2 months with mean weight loss of 7 kg in the fibre group and 6 kg in the placebo group ($p<0.05$). Mean blood pressure decreased by 10/5 mmHg in the fibre group and by 13/5 mmHg in placebo ($p<0.01$). The second lasted for 3 months with a mean weight loss of 6.2 kg in the fibre group and 4.1 kg in placebo group ($p<0.05$). Blood pressure decreased from baseline by 6/3 mmHg in the fibre group and 6/0 mmHg in the placebo group ($p<0.05$ for diastolic blood pressure in the fibre group). It was not reported if the fibre was insoluble or soluble or a mixture (Rössner et al 1986).

A 12 week dietary intervention study was conducted in 200 mild hypertensives (diastolic blood pressure 90-100 mmHg) by the Australian National Health and Medical Research Council. They were randomised to a normal diet ($n=55$), high potassium diet ($n=52$), low sodium diet ($n=52$), or high potassium/low sodium diet ($n=53$). Blood pressure fell significantly greater (3.5-5 mmHg systolic/ 2.5-4 mmHg diastolic blood pressure) in all three diet interventions compared to normal diet, with no apparent additive effect of the high potassium/low sodium combination (Chalmers et al 1986).

A Birmingham study assessed the effect on blood pressure and weight in 20

men and 14 women with poorly controlled essential hypertension, of (a) a high fibre, low fat and low sodium diet group (N=17) compared with (b) a usual dietary control group (N=17). Despite a significant reduction of 18/12 mmHg of blood pressure, and 1.9 kg in weight on average in the high fibre, low fat, low sodium diet group, these reductions were not significantly different from the reductions in the control group. However, there was a significant increase in the number of patients in the high fibre, low fat, low sodium diet group with controlled blood pressure at the end of the treatment period. There was no change in the cholesterol values in either group, all of whom were normo-lipid initially (Dodson et al 1989).

The Hypertension Prevention Trial Research Group randomised 841 healthy men and women 25 to 49 years of age with diastolic blood pressures 78 to 89 mmHg to either one of four dietary groups or a control group. The dietary groups were seen in group sessions for caloric restriction alone, reduced sodium alone, caloric restriction with reduced sodium, or reduced sodium with increased potassium. After 3 years the greatest reductions (2/2 mmHg) were seen in the caloric restriction group, and non-significant changes were seen in the sodium restriction groups (Hypertension Prevention Trial Research Group 1990).

Sciarrone et al used a factorial design to investigate the effect of salt restriction and a low-fat/high-fibre diet, in hypertensive subjects. Sodium or sodium-placebo was added to normal-fat/normal-fibre and low-fat/high fibre groups over 8 weeks. 95 hypertensives were randomised to the 2x2 design. Supine systolic blood pressure was significantly reduced by the low sodium diet compared to changes in low-fat/high-fibre group, and cholesterol was significantly reduced by the low-fat/high fibre diet. Weight decreased slightly in all groups, non-significantly (Sciarrone et al 1992).

The Trials of Hypertension Prevention (TOHP) Collaborative Research Group randomised 2,182 men and women 30-54 years to 7 different interventions with a control group for each intervention. Weight reduction (3.9 kg after 18 months) lowered blood pressure by 3/2 mmHg, and sodium intake reduction lowered it on average by 2/1 mmHg. Stress management or supplement with either calcium,

magnesium, fish oil or potassium did not affect blood pressure (TOHP Collaborative Research Group 1992).

Non-pharmacological interventions, primarily dietary, have also been compared to drug treatment. Berglund et al compared dietary treatment (weight reduction, sodium and alcohol restriction, increase potassium intake and ratio of polyunsaturated to saturated fat) with drug treatment in 61 men aged 40-69 years. After one year, drug treatment significantly lowered blood pressure, but dietary treatment significantly lowered the other cardiovascular risk factor, lipids, but not blood pressure (Berglund et al 1989).

In a complicated study design, Oberman et al evaluated the effect of usual, low sodium-high potassium or weight loss diet with placebo, chlorthalidone or atenolol. The study was called the Trial of Anti-hypertensive Interventions and Management (TAIM). In all, 692 men and women between 21-65 years of age were randomised to 9 different treatment groups and change in risk was assessed using the Framingham model. Risk was found to be reduced, except in the 'chlorthalidone alone' group, with the greatest reduction being in the 'weight loss diet taking atenolol' group (Oberman et al 1990).

Non-pharmacological therapy, including a reduced calorie diet, low-salt diet, low intensity exercise and mental relaxation (n=33) was compared with propranolol (n=23) or placebo (n=23) over 12 weeks, in men over the age of 30 years, with entry diastolic blood pressures 95-105 mmHg and weight no greater than 135% of ideal. In addition to blood pressure changes, exercise performance, lipoprotein levels and quality of life variables were evaluated. Non-pharmacological treatment lowered blood pressure as well as propranolol. It also significantly lowered body mass index, total cholesterol, low density lipoprotein (LDL) cholesterol, increased exercise tolerance, and participants reported that they felt more energetic and had greater sexual satisfaction (Kostis et al 1992).

All of the drug studies described in the previous section have included

mortality analysis. Excluding Morisky's study (Morisky et al 1980) and Patel et al (Patel et al 1985), there have been few such reports evaluating the ultimate impact of non-pharmacological or nutritional-hygienic advice.

In a recent study, the Treatment of Mild Hypertension Study Research Group used non-pharmacological treatment (lowering weight, sodium intake, alcohol intake and increased physical activity) as the control intervention in a multi-drug trial in which all drug regimens included this as well. The drugs evaluated were chlorthalidone, acebutolol, doxazosin, amlodipine and enalapril. All groups were followed for an average of 4.4 years. Drug treatment groups had greater blood pressure lowering and significantly fewer cardiovascular and other clinical events than the nutritional hygiene group (Neaton et al 1993).

Finally, there have been reviews of the effects of various non-pharmacological interventions which have helped to shed light on the effectiveness of such interventions. In a review of the effect that weight reduction has on blood pressure, Berchtold et al concluded that weight reduction does lower blood pressure in most obese patients with hypertension. They advocate its use as the 'first and most important step of any rational therapeutic strategy' for any obese hypertensive patient (Berchtold et al 1982). Staessen et al agreed with this view in a similar review (Staessen et al 1985).

In a wide ranging review of the effects of vegetarian diet on blood pressure, Rouse and Beilin presented a factor analysis of data from their controlled vegetarian studies and showed that blood pressure changes were significantly related to the factor representing increased intake of polyunsaturated fat, fibre, vitamin C, Vitamin E, calcium, magnesium and a fall in the intake of protein (Rouse & Beilin 1984).

In 1986, the Royal Society of Medicine convened a round table discussion in London on the role of dietary salt in hypertension care and its implications for public health policies. Experts reviewed the evidence which had accumulated to that time, and concluded that, although the effect of sodium intake on blood pressure was well established, it was relatively small, and the profound problems with compliance

mediated against full effects being achieved (Wood 1986). This was the conclusion drawn by Pickering in his classic text 'High Blood Pressure' nearly 20 years previously (Pickering 1968). Despite this conclusion, a number of researchers have continued to use this as an intervention strategy for evaluation in larger groups and for extended periods.

1.2.4. Impact of anti-hypertensive treatment - summary

A number of issues need to be addressed when considering the effect of treatment. They can be summarised as follows: the comparison of the effect of anti-hypertensive treatment with population surveys, study population size, the level to which blood pressure should be reduced, the cost of such reductions to individuals and society as well as the effect of specific agents.

There are difficulties in assessing the full potential of treatment when comparing achieved levels of pressure with the levels of blood pressure from prospective epidemiological surveys. The vast majority of data from these surveys are for men, while most of the intervention trials have included women. The Renfrew and Paisley survey, which does include women, highlights the very different cardiovascular experience of women (Isles et al 1992). In addition, the surveys such as Framingham and the Whitehall study indicate that systolic blood pressure has the stronger correlation with cardiovascular/coronary heart disease mortality, yet many of the drug studies reviewed above focused on the reductions in diastolic blood pressure.

Another issue is the underlying assumption of a number of commentators that, if one reduces blood pressure, the subsequent reduction in risk ought to be equivalent to the risk associated with that lower level of blood pressure in the prospective trials (Weber 1987, Reid 1988, Fletcher & Bulpitt 1992). If the vascular damage due to raised blood pressure develops over an extended period of time, is it logical to assume it to be reversed entirely (or at all) with the lowering of that pressure in a limited number of years.

There has been an increase in the size of study populations over the years. The VA studies included 143 men in the moderate/severe hypertension study (VA Cooperative Study Group 1967) and 380 men in the mild/moderate study (VA Cooperative Study Group 1970). The MRC trial in mild hypertension had 17,354 (MRC Working Party 1985) and the elderly study had 4,396 participants (MRC Working Party 1992). Unfortunately, there has not been a proportional increase in the clarity of results. It is only with meta-analysis that broader conclusions can be drawn (MacMahon et al 1990, Collins et al 1990).

How far particularly diastolic blood pressure should be lowered has generated a great deal of debate. Cruickshank first raised this concern in 1987 (Cruickshank et al 1987) and in a further paper in 1988 (Cruickshank 1988). A rise in coronary heart disease mortality at levels below 75 mmHg were found in the DHSS Computing Project population (Fletcher et al 1988) and also in the Glasgow Blood Pressure Clinic population (Waller et al 1988). MacMahon's meta-analysis refutes this concern (MacMahon et al 1990), but in a well argued review of the relevant clinical and trial data, Fletcher and Bulpitt conclude that it is still unclear how far below 85 mmHg diastolic blood pressure should be lowered (Fletcher & Bulpitt 1992).

Despite the above difficulties, the majority of anecdotal, retrospective and prospective studies indicate that, even in the mild range of blood pressure elevation, treatment demonstrates some cardiovascular benefits, particularly cerebrovascular,which are particularly pronounced in older populations. Therefore, such results should be incorporated into clinical practice and continue to be so as they emerge.

However, there are experts who argue against this without first evaluating the individual and societal 'cost'. Ramsay voices caution in the light of drug side effects and, based on the trial results at that time, the need to treat 25 people for 20 years in order to postpone one cardiovascular death (Ramsay 1985). Yet, Smith, in an economic analysis of the societal benefits of lowering stroke rates with anti-hypertensive drug treatment (based on the rates obtained in the VA studies),

postulated substantial economic benefit for the United Kingdom (Smith 1990). Maynard estimates the cost of anti-hypertensive drug treatment to prevent stroke between the ages of 45-65 years to be £940/Quality Adjusted Life year (QALY). In comparison, cholesterol testing and lowering by diet in all adults aged 40-69 years is estimated to cost £220/QALY, or by drug treatment in all adults 25-39 years as £1,480/QALY (Maynard 1992). Fletcher identifies a number of variables and basic assumptions that affect economic analysis in a review of these techniques, and advises caution in their interpretation (Fletcher 1992).

Finally, what is the most appropriate drug? Most of the previously reviewed drug treatment studies used thiazide diuretics or beta-blockers alone or in combination or in comparison. At the moment, in light of the positive studies in the elderly, diuretics appear to be the most beneficial. Future studies are required to identify whether the newer classes of agents, including the angiotension converting enzyme inhibitors and calcium antagonists, have equivalent or superior effects with fewer side effects.

1.3. Epidemiology of hypertension and other cardiovascular risk factors

What are these other 'indicators of CHD risk'? Hopkins and Williams in a far ranging review in 1981 found evidence for 246 suggested coronary risk factors in the literature at that time! However, they concluded that hypertension, hypercholesterolaemia, cigarette smoking, diabetes, age, sex and strong familial predisposition were the generally accepted major risk factors for early occurrence of CHD (Hopkins & Williams, 1981).

The DHSS Hypertension Care Computing Project and the Glasgow Blood Pressure Clinic have shown that there are factors that statistically correlate with mortality/survival in their populations of hypertensive patients observed over a number of years. In the 1979 review of 'risk factors for death...', the DHSS project identified age, impaired renal function, smoking and systolic blood pressure before treatment as well as proteinuria, history of myocardial infarction, retinal changes of

accelerated hypertension as independent risk factors for cardiovascular death. Increased weight and serum cholesterol were not associated independently in this analysis (Bulpitt et al 1979).

By 1986, with nearly twice the hypertensive population to review (5,451 vs 2,587) and nearly three times the number of deaths to analyse (411 vs 156), the DHSS project staff assessed their data from a survival point of view. Survival was impaired by cigarette smoking, previous history of myocardial infarction or stroke, diagnosis of angina, impaired renal function and raised blood sugar. Again serum cholesterol was reported as not being an independent risk factor. However, cholesterol values were available for only 49% of the study population (Bulpitt et al 1986).

The Glasgow Blood Pressure Clinic review of mortality strongly indicated that all cause and stroke mortality were reduced by treatment. It was less clear as to the effect on ischaemic heart disease. Age, male sex, blood pressure and the presence of secondary hypertension were associated with increased mortality. In addition, cigarette smoking, a history of myocardial infarction, angina pectoris or cerebrovascular accident, an increased concentration of serum urea and ECG abnormality were also associated with increased mortality. They were unable to study the effect of serum cholesterol due to lack of data. Another issue, brought out by the Glasgow mortality study, was the demonstration that, despite treatment, the mortality rates remained higher than for the 'normal' population, indicating that more than hypertension was implicated in the long term cardiovascular mortality of these individuals (Isles et al 1986).

This excess mortality was also identified in the hypertensive population attending a clinic in Dalby, Sweden. Lindholm and his colleagues have been following up this community based population since 1972. After 10 years of follow-up, they found that the relative odds (risk) of MI in male hypertensives was 3.8 in comparison to a normotensive population from the same community. The estimates calculated for smokers was 4.9 and non-smokers 2.2. This again supports the concept

that more than hypertension needs to be addressed in caring for hypertensive populations. Both hypertensives and controls were re-examined in 1988-89. Assessment included glucose tolerance and cholesterol levels. There was a much higher prevalence of disturbed glucose metabolism in the hypertensive group which appeared to be related to some drug treatments. Those patients on a calcium antagonist or ACE inhibitor had levels similar to the control group (Lindholm, 1991).

1.3.1. Epidemiology of cardiovascular risk

Long term prospective epidemiological studies in 'normal' populations can shed further light on the relationships between cardiovascular risk factors. The following studies have involved more than blood pressure measurement. The blood pressure results from some of these studies have been previously cited in relation to the epidemiology of hypertension discussion (1.1.). The limitations of such, generally one off, examinations have also been cited.

Craig et al in 1989 reviewed 54 published studies to examine the relationship between smoking and serum lipoprotein concentrations in adults. In particular, this meta-analysis found that serum cholesterol concentrations were 3% higher in smokers compared with non-smokers, and high density lipoprotein cholesterol was 5.7% lower (Craig et al 1989).

While excess weight and alcohol consumption are not identified in the following multiple risk factor surveys as relating independently to increased cardiovascular or coronary mortality, they have been shown to contribute to higher levels of hypertension, which is a strong independently linked risk factor. The Kaiser-Permanente study of 87,000 men and women, showed that blood pressure increased with alcohol consumption even when controlling for weight and tobacco use (Friedman et al 1982). A household survey of drinking patterns and blood pressure in 1,630 Americans, showed a significant increase in systolic blood pressure with increasing alcohol consumption. Those reporting 'less than weekly drinking'

had lower blood pressures than abstainers (Russell et al 1991).

Sonne-Holm et al evaluated nearly 1,000 obese Danish men with Body Mass Index (BMI) > 31, after first attending for a military physical examination, and a randomised control group of slightly over 1,000 men with BMI < 31. At initial examination, prevalence of hypertension ($\geq$160/95) was greater as BMI increased. At a follow-up 4 - 40 years later, hypertension was more prevalent in those individuals whose weight had increased and less so for those whose weight had decreased from initial values regardless of starting levels of blood pressure (Sonne-Holm et al 1989).

One of the first prospective studies of a number of risk factors was undertaken in Göteborg, Sweden and published in 1973. Wilhelmsen et al followed 834, 50 year old men without signs of coronary heart disease, for 9 years. Of the 9 factors analysed by a multiple logistic model, high serum cholesterol, smoking, high systolic blood pressure, dyspnoea and registration by the Temperance Board were found to significantly increase the risk of experiencing events related to coronary heart disease (Wilhelmsen et al 1973).

In the Seven Countries Studies, 75% of the coronary mortality variance was accounted for by differences in mean serum cholesterol and blood pressure. When looking at the risk for individuals in the countries, serum cholesterol, blood pressure and smoking were highly significant for coronary death in all regions except Japan (Keys et al 1984).

The Pooling Project and Framingham studies were the first large reviews to demonstrate the additive nature of cardiovascular risk factors in individuals. In the Pooling Project, the risk factors considered in addition to blood pressure, were serum cholesterol, desirable weight for height, smoking habits and ECG abnormalities other than myocardial infarction (MI) (evidence of previous MI was an exclusion criteria). Endpoints assessed after 10 years of follow-up in 5 year increments, included non-fatal and fatal MI, and sudden CHD death. For this population, it was found that the 20% of the population at highest risk yielded 40% of all first coronary events. They

concluded that the risk relationship of blood pressure, serum cholesterol and cigarette smoking to susceptibility to CHD was 'consistent, strong, graded and independent' and had 'predictive ability' (Pooling Project Research Group 1978).

In the ongoing Framingham Heart Study, smoking status, left ventricular hypertrophy on electrocardiogram, and from 1971-74 review, high density lipoprotein (HDL) cholesterol were assessed. Utilising a multiple logistic model to analyse risk, it was found that when cigarette smoking, increased systolic blood pressure and increased total cholesterol were present, the 6 year risk of coronary artery disease (CAD) was 40% greater in women and 100% greater in men than for individuals who were non-smokers, had normal systolic blood pressure and normal levels of cholesterol. The 6 year rates were calculated from 16 years of follow-up data available at that time (Wilson et al 1987).

The additive nature of cardiovascular risk factors has been confirmed in a number of other surveys. In the MRFIT screenees, death rates were analysed by quintile of blood pressure and cholesterol as well as by smoking/non-smoking status, and were cross tabulated for combinations of these risk factors. Again it was found that serum cholesterol, hypertension and smoking each independently contributed to coronary risk. In addition, there was a 'distinct escalation of risk noted for combinations of these risk factors' (Kannel et al 1986).

The British Regional Heart Study examined 7,735 40-59 year old men from 24 towns in England, Wales and Scotland. After 8 years of follow-up, a number of factors were found by multivariate analysis to contribute to the risk of developing ischaemic heart disease. These were age, mean blood pressure (systolic blood pressure + (2 x diastolic blood pressure))÷3), serum total cholesterol, years of cigarette smoking, and the presence or absence of the following: myocardial infarction or ischaemia on electrocardiogram, (definite or possible) angina, recall of a diagnosis of ischaemic heart disease or diabetes made by a doctor, and parental death from "heart disease" (Shaper et al 1986).

The Renfrew and Paisley Survey demonstrated a somewhat different risk factor and mortality profile for women. In comparison with men, the women had a higher average plasma cholesterol (6.4 vs 5.9 mmol/l), fewer smoked (44.2% vs 83.2%) more were obese (BMI >29), but they had a similar diastolic blood pressure to the men (85 vs 86 mmHg). The relative risk was similar between the sexes, but the overall absolute risk and attributable risk were less for women with similar risk levels to that of the men (Isles et al 1992).

To clarify further the relationships between risk factors and cardiovascular mortality, the MONICA project, co-ordinated by WHO, was started in 1982 to assess worldwide trends in myocardial infarctions, strokes and their determinants over the subsequent decade. Using a standardised protocol, data are being collected in 41 Collaborating Centres with 118 Reporting Units. One of the unique features of this collaborative venture is that each centre is self funding and allowed to investigate additional hypotheses as 'local options' as well as the 'core protocol'. Overall, it is anticipated that this study will provide the opportunity to compare results from centres and reporting units with contrasting profiles of risk factors and events as well as differing patterns of risk factor and mortality change (WHO MONICA Project Principal Investigators 1988).

The Scottish Heart Health Study, which includes the MONICA core protocol, investigated coronary risk factors and lifestyle in 10,359 men and women between the ages of 40-59 years in 22 districts in Scotland. Standardised mortality ratios for coronary heart disease in both sexes were obtained for these districts. The mean risk factor values for men from each district were entered into a predictive formula derived from the European cohort of the Seven Countries Study and the American Pooling Project. Cigarette smoking and blood pressure were able to explain a portion of the regional variation in mortality. Cholesterol did not, but it was generally high and varied less between the districts. Women's data were not entered into a predictive formula as 'data for prediction in women are much weaker' (Tunstall-Pedoe et al 1989).

Several epidemiological surveys have demonstrated the 'clustering' effect of cardiovascular risk factors. That is, the major cardiovascular risk factors co-exist more often than would be expected by chance. In the Australian Risk Factor Prevalence Study of over 5,000 men and women, 40% of the untreated hypertensives and more than 50% of the treated hypertensives had total cholesterol > 6.5 mmol/l, while only 30% of those with normal blood pressure had cholesterol greater than this value (MacMahon et al 1985). The Lipid Research Clinics Program Prevalence Study showed similar profiles in over 4,000 men and nearly 4,000 women (Criqui et al 1986). The concept of 'clustering' could be considered a circular argument in that surveys such as the MRFIT screenees and the Framingham study have identified that when these factors are present together, there is an increased chance of that individual dying from cardiovascular disease, ie. that they are risk factors. The benefit of these two studies is to confirm that the apparent synergistic relationship between risk factors identified in the mortality studies, has a basis in the actual occurrence of these factors in a population.

1.3.2. Hypertension trials and cardiovascular risk factors

The management committee of the Australian National Blood Pressure Study reported on covariates which influenced ischaemic heart disease and cerebrovascular disease events in a study of mild hypertension. These factors were older age, male gender, cigarette smoking, and higher systolic blood pressure at screening. Treatment was more beneficial in smokers with lower weight, and, in a preliminary analysis, in individuals with lower serum cholesterol (Management Committee of the Australian National Blood Pressure Study 1984).

In the MRC trial of treatment of mild hypertension in men and women, the entry characteristics of age, male sex and cigarette smoking were significantly related to stroke, coronary events, all cardiovascular events and all cause mortality by logistic regressions. Elevated serum cholesterol and an electrocardiogram showing an ischaemic pattern on entry, were significantly related to coronary events, all

cardiovascular events and all cause mortality. BMI was only related to coronary events (MRC Working Party 1985).

The age and sex, history of cardiovascular disease, smoking and non-smoking sub-group analysis from the EWPHE trial demonstrated there was similar percentage reduction in events for those with a history of cardiovascular disease and over the age of 70 years as for those between the ages of 60-69 years. Little benefit was demonstrated for those over the age of 80 years. As in the MRC trial in mild hypertension, smoking did not influence diuretic treatment outcomes (Amery et al 1986).

In a sub-group analysis of 686 treated hypertensives participating in the Primary Prevention Trial in Göteborg, Samuelsson et al demonstrated a significant reduction in cardiovascular and coronary morbidity in individuals who were able to achieve a substantial reduction in both blood pressure and serum cholesterol (Samuelsson et al 1987).

1.3.3. Population cardiovascular risk factor epidemiology

There is some evidence that reductions in ischaemic heart disease (IHD) and cardiovascular rates parallel reductions in risk factor levels in general populations. Sigfusson et al compared trends in mortality and morbidity with observed levels of risk factors from population surveys conducted in Iceland between 1968 and 1988. They analysed smoking, total serum cholesterol and systolic blood pressure and assessed risk using Cox's proportional hazard model derived from data obtained from an unpublished study done in Reykjavik between 1968-1985. The decrease in mortality, predicted by the decrease in risk factor levels, coincided with the observed decrease in the population's cardiovascular mortality (Sigfusson et al 1991).

Nissinen and colleagues, using the first MONICA survey data collected in Finland, compared the risk factor levels in North Karelia, where a community based multiple risk factor intervention program had been going on for the previous ten years, with levels in their reference area. The community project focused on reducing smoking, promoting a cholesterol lowering diet and on systematic care for

hypertension. Previous research had demonstrated higher levels of cardiovascular risk factors in North Karelia but this survey showed a general decrease to the levels seen in the reference area. There had also been a decline in cardiovascular disease mortality in North Karelia, which is attributed to the change in risk factor level (Nissinen et al 1987).

During the 1970's a community based multiple risk factor intervention programme entitled the Community Syndrome of Hypertension, Atherosclerosis and Diabetes (CHAD) programme was implemented by specially trained physician/nurse teams in four housing projects in Jerusalem. The aims of the programme were to reduce the prevalence of hypertension, hypercholesterolaemia, and overweight and to change dietary, smoking and exercise behaviours. The prevalence of risk factors after 5 years of the programme in 524 men and women, was compared with a control population of 1,512 men and women living in an adjacent neighbourhood who were screened and received routine medical care during the same time period. The prevalence of elevated blood pressure ($\geq$ 160/95 mmHg) was significantly reduced by 20%, hypercholesterolaemia ($\geq$250 mg/dl or 6.5 mmol/l) was significantly reduced by 23% when standardised for age and sex, smoking was significantly reduced by 11% and overweight (BMI > 28) was significantly reduced by 13% when compared with the differences observed in the control population (Abramson et al 1981).

Unfortunately, other specific trials of population intervention have not had such positive results. The WHO European Trial of Multifactorial Prevention of Coronary Heart Disease studied 60,000 male factory workers in 4 European countries including the United Kingdom. The factors addressed were cholesterol, smoking, exercise, and systolic blood pressure > 160 mmHg. The interventions consisted of a low fat, increase in polyunsaturated fat, high fibre diet; stop smoking advice; exercise for the sedentary; and treatment for systolic blood pressure > 160 mmHg. Risk factor changes were assessed by random sampling of approximately

10% of their population. The reductions in CHD mortality in the total intervention group were not significantly different from the control group. However, it was found that the benefit of the interventions were significantly related to the extent of risk factor change (WHO European Collaborative Group 1986).

The results from the multifactor primary prevention trial in Göteborg were similarly disappointing. After 10 years of follow-up, risk factor levels changed substantially in the control groups as well as the intervention group. This was a population based study with 10,000 men in an intervention group and an equivalent number in 2 control groups. Random sampling was done to ascertain levels of risk factors in one of the control groups and in the intervention group at a 10 year final examination. The second control group was not examined or interviewed. One quarter of the intervention group did not participate. This subgroup experienced twice the total mortality of those who participated in the intervention group. Thus it was found that risk factor reduction, all cause mortality, stroke and coronary heart disease incidence was not significantly different between the groups in this study on an intention to treat basis (Wilhelmsen et al 1986).

Both of these studies suffer from methodological difficulties. The small random sampling technique, required due to the resource implications of attempting to test the entire study population, may have produced samples that were not truly representative. In addition, with the world-wide media coverage of cardiovascular health issues in the last two decades, it would have been impossible to prevent control populations from receiving and acting upon such information.

1.3.4. Multiple risk factor intervention studies

Due to the population size required, complexity of conducting and the difficulties in interpreting results, there have been few multiple risk factor intervention studies with mortality follow-up. The Oslo Study's interventions, in 40-49 year old men, consisted of a diet low in saturated fat, with some polyunsaturated fat and high in fibre; and stop smoking advice. The intervention and control group, each contained more than 600 participants and there was a significant decrease in

MI, sudden death and CVA in the dietary intervention group. Overall mortality was decreased but not significantly in comparison with the control group (Hjermann et al 1981).

The Multiple Risk Factor Intervention Trial (MRFIT) randomised more than 12,000 men to special intervention or usual care. In the special intervention group, blood pressure was lowered by drug treatment, smokers were advised to stop and a diet low in saturated fat, high in polyunsaturated fat which was low in calories for those who were overweight, was prescribed. There was no significant difference in cardiovascular disease mortality or all cause mortality after 10.5 years of follow-up between the special intervention or usual care groups (MRFIT Research Group 1990b). However, post-hoc analysis of the 771 men in the special intervention group and 739 men in the usual care group, with entry diastolic blood pressure greater than 100 mmHg and on no treatment, showed a significantly lower CHD and all cause mortality in the special intervention than the usual care group (MRFIT Research Group 1990a).

The Multifactorial Primary Prevention of Cardiovascular Diseases in Middle-aged Men Trial was conducted in 40 to 55 year old Finnish business executives between 1974 and 1980. There were 612 in the intervention group, 610 in a high risk control group and 540 in a low risk control group. The intervention group was given, as appropriate, dietary advice to decrease cholesterol and weight, drug treatment to lower blood pressure and cholesterol, stop smoking advice and a program to increase physical activity. The intervention group experienced a significant reduction in risk factor levels compared with control groups yet had an increase in the incidence of coronary events over the first 5 years of follow-up. This was not statistically significant ($p=0.057$). The authors relate this result to the drug treatments used to lower blood pressure (beta blockers) and cholesterol (clofibrate). The individuals treated with these agents had an associated increased incidence of coronary events compared with those who received other treatment or no treatment (Miettinen et al

1985). Unfortunately, the 15 year mortality follow-up of this study was also negative, with continuing higher coronary rates in the intervention group. The authors discussed their findings in depth with no firm conclusions save 'research on the selection and (inter)actions of methods, including drugs and life-style changes currently in use for primary prevention, is still warranted' (Strandberg et al 1991).

Overall results of multiple risk factor intervention studies, either in community populations or high-risk groups have been generally very disappointing. It may well be that the reverse of the synergistic interaction of factors to increase risk does not operate in risk reduction. In addition, as has been previously stated, changes in the "control" groups have been impossible to prevent due to the wide-spread availability of health promotion and disease prevention information in the world.

1.4. Hypertension follow-up in the United Kingdom

Unfortunately, it has also been clear that the actual detection, and particularly the follow-up of identified hypertensives, has been less than adequate in the United Kingdom. The Renfrew Study showed that out of 422 patients, whose diastolic blood pressure was greater than 100 mmHg on a second reading, and whose health records were traced, 54.5% had not been previously identified as hypertensive (Hawthorne et al 1974).

Miall and Chinn, in their final Welsh survey, found that only 24% of men and 45% of women with phase IV diastolic blood pressures $\geq$110 mmHg had ever received treatment. For those who were receiving treatment, 27% of the men and 24% of the women had diastolic blood pressures $\geq$110 mmHg (Miall & Chinn 1974). Heller and Rose, in their companion papers in 1977, found only 12% of identified hypertensive patients in hospital and 38% of those in general practice were receiving treatment for their hypertension (Heller & Rose 1977a,b).

In a paper about patients who had regularly attended the Glasgow Blood Pressure Clinic during its first 10 years of operation, Johnston et al were able to report on only 16% of the 3500 patient enrolled who had visits recorded continuously over the three years following initial registration. Of these 562 patients, only 27.6%

had systolic blood pressure ≤139 mmHg and 22.1% had diastolic blood pressure ≤89 mmHg after 3 years of attendance (Johnston et al 1980).

In a survey of the general practice records from 1968-1977 of 1000 men over the age of 20 living in the north east of Scotland, only 34% had a blood pressure recorded. Of those recorded 34% had levels >160/100 but only 56% of those with elevated readings had a recorded follow-up reading (Ritchie & Currie 1983).

Kurji and Haines in a review of records (1972-1982) in 18 practices in North West London found 53% of patients had at least one blood pressure measurement recorded, but 69% of the hypertensives had periods of more than 1 year between blood pressure recordings (Kurji & Haines 1984). Michael found only 22% of patients from inner London practices and 43% from outer London practices had a blood pressure recorded in their notes (Michael 1984).

Stern conducted a review of the management of hypertension in 12 Oxfordshire general practices. Of the 2371 hypertensive patients on drug therapy, 53% had last recorded systolic blood pressure <155 mmHg and 40% had last recorded diastolic blood pressure <90 mmHg (Stern 1986).

In a follow-up to Hawthorne's Renfrew study, Smith et al evaluated the blood pressure status of the 10,000 participants in the Scottish Heart Health Study. There was virtually no change in the intervening years in the control of blood pressure. They found that 53% of men and 46% of women who were found to be hypertensive had previously been undiagnosed. Only 25% of the men and 42% of the women, identified as hypertensive, had satisfactorily controlled blood pressure (Smith et al 1990).

The previous catalogue of under-identification and treatment is disappointing, particularly in the light of Hart's work which showed as early as 1970 that is was possible to screen (Hart 1970) and follow-up identified hypertensives in general practice (Hart 1974, Hart 1993).

1.5. Computer based patient information systems

It is acknowledged that computerised patient information can vastly assist the

monitoring and assessment of any disease process. It can facilitate the standardisation of information recorded, its retrieval, and analysis (Slack et al 1966, Whiting-O'Keefe et al 1985, McDonald & Tierney 1988).

The Glasgow Blood Pressure Clinic and the DHSS Hypertension Care Computing Project gathered such data to monitor the long-term care of hypertensive patients since 1968 and 1971 respectively. This involved a number of hospital sites and clinicians (Glasgow Blood Pressure Clinic 1972, Beilin 1974).

Despite efforts to make the systems 'user friendly', both had multiple paged forms that required meticulous completion by an experienced clinician, data input by specialist computer personnel, a turn around time of at least a week before computerised records were added to the patient's notes, and the raw data were only accessible by experienced computer staff (Glasgow Blood Pressure Clinic 1972, Beilin et al 1974).

Other centres also developed systems to deal with the follow-up of hypertensive patients using mainframe computers. One of the earliest reports came from the Bronx HDFP centre. They set up a system for use by the nurses in the study at each clinic visit. In addition, they met regularly with their physician supervisor to review summary reports from the system (Wassertheil-Smoller et al 1975). Another came from a group at Wayne State University where a system was developed in conjunction with the university's computing centre (Laurent et al 1980). The involvement of the nurses in both studies will be discussed in the next section.

A group at the Harvard Community Health Plan in Massachusetts, evaluated a surveillance and reminder system for the follow-up of patients with newly discovered elevated diastolic blood pressure. Of those in the experimental group with computer generated reminders, 98% had follow-up attempted or achieved after 6-24 months, compared to only 46% of the control group (Barnett et al 1983).

A computer assisted shared care scheme in hypertension was started in Aberdeen in 1980. Patients are assessed at the specialist clinic at Aberdeen Royal Infirmary, and, once blood pressure is stabilised, patients are transferred back to

their general practitioner. Doctors and patients are reminded by the system to organise follow-up visits (Petrie et al 1985). Over 250 general practitioners participate, and over 3300 patients had been seen by 1989 (Petrie et al 1989).

In Toronto, a controlled trial of computer assisted management of hypertension in primary care showed that those patients whose general practitioner had feedback from the computer had lower average blood pressure, yet were seen for fewer visits. Also fewer dropped out of active treatment (McAlister 1986).

Several systems have been developed that not only monitor care but assist in medical decision making as an 'expert system', ie. '..a program that symbolically encodes concepts derived from experts in a field and uses that knowledge to provide the kind of problem analysis and advice that the expert might provide' (Shortliffe 1987).

The ARTEMIS system for the management of hypertensive patients has been developing in Paris since 1975. By 1990, data from more than 22,000 patients with more than 70,000 outpatient and 20,000 inpatient visits were coded on the system. The knowledge base utilises dynamic reasoning which is expressed by means of more than 800 production rules. By integrating the clinical data and rules, it predicts for each patient, his/her cardiovascular risk, risk of dropping-out, risk of insufficient blood pressure control and probable blood pressure level. It was prospectively evaluated by comparison with expert specialists' assessment of 80 new referrals, and agreement with the specialists was achieved in 58% to 89% in regards to investigations proposed. These results are difficult to assess since the differences between the specialists was not reported, nor was a pre-set acceptable standard identified (Degoulet al 1990).

Hypertension-aid in physician treatment (HTN-APT) was developed at the Mayo Clinic to assist in the management of hypertension. It was developed to run on International Business Machines Corporation (IBM) personal computers and is a database system based more on clinical judgements of a panel of advisors than patient

data, a simpler system than ARTEMIS. In a small evaluation, it was found to be in general agreement for choice of drug treatment by 8 family physicians who evaluated drug treatment choices for a set of 20 hypertensive patients (Siepmann & Bachman 1987).

1.6. Role of the nurse practitioner

Nurses began to extend their scope of practice into areas previously considered the sphere of their medical colleagues in the 1960's and 1970's. Particularly in North America, the role of the nurse practitioner developed in response to the limited availability of medical care in rural and inner city areas (Stilwell 1982, Jones 1984). The nurse practitioner role has been defined by Prescott and Driscoll as:

> 'a blending of medical or cure activities with the supportive and health promotion activities associated with the traditional nursing care function. It is this unique combination of care and cure functions that distinguishes the nurse practitioner from other primary care givers.'
>
> (Prescott & Driscoll 1979)

In the UK, with the growing interest in nurses extending their roles, the Department of Health and Social Security published Health Circular HC(77) 22 in 1977. The role included tasks previously done by physicians but now delegated by the physician, but with the responsibility for the patient and overall management of treatment remaining with the physician. With the advent of the United Kingdom Central Council for Nursing, Midwifery and Health Visiting, this advice has been superseded by the recent revision of their Code of Professional Practice (UKCC 1992) and Scope of Professional Practice (UKCC 1992). The emphasis has shifted from the delegation of tasks by physicians, to each nurse taking responsibility and being accountable for his/her own practice (UKCC 1992).

Sox reviewed 40 published studies presenting observations of patient care provided by nurse practitioners and/or physician assistants. Of these, 21 were direct comparisons with care given by physicians. A substantial proportion of these studies (6) were in paediatrics. He concluded that in the ambulatory care settings in which it was evaluated, these studies showed nurse practitioner follow-up to be at least

equivalent to the care provided by physicians (Sox 1979).

Nurses have been involved in screening for hypertension and caring for the individuals subsequently found to be hypertensive in a variety of settings, since the mid-1960's, although they had some involvement in hypertension research as far back as 1950 (Frant & Groen 1950). Unfortunately, many of these studies have small populations with scant data reported, were limited in duration and anecdotal in nature.

One of the earliest nurse clinics was set up at the University of Kansas Medical Center. In an evaluation of 66 chronically ill patients (1/3 were hypertensive) who were randomised to either nurse or routine medical follow-up for one year, the 33 patients followed by the nurse expressed 'greater satisfaction' with their care. Within the nurse clinic there was better adherence to appointments, fewer complaints, and fewer calls upon physicians for minor ailments, in addition to lower overall costs (Lewis & Resnik 1967). Similar results were obtained by Schulman and Wood. They reviewed 110 general medical patients, 51 of whom were hypertensive, who were cared for by a nurse practitioner over 6 months (Schulman & Wood 1972).

Clark and Dunn reported on a study done in Kansas City, in which a nurse clinician followed 32 hypertensive patients with initial diastolic blood pressures 100-125 mmHg for 15 weeks at fortnightly intervals. Care included blood pressure measurement, medication adjustment according to an agreed protocol, and monitoring of side effects. 20 of the 32 patients (62%) had diastolic blood pressure < 90 mmHg on two consecutive visits without notable side effects (Clark & Dunn 1976). This was a higher percentage than the 48.5% reported by Logan et al (Logan et al 1979).

At Wayne State University Medical School in Detroit, Michigan, a clinic was set up in 1975 to follow-up hypertensives using nurse specialists and a computer based patient information system. During the first and subsequent visits, each patient was seen by one of the nurses who obtained a medical history, measured height, weight, blood pressure and heart rate. They also counselled patients regarding the

importance of compliance to treatment and the complications of hypertension. Physical examinations were completed by the clinic physician. By 1980, they had seen 1,030 new patients and conducted 5,873 follow-up visits (Laurent et al 1980).

Ramsay et al compared nurse practitioner versus medical follow-up over 15 months in matched groups of 40 out-patients. Diastolic blood pressure was reduced on average by 12 mmHg compared to 7 mmHg, weight in obese patients decreased by 2.7 kg compared with 1.2 kg loss in obese patients in the physician treated group, and there was no difference between the groups for rates of attendance (Ramsay et al 1982). Watkins and Wagner also found no difference in the level of blood pressure control in their review comparing 3 groups of patients: 61 patients followed by physicians alone, 50 patients followed by nurse practitioners alone and 50 patients who were followed by both (Watkins & Wagner 1982).

One study with substantially more information was carried out by a team from Cornell University who set up a work site screening and follow-up program at Gimbels' department store in 1973. The nurses screened 1,674 men and women, assisted in the assessment of those found to be hypertensive, and followed-up patients at their work site under medical supervision. After 1 year, 97% (94 individuals) of those enrolled in the follow-up program were still participating. Systolic blood pressure decreased on average by 27 mmHg and diastolic pressure by 13 mmHg from initial values (Alderman & Schoenbaum 1975).

A very few studies have compared nurse practitioner follow-up with medical follow-up of hypertension. In a community based project in Memphis, Tennessee and the surrounding Shelby County, Runyan compared follow-up care received for diabetes, hypertension, cardiac disease or a combination of these provided by nurse practitioners in decentralised clinics near the patients' homes. This form of care for 1,006 patients was compared with traditional hospital based follow-up for 498 patients aged 40-79 years. Overall, there was less hospital utilisation by patients followed by the nurse practitioners. Diastolic blood pressure was significantly

reduced when compared with starting values (8 mmHg) as well as in comparison with the change in the control group (8 vs. 0 mmHg) who were attending hospital (Runyan 1975).

Another work site study, carried out in Canada by Logan et al, randomised hypertensives to work site care by specially trained nurses or to management by the patient's family doctor. The referral letter to the family doctor included information on the evaluation, management and target blood pressure, and protocol to be followed by the nurse. The nurses measured blood pressure, reviewed drug treatment, and sent a summary of every visit to the family physician. The supervising physician dealt with difficult problems and reviewed patients' charts weekly. Nearly 22,000 were screened to find the 457 employees who were eligible and agreed to participate. After 6 months, more patients in the nurse group had reached their target blood pressure (48.5% vs 27.5%), more were prescribed treatment (95% vs 63%) and a tablet count showed 68% vs 49% were taking their medications as prescribed (Logan et al 1979).

In a follow-up study, Logan et al looked at the cost effectiveness of involving an occupational health nurse in the routine follow-up of hypertensives compared with a similar group receiving regular health care from their family physician. After screening, 97 employees were randomised to be seen by the nurses and 97 to receive his/her regular care. The nurses were to ensure that patients in their group saw their family physician and arrange further appointments if one was missed. They measured blood pressure, reviewed drug treatment and compliance to medication, and whether each was reviewed by his personal physician. After obtaining the approval of an employee's physician, the nurses were allowed to counsel the patient regarding compliance strategies. Due to this doubling-up of professional effort, without significant differences emerging between the groups, the costs of caring for the employees in the nurse group were significantly greater than those being cared for solely by their personal physician (Logan et al 1983).

Lindholm anecdotally reviewed the efficacy of district nurses following up

hypertensive patients in the community at the nurses' surgeries, between yearly visits with the district physicians. He reviewed the records of 223 patients referred and followed for an average of approximately 16 months. Less than half continued follow-up, frequently due to having their blood pressure measured during visits to the district physicians for other chronic disease. For those who continued to attend, 86% maintained their treatment goal (Lindholm 1984).

Viskoper and Silverberg described the positive results obtained by family clinic nurse/physician teams in hypertension detection and follow-up in Israel. The nurses conducted hypertension screening in the community and at worksites, and followed up patients, after an initial medical examination. They measured blood pressure and weight, monitored compliance, offered health education, and tracked non-attenders. The results from a number of Israeli studies are summarised including those from the CHAD study presented above. In one study reported, 73-92% of patients had an average diastolic blood pressure < 95 mmHg after 2-4 years of follow-up. It is difficult to ascertain the contribution of nurse practitioner care as a number of other innovations were instituted over the same period (staff education, structured clinical notes including proformas, and hospital consultant visits to the family clinics) (Viskoper & Silverberg 1985). A review of the last two blood pressures recorded before the physician/nurse teams took over care, compared with the last two recordings 2 years after, in 4,255 patients, showed that 82.4% had diastolic blood pressure < 95 mmHg with physician/nurse care compared to only 42.1% under physician only care (Silverberg et al 1982).

While the majority of the above studies, except for the Israelis', looked at the effectiveness of nurses participating in routine care of relatively small numbers of individuals with hypertension, other studies have used nurses to evaluate the effectiveness of hypertension treatment under clinical trial conditions. In the United States, the Hypertension, Detection and Follow-up program depended on nursing and para-medical staff to screen for hypertension and offer the majority of the care in

specialist clinics. The nurse practitioners followed the patients as a physician would, changing medication and providing health counselling. In addition, they were responsible for the training of paramedical assistants (Robinson 1974, Wassertheil-Smoller et al 1975). Nurses have continued in this role, and, for example, they managed the clinics in the recent SHEP study (SHEP Co-operative Research Group 1991).

The first large trial to use nurses extensively in the United Kingdom was the Medical Research Council's trial for mild hypertension which was begun in the 1970's. The pilot study of 25 centres from a variety of health care screening and care settings demonstrated a number of problems. These included poor quality trial data attributable to lack of standardisation and inexperienced staff, and slow recruitment due to cumbersome screening procedures. It was found that the general practice centres that employed nurses were the most effective in carrying out the pilot study (MRC Working Party 1977). Barnes established the training and review methods (Barnes 1981) which continue to facilitate large scale research projects today in the MRC's 'general practice research framework', including the recently published Hypertension In the Elderly trial (MRC Working Party 1992).

In the original trial, after training, the nurses screened, recorded electrocardiograms, measured height and weight, and undertook urine testing. During follow-up visits they continued to measure blood pressure using the standardised MRC method, titrated drug doses and generally reviewed each participant. Annually, the supervising physician conducted a review. Trial techniques were reviewed regularly under the trial's quality control scheme (Barnes 1981; MRC Working Party 1985).

It is now standard practice to use nurses to collect data in epidemiology survey work. These studies have included the British Regional Heart Study (Shaper et al 1981), the Scottish Heart Health Study (Tunstall-Pedoe et al 1989), and the Nine Towns Study (Bruce et al 1993).

In the Göteberg hypertension clinic which cared for the hypertensive

participants in their Primary Prevention Trial, the nurses conducted the first two clinic visits, where they measured blood pressure, obtained an ECG and blood for tests. During follow-up, the patients attended one of the clinic's physicians for annual review, but saw one of the nurses up to six times in the interim, to assess the control of blood pressure, advised smokers to stop, and those with cholesterol > 6.7 mmol/l to lower the saturated fat content of their diet (Samuelsson 1985).

In Coope and Warrender's randomised trial of treatment of hypertension in elderly patients in primary care, the trial nurses screened 10,718 patients in 13 general practices to identify the 884 participants. They reviewed the medical records regularly of all participants, administered and assisted with the completion of the trial symptom questionnaires where necessary, carried out home visits, sent out appointment reminders and generally implemented the trial protocol with back-up of each patient's general practitioner (Coope & Warender 1986).

There have also been a number of initiatives by individual nurses or groups of nurses to establish screening and follow-up programmes in general practice in the United Kingdom (Antrobus 1983, Antrobus 1984, Carroll-Williams & Allen 1984, Hawke 1984, Bracey & Blythe 1985, Kenkre et al 1985, Jewell & Hope 1988, Hudson 1993).

Other initiatives have been developed by multi-disciplinary teams which have included nurses. At the Veterans' Administration Outpatient Clinic in New Bedford, Massachusetts, a multi-disciplinary small group educational program was set up by the clinic's nurse practitioners. The report followed up 66 participants up to 3 years after attending. Two thirds of the participants reported more positive health behaviours compared with an initial assessment. Least change occurred in the areas of smoking and weight reduction (Wyka-Fitzgerald et al 1984).

In the United Kingdom, the Oxford Prevention of Heart Attack and Stroke project used specially trained nurses to screen and counsel patients in 3 general practices in Oxford. One nurse acted as 'facilitator' to the project (Fullard et al 1984). The nurses measured blood pressure and weight, checked diet, smoking and

drinking habits, and assessed general well-being. They counselled patients regarding weight loss, smoking cessation, and monitored anti-hypertensive drug therapy (Anderson 1984, Fullard et al 1987).

The results of the Oxford study has lead to the employment of a number of 'facilitators' by health boards in England and Wales. Their role is to support general practices in establishing nurse run prevention clinics (Holmes, 1986). A follow-up audit of hypertensive patients ($\geq$160/90 mmHg) identified at screening in the three original practices demonstrated improvement in blood pressure control. The percentage of patients with diastolic blood pressure $\geq$100 mmHg decreased from 15.8% to 8.1% over 3 years. The changes in smoking habits and weight were very modest (Mant et al 1989).

Robson et al demonstrated the effectiveness of a health promotion nurse employed in general practice for the routine screening and recording of blood pressure, smoking status, family history of ischaemic heart disease and serum cholesterol. All 30-64 year old patients were randomised to nurse follow-up for health promotion or continued care by the general practitioners who were also engaged in preventive activities with their patients. The group cared for by the nurse had significantly more frequent blood pressure recordings and follow-up visits, smoking status identified and family history recorded (Robson et al 1989).

Two recent studies have reported on the effect of health promotion screening and risk factor follow-up by practice nurses in general practice (OXCHECK Study Group 1994, Family Heart Study Group 1994). The Oxford group's study screened 6,124 men and women, approximately one third were followed up by the nurses for one year and compared with a non-intervention control group. Results were very modest reductions in blood pressure (3/2 mmHg), total cholesterol (0.1 mmol/l) and smoking (0.5%) compared with controls (OXCHECK Study Group 1994).

The British Family Heart Study screened 12,472 men and women in 13 towns with an approximately 2/3 size internal comparison group and an external comparison group approximately 1/3 larger than the intervention group. On an

intention to treat basis, an overall reduction of 12% in coronary risk was determined using the Dundee risk scoring system (Tunstall-Pedoe 1991). There were modest reductions in blood pressure (8/3 mmHg), total cholesterol (0.1 mmol/l) and smoking (3.5%) compared with external controls (Family Heart Study Group 1994). Blood pressure reductions are in keeping with a number of clinical trials that have also shown reductions in cardiovascular mortality (Management Committee 1980, MRC Working Party 1985).

While these last two studies call into question the effectiveness of health promotion and screening in the general population (Stott 1994), they have also been used to discredit the value of nurses working more independently within the general practice primary care team (Cassidy 1994). Yet, the conclusion drawn from the above review is that, in terms of hypertension research, screening and follow-up, nurses have played an effective role.

This role for nurses has been accepted by a number of experts in the field of hypertension research and care. As early as 1981, the proceedings of a symposium on hypertension was published in the Nursing Clinics of North America with 6 papers by 13 nurse authors describing various aspects of hypertension detection and follow-up (Hill & McCombs 1981). By 1985, nurses were following up more than 100,000 hypertensive patients, as part of nurse/physician teams, in over 600 family clinics in Israel (Viskoper & Silverberg 1985). Beevers and MacGregor in their book 'Hypertension in Practice' make many references to the role practice nurses can play in the long term care of hypertensive patients (Beevers & MacGregor 1987). In Laragh and Brenner's two volume textbook: Hypertension: Pathophysiology, Diagnosis and Management, a chapter is written by two nurses describing the 'Nursing Management of the Hypertensive Patient' (Marion & Ryan 1990).

1.7. Scope of Thesis

In this chapter, the background and epidemiology of hypertension and other cardiovascular risk factors has been presented. The effects of pharmacological and

non-pharmacological treatment have been outlined, the usefulness of computer based patient information systems and the role of the nurse practitioner in hypertension research and follow-up have been described.

This review has demonstrated that increased levels of blood pressure are associated with increased mortality, particularly due to cardiovascular causes (MacMahon et al 1990). In addition, the effectiveness of anti-hypertensive treatment is particularly significant in relation to cerebrovascular mortality (Collins et al 1990) and that the cardiovascular mortality reductions seen with anti-hypertensive drug treatment are greater in the elderly (SHEP 1991, Dahlöf 1991, MRC Working Party 1992).

However, adequate long term follow-up of patients with hypertension is yet to be achieved, with less than half of the women and only a quarter of the men identified as hypertensive in the Scottish Heart Health Survey, found to have controlled diastolic blood pressure between 85-90 mmHg (Smith et al 1990).

The benefits of a computer based patient information system and how it can facilitate the collection, retrieval and analysis of data has been presented. Personal microcomputers provide the opportunity for further development of such systems (Lilford & Chard 1981).

The role nurses can play in the care of hypertensive patients has also been illuminated. Nurse practitioner follow-up in a number of outpatient settings has been judged to be at least equivalent to physician follow-up (Sox 1979).

Therefore, with the help of the Scottish Chest, Heart and Stroke Association, a clinic was set up in 1981 utilising a nurse practitioner and a microcomputer based patient information system to follow-up patients with hypertension. Data were collected for a period of 8 years with 1091 patients enrolled, and a total of 705 continuing to attend at the end of 8 years. The aim of the work presented in subsequent chapters is to evaluate that follow-up care and related projects.

Chapter 2. Methods

2.0. Summary

In this chapter, the structure and functioning of the blood pressure clinic are described. The data sets, their rationale, and description of the databases used, are included. Examples of computer output are shown. The statistical methods used for analysis are also presented.

2.1. Introduction

The nurse practitioner clinic with microcomputer patient information system, was inaugurated in September 1981 within the Department of Materia Medica at Stobhill General Hospital, Glasgow, G21 3UW. Funding was obtained from the Scottish Chest, Heart and Stroke Association for the first 2 years of operation. The original Commodore PET computer system was funded by the Greater Glasgow Health Board and was replaced by an Apricot system.

2.2. Aims

The primary aims of the clinic were to assess the effectiveness of:

1. offering standardised anti-hypertensive care by the same specialist nursing staff with expert physician backup.
2. using a computerised patient information system to facilitate the follow-up of individuals identified as having hypertension.
3. new pharmacological and non-pharmacological treatments to reduce cardiovascular risk in hypertension.

2.3. A nurse practitioner hypertension follow-up clinic.

2.3.1. Clinic staff

The nurse practitioner saw patients, organised and managed day-to-day activities, collated and analysed the data generated. In addition to the nurse practitioner, the dedicated clinic staff included a part-time receptionist, and eventually an additional part-time clerk. By the second year, an auxiliary nurse was assigned to the clinic from the outpatient department for the three sessions per week the clinic was held. During the third year of operation, a second nurse practitioner joined the clinic part-

time due to the increasing patient population.

Medical staff were 'on call' to each clinic session with every effort made to have the same physician covering the clinic the same day each week. In this way patients generally were seen by the same nurse practitioner and physician for follow-up.

2.3.2. Patient population

Patients were recruited from the department's general medical clinics. Initial assessment occurred at these general medical clinics, to which patients had been referred by their general practitioner or other hospital consultant. Therefore, over the 8 years of the clinic, 1091 patients entered the nurse practitioner clinic for long term follow-up.

2.3.3. Clinic Management

A protocol for the management of hypertension in the clinic was developed in consultation with the three senior physicians whose patients would be attending the clinic after initial outpatient assessment. The flow chart summarising the protocol is given in Figure 2.1 (Curzio 1983). The rationale for the target blood pressures is discussed in section 2.3.4.

An initial blood pressure data form (Figure 2.2) was completed either by one of the physicians or one of the nurse practitioners prior to the patient first attending the Hypertension Clinic for long term follow-up. The form changed with the introduction of the Apricot system which is described in detail in section 2.4.2 (Figure 2.3).

The initial data were then entered into the clinic database by the clinic secretary or one of the nurse practitioners. A first appointment letter was sent to the patient with directions on how to get to the clinic.

Each patient was issued with a specially designed Blood Pressure Information and Appointment Card. In addition to the date and time of the next appointment, there was space for supine and erect readings and current anti-hypertensive drug treatment. Staff names and the clinic telephone number were on the back of the

Figure 2.1. Main follow-up protocol flowchart.

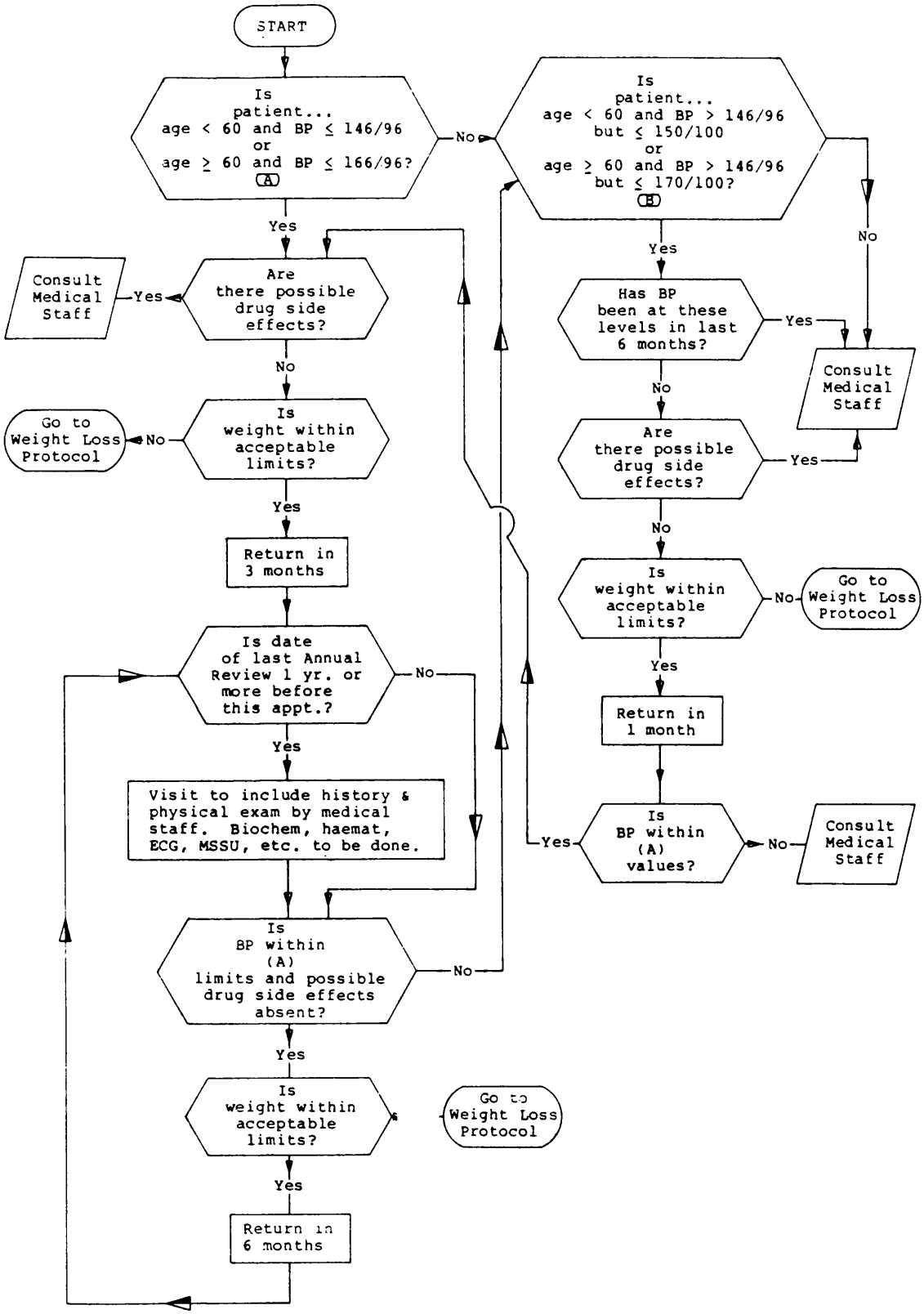


Figure 2.2. Initial blood pressure data form for PET system.

B.P. DATA INITIAL

NAME _____ GP NAME _____
ADDRESS _____ ADDRESS _____
_____ _____
_____ _____
UNIT No _____

SEX: MALE = 1 _____
FEMALE = 2
DATE OF BIRTH (day,
month, year)
_____

HEIGHT _____ METRES
WEIGHT _____ kg
OBESITY NONE = 0 ____
MOD. = 1
SEVERE = 2
SMOKING NEVER = 0 ____
PRESENT = 1 PIPE = 3
PAST = 2 CIGAR = 4
No CIG/DAY _____
ALCOHOL NONE = 0 _____
MOD = 1
HEAVY = 2
FAMILY HISTORY
HYPERTENSION
YES = 1 NO = 0 _____
PERSONAL HISTORY OF:
(YES = 1 NO = 0)
Myocardial Inf. _____
Angina _____
C.C.F. _____
C.V.A. _____
Per. Vasc. Dis. _____
C.O.A. D. _____
PREVIOUS TREATMENT
(Up to this visit)
YES = 1 NO = 0 _____
Details
_____
_____
_____

PRESENT TREATMENT
(On leaving the clinic)
Beta Blocker _____
NONE = 0
ATENOLOL = 1
PROPRANOLOL = 2
METOPROLOL = 3
OXPRENOLOL = 4
OTHER = 5
DOSE ____ mg
Diuretic _____
NONE = 0
THIAZIDE = 1
K SPARING = 2
LOOP = 3
COMBINATION = 4
OTHER = 5
DOSE ____ mg
Vasodilator _____
NONE = 0
PRAZOSIN = 1
HYDRALAZINE = 2
ENDRALAZINE = 3
CAPTOPRIL = 4
NIFEDIPINE = 5
DOSE ____ mg
Centrally Acting _____
NONE = 0
METHYLDOPA = 1
CLONIDINE = 2
OTHER = 3
DOSE ____ mg
ADVERSE EFFECTS
YES = 1 NO = 0 _____
Details
_____
_____
_____

Figure 2.2. Initial blood pressure data form for PET system (cont'd)

DETAILS AT INITIAL VISIT

Type of Hypertension _____

ESSENTIAL = 1 PREGNANCY = 4

ACCELERATED = 2 OTHER = 5

PILL = 3

SUPINE DATA

Sys. B.P. _____

Dias. B.P. _____

Heart Rate _____

ERECT DATA

Sys. B.P. _____

Dias. B.P. _____

Heart Rate _____

TARGET B.P. (Sys,Dias)

_____

ARE BIOCHEMICAL DATA AVAILABLE?

YES = 1 NO = 0 _____

CHOLESTEROL _____ date of Biochem update

GLUCOSE _____ _____

URATE _____ (1 yr after last data obtained)

POTASSIUM _____

CREATININE _____

GAMMA G.T. _____

URINE GLUCOSE _____

PRESENT = 1 ABSENT = 0

URINE PROTEIN _____

PRESENT = 1 ABSENT = 0

ECG LVH _____

PRESENT = 1 ABSENT = 0

DATE OF NEXT APPOINTMENT

(Day, month, year)

_____

Figure 2.3. Initial blood pressure data form for Apricot system.

Initial BP DATA - Apricot Microcomputer System

Patient Surname: _____
Forename: _____
Address - Street: _____
Town: _____
Post Code: _____
Tele: _____
Unit No: _____
GP Surname: _____
Forename: _____
Address-Health Centre: _____
Street: _____
Town: _____
Post Code: _____
Tele: _____
Sex (M or F) : _____
Date of Birth: ___/___/___
Ht: _____ (M)
Current Wt: _____ (Kg)
Smoking (cigs/day) : _____
Alcohol Intake (gm/wk): _____(1/2 pint or 1 gl wine or a sherry=10 gm)

Evidence of LVH on ECG: Y or N
Family History of Hypertension:

_____
Patients Risks Factors: eg. MI, CCF, COAD, CVA, ANGINA

_____
Any Other Relevant Conditions:

_____
Date of Next Visit: ___/___/___
Initial Data - Date: ___/___/___
Wt: _____ (Kg)
Type of Hypertension: _____
Supine Data SBP:_____ DBP:_____ HR:_____
Erect Data SBP:_____ DBP:_____ HR:_____
Target BP SBP:_____ DBP:_____
Appt Cycle: _____
BP Control: _____
Date of Annual Review: ___/___/___
Cholesterol: _____
Glucose: _____
Urate: _____
Potassium: _____
Creatinine: _____
Gamma GT: _____
Protein in Urine: Y or N
Glucose in Urine: Y or N
Current Treatment
Beta Blocker: _____
Diuretic: _____
Vasodilator: _____
Centrally Active Drug: _____
Other: _____
Adverse Reactions:

_____

card to facilitate contact. In addition, there were explanatory notes to the patient and general practitioner (Figure 2.4). The card was updated at the end of each clinic visit and patients were encouraged to carry it.

An appointment was arranged with each patient at the end of the clinic visit based on the need for follow-up and personal preference for time and day of the week. If unable to attend, all patients were encouraged to telephone for another appointment. When a patient did not attend, two further appointments were arranged before a letter was sent to the general practitioner reporting the failure to attend, and stating that no further appointments would be made unless requested to do so.

A master name and address file with GP noted was kept in the clinic office for quick reference. This file was used frequently to determine if a patient was on the database, to obtain a patient's telephone number and to identify the patient's general practitioner. In addition, if a patient was no longer being followed up, the reason was noted on the bottom of the card with the date it was recorded.

2.3.4. Measurement of weight

At each visit the nurse practitioner or auxiliary nurse would weigh each patient in kilograms on an Avery balance scale, which was calibrated regularly. Height in metres was measured during the first clinic visit if it had not been previously recorded in the case notes.

A Body Mass Index (BMI) was determined for each patient. BMI is calculated by dividing an individual's weight in kilograms by the square of their height:

$$\frac{\text{weight (kg)}}{\text{height}^2\text{(m)}}$$

Garrow demonstrated the correlation between BMI, first put forward by Quetelet in the 17th century, and overall mortality using insurance company data. The gradings are as follows:

Figure 2.4. Blood pressure information and appointment card.

To the patient:

1. Keep this card with you and bring it to the clinic.
2. Show it to your family doctor when you attend his surgery.
3. If you have an accident or enter hospital, show this card.
5. Bring your tablets each visit.
6. If you are unable to attend for an appointment, please telephone the nurse, Joan Curzio (041-558-0111 Ext. 278) for another one.
7. If you have a question about your blood pressure that needs to be answered before your next appointment please feel free to telephone.

To the doctor:

If the drug dose is changed, please write the new dose on the card in the appropriate column, together with any blood pressures recorded by you, on the line below the next appointment date.

Further information or assistance in management can be obtained from:
Prof. Reid, Dr. Rubin, Dr. Elliott or the 8A BP Clinic at Stobhill General Hospital
(041-558-0111 Ext. 278)

83-386-22

Stobhill General Hospital

Blood Pressure Information and Appointment Card

Name _____

Address _____

_____

Hospital No. _____

Please carry this card with you

8A Blood Pressure Clinic

Name of family doctor

Dr. _____

MEDICATION and DOSE

APPOINTMENT		BLOOD PRESSURE This Visit					
DATE	TIME	Lying	Standing				

BMI 20 - 24.9	Grade 0
BMI 25 - 29.9	Grade I
BMI $\geq$ 30 $<$ 40	Grade II
BMI $\geq$ 40	Grade III

(Garrow 1981). This index has been validated in other populations (Goldourt & Medalie 1974, Bray 1978, Bray 1985). Thus those individuals with BMI $>$ 30, being at greatest risk, were targeted for repeated counselling regarding weight reduction.

2.3.5. Measurement of blood pressure

Blood pressure was measured by the nurse practitioner using a Sentron semi-automatic sphygmomanometer (C R Bard International, Pennywell Industrial Estate, Sunderland, SR4 9EW). A semi-automatic device was chosen to maintain consistency of readings by a regularly calibrated device. Calibration procedures were carried out quarterly on both devices used in the clinic.

The Sentron measures blood pressure oscillometrically, by sensing the pulse waves through the cuff as the pressure is released. If the pulse sensations are outwith pre-set norms (possibly due to arm movement or a low heart rate, ie. less than 44 beats per minute), the machine will re-inflate and begin the measurement again. The machine will zero if it is unable to obtain an acceptable reading after 3 re-inflations.

Small (22 cm x 10 cm), regular (31 x 12 cm) and large (39 cm x 16 cm) cuffs, with velcro fastenings, were available at all times in the clinic. An appropriate sized cuff, based on the cuff markings, was applied to the right upper arm of each patient to ensure the cuff bladder would encircle at least 80% of the circumference of the arm as recommended (Petrie et al 1986).

Since the Sentron re-sets itself after each reading, basing the pressure level of inflation for a reading on the level of the preceding measurement, two supine and two erect measurements were obtained after a short period of rest. The second measurement of each was recorded in the database.

2.3.6. Target blood pressure

Target blood pressures were determined for all patients, and failure to reach these targets was the criterion for referral to medical staff for further treatment. The targets were globally based on age. For those individuals less than 60 years of age, the target blood pressure was less than 140/90, and for those over 60 it was less than 160/90. However, targets were further individualised for a few patients, as required, so that if a patient had a problem such as polycystic kidneys the target would be lowered to 135/85, in order to protect renal function.

The use of target or goal blood pressures is now common. These levels are somewhat less than the 160/90 mmHg recently recommended by the British Hypertension Society (Sever et al 1993), but higher than the 120-130/80 mmHg for young patients and 140/90 mmHg for elderly patients recommended by the World Health Organisation and the International Society of Hypertension (WHO/ISH Mild Hypertension Liaison Committee 1993).

2.3.7. Patient interview

During the subsequent interview, patient well-being and compliance were assessed by the nurse practitioner. Poorly controlled blood pressure and possible drug side-effects, as well as other medical problems, were referred to the backup medical staff. Drug treatment changes were instituted only by medical staff.

2.3.8. Health education and counselling

Obese patients, particularly those with BMI $>$ 30 were advised to lose weight. The protocol developed for weight reduction advice is given in Figure 2.5. Patients were given the option to see one of the hospital dietitians for specialist advice or to receive support only from the clinic nurse practitioner. In addition, patients were encouraged to take prescribed medication regularly and smokers to stop smoking. Health education material obtained from the Greater Glasgow Health Board and from the Dietetics Department of Stobhill Hospital were used to support these health education messages. In addition, several leaflets were prepared by clinic staff. A list of the various materials used is shown in Table 2.1.

Figure 2.5. Weight reduction protocol flowchart.

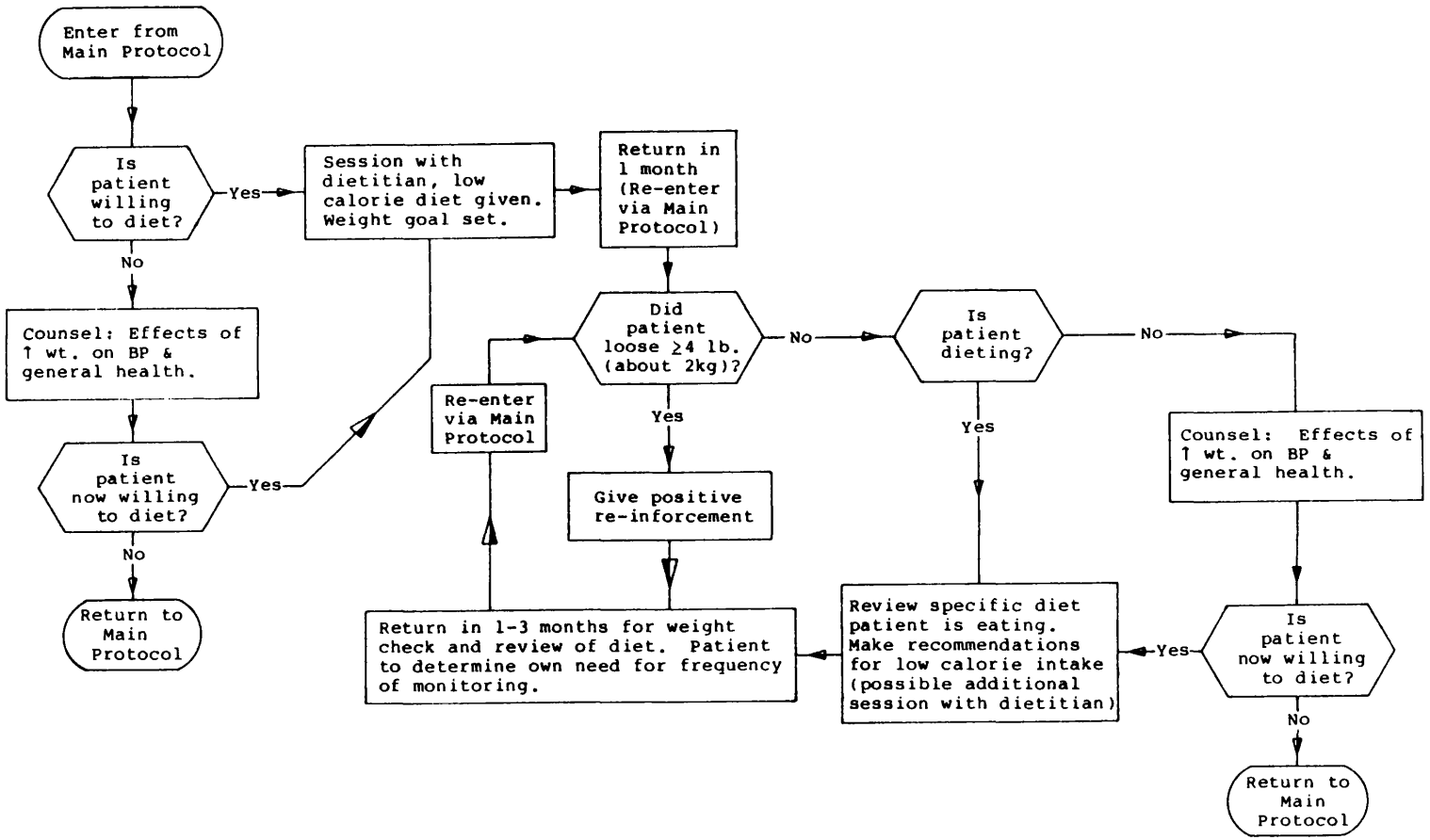


Table 2.1. Health education materials.

Is it blood pressure
British Heart Foundation

Do you understand these numbers?
Stobhill Hypertension Clinic

Dieting Advice
Stobhill Hypertension Clinic

Coming down lightly
Good Hearted Glasgow weight reduction leaflet

Giving up smoking: Let your body breathe
Scottish Health Education Group

So you want to stop smoking
Scottish Health Education Group

Copies of several in-depth paperback books on hypertension were available on loan from the clinic. The clinic had two copies of 'High Blood Pressure: What it means for you and how to control it' (O'Brien & O'Malley 1982) and 4 copies of 'Churchill Livingstone Patient Handbook 7: High blood pressure'(Lewis 1981). These were made available to new patients and those who expressed an interest, to provide additional information about hypertension.

2.3.9. Annual review

Each year all patients underwent an 'Annual Review' in addition to the routine clinic assessment. The nurse practitioner obtained a blood sample for analysis by the hospital's Biochemistry and Haematology departments for the tests listed in Table 2.2. A mid-stream specimen of urine was obtained for multi-stix dipstick assessment in the clinic, and culture and sensitivity assessment by the hospital's Bacteriology Department. Each patient's current address, general practitioner and smoking status were reviewed and updated. A 12-lead electrocardiogram (ECG) was done in the hospital's ECG Department.

The majority of the routine biochemistry tests were measured by an SMA-12. Total cholesterol was measured enzymatically on a Technicon RA1000. Haematological samples were auto-analysed. For the studies described in Chapters 5 and 6, triglyceride was measured enzymatically on a Technicon RA1000, very low density lipoprotein cholesterol (VLDL) was isolated by ultracentrifugation and high density lipoprotein cholesterol (HDL) by precipitation using heparin/manganese.

The physician interviewed the patient and conducted a physical examination with particular reference to reviewing each patient's optic fundi and heart sounds. For those patients also entered onto the Glasgow Blood Pressure Clinic (GBPC) database (Glasgow Blood Pressure Clinic 1972), a GBPC Annual Review form was completed.

2.3.10. Drug treatment

Drug treatment choice and treatment changes were the province of the medical staff. 'Stepped Care' was the underlying principle of care in the early and

Table 2.2. Annual review blood tests.

Biochemistry	Haematology
Total cholesterol*	RBCs
Random glucose*	WBCs
Sodium	Haemoglobin
Potassium*	Haematocrit
Chloride	MCV
Bicarbonate	MCH
Creatinine*	MCHC
Urea	RDW
Calcium	Platelets
Phosphate	Pct
Urate*	MPV
Total Protein	PDW
Albumin	Lymphocytes (percentage)
Alkphosphatase	Lymphocytes (number)
Bilirubin	
AST	
ALT	
GammaGT*	

* entered into database

mid-1980's. The efficacy of this approach had been validated in the Hypertension, Detection and Follow-up Program (HDFP Cooperative Group 1979). Newly diagnosed hypertensives without contraindications, were treated as described in Table 2.3. The first choice was a beta blocker with the addition of a thiazide diuretic and then a vasodilator if blood pressure control was not obtained.

With the advent of angiotensin converting enzyme inhibitors and calcium channel blockers in the mid-1980's treatment choices shifted to these newer agents. The changes in drug treatment are highlighted in Chapter 3.

2.4. Microcomputer patient information system

2.4.1. Data

The data stored in the database for each patient were those which were identified by the senior medical staff, at the beginning of the project, as being the most relevant for the follow-up of hypertension. Storage space was particularly limited in the original system and therefore only 100 items of information were obtained for each patient (Table 2.4).

Information included weight, smoking, family history, drug treatment, biochemistry and blood pressure measurements. This data set facilitated the monitoring of each patient for the development of diabetes or renal disease, in addition to the review of blood pressure and anti-hypertensive treatment. Such monitoring is important since diabetes is an independent cardiovascular risk factor (Kannel & McGee 1979) and renal disease can make the control of blood pressure more difficult as well as influence the risk of developing malignant hypertension (Kincaid-Smith 1985).

2.4.2. Hardware and software development

Over the 8 years the clinic was held at Stobhill General Hospital, the computer database underwent several refinements due to the improvements in available computer hardware and programming software. However, the core data did not change.

Version 1.0 of the software was written in PET BASIC to run on a

Table 2.3. Drug treatment regimen: 'Stepped Care'.

Step 1	Beta blocker or thiazide diuretic
Step 2	(if blood pressure were uncontrolled on Step 1 medication) the alternative drug not used in Step 1 added for a combination of beta blocker plus diuretic or diuretic plus beta blocker
Step 3	(if blood pressure continues uncontrolled on Step 2 medication) add in a vasodilator which initially was hydralazine or prazosin and later a calcium antagonist (Nifedipine) or ACE inhibitor (Captopril or Enalapril)

Table 2.4. Data identified for inclusion into the database.

Record	Patient Details
1	Patient Number
2-5	Name
6-16	Address
20	Unit number
21	Sex (1=male,2=female)
22	Date of birth
23	Age
24	Height (m)
25	Weight (kg)
	Risk factors;
26	Obesity (none,moderate,severe)
27	Smoking (yes/no)
28	No. of cigarettes/day
29	Alcohol use (none,moderate,heavy)
	History:
31	Family history of hypertension
32	Patient's history of: MI
33	angina
34	CCF
35	CVA
36	PVD
37	COAD
	Previous treatment:
38	Any previous treatment (yes/no)
39	Details
	Present treatment:
47	Beta blocker (none, atenolol, propranolol, metoprolol, oxprenolol, other)
48	Dose of beta blocker
49	Diuretic (none, thiazide, k sparing, loop, combination, other)
50	Dose of diuretic
51	Vasodilator (none, prazosin, hydralazine, other)
52	Dose of vasodilator
53	Centrally acting drug (none, methyldopa, clonidine, other)
54	Dose of CA drug
	Adverse effects:
55	Present (yes/no)
56	Details

Record	Patient Details
	Initial BP data:
63	Type of hypertension (essential, accelerated, due to contraceptive, first diagnosed during pregnancy, other)
64	Supine systolic BP
65	Supine diastolic BP
66	Supine heart rate
67	Erect systolic BP
68	Erect diastolic BP
69	Erect heart rate
70	Target systolic BP
71	Target diastolic BP
	Biochemical data:
72	Serum cholesterol
73	Serum glucose
74	Serum urate
75	Serum potassium
76	Serum creatinine
77	Serum γGT
78	Presence of protein in urine (yes/no)
30	Presence of glucose in urine (yes/no)
	2nd last visit:
82	Supine systolic BP
83	Supine diastolic BP
84	Supine heart rate
85	Erect systolic BP
86	Erect diastolic BP
87	Erect heart rate
	Last visit:
88	Supine systolic BP
89	Supine diastolic BP
90	Supine heart rate
91	Erect systolic BP
92	Erect diastolic BP
93	Erect heart rate
	Miscellaneous data:
79	ECG: Presence of left ventricular hypertrophy
80	Most recent weight (kg)
81	Current treatment drug
94	Date for update of biochemical data
95	Appointment cycle
96	Estimate of patient's compliance
97	Estimate of BP control
98	Date file was last updated
99	Date of next clinic appointment
100	Number of appointments missed

Commodore PET4040 and then a PET8000. It was capable of outputting a full summary (Figure 2.6), a partial summary of the data held on each patient (Figure 2.7), as well as printing the entire database in total or by appointment date. The partial summary was updated at each clinic visit by the nurse practitioner. The database was then updated, and the hand-written updated partial summary filed in the patient's case notes for future reference. Each 360,000 byte disk held data for approximately 250 patients. This set-up supported the patient information system for the first three years (Kelman et al 1982).

During the fourth year of operation, data were manually transferred into an enhanced Version 2.0 of the software written in dBaseII (Ashton-Tate) designed to work on an 256K RAM Apricot PC. An added feature of this version was an option to output standard letters in batch mode, many of which had been generated individually using the Commodore's word processor. These included letters to patients regarding appointments (Figure 2.8), and letters to general practitioners about routine follow-up visits (Figure 2.9) or patients who failed to attend and who might have died or were known to be dead. The last letter was sent with a brief form for completion by the general practitioner (Figure 2.10).

The output used in the clinic now included all data held in the system for that individual (Figure 2.11). Each printout continued to be updated in the clinic with the updated data used to amend the database after the clinic session. The manually updated printout continued to be filed in the patient's case notes. Data from patients who were no longer attending or who had moved or died were transferred to either a 'Lost-to-follow-up' file or 'dead' file, leaving data for patients currently attending in the active file.

Version 2.0 processed data more quickly, was able to handle a much larger data set per disk (900+ records) and allowed for the electronic transfer of data to other software packages and other hardware platforms for data analysis.

Finally, a local area network (LAN) was installed connecting a number of Apricot machines in the department to a 20 mega-byte hard disk file server. There

Figure 2.6. Partial summary of data for each patient held in PET system.
(all data presented here are fictitious)

```
                BLOOD PRESSURE CLINIC          DATE 291181

                ---------------------

PATIENT         124   IVOR PALSHIRE      DATE OF APPT. 010983
                8 GREEN STREET  GLASGOW
UNIT NO. 123456


MOST RECENT WEIGHT 72

CURRENT TREATMENT
-----------------
BETA BLOCKER 1 160

BLOOD PRESSURE DATA
-------------------
                INITIAL          2ND LAST VISIT      LAST VISIT
SUP   SYS.B.P.  178                   154                146
     DIAS.B.P.  98                    92                 84
    HEART RATE  88                    65                 62

ERECT SYS.B.P.  180                   168                142
     DIAS.B.P.  106                   100                86
    HEART RATE  95                    72                 62

******** TARGET B.P. 150  /90 ********


BIOCHEM. DUE TO BE UPDATED ON 200682

APPOINTMENT CYCLE
COMPLIANCE
B.P. CONTROL
DATE OF NEXT APPOINTMENT
```

Figure 2.7. Full summary of data for each patient held in PET system.
(all data presented here are fictitious)

```
                BLOOD PRESSURE CLINIC          DATE 291181

                ---------------------
PATIENT NO.             124   UNIT NO. 123456  TYPE OF HYP.1
NAME    IVOR PALSHIRE
ADDRESS 8 GREEN STREET  GLASGOW

SEX  1                  AGE 57             DATE OF BIRTH 030924
INITIAL WT(KG) 81                          HEIGHT (M) 1.72
PRESENT WT(KG) 72

RISK FACTORS
------------
OBESITY 0         SMOKING 1                ALCOHOL 0
                  40   CIGS/DAY

********** FAMILY HISTORY OF HYPERTENSION ************

PATIENT'S HISTORY
-----------------
PER. VASC. DISEASE

BLOOD PRESSURE DATA
-------------------
                  INITIAL           2ND LAST VISIT      LAST VISIT
SUP   SYS.B.P.    178                    154                146
     DIAS.B.P.    98                     92                 84
    HEART RATE    88                     65                 62

ERECT SYS.B.P.    180                    168                142
     DIAS.B.P.    106                    100                86
    HEART RATE    95                     72                 62

******** TARGET B.P. 150  /90 ********

BIOCHEMICAL DATA
----------------
CHOLESTEROL 4.7       GLUCOSE 6          URATE 0.44
POTASSIUM   4.2    CREATININE 101    GAMMA GT 26

BIOCHEM. DUE TO BE UPDATED ON 200682

PREVIOUS TREATMENT  PROPRANOLOL
-----------------

CURRENT TREATMENT
-----------------
BETA BLOCKER 1 160

ASSESSMENT OF COMPLIANCE   3
ASSESSMENT OF B.P. CONTROL 3
APPOINTMENT CYCLE          8
NEXT APPOINTMENT      051282
NO. OF APPTS. MISSED
FILE LAST UPDATED ON  291181
```

Figure 2.8. First, follow-up, and missed appointment letters to patients, generated by the Apricot system. *(all data presented here are fictitious)*

Ms Elizabeth Hogg 10/04/85
5 Kingsway
KIRKINTILLOCH G66

Dear Ms Hogg

Your next appointment at the Blood Pressure Clinic in Ward 8A is at 11.00 am on 26/06/85.
Instead of going to the Outpatient Department, please come along to the Department of Materia Medica, Ward 8A. It is therefore not necessary for you to check in at the Appointments Desk, just come straight to this clinic.

A map is enclosed with this letter to help you find your way. Once inside the hospital you can follow the signs for Wards 9-14. The Department of Materia Medica is in that part of the main corridor towards the front of the building complex.

If you are unable to come at this time, please telephone me, or the receptionist, Mrs Richardson, any morning at the above number, ext. 278. We can then make an appointment that is more convenient for you.

Yours sincerely,

Mrs Joan Curzio
Research Nurse

10/07/85

Ms Elizabeth Hogg
5 Kingsway
KIRKINTILLOCH G66

Dear Ms Hogg

Your next appointment at the Blood Pressure Clinic in Ward 8A is at 11.00 am on 26/06/85.

If you are unable to come at this time, please telephone me, or the receptionist, Mrs Richardson, any morning at the above number, ext. 278. We can then make an appointment that is more convenient for you.

Yours sincerely,

Mrs Joan Curzio
Research Nurse

10/07/85

Ms Elizabeth Hogg
5 Kingsway
KIRKINTILLOCH G66

Dear Ms Hogg

I am sorry that you were unable to come to your appointment at the Blood Pressure Clinic. Could you please come in at 10.30 on 20/06/85.

If you are unable to come at this time, please telephone me, or the receptionist, Mrs Richardson, any morning at the above number, ext. 278. We can then make an appointment that is more convenient for you.

Yours sincerely,

Mrs Joan Curzio
Research Nurse

Figure 2.9. Letter sent to each patient's general practitioner after a visit.
(all data presented here are fictitious)

29/02/85

Dr J Yard
Union Street
KIRKINTILLOCH G66

Dear Dr Yard

re: Elizabeth Hogg, D.O.B. 04/07/26, Unit No. 008039
5 Kingsway, KIRKINTILLOCH G66

Your patient was seen on 27/02/85 at the 8A Blood Pressure Clinic at Stobhill Hospital. Her blood pressure was 150/88 lying and 146/81 standing. Heart rate was 86 beats per minute lying and 101 standing.

Her current treatment is

Bendrofluazide 5 mg
Nifedipine Retard 20 mg b.d.

to be taken daily. I have asked her to continue on this regimen. A further visit has been arranged for 8 weeks.

Yours sincerely,

John L. Reid
Professor of Materia Medica

Figure 2.10. Letter sent to each patient's general practitioner when patient has not attended and might have died. *(all data presented here are fictitious)*

29/02/85

Dr J Yard
Union Street
KIRKINTILLOCH G66

Dear Dr Yard

re: Elizabeth Hogg, D.O.B. 04/07/26, Unit No. 008039
5 Kingsway, KIRKINTILLOCH G66

The above named patient has been managed at the Hypertension Clinic at Stobhill Hospital and our records indicate that she has been under your care. She has failed to keep a recent appointment and I understand that she has died. I would be most grateful if you could please provide us with some information, not only to allow us to update our case records, but also to reduce the likelihood of distressing the family with enquiries or further appointments.

Yours sincerely,

John L. Reid
Professor of Materia Medica

Blood Pressure Patient Information

Patient's Name..... Case No.....

Patient's Address.....

Please complete and delete as appropriate

1. This patient is not now under my care and I have no record of him.
2. I believe this patient has recently been under the care of Dr..... of.....
3. This patient is alive and wishes a further appointment.
4. I confirm that the patient died on .....
5. The patient died at home
   in .....hospital
6. The cause of death was.....
7. Do you believe death was directly related to cardiovascular disease (myocardial infarction) (stroke) (other.....)
8. A post mortem was/was not performed.

Signed.....Date.....

name and address of GP/Hospital Dr.

.....

Figure 2.11. Full summary of data held in Apricot system for each patient. *(all data presented here are fictitious)*

```
                    --STOBHILL BLOOD PRESSURE CLINIC--

NAME          Elizabeth Hogg
ADDRESS       5 Kingsway
              KIRKINTILLOCH , G66
TEL.          776-55555                        UNIT NO. 008039
-------------------------------------------------------------------
G.P.          DR J. Yard
ADDRESS         , Union Street
              KIRKINTILLOCH  , G66
TEL.          041-776-1111
-------------------------------------------------------------------
DATE OF LAST APPT.  15/11/84
DATE OF NEXT APPT.  27/04/85
                                               RISK FACTORS
SEX           F
DATE OF BIRTH     04/7/26                      SMOKING (CIGS/DAY)   0
AGE               59                           ALCOHOL (GM/WK)      50
HEIGHT (M)        1.51                         OBESITY INDEX        24.16
WEIGHT (KG)       55.1                         LVH                  N

PATIENTs HISTORY
OTHER CONDITIONS  Ex lung tumour
FAMILY HISTORY
-------------------------------------------------------------------
BLOOD PRESSURE DATA

              INITIAL          2nd LAST VISIT          LAST VISIT

SUPINE        DATE  00/00/81   15/11/84                27/02/85
              SBP   240        166                     150
              DBP   130        93                      88
              HR    100        93                      86

ERECT         SBP   220        167                     146
              DBP   122        93                      81
              HR    112        96                      101

TARGET BLOOD PRESSURE 140/90
-------------------------------------------------------------------
CURRENT TREATMENT

BETA BLOCKER
DIURETIC                 Bendrofluazide 5 mg
VASODILATOR              Nifedipine Retard 20 mg b.d.
CENTRALLY ACTING DRUG
OTHER THERAPY
ADVERSE EFFECTS          RAYNAUD'S-ATENOLOL, REFLEX TACH-PRAZOSIN
-------------------------------------------------------------------
APPOINTMENT CYCLE        8 WKS          INITIAL WT. (KG)       52.2
NO. OF APPTS.MISSED      4              INITIAL OBESITY INDEX  22.89
BP CONTROL (SUBJ)        S
DATE FOR ANNUAL REVIEW 00/08/85   TYPE OF HYPERTENSION - ESSENTIAL
-------------------------------------------------------------------
BIOCHEMISTRY      CHOLESTEROL 8.1   GLUCOSE    5.7    URATE    0.2
                  CREATININE  100   POTASSIUM  4.2    GAMMA GT 34

              PROTEIN IN URINE N              GLUCOSE IN URINE N
```

were no further changes to the Hypertension clinic database structure or dedicated software, but the LAN allowed password protected access to the database from a number of stations and allowed for a larger database.

2.5. Clinical Audit

From the first year, pertinent data were tabulated annually as of 1 September and reported to the rest of the team. A complete copy of the database was obtained and archived for future analysis. Age, sex, weight, blood pressure ranges and drug treatment regimes were a particular focus. Serum cholesterol values were added to the review in the fourth year. In the fifth year, risk factor changes were assessed for the cohort of patients who had attended the clinic from its first year. An overview of these data can be found in Chapter 3.

2.6. Statistical analysis

During years 1-3 (1981-1984), data were analysed manually. Once the Apricot personal computer was available, data were analysed using LOTUS 123 version 1.0 (Lotus Corporation) and dBase II (Ashton-Tate). It was also exported to the university's ICL 3980 mainframe computer for further analysis by MINITAB, SPSSx, BMDP and RUMMAGE. Parametric and non-parametric tests, were applied as appropriate to the data.

Latterly, Quattro Pro version 3 (Borland) was used to edit and graph the data. In addition, MINITAB version 8 for the personal computer, was used to analyse additional audit data in Chapter 3. One way analysis of variance and chi-square tests were used.

The data from Chapter 4, the comparison with conventional hypertension care, were evaluated using SPSSx and MINITAB on the ICL 3980 mainframe. The mortality sub-routine of BMDP was used on the same system. The life-table analysis was generated according to the method described by Armitage (Armitage 1971) and was calculated without computer assistance.

Data were analysed for the Cholesterol Diet Study in Chapter 5, by repeated measures analysis of variance (ANOVA) and covariance (ANCOVA). For the

ANCOVA, entry values were used as the covariates where appropriate. Bonferroni multiple comparisons and an overall confidence level of 95% were also derived using RUMMAGE. Correlation analysis was undertaken as indicated using MINITAB. Both of these statistical packages were run on the ICL 3980 mainframe.

The analysis of the guar study reported in Chapter 6, was carried out using MINITAB on the ICL 3980 mainframe and undertaken on an intention-to-treat basis. The changes in parameters were investigated by one way ANOVA. Power calculations were undertaken based on the method described by Day and Graham (Day & Graham 1989).

In Chapter 7, the evaluation of changing emphasis from hypertension follow-up to multiple cardiovascular risk factor intervention, data were analysed using the spreadsheet software Quattro Pro version 3 and version 4 as well as MINITAB version 8 for the personal computer. It is presented as mean $\pm$standard deviation and percentages. One way analysis of variance, paired t-test and chi-squares were determined as appropriate.

Final spreadsheet analyses were undertaken and graphs generated using Quattro Pro for Windows version 5.0.

2.7. Ethical approval

All studies contained in this work have been passed by the local Stobhill Hospital/Northern District Research Ethical Committee.

Chapter 3. Clinical Overview: 8 years of nurse practitioner care

3.0. Summary

A compilation of data from the 8 years of the nurse practitioner clinic is presented in this chapter. Results for the population continuing to attend at the end of each clinic year are included. Comparisons are made between those who entered the clinic each year.

3.1. Introduction

In 1981 when the Stobhill Clinic began, the clinic team realised the opportunity provided by having computer based clinical information. From the first year, regular annual compilations of sections of the data were carried out. It is now considered mandatory to review one's clinical practice, ie. audit.

The reviewing of clinical information has been a hallmark of medical practice for several millennia. Prior to the introduction of controlled clinical trials, it was one of the few ways in which advances in care were made. The regular systematic collection of information to compare against pre-set standards is a modern refinement. This form of review, now generally referred to as audit, was first seriously proposed by Donabedian in 1966 in the United States.

In an invited review of the methods for evaluating the quality of medical care research in the United States available at that time, Donabedian began talking about the need to identify the structure, process and outcome of care. The structure of care is the available resources that can be called upon to provide care, ie. educated nurses, specialist devices, etc. The process is how care is given. The outcome is the result. All three facets of care need to be evaluated in order to assess quality (Donabedian 1966).

Subsequent workers, particularly nurses in the United Kingdom, have taken up these concepts and have established a labour intensive, convoluted process of assessment called 'Standards of Care'. In this system specific standard statements are articulated with accompanying measurable structural, procedural and outcome

measures delineated (Kitson 1989).

In the United Kingdom, medical audit came to prominence with the publication of the government white paper 'Working for Patients' in 1989 (Dept of Health 1989). In particular, the follow-up discussion document 'NHS Working Paper 6: Medical Audit', firmly threw down the gauntlet to medical practitioners. It outlined the requirement for the development of audit in each and every hospital with a locally appointed medical audit committee. There is also provision for audit committees to be set up at district and regional level and in general practice. It is interesting to note that it did not specify methods, it only demanded action (Dept of Health 1989).

It is important to be aware that recent thinking considers research and audit as two distinctly different activities with many aspects in common (Patterson 1986, Smith 1992). The impression in Donabedian's early work is that quality assessment is a form of research (Donabedian 1966).

Research can be defined as a:

> "rigorous and systematic enquiry, conducted on a scale and using methods commensurate with the issue to be investigated, and designed to lead to generalisable contributions to knowledge."
>
> (Strategy for Research in Nursing 1993)

Richard Smith in an editorial in the BMJ in 1992 reported on a meeting discussing the differences between research and audit (Table 3.1) as well as the similarities. Each ask questions, has a defined purpose, require logical thought and both use similar methods. A list of some of the more commonly used methods alluded to is given in Table 3.2. (Smith 1992). Patterson came to much the same conclusion in an earlier discussion in the Journal of the Royal College of General Practitioners (Patterson 1986).

The current review of a multi-disciplinary project, utilises some of the techniques employed in medical audit as outlined above and does not utilise the nursing standards of care methodology advocated by Kitson (Kitson 1989). This research project has benefited from and been extended by the continuous internal

Table 3.1. Differences between research and audit.

Research	Audit
discovers right thing to do	ensures the thing is done right
one off	ongoing
complex, specialist data	routine data
controlled, limited	covers everything done
can generalise from	limited to local results and circumstances
can assess audit methods	can provide background for research

(Smith 1992)

Table 3.2. Similarities in research and audit techniques.

Peer Review
Questionnaires/surveys
Direct observation
Self recording by staff
Statistical assessment
Spot checks of data/records
Trend analyses
Comparative analyses

(Smith 1992)

audit carried out while it progressed.

This chapter presents an overview of the annual clinical review of data. Further chapters deal with specific in-depth studies generated directly from the questions posed by the annual reviews.

3.2. Aims

The concern each year was to review the data to answer the question:

'Are we doing what we think we are doing?'

which then extended itself to the questions:

1. Are we controlling blood pressure?
2. What drugs are being used?
3. How many patients are overweight and are they loosing weight?
4. Have the smokers attending the clinic stopped smoking?
5. Who are we seeing?
6. How many patients are we seeing and how often?
7. How many patients are lost to follow-up and why?

In 1985, an additional question was asked:

What is the range of biochemical indices in our population, particularly glucose and cholesterol?

3.3. Methods

A complete copy of the clinic database was obtained on floppy disk annually at the beginning of September. Blood pressure, weight, enrolment, and lost to follow-up, were analysed yearly. Data were also analysed by years of follow-up, ie. by years of attendance.

Blood pressure was reviewed by assessing the percentage of patients with systolic blood pressure (SBP) >180, >150 & ≤ 180, and ≤ 150 mmHg and diastolic blood pressure (DBP) >110, >90 & ≤ 110, and ≤ 90 mmHg. These distributions were determined for initial blood pressures as well as last blood pressure measured during each year for those patients continuing to attend but not involved in a clinical trial ($<$ 10% of population any year). Population averages and

standard deviations were also calculated.

Initial and end of first year of attendance blood pressures were compared for patients entering each year. The reductions in blood pressure achieved during their 1-12 months in the clinic were calculated and compared.

Target blood pressures were set for each patient as described in Chapter 2. These generally were 160/90 for patients $\geq$60 years old and 140/90 for those $<$ 60 years of age. The percentages of the population within target, 10 and 15 mmHg of their systolic blood pressure targets and within target, 5 and 10 mmHg of diastolic pressure targets were calculated.

Drug treatment was reviewed at the end of the first (1981/82), fifth (1985/86) and eighth (1988/89) years. The types of drugs used as well as specific drugs were identified. The percentage of patients on mono, double and triple therapy was also noted. The drug treatment prescribed for those first attending these years has also been identified and compared.

Change in weight over time was investigated. The group of patients attending during the first 3 years had their first year's weights compared with their weights after three years of attendance. In Year 8 (1988/89), weights were assessed and compared to initial weights upon entry to the clinic. Initial and end of first year of attendance weights were compared for patients entering each year. The reductions in weight achieved by the end of their first clinic year, were calculated and compared.

Smoking was recorded at entry, and, from Year 4 (1984/85), current smoking habit was included as part of every annual review. The number of cigarettes smoked per day was recorded. Patients who reported smoking cigars or pipes were rated as smokers. The percentage of smokers of each sex entering the clinic each year was also noted.

Alcohol intake was initially rated as 'none', 'moderate' or 'heavy'. With the advent of version 2 of the database system, alcohol intake was recorded as grams of alcohol consumed per week (10 grams = 1 unit).

Cholesterol and glucose values were measured at least annually from 1985 onwards, with the first year values assessed retrospectively in 1985 by entering the data from an archived printout. Potassium, creatinine, urate and gamma-GT were also checked annually at annual review.

With the Commodore system, printouts of data were analysed manually for Years 1-3 (1981-1984). The Apricot system from Year 4 (1984/85) allowed most of the analysis to be carried out using dBase II then dBase III, once it was available, as well as LOTUS 123 version 1.0. Follow-up analysis was undertaken using Quattro Pro 3.0, Quattro Pro 5 for Windows and MINITAB version 8 for the personal computer. The partitioning method described by Siegel and Castellan was used for the chi-square post-hoc analysis to identify where the significant differences were in the contingency tables (Siegel & Castellan 1988). for those t-test analysis with differences in sample size, the method described by Snedecor and Cochran was used (Snedecor & Cochran 1967).

3.4. Results

3.4.1. Are we controlling blood pressure?

The assessment of blood pressure was the major focus of the clinic and it was summarised in several ways. Blood pressure distribution was assessed each year as an indication of control (Figures 3.1. and 3.2). There was no significant difference in the total population's initial systolic or diastolic blood pressure distribution over the 8 years.

There were significant changes in the distribution between initial and last visit blood pressures each year by chi-square analysis for those patients continuing to attend (Table 3.3). The distributions of last visit blood pressures were significantly different between years for systolic ($X^2=24.94507$, df=14, $p<0.05$) and diastolic blood pressure ($X^2=30.69702$, df=14, $p<0.01$). Partitioning revealed that Year 7 last visit distribution was significantly different from Year 3 for systolic ($X^2=8.326$, df=1, $p<0.005$) and diastolic blood pressure ($X^2=16.474$, df=1, $p<0.0005$) and Year 6 was significantly different from Year 3 for diastolic blood pressure only

Figure 3.1. Distribution of initial and last visit systolic blood pressures.

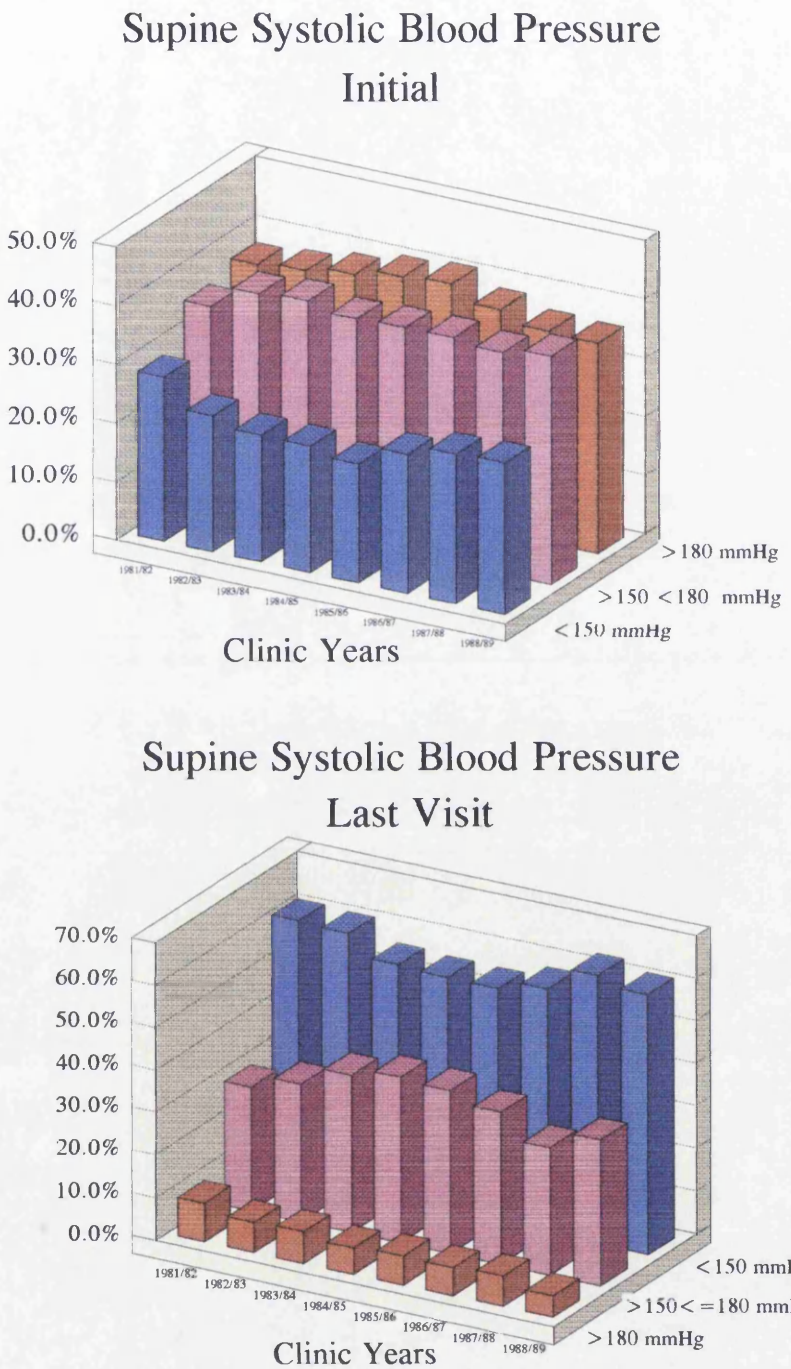


Figure 3.2. Distribution of initial and last visit diastolic blood pressures.

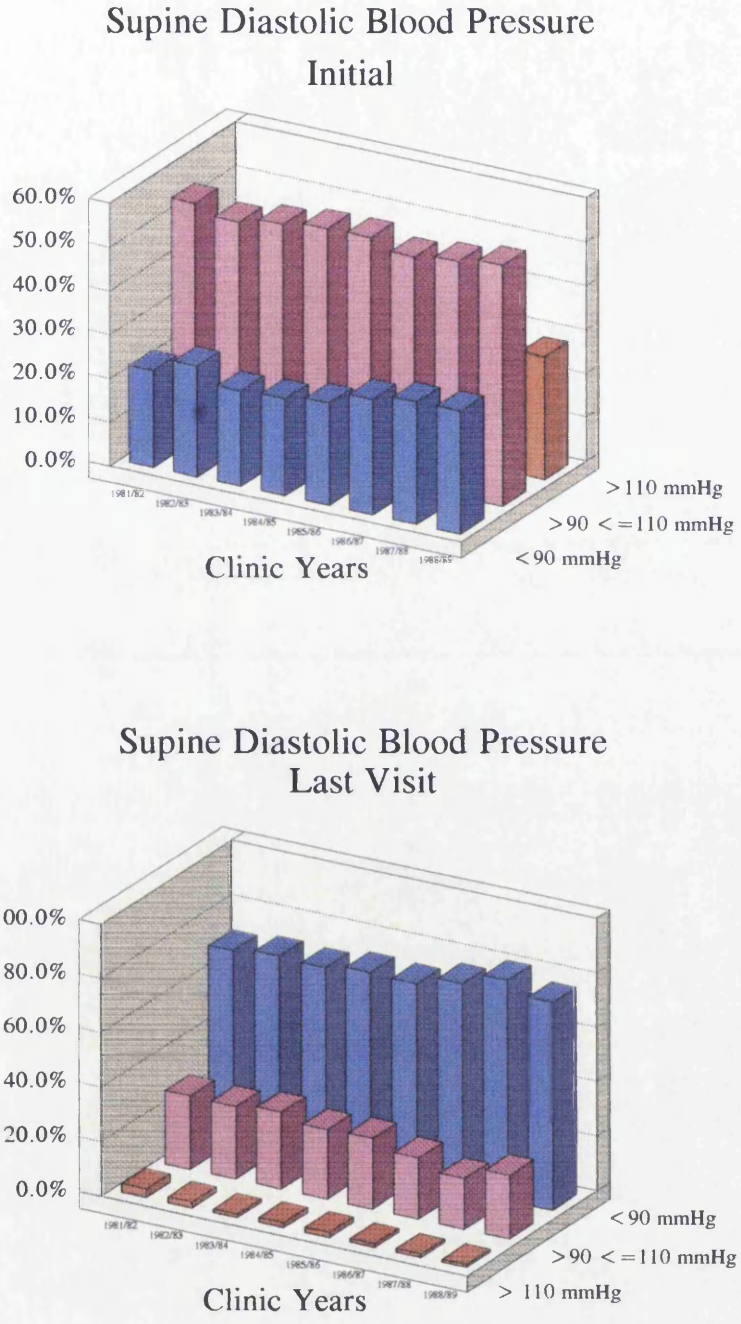


Table 3.3. Chi-square analysis results comparing initial with last visit blood pressure distributions each year for population continuing to attend.

	df	Chi-square	p value
Systolic blood pressure			
Year 1 1981/82	2	60.223	< 0.0005
Year 2 1982/83	2	115.084	< 0.0005
Year 3 1983/84	2	150.952	< 0.0005
Year 4 1984/85	2	193.315	< 0.0005
Year 5 1985/86	2	211.585	< 0.0005
Year 6 1986/87	2	225.606	< 0.0005
Year 7 1987/88	2	232.533	< 0.0005
Year 8 1988/89	2	264.286	< 0.0005
Diastolic blood pressure			
Year 1 1981/82	2	230.381	< 0.0005
Year 2 1982/83	2	273.513	< 0.0005
Year 3 1983/84	2	230.381	< 0.0005
Year 4 1984/85	2	273.513	< 0.0005
Year 5 1985/86	2	273.692	< 0.0005
Year 6 1986/87	2	333.557	< 0.0005
Year 7 1987/88	2	370.938	< 0.0005
Year 8 1988/89	2	352.869	< 0.0005

($X^2=5.603$, df=1, $p<0.025$). To evaluate these differences further, the blood pressures of those entering as new patients each year were also analysed.

Average initial blood pressures for those entering the clinic each year are plotted with the total population average initial blood pressure for that year, in Figure 3.3. One-way analysis of variance yielded significant differences between years for systolic blood pressure ($p<0.001$) and diastolic blood pressure ($p<0.001$). Tukey post hoc multiple comparisons (MINITAB 1991) showed that those entering Years 6 and 7 had significantly lower systolic and diastolic blood pressures at entry compared to earlier years (Table 3.4).

One-way analysis of variance of last visit systolic blood pressure for end of first year of attendance for those entering each year was non-significant. The end of first year of attendance diastolic blood pressure was statistically significant ($p<0.05$), but Tukey post hoc multiple comparisons failed to identify a significant difference between any two years, thus indicating that any between year differences in blood pressure control achieved within the first few months of attendance, are marginal.

Mean systolic and diastolic blood pressures compared with entry values are shown in Figure 3.4. As with the shift in blood pressure distribution, there is a significant difference between entry and last visit mean values each year ($p<0.001$). There is a significant difference in mean last visit diastolic blood pressure between the Year 1 population of 191 and the Year 8 population of 700 patients (88 ± 10 vs 84 ± 10 mmHg) at $p<0.001$ by unpaired t-test which was corrected for unequal sample size according to the method described by Snedecor and Cochran (Snedecor & Cochran 1967).

Blood pressure was also evaluated against the target blood pressure set for each patient and these are reported for Year 5 (1985/86) and Year 8 (1988/89) as a comparison (Table 3.5). 75% of patients were within 15 mmHg of their systolic targets for both years assessed, while 92% were within 10 mmHg of their diastolic target.

Figure 3.3. New patient versus total population mean initial blood pressure.

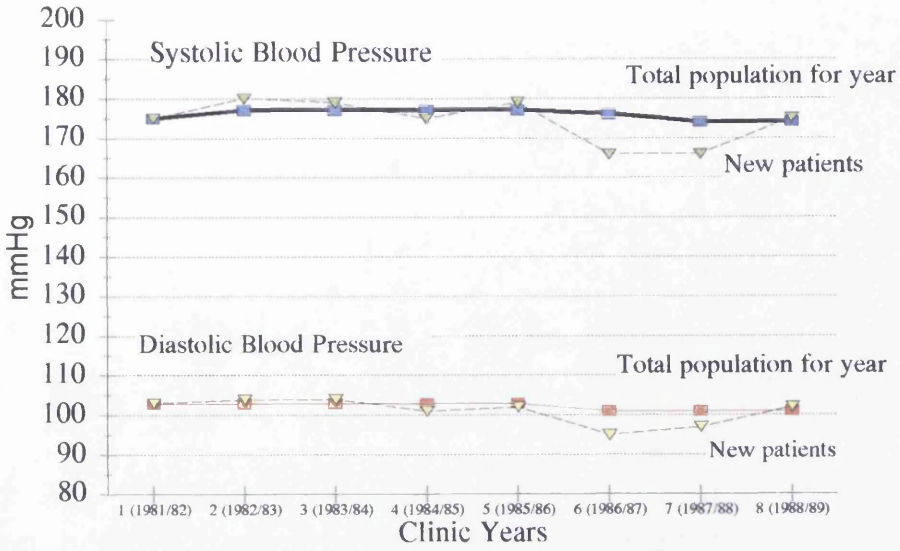


Table 3.4. Tukey confidence intervals comparing initial blood pressures of new patients entering each year.

Initial Systolic Blood Pressure

Years	Year 1 1981/82	Year 2 1982/83	Year 3 1983/84	Year 4 1984/85	Year 5 1985/86	Year 6 1986/87	Year 7 1987/88
2 1982/83	-15.98 4.23						
3 1983/84	-14.77 5.67	-10.44 13.08					
4 1984/85	-11.17 9.32	-6.83 16.73	-8.25 15.51				
5 1985/86	-16.29 7.72	-11.75 14.93	13.16 13.69	-16.81 10.09			
6 1986/87	-1.42 18.09	2.85 25.57*	1.43 23.34 *	-2.23 20.74	-0.46 25.70		
7 1987/88	-2.19 18.86	2.18 26.24*	0.76 25.01*	-2.89 21.41	-1.05 26.28	-11.74 11.74	
8 1988/89	-10.44 10.30	-6.09 17.69	-7.50 16.46	-11.16 12.86	-9.33 17.76	-20.00 3.19	-20.65 3.85

Initial Diastolic Blood Pressure

Years	Year 1 1981/82	Year 2 1982/83	Year 3 1983/84	Year 4 1984/85	Year 5 1985/86	Year 6 1986/87	Year 7 1987/88
2 1982/83	-6.00 4.37						
3 1983/84	-6.66 3.83	-6.63 5.44					
4 1984/85	-3.81 6.71	-3.78 8.31	-3.23 8.96				
5 1985/86	-5.04 7.34	-4.91 18.84	-4.35 9.48	-7.23 6.63			
6 1986/87	2.68 12.69*	2.67 14.33*	3.22 14.98*	0.34 12.13*	-0.21 13.28		
7 1987/88	0.68 11.48*	0.73 13.07*	1.27 13.72*	-1.60 10.87	-2.11 11.97	-7.63 4.42	
8 1988/89	-3.95 8.29	-3.91 8.299	-3.37 8.93	-6.24 6.09	-6.76 7.20	-12.26 -0.37*	-11.00 1.58

*$p < 0.05$

Figure 3.4. Blood pressure means and standard deviations.

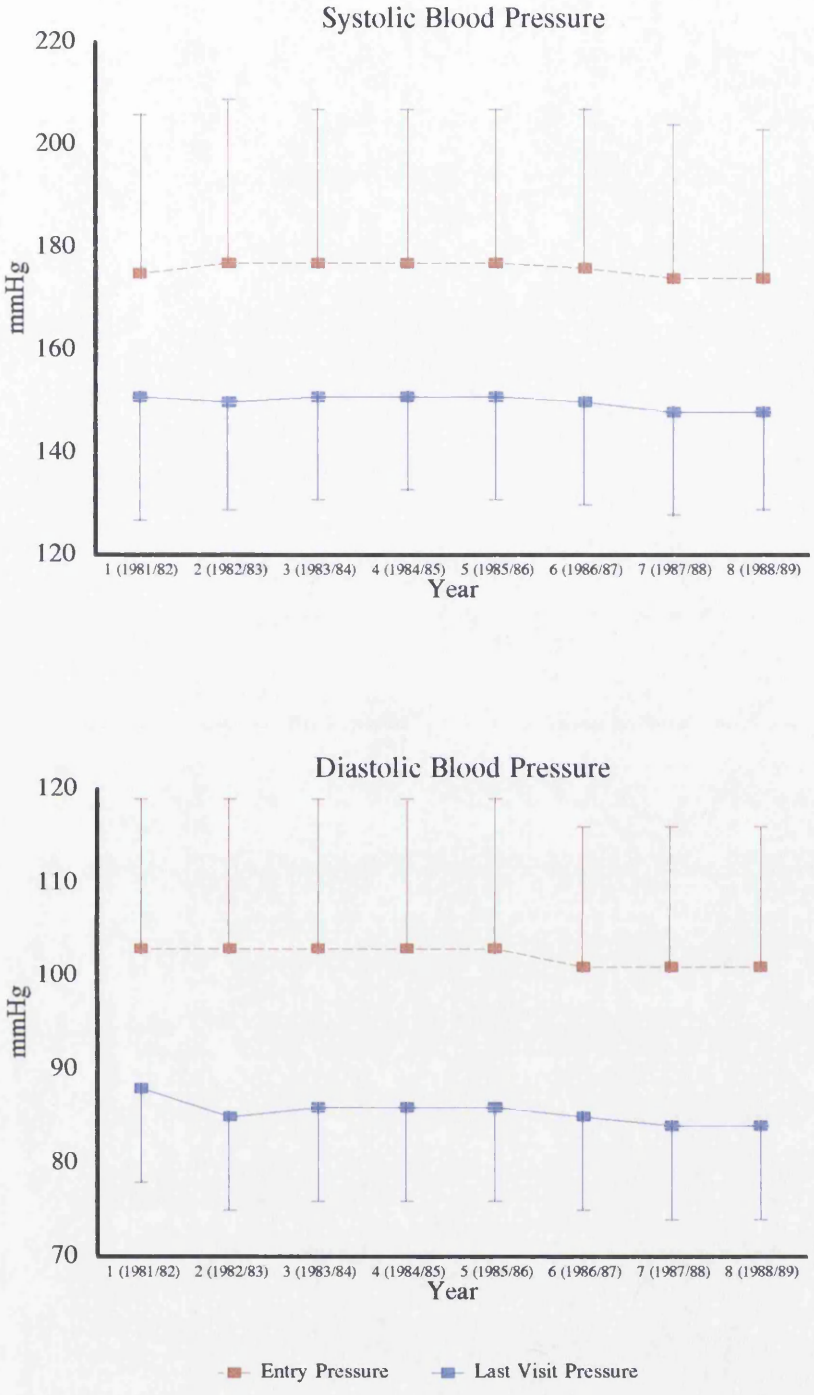


Table 3.5. Percentage of patients within 10 and 15 mmHg of systolic blood pressure target as well as within 5 and 10 mmHg of diastolic blood pressure target.

	Year 5 (1985/86)	Year 8 (1988/89)
Systolic Blood Pressure		
within target	44%	47%
within 10 mmHg	68%	71%
within 15 mmHg	76%	79%
Diastolic Blood Pressure		
within target	71%	75%
within 5 mmHg	84%	87%
within 10 mmHg	92%	92%

3.4.2. What drugs are being used?

Drug treatment strategies changed slowly over the years of the clinic. Initially, step-care was the advocated regimen. The percentage of patients receiving specific drugs and combinations is given in Table 3.6. The use of beta blocking and diuretic agents has declined, whereas the use of calcium antagonists and angiotensin converting enzyme (ACE) inhibitors has increased. Centrally acting agents (e.g. methyldopa, clonidine, etc) were no longer being prescribed by Year 8 (1988/89). Despite its declining use, atenolol was still the most commonly prescribed medication for the treatment of high blood pressure in this clinic.

The choice of drugs used in combination also changed over time (Table 3.7). The use of the beta blocker-diuretic combination was reduced to a third of its initial use by Year 8 (1988/89) when compared to Year 1 (1981/82), while the use of diuretics combined with vasodilators increased.

The percentage of patients who continued to attend the clinic on no treatment remained similar over time (Table 3.8). The percentage of patients taking only a single agent increased from 25% to 40%, whereas the use of triple therapy declined by half (21% to 10%). Despite these apparent major shifts in the number of drugs prescribed per patient to control blood pressure, there was no significant difference in the distribution by chi-square analysis.

3.4.3. How many patients are overweight and are they losing weight?

It was noted during the first year that many patients in the clinic were obese. The distribution of body mass indexes (BMI) did not change over the years for the clinic population as a whole (Figure 3.5), but it became apparent that some patients lost weight, while others gained. Changes in weight were investigated by comparing differences between Year 1 and Year 3 with differences between Initial and Year 8 weights, by sex. The distribution of weight gain/loss changed significantly for men between the two assessments (Figure 3.6). Despite an increase of a more than half in the percentage of men losing greater than 2 kg over time (22% vs 36%), the percentage gaining more than 2 kg doubled (13% vs 27%) (X^2=17.332,

Table 3.6. Changes in anti-hypertensive drug treatment over time.

Drug Treatment	Year 1 (1981/82)	Year 5 (1985/86)	Year 8 (1988/89)
Beta blockers	70%	57%	52%
Atenolol	64%	53%	49%
Propranolol	6%	2%	2%
Metoprolol		1%	1%
Other beta blockers		1%	
Diuretics	58%	46%	33%
Neo-Naclex	43%	16%	13%
Chlorthalidone	11%	22%	12%
Frusemide	3%	4%	6%
Modiuretic	1%	2%	1%
Other diuretics		2%	1%
Vasodilators	21%	44%	54%
Nifedipine Retard	4%	25%	27%
Verapamil		6%	6%
Diltiazem			3%
Captopril	3%	1%	1%
Enalapril		10%	14%
Prazosin	4%	2%	1%
Doxazosin			1%
Hydralazine	10%	4%	1%
Centrally Acting (alone or in combination)	3%	1%	
Other Drug Treatment			
GTN			4%
Aspirin			4%
Dipyridamole			1%

Table 3.7. Changes in anti-hypertensive drug treatment combinations over time.

Drug Treatment	Year 1 (1981/82)	Year 5 (1985/86)	Year 8 (1988/89)
Monotherapy			
Beta blocker alone	19%	15%	20%
Diuretic alone	5%	3%	3%
Vasodilator alone		13%	17%
Combinations			
Beta blocker + diuretic	51%	18%	10%
Atenolol + bendrofluazide	15%	8%	3%
Atenolol + chlorthalidone	36%	20%	6%
Beta blocker + diuretic + vasodilator	19%	16%	9%
Beta blocker + vasodilator	1%	7%	12%
Diuretic + vasodilator	1%	7%	11%

Table 3.8. Changes in the number of drugs prescribed per patient over time.

	Year 1 (1981/82)	Year 5 (1985/86)	Year 8 (1988/89)
No treatment	17%	18%	15%
Single drug	25%	31%	40%
Two drugs	37%	32%	33%
Three drugs	21%	15%	10%

Figure 3.5. Distribution of last visit body mass indexes over 8 years.

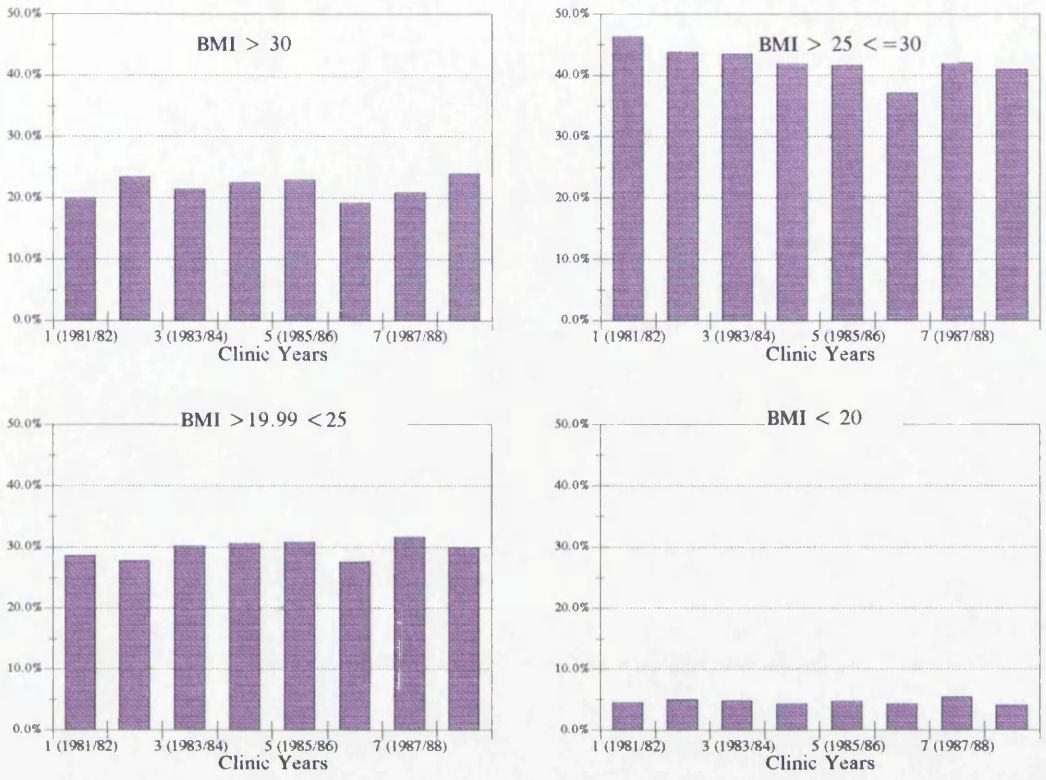
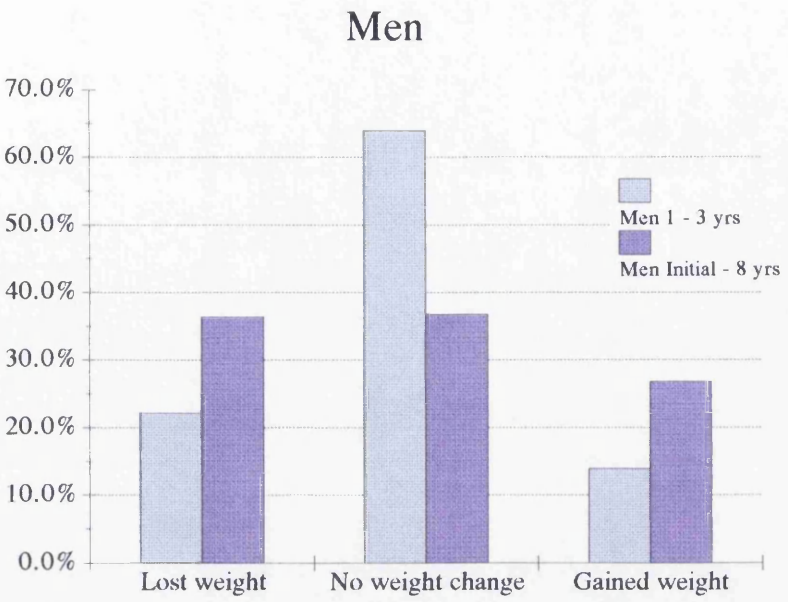
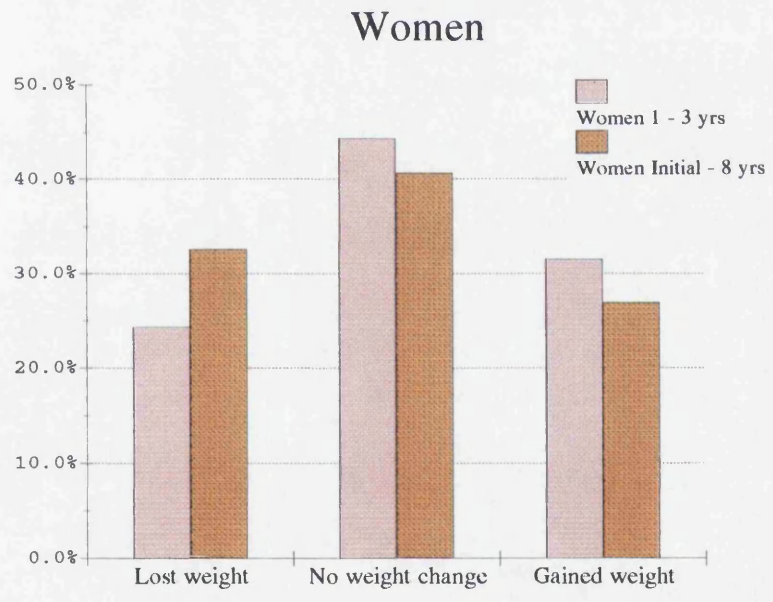


Figure 3.6. Weight changes in men and women compared Year 1 with Year 3, and Initial with Year 8.





df=2, $p<0.0005$). This indicated, that by Year 8, the distribution of weight change in men was similar to that seen in women.

In addition, for those continuing to attend at the end of Years 5 and 8, changes in weight were compared by initial BMI gradings for all patients. There were no significant differences in the Year 5 population. In Year 8, patients with an initial BMI of 25.00 - 30.00, on average lost 1.0 kg in weight over their attendance in the clinic (3 months-8 years) compared to 0.2 kg gain for those with initially normal grade of 20.00 - 24.99 ($p<0.05$). Obese men with initial BMI > 30 lost 1.5 kg on average compared to a gain of 0.5 kg in males with initial BMI 20.00 - 24.99 ($p<0.05$).

A similar analysis undertaken in new patients showed a 1.3 kg reduction in weight in those with initial BMI > 30 of during their first year of attendance. One-way analysis of variance showed that this was a significant reduction in weight in comparison to those with BMI 20-24.99 who had gained 0.4 kg by the end of their first year of attendance ($p<0.001$). Thus, the average weight changes identified between initial and Year 8 weights occurred during the first year and were maintained over time.

3.4.4. Have the smokers attending the clinic stopped smoking?

The percentage of patients who reported that they smoked generally declined over time apart from a slight increase in Year 4 (1984/85) when there was a change over in computing systems. All smoking data were entered prospectively as patients attended that year, so that at the time of the end of year audit, 21% of patients had not had their smoking status updated (Table 3.9). The changes in smoking over time, excluding Year 4 data, were not significant by chi-square analysis. There was no significant difference in the proportion of men and women smoking.

The number of cigarettes reported to be smoked each day by smokers declined over the years. In Year 1 (1981/82), 20% of smokers smoked more than 20 cigarettes per day, while by Year 8 (1988/89) 7% reported smoking more than 20 cigarettes per day. Those reporting smoking 10 or fewer cigarettes per day increased

Table 3.9. Percentage of patients reporting smoking at the end of each year compared with percentage of new patients that year who reported smoking.

	YEAR	Percentage Total Population	Percentage Without Smoking Information	Percentage New Patients
1	1981/82	39.1%	3.1%	40.3%
2	1982/83	34.1%	2.0%	26.5%
3	1983/84	35.0%	4.3%	36.6%
4	1984/85	36.1%	21.0%	32.4%
5	1985/86	32.6%	7.4%	26.3%
6	1986/87	31.3%	4.3%	31.8%
7	1987/88	28.4%	1%	22.6%
8	1988/89	27.8%	<1%	30.7%

from 44% to 57%. These shifts in the number of cigarettes smoked were significant over time by chi-square analysis, again excluding Year 4 data ($X^2=25.840$, df=12, $p<0.025$).

At the end of Year 3, smoking levels were compared with entry levels for all reported smokers (31.1% vs 29.3%), males (30.2% vs 26.3%) and females (33.3% vs 31.8%), thus showing very modest reductions during attendance at the clinic (1 month - 3 years). Smoking rates by sex in the clinic are plotted against the Scottish national averages (Information & Statistic Division 1990) for the same year in Figure 3.7. The rates for the 1986 MONICA survey in North Glasgow are also noted in the figure (Smith et al 1988). The percentage of clinic patients of each sex who smoke was consistently less than that for the general Scottish population and for the North of Glasgow. While the percentage of female smokers in the general population increased slightly with time, in the clinic, the percentage decreased.

Changes in smoking were analysed at the Year 5 (1984/85) annual review by comparing current status to the previous year's status for each patient, thus identifying more activity in attempts to change smoking habits than the stop smoking rate indicated (Table 3.10). Unfortunately, the 3.1% (11) patients who reported that they had stopped smoking, was offset by the 0.8% (3) who admitted that they had resumed, as was the 5.3% (19) who reported a decrease in the number of cigarettes smoked per day, by the 2.8% (10) who admitted smoking an increased number of cigarettes per day, from the previous year.

3.4.5. Who are we seeing? - Age/sex distribution

Initially, there was a relatively equal distribution of males and females in the clinic (48% vs 52%). However, latterly the men were outnumbered by the women (43% vs 57%), but the change in distribution between Years 1 and 8, was not significant by chi-square analysis (Table 3.11). There was no significant difference in the sex ratio of new patients that entered each year.

A summary of the percentage of each sex by age group over the 8 years of the clinic is given in Table 3.12. During the early years of the clinic, there were more

Figure 3.7. Smoking levels compared with Scottish percentages by sex including results from the North Glasgow cohort of the MONICA project.

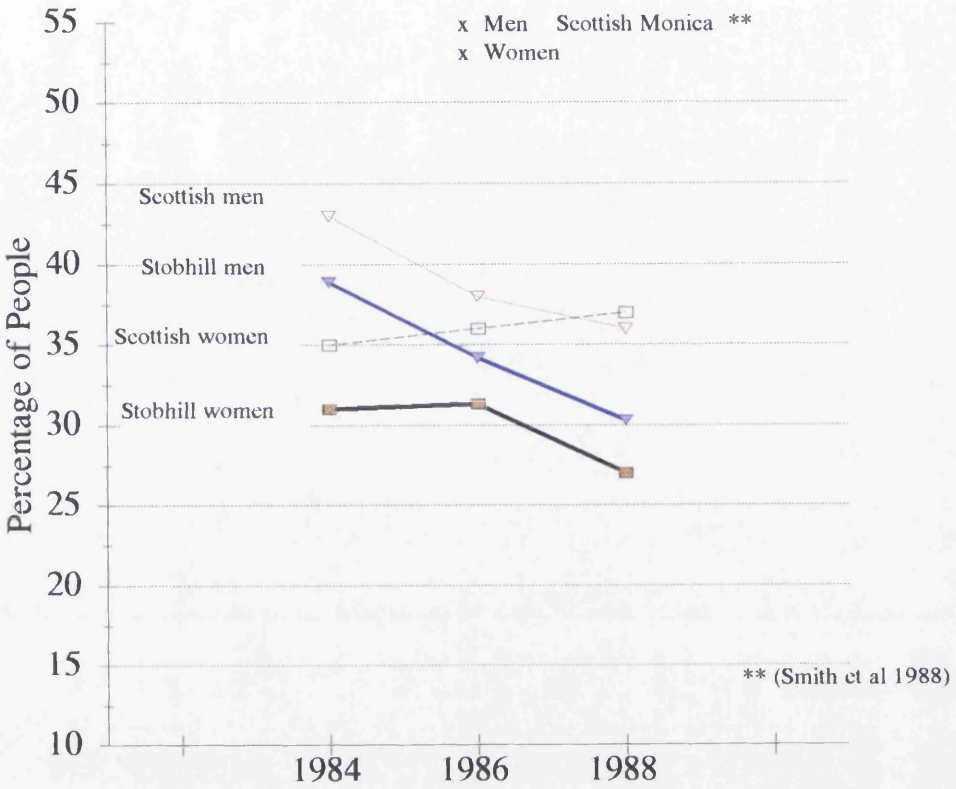


Table 3.10. Changes in reported smoking status between Year 4 (1984/85) and Year 5 (1985/86) for patients with smoking data both years.

	Number	Percentage of Population with Smoking Data both years
Smoking	119	33.1%
Stopped smoking	11	3.1%
Decreased number smoked	19	5.3%
Resumed smoking	3	0.8%
Increased number smoked	10	2.8%

Table 3.11. Percentage of males and females continuing to attend each year.

	Males	Females
1 1981/82	48% (101)	52% (108)
2 1982/83	49% (155)	51% (160)
3 1983/84	46% (187)	54% (216)
4 1984/85	47% (233)	53% (261)
5 1985/86	45% (239)	55% (294)
6 1986/87	44% (276)	56% (350)
7 1987/88	42% (274)	58% (371)
8 1988/89	43% (302)	57% (403)

Table 3.12. Percentage of sex by age group over 8 years.

	Year 1 (1981/82)	Year 2 (1982/83)	Year 3 (1983/84)	Year 4 (1984/85	Year 5 (1985/86)	Year 6 (1986/87)	Year 7 (1987/88)	Year 8 (1988/89)
Men								
≤ 20 years	1%	1%	2%		1%			
21 - ≤ 30 years	3%	3%	3%	3%	4%	4%	4%	5%
31 - ≤ 40 years	8%	7%	6%	9%	8%	10%	8%	6%
41 - ≤ 50 years	15%	21%	19%	18%	17%	17%	19%	19%
51 - ≤ 60 years	37%	36%	35%	33%	34%	33%	29%	31%
61 - ≤ 70 years	33%	27%	31%	30%	31%	28%	30%	28%
71 - ≤ 80 years	4%	3%	4%	6%	6%	7%	10%	10%
> 80 years		1%						1%
Women								
≤ 20 years						1%		
21 - ≤ 30 years	11%	15%	12%	10%	9%	9%	8%	6%
31 - ≤ 40 years	11%	11%	8%	11%	10%	9%	11%	10%
41 - ≤ 50 years	23%	22%	24%	22%	21%	20%	18%	17%
51 - ≤ 60 years	33%	31%	28%	28%	27%	29%	29%	34%
61 - ≤ 70 years	15%	14%	19%	22%	25%	25%	24%	24%
71 - ≤ 80 years	7%	7%	7%	6%	7%	8%	9%	9%
> 80 years	1%	2%						

younger women and older men. Initially 22% of the women versus 12% of the men were 40 years old or younger, while 37% of the men versus 22% of the women were over 60 years of age. The percentage of younger women declined and the percentage of older women increased. By Year 8 (1988/89) 16% of the women were 40 years old or younger and 33% were over 60 years. These shifts in distribution were non-significant by chi-square analysis and represent an aging clinic population continuing to attend.

3.4.6. How many are we seeing and how often? - Enrolment and attendance

There were 247 patients enrolled from the outpatient clinics during the first year of operation. In subsequent years enrolment of new patients to the clinic averaged about 125 per year. Non-attendance rates averaged about 10% per year as did cancellations. The population continuing to attend grew yearly by approximately 100 patients per years. Annual totals are given in Table 3.13.

The number of years of attendance is given in Table 3.14. Nearly half of those who enrolled during the first year of operation had last visit data in Year 8.

3.4.7. How many were lost to follow-up?

Those patients no longer attending were tracked and the reasons noted. A summary by year is given in Table 3.15. It can be seen that relatively few patients were lost to follow-up through non-attendance. The general practitioners of those who failed to attend were notified, to give them the opportunity to 'recapture' their patient's care.

The 146 who failed to attend over the 8 years included 13 patients who were repeat attenders. One lady re-entered the clinic 4 times after failing to attend for three appointments each time. In total, only 123 individuals (11%) out of the 1091 referred were lost due to non-attendance. The other major reasons for patients not attending were (a) returning to their general practitioner for care either at their own request or that of their general practitioner (9%), and (b) death (8%).

Table 3.13. Number of patients enrolled each year and continuing to attend.

		Number Enrolled	Number Currently Attending
Year 1	1981/82	247	209
Year 2	1982/83	129	315
Year 3	1983/84	120	403
Year 4	1984/85	121	494
Year 5	1985/86	95	533
Year 6	1986/87	134	626
Year 7	1987/88	137	645
Year 8	1988/89	108	705
	Total	1091	

Table 3.14. Years of attendance.

Number of Years of Attendance	Number of Patients Attending
8	112
7	86
6	98
5	83
4	105
3	140
2	177
1	251

Table 3.15. Disposition of patients who left the clinic.

	Year 1 (1981/82)	Year 2 (1982/83)	Year 3 (1983/84)	Year 4 (1984/85)	Year 5 (1985/86)	Year 6 (1986/87)	Year 7 (1987/88)	Year 8 (1988/89)	Total
Failed to attend (DNA)	7	7	14	16	20	18	33	31	146
Percentage of total attending	3%	2%	3%	3%	4%	3%	5%	4%	
Died	3	7	12	12	12	8	8	21	83
To General Practitioner Care	3	7	4	9	13	12	14	31	93
To Medical/ Obstetric Clinic	4	3	1	3	1	5	1	2	20
Moved from district	3	1	1	7	2	5	4	6	29
To Medical Clinic	7	1		2	1		1	4	16
To Cardiology Clinic				3		1	2	3	9
To Renal Unit		2	1		1		2		6
To other BP Clinic	1		1		1	3			6
Discharged	2		1	1	4	2	2	7	19
Other						1	1	4	6
Yearly Totals	30	28	35	53	55	55	68	109	433
Percentage of Total Attending	14%	8%	9%	11%	10%	9%	11%	15%	

3.4.8. What happened to biochemical indices, particularly cholesterol and glucose?

The mean and standard deviations for all biochemical indices each year are given in Table 3.16. Total cholesterol decreased significantly between Year 6 (1986/87) and Year 7 (1987/88) at $p<0.001$ by unpaired t-test. The changes in cholesterol will be presented in detail in Chapters 5 and 7. There was a non-significant rise in blood glucose between Year 1 (1981/82) and Year 4 (1984/85). The standard deviation for GammaGT was greater than the mean due to a small number of patients who had quite elevated levels due to admitted excessive alcohol intake.

3.5. Discussion

The annual review of clinic data has shown the impact of nurse practitioner care in the population continuing to attend at the end of each year. First and foremost, blood pressure rapidly came under control, and control was maintained over time for the majority of patients. In addition, drug treatment regimens were simplified, with more patients taking less drug therapy without loss of blood pressure control. This level of control is in sharp contrast to that which has been previously reported in general practice in Scotland (Hawthorne et al 1974, Ritchie & Currie 1983, Smith et al 1990). The level of diastolic blood pressure achieved is in keeping with that obtained within clinical trials such as the HDFP (HDFP Cooperative Group 1979).

Despite differences observed between years in the initial systolic blood pressures of new patients, by the end of their first year of attendance there were no significant differences in last visit pressure. Bulpitt et al demonstrated, using the DHSS computing project data, that achieved blood pressure predicted outcome far better than initial or entry measurements (Bulpitt et al 1988).

Body mass index did not change. Very modest (1.3 kg), but significant, reductions were noted in those with $BMI>30$ within their first year of attendance.

Table 3.16. Biochemical indices over 8 years.

	Year 1 (1981/82) n Mean s.d.	Year 2 (1982/83) n Mean s.d.	Year 3 (1983/84) n Mean s.d.	Year 4 (1984/85) n Mean s.d.	Year 5 (1985/86) n Mean s.d.	Year 6 (1986/87) n Mean s.d.	Year 7 (1987/88) n Mean s.d.	Year 8 (1988/89) n Mean s.d.
Total Cholesterol	165 6.4 ±1.4	217 6.3 ±1.6	250 6.3 ±1.2	332 6.6 ±1.2	408 6.5 ±1.3	550 6.5 ±1.3	622 6.2 ±1.2	696 6.2 ±1.2
Glucose	127 5.6 ±2.3	209 5.4 ±1.7	310 5.6 ±1.6	425 5.9 ±1.9	472 6.0 ±1.8	566 5.9 ±2.2	612 5.9 ±2.0	678 6.0 ±2.2
Urate	164 0.38 ±0.10	265 0.38 ±0.10	371 0.35 ±0.09	467 0.30 ±0.10	490 0.31 ±0.10	592 0.33 ±0.10	629 0.34 ±0.09	686 0.34 ±0.09
Potassium	160 4.1 ±0.5	262 4.0 ±0.4	382 4.1 ±0.4	482 4.1 ±0.4	498 4.0 ±0.4	588 4.1 ±0.4	632 4.1 ±0.4	690 4.1 ±0.4
Creatinine	162 102 ±48	267 97 ±44	385 101 ±35	483 100 ±32	503 97 ±30	591 97 ±36	638 93 ±36	698 92 ±32
GammaGT	148 42 ±34	251 40 ±60	369 37 ±54	470 36 ±45	486 38 ±60	576 36 ±44	627 33 ±48	680 32 ±42

Similar reductions were observed when comparing initial weight with last visit weight for those continuing to attend at the end of Year 8. Therefore, the average reduction in weight observed during the first year in the nurse practitioner clinic were present over time. These changes are similar to other reports of long term weight reduction in an outpatient hypertension clinic (Straznicky et al 1991).

Reported levels of smoking declined over the years and were much reduced compared to Scottish averages (Figure 3.7). Reporting bias cannot be ruled out, but it would appear that a number of these patients had stopped smoking prior to their attending, so that those who continued to smoke were likely to be individuals who found it difficult to stop. Yet, a few more managed to stop each year.

Continued attendance in this clinic has been shown to be high, with only 11% of those enrolled lost due to non-attendance, and 65% continuing to attend at the end of 8 years. This result is in marked contrast to a report from the Glasgow Blood Pressure Clinic which was only able to report on the 16% of its enrolled population who had 3 years of continuous data (Johnston et al 1980).

It is unlikely that the participation in clinical trials of patients attending the nurse practitioner clinic has affected these results as patients may or may not have had uncontrolled blood pressure at the time of their recruitment, and no more than 10% of the population participated any year. In addition, if a patient was in a clinical trial at the time of the annual audit, their data were withheld from the analysis.

A vast quantity of routine clinical data have been generated over the course of this project. The regular annual reviews and other analyses have stimulated the development of a number of projects which are presented in subsequent chapters of this thesis.

Chapter 4. Comparison of nurse practitioner care with conventional hypertension clinics

4.0. Summary

In this chapter, the nurse practitioner clinic (NPC) is compared with a conventional hypertension clinic (CHC). Clinical care of patients enrolled in both clinics between 1 September 1981 and 1 September 1982 is compared initially at entry, and after 1 and 4 years of follow-up. Mortality over 6 years is reported and discussed.

4.1. Introduction

Nurses, working in a variety of settings, have been involved in screening for hypertension and caring for the individuals subsequently found to be hypertensive since the mid-1960's as described in detail in Chapter 1. Much of this original work was carried out in North America. In addition to traditional outpatient clinics and community clinics, the care settings have included department stores (Alderman & Scholenbaum 1975), and other worksites (Logan et al 1979, Logan et al 1983).

One of the few comparisons reported was Runyan's community care study which compared follow-up care received for diabetes, hypertension, cardiac disease or a combination of these provided by nurse practitioners in decentralised clinics near their homes. Overall there was less hospital utilisation by patients followed by the nurse practitioners. Diastolic blood pressure was also significantly reduced (Runyan 1975).

In a Canadian study, Ramsay et al compared nurse practitioner versus medical follow-up in matched groups of 40 out-patients over 15 months. Diastolic blood pressure was reduced and weight decreased in obese patients cared for by the nurse practitioner. There was no difference between the groups for levels of attendance (Ramsay et al 1982).

An Israeli comparison study which followed 5,541 hypertensive patients attending community family health clinics, demonstrated improvements in the percentage of patients with controlled diastolic blood pressure. During care by a

physician alone, only 42.1% had an average diastolic blood pressure < 95 mmHg over 2 visits, while 2 years after commencing care by nurse/physician teams, 84.6% had diastolic blood pressures at these levels (Viskoper & Silverberg 1985).

Unfortunately, of the studies reported above and in Chapter 1, only Ramsay's compared the care provided by nurses/nurse practitioners in a hospital outpatient clinic with traditional medical hospital outpatient follow-up (Ramsay et al 1982). Most of these report on short term follow up of less than two years except for the controlled clinical trials. In addition, only the controlled clinical trials looked at mortality over time as well as degrees of blood pressure control.

In order to assess the impact of our nurse practitioner clinic method of follow-up care, a study was devised to compare patients enrolled during the first year of operation with a group who had been seen in conventional hypertension clinics in two other teaching hospitals within the Greater Glasgow Health Board. They first attended during the same year, and their information was collected prospectively and incorporated into the Glasgow Blood Pressure Clinic (GBPC) database (Glasgow Blood Pressure Clinic 1972). Clinical data were compared initially, and after one year and 4 years. Mortality was analysed over 6 years of follow-up.

4.2. Methods

4.2.1. Referral sources

Referrals to all three hospitals for the management of hypertension came from general practitioners (secondary referral) or hospital specialists (tertiary referral). Patients at each clinic were initially seen by a physician, and it was the agreed policy of all the clinics to continue hospital based care for these patients.

4.2.2. Nurse Practitioner Clinic (NPC)

The NPC patients were seen by one of two experienced nurse practitioners for follow-up. The NPC is explained in detail in Chapter 2, but briefly the nurse practitioners measured blood pressure, body weight, and assessed general wellbeing. Patients were counselled regarding weight, smoking and compliance with drug and

diet therapy. They were referred to medical staff for assessment of possible drug side effects or for poorly controlled blood pressure. Annually, patients were seen by a clinic physician and given a physical examination. Urinalysis and 12-lead electrocardiogram were carried out, and a venous blood sample was taken for biochemical analysis, including non-fasting glucose and total cholesterol.

Drug treatment in the NPC was based upon a step care approach as recommended by the United States National Committee on Detection, Evaluation and Treatment of High Blood Pressure (Joint Committee 1977). A beta blocker was first choice with the addition of a diuretic and vasodilator added, as required, to achieve target blood pressure. Treatment decisions were taken by medical staff. Target blood pressures were set according to age, with those patients under 60 years of age having a target of $\leq$ 150/90 mmHg and those over 60 years a target of $\leq$ 165/95 mmHg.

4.2.3. Conventional Hypertension Clinics (CHC)

In the CHC, patients were seen regularly by senior or junior medical staff. Several papers have described the functioning of these clinics (Ramsay et al 1978,Isles et al 1986). Blood pressure and weight were measured at each visit and drug treatment recorded. An annual review, similar to that undertaken in the NPC, was part of the routine follow-up. Drug treatment was broadly similar, but less formalised, than the NPC's step care.

4.2.4. Data compared

NPC data were stored as previously described on a succession of microcomputers using software developed in house (Kelman et al 1982). The CHC data were stored on the Greater Glasgow Health Board's ICL mainframe computer using the GBPC's 'SWITCH' system (Kennedy 1968). The subset of data for those patients enrolled between 1 September 1981 and 31 August 1982 from the other two teaching hospitals contributing data to this system was obtained on a micro-floppy disc compatible with the NPC's microcomputer system. Thus both sets of data were collected prospectively.

Due to a substantial lack of data beyond four years in the CHC group, analysis

was limited to attendance levels, supine blood pressure, weight, drug treatment, and routine biochemistry at the end of the first and fourth years of attendance. In addition, an assessment of the six year mortality in both populations was performed.

In order to obtain mortality data, all patients were traced up to 1 September 1987. Patients enrolled onto the GBPC's 'SWITCH' system are recorded with the Registrar General's office in Edinburgh, so that notification is given within 6 months if these individuals die. A copy of the death certificate is sent to and stored in the 'SWITCH' office.

The NPC, when notified of a death, sent a letter to the patient's general practitioner asking for the cause of death. This information was used for analysis unless the patient had been enrolled onto 'SWITCH', in which case the death certificate cause of death was utilised. All NPC patients not enrolled onto 'SWITCH', and no longer attending, were traced via correspondence with their general practitioner. The cause of death was noted for those who had died since leaving the NPC.

4.2.5. Data analysis

Data were analysed using either LOTUS 1-2-3 (Version 1A) on the microcomputer, or SPSSx, MINITAB and BMDP on the Glasgow University ICL 3980 mainframe computer. Results are presented as means for initial, first year and fourth year data. Parametric and non-parametric tests were undertaken as appropriate. Life table analysis was done according to the method described Armitage (Armitage 1971) and without computer assistance.

4.3. Results

4.3.1. Results - All patients

There were 247 patients enrolled in the NPC clinic and 229 enrolled in the CHC clinics from 1 September 1981 to 31 August 1982. A summary of initial data for each group is presented in Table 4.1. The patients attending the NPC were older (51 vs 48 yrs) than patients attending the CHC ($p<0.02$), starting blood pressures were not different but almost reach significance with $p < 0.06$ for supine systolic

Table 4.1. Initial profile of all patients (Mean ±s.d. or percentage).

	NURSE PRACTITIONER CLINIC	CONVENTIONAL HYPERTENSION CLINIC	SIGNIFICANCE
Age (years)	51 ±13	48 ±14	$p < 0.02$
Sex (M/F)	119/128	112/117	
Body Mass Index	27.21 ±4.54	26.90 ±4.56	
% Smokers	41%	47%	
Supine Systolic Blood Pressure	175 ±31	169 ±30	$p < 0.06$
% with SBP <= 150 mmHg	28%	29%	
Supine Diastolic Blood Pressure	103 ±16	101 ±14	$p < 0.08$
% with DBP <= 90 mmHg	23%	25%	
Cholesterol (mmol/l)	6.3 ±1.4	6.2 ±1.7	
Glucose (mmol/l)	5.9 ±2.1	5.3 ±1.8	$p < 0.10$
Potassium (mmol/l)	4.0 ±0.5	3.9 ±0.7	
Urate (mmol/l)	0.38 ±0.12	0.34 ±0.10	
Creatinine (μmol/l)	100 ±45	97 ±69	
Gamma GT (iu/l)	41 ±33	33 ±42	$p < 0.10$

blood pressure and $p < 0.08$ for supine diastolic blood pressure.

Follow up attendance differed markedly between the clinics over the four years (Table 4.2). By four years, 70% of the NPC patients but only 33% of CHC were continuing to attend. There were also profound differences in favour of the NPC in the number of patients who had routine follow-up biochemistry data available at four years (Table 4.3). While the NPC had values obtained in 91-100% of the patients attending, for each of the 6 biochemistry indices under consideration, only 13%-75% of the patients in the CHC had values for each of these biochemistry results.

Blood pressure control improved from initial values in both clinics during the four years of follow-up care (Figure 4.1). At the end of the first year, the average decrease in diastolic blood pressure of 15 mmHg in the NPC was statistically significantly greater than the 9 mmHg decrease in the CHC ($p<0.005$).

Diastolic blood pressure was also statistically significantly lower in the NPC at four years ($p<0.005$), with average diastolic blood pressure 85 $\pm$9 mmHg in the NPC and 89 $\pm$9 mmHg in the CHC. There were no statistically significant differences in systolic blood pressure between the groups at any of the time points.

Drug treatment initially and at the end of the first year are shown in Table 4.4. Drug treatment regimens approximated 'step care' by the end of the first year. However, there were more patients receiving no treatment in the CHC initially and at the end of the first year.

Thus, preliminary data analysis revealed statistically significant age and diastolic blood pressure differences as well as minor differences in sex distribution between the groups. Further analysis was undertaken, as these differences might have influenced drug treatment choices and acceptability of blood pressure levels. This further analysis controlled for age and sex.

4.3.2. Results - Age and sex matched groups

Patients were matched retrospectively for sex and age (within 5 years), and 198 patient pairs were obtained from the original NPC and CHC cohorts. A summary of the initial data for these matched groups from each clinic is given in

Table 4.2. Attendance over 4 years in all patients.

	NURSE PRACTITIONER CLINIC	CONVENTIONAL HYPERTENSION CLINIC	SIGNIFICANCE
Initial Enrolment	247 (100%)	229 (100%)	
At One Year	191 (77%)	167 (73%)	n.s.
At Four Years	173 (70%)	76 (33%)	$p < 0.001$*

* Chi-square $X^2 = 64.692$, df=1

Table 4.3. Biochemistry results after 4 years of follow-up in all patients.

	NURSE PRACTITIONER CLINIC (N=173/247)	CONVENTIONAL HYPERTENSION CLINIC (N=76/229)
	N=	N=
Cholesterol (mmol/l)	158 6.6 ±1.3	35 6.3 ±1.7
Glucose (mmol/l)	164 6.1 ±2.3	10 5.9 ±1.1
Potassium (mmol/l)	172 4.0 ±0.4	57 4.2 ±0.5
Urate (mmol/l)	172 0.38 ±0.09	45 0.39 ±0.10
Creatinine (μmol/l)	173 98 ±27	57 101 ±50
Gamma GT (iu/l)	173 35 ±32	51 37 ±46

Figure 4.1. Systolic and diastolic blood pressures for all patients.

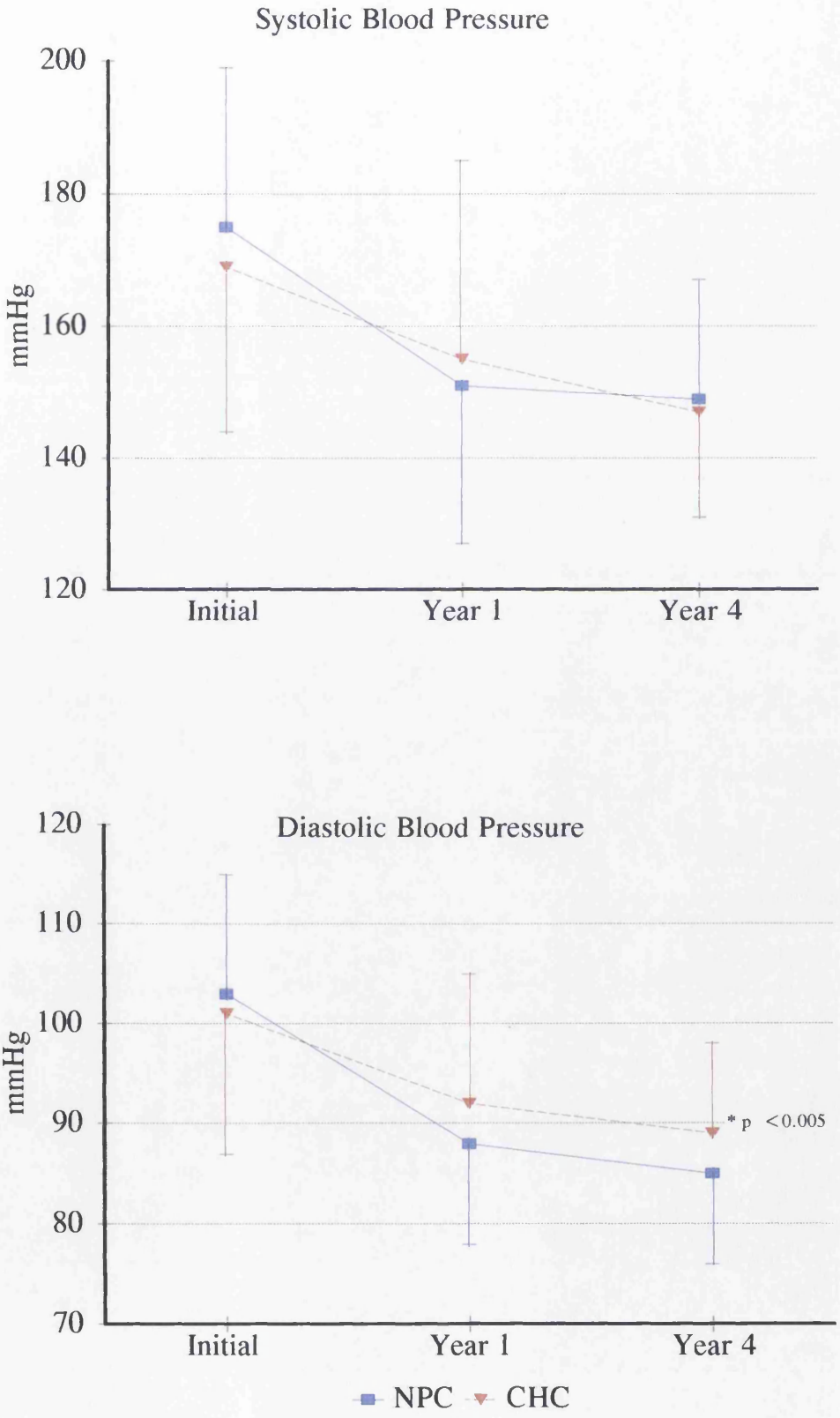


Table 4.4. Drug treatment regimens initially and at the end of the first year of follow-up in all patients.

	NURSE PRACTITIONER CLINIC		CONVENTIONAL HYPERTENSION CLINIC	
	Initially	End of First Year	Initially	End of First Year
Beta Blocker Alone	46 (19%)	37 (19%)	24 (10%)	20 (12%)
Diuretic Alone	9 (4%)	11 (6%)	15 (7%)	10 (6%)
Vasodilator Alone	0	1	2	2
Beta Blocker and Diuretic	76 (31%)	63 (33%)	55 (24%)	50 (30%)
Beta Blocker and Vasodilator	7 (3%)	8 (4%)	2	1
Diuretic and Vasodilator	0	1	2	3 (2%)
Beta Blocker, Diuretic and Vasodilator	48 (19%)	38 (20%)	12 (5%)	17 (7%)
No Treatment	51 (21%)	23 (12%)	82 (36%)	49 (29%)

Table 4.5. There were no significant differences in obesity, supine systolic blood pressure, supine diastolic blood pressure, percentage of regular to heavy drinkers, percentage of patients diagnosed as having essential hypertension or most biochemical indices. Gammaglutamyltransferase (Gamma GT) and urate were higher in the NPC, fewer patients were untreated and there were fewer reported smokers in that group.

Out of the 198 age and sex matched patients from each clinic, 160 in the NPC clinic and 147 in the CHC clinic were still attending at the end of the first year, but at the end of the fourth year there were 136 patients continuing in the NPC and only 70 in the CHC. Even after one year there was a greater loss to follow-up (26%) in the CHC compared to the NPC (19%). By the end of four years, 65% of the CHC were not attending for follow-up while only 31% of the NPC were no longer attending ($p < 0.001$). The disposition of those patients no longer attending after 4 years is presented in Table 4.6.

As can be seen in Table 4.5, there were no significant differences between the NPC or CHC groups in mean starting supine systolic or diastolic blood pressure. Supine blood pressures for the first and fourth years and their average differences from initial values are given in Table 4.7. The percentages of patients with controlled blood pressure for their age at the end of one and four years compared with initial levels are in Figure 4.2. First year systolic blood pressure for the 114 remaining age and sex matched pairs was significantly different ($p < 0.05$) by paired t-test. Overall, the NPC group achieved a greater reduction in both systolic and diastolic blood pressure over the first year of attendance, and had a higher percentage of patients with blood pressures less than or equal to the predetermined target. The difference in diastolic blood pressure extended into the fourth year for those patients continuing to attend.

Obesity was assessed in both groups using Body Mass Index (BMI) (WT/HT^2). There was no difference in starting BMIs between the groups, or in weight change at the end of the first year. By the end of the fourth year there was no difference in

Table 4.5. Initial profile of age and sex matched groups (Mean ±s.d. or percentage).

	NURSE PRACTITIONER CLINIC	CONVENTIONAL HYPERTENSION CLINIC	SIGNIFICANCE
Age (years)	50 ±13	49 ±13	
Sex	M 92 F 106	M 92 F 106	
Obesity Index	26.95 ±4.30	27.08 ±5.12	
% Smokers	37%	46%	
% Regular to Heavy Drinkers	29%	26%	
Supine Systolic Blood Pressure	173 ±32	171 ±30	
% Controlled SBP ($\leq$150 mmHg)	30%	27%	
Supine Diastolic Blood Pressure	102 ±15	101 ±14	
% Controlled DBP ($\leq$90 mmHg)	24%	25%	
% Untreated	22%	32%	$p<0.05$
% Essential Hypertension	87%	80%	
Cholesterol (mmol/l)	6.4 ±1.3	6.3 ±1.5	
Glucose (mmol/l)	5.9 ±2.3	5.3 ±1.8	
Urate (mmol/l)	0.38 ±0.12	0.35 ±0.09	$p<0.05$
Potassium (mmol/l)	4.0 ±0.5	3.9 ±0.5	
Creatinine (umol/l)	102 ±50	98 ±74	
Gamma GT (IU/l)	40 ±33	28 ±31	$p<0.01$

Table 4.6. Disposition of age and sex matched groups no longer attending after 4 years.+

	NURSE PRACTITIONER CLINIC	CONVENTIONAL HYPERTENSION CLINIC
Moved	8 (4%)	0
To Other Medical Care (other clinics, hospital admission, GPs)	21 (11%)	12 (6%)
Discharged	1	30 (15%)
Died (during first 4 years of attending)	18 (9%)	17 (9%)
Non-attendance/ Lost to Follow-up	15 (8%)	68 (34%)

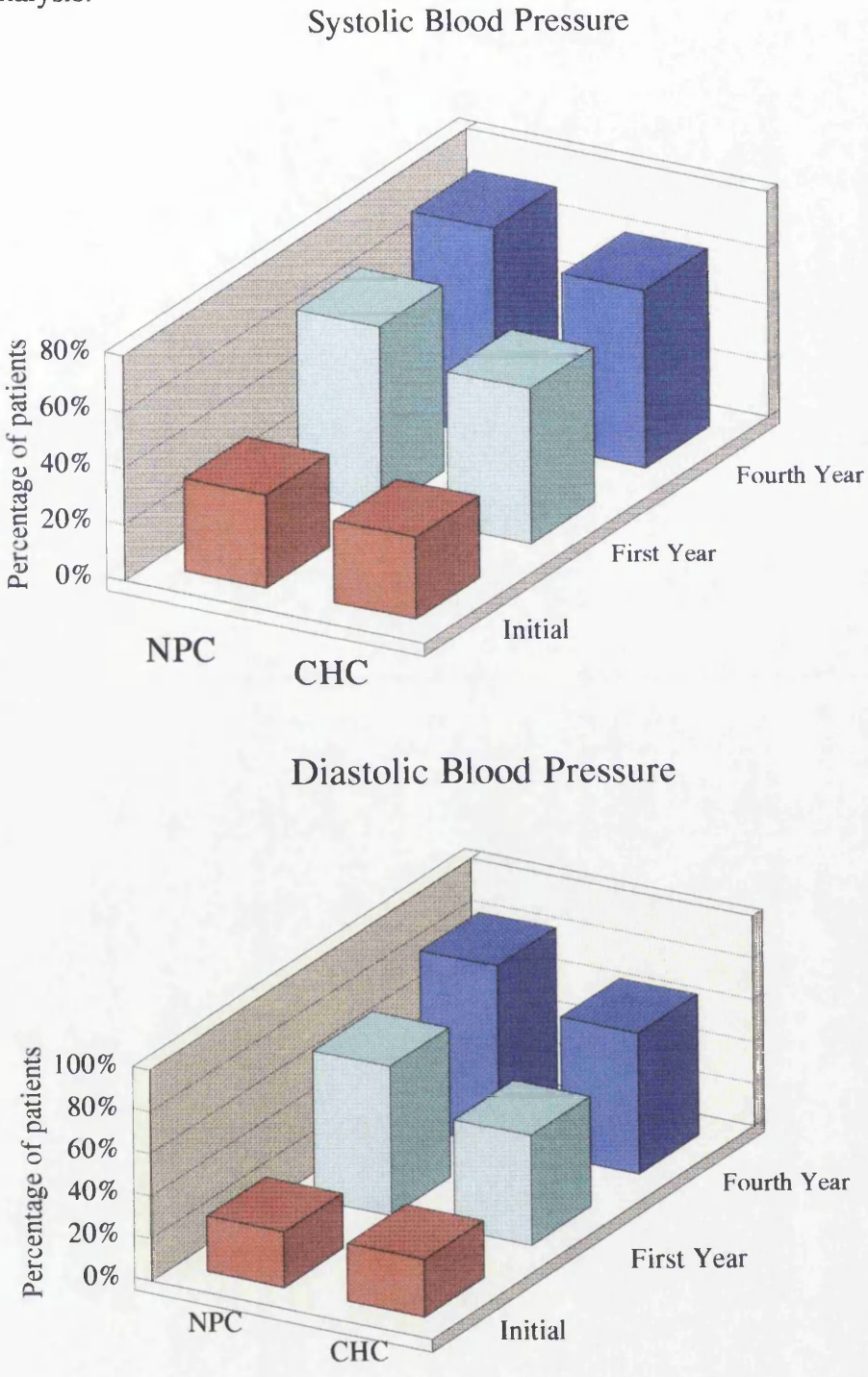
+ adjusted $X^2=54.1, df=4, p<0.001$

Table 4.7. First and fourth year supine systolic and diastolic blood pressures and differences from initial blood pressure values in age and sex matched groups.

	NURSE PRACTITIONER CLINIC	CONVENTIONAL HYPERTENSION CLINIC	
Systolic Blood Pressure			
	$\bar{X}$/s.d.	$\bar{X}$/s.d.	95% Confidence Interval
Year 1	152 ±24	156 ±32	
Difference Year1-Initial	-24 ±33	-16 ±30	-14.5, -0.4+
Year 4	150 ±18	147 ±20	
Difference Year4-Initial	-24 ±30	-26 ±29	-5.9, 11.1
Diastolic Blood Pressure			
Year 1	88 ±10	92 ±13	
Difference Year1-Initial	-15 ±18	-9 ±15	-9.9, -2.5*
Year 4	85 ±9	89 ±8	
Difference Year4-Initial	-18 ±16	-13 ±16	-9.5, -0.4+

+$p < .05$
*$p < .005$ by unpaired t-test

Figure 4.2. Percentage of patients whose blood pressures were considered to be 'controlled' adequately ($\leq$150/90 mmHg for age $\leq$ 60 years and $\leq$160/95 mmHg for age > 60 years) in the age and sex matched analysis.



the mean change in weight from initial values for either group (0.3 kg vs. 0.9 kg). However, in severely obese patients with initial BMIs > 30 in both groups, the NPC patients had a mean loss of 2.8 kg versus a 0.5 kg loss in the CHC (Figure 4.3).

Initial drug treatment did differ between the groups. By the end of the first year there were fewer NPC patients on no drug treatment, more on a beta-blocker alone, and more on triple therapy with a beta-blocker, diuretic and a vasodilator. (The vasodilator category included hydralazine or prazosin in early years, and calcium antagonists, or ACE inhibitors in later years.) At the end of four years there were more NPC patients on no drug treatment, and the treatment regimens in the clinics were similar for those continuing to attend (Table 4.8). The number of drugs prescribed in each clinic was highly significantly different initially and continued to be significantly different at 4 years (Table 4.9).

More NPC patients had initial and follow-up biochemistry undertaken, and, thus, more results recorded and available for analysis. There was no difference by unpaired t-test between the groups for cholesterol, glucose, or creatinine, initially or at the end of the first or fourth years (Table 4.10). Gamma GT was initially significantly different ($p<0.01$) as was urate ($p<0.05$), but there was no difference at the end of the first and fourth years. Potassium was significantly different at the end of four years ($p<0.05$), but levels were within the clinically acceptable range.

The disparity in the size of the groups at four years precluded further analysis, but emphasised the superiority of the NPC in collecting clinical information. Measurement of cholesterol and glucose in all patients at annual review was the agreed policy at both clinics as was continued hospital based follow-up.

The total number of deaths in each group over the four year study was similar (Table 4.6) and the collection of mortality data was extended for a further 2 years in order to compare the rates with those previously measured in the Glasgow Blood Pressure Clinic (Isles et al 1986). At six years, the number of deaths in each group was not significantly different, with 25 in the NPC and 29 in the CHC. The

Figure 4.3. Mean and 95% confidence intervals for weight change after 4 years in patients with initial BMI > 30.

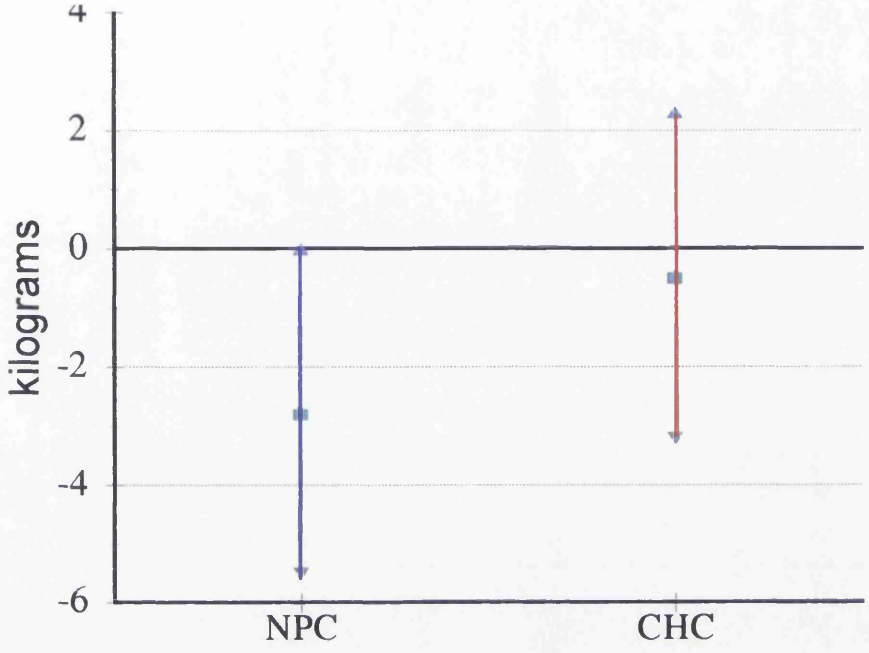


Table 4.8. Drug treatment initially and at the end of 4 years in age and sex matched groups.

	Initially+		Fourth Year++	
	NURSE PRACTITIONER CLINIC (N=198)	CONVENTIONAL HYPERTENSION CLINIC (N=198)	NURSE PRACTITIONER CLINIC (N=136)	CONVENTIONAL HYPERTENSION CLINIC (N= 70)
No drug treatment	43 (22%)	63 (32%)	21 (15%)	6 (9%)
Beta-blocker alone	40 (20%)	25 (13%)	25 (18%)	7 (10%)
Diuretic alone	8 (4%)	15 (8%)	6 (4%)	4 (6%)
Vasodilator* alone	0	1	8 (6%)	1 (1%)
Beta-blocker and diuretic	53 (27%)	53 (27%)	34 (25%)	20 (29%)
Beta-blocker and vasodilator	7 (4%)	6 (3%)	12 (9%)	3 (4%)
Diuretic and vasodilator	0	5 (3%)	7 (5%)	4 (6%)
Diuretic and Methyldopa	0	11 (6%)	0	1 (1%)
Beta blocker and diuretic and vasodilator	41 (21%)	9 (5%)	23 (17%)	21 (30%)
Other treatment	6 (3%)	10 (5%)	0	3 (4%)

*Vasodilator=alpha blocker or calcium antagonist or ACE inhibitor or direct vasodilator such as hydralazine

\+ adjusted $X^2=30.221$, df=6, $p<0.0005$ (cells with < 5 not included in analysis)
++ n.s.

Table 4.9. Number of drugs prescribed initially and at the end of 4 years in age and sex matched groups.

	Initially+		Fourth Year++	
	NURSE PRACTITIONER CLINIC (N=198)	CONVENTIONAL HYPERTENSION CLINIC (N=198)	NURSE PRACTITIONER CLINIC (N=136)	CONVENTIONAL HYPERTENSION CLINIC (N= 70)
No drug treatment	43	63	21	6
One Drug	48	41	39	12
Two Drugs	60	75	53	28
Three Drugs	41	9	23	21

\+ X^2=26.432, df=3, p<0.0005

++ X^2= 7.893, df=3, p<0.05

Table 4.10. Fourth year biochemistry results in age and sex matched groups.

	NURSE PRACTITIONER CLINIC (n=136)		CONVENTIONAL HYPERTENSION CLINIC (n= 70)	
	%	X/s.d.	%	X/s.d.
Cholesterol (mmol/l)	93	6.7 ±1.3	44	6.5 ±1.4
Glucose (mmol/l)	96	6.0 ±2.3	14	5.9 ±1.2
Urate (mmol/l)	99	0.31 ±.10	57	0.39 ±.11
Potassium (mmol/l)	99	4.0 ±0.4	77	4.2+ ±0.6
Creatinine (umol/l)	100	98 ±28	77	101 ±52
Gamma GT (IU/l)	99	34 ±31	66	37 ±49

+ $p < 0.05$

percentage of cardiovascular deaths was higher in the CHC at 79% (n=23) of deaths compared with 68% (n=17) in the NPC, but it was not statistically significant. Life table analysis showed that the cumulative probability of surviving 6 years was 87% in the NPC and 85% in the CHC (Table 4.11). Mortality in both clinics in the early 1980's appeared to be better than that reported for the Glasgow Blood Pressure Clinic in earlier years (Isles et al 1986).

4.4. Discussion

It has been demonstrated that a clinic utilising nurse practitioners with a microcomputer patient information system and physician back-up is effective (Rubin 1984). Similar approaches involving nurses have been developed in a number of countries for the long term management of hypertension. These nurses have worked successfully in occupational health settings (Alderman & Scholenbaum 1975, Logan et al 1979, Logan et al 1983), hospital outpatient clinics (Lewis & Resnik 1967, Clark & Dunn 1976, Laurent et al 1980, Wyka-Fitzgerald et al 1984), the community (Lindholm 1982), and in general practice (Mant et al 1989). However, all of the above mentioned studies looked at these clinical efforts alone and not in comparison with other forms of outpatient hypertension follow-up care.

Runyan compared follow-up care received for diabetes, hypertension, cardiac disease or a combination of these conditions provided by nurse practitioners in decentralised clinics near to their homes. This form of care was compared with traditional hospital based follow-up. Overall, there was less hospital utilisation by patients being followed by the nurse practitioners. Diastolic blood pressure was statistically significantly reduced in the nurse practitioner patients when compared with starting values for the group, as well as in comparison with the change in diastolic blood pressure of the control group (Runyan 1975). However, since this study compared care in the community with hospital follow-up, it is difficult to know how much the nurse practitioner affected outcome versus the switch to care in the community.

A more comparable study to the current one, was carried out by Ramsay

Table 4.11. Life table analysis.

Year	x Year after Tx	Px Probability of surviving each year		qx Probability of dying each year		Lx No. alive on each anniversary		dx No. dying during each year	
		NPC	CHC	NPC	CHC	NPC	CHC	NPC	CHC
1981/82	0	.980	.985	.020	.015	198	198	4	3
1982/83	1	.979	.959	.021	.041	194	195	4	8
1983/84	2	.979	.995	.021	.005	190	187	4	1
1984/85	3	.968	.973	.032	.027	186	186	6	5
1985/86	4	.972	.967	.028	.033	180	181	5	6
1986/87	5	.989	.966	.011	.034	175	175	2	6
	6					173	169		

et al in 1982 which investigated the care provided in a hospital outpatient setting by a nurse practitioner, and compared it with medical follow-up. The groups were small (40 patients) and follow-up was limited to 15 months. Blood pressure, weight and attendance were the only variables studied. For those continuing to attend, the nurse practitioner clinic had statistically significantly better blood pressure control and weight loss, but there was no difference in attendance or dropout rate (Ramsay et al 1982).

Therefore, the current study is important since it does compare data collected prospectively from two very different forms of hospital outpatient care in groups of 198 patients over an extended period of time. The results demonstrate that nurse practitioner follow-up is more effective than conventional medical clinics for the long term management of hypertension. The groups were well matched, with only three of sixteen initial variables being different (Table 4.5). By the end of the first year, the major difference between the two groups was the degree of blood pressure control. The NPC group had a greater reduction in both supine systolic and diastolic blood pressure. This trend continued and the NPC still had a greater percentage of patients with controlled systolic and diastolic blood pressure at the end of the fourth year (Figure 4.2). This is statistically significant and clinically relevant since the major aim of both clinics is the control of blood pressure.

The average decrease in first year blood pressure from initial values in the NPC group of 15 mmHg is similar to the 16 mmHg decrease found by Alderman and Schoenbaum's 1975 study of nurses following up hypertensive department store employees, but greater than the 12 mmHg decrease reported by Ramsay et al in their nurse practitioner group in 1982 after 15 months of follow-up (Ramsay et al 1982).

Target blood pressures were achieved after 4 years in 85% of the NPC patients. This compares favourably to several Israeli studies which revealed 84.6% control in 5,541 patients after 2 years of follow-up and 73% control in 1,283 patients followed for 4 years (Viskoper & Silverberg 1985).

Analysis at the end of four years of follow-up was hampered by the differences

in numbers of patients continuing to attend each clinic (136 at NPC vs. 70 at CHC in the age-sex matched groups). This observation alone was of considerable importance as the declared aim of both clinics was to provide long term hospital based care and supervision. The modest but greater reduction in weight in those who were obese at presentation in the NPC group reflected a particular emphasis on weight reduction and other dietary advice. It was consistent with earlier findings (Curzio 1987) and with the work of Israeli nurse/physician teams (Viskoper & Silverberg 1985).

The lack of biochemical data in the CHC after 4 years of follow-up (Table 4.3), precluded the identification in that population of individuals with developing diabetes, gout, renal failure, liver failure, hypokalaemia, and adverse changes in total cholesterol. Adverse effects on total cholesterol identified in the nurse practitioner clinic population stimulated changes in treatment strategies and the development of several projects to evaluate these changes (Chapter 5 and Chapter 7).

Mortality between the age-sex matched groups over 6 years was not significantly different, but fewer deaths were attributed to cardiovascular disease in the NPC. However, the groups are small, and 6 years is a relatively short time to evaluate the impact of a strategy of care on mortality, but no other clinically based study has assessed mortality in groups receiving alternative forms of follow-up.

4.5. Conclusions

A follow-up clinic, which utilises nurse practitioners for the management of hypertension, has shown better blood pressure control in a greater proportion of patients, maintained contact with a greater percentage of patients and collected data more reliably over the years on the risk factors needed to assess the effectiveness of care in the long term.

Chapter 5. Effect of intensive lipid lowering dietary advice on hypercholesterolaemia in treated hypertensives

5.0. Summary

The introduction of regular, consistent lipid lowering advice in the clinic came in the form of a clinical trial to evaluate the effectiveness of intensive dietary intervention by dietitians over a 6 month period, which is reported in this chapter.

5.1. Introduction

It is well recognised that patients with both hypertension and hypercholesterolaemia are at greater risk of cardiovascular disease, regardless of their sex, than individuals with only one of these risk factors. Kannel and Dawber demonstrated this in the Framingham cohort (Kannel & Dawber 1974) as did The Renfrew and Paisley Survey (Isles et al 1992).

These major cardiovascular risk factors have been found to co-exist more than would be expected by chance. This 'clustering' of risk factors has been reported from Australia (MacMahon et al 1985) and the United States in the Lipid Research Clinics Program Prevalence Study (Criqui et al 1986). Such clustering was also noted in the Stobhill Hypertension Clinic, with 45% of the patients having total cholesterol > 6.5 mmol/l in 1987.

In addition, it has been postulated that the lack of efficacy of anti-hypertensive drug treatment regarding the reductions in coronary heart disease and cardiovascular disease may be due to lack of attention paid to co-existing risk factors (Reid 1988). Therefore, it has been suggested that, in addition to reduction of blood pressure, these patients may well require lipid lowering interventions.

5.1.1. Dietary intervention for hypercholesterolaemia

The first line of treatment advocated for hypercholesterolaemia is dietary modification. This recommendation comes from the European Atherosclerosis Society (Study Group, European Atherosclerosis Society 1987) and British Hyperlipidaemia Association (Shepherd et al 1987). The American Heart Association 1988 Consensus Conference also identified it as the 'first logical step of treatment',

but this group also admitted that its efficacy has not been proven (Gotto 1989).

Despite the obvious need for dietary intervention studies, there have been surprisingly few carried out, and only a minority investigated dietary changes alone in high risk individuals.

5.1.2. Studies in normolipidaemic individuals free of cardiovascular disease

There have been studies that have assessed the impact of diet on lipid levels in healthy normolipidaemic individuals free of cardiovascular disease. Lewis and colleagues assessed a variety of diets, each lasting 5 weeks, in a group of 12 normolipid monks, and found that there was a significant reduction with the intake of a fat-modified, fibre rich diet (Lewis et al 1981).

Weintraub et al assessed chronic and acute effects of different types of dietary fat in 8 normolipidaemic males under hospital conditions. Each diet was taken for 25 days, and the greatest reduction in total cholesterol occurred on the diet high in w-3 polyunsaturated fatty acids which are found in fish (Weintraub et al 1988).

Mensink and Katan assessed the impact of diets high in monounsaturated and polyunsaturated fats for 36 days in a group of 83 healthy men and women students after 17 days on a high saturated fat diet. They concluded that both diets were equally effective in lowering low density lipoprotein cholesterol (Mensink & Katan 1989).

All of these studies which were carried out in small numbers of normolipid individuals for relatively short periods of time, and only investigated the efficacy of diet in lowering cholesterol and lipoproteins. None assessed the long term impact of diet on mortality.

5.1.3. Studies in institutionalised individuals

Other investigators have manipulated the diets of institutionalised individuals with a range of lipid levels and whose diet can be more readily controlled. In the landmark Los Angeles Veterans Administration study, men living at the VA hostel were randomised to one of two dining rooms. In one dining room, the diet served

had polyunsaturated fat substituted for saturated fat, and the cholesterol content was decreased. Over 6-8 years, the morbidity and mortality of the 424 men eating in this dining room were compared with that of 422 men eating the usual diet offered in the other dining room. Cardiovascular mortality was statistically significantly less in the intervention group, but there was no difference between the groups for all cause mortality (Dayton et al 1969).

In the Finnish Mental Hospital Study, men from 1 of 2 hospitals were given a diet in which polyunsaturated fat was substituted for saturated fat and the cholesterol content was reduced, while the men in the other hospital consumed a usual diet. After 6 years, the subjects in each hospital changed to the alternative diet for a further 6 years. Coronary heart disease (CHD) and all cause mortality was assessed in the approximately 4000 participants. For those consuming the modified fat diet, CHD mortality was significantly reduced, and all cause mortality was decreased, but not significantly, over the time the participants partook of the intervention diet (Turpeinen 1979).

Keys et al studied the effects of a variety of diets in groups of 24-38 mentally retarded residents of a state hospital and school to assess the variability in individual serum cholesterol response to changes in diet. The studies lasted from 3 to 10 weeks and the authors found a lack of consistency in responsiveness to dietary change in individuals between experiments (Jacobs et al 1983)

The Minnesota Coronary Survey was conducted in 4,393 men and 4,664 women patients in 6 state mental hospitals and one nursing home in the late 1960's and early 1970's. This study used a diet low in saturated fat, high in polyunsaturated fat and low in cholesterol content. Most of the participants were on the diet for less than 2 years, but mortality was tracked for five years with no significant differences noted between the groups (Frantz et al 1989).

5.1.4. Diet studies in high risk groups

Several studies have investigated diet in post-myocardial infarction (MI) patients. Researchers from a group of London hospitals, assessed a 'fat modified'

diet (decreased amount of saturated fat only) compared to usual diet in a group of post-MI men. In total, 264 subjects were randomised to either diet. There was no difference in relapse rate, ie. further MI or death due to MI, between the groups (Research Committee 1965). The Diet and Reinfarction Trial (DART) randomised 2033 post-MI males to one of three diets for two years. The diets were 1) low in saturated fat, high in polyunsaturated fat, 2) at least 2 weekly portions of fatty fish, and 3) high in fibre. There was no significant reduction of total cholesterol in the fish or high fibre diet groups, and only a modest reduction of 3.6% in the low fat diet group. However, there was a 29% reduction in all cause mortality in the fish diet group (Burr et al 1989).

The Leiden Intervention Trial looked at angiographically assessed coronary artery lesion progression in 35 men and 4 women with angina who consumed a vegetarian diet for 2 years. Lesion progression correlated with total/HDL cholesterol ratio. Progression was significant in patients with higher values of the ratio (8.1 $\pm$1.7 vs 5.8 $\pm$1.2). No progression was observed in patients either with lower ratios or who had initial high values which were significantly lowered by the intervention (Arntzenius et al 1985).

The St Thomas' Atherosclerosis Regression Study (STARS) used a low fat diet, high in omega-3 and omega-6 polyunsaturated fat and high in fibre, particularly soluble fibre in the form of pectin. This study demonstrated an increase in the frequency of luminal widening and fewer cardiac events in the diet only group of 26 middle aged men with history of angina or MI compared to 23 untreated controls on their usual diet. Another group who received cholstyramine in addition to diet also showed an increased mean coronary diameter (Watts et al 1992).

5.1.5. Multiple risk factor studies

A number of the multiple risk factor studies have used diet as their sole intervention for hyperlipidaemia. The Oslo, MRFIT and European Trial of Multifactorial Prevention of Coronary Heart Disease studies have been described in

detail in Chapter 1. In the Oslo Study a diet low in saturated fat, having some polyunsaturated fat and high in fibre was used (Hjermann et al 1981). The diet in MRFIT was low in saturated fat, high in polyunsaturated fat and low in calories for those who were overweight (MRFIT Research Group, 1990). The World Health Organisation European Trial of Multifactorial Prevention of Coronary Heart Disease dietary advice consisted of a cholesterol lowering diet that was low in fat, had an increase in polyunsaturated fat, and was high in fibre (WHO European Collaborative Group 1986).

The Toledo Exercise and Diet Study assessed whether exercise was additive to diet in a group consisting predominantly of women (49 of 66), with hyperlipidaemia, moderate to low fitness and a high fat, high cholesterol diet. Greatest reductions in total cholesterol were observed after 8 weeks of diet with no further reductions by 6 months. There was no difference between the groups at the end of 26 weeks (Leighton et al 1990).

The Lifestyle Heart Trial instituted a low fat vegetarian diet, stop smoking counselling, stress management training and moderate exercise in 28 patients, and compared them with a group of 20 in a usual care group. All participants had angiographically documented coronary artery disease. After 1 year, intervention group subjects' average percentage stenosis was less while it was increased in the control group. The intervention group also reported reduced frequency, severity and duration of angina (Ornish et al 1990).

There is some difficulty in assessing the absolute impact of a single component of a multiple risk intervention. This is particularly so as the above studies were designed to investigate the effect of the combination of interventions.

5.1.6. Summary of diet studies

The majority of the studies presented above (10 of 15) were conducted in men. The Mensink and Martin study, DART, Leiden Intervention Trial, and Toledo Exercise and Diet Study together, involved a total of 89 women. Only the Minnesota Coronary Survey involved a substantial number of women (4,000), but this study is

weak in that it reports 5 year mortality after less than a year of dietary intervention which occurred only when the patients were hospitalised.

The decreases in total cholesterol reported in the intervention groups of these studies range from 3.6% in the DART study (Burr et al 1989) to 29% reported by Lewis (Lewis et al 1981). This is a wide range of effectiveness, and it is interesting to note that the smallest percentage decrease in total cholesterol occurred in high risk angina patients.

5.1.7. Discussion of the impact of dietary intervention

The true magnitude of the cholesterol reduction induced by dietary modification, and its independent impact on coronary heart disease (CHD), was unclear until recently. The epidemiological evidence from around the world that people with lower levels of cholesterol have significantly lower mortality due to cardiovascular disease is impressive. The Seven Countries Study (Keys et al 1984), the Donolo-Tel Aviv Prospective Coronary Artery Disease Study (Brunner et al 1987) the MRFIT screening cohort (Martin et al 1986) and the more recent Whitehall Study (Smith et al 1992) have shown this relationship.

In addition, studies that have looked at diet consumed and cardiovascular disease, have found that groups with higher intakes of saturated fat have higher CHD mortality. The Western Electric Study scored dietary intake according to fat intake and found a positive association, prospectively, between the mean base-line diet score and the 19 year CHD risk (Shekelle et al 1981). A similar scoring was used in the Ireland-Boston Diet-Heart Study with similar CHD mortality correlations to fat intake, but with additional decreased risk associated with higher fibre intake (Kushi et al 1985). Keys et al also found this relationship when looking at the 15 year mortality in the Seven Countries Study, as well as an inverse relationship between the intake of mono-unsaturated fatty acids and CHD (Keys et al 1986).

However, the evidence from individual clinical trials that lowering total cholesterol by dietary means decreases cardiovascular, coronary heart disease or all

cause death rates is conflicting. As previously presented, the Finnish Mental Hospital Study (Turpeinen 1979) and the Veterans' Hospital Study (Dayton et al 1969) showed reductions in CHD (but not overall mortality), while the Minnesota Coronary Survey (Frantz et al 1989) and the Middlesex post-MI study (Research Committee 1965) showed no significant effect.

There has been, and there continues to be, a controversy with respect to the impact of primary and secondary prevention trials on total mortality. Three major reviews were published in 1990 considering a number of the studies reviewed above as well as lipid lowering drug trials. Other experts have followed, and a further set, known as the 'Cholesterol Papers', were published in the British Medical Journal in 1994 (Law et al 1994a, Law et al 1994b, Law et al 1994c).

Muldoon, Manuck and Matthews looked at 6 randomised primary prevention trials. They concluded that the association between reduced cholesterol levels and non-cardiovascular deaths warrants further investigation. In addition, the apparent lack of effect of cholesterol lowering on all cause mortality 'justifies a more cautious appraisal of the probable benefits of reducing cholesterol concentrations in the general population' (Muldoon et al 1990).

Rossouw, Lewis and Rifkind reviewed 7 secondary prevention trials and concluded that if 'gains are achieved in cardiac morbidity alone and not overall mortality this remains a net gain'. They argued that longer term follow-up of up to 15 years may be required to demonstrate positive effects on mortality (Rossouw et al 1990).

Holme reviewed 19 studies including primary and secondary prevention trials which used single or multiple risk interventions. This review concluded that for each 1% reduction in total cholesterol there results an estimated 2.5% reduction in CHD incidence. However, it was briefly pointed out that what was gained by CHD reduction was lost on other fatal end points (Holme 1990).

It is interesting to observe that the concerns expressed by Muldoon, Manuck, and Matthews regarding non-cardiovascular deaths is 'downplayed' by not only

Rossouw, Lewis and Rifkind but by Holme as well. Muldoon and Rossouw continued their discussions in an exchange of letters in a subsequent issue of the New England Journal of Medicine (Muldoon et al 1991; Rossouw et al 1991). Others have taken up the concerns expressed by Muldoon et al, Smith and Pekkanen called for a moratorium on the use of lipid lowering drugs (Smith & Pekkanen 1992) and Oliver, in a BMJ editorial, agreed except in the case of high risk individuals (Oliver 1992).

Smith et al confirmed this concept of the value of lowering cholesterol in high risk individuals in a meta-analysis of 35 single factor dietary or drug treatment trials. Trials were stratified by the low, medium and high risk of coronary heart disease experienced in each trial's control population. Benefit of treatment in terms of total mortality as well as coronary heart disease mortality, was only seen in those at high risk, with no benefit for those at medium risk, and adverse effects noted in those at low risk. In addition, the adverse effects on total mortality appeared to be confined to the drug treatment trials and not the dietary trials, indicating that cholesterol lowering itself doesn't increase the risk of non-coronary death (Smith et al 1993).

Law et al in the 'Cholesterol Papers' noted a systematic underestimation of the association between cholesterol concentration and ischaemic heart disease due to regression dilution bias, and a surrogate dilution effect. Using data from 21,515 males aged 35-64 years from the British United Provident Association (BUPA) physical examinations, they demonstrated that the relationship between the two is stronger than previously shown and is age related, decreasing with increasing age. They estimated that a 10% reduction in cholesterol in a man aged 60 years is associated with a 30% reduction in ischaemic heart disease, and not 20% as previously thought (Law et al 1994a).

In a companion paper, Law et al conducted a meta-analysis of 10 prospective cohort studies, 3 international studies in different communities and 28 randomised controlled trials with mortality data. They concluded that the full effect of the reduction in risk is achieved within 5 years (Law et al 1994b).

Thus the 'consensus' view is that lipid-lowering interventions are a means of reducing cardiovascular mortality and morbidity, particularly in individuals at high risk of coronary heart disease. Diet is invariably the first choice lipid-lowering intervention. Most of the previously cited diet efficacy studies were carried out in normolipidic individuals for relatively short periods of time, so that, additional longer assessment of lipid lowering diet alone in high risk individuals of both sexes is warranted.

5.2. Study aims

This study was designed to assess the impact of dietary advice for serum cholesterol reduction, over a 6 month period, in treated male and female hypertensives who were at additional cardiovascular risk with cholesterol levels greater than 6.5 mmol/l, the level above which both the British Hyperlipidaemia Association (Shepherd et al 1987) and the European Atherosclerosis Society (Study Group 1987) recommend 'action'.

5.3. Methods

5.3.1. Patients, anti-hypertensive drug treatment and stratification

A total of 141 well controlled hypertensive patients from the nurse practitioner Blood Pressure Clinic at Stobhill (described in Chapter 2) and who were found at annual clinical review to also have hypercholesterolaemia (defined as a serum total cholesterol > 6.5 mmol/l), entered this controlled trial. These patients had been attending the clinic regularly 1-3 times per year for from 2 months to 6½ years prior to recruitment and were invited to participate after being informed of their cholesterol levels.

Of the original 141 patients, 116 completed the study and an additional 8 patients attended all but the 6 month visit. Of the remaining 17 patients: 7 defaulted, 4 formally withdrew and the other 6 dropped out for various incidental reasons. The results therefore relate to the 124 patients who completed at least 3 months of the study.

Anti-hypertensive drug treatment was not changed over the course of the study

(Table 5.1). Enrolled patients were stratified by anti-hypertensive drug treatment and then randomly assigned to one of 2 groups: Group 1,-*Advice Group* received intensive and specific dietary advice for cholesterol reduction from a specialist dietitian and Group 2,-*No Advice Group*, attended the same sequence of clinic visits, but did not consult with the dietitian and received no specific dietary advice.

5.3.2. Other risk factor interventions

Patients had previously been given advice to stop smoking if a smoker and a weight reducing diet if obese (body mass index > 30). It had not been clinic policy at that time to routinely give detailed advice about cholesterol lowering diets or sodium intake. Patients received no additional advice over the 6 months of the study for these risk factors.

5.3.3. Visit schedule and measurement techniques

Following recruitment, patients reported after an overnight fast for an initial entry (baseline) visit, and then at 1, 3 and 6 months for further measurements of weight, blood pressure, serum total cholesterol, triglyceride and high density lipoprotein (HDL) cholesterol. At entry to the study and at 6 months, low-density lipoprotein (LDL) cholesterol and very low-density lipoprotein (VLDL) cholesterol were also measured.

Blood pressure measurement, weight measurement, and laboratory lipid analysis were carried out as described in Chapter 2.

5.3.4. Dietary advice and diet questionnaire

Patients in the Advice Group were seen by a hospital dietitian at each visit for diet history and specific individualised dietary advice. Diet I (Figure 5.1) was the basis for advice with those patients who had not been following a low cholesterol/high polyunsaturated fat/high fibre diet and whose previous cholesterol was > 6.5 but < 8.0 mmol/l. This diet followed the guidelines of the National Advisory Committee on Nutrition Education (NACNE) and the Committee on Medical Aspects of Food Policy (COMA) who recommend a reduction in fat to 30%

Table 5.1. Anti-hypertensive drug treatment of patients studied.

	DIETARY ADVICE N=61	NO DIETARY ADVICE N=63
No treatment	7%	13%
Beta blocker alone	18%	17%
Diuretic alone	3%	3%
Calcium antagonist alone	13%	3%
ACE inhibitor alone	3%	5%
Beta blocker + diuretic	21%	22%
Beta blocker + calcium antagonist	11%	6%
Diuretic + calcium antagonist	2%	3%
Diuretic + ACE inhibitor	7%	5%
Beta blocker + diuretic + calcium antagonist	10%	14%
Other drug treatment	5%	8%

Figure 5.1. Diet I. (Front of sheet is at bottom, and inside on top of figure).

Diet 1

Diet For Those With High Blood Fat Levels (Cholesterol)

1) Eat Less Dairy Produce.
2) Reduce the amount of Cheese eaten, try Cottage Cheese instead.
3) Use Skimmed or Semi-Skimmed Milk (Do not take cream in any form).
4) Restrict Eggs to 2 - 3 per week.
5) Eat less Meat and cut off visible fat, include more Fish & Poultry in your diet.
6) Avoid Pies, Pastries etc., as these are a high source of fat.
7) Use Polyunsaturated Margarine e.g.,Flora or Low Fat Spread.
8) Corn Oil, Sunflower Oil (Flora, Mazola, etc.,) to be used for Cooking, Oils labelled simply "Vegetable Oil" are not suitable. Food should be grilled.
9) "Low Fat" products are a better choice to make.
10) Eat plenty fresh Fruit, Vegetables and Salads. Use only oil free salad dressing.
11) If overweight a Low Calorie Diet is advised.
12) Increase the fibre content of your diet by choosing Brown Bread, High Fibre Cereals, Wholewheat Pasta and Brown Rice.

TO LOSE WEIGHT

1) Cut Out Sugar In all Forms. (No Lemonade, Squash, Sweets, Cakes, Jam, Marmalade, Ice Cream).

2) Use Margarine/Oil sparingly (Avoid Fried Foods) including oils.

3) Take average helpings of Meat, Fish, Poultry, Eggs (3/week) and Cheese (1/4 lb/week). If taken in excess these foods can prevent weight loss.

4) Reduce the amount of Bread and Potatoes you eat.

5) Eat plenty Vegetables, Salads and Fresh Fruit.

6) Alcoholic drinks are a high source of calories and should be restricted.

7) Care should be taken with foods labelled "low calorie" they often have a significant calorie value.

Check Your Weight Against the Chart Below

MEN		WOMEN	
Height	Weight	Height	Weight
5'3"	9st 8lb	4'11"-6'	8st 3 lb - 11st 11lb
5'4"	9st 10lb	5' - 6'	8st 5lb - 12st 2lb
5'5"	10st 1lb	5'1"-6'	8st 7lb - 12st 7lb
5'6"	10st 4lb	5'2"-6'	8st 9lb - 12st 11lb
5'7"	10st 8lb	5'3"-6'	8st12lb - 13st1lb
5'8"	10st11lb	5'4"-6'	9st 1lb - 13st4lb
5'9"	11st 2lb	5'5"-6'	9st 6lb - 13st 8lb
5'10"	11st 6lb	5'6"-6'	9st 8lb - 13st11lb
5'11"	11st11lb	5'7"-6'	9st11lb - 14st2lb
6'	12st2lb	5'8"-6'	10st2lb - 14st6lb
6'1"	12st7lb	5'9"-6'	10st6lb - 14st10lb
6'2"	12st11lb	5'10"-6'	10st10lb - 15st1lb
6'3"	13st1lb	5'11"-6'	11st - 15st4lb

STOBHILL GENERAL HOSPITAL

(Dietetic Department)

Healthy Eating Can Help Prevent Heart Disease, A Few Simple Dietary Changes Can Be Beneficial

1) EAT LESS FAT

2) EAT LESS SUGAR

3) EAT MORE FIBRE (Wholemeal Bread, Fruit and Vegetables)

4) DO NOT ADD SALT AT TABLE

5) AVOID BEING OVERWEIGHT

DO NOT SMOKE

of total energy intake, an increase in fibre to approximately 30 g, a reduction in the amount of refined sugar consumed and restriction to no more than 3 eggs per week (National Advisory Committee on Nutrition Education 1983, Committee on Medical Aspects of Food Policy 1984).

Diet II (Figure 5.2) was used for patients who had previously been following a relatively low cholesterol/high polyunsaturated fat/high fibre diet, or whose previous cholesterol values were > 8.0 mmol/l. This diet incorporated Diet I, but cholesterol intake was restricted to less than 250 mg daily by a reduction in the consumption of meat, and the restriction to 1 egg per week.

In addition, all overweight patients were also given weight reduction dietary advice (smaller portions, lower calorie food choices, etc).

A food frequency questionnaire was devised by the study dietitians to assess the dietary intake of saturated fat, polyunsaturated fat and fibre (Figure 5.3a and Figure 5.3b). All patients completed this questionnaire at entry and at the end of the study to measure the reported change in diet.

The study dietitians rated the contribution of each food frequency to a low cholesterol, high polyunsaturated fat, high fibre diet (Figure 5.4). A negative score indicated a diet high in saturated fat, low in polyunsaturated fat and low in fibre, while a high positive score indicated a diet low in saturated fat, high in polyunsaturated fat and high in fibre. The potential impact of each reported dietary change on an individual's total cholesterol was also rated. Changes in food frequency were identified by comparison of diet questionnaire responses at 6 months with entry responses (Figure 5.5). A positive change score indicated an 'improved' diet while a negative score indicated the individual's diet was higher in saturated fat, lower in polyunsaturated fat or fibre than previously reported.

5.3.5. Data analysis

Data were analysed by repeated measures analysis of variance (ANOVA) and covariance (ANCOVA). For the ANCOVA, entry values were used as the covariates where appropriate. Bonferroni multiple comparisons and an overall confidence level

Figure 5.2. Diet II.

Stobhill Hospital

LOW CHOLESTEROL DIET TYPE II

FAT — Total fat intake should be reduced.

Modify fat by using fats of plant origin in place of fats of animal origin, e.g., Polyunsaturated margarine instead of butter (1/2 lb. per week) Corn or sunflower oil instead of cooking fat or vegetable oil.

CHOLESTEROL — Foods with a high cholesterol, high saturated fat content must not be taken (see list below).

Meat — must be very lean and taken no more than once per day. Include more chicken, turkey and fish in your diet.

Eggs — should be restricted to one per week.

Cheese — has a very high cholesterol/high fat content and only low fat cottage cheese should be taken.

FIBRE — Increase the fibre in your diet by using wholemeal bread, bran cereal (All Bran, Weetabix, etc.) Fruit, Vegetables and Pulses (Peas, Beans, Lentils).

WEIGHT — It is important you achieve and maintain your ideal weight. If overweight, omit sugar and all foods containing sugar. Eat small helpings, and reduce alcohol consumption.

HIGH CHOLESTEROL/SATURATED FAT FOODS	LOW CHOLESTEROL/POLYUNSATURATED FAT FOODS
Milk, "St. Ivel 5 Pints", Semi-skimmed milk, Evaporated Milk, Condensed Milk, Coffee mate, "Compliment", Dream Topping	Fresh Skimmed Milk, Skimmed Milk Powder, e.g., Marvel.
Cheese - all varieties except Low Fat Cottage Cheese	Low Fat Yogurt
Egg Yolk	Low Fat Cottage Cheese
Butter, ordinary Margarine, St. Ivel Gold, Vegetable Oil, Lard, Suet	Egg White
Olive oil, Mayonnaise, Salad Dressing	Flora or Polyunsaturated Margarine
Lemon Curd	Mazola, Corn Oil, Sunflower Oil, Flora Oil or White Flora
Fatty Meat, Sausages, Bacon, Liver, Kidney, Tripe, Sweetbreads, Spam, Pate, Meat Paste, Black Pudding	Sugar, Jam, Marmalade
Shellfish, Fish Roe	Lean Meat - no oftener than once/day.
Cakes, Biscuits, Pastry unless made with Corn Oil	Turkey, Chicken, Chicken Roll, White Fish, Smoked Fish, Herring, Kippers, Salmon, Tuna, Pilchards and Sardines (drain off oil)
Crisps, Chips	Bread Rolls, Oatcakes, Ryvita, Plain Biscuits, Breakfast Cereal, Porridge, Potatoes, Rice, Pasta, Beans, Skimmed Milk Puddings, Jellies.
Puddings containing egg or fat	Fruit, Vegetables
Cream Soups, Kidney Soup	Broth, Lentil, Vegetable and Potato Soup
Chocolate, Ice Cream	Boiled Sweets, Pastilles, Gums
	Lemonade, Squash

Figure 5.3a. Food frequency questionnaire - front.

8A BLOOD PRESSURE CLINIC

Cholesterol Study Questionnaire

Please answer these questions as best as you can...
(underlining or circling your answer where applicable)

---

1. Bread: How many slices of bread or rolls do you eat on average each day?

   _____

   What type of bread or rolls do you normally eat?

   White Brown Wholemeal High fibre

---

2. a. What would you normally spread on the bread or roll?

   Nothing Block margarine Polyunsaturated margarine

   Butter Low fat spread Other _____ (please give)

   b. Do you like it thick or thin?

   c. Can you name the brand you normally use? _____

---

3. Milk: What kind of milk do you use?

   Skim Semi skim Low fat Ordinary Pasteurised

   How much milk do you use every day?

   None Only in tea or coffee

   1/2 pint every day 1 pint every day

---

4. Meat Products (Underline or circle which you eat regularly, every week)

   Meat (beef,including mince), lamb, pork, bacon and ham (not sausages)

   Chicken and poultry

   Tinned meat and made up meats-Corned beef, Pies, Bridies, Sausage rolls, Burgers, Haggis, Black pudding, Sausage, Sausages

   Fish

   How often do you eat cheese or cheese dishes (such as macaroni cheese)?

   Never Every day Twice per week

   How many eggs do you eat per week?

(please turn over and answer questions on back of sheet)

Figure 5.3b. Food frequency questionnaire - back.

5. Which of the following foods would you normally fry?

   Chops Steaks Sausages Bacon Fish Burgers

6. With what do you fry foods?

   Lard Dripping Vegetable oil Corn oil Sunflower oil

7. How often do you take chips or crisps each week?

   Never Every day 4 times per week once weekly

8. How often do you have rice or pasta (such as spaghetti) each week?

   _____

9. Do you use sugar in tea or coffee? Yes No

   If yes, how much?

10. Do you have fizzy soft drinks? (like lemonade, cola,etc.)

    Never Up to 1/2 bottle/week 1 bottle/week More

11. Do you regularly eat...?

Cakes	Never	Daily	Weekly
Biscuits	Never	Daily	Weekly
Sweets	Never	Daily	Weekly

12. Approximately how much alcohol do you drink each week?

    None ____Pub measures of whisky, vodka, or other spirits

    ____Pints of beer ____Glasses of wine or sherry

Thank you for completing this questionnaire, your cooperation is appreciated.

8A Blood Pressure Clinic Staff

Figure 5.4. Initial diet scoring system.

Number of slices & type of bread

2 slices brown = 1.0
1 slice brown = 0.5
white+brown = 0
2 slices white =-1.0
1 slice white =-0.5

Spread Type

polyunsaturated = 1.0
low fat spread = 1.0
low fat/polyun-saturated+butter = 0
block margarine =-0.5
butter/lard =-1.0

Thick/thin

thick butter =-0.5
thick block =-0.25
(if using polyunsaturated or lowfat spread-no score)

Kind of Milk

1 pint =-1.0
(except skimmed milk)
1/2 pint =-0.5
(except skimmed milk)
in coffee/tea =-0.25
(except skimmed)
no milk = 2.0

Meats eaten regularly

2 meats =-1.0

Chicken, poultry

Chicken = 1.0

Prepared meats eaten regularly

2 meats =-1.0

Fish

Fish = 1.0

Amount of cheese

Daily =-3.5
x4/ week =-2.0
x3/ week =-1.5
x2/ week =-1.0
x1/ week =-0.5
seldom = 1.75
none = 3.5

Number of Eggs

2 eggs =-1.0
(over 1/wk)
1 egg only = 1.0
no eggs = 2.0

Fried Foods

2 foods =-1.0
no fried foods = 1.0

Types of fat

lard/dripping =-1.0
vegetable oil =-0.5
cheapest =-0.5
vegetable +
polyunsaturated = 0.5
polyunsaturated = 1.0

Frequency of Chips/Crisps

daily =-3.5
x4/wk =-2.0
x2/wk =-1.0
x1/wk =-0.5
rarely,seldom =-0.25
never = 1.0

Frequency of Pasta/Rice

2 servings/wk= 1.0
serving/wk = 0.5
no servings =-1.0

Frequency of Cakes

daily =-1.5
weekly =-0.5
seldom = 0.5
never = 1.5

Frequency of biscuits

daily =-1.5
weekly =-0.5
seldom = 0.5
never = 1.5

Figure 5.5. Change in diet, scoring system.

Bread type
white to brown combo= 1.0
white to white+brown combo= 0.5
white+brown combo to brown combo= 0.5

Spread type
saturated to polyunsaturated/low fat = 1.0
block margarine to polyunsaturated = 0.5
saturated+lowfat to lowfat = 0.5
saturated to lowfat+saturated = 0.5
saturated to block = 0.5

Thick/thin
thick to thin = 1.0
average to thin = 0.5
thin to 0 = 0.5

Kind of Milk
whole to semi-skimmed/low fat = 1.0
semi-skimmed/low fat to skimmed = 1.0
whole to skimmed = 2.0

Amount of milk
1 pint to 1/2 pint = 1.0
1 pint to tea/coffee only = 1.5
1 pint to none = 2.0
1/2 pint to tea/coffee only = 0.5
1/2 pint to none = 1.0
more than 1 pint to 1/2 pint = 1.5
tea/coffee to 1 pint =-1.5
tea/coffee only to more than 1 pint =-2.0

Meats eaten regularly
decrease by 2 = 1.0

Chicken, poultry
not eating regularly to eating regularly = 1.0

Prepared meats eaten regularly
decrease by 2 = 1.0

Fish
not eating regularly to eating regularly = 1.0

Amount of cheese
daily to x4/wk = 1.5
daily to x3/wk = 2.0
daily to x2/wk = 2.5
daily to x1/wk = 3.0
daily to none = 3.5
daily to seldom = 3.25
x3/wk to x1/wk = 1.0
x2/wk to x1/wk = 0.5
x2/wk to seldom = 0.75
x2/wk to none = 1.0
x1/wk to none = 0.5

Number of Eggs
decrease of 2 eggs/wk = 1.0

Fried Foods
decrease of 2 = 1.0
decrease of 1 = 0.5

Types of fat
lard/dripping to vegetable oil = 0.5
lard/dripping to polyunsaturated oil (corn/sunflower) = 1.0
vegetable oil to polyunsaturated oil (corn/sunflower) = 0.5

Frequency of Chips/crisps
every day to x4/wk = 1.0
every day to x1/wk = 2.0
every day to none = 2.5
x4/wk to x1/wk = 1.0
x1/wk to never = 0.5
rarely,seldom to never = 0.25

Frequency of Pasta/rice
increased servings by 2 = 1.0
0 to 1 serving = 0.5

Frequency of cakes
daily to weekly = 1.0
daily to never = 1.5
daily to seldom = 1.25
weekly to never = 0.5
seldom to never = 0.25

Frequency of biscuits
daily to weekly = 1.0
daily to never = 1.5
daily to seldom = 1.25
weekly to never = 0.5
seldom to never = 0.25

of 95% were also derived using RUMMAGE. Correlation analysis was undertaken as indicated using MINITAB. Both of these statistical packages were run on the University's ICL 3980 mainframe computer.

5.4. Results

5.4.1. Group demographics

The groups were well matched for age, sex, reported cigarette and alcohol consumption, blood pressure, last clinic cholesterol and length of time followed in the clinic (Table 5.2). The groups were balanced for the types of anti-hypertensive drugs in accord with the study design (Table 5.1). There were minor differences in the percentage of patients taking a calcium antagonist alone, and those taking a beta blocker with a calcium antagonist, but these differences were not significant by chi-square analysis. The significant differences between the groups at entry were in regards to body weight (Table 5.2), HDL and HDL/LDL ratio (Table 5.3).

Blood pressure in both groups at all visits is plotted in Figure 5.6. There was a significant decrease in blood pressure in the No Advice Group over the 6 months of the study ($p < 0.05$) by ANOVA, with blood pressures similar in both groups until the 6 month visit. There was no correlation between changes in blood pressure and changes in weight for either group.

5.4.2. Weight

Since weight differed between the groups at entry, the change in weight in each group over the 6 months of the study was compared by ANCOVA, which accounts for the entry difference. Weight decreased in the Advice Group by an average of 2.6 kg, but by only 0.5 kg in the No Advice Group (Figure 5.7), and this difference in weight reduction between the groups was significant ($p < 0.01$). Confidence intervals for weight change in each group are given in Table 5.4.

5.4.3. Total cholesterol and lipoproteins

Both groups showed decreases between the fasting cholesterol measured at entry to the study and previous random cholesterol values obtained in the clinic at routine annual review for several years previously (Figure 5.8). On average, total

Table 5.2. Demographic features of patients studied.

	DIETARY ADVICE N=61	NO DIETARY ADVICE N=63
Sex (M/F)	27/34	34/29
Age (years)	57 ±9	56 ±8
Age Range (years)	37-77	32-72
Weight (kg)	71.7 ±12	76.2 ±16 **
Smokers	30%	33%
Alcohol use $\geq$ 200 gm/week	11%	8%
Last clinic cholesterol (mmol/l)	7.7 ±0.8	7.5 ±0.8
Systolic Blood Pressure (mmHg)	150 ±17	149 ±15
Diastolic Blood Pressure (mmHg)	85 ±9	86 ±9
Average length of follow-up (months)	37 ±22	41 ±25
Range of follow-up (months)	1-72	2-78
Number followed for < 6 months	3	6

**$p < 0.01$

Table 5.3. Triglyceride and lipoproteins (Mean ±s.d.) at entry and after 6 months.

	ENTRY		6 MONTHS	
	DIETARY ADVICE	NO DIETARY ADVICE	DIETARY ADVICE	NO DIETARY ADVICE
Triglyceride mmol/l	2.0 ±1.1	2.2 ±1.0	1.9 ±1.1	2.0 ±0.8
Cholesterol mmol/l	7.1 ±0.8	7.1 ±0.8	6.8 ±0.9	6.9 ±0.8
VLDL mmol/l	0.7 ±0.4	0.8 ±0.4	0.6 ±0.4	0.7 ±0.4
LDL mmol/l	5.0 ±0.8	5.1 ±0.7	4.7 ±0.8	4.9 ±0.8
HDL mmol/l	1.4 ±0.4	1.3 ±0.3*	1.4 ±0.4	1.3 ±0.3*
HDL/LDL Ratio	0.30 ±0.11	0.26 ±0.07*	0.32 ±0.13	0.27 ±0.07* +
HDL/ Cholesterol Ratio	0.21 ±0.06	0.19 ±0.05*	0.22 ±0.08	0.19 ±0.04*

*$p < 0.05$ for between group differences at each time

+$p < 0.05$ by ANCOVA for between groups

Figure 5.6. Supine systolic and diastolic blood pressure in both groups over course of study.

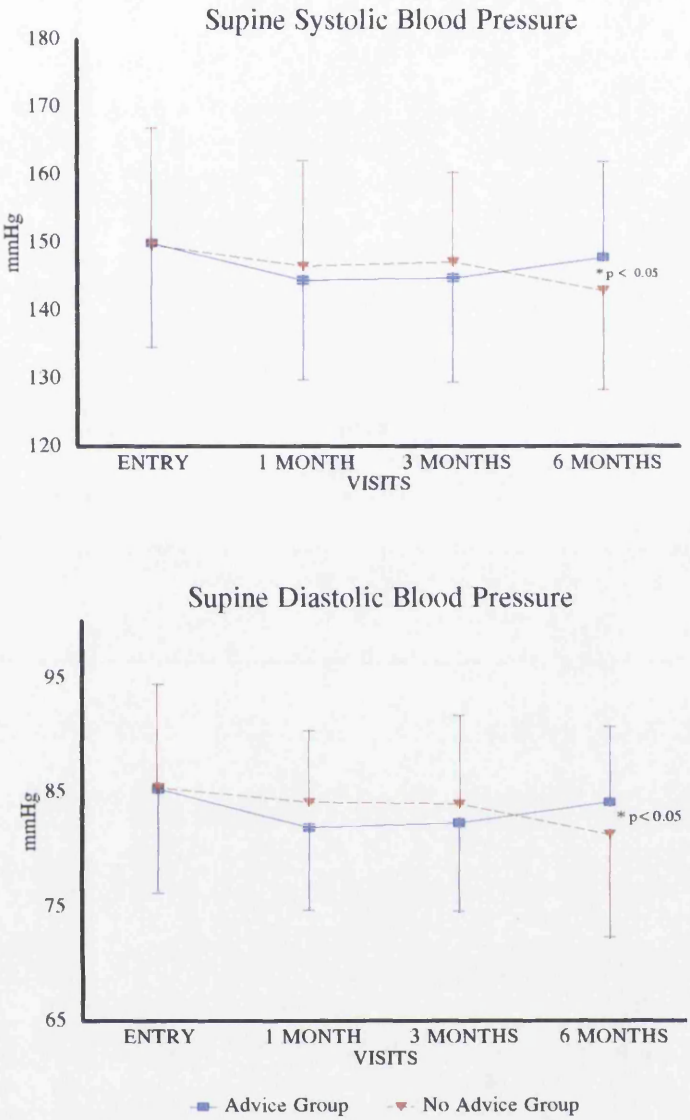


Figure 5.7. Weight (kg) in both groups over course of study.

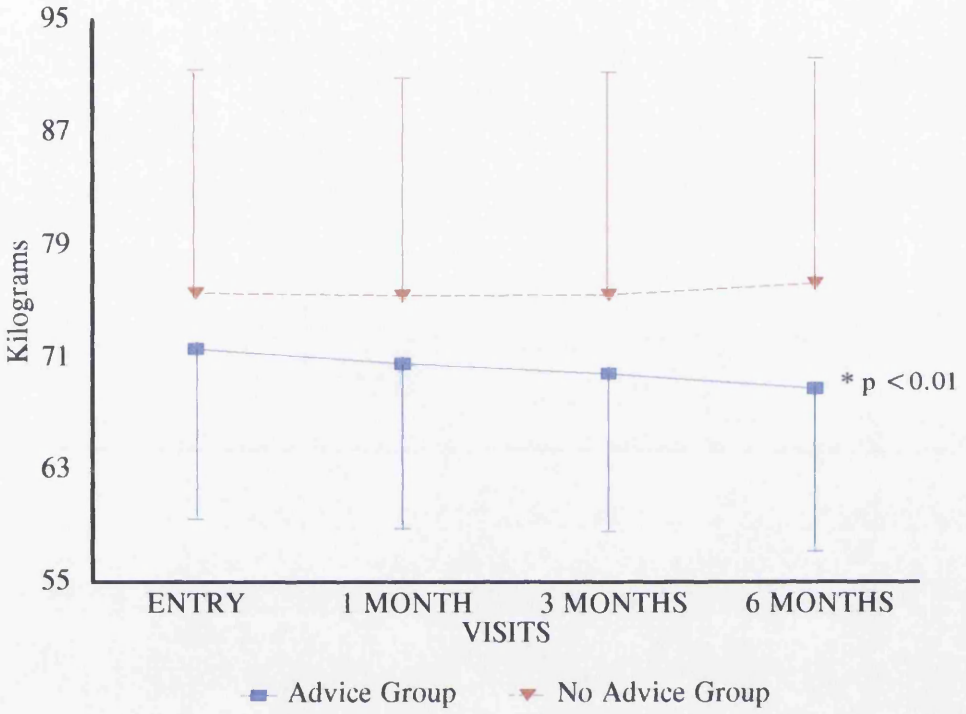
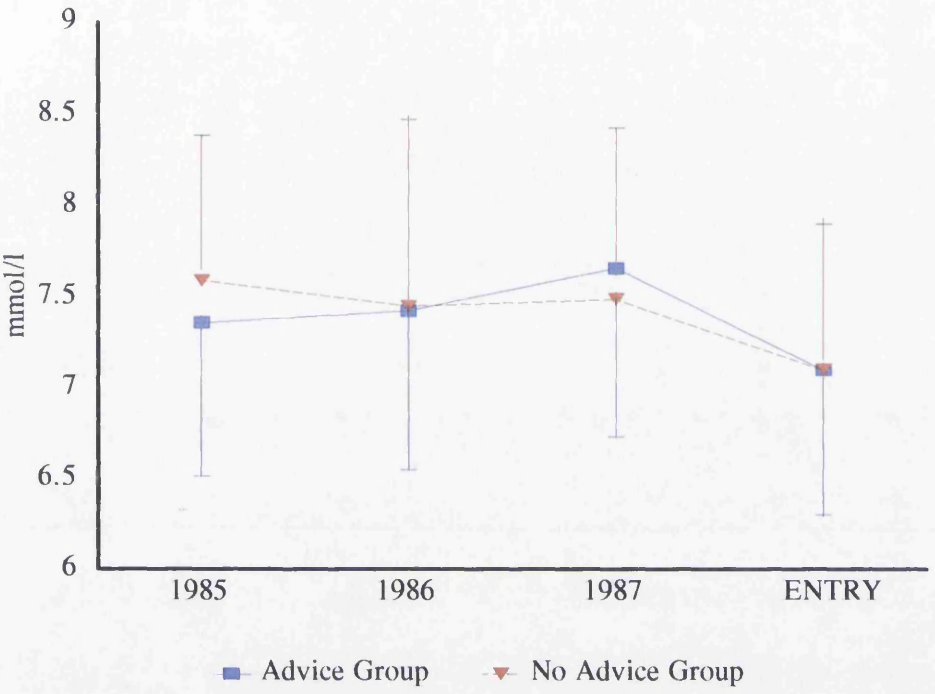


Table 5.4. Change in weight between the groups (kg).

	DIETARY ADVICE	NO DIETARY ADVICE
Weight Difference (Mean ±s.d.)	-2.6 ±3.0	-0.5 ±2.4*
Confidence Interval	(-3.14, -1.8)	(-1.2, 0.2)
Significance within	$p < 0.001$	$p = 0.15$

*significant difference between the groups for change in weight ($p < 0.01$)

Figure 5.8. Average cholesterol at annual review for previous 3 years compared to entry values for each group.



cholesterol had decreased by 0.5 ±0.6 mmol/l in the Advice Group and 0.4 ±0.7 mmol/l in the No Advice Group between last annual review and entry to the study.

During the study period, the average decrease in total cholesterol was 0.33 ±0.65 mmol/l in the Advice Group ($p<0.05$) and 0.27 ±0.72 mmol/l in the No Advice Group (n.s.). Using ANCOVA, a statistically significant group effect was observed ($p<0.05$) at 1 month (Figure 5.9), but there was no difference between the groups at 6 months. The change in total cholesterol ranged from -31% to +12% of baseline (mean -4%) in the Advice Group, and from -26% to +16% (mean -3%) in the No Advice Group.

The changes from previous annual review levels to entry represented a decrease of 7% in the Advice Group, and 5% in the No Advice Group and these were at least as great as the reductions induced by formal dietary advice. Further reductions during the dietary study resulted in cumulative reductions in the order of 12% and 7%.

The lipoprotein results are shown in Table 5.3. Small changes were observed in both groups over the course of the study. Only the HDL/LDL ratio showed a statistically significant difference between the groups ($p<0.05$) by ANCOVA, with the Advice Group's mean ratio increasing from 0.30 to 0.32 and the No Advice Group from 0.26 to 0.27.

5.4.4. Changes in weight and cholesterol

There was no significant correlation between the change in weight and the change in cholesterol for all participants ($r=0.1$) (Figure 5.10). Furthermore, the changes in weight and cholesterol analysed by anti-hypertensive drug treatment using ANOVA, showed no statistical significant differences between drug treatments (Table 5.5).

5.4.5. Diet and diet scores

The diets reported by each group were similar at entry. In the Advice Group 41% were prescribed Diet I and 59% Diet II at entry. At three months 10 of the 25 patients on Diet I were prescribed Diet II as total cholesterol in these individuals had

Figure 5.9. Total cholesterol (mmol/l) for each group over course of study.

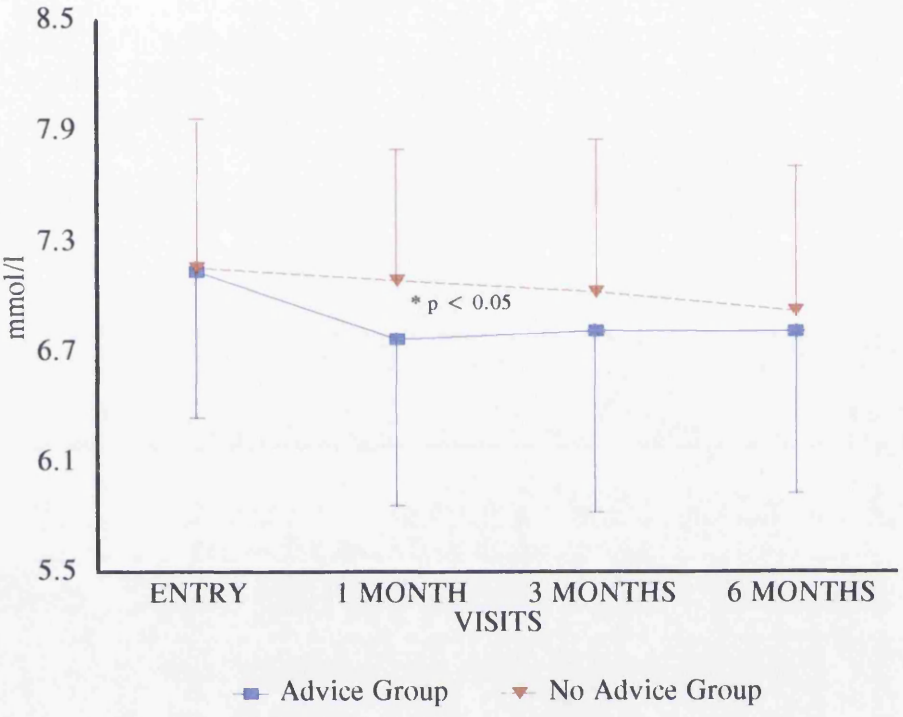


Figure 5.10. Changes in weight (kg) plotted against changes in total cholesterol (mmol/l).

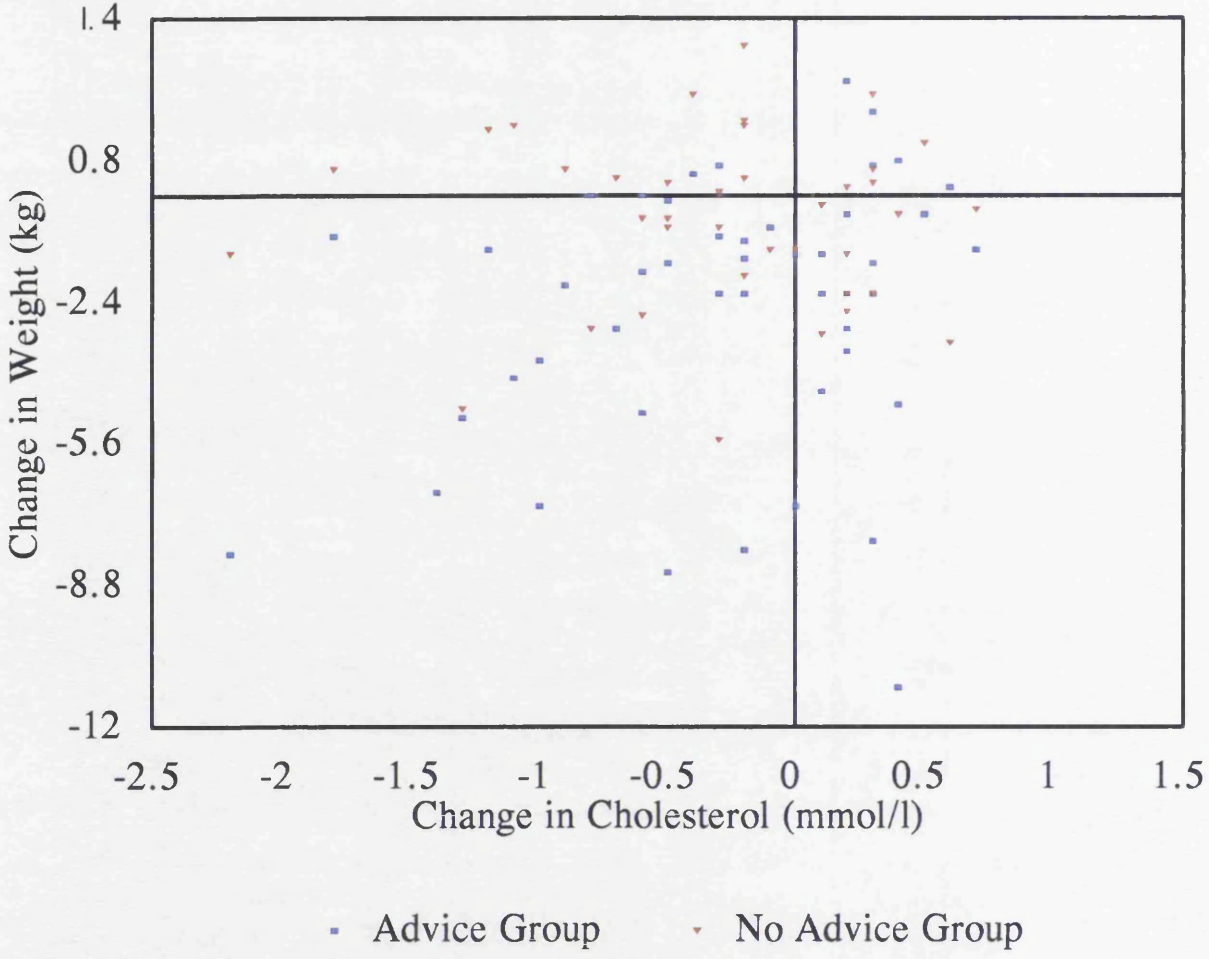


Table 5.5. Change in total cholesterol (mmol/l) in groups by drug treatment between entry and 6 month visits.

	N	Dietary Advice (mmol/l)	N	No Dietary Advice (mmol/l)
Lipid Neutral+ or no treatment	15	-0.6 ±0.8	11	0.0 ±0.7
Beta blocker alone	10	0.1 ±0.4	11	-0.3 ±0.7
Beta blocker and diuretic	10	-0.4 ±0.6	12	-0.4 ±0.6
Beta blocker, diuretic and calcium antagonist	6	-0.6 ±0.6	8	-0.1 ±0.8
Other@	13	-0.1 ±0.5	13	-0.5 ±0.8

+ monotherapy or combination of calcium antagonist and ACE inhibitors as well as no treatment

@diuretic with calcium antagonist or ACE inhibitor, or triple therapy including hydralazine

not fallen below 6.5 mmol/l. In total, during the last three months of the study, 75% of the Advice Group were prescribed Diet II.

The end of study questionnaire results showed that those in the Advice Group who reported a decrease in the frequency of eating foods high in saturated fat, and an increase in the frequency of eating foods high in polyunsaturated fat and fibre. The No Advice Group reported little change in diet over the course of the study (Table 5.6).

Both groups' entry diets were negatively rated, indicating that on average both groups were generally consuming diets high in saturated fat, low in polyunsaturated fat and low in fibre. The Advice Group's average score was -3.3 $\pm$6.0 and the No Advice Group's average score was -1.4 $\pm$5.6. Despite the Advice Group's 'worse diet' as indicated by the more negative score, there was no statistically significant difference between the average scores at entry.

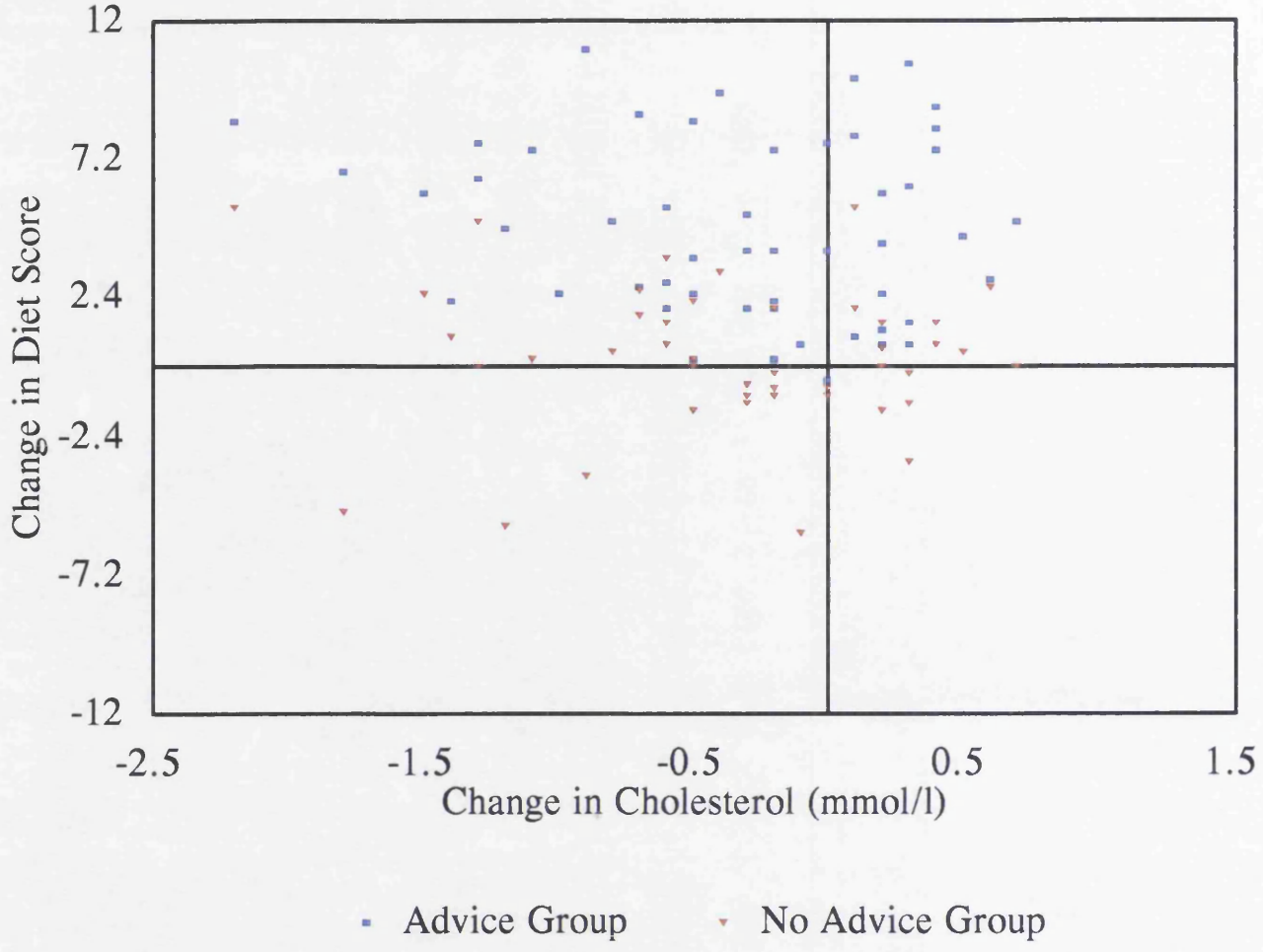
With specific individualised dietary advice, the Advice Group scored an average change of 4.6 $\pm$3.2 while the No Advice Group changed little with an average change of only 0.4 $\pm$2.3. This was a statistically significant difference between the groups ($p < 0.05$). Yet, 50% or less of the Advice Group reported having instituted the majority of the dietary changes listed in Table 5.6. Only a decrease in the quantity of eggs eaten, was reported by 68% of the Advice Group.

The change in diet score is plotted against the change in total cholesterol for each group in Figure 5.11. It is apparent that most individuals in the Advice Group reported some positive dietary changes and had a corresponding decrease in total cholesterol. However, it is also interesting to note the sub-group who reported substantial dietary changes with little impact on their total cholesterol levels (blue rectangles in upper right quadrant) as well as those in the No Advice Group who indicated they were eating a 'worse diet' at 6 months but still lowered their cholesterol (red triangles in lower left quadrant). These results call in to question the assumption that dietary intervention lowers cholesterol.

Table 5.6. Number of patients in each group reporting dietary changes on end of study questionnaire compared with entry responses for questions regarding fibre, saturated and polyunsaturated fat intake.(Some patients did not answer all questions).

Reported Dietary Changes In	Dietary Advice N=56			No Dietary Advice N=56		
	Positive Change	Negative Change	No Change	Positive Change	Negative Change	No Change
Type of bread (ie. White to Wholemeal)	26	3	23	8	10	37
Quantity of bread	15	14	20	11	7	24
Frequency of pasta	14	6	33	10	10	24
Type of spread (ie. Butter to polyunsaturated margarine)	30	1	23	10	2	41
Amount of spread (ie. thick to thin)	7	3	38	3	1	38
Cooking fat used	29	0	26	8	8	36
Frequency of fried foods	27	8	20	15	14	22
Frequency of chips	18	8	26	6	7	36
Type of milk (ie. whole to semi-skimmed)	31	0	22	6	7	34
Amount of milk	12	7	36	6	11	36
Frequency of cheese	27	1	23	12	6	33
Frequency of meat	29	11	17	14	20	21
Frequency of prepared meats	26	4	24	18	15	21
Quantity of eggs	38	4	11	18	14	24
Frequency of fish	15	1	36	8	3	45
Frequency of poultry	8	3	43	2	7	47

Figure 5.11. Changes in diet score plotted against changes in total cholesterol (mmol/l).



5.5. Discussion

This study is important since it attempted to intervene in a high risk group of hypertensive hyperlipidaemics of both sexes using diet alone. The significant reduction in blood pressure of 7/4 mmHg at 6 months compared to entry values in the No Advice Group, compared with little change (2/1 mmHg) in the Advice Group, might be explained by the extra attention paid to this group's blood pressure by the increased frequency of clinic visits required of the study. However, both groups average blood pressures were virtually the same up to and including the 3 month visit (Figure 5.6). Differences in blood pressure only emerged at the 6 month visit when the No Advice Group's mean decreased (4/3 mmHg) and the Advice Group's mean blood pressure increased (3/2 mmHg) compared to 3 month visit means.

The significant reduction in weight in the Advice Group reflected the intensive dietary therapy which included weight reduction advice for the obese. The change in weight did not correlate with changes in cholesterol (Figure 5.9) or blood pressure. The lack of correlation between weight and blood pressure reduction is at odds with studies which have shown that lowering weight lowers blood pressure (Staessen J et al 1985).

The explanation for the fall in total cholesterol in both groups after identification for entry to the study is not clear (Figure 5.8). Many of the patients have had stable consistent measurements of high cholesterol over many years. It could be a result of self-induced diet changes following 'labelling' as hyperlipidaemic as the informed consent obtained for the clinical trial made all patients aware that their blood cholesterols were elevated. In addition, while the study was underway a major public health programme 'Good Hearted Glasgow' was initiated in the city. Its publicity may have contributed to an increased awareness of cardiovascular risk factors and lipids and diet in particular.

Food frequency questionnaires have been shown to be as adequate an assessment of intake as diet diaries (Salvini et al 1989) or diet recall (Suitor et al

1989). Deriving a score for the potential impact on total cholesterol of a particular change in eating habit has facilitated a quantification of changes in diet and allowed for the plotting of the reported change in diet with change in weight (Figure 5.10) and total cholesterol (Figure 5.11).

From both plots it is apparent that for some people, the change in weight and reported dietary changes, were reflected by a change in cholesterol. However, particularly for cholesterol, it was evident that for about a third of the Advice Group who reported substantial changes in their diet (Change Score ≥ 5), their total cholesterols actually increased over the time of the study. 'Responders' and 'non-responders' to diet have been identified in the past (Jacobs et al 1983). However, there is no explanation for those few individuals in the No Advice Group who indicated they were eating a higher fat, higher cholesterol diet lower in fibre at the end of the study, yet had a decrease in total cholesterol (Figure 5.11).

Ramsay et al compared the preliminary results from this study with a number of the dietary intervention trials in a variety of settings. The percentage change in cholesterol was assessed to be the reduction in the intervention group minus the change in the control group in each trial. Thus in this study, net reduction was 2% from entry and 5% from last annual review. With such limited results they questioned the efficacy of dietary treatment and the cost benefits due to the investment in professional staff time required for its implementation (Ramsay et al 1991). This is a valid concern with ever shrinking health care resources, and in addition, it raises the concern as to why dietary intervention appears to be less effective in high risk groups.

Despite statistical significance in some parameters, all of the changes seen in this study were modest in clinical terms. At the end of the study, 56% of patients in the Advice Group and 57% in the No Advice Group still had total cholesterol > 6.5 mmol/l.

5.6. Conclusions

This study has shown that intensive dietary intervention may not significantly improve on the impact of merely telling individuals they are hyperlipidaemic, as nearly 50% in both groups managed to lower their cholesterols to below 6.5 mmol/l. This has cost implications as the cost of telling an individual they are hypercholesterolaemic is far less than intensive individualised dietary counselling by highly trained dietitians.

It has also shown that diet can only be the first course of treatment. Additional lipid lowering strategies will be required in many of those remaining individuals with elevated lipids.

Chapter 6. A placebo controlled study of guar gum in hyperlipidemia and/or obese essential hypertension

6.0. Summary

In this chapter, a study which evaluated the effect of guar gum (guar) on weight, blood pressure and lipids after 6 months of active treatment in a placebo controlled, double blind study is reported.

6.1. Introduction

As previously noted, it has been shown that the major cardiovascular risk factors occur more frequently together in individuals than would be expected by mere chance (Criqui et al 1980, Criqui et al 1986).

By 1986 in the Stobhill Clinic, there were 526 patients continuing to attend, with a mean blood pressure of 151 $\pm$19/86 $\pm$10 mmHg. 31% of patients had systolic blood pressures more than 10 mmHg above their target levels, and 16% of patients had diastolic blood pressures more than 5 mmHg above their target levels. 44% had total plasma cholesterol values > 6.5 mmol/l, 23% had a BMI > 30 and 33% continued to report that they smoked.

There was no difference in the distribution of obesity or smoking in the subset of hyperlipidaemic hypertensives from the total hypertensive population. The multiple risk of many of these patients warrants attempts to find a single therapeutic intervention that would be able to address more than one risk factor.

6.1.1. Role of fibre in cardiovascular disease

Epidemiological surveys of international diets have highlighted correlations between dietary fibre intake and rates of cardiovascular disease, and a Californian study indicated that this relationship may well be independent of the relationships identified with saturated fat and cholesterol intake.

Morris et al from the department of Community Health, London School of Hygiene and Tropical Medicine, in 1977 reviewed the CHD rates among 337 healthy middle-aged working men from London who had participated in seven-day individual

weighed dietary surveys 10-20 years before. The data were re-analysed, correlating various dietary factors with CHD incidence. Correlations were observed with increasing levels of the known risk factors of systolic blood pressure, total cholesterol and smoking in 270 in whom this information was available for analysis. The dietary factors identified with decreased CHD incidence were increasing levels of calorie and fibre intake, and multiple regression analysis showed that the effect of each was independent. There was no association between blood pressure and the nutrient factors studied (Morris et al 1977).

The Ireland-Boston Diet-Heart Study followed 563 men of Irish descendent, between the ages of 30 and 69 who lived in the Boston area for at least 10 years, and 572 brothers of the Boston men who were still living in Ireland. A third group of 373 men who were born in the Boston area but whose parents had emigrated from Ireland were also followed up for 20 years. Dietary intake was assessed at baseline as was blood pressure, 12-lead ECG, smoking habits, serum cholesterol level, triceps and subscapular skin-fold thicknesses, height and weight. 20 year mortality for CHD did not differ significantly between the three groups. However, for the entire population of 1001 men, initial analysis showed increased CHD mortality with lower vegetable food score which included a fibre intake sub-score ($p<0.02$). Unfortunately, this inverse association with fibre became non-significant ($p=0.05$) with adjustment for other risk factors (Kushi et al 1985).

Khaw and Barrett-Connor recorded 12 year ischaemic heart disease mortality prospectively in a group of 859 Californian men and women after obtaining a baseline survey of 24 hour dietary fibre intake. They also obtained data on the levels of known cardiovascular risk factors. Overall mean fibre intake was approximately 12g/24 hours. Mortality was assessed for $<$ 16 g/24 hours and $>$ 16 g/24 hours intakes. Relative risk of ischaemic heart disease in the higher fibre group was .33 (C.I. = 0.14-0.77) with p value of 0.01 in the males and .37 (C.I. = 0.11-1.24) with p value of 0.16 in the females. Dietary fibre correlated negatively at marginal levels

of significance in men only for diastolic blood pressure, body mass index and plasma cholesterol. There was no relationship with smoking in either sex. Multi-variate analysis adjusting for age, systolic blood pressure or diastolic blood pressure, plasma cholesterol, fasting plasma glucose, obesity and smoking habit continued to demonstrate a significant inverse association between dietary fibre intake and ischaemic heart disease mortality in both sexes (Khaw & Barrett-Connor 1987).

Turning from the prospective surveys to intervention trials reveals mixed results of diets rich in fibre when used alone or more frequently in conjunction with other risk factor interventions, as reviewed in the introduction of Chapter 5. In the Diet and Reinfarction Trial (DART) in post MI males there was no significant difference in cholesterol levels or mortality in the high fibre group (Burr et al 1989), and in the Leiden Intervention Trial angiographically assessed coronary artery lesion progression was not observed in those who had high total/HDL cholesterol which was significantly lowered by the intervention (Arntzenius et al 1985).

Several of the multiple risk factor intervention studies have used high fibre as an added component to a high polyunsaturated, low saturated fat diet. These include the Oslo Study (Hjermann et al 1981), and the WHO European Trial of Multifactorial Prevention of Coronary Heart Disease study (WHO European Collaborative Group 1986). Unfortunately, since high fibre content was only a component of these diets, it is impossible to differentiate the effect of fibre from the effect of other dietary constituents.

6.1.2. Effect of adding fibre to the diet

Several multi-faceted diet studies have included an increased fibre intake as a component, while other researchers have investigated the effects of only increasing the dietary fibre content. Physiological parameters such as plasma or serum lipids, blood pressure, weight, blood glucose and insulin levels have been used as endpoints. The studies investigating the effects on blood pressure have been reviewed in Chapter 1.

In a review of the effects of vegetarian diet on blood pressure, Rouse and Beilin identified a number of important methodological issues in interpreting dietary studies, including the measurement of blood pressure, assessment of dietary intake, confounding nutrient interactions and statistical methods. A factor analysis conducted on data from their controlled vegetarian studies showed that blood pressure changes significantly correlated to the factor representing increased intake of polyunsaturated fat, fibre, vitamin C, Vitamin E, calcium, magnesium and a fall in the intake of protein. They do not address the contribution which fibre has to this factor. They conclude that despite the lack of good data with respect to the effects of 'dietary fibre', what data there are suggest that this nutrient may be important (Rouse & Beilin 1984).

Jenkins et al compared 36 g/day doses of wheat bran, pectin and guar in young healthy normolipid males. In those individuals who completed each course, those taking the guar (7 volunteers) had a significant reduction (16%) in their serum cholesterols (Jenkins et al 1975).

In the Netherlands, Stasse-Wolthuis et al divided 62 healthy normotensive volunteers with cholesterol values < 5.17 mmol/l and diastolic blood pressure < 90 mmHg, into 4 groups after an initial 2.5 week period of a low-fibre diet. One group continued on the low fibre diet (18g/day), the second group were given a diet rich in vegetables and fruit (43 g/day of fibre), the third group was supplemented with citrus pectin (28g/day of fibre) and the fourth group was supplemented with wheat bran (37g/day of fibre). All other food, except 100 kcal/day, was also provided. There was a significant decrease in cholesterol in the pectin group, but no changes in HDL cholesterol. Fecal output was generally increased in the pectin and bran groups. Not surprisingly, there was no change in blood pressure in these normotensive subjects (Stasse-Wolthuis et al 1980).

Haskell et al conducted a series of experiments with various forms of water-soluble dietary fibre (WSDF). They demonstrated acacia gum had little lipid

lowering effect, while guar alone or in combination with other WSDF did significantly lower lipids. A month long dose ranging study with a placebo, 5, 10 and 15 g/day dose of guar in groups of 12 or 13 showed increasing reductions in total and LDL cholesterol with increasing dose. There was no gender effect nor were there significant weight changes in any of the groups (Haskell et al 1992).

Jenkins et al investigated the effect of 4 months of treatment with soluble or insoluble fibre in 43 hyperlipidaemics (15 men, 20 women) who had been on a low cholesterol diet for at least 2 months in an open study. Total cholesterol, LDL cholesterol and HDL cholesterol were significantly reduced by an additional 5%, 5% and 3% respectively during treatment with the soluble fibre compared with the reduction during insoluble fibre treatment (Jenkins et al 1993).

6.1.3. Role of guar in addressing single cardiovascular risk factors

Guar is a soluble fibre obtained from the cluster bean plant Cyamopsis tetragonoloba also called Cyamopsis psoraloides. It has been used for a number of years to treat diabetes by retarding glucose absorption from the gut. Jenkins et al assessed the effect of various fibres in groups of 4-6 individuals who underwent a 50 g. glucose tolerance test. Guar significantly reduced hyperglycemia by 50% ($p<0.01$). The viscosity of the various fibre preparations correlated with the reduction in maximum rise in blood glucose concentration (Jenkins et al 1978) and the continued effect has been demonstrated after 1 year of treatment in 11 diabetics (Jenkins et al 1980a).

Blackburn et al investigated possible mechanisms of action of guar in the gut by assessing gastric emptying time, intestinal absorption and the 'unstirred water layer' in the small intestine. Guar was shown to decrease glucose tolerance, delay gastric emptying and decrease glucose absorption from the intestine. However, there was no correlation between change in gastric emptying and the peak increase in blood glucose concentration (Blackburn et al 1984).

Jenkins et al have carried out a series of small uncontrolled studies which have

shown significant reductions in total cholesterol compared with pectin and wheat fibre (Jenkins et al 1975), after 2 weeks of treatment in 10 hyperlipidaemics (Jenkins et al 1979), and after 6 months of treatment in 8 normolipidaemic diabetics (Jenkins 1980a). They also compared either guar crispbread, hydrated guar, semi-hydrated guar or cholestyramine with small groups of hyperlipidaemic patients, and found the guar crispbread to be more acceptable to patients. Weight was also significantly reduced by 1.5 kg on average in the 7 patients who completed the 8 week course of crispbread (Jenkins et al 1980b).

A 12 month study of active guar (6 g tds), following a 4 week placebo period, was conducted in 19 hypercholesterolaemic ($>$ 6.5 mmol/l) Australians. 2 patients withdrew due to severe diarrhoea initially, another 4 withdrew after 3 months. Guar was taken in a flavoured guar formulation mixed with 170 ml of water, half taken before and the rest during each meal. It contained an inhibitor of gelation which prevented the guar jelling until it reached the acidic contents of the stomach. Of the 13 who completed 12 months of treatment, a significant reduction in serum cholesterol and LDL cholesterol was observed by analysis of variance ($p<0.001$) (Simons et al 1982).

Kirsten et al assessed the influence of 4 g guar dissolved in 200 ml of water taken 3 times per day, on serum lipids in 13 hyperlipidaemic patients over a 60 day period. Values were compared with pre and post study assessments. There was a significant reduction in total cholesterol (13%) and LDL cholesterol (0.64 $\pm$0.52 mmol/l). However, HDL cholesterol was significantly decreased at 30 days, but returned to pre-treatment levels after 60 days of treatment (Kirsten et al 1990).

A few studies have been conducted with a more rigorous study design. Khan et al published the results of a double-blind placebo controlled study using 600mg capsules of guar and matching glucose capsules. 18 men and 6 women were randomised to take 5 capsules 3 times per day, ie. a total of 9.0 g. of guar or placebo, for a 4 week period. There was no change in body weight, but total

cholesterol decreased by 16.6% ($p<0.05$) and LDL cholesterol by 25.6% ($p<0.05$) in the guar group. There were no significant lipid changes in the control group (Khan et al 1981).

A Scandinavian study showed guar to have a significant effect on weight in hypercholesterolaemic females after 4 months of treatment. Tuomilehto et al randomised 33 hypercholesterolaemic females (cholesterol > 7.6 mmol/l) to 3 groups. Group 1 received 5 g of guar granules 3 times per day mixed with a small amount of food or drink, group 2 received placebo (5 g wheat flour without fibre 3 times per day) and group 3 received no treatment. Mean weight was statistically significantly decreased by 2.5 kg in the guar group ($p<0.0005$), but there was no change in total serum cholesterol in any of the groups (Tuomilehto et al 1980).

Subsequently, these investigators conducted a double-blind cross over study using the same treatment regimen and placebo in 10 obese hypercholesterolaemic patients who were receiving long term anti-hypertensive treatment. Each phase lasted for 3 months. Serum cholesterol statistically significantly decreased during the guar phase of treatment ($p<0.001$) by ANCOVA, controlling for change in body mass index, since weight had significantly decreased during the trial 'run-in' phase. No significant weight change was observed in the 'active treatment' phase of this study (Tuomilehto et al 1983).

A guar containing 'snack' type bar was developed by McIvor et al in Baltimore. The first study, in 1985, with 5 type 2 diabetics, failed to show any significant reduction in cholesterol, glucose or weight over a 16 week period, despite the subjects taking 4-6 bars per day (approximately 26-40 mg/day) (McIvor et al 1985). In a second study reported the following year, they had equally negative results. They randomised 16 type 2 diabetics to either guar or placebo bars for 6 months. LDL cholesterol was significantly reduced only in males on guar compared to males on placebo. All other parameters were unchanged (McIvor et al 1986).

Lalor et al used a double blind, double dummy method to compare the

effectiveness of guar, metformin and placebo on fasting glucose and lipid levels, and body weight in 19 obese type 2 diabetics. Each treatment period lasted 12 weeks. Both the guar and metformin were equally effective in lowering blood glucose, while cholesterol was only reduced in a sub-group of 6 hyperlipidaemics (cholesterol > 6.5 mmol/l). There was no change in body weight over the course of the entire study (Lalor et al 1990).

Another double blind, placebo controlled study was carried out in Finland with 17 mildly hypercholesterolaemic (>5.7 mmol/l), insulin-dependent diabetics. The guar group (N=9) received 5 g. granulated guar, and the control group (N=8) received a wheat flour placebo, each four times per day before meals for 6 weeks. Weight was unchanged. Glycosylated haemoglobin and plasma glucose concentration did decrease significantly in the guar group, but the changes were not significantly different from those in the wheat flour group. Serum total cholesterol decreased significantly in the guar group when compared with the change in the wheat flour group (-1.0 mmol/l vs. +0.1 mmol/l). Three guar patients reduced their insulin doses over the course of the study (Vuorinen-Markkola et al 1992).

A study, from Sweden, evaluated the effect of guar on glucose and lipid metabolism, blood pressure and fibrinolysis in a double-blind, placebo controlled cross-over study. 25 healthy, non-obese middle-aged men taking no medication were recruited from a normal population. 10 g of guar or granulated jelling starch in a glass of water was given 3 times per day before meals for 6 weeks after a 2 week run-in period without treatment. The second 6 week period on the opposite treatment was completed after a 2 week wash-out period. There was no change in body weight, fibrinogen concentration, renin activity or plasma aldosterone. Systolic and diastolic blood pressures decreased significantly compared to entry values (6 $\pm$9/3 $\pm$2 mmHg,$p<0.001$), and both returned to pre-treatment values post-study. Blood glucose decreased significantly (0.3 $\pm$0.2 mmol/l,$p<0.001$) but insulin did not. Glucose disposal, as measured by the euglycemic-clamp, significantly increased

($p<0.001$). Cholesterol and triglycerides decreased significantly by 0.6 $\pm$0.3 mmol/l ($p<0.001$) and 0.2 $\pm$0.6 mmol/l ($p<0.05$). Basal glucose uptake by abdominal fat cells increased ($p<0.001$) and maximally stimulated glucose uptake increased as well ($p<0.01$) (Landin et al 1992).

A study undertaken locally suggested that guar was an efficacious adjunct to diet therapy in the grossly obese (personal communication, A. Lakhdar).

6.1.4. Discussion of the role of fibre

There is more than the average amount of difficulty when trying to interpret dietary studies. In the epidemiological surveys carried out in Boston/Ireland (Kushi et al 1985) and California (Khaw et al 1987) the 20 and 12 year mortality results were correlated only with an initial survey of food recall. This fails to address the issues of dietary intake affected by seasons and changing cultural habits over time. Unfortunately, the Seven Countries study which actually had subsamples of participants weigh their dietary intakes over a set period of time, with duplicate samples of food chemically analysed for nutrient content, with this being repeated at 5 yearly intervals, did not report on fresh fruit/vegetable or fibre intake (Keys et al 1986).

In particular when evaluating the studies involving guar, the difficulties are best summed up by Todd et al in 1990 when they reviewed the use of guar as a dietary adjunct in hypercholesterolaemia. Difficulties identified in interpreting the results of completed studies include the differences in type of formulation used (ie. powder, granules, coated), dosages administered, whether taken hydrated with water or unhydrated with food, the problems with blinding due to the high frequency of side effects in the guar groups and the limited power of most studies due to small population size (Todd et al 1990).

Nearly half of the studies reported above did not have a control group nor were they blinded. Most studies lasted 4-6 weeks. In only 3 studies did the guar treatment period last for more than 3 months. Tuomilehto's study in obese women

was 4 months long (Tuomilehto et al 1980), Simons' study from Australia was 12 months (Simons et al 1982), and McIvor's second study was 6 months (McIvor et al 1986).

Therefore, with the accumulated evidence that increased dietary fibre had been associated with lowering blood pressure, and guar appeared to have an effect in lowering weight and lipids in some studies, a study was devised to investigate further these potential benefits in patients attending the nurse practitioner follow-up clinic.

6.2. Study aims

The aims of this double blind, placebo controlled study were to evaluate the effect of guar on:

1. lipids in hyperlipidaemic hypertensive patients with cholesterol > 6.5 mmol/l,
2. weight in obese hypertensive patients with body mass index > 30,
3. blood pressure in essential hypertensives.

6.3. Methods

6.3.1. Outline of Study

In total, 36 patients of either sex between the ages of 18 and 70 years with a last clinic blood pressure < 180/100, were to be recruited. For analysis purposes:

- 12 patients were to have BMI > 30 and total cholesterol < 6.5 mmol/l,
- 12 were to have BMI > 30 and total cholesterol > 6.5 mmol/l, and
- 12 were to have BMI between 20 and 25 and total cholesterol > 6.5 mmol/l.

Power calculations indicated with this group size the study had 92% power to detect 1 mmol/l change in total cholesterol, 97% power to detect a standard deviation change in weight, systolic and diastolic blood pressure by the method described by Day and Graham (Day & Graham 1989).

Patients were excluded if their last clinic blood pressures were > 180/100 mmHg, they were pregnant or lactating women, or of child bearing potential and not using a reliable form of contraception, had a history of hiatus hernia or gastro-intestinal disease or were currently taking a thiazide diuretic. Patients were to be

withdrawn if an adverse drug reaction occurred such as excessive flatulence or diarrhoea, as well as if they expressed a desire to withdraw.

Attempts were made, when selecting participants, to control for: age, sex, smoking status, and drug treatment. Drug treatment, including anti-hypertensive therapy, were to be kept constant throughout the study period. Patients taking a thiazide diuretic would have it withdrawn 6 weeks prior to entry to the study and were included only if after 6 weeks with no thiazide therapy they continued to meet the other entry criteria.

Hypercholesterolaemic patients were asked to continue their low cholesterol/high polyunsaturated fat, high fibre diets and overweight patients were encouraged to attempt to modify their caloric intakes.

Patients attended over a 7 month period with entry, 1 month, 2 month, 4 month and 7 month visits according to the schedule of visits outlined in Table 6.1. This allowed for the initiation of the bran control in an increasing dose in all patients during a month prior to the start of the 6 month active treatment phase.

Dropouts due to drug side effects were to be recalled for a 6 month (from start of active treatment) visit for an assessment so that their data could be included in an intention-to-treat analysis. Dropouts due to other reasons were to be replaced to maintain the proposed group sizes.

Informed written consent was obtained prior to entry to the study, and patients were provided with a Patient Information Sheet which they could keep for reference (Figure 6.1).

6.3.2. Study Measurements

Supine and erect blood pressures were measured using a Sentron semi-automatic sphygmomanometer as described in Chapter 2, using an appropriate size cuff depending upon the individual's upper arm circumference, and the cuff size remained standard for each patient throughout the course of the study. A series of 5

Table 6.1. Visit and assessment schedule.

Visit	Month	Assessments
0	0	Height and weight, supine and erect blood pressure with heart rate Start placebo before meals: 1 sachet per day first week 2 sachets per day second week 3 sachets per day third week continue t.d.s. until next visit
1	1	Weight, supine and erect blood pressure with heart rate Fasting total cholesterol,LDL cholesterol,HDL cholesterol,triglycerides Compliance check Start double blinded active treatment phase (guar 5g. t.d.s. or bran control t.d.s.) as per Visit 0: 1 sachet per day first week 2 sachets per day second week 3 sachets per day third week continue t.d.s. until next visit
2	2	Weight, supine and erect blood pressure with heart rate Compliance check Maintain guar/control dose.
3	4	Weight, supine and erect blood pressure with heart rate Compliance check Maintain guar/control dose
4	7	Weight, supine and erect blood pressure with heart rate Fasting total cholesterol,LDL cholesterol,HDL cholesterol,triglycerides Compliance check

Figure 6.1. Patient Information Sheet given to all participants.

Patient Information Sheet

Study: To examine the effect of guar gum in overweight patients and patients with elevated cholesterol, who also are hypertensive (have high blood pressure).

Guar gum is a plant fibre in a concentrated form. It has been shown to lower cholesterol and to help overweight people loose weight. We wish to assess these effects in people with high blood pressure.

We wish to treat you with guar gum for up to 6 months to examine its effect on either your weight or cholesterol, or both if you have both health problems. We also wish to compare the effects with an inactive treatment. At some time during the study you will be taking inactive sachets.

You will be required to attend the Blood Pressure Clinic monthly for 2 months, then at 2 and 3 months. We will ask you to come fasting at the first monthly visit and at your last visit of the study for a blood sample to check your cholesterol and other blood fat levels.

You should continue your routine blood pressure medication throughout the period of the study. Your blood pressure will be monitored at each visit as well as your general well being. No serious side effects are expected but you may experience an increase in flatulence ("wind") and an increased frequency of bowel motions during the first week or so of treatment.

If you have any questions about this study now or in the future, please ask Mrs Curzio, Dr Lees or Professor Reid at the Blood Pressure Clinic, Stobhill Hospital (041-558-0111 Ext 278). In an emergency contact Mrs Curzio (Bishopton 862061).

supine and then 5 erect blood pressure measurements were obtained at one minute intervals after 5 minutes resting. The mean of these supine and erect readings was determined and used for data analysis.

Venous blood samples were obtained for total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol and VLDL cholesterol at Visits 1 (just prior to starting the active treatment phase, after 1 month bran control) and visit 4 (after 6 months in the active treatment phase). Patients were asked to fast from 10 pm the evening before each sample. These samples were assayed in the Stobhill Biochemistry Laboratory as described in Chapter 2.

6.3.3. Randomisation and drug dosage

Guar 5 g. was packaged in plain white, unmarked sachets, as was the wheat bran control. A statistician not directly involved in the study, randomised an equal number of participants in each of the three categories within the study, (overweight with normal lipids, overweight with hyperlipidaemia, normal weight with hyperlipidaemia) to each treatment.

At entry during Visit 0, all patients were asked to start one sachet per day of the wheat bran control preparation for the first week, then to increase the dose to two sachets per day the second week and to three sachets per day the third week, in order to build a tolerance to the high fibre load. They were asked to continue three sachets per day until the next visit.

At visit 1, a month after Visit 0, all patients were informed that they were now to receive a 'higher dose' and would therefore need to acclimatise their bodies to this higher dose by following the same increasing dosing schedule as they had done after Visit 0. In this way, the participants who were randomised to the active guar treatment would be able to develop tolerance to the high soluble fibre load.

6.3.4. Statistical analysis

It was originally proposed to analyse the change in weight, cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, VLDL cholesterol, supine and

erect blood pressure and heart rate between baseline (Visit 1, after 1 month of bran control) and after 6 months of the active treatment phase (Visit 4). The analysis would utilise an analysis of covariance (ANCOVA) such that weight would be the covariate for the cholesterol analysis, cholesterol would be the covariate for the weight analysis and cholesterol plus weight would be the covariates for the blood pressure analysis. Power calculations were carried out according to the method described by Day and Graham (Day & Graham 1989).

Analysis was undertaken on an intention to treat basis. Unfortunately, the analysis of co-variance could not be carried out as the main treatment groups were not homogeneous. One way analysis of variance (ANOVA) using MINITAB on the ICL 3980 mainframe computer, was carried out on the change in weight, cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, VLDL cholesterol, supine and erect blood pressure and heart rate between baseline (visit 1) and after 6 months of the active treatment phase (visit 4) for all patients with data obtained on an intention-to-treat basis.

Further one way analysis of variance analysis was undertaken by partitioning the data into 2 sub-groups of:

1) those patients who were obese with and without hyperlipidemia

2) those who were hyperlipidaemic with and without obesity.

Factors were then analysed accordingly.

6.4. Results

6.4.1. Details of patients studied

As previously stated, the protocol sought to recruit 36 hypertensive patients from the Blood Pressure Clinic. In total, 39 patients, 16 males and 23 females, were recruited to the study (Table 6.2). Withdrawals from the study were in excess of those anticipated, however, with half of the early withdrawals being due to intolerance of the bran control preparation. Thus 31 patients commenced active treatment. On an intention to treat basis, data were obtained for 29 patients, 12 males

Table 6.2. Patient recruitment.

	Men	Women
Entered into placebo phase	16	23
Entered active treatment	13	18
Withdrew from active treatment	1	5
Continued study visits, but stopped treatment	3	1
Completed study	9	12

and 17 females. One of the patients who withdrew from active treatment is not included as he failed to attend his clinic appointments. The other withdrawal from active treatment for whom intention to treat data were not obtained, had been started on a thiazide diuretic by her general practitioner prior to her final visit. Reasons for withdrawal from either phase of the study are listed in Table 6.3.

The distribution between active treatment with guar and the bran control for all patients, the obese and the lipid sub-groups are in given Table 6.4. Anti-hypertensive treatment was not changed over the course of the study. There were only 5 smokers in the 29 patients who completed the study on an intention-to-treat basis. The smokers were evenly distributed throughout all groups.

6.4.2. Blood Pressure

Mean supine systolic blood pressure for all patients, obese and lipid sub-groups are shown in Figure 6.2. Supine diastolic blood pressure is plotted for all patients and the 2 sub-groups in Figure 6.3. Oneway ANOVA of the differences in blood pressures between entry and after 6 months of active treatment, showed no statistically significant difference between the guar and bran control for all patients or the 2 sub-groups.

The average difference of 11 mmHg between entry supine systolic blood pressures in the obese sub-group was not significant due to the variability of blood pressure within each treatment group ($\pm$16 mmHg in guar and $\pm$10 mmHg in the bran controls). There was a similar difference of 8 mmHg in the lipid sub-group and this was also not significant due to the within treatment group variability ($\pm$16 mmHg in the guar and $\pm$18 in the bran controls).

6.4.3. Weight

Mean weights for all patients and the 2 sub-groups are presented in Figure 6.4. Once the treatment code was broken, initial weights were found to be quite different between the treatment groups for all patients and the 2 sub-groups, with the guar average weight being more than 10 kilograms heavier than the bran control. Analysis

Table 6.3. Reason for withdrawal from control or active treatment or stopping treatment.

Withdrew during placebo period

Did not return for Visit 1	2
Did not wish to participate in a clinical trial	2
Unable to tolerate bran control	4

Withdrew during active treatment

	Guar	Bran Control
Unpalatable, difficult to mix with foods	1	
Developed gastroenteritis, or diarrhoea or increased frequency of bowel motions	2	
Failed to attend follow-up appointments		1
Depression, swollen ankles, nausea and vomiting		1
GP started thiazide (but had also stopped treatment after episode of nausea/vomiting)		1

Continued study visits but stopped treatment

	Guar	Bran Control
Difficult to remember to take	1	
Fractured bone in foot, unable to move around (increased frequency of bowel motions)	1	
Increased thirst and nausea	1	
Skin rash		1

Table 6.4. Group distributions.

All Patients		
N=29	13 Guar	6 men
		7 women
	16 Bran Control	6 men
		10 women
Obese Sub-Group		
N=20	10 Guar	4 men
		6 women
	10 Bran Control	3 men
		7 women
Lipid Sub-Group		
N=18	8 Guar	3 men
		5 women
	10 Bran Control	3 men
		7 women

Figure 6.2. Mean supine systolic blood pressure for all patients, obese and lipid sub-groups.

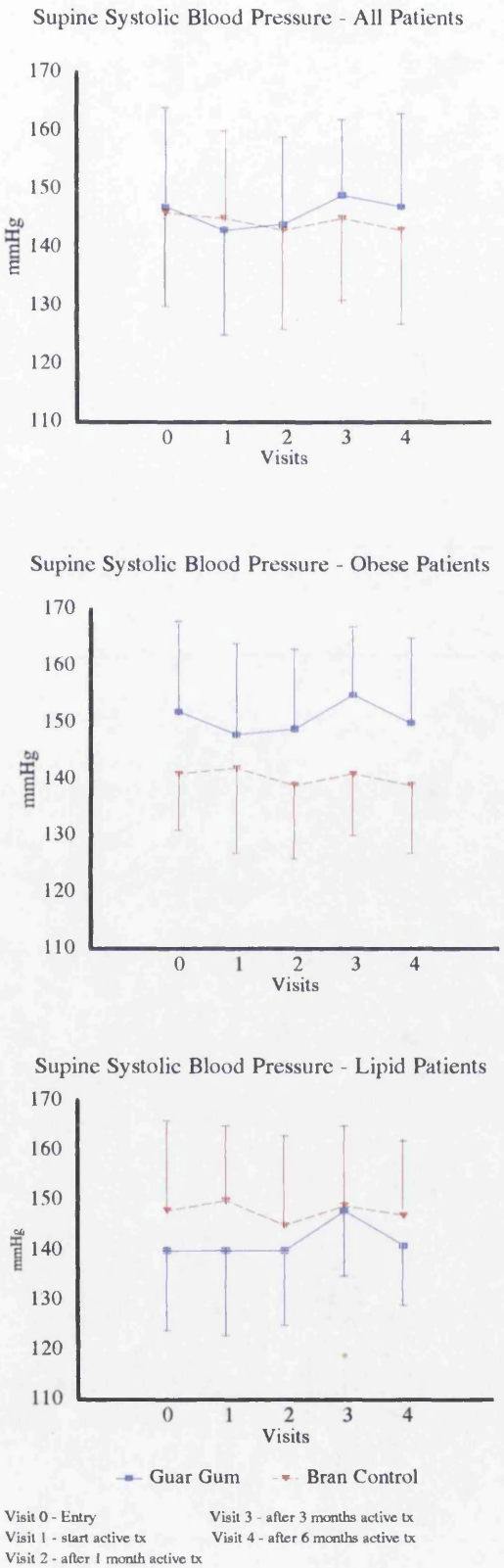


Figure 6.3. Mean supine diastolic blood pressure for all patients, obese and lipid sub-groups.

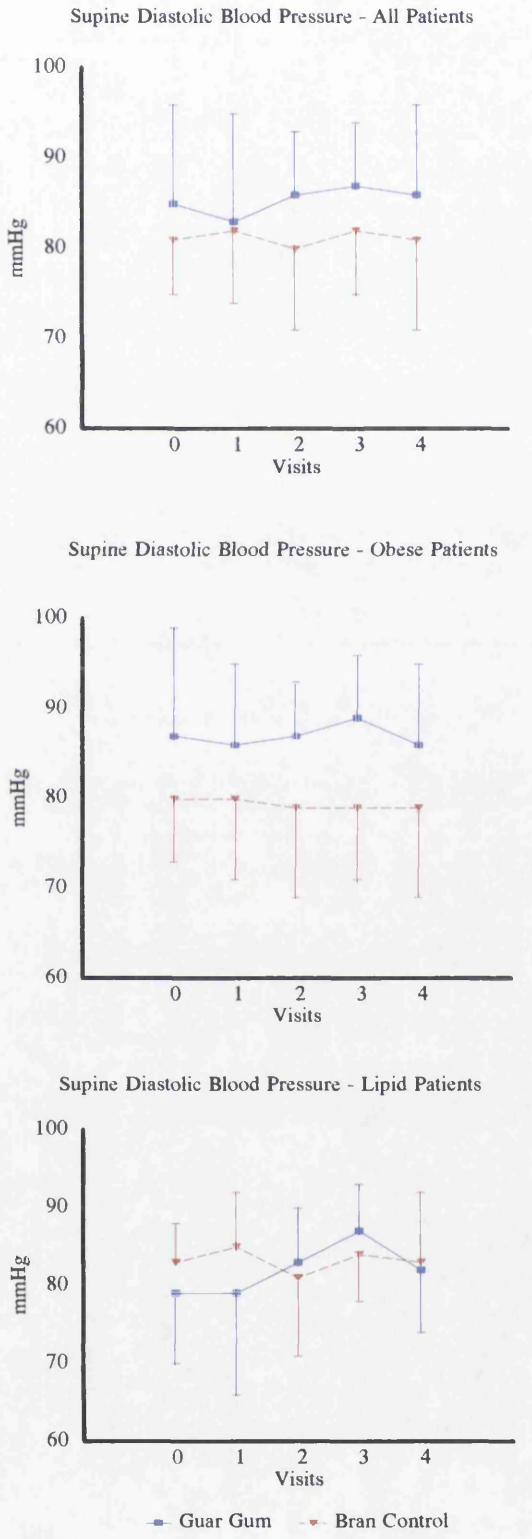
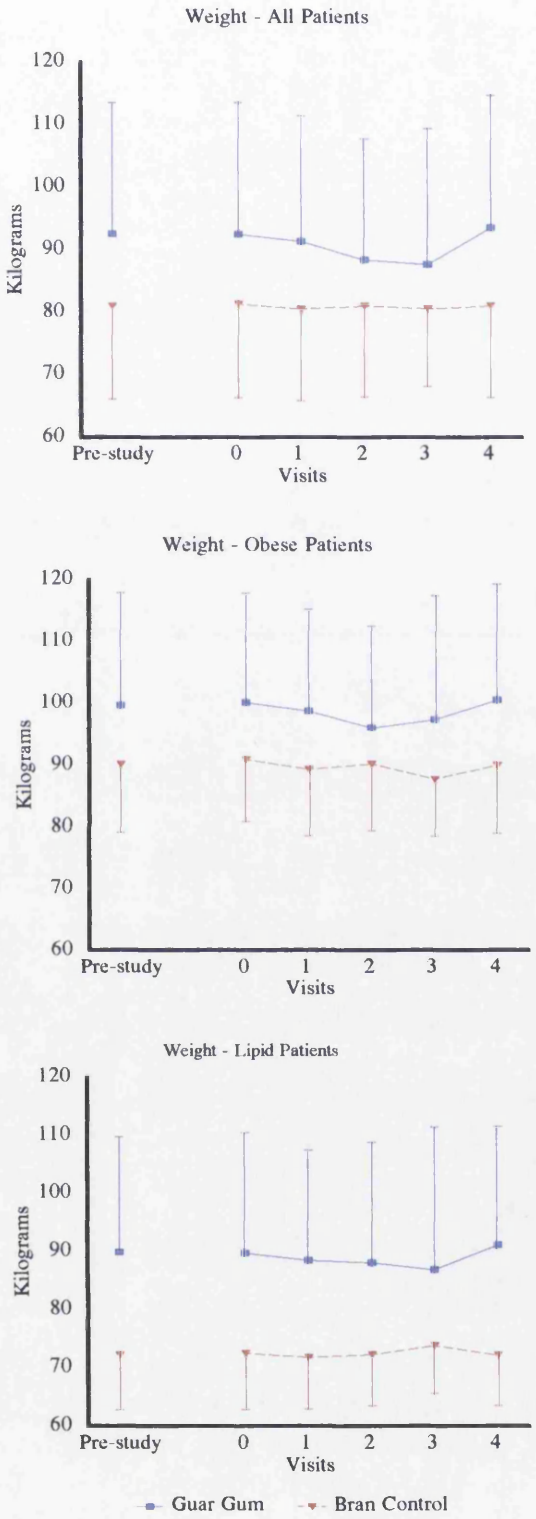


Figure 6.4. Mean weight in kilograms for all patients, obese and lipid sub-groups.



of co-variance (ANCOVA) using pre-study weight as the covariate, revealed no statistically significant difference in the changes in weight for either the guar or control groups over the course of the study for all patients, or for either of the 2 sub-groups.

6.4.4. Lipids

Total cholesterol for all patients, obese and lipid sub-groups is presented in Figure 6.5, and other lipid results are presented in Table 6.5. Data are first presented for all patients and then for the obese and lipid sub-groups. There were no statistically significant differences in the lipid measurements between the treatments for all patients or in either of the 2 sub-groups analysed.

A small reduction (6%) in total cholesterol in the guar treatment group of the lipid sub-group was significant only when compared with initial values in that group by paired t-test ($p<0.05$, 95% C.I. -1.013,-0.012). A similar small reduction (7%) in LDL-cholesterol was not significant ($p<0.08$,95% C.I. -0.947,0.072) when compared with initial values for that treatment group.

6.4.5. Tolerance and symptoms

The fibre preparations were poorly tolerated with overall 13 of the 29 patients analysed reporting changes in their bowel habits, 8 in the guar treatment group and 5 taking the bran control (Table 6.6). Only 20 patients were able to reach the maximum dose of 3 sachets (15 g) per day (Table 6.7). Of the 11 patients who stopped treatment, 8 were taking guar. An additional 2 patients in the bran control group admitted to very poor compliance over the course of the study (Table 6.8). Finally, 5 of 6 patients in the guar group, while in the active treatment phase reported great difficulty in mixing it with foods and generally found treatment unpalatable.

6.5. Discussion

The current study design attempted to overcome many of the difficulties previously discussed by using a double-blind, placebo controlled design with a 6

Figure 6.5. Mean total cholesterol for all patients, obese and lipid sub-groups.

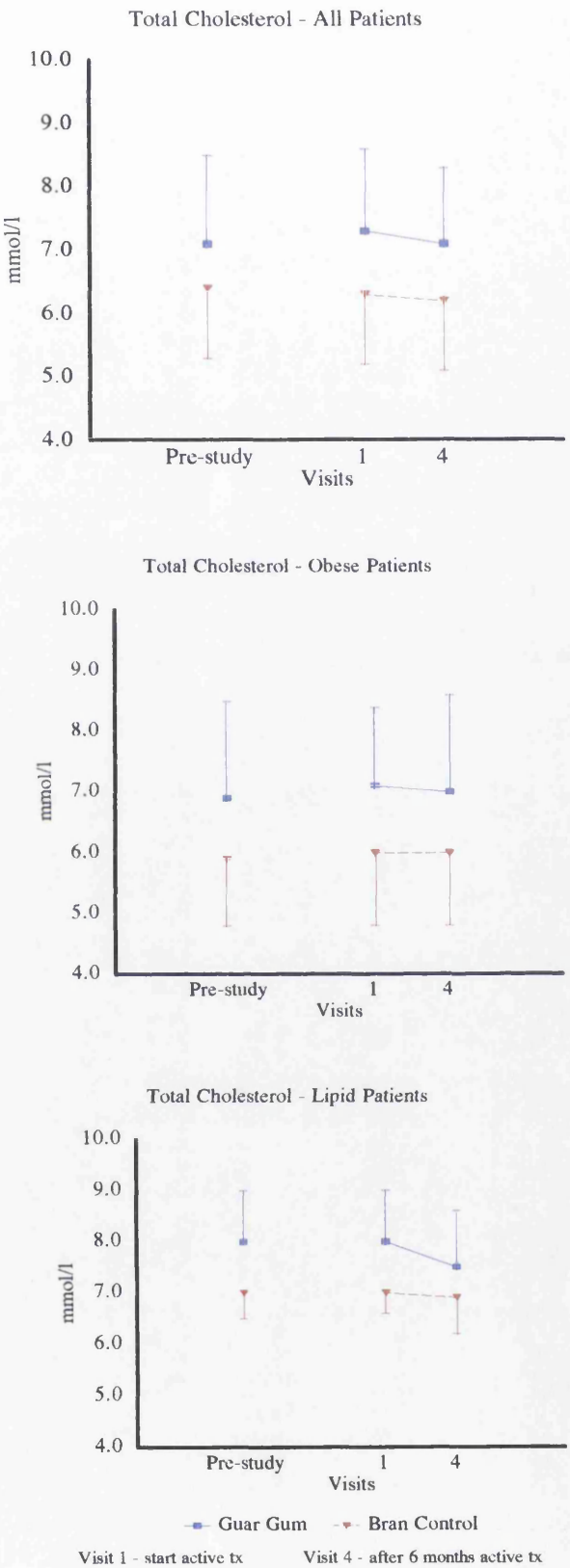


Table 6.5. Lipid values initially (after 1 month bran control) and after 6 months of treatment.

ALL PATIENTS	**Initial**	**6 Months**
Triglycerides (mmol/l)		
Guar Group	2.1 ±1.0	2.2 ±0.9
Bran Control Group	1.7 ±0.9	1.7 ±0.9
Total cholesterol (mmol/l)		
Guar Group	7.3 ±1.3	7.1 ±1.2
Bran Control Group	6.3 ±1.1	6.2 ±1.1
HDL-cholesterol (mmol/l)		
Guar Group	1.3 ±0.3	1.3 ±0.3
Bran Control Group	1.4 ±0.5	1.5 ±0.5
LDL-cholesterol (mmol/l)		
Guar Group	5.2 ±1.2	5.1 ±1.1
Bran Control Group	4.3 ±0.9	4.3 ±1.0
VLDL-cholesterol (mmol/l)		
Guar Group	0.8 ±0.5	0.8 ±0.4
Bran Control Group	0.6 ±0.3	0.6 ±0.2
OBESE PATIENTS	**Initial**	**6 Months**
Triglycerides (mmol/l)		
Guar Group	2.3 ±1.0	2.4 ±0.9
Bran Control Group	2.1 ±1.0	2.0 ±0.9
Total cholesterol (mmol/l)		
Guar Group	7.1 ±1.3	7.0 ±1.3
Bran Control Group	6.0 ±1.2	6.0 ±1.2
HDL-cholesterol (mmol/l)		
Guar Group	1.3 ±0.3	1.3 ±0.3
Bran Control Group	1.3 ±0.5	1.4 ±0.5
LDL-cholesterol (mmol/l)		
Guar Group	4.9 ±1.1	5.0 ±1.2
Bran Control Group	4.0 ±1.0	4.0 ±1.0
VLDL-cholesterol (mmol/l)		
Guar Group	0.9 ±0.5	0.9 ±0.5
Bran Control Group	0.7 ±0.3	0.6 ±0.2
LIPID PATIENTS	**Initial**	**6 Months**
Triglycerides (mmol/l)		
Guar Group	2.0 ±0.8	1.9 ±0.9
Bran Control Group	1.4 ±0.7	1.4 ±0.4
Total cholesterol (mmol/l)		
Guar Group	8.0 ±1.0	7.5 ±1.1
Bran Control Group	7.0 ±0.4	6.9 ±0.7
HDL-cholesterol (mmol/l)		
Guar Group	1.4 ±0.3	1.4 ±0.3
Bran Control Group	1.6 ±0.5	1.7 ±0.4
LDL-cholesterol (mmol/l)		
Guar Group	5.8 ±0.9	5.4 ±0.9
Bran Control Group	4.9 ±0.5	4.9 ±0.6
VLDL-cholesterol (mmol/l)		
Guar Group	0.8 ±0.5	0.8 ±0.5
Bran Control Group	0.5 ±0.3	0.5 ±0.2

Table 6.6. Reported adverse effects of treatment - patients enrolled into active treatment phase.

Guar

Patient number	Adverse Effects
102	none reported
104	increased frequency of bowel motions
108	slight increased frequency of diarrhoea
109	increase in abdominal cramping if took 3 sachets/day
112	diarrhoea and abdominal pain, diagnosed episode of gastroenteritis
203	increased bowel frequency and flatulence, thirst and nausea
204	diarrhoea with 3 sachets/day
209	none reported
210	"turns stomach at times"
211	none reported
301	increased frequency of bowel motions
303	increased indigestion with 3 sachets/day, abdominal cramp and constipation
310	none reported

Bran Control

Patient number	Adverse Effects
103	none reported
107	slight change in bowel habits
110	none reported
111	increased frequency of bowel motions
202	none reported
205	skin rash after 10 days of increasing dose, resolved once treatment stopped
206	none reported
207	none reported
208	improved previous problem with constipation
212	increased flatulence, episode gastroenteritis visit 3, indigestion visit 4
302	increased frequency of stools
304	none reported
305	none reported
307	depression, swollen ankles, nausea, vomiting
309	some tiredness at visit 2 with decreased frequency of bowel motions
311	increased hunger

Table 6.7. Maximum dose attempted by each patient during active treatment phase.

Guar

Patient number	Maximum dose
102	3 sachets/day
104	3 sachets/day
108	3 sachets/day
109	2 sachets/day
112	1 sachet/day
203	2 sachets/day
204	2 sachets/day
209	1 sachets/day
210	3 sachets/day
211	2 sachets/day
301	3 sachets/day
303	3 sachets/day
310	2 sachets/day

Bran Control

Patient number	Maximum dose
103	3 sachets/day
107	3 sachets/day
110	3 sachets/day
111	3 sachets/day
202	3 sachets/day
205	2 sachets/day
206	3 sachets/day
207	3 sachets/day
208	3 sachets/day
212	3 sachets/day
302	3 sachets/day
304	3 sachets/day in 2 doses
305	3 sachets/day
307	1 sachet/day
309	3 sachets/day
311	3 sachets/day

Table 6.8. Reasons for stopping treatment or poor compliance during active treatment phase and first month of bran control study.

Guar

Patient number	Reason given
102	Stopped after visit 3, difficult to take
104	Stopped after visit 2, fractured bone in foot-unable to get around
108	stopped before visit 2, difficult to mix with food
112	stopped several days after visit 1
201+	stopped 2 weeks after visit 2 due to increased bowel motions and diarrhoea
203	stopped after visit 3, increased thirst and nausea
209	failed to attend visit 2
211	stopped after visit 2, unable to tolerate in food

Bran Control

Patient number	Reason given
101++	stopped after episode of nausea and vomiting 2 weeks before visit 3
205	stopped 10 days after visit 1, skin rash
206*	taking sachets "as he minds", difficulty taking it regularly
207*	intermittently stopped treatment, forgot to take them on holiday
307	depression, swollen ankles, nausea, vomiting 3 weeks after visit 1

Stopped during bran control period

Patient number	Reason given
101(R)	never returned for follow-up
109(R)	found bran control difficult to mix with food, it "sickened" her
204(R)	frequent bowel motions, some rectal bleeding
206(R)	not attend for visit 1
211(R)	decided didn't wish to participate in a clinical trial
308(R)	developed indigestion and mild headache
312(R)	unable to tolerate control, found it unpalatable
-----	decided didn't wish to participate in a clinical trial

\+ did not return for follow-up, not included in analysis.
++ patient's data not included in analysis, GP had prescribed thiazide.
* poor compliance.

month active treatment phase. Initial power calculations indicated that it had 92% power to detect a 1 mmol/l change in total cholesterol, 97% power to detect a one standard deviation change in weight, and 97% power to detect a one standard deviation change in supine systolic and diastolic pressure. Unfortunately, due to the high incidence of side effects and poor compliance, the study, analysed on an intention-to-treat basis, had 81% power to detect a 1 mmol/l change in total cholesterol, 61% power to detect a one standard deviation change in weight, and 76% power to detect a one standard deviation change in supine systolic and diastolic pressure.

Changes in total cholesterol in the hyperlipidaemic guar treatment group, although not significant when compared with the changes in the bran control group, are in keeping with the significant changes reported by other randomised controlled studies (Khan et al 1981, Simons et al 1982, Tuomilehto et al 1983, Kirsten et al 1985, Landin et al 1992, Vuorinen-Markkola et al 1992). In addition, the patients recruited to this study had been on a low cholesterol/low fat and high dietary fibre diet for more than 6 months prior to entering the study, as had about half of the positive guar studies previously cited (Simons et al 1982, Tuomilehto et al 1983, Kirsten et al 1989).

In contrast, Lalor et al showed significant reductions in cholesterol only in a sub-group of hyperlipidaemics with total cholesterol > 6.5 mmol/l (Lalor et al 1990). Of these more controlled, rigorous guar studies, Tuomilehto's all female study showed no significant reduction in total cholesterol despite the population being hyperlipidaemic (Tuomilehto et al 1980). The lack of change in McIvor's guar granola bar studies may well have been due to the guar preparation used and the fact that both study populations had normal cholesterol values initially (McIvor et al 1985, McIvor et al 1986).

The lack of change in body weight in this study is also in keeping with most of the other studies of the effectiveness of guar in obese individuals (Simons et al 1982,

Lalor et al 1990, Landin et al 1992). Again, in these other studies, only Tuomilehto's early study in 1980 demonstrated a 2.5 kg weight reduction in the guar group compared with 0.4 kg reduction in a placebo and 0.6 kg reduction in a no treatment group (Tuomilehto et al 1980).

The effect of guar on blood pressure has not been widely studied, although there has been work carried out on the effects of other forms of dietary fibre, with mixed results (Stasse-Wolthuis et al 1980, Wright et al 1979, Silman 1980, Fehily et al 1986). The effect of vegetarian diets on blood pressure has also been studied (Rouse et al 1984, Margetts et al 1985). Landin et al showed a significant reduction in both systolic and diastolic blood pressure after 6 weeks of guar in a normotensive population on no blood pressure lowering treatment (Landin et al 1992). These negative results in a treated group of hypertensives are in agreement with Wright's hypertensive group (Wright et al 1979) and Margett's normal population (Margett et al 1987). These last two studies used insoluble dietary fibre.

Twelve patients withdrew from the current study for reasons related to the trial treatment. There was no significant difference in the withdrawal rate between guar and the bran controls. Most studies described above, except Khan's in which the guar was in capsule form (Khan et al 1981), and which reported on side effects, noted a substantial number of participants reporting flatulence and increase frequency of bowel motions. These types of side effects are socially unacceptable and, therefore, limit the usefulness of guar preparations, even if more positive results had been found.

The place of more palatable forms of water soluble dietary fibre in the treatment of hyperlipidemia is being pursued. Jenkins et al published a cross-over study evaluating the addition of either soluble or insoluble forms of fibre to a low cholesterol/low fat diet in 43 volunteers. Total, LDL and HDL cholesterol were significantly lower when these individuals consumed the diet with additional soluble fibre. The diets were described as being 'well accepted'(Jenkins et al 1993), the

opposite reaction to guar of most of the subjects in this study.

6.6. Conclusions

In conclusion, the results from the current guar study and review of the literature indicate that lipid lowering is the only risk factor addressable by increasing dietary soluble fibre intake. There is little or no evidence to support effects on either weight or blood pressure.

Chapter 7. Hypertension to multiple risk intervention

7.0. Summary

A report of the impact of changing the emphasis of care in the nurse practitioner clinic from hypertension follow-up to multiple cardiovascular risk factor reduction is presented in this chapter.

7.1. Introduction

There was concern in the world of hypertension research with the realisation that lowering blood pressure did not have the efficacy anticipated, particularly in regards to coronary heart disease (CHD) mortality. In 1986 MacMahon et al compared the pooled mortality and morbidity results from nine randomised trials of anti-hypertensive drug treatment with the associated difference of an equivalent reduction in diastolic blood pressure in two large prospective, observational studies. The effect on stroke mortality was about 80% of predicted, but that for CHD mortality was only about 36% of predicted reductions. They postulated that this short fall may well have been influenced by other 'indicators of CHD risk' and/or the metabolic side effects of the anti-hypertensive drug treatment used in these trials (MacMahon et al 1986).

Weber, in reviewing 5 of these intervention trials, came to very similar conclusions (Weber, 1987), as did Reid in an editorial review in 1988 (Reid, 1988).

A subsequent meta-analysis, taking into account the more recent hypertension in the elderly trials' results, demonstrated that stroke rates in the treatment groups were reduced, in keeping with the potential predicted by the observational studies. However, the coronary heart disease mortality reductions were less than predicted, as previously found (Collins et al 1990).

7.1.1. Multiple risk factor intervention

The epidemiological evidence, as reviewed in Chapter 1, indicates that there is a synergistic effect on mortality of increasing the number of risk factors, ie. that it is more than additive, in women (Isles et al 1992), as well as in men (Kannel et al

1986, Shaper et al 1986, Isles et al 1992). Results from community surveys of risk factors over time indicate that changes in risk factor levels parallel ischaemic heart disease rate changes in general populations (Nissinen et al 1987, Sigfusson et al 1991).

The few large, prospective trials of community and high risk group multiple risk factor intervention have failed to show a consistent, significant impact on cardiovascular mortality. The WHO European Trial of Multifactorial Prevention of Coronary Heart Disease found no mortality differences between the intervention and control groups but did determine that the benefit of the interventions were significantly related to the extent which risk factors were changed (WHO European Collaborative Group 1986). Nor were there significant differences found in the Göteborg multifactor primary prevention trial (Wilhelmsen et al 1986).

The results from MRFIT in the United States and the Finnish Multifactorial Primary Prevention of Cardiovascular Diseases in Middle-aged Men Trial were equally disappointing (MRFIT Research Group 1990b, Strandberg et al 1991). Only a post-hoc analysis of the men who entered the MRFIT with diastolic blood pressure > 100 mmHg on no anti-hypertensive drug treatment showed significant CHD and all cause mortality reductions in the special intervention compared to the usual care group (MRFIT Research Group 1990a).

7.1.2. Cardiovascular risk factors in the nurse practitioner hypertension clinic

High levels of cardiovascular risk factors had been noted in the Stobhill cohort (Chapter 3). Unfortunately, there was only limited success in dealing with most of them in the context of a hypertension follow-up clinic. A review of 175 patients who were continuous attenders for the first 4 years of follow-up, revealed statistically significant improvement in blood pressure control. At 4 years, 78% had systolic blood pressures within 10 mmHg of their target levels, and 93% had diastolic blood pressure within 5 mmHg of their target levels. There was also a statistically significant decrease in the percentage of males who reported that they smoked

(Curzio et al 1987).

Unfortunately, body weight and the percentage of female smokers did not change. In addition, serum cholesterol and glucose increased from the first to the fourth year. These increases appeared to be limited to those patients taking a thiazide diuretic alone or in combination with other anti-hypertensive drug treatment (Table 7.1) (Curzio et al 1987).

Of those patients with a cholesterol measurement recorded on the database, 46.7% of the patients had values > 6.5 mmol/l, which is the level above which both the British Hyperlipidaemia Association (Shepherd et al 1987) and the European Atherosclerosis Society (EAS) (EAS Study Group 1987) recommend 'action'.

At this time then, the clinic was successful at doing what it set out to do, ie. control of blood pressure, but was far less so in dealing with other cardiovascular risk factors. There was now a need to address the other major known cardiovascular risk factors vigorously, as current knowledge indicated that the greatest benefit in multiple risk factor intervention appeared to be in those at higher risk.

7.2. Methods

Starting in 1987, a change in emphasis and focus within the clinic was instituted and the title was changed from 'Hypertension' clinic to 'Cardiovascular Risk Factor' clinic. At each visit, patients were reminded of the status of their other cardiovascular risk factors in addition to their blood pressures. The concept of 'overall cardiovascular risk' was introduced, and patients advised as to whether they were at more or less risk due to the level of their risk factors. The additive nature of having more than one cardiovascular risk factor was included in the discussions. The patient information card given to every patient and updated after each clinic visit was revised to include weight and total cholesterol values (Figure 7.1).

Blood pressure, compliance to anti-hypertensive and lipid lowering drug regimens continued to be monitored. Target blood pressures were still used and at times further individualised based on overall risk, ie. a young male with polycystic

Table 7.1. Mean (±sd) of serum cholesterol and glucose measurements (mmol/l) in patient at years 1 and 4.

	Cholesterol			Glucose		
	1st year	**n**	**4th year**	**1st year**	**n**	**4th year**
All patients	6.42 ±1.28	127	6.63 ±1.31**	5.51 ±1.89	101	6.08 ±2.46**
No drug treatment	6.60 ±1.84	13	6.66 ±1.14	5.03 ±0.36	10	5.55 ±0.86
Thiazide+other drugs	6.51 ±1.21	52	6.93 ±1.14**	5.11 ±0.90	37	6.03 ±1.64**
ß blocker+thiazide	6.50 ±1.26	22	6.81 ±1.13*	5.03 ±0.72	18	5.61 ±1.44
ß blocker alone	6.37 ±1.05	15	6.09 ±1.12	5.16 ±1.01	10	5.45 ±0.71
Thiazide stopped	5.97 ±0.87	23	6.00 ±0.9	5.69 ±1.60	15	5.70 ±1.22

* $p<0.05$
** $p<0.01$

Figure 7.1. Patient information card for the Cardiovascular Clinic.

To the patient:

1. Keep this card with you and bring it to the clinic.
2. Show it to your family doctor when you attend his surgery.
3. If you have an accident or enter hospital, show this card.
5. Bring your tablets each visit.
6. If this appointment is not suitable please write to the out-patient department for an alternative date.
7. If you have a question about your blood pressure that needs to be answered before your next appointment please feel free to telephone. (041-558-0111 ext 3087)

To the doctor:

If the drug dose is changed, please write the new dose on the card in the appropriate column, together with any blood pressures recorded by you, on the line below the next appointment date.

Further information or assistance in management can be obtained from:
Prof. Reid, Dr. Elliott or the Cardiovascular Clinic at Stobhill General Hospital
(041-558-0111 Ext. 3087)

83-386-22

Stobhill General Hospital

Cardiovascular Clinic

Information Card

Name _____

Address _____

_____

Hospital No. _____

Please carry this card with you

Name of family doctor

Dr. _____

MEDICATION and DOSE

Date	Cholesterol	Weight	BLOOD PRESSURE This Visit					
			Lying	Standing				

kidneys would have a target of 135/85.

The impact of increased weight on blood pressure had previously been stressed with obese patients, ie. those patients having BMIs > 30. This strategy continued, and the contributing role which obesity has in overall cardiovascular risk communicated. The patient dietary information as previously described in Chapter 2, was also continued.

Smoking status was reviewed on at least an annual basis. Identified smokers, were now strongly encouraged to stop smoking, and the impact of smoking on overall cardiovascular risk was emphasised. The pamphlet 'SO YOU WANT TO STOP SMOKING' (Scottish Health Education Group 1986) which describes a method of stopping smoking, was given to each smoker.

Patients with cholesterol values > 6.5 mmol/l were invited to participate in the Cholesterol/Diet Study (see Chap 5). For those who declined or were already on lipid lowering medication, their diets were reviewed. Advice was given and/or followed-up by the clinic nurse practitioners. Those already receiving lipid lowering medication or with cholesterol values greater than 8.0 mmol/l were given Diet II (Figure 5.2). Those who had not previously been on a lipid lowering diet, and whose cholesterol was between 6.5 and 8.0 mmol/l, were given Diet I (Figure 5.1). These diet sheets were devised by the Stobhill Dietetics Department and were also used in the Cholesterol/Diet study described in Chapter 5. At subsequent visits, diet was reviewed and difficulties discussed. If patients had particular difficulty or were diabetic, they were referred to the hospital dietitians for specialist advice. Patients with borderline cholesterol values, ie. between 6.0 and 6.5 mmol/l, were given advice regarding a 'healthy diet' and provided with guidelines developed by the Good Hearted Glasgow programme (Figure 7.2).

Total cholesterol was evaluated in relation to the levels at which 'no action' and 'action' has been recommended by the British Hyperlipidaemia Association (Shepherd et al 1987) and the European Atherosclerosis Society (Study Group 1987).

Figure 7.2. Good Hearted Glasgow 'Healthy Eating' diet sheet (text only).

HEALTHIER EATING

Many of the modern diseases, including heart disease, are partly caused by faulty diet. Nearly all the experts agree that the average diet contains too much fat and sugar and not enough fibre. The following are suggestions for improvement:

1. CUT DOWN ON FAT

- avoid frying. Grill instead and let all the grease drain away.
- use less butter and margarine. Cut thicker slices of bread and spread the butter or margarine thinly.
- Try a low fat spread.
- Go easy on cakes, pastries and biscuits - many are surprisingly rich in fat, as well as sugar.
- Trim fat off meat. Look out for lean cuts.
- Make more use of fish and chicken.
- Save on cream, which is high in fat, serve natural yogurt instead, with fruit, salads, etc.
- Try semi-skimmed milk, instead of whole milk.
- Use a cheese which is lower in fat e.g. Edam, Camembert, Cheese Spread, Processed Cheese, or the new low fat 'Cheddar' type. Cottage cheese and skimmed milk are very low in fat.

Lack of fibre not only causes constipation, but it may be associated with other bowel disorders.

2. INCREASE FIBRE

- Eat more bread, especially wholemeal. All bread contains fibre, but wholemeal bread contains three times as much fibre as white bread.
- Eat more potatoes, but don't cook with fat (e.g. chips)
- Try more vegetable based dishes. Peas and beans can be substituted for part of the meat in a dish. This increases the fibre and reduces the fat.
- Choose a high fibre breakfast cereal e.g. muesli. 'Bran' cereals have a high fibre content. Avoid adding sugar.

To sum up, replace sweet and fatty foods, e.g. cakes, pastries, biscuits, chocolate, fizzy drinks and sweets with more bread, potatoes, fruit and vegetables.

Good Hearted
Glasgow

Thus those with cholesterol ≤ 5.2 mmol/l, > 5.2 mmol/l ≤ 6.5 mmol/l and > 6.5 mmol/l were tabulated for each year and compared.

Alcohol intake was reviewed at least annually. Males reporting a greater than 200 gms of alcohol intake per week (20 units), were advised to reduce consumption to 200 gms or less and females to less than 140 gms (14 units) per week. If gamma GT was greater than 40 iu/l at annual review, alcohol intake was reviewed, and the above advice reinforced. The pamphlet 'That's the Limit' was used to support the advice given by the nurse practitioners (Health Education Authority 1886).

Data analysis was undertaken using Quattro Pro version 3 and version 4 as well as MINITAB version 8 for the personal computer. Means, standard deviations and percentages were analysed by one-way ANOVA, paired t-test and chi-square analysis as appropriate. As patients were not randomised, this is not a comparison of interventions but audit.

7.3. Results

The analysis group consisted of the 551 patients who had attended the clinic from 1987 or before, and who were still attending at the beginning of September 1989. This permitted comparison of their risk factors and blood pressures between 1987 on the old regimen and 1989 on the new regimen. Patients enrolled after 1987 or who were no longer attending by 1989, were not included.

This sub-population included 250 males and 301 females, with an average age of 53.8 years. The males (average age of 54.9 years) were slightly older than the females (average age of 52.8 years) and the distribution of age by sex is presented in Figure 7.3.

There was no difference in average blood pressures over the 2 years of change to risk factor follow-up from hypertension follow-up. Mean values for initial, 1987 and 1989 supine blood pressures with standard deviations are shown in Figure 7.4. and the percentage of patients with varying degrees of control for each time point are illustrated in Figure 7.5. for systolic blood pressure and in Figure 7.6. for diastolic blood pressure. There was an improvement in the percentage of patients with systolic

Figure 7.3. Distribution of age by sex.

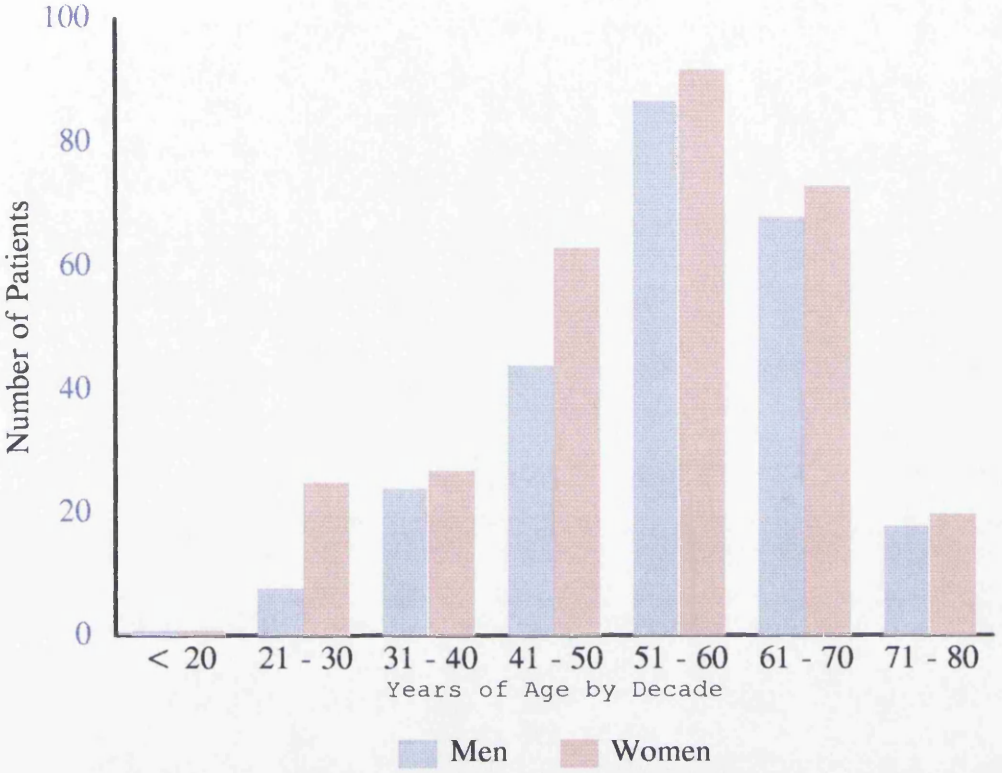


Figure 7.4. Initial, 1987 and 1989 supine blood pressure means and standard deviations.

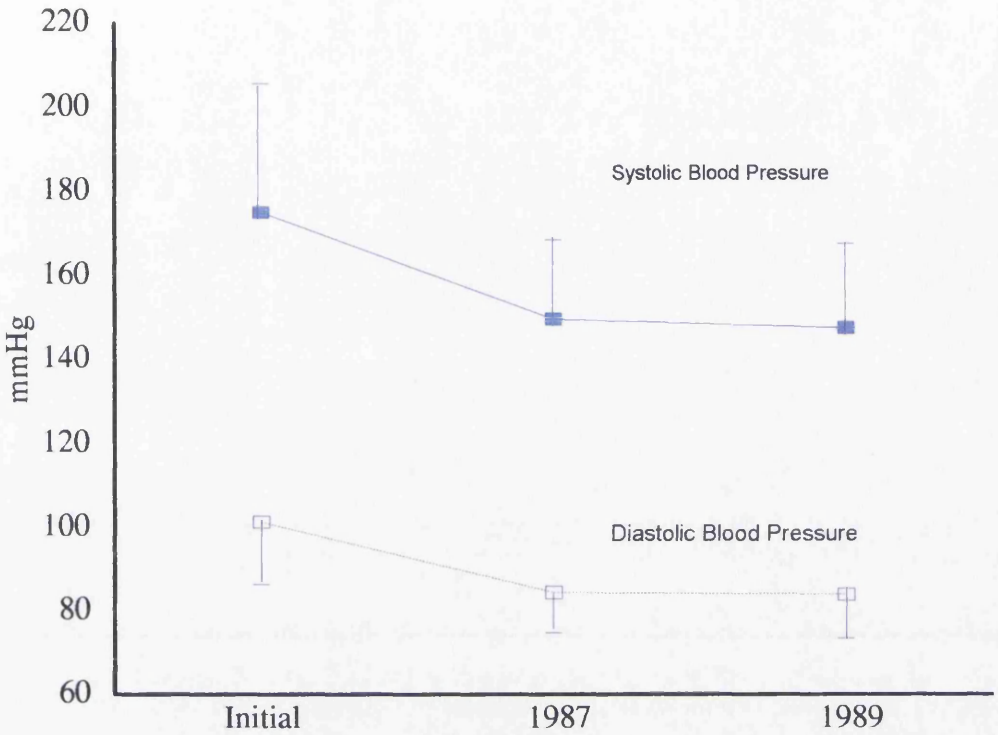


Figure 7.5. Initial, 1987 and 1989 supine systolic blood pressure distributions.

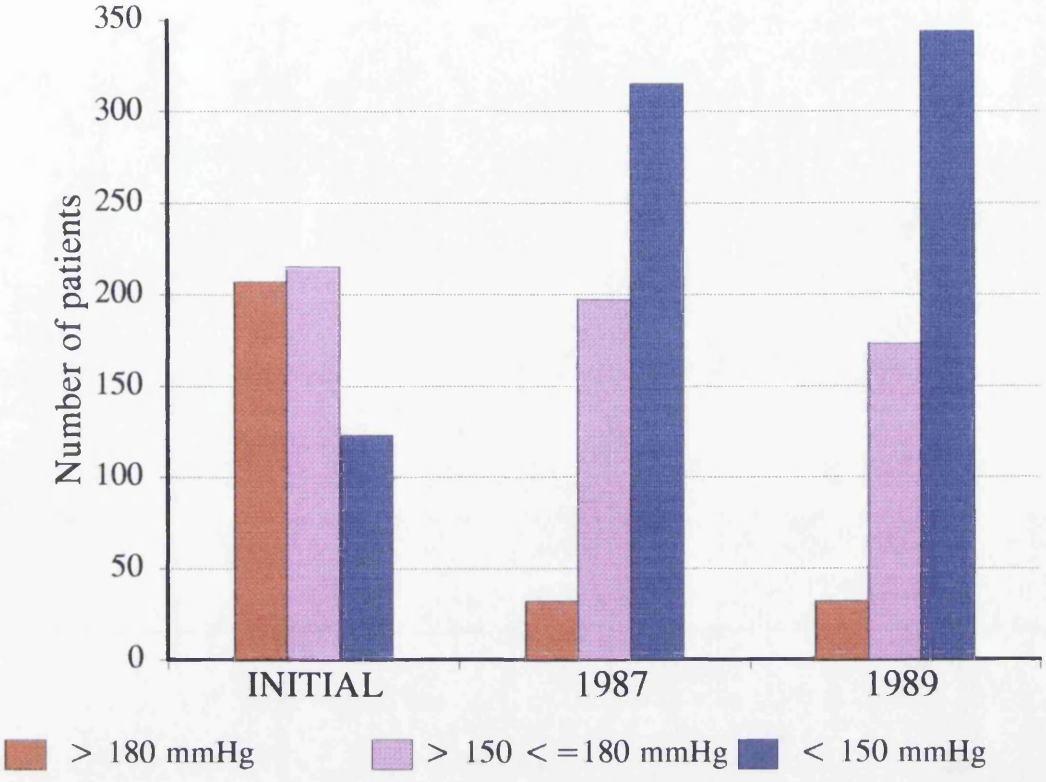
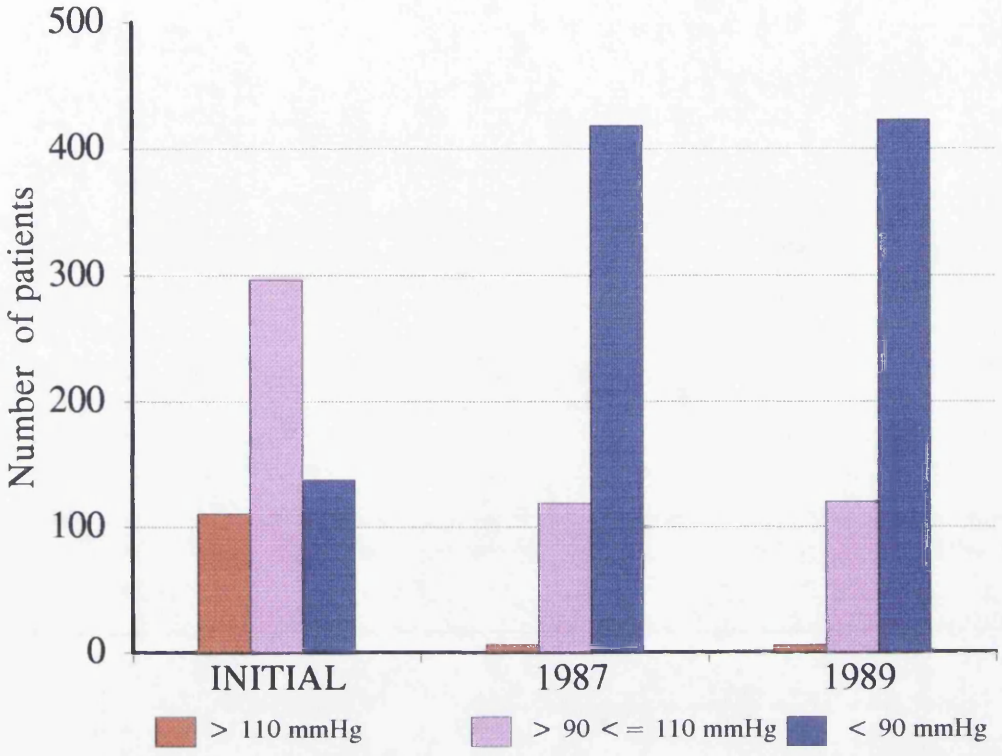


Figure 7.6. Initial, 1987 and 1989 supine diastolic blood pressure distributions.



blood pressure within 10 mmHg of their target pressures which increased from 68% to 73%, and also in the percentage within 15 mmHg, which changed from 77.3% to 81.7%. There was little change in the percentage within 5 mmHg of target diastolic pressure which remained satisfactory at 90% and 89% respectively, or in the percentage of those within 10 mmHg of target diastolic blood pressure which was 95.7% and 93.7% respectively.

The greatest reduction in supine systolic blood pressure (15 mmHg) between 1987 and 1989 was seen in patients whose systolic blood pressure was in the upper quartile in 1987 ($p<0.001$). This reduction was significantly different from the reduction in the third quartile and the increases seen in quartiles 1 and 2. A similar profile was observed for supine diastolic blood pressure in which all the quartiles were significantly different ($p<0.001$) (Figure 7.7). Thus those with the highest blood pressures experienced the greatest reductions in blood pressure.

Overall, average weight changed very little, decreasing by 0.4 $\pm$5.3 kg between 1987 and 1989 in the total population. However, 1987 BMI values did show a statistically significant difference in weight reduction between 1.3 kg loss on average within the very obese group (BMI > 30) and the 0.3 kg gain in the desirable weight range group (BMI 20.00 - 24.99). This was also the case between the 1.0 kg loss in the mild-moderately obese group (BMI 25.00 - 30.00) and the 0.3 kg gain in the desirable weight group ($p<0.001$) by one-way analysis of variance with Tukey post-hoc analysis. This is summarised using 95% confidence intervals in Figure 7.8.

The percentage of patients who identified themselves as smokers when reporting smoking/non-smoking status for both years, decreased marginally from 30.6% to 29.5%. In total, 15 smokers (9.3%) reported that they had stopped smoking, and 43 reported a decrease in the number of cigarettes smoked per day. Unfortunately, 9 patients resumed smoking and 26 reported an increase in the number of cigarettes smoked per day. Of the 161 identified smokers in 1987, 36% reported they had either stopped smoking or decreased the number of cigarettes

Figure 7.7. Mean changes in blood pressure by 1987 quartiles.

Systolic Blood Pressure $p<0.001$

Quartile

```
LEVEL  N      MEAN     STDEV  ---+---------+---------+---------+---
1      140     6.99     15.18                                (---*--)
2      136     2.22     14.49                           (---*--)
3      131    -3.45     16.67                      (---*--)
4      135   -14.67     22.42   (---*--)
                               ---+---------+---------+---------+---
POOLED STDEV =    17.45        -16.0       -8.0        0.0         8.0
```

Confidence Intervals for Tukey Multiple Comparisons

Quartile	1	2	3
2	-0.62 10.16		
3	5.00 15.89	0.19 11.15	
4	16.26 27.06	11.45 22.33	5.72 16.71

Diastolic Blood Pressure $p<0.001$

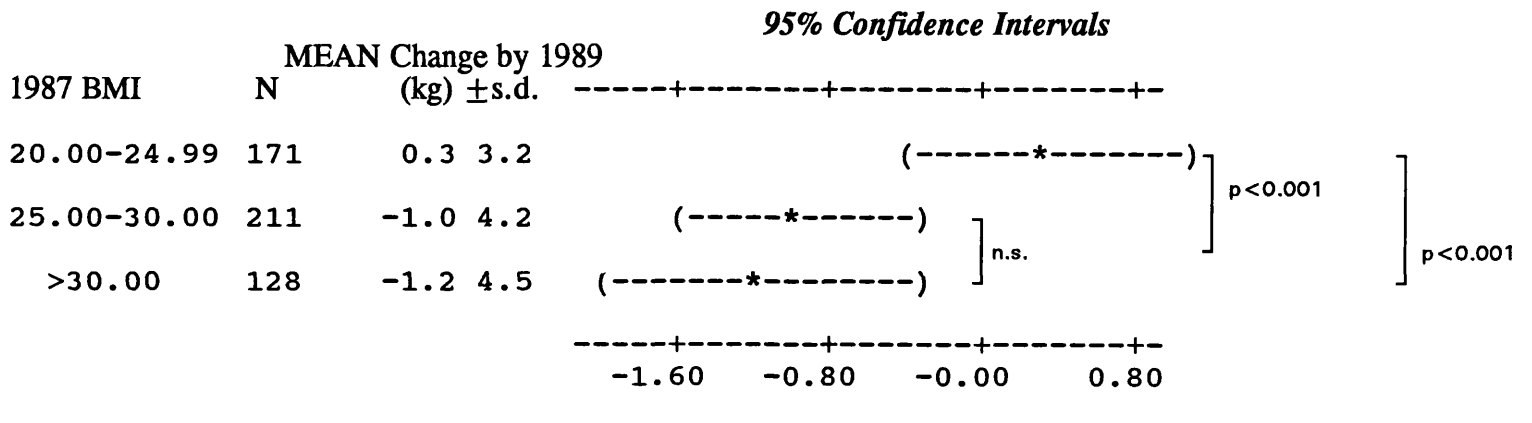
Quartile

```
LEVEL  N      MEAN     STDEV  ---------+---------+---------+-------
1      137    5.657    10.852                                (--*---)
2      142    1.458     8.276                          (--*--)
3      137   -1.978     8.138                    (--*--)
4      126   -7.548    12.284  (---*--)
                               ---------+---------+---------+-------
POOLED STDEV =    9.976                -5.0        0.0         5.0
```

Confidence Intervals for Tukey Multiple Comparisons

Quartile	1	2	3
2	1.133 7.266		
3	4.541 10.729	0.369 6.502	
4	10.044 16.365	5.871 12.139	2.409 8.730

Figure 7.8. Means and standard deviations and 95% Confidence Intervals for changes in weight by 1987 BMI grading.



smoked per day while 22% had either resumed smoking or increased the number of cigarettes smoked per day. There was a net reduction of 6 smokers (3.7%) between the two years.

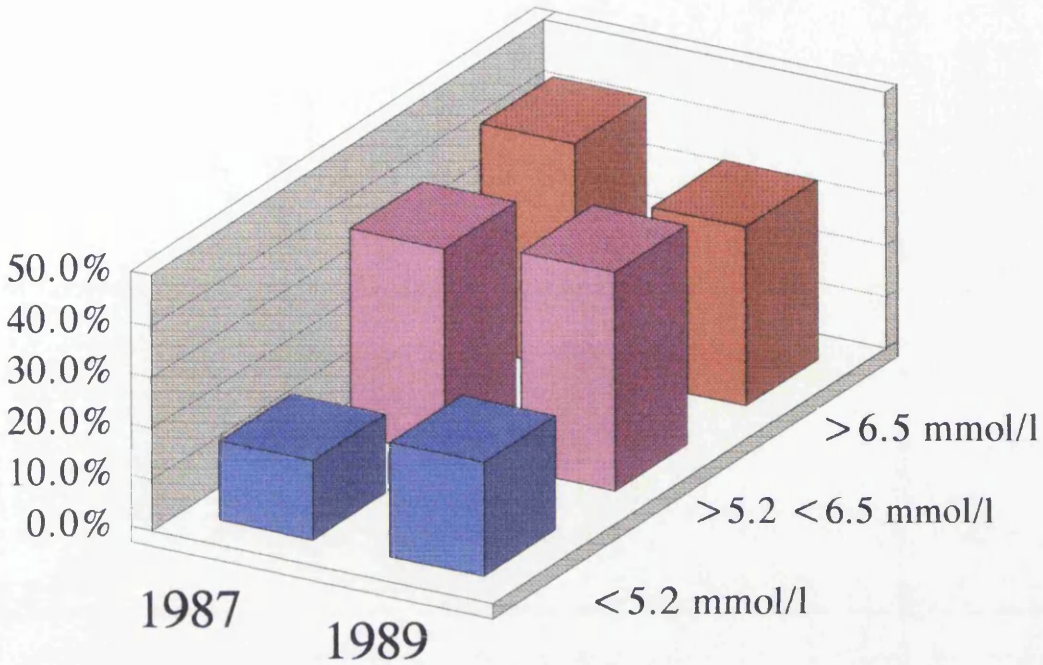
Total plasma cholesterol decreased significantly from 6.5 $\pm$1.3 mmol/l in 1987 to 6.3 $\pm$1.2 mmol/l in 1989 ($p < 0.001$). The shift in the proportion of patients with values > 6.5 mmol/l, > 5.2 and $\leq$ 6.5 mmol/l and $\leq$ 5.2 mmol/l along with cumulative distributions for each year are given in Figure 7.9. Chi-square analysis of the proportional shift demonstrated it to be statistically significant ($X^2=12.36$, df=2, $p<0.005$). The change in cholesterol was also evaluated by comparing the average reduction between the quartiles, and as with blood pressure and weight, those in the upper quartiles experienced significant reductions ($p<0.001$) (Figure 7.10). The percentage differences in the cholesterol reductions between quartiles are +1.8%, -2.3%, -7.0% and -11.5%.

There were no differences in reported alcohol use (Table 7.2). Gamma GT values are also given in the table for all patients with values in 1987 and 1989 as well as for those patients with reported alcohol intake > 200 gms/week (20 units). There was no correlation in either year between reported levels of alcohol intake and Gamma GT values ($r=0.2$, both years).

Changes in the use of diuretics in this population are shown in Table 7.3. Also noted is the change in diuretic use in those individuals with total plasma cholesterol > 6.5 mmol/l. There is a statistically significant reduction in the use of diuretics overall ($X^2=4.875$, df=1, $p<0.05$) and especially in those individuals with cholesterol > 6.5 mmol/l ($X^2=15.1$, df=1, $p< 0.0005$). For comparison, the use of atenolol, which changed very little over this time course, is shown.

In conclusion, the risk factor changes seen after two years of a multiple risk factor intervention approach are summarised in Table 7.4 with the 1987 values compared with 1989.

Figure 7.9. The shift in the distribution of total cholesterol between 1987 and 1989.



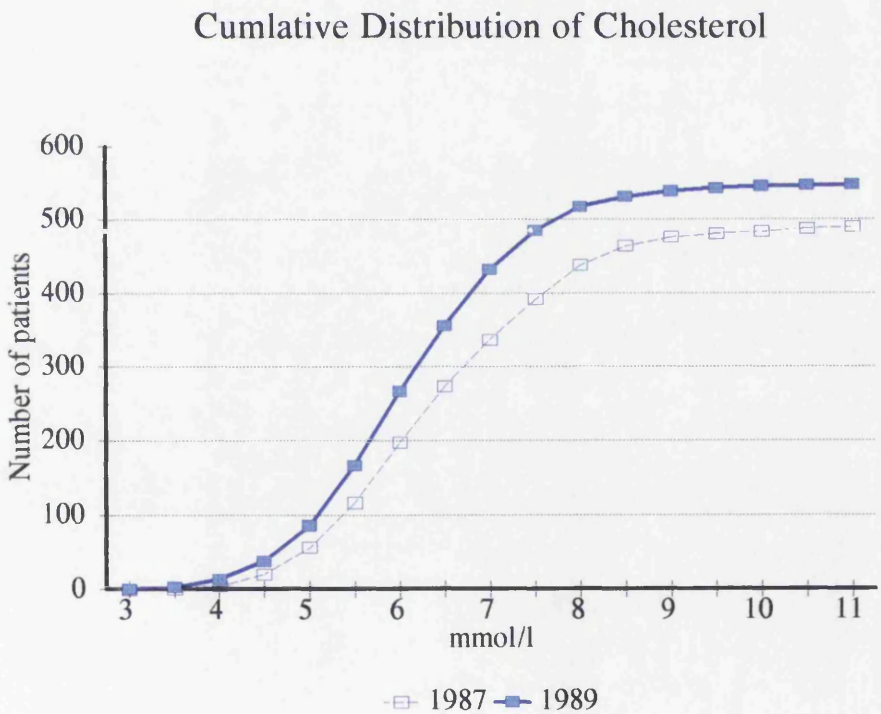
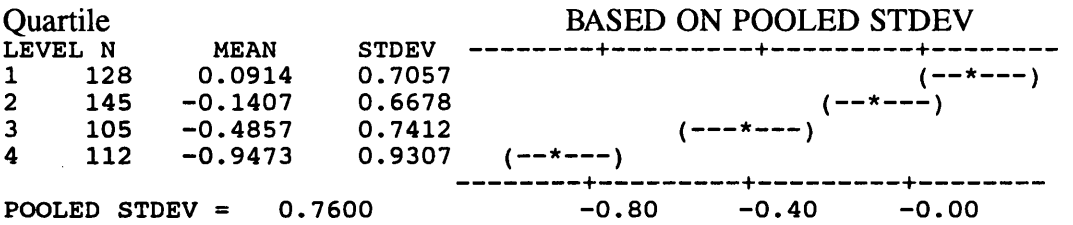


Figure 7.10. Mean changes in cholesterol by 1987 quartiles.



Confidence Intervals for Tukey Multiple Comparisons

Quartile	1	2	3
2	-0.0045 0.4687		
3	0.3202 0.8340	0.0950 0.5950	
4	0.7863 1.2911	0.5612 1.0520	0.1966 0.7266

Table 7.2. Changes in reported alcohol intake and gamma GT between 1987 and 1989.

	1987	**1989**
Percentage of patients reporting alcohol intake > 200 gms/wk (20 units)	9.5%	8.4%
Gamma GT (iu/l)	35 ±44	34 ±49
Gamma GT (iu/l) for those reporting >200 gms/wk (20 units)	60 ±43	62 ±88
Gamma GT (iu/l) for those reporting >200 gms/wk (20 units) in 1987	60 ±43	61 ±65

Table 7.3. Diuretic drug use in 1987 and 1989.

	1987	**1989**
Percentage of all patients prescribed diuretics	44%	37%*
Percentage of only those patients prescribed diuretics with cholesterol > 6.5 mmol/l	51%	33% **
Percentage of all patients prescribed atenolol	54%	53%

*$p < 0.05$
**$p < 0.001$

Table 7.4. Summary of risk factors for change in clinic emphasis.

	N=551	
	1987	**1989**
Blood pressure (mmHg)	150 ±19 84 ±10	148 ±20 84 ±10
Smokers	31 %	29 %
Alcohol intake > 200 gms/week (20 units)	9.5%	8.4%
% Gamma GT > 80 iu/l	8.2%	6.9%
BMI > 30	24 %	23 %
Cholesterol (mmol/l)	6.5 ±1.3	6.2 ±1.2 *
Cholesterol > 6.5 mmol/l >5.2 ≤6.5 mmol/l < 5.2 mmol/l	 44 % 40 % 15 %	 35 % 43 % ** 22 %

* $p < 0.001$
** $p < 0.005$ $X^2 = 12.36$, df=2

7.4. Discussion

This assessment demonstrates the feasibility of altering the emphasis of care in an outpatient nurse practitioner clinic setting. There was a small improvement in the percentage of patients with systolic blood pressure within 10 mmHg and 15 mmHg of their target pressures and no deterioration in the high level of diastolic blood pressure control in this population. Total plasma cholesterol significantly decreased as did the percentage of patients with values > 6.5 mmol/l, 34.9% of the population continued to have cholesterol values > 6.5 mmol/l. Weight decreased significantly in those with BMI > 30 in 1987. Unfortunately, there was no significant change in reported smoking habits or alcohol intake in those reporting more than 200 gms/week in 1987.

The greatest reductions in blood pressure, weight and cholesterol were observed in those in the highest quartile for each in 1987. This indicated that those at highest risk, are in fact those who are most able to reduce their risks through multi-factor intervention. There was a similar conclusion drawn in the British Family Heart Study (Family Heart Study Group 1994).

The overall population results are generally modest, but are better in some respects than reports of risk factor changes in other hypertensive populations, and are in keeping with the changes reported from controlled trials of multiple risk factor intervention, which also evaluated the effect on mortality. Comparison with all factors addressed in the nurse practitioner clinic is impossible as other studies focused on different combinations of factors. In addition the majority of the controlled trials have been conducted in middle-aged men.

However, it is interesting to consider the reports of clinical experience of risk factor change in other hypertension clinics. First, most reports note a substantial percentage of their populations with controlled blood pressure. In the Dalby, Sweden population, about 75% of the population had blood pressure within their targets of ≤160/95 mmHg for 40-59 year olds, ≤180/100 mmHg for 60+ year olds, and 5-10 mmHg lower for diabetics. All of these targets were higher than the ones used in the

nurse practitioner clinic. The cholesterol levels were not used for comparison with the Dalby control group until 1989. However, Lindholm did declare the need for full risk factor intervention in such populations (Lindholm, 1991).

Straznicky et al reported on 5 years of follow-up dealing with risk factors in the setting of an Australian hypertension clinic, in 131 men and women. A number of factors are compared with the nurse practitioner clinic values for comparable data, in Table 7.5. The Australians were heavier, smoked less and had lower cholesterols. The level of achieved diastolic blood pressure was similar, while more Australians stopped smoking, but there was a greater effect of dietary intervention in the nurse practitioner clinic. They concluded that the programme 'produced little evidence of improvement in risk factors...' despite a high proportion of patients having controlled blood pressure and decreasing the percentage of smokers by half (Straznicky et al 1991).

As for the controlled intervention trials, the Oslo Study interventions were dietary to lower serum cholesterol, and stop smoking advice. Initially risk factor levels were high in that mean cholesterol was 8.5 mmol/l in each group, and 79% were smokers (Hjermann et al 1981). These values are far higher than the 6.5 mmol/l average total serum cholesterol, and 30.6% smokers in the nurse practitioner clinic population. The resultant changes in the Oslo Study were greater than those that were achieved in the nurse practitioner clinic. Total serum cholesterol decreased by 13% in the Oslo intervention group compared with the control group during the 5 years. This is greater than the 5% reduction seen over 2 years in the nurse practitioner clinic. Smoking levels expressed as number of cigarettes smoked per man per day decreased by 45% in the Oslo Study intervention group. An equivalent calculation for the nurse practitioner clinic population yielded a reduction of 11% for the number of cigarettes smoked per person per day between 1987 and 1989.

The hypertensive population within the Primary Prevention Trial in Göteberg, Sweden were cared for in a specialist follow-up clinic staffed by a combination of

Table 7.5. Comparison of risk factors in an Australian outpatient hypertension clinic and the nurse practitioner clinic.

	Australian Clinic N = 131	**Nurse Practitioner Clinic** N = 551
Entry diastolic blood pressure (mmHg)	101 ±17	102 ±15
Last visit diastolic blood pressure (mmHg)	82 ±10	84 ±10
Percentage with diastolic blood pressure ≤ 90 mmHg	83%	77%
Total cholesterol (mmol/l) in 1987	6.0 ±1.1	6.5 ±1.3
Total cholesterol (mmol/l) in 1989	6.1 ±1.1	6.3 ±1.2
Percentage continuing to smoke cigarettes at last visit	9.9%	29.5%
Percentage above desirable weight range BMI (20.00 - 24.99)		
Men	88.7%	67.6%
Women	85.3%	56.8%
Mean weight reduction (kg)	1.4	0.4

nurses and physicians. Patients were advised to stop smoking and lower the content of saturated fat in their diets if total cholesterol was > 6.7 mmol/l. The blood pressure target used by this group was < 160/95 mmHg. A summary of blood pressure, cholesterol and smoking in this population in comparison with the nurse practitioner clinic population is given in Table 7.6. After 10 years, blood pressure and cholesterol levels were similar to those achieved at two years in the nurse practitioner clinic, and they achieved a significant reduction in the percentage of smokers (Samuelsson, 1985). As previously noted, this sub-group demonstrated a significant reduction in cardiovascular and coronary morbidity in those individuals who were able to achieve a substantial reduction in both blood pressure and serum cholesterol (Samuelsson et al 1987).

In the Multiple Risk Factor Intervention Trial (MRFIT) the methods used to address each risk factor were similar to ones employed here: drug treatment to lower blood pressure, dietary advice to lower serum cholesterol, and stop smoking advice to reduce the number of smokers. Reductions in the MRFIT were greater in the special intervention group. A summary of the MRFIT intervention group's results at 2 years and nurse practitioner clinic data for the same factors are given in Table 7.7 (MRFIT Research Group 1982). The level of achieved blood pressure and total cholesterol were similar for both, but MRFIT had a slightly higher percentage of patients continuing to smoke.

7.5. Conclusions

In conclusion the implementation of a multiple risk factor approach in a hypertension follow-up clinic did not adversely affect blood pressure control. This approach had a small but significant impact on hyperlipidaemia, but only a limited effect on obesity, despite a statistically significant reduction in weight for those with BMI > 30 in 1987. In addition, it was noted that those in the highest quartile of blood pressure, weight and total cholesterol experienced significant reductions in response to a change in emphasis of care from hypertension to multiple risk factor.

Table 7.6. Comparison of risk factors between hypertension follow-up clinic of Göteborg Primary Prevention Trial and the nurse practitioner clinic.

	Göteborg+ Clinic			Nurse Practitioner Clinic	
	Initially	5 yrs	10 yrs	Initially	2 yrs
Average Diastolic Blood pressure (mmHg)	106 ±13	91 ±9	89 ±8	102 ±15	84 ±10
Total serum Cholesterol (mmol/l)	6.6 ±1.2	------	6.2 ±1.5	6.5 ±1.2	6.2 ±1.3
Percentage Reporting Cigarette smoking	34%	------	24%	31%	30%

+(Samuelsson 1985)

Table 7.7. Comparison of risk factors between MRFIT Special Intervention Group at 24 months of follow-up and the nurse practitioner clinic.

	MRFIT+ N=5,995	**Nurse Practitioner Clinic** N=551
Average diastolic Blood pressure (mmHg)	83	84
Total serum Cholesterol (mmol/l)	6.2	6.2
Percentage reporting Cigarette smoking	35%	29%

+(Multiple Risk Factor Intervention Trial Research Group 1982)

Finally, this study has demonstrated the need for the development of alternative strategies to encourage patients to stop smoking, modify alcohol intake and lose weight, as well as the identification of additional methods for further reducing hyperlipidaemia.

Chapter 8. Final discussion and conclusions

8.0. Summary

A discussion of the impact of 8 years of nurse practitioner care is presented in this chapter as well as an assessment of the various cardiovascular risk factor reduction interventions investigated.

8.1. Introduction

The project has provided the opportunity to assess the impact of care provided by nurse practitioners with a computerised patient information system over an extended period of time in a Scottish urban setting. Nurse practitioner care was evaluated by determining the achieved level of blood pressure control each year and the results of cardiovascular risk factor interventions in Chapters 3 and 7, and, by comparison with patients enrolled in conventional hypertension clinics (CHC) in Chapter 4. In addition, the success or otherwise of a variety of cardiovascular risk factor interventions have been evaluated singly or in combination.

8.2. The nurse practitioner clinic

Although the major clinical trials in hypertension, including the HDFP (Robinson 1974), MRC mild hypertension trial (Barnes 1981), the Göteberg Primary Prevention Trial (Samuelsson 1985) and the MRC hypertension in the elderly trial (MRC Working Party 1992), have used nurses to care for patients and carry out the trials, few trials have been set up to evaluate the care of high risk individuals by nurses specifically or as a variable (Ramsay et al 1982, Watkins & Wagner 1982). However, a number of studies have looked at the health promotion role in general practice (Fullard et al 1984, Mant et al 1989, Robson et al 1989, OXCHECK Study Group 1994, Family Heart Study Group 1994).

This is one of the largest reported populations (1091 patients) to be followed by nurse practitioners. The few large population studies evaluating nurse practitioner care, have all been based in the community and for shorter durations of time (Runyan 1975, Abramson et al 1981). Many of the outpatient studies have been small without a

control group (Schulman & Wood 1972, Clark & Dunn 1976, Laurent 1980).

More patients continued to attend the nurse practitioner clinic after 4 years than conventional hypertension care (69% vs 35%), and there was more current relevant clinical data for each patient (Chapter 3). After 8 years, 65% of the patients enrolled in the nurse practitioner clinic continued to attend, and 53% of those had attended for 5 or more years. This is directly comparable to the rates observed in an Australian medical clinic (Straznicky et al 1991).

No other studies have been identified which have attempted to investigate the impact of nurse practitioner care on mortality. The study reported in Chapter 3 had limited power and showed no significant difference between the groups, but there were fewer deaths (25 vs 29), and fewer cardiovascular deaths amongst the patients attending the nurse practitioner clinic.

8.3. Computer based patient information system

Computer-based patient information systems are now commonplace. The original version of the Stobhill programme was one of the first microcomputer based programmes published to follow-up hypertensive patients (Kelman et al 1982). It has been followed by many others including one in Australia (Straznicky et al 1991). In the United Kingdom, only the DHSS Hypertension Care Computing Project (Beilin et al 1974), the Glasgow Blood Pressure Clinic (Glasgow Blood Pressure Clinic 1972) and the Aberdeen shared care scheme (Petrie et al 1985), all mainframe computer projects, have followed hypertensive patients longer.

The compact dataset has facilitated the collection of data. As seen in Chapter 4, smoking follow-up was virtually unavailable in the Conventional Hypertension Care group, whereas the completeness of information in the Nurse Practitioner Clinic was far greater than that reported for paper based systems. For example, Stern found that 56% of 2371 hypertensives cared for in general practice, had no record of each individual's smoking habit, 69% had no record of weight, and cholesterol was not reported on (Stern 1986).

8.4. Cardiovascular risk factor intervention

The greatest impact on cardiovascular risk factors in the nurse practitioner clinic was seen in those individuals with values in the highest quartile for blood pressure, weight and total cholesterol (Chapter 7). The effect of 'regression to the mean' in these patients cannot be ruled out totally, but the rise in the lowest quartile is less than half the reductions seen in the highest quartile for each variable. This is of particular importance, as these are the individuals who have the highest cardiovascular risk as shown by epidemiological surveys (Pooling Project Research Group 1978, Kannel et al 1986, Isles et al 1992, Law et al 1994) but who have also been shown to benefit most from intervention (Smith et al 1993).

The results of international studies of multiple cardiovascular risk factor interventions and their effects on mortality have been disappointing (MRFIT Research Group 1990, Miettinen et al 1985, WHO European Collaborative Group 1986). The impact of risk factor intervention in the nurse practitioner clinic is consistent with the reductions seen in these international controlled trials and are in keeping with the results obtained by other clinical groups (Straznicky et al 1991).

8.4.1. Blood pressure

The nurse practitioner clinic has been most successful at dealing with hypertension. Blood pressure was relatively easily controlled soon after referral to the clinic. This was true for those individuals enrolled during the first year, many of whom came from medical follow-up clinics, as well as those enrolled in subsequent years from general practice referrals (Chapter 3). The success in terms of blood pressure control exceeded that achieved by the Glasgow Blood Pressure Clinic in its early years (Johnston et al 1980). Blood pressure control is important as Isles et al and Bulpitt et al has shown that the achieved level of blood pressure predicts mortality outcome (Isles et al 1986, Bulpitt et al 1988).

Blood pressure control in the nurse practitioner clinic was better than conventional hypertension care offered within the Glasgow Blood Pressure Clinic at

one year for both systolic and diastolic blood pressure, and the significant difference in the degree of diastolic blood pressure control was still present after 4 years of follow-up for those patients continuing to attend (Chapter 4). Blood pressure control was better than that reported in Stern's review of management in general practice (Stern 1986).

Guar has no significant effect on blood pressure compared with a bran control, over a 6 month treatment period, in the hypertensives with or without hyperlipidaemia or obesity (Chapter 6).

There was no loss of blood pressure control with the change of emphasis in care from hypertension follow-up to multiple risk factor intervention. Indeed, a small improvement in the percentage of patients with systolic blood pressure within 10 mmHg of their target levels were noted (Chapter 7). These results are in keeping with those reported for the MRFIT intervention group (MRFIT 1982), the Göteborg Primary Prevention Trial (Samuelsson 1985), and the Medical Research Council's trial of treatment of hypertension in older adults (MRC Working Party 1992) as well as the clinical experience reported from Australia (Straznicky et al 1991) and Lindholm in Sweden (Lindholm 1991).

8.4.2. Weight

Average body weight did not significantly increase over time in the clinic, nor did it decrease (Chapter 3). There were positive reductions in weight in the severely obese (BMI >30). There was a mean loss over 4 years of 2.8 kg compared to a loss of 0.5 kg in the conventional hypertension clinic group (Chapter 4). A similar reduction in weight was found over the 6 months of the cholesterol diet study in which the group receiving intensive specialist low saturated, high polyunsaturated fat, high fibre diet counselling by dietitians lost significantly more weight (2.6 kg) than the non-intervention group's 0.5 kg (Chapter 5). There was no change in weight with 6 month treatment with Guar (Chapter 6).

A modest, but significant difference in weight reduction also occurred with the

change in emphasis from hypertension follow-up to multiple risk factor intervention. The obese sub-group (BMI > 30) had the greater reduction in weight of 1.3 kg on average, compared with the mild to moderate obese sub-group (BMI 25-30) with a weight reduction of 1.0 kg on average, while in contrast, the desirable weight sub-group (BMI 20-25) gained 0.3 kg on average (Chapter 7). These results are in keeping with clinical reports (Straznicky et al 1991).

8.4.3. Plasma total cholesterol

Plasma total cholesterol and glucose measurements were measured at least annually from 1985 and were always recorded in the database . An initial rise in both measurements over the first 4 years of attendance appeared to be associated with the long term use of thiazide diuretics (Chapter 7). These results stimulated further research studies and changes in care including the cholesterol diet study (Chapter 5), the Guar Gum study (Chapter 6) and the change in emphasis of care to multiple risk intervention (Chapter 7).

There was a change in plasma total cholesterol within the patients attending at the time of the change of emphasis to multiple risk factor intervention. This change was small in absolute terms (0.2 mmol/l on average), but it significantly shifted the distribution. The percentage of patients with cholesterol > 6.5 mmol/l decreased from 44% to 35%, and those with values < 5.2 mmol/l increased from 16% to 19%. In addition, the patients with cholesterols in the highest quartile in 1987, had reduced their cholesterols by 11.5% (Chapter 7).

However, there were only modest changes in cholesterol under the controlled conditions of the cholesterol diet study and these were significant in the 'advice' group only after 1 month, but not at 6 months. The changes in total cholesterol at entry into the study compared with the previous annual review value were at least as great as that which occurred within the study. Cumulative change from last annual review to the end of the 6 month intervention showed a 12% reduction in the Advice Group and a 7% reduction in the No Advice Group (Chapter 5).

Ramsay et al questioned the effectiveness of dietary intervention for hyperlipidaemia due to its limited impact (Ramsay et al 1991). However, this limited effect may be due to a dilution of risk when populations are analysed without special reference to evaluating quartile changes.

In the Guar study, the observed lipid lowering in the hyperlipidaemic group was non-significant. The limited power of the study was brought about by substantial withdrawals in both the bran 'run in' and active treatment phases, due to socially unacceptable side effects including flatulence and increased bowel motions (Chapter 6).

8.4.4. Smoking

Reported smoking levels decreased very slowly over time (Chapter 3). Changes in smoking behaviour, including a decrease in the number of cigarettes smoked and stopping, showed greater activity in the assessment made between years 6 and 8 (36% of smokers) with the change in emphasis of care (Chapter 7) than between years 4 and 5 of routine follow-up (23.1% of smokers). Unfortunately, the percentage of those resuming smoking or increasing the reported number of cigarettes smoked was greater at 22% between year 6 and 8 than the 10% between year 4 and 5. These results are in keeping with a number of 'stop smoking' studies (Sanders et al 1989). It is only with the advent of nicotine patches that significant decreases in smoking rates have been achieved (Imperial Cancer Research Fund General Practice Research Group 1993).

8.5. Conclusions

In conclusion the following have been shown:

1. Nurse practitioner care is at least as good as conventional medical care for the long term follow up of hypertensive patients.
2. Nurse practitioner care is more effective in terms of maintaining follow-up and adherence to management protocols.
3. A microcomputer patient information system can facilitate the every day management of an outpatient clinic as well as providing data for research and audit.

4. A nurse practitioner clinic with a computer based patient information system is capable of responding to and integrating the developments in knowledge and understanding which demand change in the provision of care.
5. Dietary intervention for hypercholesterolaemia is only a starting point in addressing the cardiovascular risk associated with raised cholesterol.
6. Guar gum has no effect on weight or blood pressure in hypertensives with or without hyperlipidaemia or obesity. The lipid lowering effect observed in some clinical trials was not confirmed due to the limited power of the study brought about by the high level of socially unacceptable side effects.
7. The success of current strategies for decreasing overall cardiovascular risk by decreasing levels of established risk factors, such as smoking, excessive alcohol consumption and weight is limited.

8.6. Future considerations

Considerations for the future following from this work are:

1. that an extensive education programme be set up for nurses to facilitate the expansion of care provided by nurse practitioners.
2. nurse practitioner clinics be associated with academic centres of excellence interested in the care of hypertensive patients, to continue the evaluation of new aspects of care using this model.
3. that studies to assess the long term mortality of this population be carried out to investigate:
   a) the overall impact of nurse practitioner follow-up,
   b) the change in emphasis from hypertension follow-up to multiple cardiovascular risk intervention.
4. further studies be undertaken to develop alternative pharmacological and non-pharmacological interventions to decrease overall cardiovascular risk. In particular, new strategies to provide more effective weight and cholesterol reduction, and smoking cessation are urgently required.

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Abbreviations

ACE inhibitor Angiotension converting enzyme inhibitor.

ANOVA Analysis of variance.

ANCOVA Analysis of co-variance.

BMI Body mass index, calculated: weight (kg)/height $(m)^2$.

CHC Convention hypertension clinics.

CHD Coronary heart disease.

DART Diet and Reinfarction Trial.

DBP Diastolic blood pressure.

DHSS Department of Health and Social Security.

ECG Electrocardiogram.

EWPHE European Working Party on High blood pressure in the Elderly.

g Grams.

GammaGT Gammaglutamyltransferase.

GBPC Glasgow Blood Pressure Clinic.

GP General practitioner.

HDFP Hypertension Detection and Follow-up Program.

HDL cholesterol High density lipoprotein cholesterol.

IHD Ischaemic heart disease.

iu/l International units per litre.

kg Kilograms.

LDL cholesterol Low density lipoprotein cholesterol.

MI Myocardial infarction.

mmHg Millimetres of mercury.

mmol/l millimoles per litre.

MONICA Monitoring of trends and determinants in cardiovascular disease study.

MRC Medical Research Council.

MRFIT Multiple Risk Factor Intervention Trial.

NPC Nurse practitioner clinic.

SBP Systolic blood pressure.

STARS St Thomas' Atherosclerosis Regression Study.

ummol/l micromoles per litre.

VA Veterans Administration.

VLDL cholesterol Very low density lipoprotein cholesterol.

WHO World Health Organisation.

WSDF Water soluble dietary fibre.