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Assessing Pharmacist's Intervention in Supporting the Management of Type 2 Diabetes in a Primary Care Setting

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To my parents and dearest sister, Nui

for their continued support and encouragement

Abstract

Type 2 diabetes mellitus is a chronic disease that is associated with substantial morbidity, mortality, and health care cost. All patients with diabetes require a high level of clinical care to prevent the development of diabetic complications. The aim of this study was to compare the impact of a pharmaceutical care diabetic clinic within a primary care setting to standard care on clinical, humanistic and process outcomes in Type 2 diabetes patients. A randomised controlled trial was conducted in 9 general practices in Greater Glasgow Health Board. All patients with Type 2 diabetes, aged 18 years or over, taking an oral antidiabetic drug were recruited and stratified by practice, age, and gender, and then randomised into an active or control group. The patients in both groups were invited to a pharmaceutical care diabetic clinic within their general practice for three visits at three-monthly intervals. Active patients received review and allocated intervention by the pharmacist while control patients received review only without intervention by the pharmacist. Allocation remained blind until after the first evaluation. The pharmacist evaluated the appropriateness of the medication for the individual and their overall diabetic care. The pharmacist prepared a list of drug-related problems and a referral where appropriate. GP referrals were actioned in the active group but held back until after the conclusion of the study in the control group. Patient outcome measures include changes in HbA1c value, systolic blood pressure, health related quality of life (HRQOL), and drug related problems (DRPs) from baseline to the end of the study for both groups.

Three hundred and eighty seven patients were targeted for recruitment to the study, of which 198 signed informed consent and attended for interview with 160 (81%) patients attending two or more clinic visits, and 82 (51%) patients attending all three clinic visits. The results demonstrated a significant change in systolic blood pressure

in the active group from clinic visit 1 to 2 (9 mmHg, $P = 0.007$) and clinic visit 1 to 3 (15 mmHg, $P = 0.001$) but no change in HbA1c and HRQOL. There were 177 DRPs in the active group at baseline which decreased to 67 at clinic visit 2. Equivalent numbers of DRPs for the control group were 179 and 114 respectively. The risk reduction in the active group was therefore 0.59 with a number needed to treat (NNT) of 4 (19 weeks). Results also demonstrated a high GP acceptance rate as evidenced by 80% of recommendations being completely agreed and only 2% rejected.

The hypothesis of this study was 'pharmaceutical care delivered by community pharmacists does improve patient outcomes of Type 2 diabetics in a primary care setting'. We conclude that two of the patient outcome measures (systolic blood pressure and DRPs) showed a significant improvement, with no reduction in HRQOL and no change in HbA1c.

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Abbreviations

ADA	American Diabetic Association
ADDQoL	The Audit of Diabetes Dependent Quality of Life
BDA	British Diabetic Association
BMI	Body mass index
BNF	British National Formula
CHD	Coronary heart disease
DCCT	The Diabetes Control and Complications Trial
DDCF	Diabetes Data Collection Form
DRP	Drug related problem
DRPs	Drug related problems
FPG	Fasting plasma glucose
GGHB	Greater Glasgow Health Board
GP	General practitioner
GPs	General practitioners
HbA1c	Haemoglobin A1c (glycosylated)
HRQOL	Health related quality of life
MI	Myocardial infarction
MRF	Medication Review Form
NNT	Number needed to treat
OGTT	Oral glucose tolerance test
OTC	Over the counter
QOL	Quality of life
RCT	Randomised controlled trial
SBP	Systolic blood pressure
SPSS	Statistical package for social sciences

UKPDS	The United Kingdom Prospective Diabetes Study
WHO	World Health Organisation

Chapter 1

Review of Literature

1.1 Introduction

Diabetes mellitus is a group of metabolic disorders characterised by chronic hyperglycaemia resulting from defects in insulin secretion, insulin action, or both (Expert Committee, 1997). The effects of diabetes include microvascular and macrovascular complications that contribute to an increase in morbidity and mortality and a reduction in the quality of life. There are two main types of diabetes mellitus: Type 1 diabetes and Type 2 diabetes.

Type 1 diabetes mellitus (previously known as insulin-dependent diabetes mellitus) develops most frequently in children and young adults, but also may occur in adults. In patients with Type 1 diabetes, the pancreatic beta cells have been destroyed by an autoimmune response causing insulin deficiency. If the balance between diet, physical activity levels and insulin dosage is not maintained, this can lead to hypoglycaemia. Patients with Type 1 diabetes need insulin treatment to survive. Failure to take insulin can result in diabetic ketoacidosis.

Type 2 diabetes mellitus, previously known as adult-onset diabetes or non-insulin-dependent diabetes, is the most prevalent form of diabetes. It is a complex metabolic disorder which may originate from insulin resistance and relative insulin secretory deficiency, either of which may be predominant (Alberti and Zimmet, 1998). Patients with this form of diabetes are not absolutely dependent on exogenous insulin for

survival and are not prone to the development of ketoacidosis except during conditions of severe stress such as those caused by infections, trauma or surgery.

The risk of developing Type 2 diabetes increases with age, obesity, and lack of physical activity. It is more common in individuals with a family history of diabetes and in members of certain ethnic groups. Most patients with Type 2 diabetes are obese, and obesity itself causes or aggravates some degree of insulin resistance (Campbell and Carlson, 1993; Kissebah et al., 1982). Type 2 diabetes is often asymptomatic in its early stages and can remain undiagnosed for many years. Such patients are at significantly higher risk for developing macrovascular and microvascular complications than the non-diabetic population (Walters et al., 1994).

In 1989 the St. Vincent Declaration set out specified targets for diabetes care and the reduction of diabetic-related complications for all countries throughout Europe (Anonymous, 1990). Results from the United Kingdom Prospective Diabetes Study (UKPDS) (UKPDS Group, 1998a; UKPDS Group, 1998d), the largest and longest clinical trial in Type 2 diabetes, have shown that intensive management of blood glucose and blood pressure can dramatically reduce the risk of developing complications.

1.2 Overview of Type 2 diabetes mellitus

1.2.1 Diagnostic criteria

The most widely used diagnostic criteria for diabetes mellitus were developed by the World Health Organisation (WHO) in 1980 (WHO, 1980) and updated in1985 (WHO, 1985). According to the 1985 WHO criteria, diabetes was diagnosed by either fasting plasma glucose (FPG) ≥ 7.8 mmol/l or 2-hour glucose concentration ≥ 11.1 mmol/l during a 75-g oral glucose tolerance test (OGTT). In 1997 the American Diabetes Association (ADA) introduced new diagnostic criteria for diabetes (Expert committee, 1997). The ADA criteria are based mainly on FPG and use a cut-off value of at least 7.0 mmol/l for diagnosis, which is lower than the WHO criteria. This lower cut-off point was chosen because the microvascular complications begin to become more prevalent at this concentration. The ADA also introduced a new intermediate category called impaired fasting glucose (fasting glucose 6.1-6.9 mmol/l), which differs from the WHO category of impaired glucose tolerance (FPG < 7.8 mmol/l and 2-h plasma glucose (2-h PG) ≥ 7.8 mmol/l and < 11.1 mmol/l). In 1999, the WHO changed the diagnostic criteria, lowering the FPG criterion to ≥ 7.0 mmol/l for the diagnosis of diabetes but retained the recommendation for the OGTT for the diagnosis of diabetes and staging of impaired glucose regulation (WHO, 1999).

Both the 1997 ADA and 1999 WHO criteria agreed to lower the diagnostic value of the FPG to facilitate identification of undiagnosed diabetes and thereby identify more people at risk of complications of diabetes at an earlier stage in their disease. Use of FPG was advocated by the ADA because it is a much simpler test than an OGTT,

can be widely applied in clinical practice and because its predictive value for microvascular complications is nearly the same as that of 2-h PG.

1.2.2 Incidence and prevalence of Type 2 diabetes

The prevalence of Type 2 diabetes is increasing not only in the United Kingdom but also around the world. The WHO Collaborating Centre for diabetes in Melbourne has estimated that the number of Type 2 diabetes patients worldwide will increase from 99 million in 1994 to 216 million in 2010 (Zimmer and McCarty, 1995). In the UK alone, according to the report by the Audit Commission (2000), it was predicted that the number of diabetic patients might double from 1.4 million (estimated as 3% of the population) to 3 million by the year 2010. This is thought to be due to a number of factors, namely an ageing population, the increasing prevalence of obesity and changes in lifestyle (Clark and Perry, 1999).

In Scotland, approximately 108,000 Scottish residents have diabetes (Cromie and Teo, 1999), equivalent to 2.1% of the estimated Scottish population of 5,119,200 (General Scotland Register Office, 2000). It is likely to increase to 6.5% by the year 2006 due to the increase in the elderly population. Each year, it is estimated that 3,850 new adult cases of diabetes are diagnosed, equal to the UK incidence of new cases, which are 100 per 100,000 each year. In addition 2,700 people are recorded annually as dying of a diabetic related complication (Cromie and Teo, 1999).

In the UK and many other countries Type 2 diabetes is a particular problem in certain ethnic minority groups, such as Asians, and African-Caribbeans where prevalence of known Type 2 diabetes rates are three to four times higher than in comparable white Caucasian populations (Audit Commission, 2000). In Scotland this group comprises

1.25% of the population, but is higher in some big cities including Edinburgh and Glasgow where ethnic communities comprise 3% of the population (Cromie and Teo, 1999).

1.2.3 Complications of Type 2 diabetes: mortality, morbidity and effects of near-normoglycaemia

Diabetic complications can be classified into two main categories, acute metabolic complications, and chronic complications. Acute complications of Type 2 diabetes include severe hyperglycaemia, leading to polyuria, increased thirst, dehydration, weight loss, blurred vision, fatigue and occasionally hyperosmotic non-ketotic coma. Patients with diabetes are also at risk of suffering from chronic complications, including microvascular complications of retinopathy, nephropathy, neuropathy, and macrovascular complications of cardiovascular, cerebrovascular, and peripheral vascular disease. Long-term complications can have serious consequence on the health and quality of life of the patient. The following review will focus mainly on chronic complications, which are major causes of mortality and morbidity amongst patients with Type 2 diabetes.

1.2.3.1 Microvascular complications: diabetic neuropathy

Diabetic neuropathy is an important cause of morbidity in patients with diabetes often leading to foot ulceration and amputation and the cost to the health service is considerable. Data from a study in Newcastle upon Tyne hospitals during 1989-1991 showed an incidence of diabetes amputation of 5.7 per 1,000 diabetic patients per year and identified that 42% of all operations were performed on diabetic patients (Deerochanawong and Alberti, 1992).

One British study of patients attending a hospital diabetes clinic (Young et al., 1993) found that diabetic peripheral neuropathy was present in more than 50 percent of Type 2 diabetic patients aged over 60 years. Studies in the UK reported that prevalence of neuropathy in Type 2 diabetes varied widely from 17.2% (Walters et al., 1992), 32.1% (Young et al., 1993) to 41.6% (Kumar et al., 1994) mainly due to differences in diagnostic criteria and selection criteria used in the studies. In addition, the prevalence rate of diabetic foot ulceration reported has ranged from 5.3% to 7.4% (Kumar et al., 1994; Reiber, 1996).

In the US foot ulcers affect up to 15% of patients with diabetes during their lifetime (Reiber, 1996). Half of all nontraumatic lower-extremity amputations occur in patients with diabetes (Leese, 1991). The prevalence of amputation in the US in 1989 was 2.8% for patients with diabetes (Mayfield et al., 1998). The direct costs for care of foot ulcers were estimated to be $145 million in 1986 (Mayfield et al., 1998).

Poor glycaemic control and long duration of diabetes increases the risk of neuropathy and amputation. A high HbA1c (>10.7%) and high fasting plasma glucose (>13.4 mmol/L) was associated with a twofold increase in risk of amputation in a Finnish population with Type 2 diabetes (Lehto et al., 1996). A study of Young et al. (1993) showed significant increasing prevalence of diabetic peripheral neuropathy with duration of diabetes, from 20.8% in 2,199 patients with diabetes duration of less than 5 years from diagnosis to 36.8% in 2,532 patients with diabetes for more than 10 years. However, the study did not specify the type of diabetes. In addition, it should be noted that the duration of Type 2 diabetes can never be accurately recorded because of the variable asymptomatic period prior to the diagnosis of the disease.

Of all possible interventions, tight glycaemic control is probably the only one that may slow the progression of the neuropathic state. As shown in the Diabetes Control and Complications Trial (DCCT), patients with Type 1 diabetes who achieved near-normal glycaemic control experienced a 69% reduction in the incidence of appearance of neuropathy and a 57% reduction in subclinical neuropathy, as compared with control subjects who received the usual treatment and subsequently had higher levels of glycaemia (DCCT Research Group, 1993). The epidemiological literature suggests a similar association in Type 2 diabetes (Klein et al., 1996; Ohkubo et al., 1995).

1.2.3.2 Microvascular complications: diabetic retinopathy

Diabetic retinopathy remains the leading cause of blindness in adults of working age in the developed world (ADA, 1998b; Evans, 1995; Leese, 1991) despite the fact that if it is detected and treated early, over 50% of blindness caused by diabetes is prevented (Rohan et al., 1989).

It is estimated that retinopathy begins to appear approximately 5 years after the onset of fasting hyperglycaemia (Jarret, 1986). Dolben et al. (1988) showed that retinopathy is related to the duration of disease and degree of hyperglycaemia and was found in up to 29% of Type 2 diabetes patients at the time of clinical diagnosis. In the UK 37% of patients with Type 2 diabetes had retinopathy at the time of diagnosis, according to the UKPDS (Aldington et al., 1994). In Type 2 diabetes (diagnosed after 30 years of age) of 15 or more years' duration, the risk of any retinopathy is approximately 78% (Neely et al., 1998).

In Type 1 diabetes, the DCCT Research Group (1993) demonstrated that tight glycaemic control was associated with a reduction in the onset and progression of

diabetes retinopathy. Studies in patients with Type 2 diabetes suggest a similar relation between level of glycaemic control and rate of retinopathy. An intervention study of Japanese Type 2 diabetic patients (Ohkubo et al., 1995) reported a 6-year cumulative development and progression of retinopathy of 7.7% in the intensively treated group (mean HbA1c 7.1%) compared with 32% in the conventionally treated group (mean HbA1c 9.4%), confirming the benefit of tight glycaemic control in Type 2 diabetes. The UKPDS also showed that intensive blood glucose control by either sulphonylureas or insulin substantially decreases the risk of microvascular complication (UKPDS Group, 1998d).

1.2.3.3 Microvascular complications: Diabetic nephropathy

Diabetes has become the leading cause of end-stage renal disease (ESRD), accounting for about one-third of all cases of ESRD in the United States (ADA, 1998a). In the UK, it is estimated that about 600 new diabetic patients start on the renal replacement therapy programme every year (Viberti et al., 1996).

Nephropathy is a potential problem for all diabetics. Patients with diabetes have a 17 fold increased risk of ESRD compared with those without diabetes (Leese, 1991). Although a smaller proportion of those with Type 2 diabetes develop ESRD, the much greater prevalence of Type 2 accounts for the fact that half of the diabetics with end-stage renal disease have Type 2 diabetes (ADA, 1998a; Viberti et al., 1996).

In patients with Type 2 diabetes, nephropathy can be present at the time of diagnosis and this may be due to delayed diagnosis and the presence of macrovascular disease and hypertension (BDA, 1995). In addition, ethnic origin is an important factor in determining the risk of nephropathy. Viberti et al. (1996) reported that

diabetic nephropathy is two-fold more commonly seen in Afro-Caribbean, Asian Indians, and Japanese patients with Type 2 diabetes than those of European origin.

Onset of diabetic nephropathy may be delayed with good glycaemic control, such as that used in the DCCT which achieved an average HbA1c level of 7.1% (DCCT Research Group, 1993). The DCCT documented that intensive control of glucose in Type 1 diabetes decreased the frequency of albuminuria by 60%. In Type 2 diabetes, a study of Ohkubo et al. (1995) showed a decrease in the frequency of development of both microalbuminuria (57%) and macroalbuminuria (70%) with intensive insulin therapy. In a long term follow-up study of a mixed Type 1 and Type 2 diabetic cohort, Hellman et al. (1997) showed that a comprehensive diabetes treatment programme resulted in reduction of total mortality, renal failure rate, and cardiac mortality. As with other microvascular complications in Type 2 diabetes, the results of the UKPDS (UKPDS Group, 1998d) indicated that intensive glycaemic control with sulphonylureas or insulin reduced the risk of diabetic nephropathy. However, UKPDS only evaluated the progression of complications in newly diagnosed patients with Type 2 diabetes. Levin et al. (2000) also showed that intensive glycaemic control (goal HbA1c 7.1%) retarded microalbuminuria in patients who had a confirmed diagnosis of Type 2 diabetes for several years (mean duration of known diabetes was 8 years).

1.2.3.4 Macrovascular complications

Coronary heart disease (CHD) mortality and morbidity rates are increased two- to four-fold among diabetic patients compared with non-diabetic persons (Laakso and Lehto, 1998), and the risk of myocardial infarction (MI) is as high as in non-diabetic people who have already had an MI (Haffner et al., 1998). As shown in a 16-year follow-up study in Framingham, the prevalence of coronary heart disease,

cerebrovascular accidents, and intermittent claudication were 1.8, 2.4, and 4.5 times greater, respectively, in patients with diabetes than in age- and sex- matched non-diabetics (Gracia et al., 1974). In the Whitehall Study all causes mortality was 42% in the diabetic patients compared with 16% in the non-diabetic patients. Moreover, the cardiovascular mortality was 26% in the diabetic group in comparison with less than 9% in non-diabetic subjects ($p < 0.0001$) (Jarrett et al., 1984).

In DCCT (1993), the risk of macrovascular disease was reduced by 41% in patients with Type 1 diabetes achieving intensive blood glucose control, although this difference was not statistically significant because of the low incidence of such complications. Macrovascular disease is a major cause of death in patients with Type 2 diabetes (Donnelly, 2001; Groeneveld et al., 1999; Roper et al., 2001; Wei, 1998).

In patients with Type 2 diabetes, the Kumamoto study (Okhubo, 1995) and the VA Cooperative study (Abraira et al., 1997), did not support the finding that intensive blood glucose control in Type 2 diabetes significantly lowers the rate of macrovascular complications. However, there were small samples in both studies (110 patients in Kumamoto study and 153 patients in VA Cooperative study) which limits its generalisability. In the UKPDS, blood glucose lowering was found to have less effect on cardiovascular complications than on microvascular complications (UKPDS Group, 1998d). There was evidence of a 16% risk reduction ($p = 0.052$) for fatal and non-fatal MI with a difference in median HbA1c of 0.9% between intensively and conventionally treated groups (7.0% versus 7.9%, respectively) (Stratton et al., 2000).

It is particularly notable that in the UKPDS sub-population of patients with hypertension, it was found that blood pressure control was more effective than blood

glucose control in reducing the risk of macrovascular complications (UKPDS Group, 1998a).

Several prospective studies have indicated that poor glycaemic control could increase the risk of cardiovascular disease. Uusitupa et al. (1993) observed a significant effect of severity of hyperglycaemia on mortality in Type 2 diabetic patients. They found that fasting plasma glucose concentration and HbA1c values at 5 years after diagnosis were higher in diabetic patients who died during the follow-up than in those who survived. Increased levels of glycosylated haemoglobin were also shown to be associated with CHD in a Finnish study of Type 2 diabetic patients (Laakso, 1996).

In addition to hyperglycaemia, other risk factors for cardiovascular mortality and morbidity in Type 2 diabetes include hypertension, obesity, and dyslipidaemia, especially hypertriglyceridaemia and low levels of high density lipoprotein cholesterol (Laakso and Lehto, 1998). As a result of the UKPDS (1998a), it was confirmed that the major causes of the increased risks of CHD in patients with diabetes are due to hyperglycaemia together with other risk factors and that glucose control alone may not improve CHD in diabetes. Therefore, all risk factors for Type 2 diabetes should be addressed. This is also supported by studies that have demonstrated that treatment of high cholesterol, blood pressure and weight loss in addition to control of blood glucose reduces the risk for macrovascular complications (Marshall, 1999; Passa, 1998; Steiner, 2000).

1.3 Studies focusing on the benefits of improved glycaemic control and primary prevention

The DCCT, which was completed in 1993, studied 1,441 patients with Type 1 diabetes mellitus (mean age 27 years) and showed that intensive therapy, which resulted in a mean HbA1c level of 7.1%, compared with conventional therapy, which resulted in a level of 9.0%, reduced progression of diabetic microvascular complications (DCCT Research Group, 1993). Although all DCCT subjects had Type 1 diabetes, there is a theoretical reason to believe that similar benefits of intensive glucose control could be found in Type 2 diabetes because hyperglycaemia has been established as the cause of the microvascular pathology in both types of diabetes (Cerveny et al., 1998).

A limited number of studies have demonstrated reduced macrovascular complications with tight glycaemic control in patients with Type 2 diabetes. The University Group Diabetes Programme (UGDP, 1982) studied 1,021 patients with Type 2 diabetes (mean age 53 years) and concluded that there was no benefit from improved glucose control induced by insulin, biguanide, or sulphonylurea therapy in preventing macrovascular diabetic complications. However, this study has been criticised due to the unnecessary discontinuation of the oral hypoglycaemic therapy after 7 years leaving only the diet and insulin groups to complete the study for an average 12.5 years.

In the Kumamoto trial (Ohkubo et al., 1995), 110 Japanese Type 2 diabetic patients were randomised to intensive or conventional insulin therapy and were followed up for 6 years. The HbA1c level at the end of the study was 7.1% in the intensively

treated group and 9.4% in the conventionally treated group. The results of the study demonstrated that tight control with multiple daily insulin injections resulted in a decrease in the onset and progression of diabetic retinopathy, nephropathy and neuropathy in comparison with conventional insulin therapy. However, the study has several limitations. It was performed in nonobese Japanese Type 2 diabetic patients. This may not be representative of Type 2 diabetes patients, especially those in Western countries. The study excluded patient with hypertension, therefore the reduction in the risk of nephropathy might be overestimated because of the significant relationship between hypertension and nephropathy. In addition, the number of participants was limited to 110 patients, and did not include patients receiving oral hypoglycaemic agents.

The UKPDS was a large, long-term, multicentre clinical trial involving 23 centres in the UK between 1977 and 1991. A total of 5,102 patients with newly diagnosed Type 2 diabetes were monitored for an average of 10 years. The study aimed to determine firstly whether intensive therapy of Type 2 diabetes (fasting plasma glucose <6 mmol/l) using oral antidiabetic drugs or insulin reduced the risk of macrovascular and microvascular complications of diabetes compared to conventional management (fasting plasma glucose <15 mmol/l) which is diet therapy and secondly whether the use of sulphonylurea, metformin, or insulin had specific advantages or disadvantages (UKPDS Group, 1998d; UKPDS Group, 1998e).

After 10 years, the results of the study showed that the mean HbA1c was 7.0% in the intensively treated group and 7.9% in the diet group (P<0.0001). This 0.9% reduction was associated with 12% fewer diabetes-related end-points in the intensively treated group (P=0.029). Diabetes-related end points were defined as sudden death, death from hyperglycaemia or hypoglycaemia, myocardial infarction, angina, heart failure,

stroke, renal failure, amputation, and eye complications. Most of this benefit was found with a 25% risk reduction in microvascular end-points (P=0.0099). The incidence of myocardial infarction was reduced by 16% in the intensively treated group, but this did not reach statistical significance (P=0.052) (UKPDS Group, 1998d). However, hypoglycaemia was more common (P<0.001) in the intensively treated group (0.7%/year for conventional treatment, 1.0%/year for chlorpropamide, 1.4%/year for glibenclamide, and 1.8%/year for insulin). Weight gain was significantly higher in the intensively treated group than in the conventional group (P<0.001).

This evidence has demonstrated that intensive lowering of blood glucose levels reduces the risk of diabetic complications, the greatest effect being on microvascular complications. However, this effect was associated with weight gain and hypoglycaemia, and therefore the risks and benefits of therapy should be carefully considered in each individual (Krentz, 1999).

In addition, patients with Type 2 diabetes (n = 1,148) who were also hypertensive were randomised to 'less tight' blood pressure control (target blood pressure < 180/105) or 'tight' control (target blood pressure <150/85). The UKPDS study also investigated any benefits of lowering blood pressure in hypertensive Type 2 diabetics and to ascertain whether the use of ACE inhibitors (captopril) or beta-blockers (atenolol) had particular therapeutic advantages or disadvantages (UKPDS Group, 1998a; UKPDS Group, 1998b). The results of the study showed a reduction in risk of developing a diabetes-related end-point (P=0.005), diabetes-related death (P=0.019), stroke (P=0.013), and microvascular disease (P=0.009) when average blood pressure of 144/82 mmHg was achieved with tight control compared with an average blood pressure of 154/87 mmHg with less tight control. Captopril and atenolol were

found to be equally effective in reducing the risk of macrovascular end points, suggesting that BP reduction in itself may be more important than the treatment used.

Based on these findings, there is clearly evidence to support diabetic patients to try to achieve and maintain long term near-normal blood glucose and blood pressure levels (Krentz, 1999). To achieve this, all patients with diabetes require a high level of health care to prevent the development of diabetic complications. This includes the need for regular monitoring of blood pressure, urine and blood glucose and foot and eye examination. The health care team has a duty to ensure that patients receive a high standard of care and also education about the disease to facilitate self-management.

1.4 Outcome measures in diabetes care

1.4.1 HbA1c monitoring

Haemoglobin A1c (HbA1c) is a reliable marker of chronic hyperglycaemia, and an appropriate predictor of diabetic complications (DCCT Research Group, 1993; UKPDS Group, 1998d). Since it is often difficult to perform an oral glucose tolerance test or obtain fasting blood samples, especially in a large-scale longitudinal study, the HbA1c test is a good alternative for assessment of glucose control. Another advantage of HbA1c is that it gives an objective assessment of glucose control over the past 2-3 months (Bunn, 1981).

Several assays to measure glycosylated haemoglobin are currently available, with high performance liquid chromatography (HPLC) still considered the reference method (DCCT Research Group, 1993; UKPDS Group, 1998d). However, most of

these methods are time-consuming and technically demanding, and the results of the assay are not available at the time of the clinic visit. It should be noted that HbA1c has different normal ranges, and that various laboratories use different measures; each laboratory should therefore report the actual range to clinicians.

1.4.2 Monitoring diabetic complications

Overt diabetic nephropathy is classified as a protein positive (1+ or greater) urine dipstick test, which represents macroalbuminuria, or an albumin concentration of greater than 300 mg/g creatinine. Dipstick tests that are negative or show positive traces of protein should be followed with screening for early diabetic nephropathy, commonly referred to as microalbuminuria which is a good predictor of mortality (especially in Type 2) and morbidity in diabetes (Vijan et al., 1997).

Microalbuminuria is usually defined as an excretion rate of albumin between 30-300 mg/day or 20-200 μg/min or a urinary albumin-to-creatinine ratio of 3-30 μg/mg. Due to the significance of microalbuminuria in the development of subsequent renal disease and because treatment may be effective at this stage, it is important to screen for this biochemical abnormality. Detection of microalbuminuria is critical in the diagnosis of early renal disease, particularly in patients with both diabetes and hypertension. An excretion rate below 30 mg/day is designated normoalbuminuria.

1.4.3 Quality of life measurement

It is being increasingly recognised that the impact of chronic illness and its treatment should be considered in terms of their influence on quality of life in addition to traditional clinical variables (Muldoon et al., 1998). Quality of life is a patient outcome measure, and its improvement is supported as one of the ultimate goals of pharmaceutical care (Hepler and Strand, 1990). While there is a growing interest in the measurement of patient's quality of life and in the number of instruments being developed (Sanders et al., 1998), there is an absence of clear agreement on a definition of quality of life (Leplege and Hunt, 1997; Muldoon et al., 1998). QOL has been defined by the WHOQOL Group (1993) as the "individuals' perceptions of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, and concerns".

To distinguish between quality of life, which refers to an assessment of all aspects of a person's life, the term 'health related quality of life (HRQOL) is frequently used in order to be more specific on those aspects that are significantly influenced by the personal health status (Guyatt et al., 1993). An assessment of HRQOL typically measures a number of domains (also known as multi-dimensional construct), including physical, emotional and social functioning (Leplege and Hunt, 1997).

In the case of diabetes and its treatment, health related quality of life considerations are of special importance. Diabetes can have considerable impact on the quality of life, with possible limitations of work, social life, family relations, sexual relationships and leisure activities. As shown in the study of Wandell and Tovi (2000), the HRQOL assessed by the Swedish Health-Related Quality of Life Survey (SWED-QUAL) was found to be poorer in elderly diabetic subjects (n = 177 respondents) than in age-

matched controls from the general population, especially regarding different aspects of physical functioning. Poor metabolic control, with HbA1c levels more than 2% over reference, was also associated with reduced cognitive function.

Glycaemic control can enhance the health related quality of life in diabetic patients by minimising the effects of hyperglycaemia and morbidity. However, Jacobson et al. (1994) reported that patients taking oral medications had more diabetes-related worries than those controlling their diabetes with diet and exercise only, and that those taking insulin reported less satisfaction with treatment and more burden of illness than those taking oral medications. Others have suggested that experiencing hypoglycaemia and the difficulty associated with intensive therapeutic regimens could have adverse effects on patient's health related quality of life (DCCT Research Group, 1993).

HRQOL was assessed in Finnish Type 2 diabetic patients aged under 65 years using the Medical Outcomes Study Short Form (SF-20) (Hanninen et al., 1998). In this study 260 diabetic subjects were compared with 177 non-diabetic age- and gender-matched controls. The results indicated that patients with Type 2 diabetes had 11-27% lower mean scores than the controls in all six dimensions. The study also showed that obesity, longer duration of diabetes, insulin treatment and impaired visual acuity were associated with poor HRQOL. Similar results were also found in the study of Keinanen-Kiukaanniemi et al. (1996) in the district of Oulu, Northern Finland. The HRQOL of 1,804 adult diabetic patients was studied by using the Nottingham Health Profile (NHP) in order to describe differences in the HRQOL between the different treatment groups and between diabetic patients and the general population. The results demonstrated that the HRQOL was poorer in diabetic subjects with tablet treatment than in the general population in all NHP dimensions.

Among the different treatment groups, they found that the diet group had a significantly better HRQOL level in all six dimensions than the tablet treatment or combined treatment (tablet and insulin) groups.

Using HRQOL measures in studies of diabetic interventions may assist in gaining a view into the effects of the intervention on the patient's health related quality of life. This information may be helpful in assessing and developing intervention programmes that achieve good control of diabetes and its complications while maximising patient's well-being in relation to health.

In diabetic patients, some studies of health related quality of life have been performed using several generic (Hanninen et al., 1998; Hiltunen and Keinanen-Kiukaanniem, 1999; Klein and Klein, 1998; Weinberger et al., 1994) or diabetes-specific questionnaires (Boyer and Earp, 1997; Bradley et al., 1999; DCCT Research Group, 1988; Goddijn et al., 1999) or with both (Anderson et al., 1997; Jacobson et al., 1994) and patients with Type 1 or Type 2 (Hiltunen et al., 1999; Klein and Klein, 1998) or only with Type 2 (Boyer and Earp, 1997; Bradley et al., 1999; Goddijn et al., 1999; Hanninen et al., 1998; Jacobson et al., 1994; Weinberger et al.,1994).

1.4.3.1 Generic health related quality of life instruments

There are a number of generic health related quality of life instruments currently available for assessing the impact of treatment on quality of life. These instruments have been developed for use in any population regardless of the specific disease. The main limitations of such instruments are that they may be less sensitive to changes in specific conditions, may not cover the appropriate areas of interest in sufficient detail, and their validation may be inappropriate for a particular study.

Conversely the use of a generic instrument allows for unexpected effects by taking a broad approach and allows for comparisons to be made across different studies, health care programmes, and patient groups (Guyatt et al., 1993; Anderson et al., 1997). Table 1.1 provides examples of widely used generic health related quality of life measures.

Table 1.1 Summary of generic QOL measures and examples of clinical trials in which they were used

Measure	Characteristics	Details
Sickness Impact Profile (SIP)	Clinical trial	Deyo et al., 1983
	Population	Outpatients with rheumatoid arthritis
	Sample size	79 patients
	No. of domains	12
	Name of domains	Physical: ambulation, mobility, body care and movement Psychosocial: communication, alertness, emotional behaviour, social interaction Independent categories: sleep and rest, eating, work, home management, recreation and pastimes
	No. of items	136
	Response scale	Tick if item applies
	Mode of administration	Self-administered
	Validity	Criterion validity
	Reliability	Test-retest reliability
	Language	US version
Nottingham Health Profile (NHP)	Clinical trial	O'Brien et al., 1993
	Population	Cardiac patients at 6 months after myocardial infarction
	Sample size	185 patients
	No. of domains	6
	Name of domains	Energy, pain, sleep, physical mobility, social isolation and emotional reactions
	No. of items	38
	Response scale	Yes/no response
	Mode of administration	Self-administered
	Validity	Construct validity: Spearman correlations with the New York Heart Association (NYHA) ranged from 0.30 to 0.52
	Reliability	Spearman correlations among domain scores ranged from 0.32 to 0.70
	Language	British version

Table 1.1 continues overleaf

Measure	Characteristics	Details
Medical Outcome Study (MOS) Short-Form General Health Survey (SF-36)	Clinical trial	Brazier et al., 1992
	Population	Patients aged 16-74 years randomly selected from two general practices in Sheffield
	Sample size	1,980 patients
	No. of domains	8
	Name of domains	Physical functioning, role limitations due to physical health problems, bodily pain, social functioning, general mental health, role limitations due to emotional problems, vitality, and general health perceptions
	No. of items	36
	Response scale	2-,3-,4-,5- or 6-point Likert scales
	Mode of administration	Self-administered
	Validity	Construct validity, the SF-36 was able to detect low levels of ill health in patients who had scored 0 on the NHP
	Reliability	Internal consistency: Cronbach's alpha greater than 0.85 Test-retest reliability: reliability coefficient greater than 0.75 for all dimensions except social functioning
	Language	British version
World Health Organisation Quality of life (WHOQOL-100)	Clinical trial	Bonomi et al., 2000
	Population	The study population consisted of three groups: healthy adults, childbearing women, and chronically ill participants
	Sample size	443 participants
	No. of domains	6
	Name of domains	Physical health, psychological state, level of independence, social relationships, environment, and spirituality
	No. of items	100
	Response scale	5-point Likert scale
	Mode of administration	Self-administered
	Validity	Construct validity: Pearson correlations with the SF-36 and Subjective Quality of Life Profile were moderate to high (r > 0.45).
	Reliability	Internal consistency: the alpha coefficient for each domain exceeded 0.80 (range 0.82-0.95). Test-retest: Intraclass correlation coefficient exceeded 0.70 for all domains (range 0.83-0.96).
	Language	US version

Sickness Impact Profile (SIP)

The SIP was developed in the United States as a behaviourally based assessment of the impact of illness on everyday life (Bergner et al., 1981). It consists of 136 yes/no items describing behaviour related to health within 12 dimensions (Table 1.1). It emphasises the impact of health upon activities and behaviour, including social functioning, rather than on feelings and perceptions. Scores range from 0 to 100, with higher scores reflecting lower quality of life.

The SIP appeared to be a generally well constructed, reliable and valid measure of functional status, though its length is not an advantage (Bergner et al., 1981; de Bruin et al., 1992). The summary by de Bruin et al. indicated alpha coefficients ranging from 0.91 to 0.95 for the overall score, from 0.84 to 0.93 for dimension scores, and from 0.60 to 0.90 for category scores. In term of validity, almost all correlations of the SIP overall score compared with 13 other health measures exceeded 0.50. However, it cannot be assumed as valid for all conditions. The estimated time to complete the 136 items is 20-30 minutes (de Bruin et al., 1992; Weinberger et al., 1991). For chronically or acutely ill patients it is likely to take even longer and this may lead to a reduced response rate.

Nottingham Health Profile (NHP)

The NHP was developed in the UK as a measure of generic health related quality of life (Hunt et al., 1981). The design and content of the NHP was influenced by the SIP, but includes questions about feelings and emotions directly rather than via changes in behaviour. It is divided into two parts. The first part consists of 38 items grouped into six dimensions (Table 1.1). The second part contains seven items that measure

the effects of health problems on paid employment, jobs around the house, social life, home life, sex life, hobbies, and holidays. This part is optional as some items, such as work and sex life, may not be applicable. Yes/no responses are used throughout the questionnaire. It is self-administered and takes approximately 10-15 minutes to complete.

Test-retest reliability is adequate, with correlations ranging from 0.77 and 0.85 in patients with chronic illness (Hunt et al., 1981). The advantages of the NHP over other generic health related QOL are that it is short, easy to administer, and easily understood by patients (Jenkinson, 1991). The NHP has been shown to be responsive in a variety of patient groups, but it tends to emphasise severe disease states and is perhaps less sensitive to minor changes in health state (Hunt et al., 1981; Jenkinson, 1991; Brazier et al., 1992).

Medical Outcomes Study (MOS) Short-Form General Health Survey

The MOS instrument includes physical, social and role functioning scales to detect behavioural dysfunction caused by health problems. The 20-item shortened form of the MOS instrument, SF-20, was published in 1988 (Stewart et al.,1988), and the SF-36 was designed later in 1992 (Ware and Sherbourne, 1992) in response to criticisms that SF-20 was too limited in scope to detect changes in health status.

The SF-36 includes multi-item scales to measure eight domains (Table 1.1). Each domain is transformed to a 0 to 100 scale, with higher scores indicating higher HRQOL. The instrument is self-administered and generally takes five to ten minutes to complete while an average of 15 minutes may be required for elderly respondents (Weinberger et al., 1991).

The strengths of the instrument include its brevity and its applicability to a variety of disease states. The SF-36 has undergone reliability and validity testing in many countries, including the United Kingdom (Brazier et al., 1992). It has been found to be reliable and valid in general populations, and populations with chronic diseases (Stewart et al., 1988; Stewart et al., 1989; Ware and Sherbourne, 1992). However, as with any brief generic health related QOL instrument, it remains possible that some aspects of life are not covered. Some have commented on the limitations of the SF-36 in that there is no assessment of cognitive function or distress (Hays and Shapiro, 1992), and that the physical activities items focus only on gross activities such as walking, bending, and kneeling, but do not cover coordinated actions (Anderson et al., 1993).

World Health Organisation Quality of Life (WHOQOL-100)

WHOQOL-100 is a newer generic health related quality of life instrument, which was developed through collaborative work to assess quality of life across various disease types, severities, and cultural subgroups (WHOQOL group, 1995). Fifteen centers around the world participated in the development and piloting of the WHOQOL pilot form (WHOQOL group, 1995). Each center explored the important aspects of quality of life and ways of asking about quality of life. There was high agreement about what aspects of life were considered important and these fell into six domains (Table 1.1). These domains contain 24 four-item facets (subscales), for a total of 96 items, plus one additional facet (four items) regarding global QOL and general health. The scores of each facet and domain are transformed to a 0 to 100 scale, a higher score represents better QOL (Bonomi et al., 2000). It was noticed that some aspects, such as safety of the environment in which they live, and their current spiritual status, are not included in other instruments. WHOQOL-100 was tested to assess its validity and

reliability in each of the centers and it was shown to be reliable and valid across cultures.

The instrument is self-administered taking generally about 10-20 minutes to complete (Bonomi et al., 2000). Although the WHOQOL can be used successfully for a comprehensive assessment of QOL in many clinical studies, its length is considered to be unsuitable for use on a daily basis and in longitudinal studies (Saxena and Orley, 1997).

The WHOQOL group recently developed a brief 24-item version, the WHOQOL-Brief (WHO, 1997). The WHOQOL-Brief contains four domains: physical, psychological, social relationships, and environment. Its reliability and validity evaluation is currently being tested in multiple countries (WHO, 1997).

1.4.3.2 Diabetes-specific quality of life instruments

Although there are well-designed generic health related quality of life instruments, these may not be specific enough to address some aspects of quality of life in diabetes such as hypoglycaemia, insulin injections, self-monitoring of blood glucose, dietary restrictions, and diabetic complications which may be critical to an individual's health related quality of life (Bradley, 1994). There have been studies measuring health status of patients with diabetes using generic measures of QOL, such as SF-36, compared to diabetes-specific measures (Jacobson et al., 1994; Anderson et al., 1997). It is important to note that whilst generic measures allow comparisons across different studies and disease groups, their need to cover a wide range of issues can make them less sensitive in identifying disease related problems and less responsive

to therapeutic effects, especially when the effects result in differences in lifestyle rather than functional health status.

There are a rather limited number of valid diabetes-specific quality of life measures (Bradley, 1994). The DQOL (Diabetes Quality of Life) was the first diabetes-specific measure to be used in a number of studies (DCCT Research Group, 1988; Jacobson et al., 1994; Parkerson et al., 1993). Alternative diabetes-specific quality of life measures include the DHP (Diabetes Health Profile), Diabetes-39, and ADDQoL (The audit of diabetes-dependent quality of life) all of which have recently been developed and validated. Table 1.2 describes clinical trials in which diabetes-specific measures have been studied in term of validity, reliability, and characteristics of the measures.

Table 1.2 Summary of diabetes-specific QOL measures and examples of clinical trials in which they were used

Measure	Characteristics	Details
Diabetes Quality Of Life (DQOL)	Clinical trial	Jacobson et al., 1994
	Population	Adult Type 1 or Type 2 diabetes patients from the outpatient department of the Joslin Diabetes Center in Boston
	Sample size	240 patients
	No. of domains	4
	Name of domains	Satisfaction, impact of diabetes, diabetes-related worry, and social and vocational worry
	No. of items	46
	Response scale	5-point Likert scale
	Mode of administration	Self-administered
	Validity	Construct validity: Pearson correlations with the SF-36 were modest (range of correlations: -0.003 to 0.60).
	Reliability	Internal consistency: Cronbach's alpha coefficients ranged from 0.47 to 0.87.
	Language	US version
Diabetes Health Profile (DHP)	Clinical trial	Goddijn et al., 1966
	Population	Dutch Type 2 diabetes patients referred by their GPs for insulin therapy
	Sample size	99 patients
	No. of domains	3
	Name of domains	Psychological distress, barriers to activity, and disinhibited eating
	No. of items	32
	Response scale	4-point Likert scale
	Mode of administration	Self-administered
	Validity	Construct validity: Spearman correlations with the RAND-36 were moderate to high ($r > 0.45$).
	Reliability	Internal consistency: Cronbach's alpha for each domain exceeded 0.70 (range 0.72-0.79).
	Language	Dutch version

Table 1.2 continues overleaf

Measure	Characteristics	Details
Diabetes-39	Clinical trial	Boyer and Earp, 1997
	Population	Adult diabetic patients from general practice and a group of outpatients from a hospital diabetes clinic
	Sample size	427
	No. of domains	5
	Name of domains	Energy and mobility, diabetes control, anxiety and worry, social burden, and sexual functioning
	No. of items	39
	Response scale	7-point rating scale
	Mode of administration	Self-administered
	Validity	Construct validity: correlations with the SF-36 were weak (weakest, r = 0.15) to strong (range 0.48-0.71).
	Reliability	Internal consistency: Cronbach's alpha for each domain exceeded 0.70 (range 0.81-0.93).
	Language	US version
The Audit of Diabetes-Dependent Quality of Life (ADDQoL)	Clinical trial	Bradley et al., 1999
	Population	The Cambridge sample (outpatient diabetes clinic attenders at Addenbrooke's hospital) and the Bromley sample (diabetes patients attending an educational programme)
	Sample size	52 outpatients with diabetes and 102 patients attending diabetes education
	No. of domains	13
	Name of domains	Employment/career, social life, family relationships, friendships, sex life, sport/leisure, travel, future (own), future of family, motivation, physical activities, other fussing, and enjoyment of food
	No. of items	13 diabetes-specific items and two general items
	Response scale	7-point rating scale for domain questions and 4-point rating scale for importance rating to allow weighting of scores
	Mode of administration	Self-administered
	Validity	Construct validity: the ADDQoL score correlated significantly with the number of complications (Spearman r = -0.21).
	Reliability	Internal consistency: Cronbach's alpha coefficient for each domain exceeded 0.80.
	Language	British version

Diabetes Quality of Life (DQOL)

The DQOL instrument was designed in the 1980s for use in the DCCT, comparing the efficacy of different insulin regimens on the development of chronic complications of Type 1 diabetes (DCCT Research Group, 1988). It was designed originally to evaluate the relative burden of an intensive diabetes treatment in comparison to standard treatment. It is particularly suited for use in diabetic populations taking insulin although it may be used in Type 2 diabetics who are on diet or oral antidiabetic treatment as demonstrated by the study of Jacobson et al. (1994).

The DQOL instrument is a 46-item, multiple choice, self-administered assessment with four subscales (Table 1.2). It uses a 5-point Likert-type scale that ranges from 1 (very satisfied, no impact, no worry) to 5 (very dissatisfied, high impact, very worried). To be more readily interpretable and less confusing, it was proposed by Jacobson et al. (1994) to transform DQOL scores to a 100 point scale where 0 represents the lowest possible quality of life, and 100 represents the highest possible quality of life.

Jacobson et al (1994) measured patients' quality of life using the DQOL and SF-36 instrument. In this study, 240 patients were assessed, of whom 111 had Type 1 diabetes and 129 had Type 2 diabetes. Patients were 18 to 80 years of age and were not excluded if they had diabetic complications. The mean age of the Type 1 diabetes patients was 44 and the mean age of the Type 2 diabetes patients was 60. Thirty-eight percent of the Type 2 diabetics were on an oral antidiabetic agent and 53% were treated with insulin. The DQOL instrument was shown to have a moderately strong correlation with SF-36 (Table 1.2), with the satisfaction and impact scales having the strongest relationships overall with the functional health status scales of the SF-36. The study also provided information about external validity with the DQOL.

Patients with different frequency and severity of diabetes complications were compared in term of their diabetes-specific quality of life. It was found that increasing severity and number of complications were associated with lower levels of satisfaction and greater impact of diabetes, while the worry scales were less sensitive to complications. As the instrument was designed for use with adolescents, Jacobson et al., (1994) commented that the social and diabetes worry scales are less relevant for adults and elderly patients.

However there was some doubt as to the sensitivity and discriminant validity of this instrument which became apparent in the DCCT (1996). Results showed no difference in quality of life between intensive and conventional diabetes treatment. Although it was concluded that intensive diabetes treatment did not lead to a deterioration in quality of life, there have been criticisms that the instrument should be able to detect differences in quality of life between the two patient groups because they had different levels of glycaemic control, different incidence rates of severe hypoglycaemia and complications (Bott et al., 1998; Bradley et al., 1999).

As with any disease- specific measure, it is unlikely that the scope of the instrument will cover all elements of change relevant to the study. For example, there are no items regarding the impact on sexual functioning. In this case, it was suggested that questions could be added if an intervention being evaluated was expected to have this particular consequence and to score these separately (Bradley, 1994).

Diabetes Health Profile (DHP)

The DHP was developed by Meadows et al. (1996) for the identification of psychological and behavioural dysfunctioning of adult insulin-dependent and insulin-requiring patients in an ambulatory care setting. The DHP contains 32 items measuring three domains: psychological distress, barriers to activity and disinhibited eating (Table 1.2). The questions are provided with 4-point Likert-type scales rated from 0-3. Each subscale score is then transformed to a common score range of 0-100, where 100 represents no function. The DHP is self-administered and takes approximately 15-20 minutes to complete (Bradley, 1994).

The DHP contains some questions regarding fear of hypoglycaemia which are less relevant in Type 2 diabetes patients and also a question concerning insulin injection, which was omitted from the study of Goddijn et al. (1999) as the subjects in that particular study were not using insulin. This study demonstrated that the DHP was not very sensitive to changes in glycaemic control, treatment modality and change in hyperglycaemic complaints, while a generic questionnaire (RAND-36) was more sensitive in this aspect.

Diabetes-39

The Diabetes-39 instrument (Boyer and Earp, 1997) contains 39 items referring to 5 domains (Table 1.2). It was developed for use with patients who have either Type 1 or Type 2 diabetes, whether managed with insulin, oral antidiabetic agents or diet alone. It uses a 7-point rating scale (from 'not at all' to 'extremely') to express how much of an influence each item has had on their health related quality of life.

Boyer and Earp (1997) reported internal reliability for the domains of the Diabetes-39 as ranging from 0.81 to 0.93 (Table 1.2), which was sufficient to support claims of internal reliability. Correlations between the Diabetes-39 and the SF-36 ranged from -0.15 to -0.64. Strong negative correlations were identified between "Energy and Mobility" and the SF-36 "Physical Functioning" scales; "Anxiety and Worry" and the SF-36 "Mental Health" scales; and "Social Burden" and SF-36 "Social Functioning" scales.

Hirsch et al. (2000) evaluated QOL scales and divided these into 'burden' type and 'satisfaction' type. They studied five QOL questionnaires, including SF-36 and Diabetes-39, in a sample of 144 patients with Type 2 diabetes who were given the questionnaires twice. In this study the Diabetes-39 instrument was classified as a 'burden' type. The results demonstrated that the Diabetes-39 scales were not sensitive to different types of therapy. The physical burden scores increased very significantly with late complications, but the scale scores showed no changes after therapeutic intervention.

The Audit of Diabetes-dependent Quality of Life (ADDQoL)

The ADDQoL was developed in the UK for use in patients with either Type 1 or Type 2 diabetes by Bradley et al. (1999). It consists of 13 diabetes-specific items and two general items (Table 1.2). Some selected items have 'not applicable' options, which are not used in the ADDQoL weighted mean. Within each diabetes-specific domain, respondents rate both impact of diabetes on each item and also the importance of those items for their health related quality of life. Impact ratings are multiplied by the corresponding importance rating to provide a score from -9 to +9 for each domain.

The ADDQoL is self-administered however no completion time has been reported (Bradley et al., 1999; Kinmonth et al., 1998).

The ADDQoL is a recently developed diabetes-specific QOL measure, and there is only preliminary evidence for its validity (Bradley et al., 1999). However, in terms of construct validity, results show differences between patients treated with insulin versus those on oral antidiabetic agent or diet treatment. Insulin users reported significantly greater negative impact of diabetes on most domains. In addition, people with greater reported complications had greater QOL impairment. Reliability for the ADDQoL has been reported: range 0.81-0.84 for Cronbach's alpha coefficient if item deleted, suggesting highly satisfactory internal consistency and reliability. Evidence for sensitivity to change of the ADDQoL has been drawn from a finding that diabetes had greater reported impact on diabetes-specific domains (such as enjoyment of food, worried about future and travel) than on standard QOL domains (such as work and social life).

1.4.4 Targets for glycaemic control and relevant measures

In 1989 the St Vincent declaration made recommendations for the care of patients with diabetes, including targets for the reduction of diabetic complications. The World Health Organisation (WHO) and the International Diabetes Federation (IDF) have drawn up a data set to monitor progress in reaching the targets of the St. Vincent declaration (Anonymous, 1990). The Desktop Guide for the management of Type 2 diabetes by the European Diabetes Policy Group (Anonymous, 1999a) recommends HbA1c (DCCT standardised) $\leq$ 6.5% and blood pressure <140/85 as a low risk group for diabetic complications.

The clinical practice recommendations of the American Diabetes Association (ADA) (1998c) suggest a treatment HbA1c standard of <7% and a blood glucose self-measurement target of 80-120 mg/dl before meals and of 100-140 mg/dl at bedtime in patients who do not have severe or unrecognised hypoglycaemia, and suggest therapeutic action when HbA1c exceeds 8%.

Diabetes UK, formerly the British Diabetic Association (Diabetes UK, 1999), in the light of the UKPDS results, has suggested that HbA1c level of 7.0% or below and fasting blood glucose levels of 4-7 mmol/l should be the target for glycaemic control in diabetic patients.

In March 1996 the Scottish Intercollegiate Guidelines Network (SIGN) published a national clinical guideline for the prevention of visual impairment in diabetes (SIGN, 1996). Further guidelines followed on the management of cardiovascular disease in diabetes (SIGN, 1997a), diabetic foot disease (SIGN, 1997b) and diabetic renal disease (SIGN, 1997c).

1.4.5 Targets for blood pressure lowering in diabetes

In the hypertension subgroup of the UK Prospective Diabetes Study (UKPDS Group, 1998a), those with Type 2 diabetes (Mean BP of 160/94 mmHg) was randomised to intensive or conventional antihypertensive treatment. The average BPs achieved were 144/82 mmHg in the intensive group and 154/87 mmHg in the conventional group. In the intensive group, treatment of hypertension was associated with a reduction in the risk of stroke (44%), deaths related to diabetes (32%) and microvascular disease (37%).

The Hypertension Optimal Treatment (HOT) study (Hansson et al., 1998) demonstrated the benefits of lowering BP to ≤ 140/85 mmHg in patients with hypertension. In patients with diabetes, there was a 51% reduction in major cardiovascular events (non-fatal MI, non-fatal stroke, and cardiovascular death) in the group with target diastolic BP < 80 mmHg, as compared to the group with a target of <90 mmHg.

Based on the significantly elevated risk of cardiovascular disease in patients with Type 2 diabetes, both the American Diabetes Association (1998c) and the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI) (Anonymous, 1997) recommend a blood pressure of less than 130/85 mmHg as a goal in diabetic patients. It should be noted that the approximate level of systolic blood pressure achieved (144 mmHg) with intensive treatment in the UKPDS (144/82 mmHg) was higher than the ADA recommendation of 130 mmHg, although the diastolic blood pressure (82 mmHg) was lower than 85 mmHg. However, it has been suggested that more aggressive treatment of high blood pressure might be useful in patients with microalbuminuria (Marshall 1999).

According to the World Health Organisation/International Society of Hypertension guidelines (Anonymous, 1999b), blood pressure in patients with diabetes should be reduced to below 140/90 mmHg. In the UK Diabetes UK (1999) has suggested that 140/80 mmHg should be the target blood pressure in diabetic patients.

In addition, aspirin treatment should be considered in patients with diabetes as a means of primary prevention of CVD. The HOT study (Hansson et al., 1998) showed that aspirin significantly reduced the frequency of major cardiovascular events by

15% and all MI by 36%. The benefit of aspirin was the same in the groups of patients with diabetes and ischaemic heart disease as it was in the whole HOT population.

1.5 Pharmaceutical Care in Type 2 diabetes

1.5.1 Concepts of Pharmaceutical Care

The process of pharmaceutical care has the patient as the main focus for activity. Pharmaceutical care has been defined as "the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life." (Hepler and Strand, 1990). The purpose of this practice philosophy is to ensure that individual patients receive the right drug, in the right dose, in the right form at the right time and to ensure that medication related health outcomes are optimised for the patient (Hepler, 1987; Hepler and Strand, 1990). In providing pharmaceutical care consistent with this philosophy, pharmacists become involved in three major functions which include identifying actual and potential drug related problems (DRPs), resolving actual DRPs, and preventing potential DRPs (Hepler and Strand, 1990).

Expanding from the traditional compounding role of pharmacists, the provision of pharmaceutical care has required pharmacists to optimise patient's therapy and to increase their relationships with patients and collaboration with other health care providers (Cipolle, 1998). This broader view of pharmacists' activities has been advanced, not only in the US, but also in many other countries (Foppe van Mil, 1999; Gilbert, 1995; Ibrahim, 1997). In the UK, pharmacists were familiar with the field of clinical pharmacy, the provision of information to patients, and cooperation with doctors. The philosophy articulated by Hepler and Strand (1990) for the development of pharmaceutical care was adopted in the UK in order to increase awareness of

pharmacists' responsibilities with respect to individual patients. The United Kingdom Clinical Pharmacy Association (UKCPA) (1996) launched a statement on pharmaceutical care intended to encourage the development and evaluation of new services to patients.

The benefits of pharmaceutical care models on patient outcomes of several disease states have been previously documented. Knoell et al. (1998), for example demonstrated a positive impact of a pharmacist-provided comprehensive education programme in an asthma outpatient clinic. A study by Varma et al. (1999) also showed improved outcomes in exercise capacity, compliance with drug therapy, knowledge of drug therapy and fewer hospital admissions in elderly patients with congestive heart failure who received education from a pharmacist, compared with control patients.

1.5.2 Interventions to improve diabetes management from previous studies

In term of diabetes management, a literature review revealed a limited number of published studies on the impact of a pharmacist intervention on patients with diabetes (Berringer et al., 1999; Coast-Senior et al., 1998; Hawkins et al., 1979; Huff et al., 1983; Jaber et al., 1996; Schilling, 1977, Wilcock, 2000). Studies during the 1970s and 1980s have primarily focused on the impact of diabetes education, and increasing patient compliance. Although disease-specific outcome measures were not consistently obtained, these studies demonstrated that pharmacist-oriented services produced a favourable impact. Since the 1990s studies have focused on drug therapy monitoring and disease outcomes and have paid closer attention to the issue of pharmaceutical care services. However, few studies have been conducted

in the UK, with those conducted mostly in the community pharmacy setting. Table 1.3 provides a summary of pharmacist interventions in the management of diabetes.

Table 1.3: Summary of pharmacist interventions in diabetic patients

References	Characteristics	Details
Schilling, 1977	Population	Diabetic patients
	Sample size	Not stated
	Site	58-bed Indian Health Service Hospital
	Research design	Intervention without either randomisation or control group
	Intervention	Pharmacist ran clinic (education, compliance assessment, monitoring, dose adjustment and referral)
	Outcome measure	Not stated
Hawkins et al., 1979	Population	Hypertensive and diabetic patients
	Sample size	349 intervention and 280 control
	Site	Medical follow-up clinic at the hospital in San Antonio, Texas
	Research design	RCT
	Intervention	Clinical pharmacist with physician review. Details not stated
	Outcome measure	BP and fasting blood sugar levels, kept-clinic-appointment rate, frequency of hospital admissions
Huff et al., 1983	Population	Diabetic patients
	Sample size	Not stated
	Site	Three ambulatory-care centers
	Research design	Intervention without either randomisation or control group
	Intervention	Diabetes-patient education
	Outcome measure	Not stated

Table 1.3 continues overleaf

References	Characteristics	Details
Van Veldhuizen-Scott et al., 1995	Population	Patients attending the educational programme at the Regional Diabetes Center in Lafayette, Indiana, from May through December 1993
	Sample size	41 patients (13 intervention group 1, 14 intervention group 2, 14 control)
	Site	Diabetes center
	Research design	RCT
	Intervention	Additional small group or individual supplementary education with follow-up telephone contact by the pharmacist
	Outcome measure	Changes in blood glucose levels, responses on a pretest and posttest questionnaire
Jaber et al., 1996	Population	African-American Type 2 diabetes patients
	Sample size	39 patients (17 intervention, 22 control)
	Site	Outpatient clinic
	Research design	RCT
	Intervention	Diabetes education, medication counselling, instruction on dietary regulation, exercise, and home glucose monitoring, and evaluation and adjustment of antidiabetes drug regimen
	Outcome measure	Fasting plasma glucose and glycated haemoglobin concentrations
Coast-Senior et al., 1998	Population	Patient with Type 2 diabetes who received insulin and were willing to perform self-monitoring of blood glucose
	Sample size	23 patients
	Site	Primary care clinics
	Research design	Intervention without either randomisation or control group
	Intervention	The pharmacists provided diabetes education, medication counselling, monitoring, and insulin initiation and/or adjustments.
	Outcome measure	Changes from baseline in glycosylated haemoglobin, fasting blood glucose, and random blood glucose measurements.

Table 1.3 continues overleaf

References	Characteristics	Details
Berringer et al., 1999	Population	Type 1 or Type 2 diabetes patients receiving prescription services from two independently owned community pharmacies in Richmond, Virginia
	Sample size	52 patients
	Site	Community pharmacy
	Research design	Intervention without either randomisation or control group
	Intervention	Routine monitoring using 'Diabetes Checklist', chart review, and identify drug-related problems and develop plan
	Outcome measure	Self-monitoring blood glucose (SMBG) results, SMBG frequency, and antidiabetes agent adherence rates
Wilcock, 2000	Population	People receiving a service from community pharmacies during three-month period.
	Sample size	Not stated
	Site	Community pharmacies in Cornwall
	Research design	Intervention without either randomisation or control group
	Intervention	Pharmacist identified diabetes-related problem, resolved the problem within the pharmacy or made GP referral if appropriate.
	Outcome measure	Number of patients given a referral slip, number of patients with pharmacist intervention

Schilling (1977) described a pharmacist involvement in a programme for monitoring and treating diabetic patients in hospital. Patients were seen by the pharmacist instead of a doctor for routine diabetes management including education, compliance assessment, alteration of medication doses based on blood and urine glucose readings and referral when appropriate. Although the report described the programme in specific details, no outcome measures were provided.

Hawkins et al. (1979) reported a randomised controlled trial assessing the effectiveness of a clinical pharmacist intervention on the management of patients with hypertension and diabetes in a pharmacist-run clinic setting. The study results indicated that the experimental group experienced higher patient satisfaction attributed to higher kept-clinic appointment and lower drop-out rates. No evidence was provided to support the claim that attendance rates equated to patient satisfaction. Fasting blood glucose in patients with diabetes were not significantly changed by the pharmacist interventions. No analysis of HbA1c was provided for comparison of longer term glycaemic control measurement. The only clinical endpoint which was reported as statistically significant was systolic blood pressure which was reported to be lower in the control group (143 to 141) compared to the intervention group from baseline to follow up (145 to 147).

Huff et al. (1983) described a reimbursed pharmacist-managed educational service successfully provided over a 10-year period. The pharmacist-educators' responsibilities included assessment, planning, instruction, and follow-up. However, objective assessment of the impact of these services on disease outcome was not published.

Van Veldhuizen-Scott et al. (1995) described a randomised, controlled study where the patients in two treatment groups received additional small group (n=13) or individual supplementary education (n=14) with the pharmacist for a two-month period. Control patients (n=14) received the standard educational programme. The authors claimed lower average weekly blood glucose levels and a decreased incidence of hyperglycaemic episodes in the treatment groups compared with the control group. However when adjusted for baseline values there was no significant difference between intervention and control groups in percentage change of glucose

over the eight weeks (P = 0.796). Analysis of HbA1c was not available due to the short duration of the study. In addition no significant change between pre-test and post-test responses was identified in general knowledge of diabetes or in perceptions/attitudes towards diabetes in general when comparing control and intervention patients (P = 0.776). Severe limitations of this study were the small numbers involved the short two month follow up and the reliance of self reported blood glucose values with only 8 patients (25%) being able to confirm self-documentation exactly as reported by their meter memory printout.

Jaber et al. (1996) reported the results of a study assessing the effectiveness of a pharmaceutical care model in African-American patients with Type 2 diabetes in an ambulatory care setting. Patients were randomised to either a pharmacist intervention or control group and followed over a 4-month period. Patients in the intervention group (n = 17) received diabetes education, medication counselling, instructions on diet, exercise, and home glucose monitoring, and evaluation and adjustment of their hypoglycaemic regimen. Follow-up was conducted on a scheduled weekly basis until targeted glycaemic control (FBG $\leq$ 6.6 mmol/l and 2-hour postprandial blood glucose < 10.0 mmol/l) was reached. Thereafter, patients came to the clinic every 2-4 weeks for the duration of the study. Patients in the control group (n = 22) continued to receive standard medical care provided by their doctors.

The authors claimed significant improvement in glycaemic control was achieved in the intervention group as evidenced by glycosylated haemoglobin and fasting plasma glucose. Fasting glucose levels at baseline and 4 month follow up were 12.7 and 11.0 for the control group and 11.1 and 8.5 in the intervention group. HbA1c values at baseline and 4 month follow up were 12.2 and 12.1 for the control group and 11.5 and 9.2 for the intervention. Although this latter decrease (P = 0.003) is considered

statistically significant it has to be cautiously interpreted. It is notable that only one hundred and fifty-six patients (17.5%) met the strict inclusion criteria and that only forty five (29%) agreed to take part with thirty nine (87%) patients completing the study. Six patients (26%) in the intervention group dropped out of the study compared to no dropouts in the control group. Of the six patients who dropped out four found it difficult to comply with the frequency of clinic visits, one was discharged due to unstable angina and one was lost to follow up. It is likely that selective exclusion of non-compliant patients in the intervention group introduced a significant bias and that the result may not have been found to be significant if an intention to treat analysis had been employed.

No significant changes in blood pressure control, lipid profile, renal function parameters, weight, or quality of life measures were noted within or between groups. However, a study with larger numbers of subjects and of longer duration needs to be carried out for further evaluation. In terms of the high frequency of attendance with this intensive approach, it might be difficult to apply this model into routine practice.

Coast-Senior et al. (1998) reported a study of clinical pharmacists working in two primary care clinics managing patients with Type 2 diabetes who either were currently treated with insulin or were initiated on insulin therapy by the pharmacists. All patients were referred to the pharmacist by their primary care providers with the aim of improving glycaemic control. The pharmacists provided diabetes education, medication counselling, monitoring and insulin initiation and/or adjustment. Twenty-three patients completed the study; fifteen (65%) were initiated on insulin by the pharmacists and eight (35%) were already using insulin. The mean length of follow-up was 27 weeks. Mean HbA1c was 11.1 ± 1.6 at baseline for control compared to 8.9 ± 1.4 at follow up for intervention. Although this was statistically significant ($P <$

0.0005) and of clinical importance the study design did not include a control group therefore it is likely that the improvement in HbA1c noted was due to the introduction of insulin. The study has many limitations in that the total number of patients were not reported only those completing the study. HRQOL was not evaluated and it is notable that 35% of patients reported hypoglycemic symptoms. Finally the study is not generalisable due to its very narrow inclusion criteria with all Type 2 patients requiring insulin.

Berringer et al. (1999) reported outcomes of a year-long pharmacist-led programme in two independent pharmacies in Richmond, Virginia. During the first 6 months of the programme, enrolled patients experienced an average decrease in their glucose values from 178.6 mg/dl to 159.3 mg/dl. Remarkably, over the 12-month study period, participants had an average adherence rate of 90% for their use of diabetes medications. One limitation of this study was that it relied on patient self report of blood glucose measure with no attempt to validate the method of self-report. As already highlighted the study by Van Veldhuizen-Scott et al. (1995) found only 8 out of 32 patients had readings which were supported by glucose meter memory records.

Another limitation was that only patients reporting 0, 6 and 12 month blood glucose levels were included in the analysis. This is likely to bias the sample as such patients may also be more compliant with therapy. No control group was included therefore we cannot rule out other factors which may have influenced the blood glucose levels. HbA1c values would have provided a more accurate measure of glucose control which would have been ideal for the six monthly reviews included in this study. A final limitation of the high adherence rate reported is the method used to evaluate adherence which calculated this by dividing the 'actual days supply' with the 'prescribed days' supply' where 'actual days supply' was calculated by number of

units purchased over the time and 'prescribed days' supply' was calculated on prescription issued over the period.

Wilcock (2000) reported an evaluation of pharmacists' intervention in community pharmacies in Cornwall. Eighty-one community pharmacists from 70 pharmacies (out of 86) attended a two-and-a-half-hours diabetes training programme. They were given a package of resources including referral forms for referring patients to a doctor or practice nurse if appropriate, and a documentation book for recording 'in-house' intervention made by pharmacists. Forty-nine pharmacies participated in the study. After a three-month period, there were only 23 patients referred back to the surgery. The top four reasons for referral included 'further advice on diet' (n=5), 'symptoms due to low/high blood glucose' (n=3), 'potential interaction with prescribed medication' (n=3), and other reasons (not specified in the report) (n=12). A total of 300 patient intervention forms were recorded from 37 pharmacies, with 12 pharmacies having no intervention recorded. Monitoring of the condition was the most common reason for advice (38% of patients), followed by advice on avoiding inappropriate over-the-counter medication (20%). However, this study did not analyse clinical outcomes such as HbA1c to assess glycaemic control, and took place over a short period of only three months. In addition outcomes of the referrals were not stated.

Conclusion

None of the studies to date have provided robust evidence of patient outcomes to support the delivery of pharmaceutical care to diabetic patients. The gold standard is normally a randomised controlled trial design. However of the three randomised controlled trials reviewed each has their limitations.

In the first RCT (Hawkins et al., 1979) a large number of subjects were reviewed over 29 months. However there was no measure of HbA1c or HRQOL. The assumption was made that attendance rates at the clinic equated to patient satisfaction. Even the attendance rates for the control group were estimates rather than actual values.

The second RCT (Van Veldhuizen-Scott et al., 1995) included very small numbers with only a two-month follow up. There was no measure of HbA1c, HRQOL and drug related problems. The authors claimed lower blood glucose in the intervention group however when adjusted for baseline values no difference was noted ($P = 0.796$).

The third RCT (Jaber et al., 1996) covered small numbers over a short four-month follow up. This study did measure HbA1c, blood pressure and QOL. No significant changes in blood pressure, lipid profile, and QOL. However the mean HbA1c for the intervention group at the end of the study was 9.2 ± 2.1, therefore it is unlikely to be clinically significant. Also this data has to be interpreted with caution as 6 (26%) patients were removed from the intervention group, four of whom could not cope with the strict regimen. No such consideration was given to removing patients from the control group therefore it is likely that we have bias in the reporting of outcomes which is likely to be significant given the small numbers.

Further research is therefore required to evaluate the impact of pharmaceutical care models in a diabetic population.

1.6 Hypothesis

Pharmaceutical care delivered by community pharmacists can improve patient outcomes of Type 2 diabetics in a primary care setting, as indicated by changes in HbA1c, systolic blood pressure (SBP), health related quality of life (HRQOL) and drug related problems (DRPs).

1.7 Aim of the present study

The aim of this study is to compare the impact of a pharmaceutical care diabetic clinic within a primary care setting to standard care on clinical, humanistic and process outcomes in Type 2 diabetics.

1.8 Objectives

1. To develop a practical pharmaceutical care model for patients with Type 2 diabetes.
2. To develop and validate suitable data collection forms to support the pharmaceutical care model.
3. To implement a pharmacist managed diabetic clinic for patients with Type 2 diabetes using the pharmaceutical care model.
4. To evaluate the pharmaceutical care model and compare clinical (HbA1c, SBP) and humanistic (HRQOL) patient outcomes in the active group receiving the pharmaceutical care model, in addition to standard care, versus the control group receiving standard care only.

5. To investigate the number and types of DRPs identified by the pharmacist, the percentage of recommendations accepted by the physician and the status of the DRPs at follow up.
6. To obtain feedback from the pharmacists to inform future service delivery.

Objective 1-2 will be covered in the pilot study, with objectives 3-6 being met in the main study.

Chapter 2

General Methodology

2.1 Literature review

A review of the literature was conducted using the electronic databases MEDLINE (1966-2000) and International Pharmaceutical Abstracts (1990-2000). The search terms used included pharmacist intervention (any of community pharmacist, clinical pharmacist, pharmacy service), pharmaceutical care, ambulatory care, pharmacotherapy, diabetes, quality of care, quality of life, outcomes, and clinical outcomes. Bibliography searches were conducted of some articles obtained, including reviews. In addition a hand search of other relevant literature was undertaken.

2.2 Study setting

It was intended that all of the pharmaceutical care clinics would take place within general medical practice settings within Greater Glasgow Health Board area (GGHB), Scotland.

2.3 Project funding

The programme was funded by the Greater Glasgow Primary Care Trust through a prescribing development fund.

2.4 Ethics committee approval

Separate applications were made for both the pilot and the main studies to the ethics committee of the Greater Glasgow Community/Primary Care Local Research Ethics Committee. Approval was granted (Appendix I and II).

The pilot study was carried out in the eight recruited general practices during July and August 1999. The main study was carried out in nine different general practices over a 12-month period from March 2000 to February 2001.

2.5 Study team

Overall there were eight members of the study team, some of whom had joint responsibilities. There was a supervisory research team who focussed on research aspects of the study and a project team which co-ordinated day to day operational aspects of the study and together these two groups comprised the study team.

The supervisory team comprised two experts in pharmaceutical care (CAM,DS) and a pharmacologist (DMcC). The project team comprised CAM (principal investigator), two clinical pharmacists (AM & RL) and a clerical assistant (KB). In addition a medical adviser (ANC) who was a consultant physician and a specialist in diabetes, was also appointed to the study team. The research student (SS) worked with both teams and was responsible for independently reporting on all aspects of the study.

In the main study the study team also included an experienced research pharmacist (ALC) to independently follow up patient outcomes at the end of the study.

2.6 Recruitment of general medical practices

The pilot study involved a convenience sample of eight out of twenty two practices currently participating in medication review clinics. The main study sample was drawn from the GGHB list of two hundred and nineteen practices excluding the eight pilot sites. Random numbers were used to identify the practices. However fifteen practices were approached in order to recruit nine practices with sufficient patient numbers to meet the predetermined study power.

2.7 Recruitment and training of pharmacists

All twenty-two pharmacists currently running general Medication Review Clinics in Glasgow were invited to participate in the pharmaceutical care diabetic clinics and required to attend a training programme. All the pharmacists who participated in the study were registered pharmacists and subject to the Royal Pharmaceutical Society of Great Britain code of ethics.

Six community pharmacists were recruited to provide the clinics in the pilot study. In addition two project pharmacists (AM & RL) also participated in the pilot clinics. All eight pharmacists received the training programme provided and had previously been working in the medication review clinics.

There were nine pharmacists who participated in the main study. All nine pharmacists completed the training programmes provided before the model was implemented. Of these, six participated in the pilot study while the remaining three were not involved in the pilot but participated only in the main study.

The training programme involved three evening sessions in November 1998, January 1999 and June 1999, and a one-day session in February 1999. The study team and appropriate specialists provided training for the pharmacists.

The first session involved a lecture providing on overview of Type 2 diabetes, pharmaceutical care of diabetic patients, and an introduction to the diabetes project, delivered by the research student. The pharmacists received a package of materials including relevant papers to support the pharmaceutical care aspects of Type 2 diabetes (BDA, 1997; SIGN, 1996; SIGN, 1997a; SIGN, 1997b; SIGN, 1997c; Strand et al., 1990; UKPDS, 1998a; UKPDS, 1998d).

The second training session was a problem-based learning workshop regarding Type 2 diabetes. This aimed to enhance the pharmacist's ability to develop diabetic care plans and solve related clinical problems. There was an interactive discussion at the end of the session. The last part of the session included practice on the use of the blood glucose meter and measuring blood pressure.

The third training session included a presentation on the diabetes clinic procedures and role playing in diabetes case scenarios. The role playing part was aimed to ensure that the pharmacists completed the data forms correctly and were able to: comply with study procedures; perform the fingerstick technique for blood glucose monitoring; measure blood pressure correctly; identify a list of drug related problem and outline a plan of action for each problem.

The fourth training session was concerned with reinforcing the study procedure and data collection methods and included a review of drug management and patient

education in Type 2 diabetes. This was presented by a specialist in diabetes (ANC) from the AYR Hospital NHS trust and the researcher (SS).

2.8 Data analysis and statistical methods

Statistical analyses were performed in both the pilot and the main study using the Statistical Package for Social Sciences (SPSS) programme version 9.0 and 10.0 for Windows. All data was entered on a SPSS database by the researcher (SS). Patients and pharmacists were all coded to ensure confidentiality. No names or address were recorded on computer profiles. The following analyses were generally considered:

1. Demographic and clinical characteristics of patients and data on the medical conditions, drugs prescribed and drug related problems were examined using descriptive statistics. Values are expressed as number, percentage, mean ± SD, and median values, as appropriate.

2. The Pearson Chi-square or Fisher' Exact test was used for nonparametric analysis to compare categorical variables.

3. Continuous variables were compared between groups using Independent-Sample T test or the Mann-Whitney U-test, in the case of skewed variables.

A two-tailed *P* value less than 0.05 was regarded as statistically significant.

Chapter 3

Pilot Study

3.1 Aim and objectives

The aim of the pilot study was to develop a pharmaceutical care model and documentation system for use in the main study.

The objectives of this pilot study were to:

1. Develop a practical pharmaceutical care model for patients with Type 2 diabetes.
   - 1.1 Develop a practical pharmaceutical care model to be used in the main study.
   - 1.2 Estimate the number of patients required for the main study.
   - 1.3 Identify and investigate problems arising from the implementation of the above process in order to improve the model.

2. Develop and validate suitable data collection forms to support the pharmaceutical care model.
   - 2.1 Develop suitable data collection forms.
   - 2.2 Test two previously validated quality of life measures and determine the most appropriate disease specific quality of life measure for the main study.
   - 2.3 Obtain the participating pharmacists' comments on the model and data collection forms during the pilot.

3.2 Methodology

3.2.1 Study setting

The project was conducted in a convenience sample of eight general practices in the Greater Glasgow Health Board area (GGHB). The practices were recruited from a total of twenty-two general practices running pharmacist led medication review clinics at the time the project began in July 1999. Each practice had one pharmacist running a clinic one day per week. A convenience sample was selected because the pharmacists were willing to participate in the training programme and were available one day per week for the 12 – 18 month period of the project. In addition the practice had to agree to participate in the pilot study and provide a suitable consultation room.

3.2.2 Patient recruitment

Patients aged 18 years and older who were diagnosed as suffering from Type 2 diabetes and receiving oral antidiabetic drugs (based on their medical record) were eligible for inclusion. They were excluded from the study if any of the following criteria were present:

(1) patients unable to provide informed consent due to cognitive or severe sensory impairment such as dementia, hearing, speech, or severe visual impairment, or

(2) serious acute or terminal illness.

A letter together with a consent form (Appendix III) was sent to prospective patients inviting them to attend the pharmaceutical care diabetic clinics. Written informed consent was obtained from all subjects before admission to the study. Within 2 weeks patients were telephoned and an appointment made, if appropriate. Patients who did

not attend a scheduled appointment were contacted again and a second clinic appointment allocated. If they did not attend the second clinic no further contact was made.

3.2.3 Development of documentation to support the pharmaceutical care model

A Medication Review Form (MRF) was used (Appendix IV, Mackie et al., 1999) to collect general data. The eight clinic pharmacists had previous experience of this MRF as it was used as a standard in all Medication Review Clinics in Glasgow. In addition a draft Diabetes Data Collection Form (DDCF) was developed by the researcher (SS) to collect additional diabetic specific information. The DDCF was presented on two pages (Appendix V). The first page included the following: demographic patient information, medical history, attendance at diabetic clinics, use of glucose monitoring, clinical objective data, history of foot examination, history of eye examination, previous therapy, and diabetic education provided at interview. This included information mainly obtained from medical records. Information not available in medical records was requested by the pharmacist directly from the patient at interview. The second page presented a list of questions for the pharmacist to ask the patient, a table in which to record the time spent on the activities in the clinic, and finally space for general comments from the pharmacists. A patient information leaflet (Appendix VI) was designed using 'plain' English providing information about diabetes with some basic advice about diabetes care.

As a measure of content validity, the draft DDCF was sent to the study team. Comments were sought in relation to whether the wording in the form was clear and whether any important areas had been omitted. Minor changes were subsequently

made to the form, which was then sent to the study team and six pharmacists for the pilot study.

After completing the training programme (see Chapter 2), the pharmacists were given a package of materials including data collection tools namely a Medication Review Form (Appendix IV), and Diabetes Data Collection Form (Appendix V), patient information leaflet (Appendix VI), two quality of life questionnaires (Appendix VII and VIII), and a GP referral form (Appendix IX).

The two quality of life questionnaires, the Audit of Diabetes Dependent Quality of Life (ADDQoL) (Appendix VII) and Diabetes-39 (Appendix VIII), were selected as they had been previously validated in Type 2 diabetic patients (Boyer, 1997; Bradley, 1999). These two questionnaires were used in the pilot study by permission from the authors.

3.2.4 Pharmaceutical care model

Six patients were booked into the pharmaceutical care clinic, which ran one day per week. Pharmacists prepared for the clinic in the morning and interviewed patients in the afternoon. The overall aim was to identify actual and potential DRPs where a DRP was defined as 'any undesirable event experienced by the patient that involves or is suspected to involve drug therapy and that actually or potentially interferes with desired patient outcomes' (Strand et al., 1990).

3.2.4.1 Morning session

During the morning session, the medical notes and computer records of all scheduled patients were reviewed in order to gather background patient information and complete the first page of the DDCF and MRF. The pharmacist explained the new type of clinic to the reception staff and supplied him/her with questionnaires and patient consent forms for every patient booked into the clinic.

3.2.4.2 Afternoon session

Patients were invited to attend the clinic in the afternoon session. Patients were asked to fill in the QOL questionnaires (either ADDQoL or Diabetes-39 allocated randomly) at the reception area before meeting with the pharmacist. At the clinic, the pharmacist introduced him/herself to the patient and explained the reason for the clinic to patients and answered all the questions about the study the patient may have. The pharmacist also obtained the completed QOL questionnaire and consent form from the patient at the start of the interview. Then the pharmacist interviewed the patient asking general and specific questions about diabetes and completed the MRF and the DDCF. During the clinic, the pharmacist educated the patient regarding DRPs which were relevant and gave the patient a diabetes leaflet. The pharmacist recorded the time spent at each step and added comments relating to the protocol and the data collection form, if appropriate.

After the clinic, the pharmacist reviewed all of the data to identify DRPs and completed a GP referral form (Appendix IX), if required.

3.2.5 Process outcomes

After completing the pilot study at the end of August 1999, the pharmacists were given a pharmacist feedback survey form (Appendix X) which asked them to comment on the clinic protocol, data collection forms, and training programme. The pharmaceutical care model was then revised based on this written feedback from the pharmacists, discussion at the training session, and peer review by the study team.

3.3 Results

3.3.1 Characteristics of patients recruited to the pilot study

Computerised records were searched in eight general practice settings in Greater Glasgow Health Board area and following screening for exclusions by the practice manager, 138 patients were identified who met the inclusion criteria. Of those, 21 (15%) refused to participate in the study and 4 (2.9%) were not contactable. Sixteen patients (12%) agreed to participate but did not subsequently attend the clinic. The remaining 97 (70%) patients participated in the study by attending the clinic of whom 96 patients completed the quality of life questionnaire.

Demographic data is provided in Table 3.1. There were approximately equal numbers of male and female patients. The majority of patients was over 60 years of age, with a mean age of 67 ± 11 years (mean ± SD).

Table 3.1: Characteristics of pilot participants

Characteristic	Number (n=97)	Percentage
Age		
40-50 years	12	12
51-60 years	16	16
61-70 years	38	39
> 70 years	31	32
Gender		
male	48	50
female	49	50

Clinical data, where available, is provided in Table 3.2. Most patients were attending diabetic clinics (92.8%) and using self-glucose monitoring at home (75.3%). Sixty-six percent of the patients were obese (BMI >27 kg/m^2), with a mean BMI of 30 ± 6.1. In addition, 34% had a history of eye problems while 11% had a history of foot problems. An indicator of glycaemic control, the HbA1c value, was 8.0 ± 2.1 %.

Table 3.2: Clinical data of patients included in the pilot study

Characteristic	Number	Percentage
Attendance at diabetic clinics		
Currently attend at hospital	44	46
Currently attend at surgery	13	14
Currently attend both	33	34
Had ever attended at hospital in the past	2	2.1
Never attended diabetic clinics	4	4.2
Last diabetic clinic attendance		
< 1 year	78	94
> 1 year	5	6.0
Self-glucose monitoring		
Using blood glucose monitoring	20	21
Using urine glucose monitoring	53	55
Never use	23	24
BMI (kg/m^2)		
< 25 kg/m^2	14	16
25-27 kg/m^2	9	10
>27 kg/m^2	64	74
History of foot exam		
normal	61	85
foot problem(s)	11	15
History of eye exam		
normal	50	60
eye problem(s)	33	40
HbA1c value		
HbA1c > 8 %	44	46
HbA1c 7- 8 %	15	16
HbA1c < 7 %	37	38

3.3.2 Documentation system and missing data

There were 97 data collection forms, 48 GP referral forms, 48 Diabetes-39 questionnaires, and 48 ADDQoL questionnaires returned to the researcher. Of the 97 data collection forms, there were missing clinical data as shown in Table 3.3.

Table 3.3: Top ten missing data in the forms returned

Missing data	Number of missing records
Liver function test	59
Albumin	58
Fasting/random blood glucose	58
Renal function (creatinine)	47
Lipid profile	45
Blood pressure	45
History of foot exam	25
Last date of attendance	14
History of eye exam	14
BMI	10

3.3.3 Time required to deliver the pharmaceutical care model

The time required to deliver the pharmaceutical care model is shown in Table 3.4. Overall the participating pharmacists took approximately one hour in retrieving patient information from the medical records, completing the data collection forms, interviewing the patient, and providing patient education.

Table 3.4: Time required for the pharmaceutical care clinic

Activity	Time per patient			
	<10 mins	**10-20 mins**	**21-30 mins**	**>30 mins**
Pre-interview	0	33	<u>48</u>	16
Interview	2	37	<u>43</u>	3
Patient education	<u>49</u>	30	1	0

Note: underlined values are the most frequently observed times.

3.3.4 Quality of life questionnaires

A summary of comparable issues between ADDQoL and Diabetes-39 is displayed in Table 3.5. In addition to the details presented in the table, it was found that there was some difficulty in score interpretation using the Diabetes-39 questionnaire. This was due to the fact that the scale was not discrete and depended on positioning of a cross.

Table 3.5: Comparison between Diabetes-39 and ADDQoL

Issues to be considered	Diabetes-39	ADDQoL
Number of questions to be completed	39 diabetes-specific questions plus two overall rating questions	13 diabetes-specific questions plus two overall rating questions
Study participant	Validated in two samples (Iowa and Carolina study) of adults in the United States.	Validated in two samples (Cambridge and Bromley sample) of adults in the United Kingdom.
Evidence of reliability and validity	Yes	Yes
Scale score for each question	0-100 (higher score indicates worse quality of life)	-9 to 9 (higher score indicates better quality of life)
Domains and number of questions for each domain	Diabetes control 12 questions Anxiety and worry 4 questions Social burden 5 questions Sexual functioning 3 questions Energy and mobility 15 questions	Employment/career Social life Family relationships Friends Sex life Sport/leisure Travel Future (own) Future of family Motivation Physical activity Others fussing Enjoyment of food (one question/domain)
Missing data	If in total more than 4 items are missing (excluding missing items sexual function scale and independent of the scale) the questionnaire will be excluded from the analysis	Provides N/A option in some domains. This is excluded from the scoring.
Valid completion (from the pilot study)	81%	92%

3.3.5 Drug related problems

3.3.5.1 Total number of drug related problems (DRPs)

One hundred and twenty seven DRPs were noted by the pharmacists for 47 (48%) of the 97 patients. DRPs most frequently involved monitoring laboratory tests (34%), changing of regimens (19%), and adjusting dose (13%). The pharmacists obtained complete GP agreement to 90 (71%) of the resolutions recommended for the drug related problems, and partial agreement to a further 26 (20%). Partial agreement was defined as GP agreeing to the recommendation but requiring to see the patient before making a change to therapy. Overall 9% of GP referrals were rejected.

3.3.5.2 Diabetes related and diabetic complication related DRPs

The pharmacist made suggestions to the GP regarding 71 diabetes related DRPs in 97 patients. The GP completely agreed with 46 out of 71 diabetes related changes (65%).

3.3.6 Summary of comments from pharmacists

The eight clinic pharmacists returned a feedback questionnaire regarding data collection forms, the package of materials, and the training programme.

3.3.6.1 Comments about the pharmaceutical care model and documentation

All eight pharmacists responded. Table 3.6 presents the pharmacists' responses to the survey questionnaire. Generally the pharmacists responded that the form was

easy to use and a useful guide when preparing the care plan and GP referral. They suggested reducing the number of records of objective data to the 3 most recent due to the difficulty and time taken in retrieving all data. In addition, the difficulty of establishing a normal range of HbA1c and some other laboratory data was also raised.

Table 3.6: General questions about the model - questionnaire completed by pharmacists after pilot study

No.	Question	Answer
1.	Comments about the data collection form	1. The form itself is relatively easy to fill and very useful when preparing GP referral form. 2. The boxes of objective data were not split properly and there was not enough space provided. 3. It was difficult to get relevant readings especially if the patient attended a hospital clinic because although they apparently make measurements they are not recorded in the surgery notes. 4. Five readings of the objective data were too much and found it was quite time consuming.
2.	Data to be included or excluded in the form	Exclude: 1. 'What is the patient's reading' in the part about glucose monitoring Include: 1. Present diabetic medication 2. Clarify 'attendance at clinics' e.g., regularly, never.
3.	Were the given package of documents and training programme adequate or inadequate?	1. One answered 'inadequate' 2. Seven answered 'adequate'
4.	How many patients on average have you booked in for each clinic?	1. All answered six patients
5.	Is this number too little, too many or about right?	1. Six pharmacists answered 'about right' 2. Two did not answer and gave a reason that there was high non-attendance rate.

The pharmacists rated number of patients booked per clinic 'about right' in the sense that when all attended there was adequate time for paper work between patients. One pharmacist said she could manage seven patients easily at one clinic. In the pilot study there was 88% attendance. Two pharmacists complained about the high non-attendance rate and therefore could not respond on whether the number of patients per visit was appropriate.

The pharmacists commented on HbA1c records. They noted that hospital results of HbA1c did not provide normal range data and the 5 readings examined in patients' notes were usually a mixture of hospital and GP readings. One pharmacist suggested excluding 'What is the patient's reading' in the part about glucose monitoring giving the reason that it was too ambiguous. It was also suggested that documentation of the liver function test data should change because most results were given as a range of enzymes. There was no simple way of documenting this in a single row within the table.

It was also suggested that if reception staff are handing out the QOL questionnaires, care must be taken to ensure that they can communicate all the necessary information to allow the patients to feel comfortable about taking part in the study and to appreciate the importance of their contribution.

The feedback from the pharmacists was discussed within the study team and some minor modifications of the data collection tools were undertaken.

3.3.6.2 Comments about the training programmes

Most of the pharmacists found the training programme and documentation provided useful and reported that it was adequate. One pharmacist indicated she was not satisfied and that she required more information, especially about the use of insulin in Type 2 diabetes.

3.4 Discussion

3.4.1 Study setting

In choosing a convenience sample, the study team recognised that the data would not be generalisable. However, the objective of the pilot study was to develop the model and data collection tools and this is best done by a team with an established relationship to prevent additional strain on team members.

3.4.2 Pharmaceutical care model and data collection forms

The pilot study was designed as a single intervention aimed primarily at arriving at a pharmaceutical care model appropriate and practical for the main study. Data from the pilot study allowed a number of points to be identified as important in revising the protocol and data collection tools. The forms were revised in term of the space and layout, the order of questions, and some items, which it was not practical to retrieve and use, were omitted.

It is important that patients actually complete the quality of life questionnaire and so the number of questions has to be considered in order to encourage completion. In this case we chose the shorter questionnaire, ADDQoL which had a 92% completion rate, for use in the main study. The other reasons for choosing the ADDQoL included ease of self-administration, and interpretation of questions and a straightforward scoring system.

The case load of approximately six patients per clinic was considered manageable for the pharmacists, with the interview lasting 20-30 minutes plus 10 minutes for patient education. This was useful information for determining the clinic schedule in the main study. It was considered likely, however that time spent would be shorter in the follow-up clinic. This duration is comparable to the study by Veldhuizen-Scott et al. (1995) who found that a one-on-one counselling intervention time took a mean time of 40 minutes.

3.4.3 Pharmacists' comments on the model and data collection form

Most of the pharmacists accepted that the training programme and materials provided were adequate to allow them to fulfill the role of the pharmacist in the diabetic clinic. However, to ensure consistency in the main study, a peer review team consisting of experienced clinical pharmacists will continue to review all GP referrals made by the pharmacists. Educational needs were also identified and would be addressed by a series of workshops to include treatment of diabetes, and further training in measuring blood pressure. Pharmacists who wished to continue to deliver the pharmaceutical care model in the main study were encouraged to enroll in ongoing peer review sessions throughout the study. These peer review sessions allowed pharmacists to discuss problem cases with their colleagues once a fortnight.

3.4.4 Problems to be solved

It was found that the normal range of HbA1c values varies between laboratories because of the lack of standardisation of the assay method. It is not possible to directly compare HbA1c values generated in different laboratories. It is therefore essential that the same laboratory is used throughout the main study and the normal reference values for this particular laboratory are used when assessing patients' glycaemic control.

The recommendations on drug related problems made by the pharmacists in this pilot study were well accepted by physicians, as indicated by the fact that 71% of the recommendations obtained complete GP agreement. Co-operation of the medical team is a critical factor in making this model work. Therefore, this is a positive finding with regard to the implementation of the model and future collaboration with the medical team in the main study.

3.4.5 Sample size for the main study

To calculate the sample size required for the main study, the study was powered to detect a clinically meaningful difference of 1.0 unit change in mean HbA1c value. From the data collected in the pilot study, the standard deviation (SD) of the mean HbA1c is 2.1. The sample size estimate was calculated on the basis of the assumption of a 2-tailed test for which the α error is 0.05 and power is 0.90. The standardised difference = clinical significant difference/SD = 1.0/2.1 = 0.48. Reading from the nomograph (Altman, 1991), gives a sample size of 170.

Therefore the minimum sample size in the main study should be 170 patients. Due to the 30% drop-out rate estimated from the pilot and the need for three visits, it was estimated that we would have to recruit many more patients into the main study, which is a randomised controlled trial design. However compared to other studies (Fischer et al., 2000; Jaber et al., 1996), participation rate in the pilot study was high. Jaber et al. (1996) studied the impact of pharmaceutical care model on Type 2 diabetes patients comparing active and control groups at baseline and a 4-month visit. The study was done in an outpatient clinic in a university hospital. Of a total of 156 eligible patients, 45 (29%) patients participated in the study. After randomisation into active and control groups, 6 of 45 patients (13%) dropped out, leaving 39 (87%) patients completing the study. The participation rate in Fischer et al. (2000) study was 46% at the initial visit. This study involved pharmaceutical care evaluation in patients with chronic disease in community pharmacies. Therefore in order to have 170 patients complete the main study we would require 370 patients to allow for a 46% follow up.

3.5 Conclusion

All the suggestions made by the pharmacists and medical adviser were incorporated into the model for the main study which was undertaken as a randomised controlled trial. The newly designed pharmaceutical care model and documentation were finalised for use in a large-scale trial to allow investigation of the impact of the pharmaceutical care model in Type 2 diabetic patients compared to standard care. Documentation to support the Pharmaceutical Care model in the main study, is given as follows:

Appendix VII	:	ADDQoL
Appendix XI	:	Patient diabetes information leaflet (Revised)
Appendix XII	:	GP referral form (Revised)
Appendix XIII	:	Patient information about the study (new)
Appendix XIV	:	Patient consent form (Revised)
Appendix XV	:	Medication review form (Revised)
Appendix XVI	:	Update medication review form (New)
Appendix XVII	:	Diabetes data collection form (Revised)
Appendix XVIII	:	Update diabetes data collection form (New)
Appendix XIX	:	Letter of thanks to patient after attending clinic 1 (new)
Appendix XX	:	Letter of thanks to patient after attending clinic 2 (new)
Appendix XXI	:	Letter of thanks to patient after attending clinic 3 (new)

Chapter 4

Method - Main Study

4.1 Aim

The aim of the study is to assess the impact of pharmaceutical care delivered by community pharmacists on the management of Type 2 diabetes using a randomised controlled trial study design.

4.2 Objectives

1. Implement a pharmacist managed diabetic clinic for patients with Type 2 diabetes using the pharmaceutical care model developed in the pilot study.

2. Evaluate the pharmaceutical care model and compare clinical (HbA1c, SBP) and humanistic (HRQOL) patient outcomes in the active group receiving the pharmaceutical care model in addition to standard care versus the control group receiving standard care only.

3. Investigate the number and types of drug related problems (DRPs) identified by the pharmacist, the percentage of recommendations accepted by the physician and the status of DRPs at follow up.

4. Obtain feedback from the pharmacists to inform future service delivery.

4.3 Study design

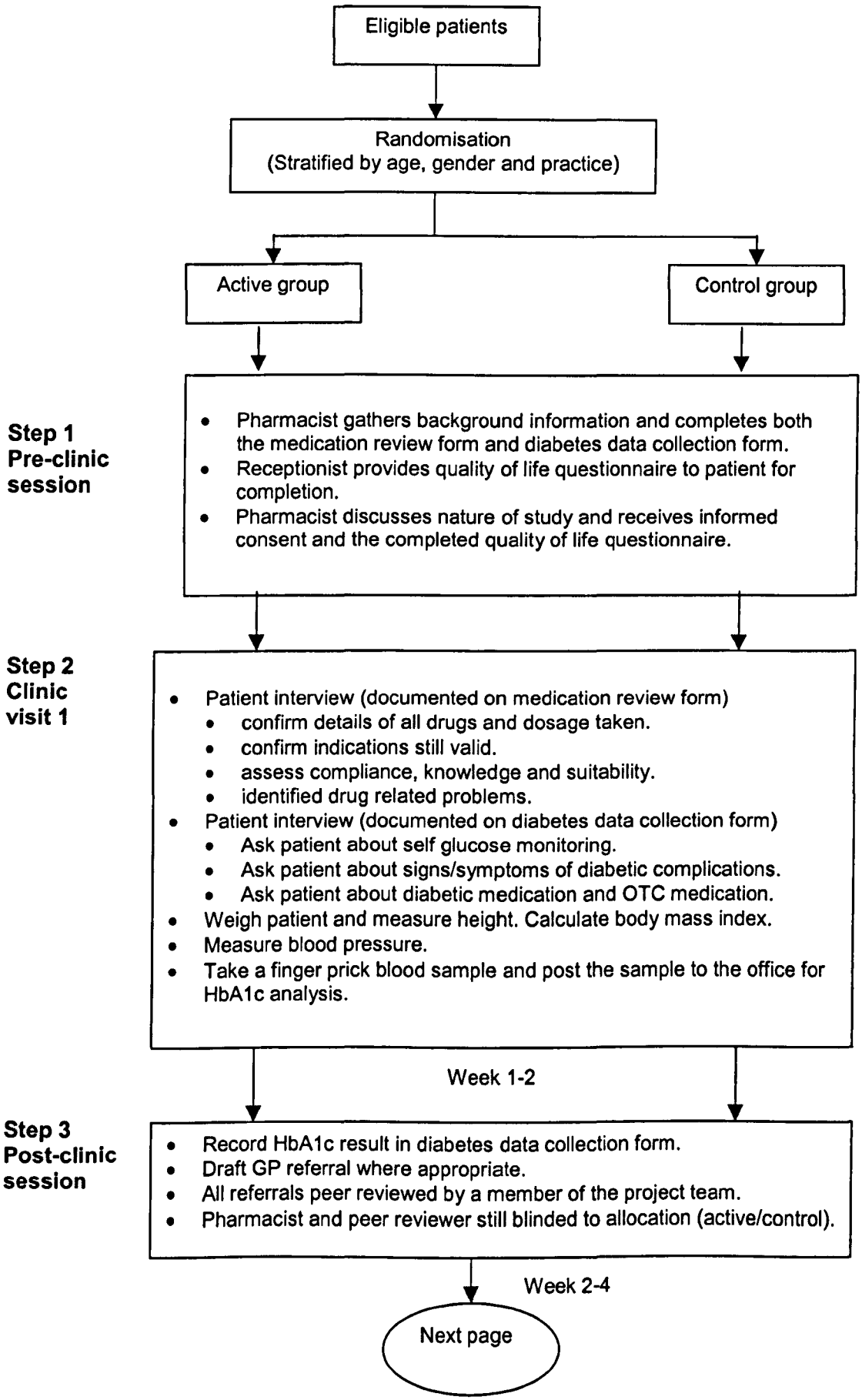
The study was conducted as a randomised controlled trial, doubled blinded at the first clinic visit. Pharmacists were blinded to the allocation at first visit only. Patients and GPs were blinded up to the point of amendment to care if one was actually made (Figure 4.1).

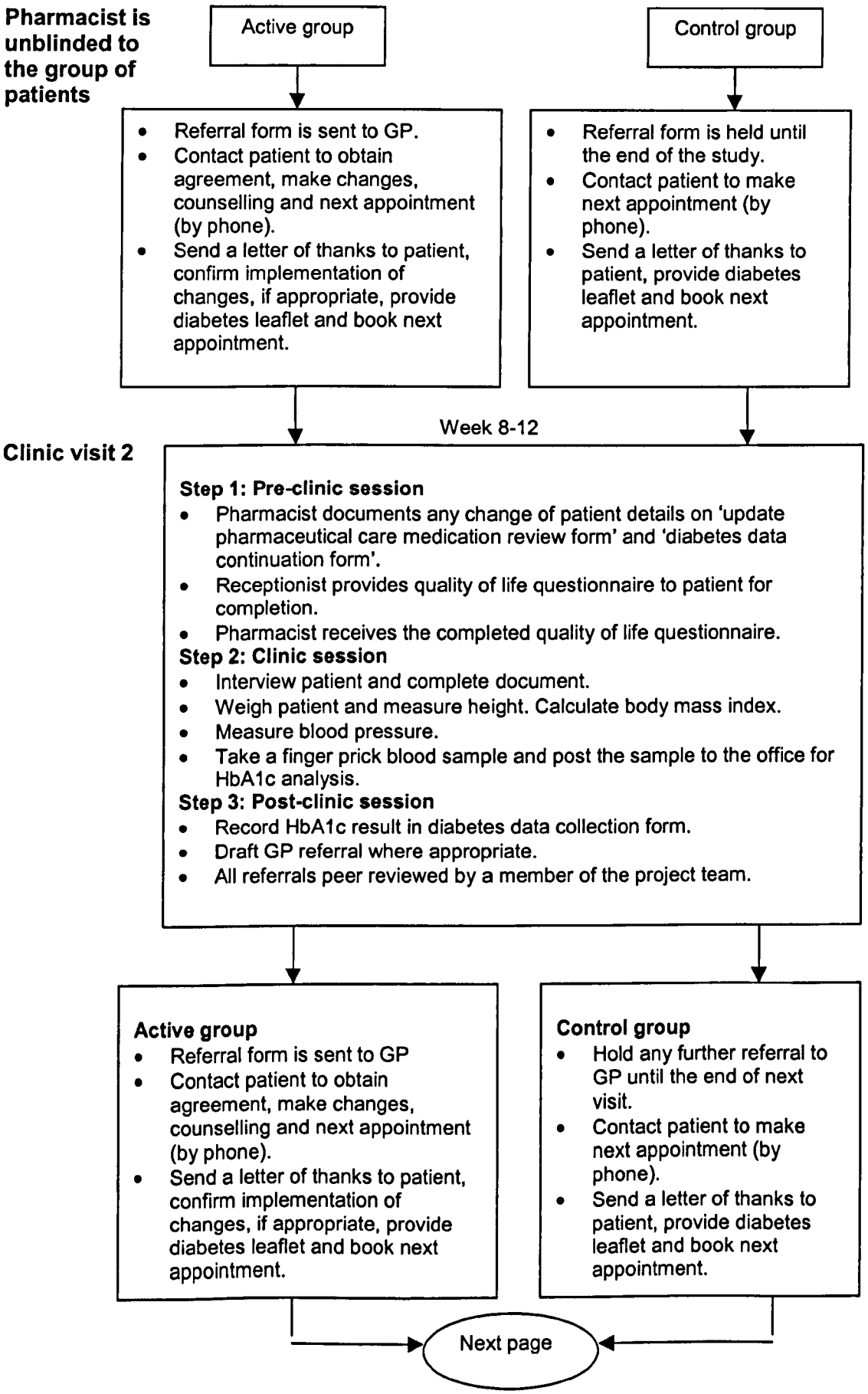
Pharmacists provided pharmaceutical care during a 12-month period from March 2000 to February 2001. Pharmacists received no additional payment for participating in the study, but were remunerated for running the clinics using standard rates in place at the time of the study (£25/hour). Participating practices and individual GPs received no payment for the study.

Patients were stratified by age, gender, and practice and then randomised into the active or control group. The enrolled patients in the control group received a pharmacist interview and usual medical care from GPs whilst the patients in the active group received usual medical care, pharmacist interview and pharmacist intervention (Figure 4.1). All patients were invited to a pharmacist run clinic within their general practice surgery for three clinic visits at approximately three-month intervals.

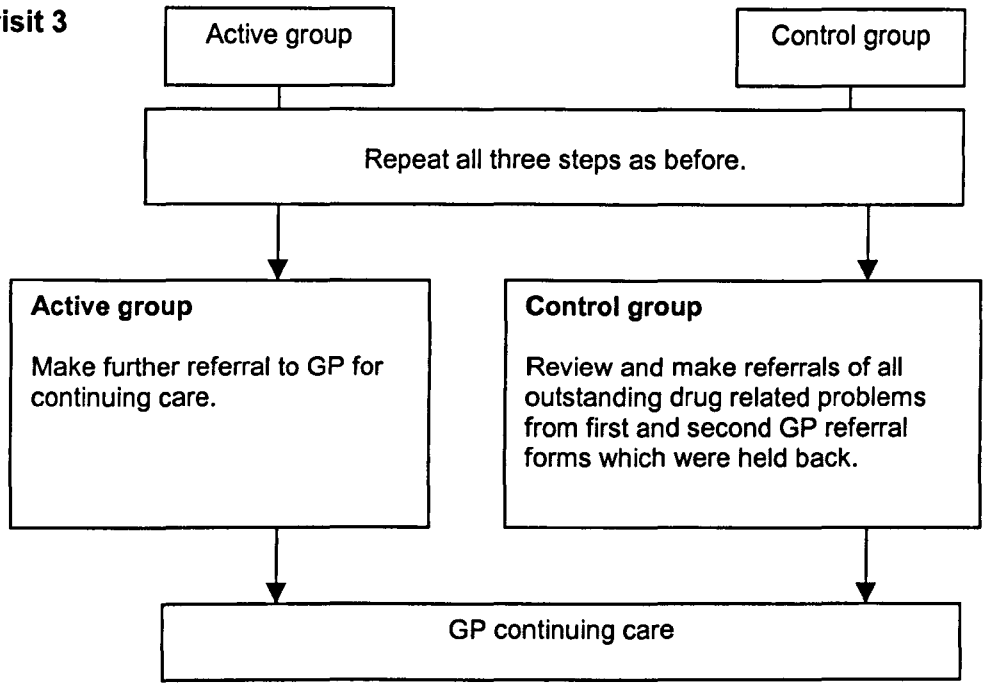
To determine the impact of the pharmacist intervention, the following outcomes were measured: changes in mean HbA1c level, changes in mean systolic blood pressure, and patient QOL, number and type of DRPs identified, and the percentage of recommendations accepted by the GP.

Figure 4.1: Flow chart of study protocol




Pharmacist is unblinded to the group of patients
Active group
Control group
• Referral form is sent to GP.
• Contact patient to obtain agreement, make changes, counselling and next appointment (by phone).
• Send a letter of thanks to patient, confirm implementation of changes, if appropriate, provide diabetes leaflet and book next appointment.
• Referral form is held until the end of the study.
• Contact patient to make next appointment (by phone).
• Send a letter of thanks to patient, provide diabetes leaflet and book next appointment.
Week 8-12
Clinic visit 2
Step 1: Pre-clinic session
• Pharmacist documents any change of patient details on 'update pharmaceutical care medication review form' and 'diabetes data continuation form'.
• Receptionist provides quality of life questionnaire to patient for completion.
• Pharmacist receives the completed quality of life questionnaire.
Step 2: Clinic session
• Interview patient and complete document.
• Weigh patient and measure height. Calculate body mass index.
• Measure blood pressure.
• Take a finger prick blood sample and post the sample to the office for HbA1c analysis.
Step 3: Post-clinic session
• Record HbA1c result in diabetes data collection form.
• Draft GP referral where appropriate.
• All referrals peer reviewed by a member of the project team.
Active group
• Referral form is sent to GP
• Contact patient to obtain agreement, make changes, counselling and next appointment (by phone).
• Send a letter of thanks to patient, confirm implementation of changes, if appropriate, provide diabetes leaflet and book next appointment.
Control group
• Hold any further referral to GP until the end of next visit.
• Contact patient to make next appointment (by phone).
• Send a letter of thanks to patient, provide diabetes leaflet and book next appointment.
Next page

Clinic visit 3



At the end of the study, the pharmacists were asked to rate how they felt about the clinics on a score of 0 (not confident) to 10 (very confident) before and after the study. A copy of the questionnaire is provided in Appendix XXII. This questionnaire was sent six months after the last clinic, together with a thank you card and a £20 Marks and Spencer voucher plus stamped envelope for returning the questionnaire. No reminder was sent.

4.4 Study setting

The study was conducted in nine general practices in Greater Glasgow Health Board area, Scotland as described in section 2.6 of the General Methods.

4.5 Patient selection

4.5.1 Eligibility criteria for participants

Patients were eligible for study if they:

1) had a diagnosis of Type 2 diabetes mellitus and were currently using an oral antidiabetic agent and
2) were aged 18 years or over and
3) had been receiving primary care from a general practitioner in one of the study practices.

4.5.2 Exclusion criteria

Patients were excluded if they met any of the following criteria:

1) Unable to obtain informed consent due to cognitive or severe sensory impairment such as dementia, hearing, speech, or severe visual impairment.
2) Serious acute or terminal illness.

These patients were identified by the practice manager from a list of eligible patients.

A final list of eligible patients was drawn up which included names, address, and telephone numbers. The clerical assistant (KB) contacted each patient by telephone, to briefly describe the study and ask whether they would like further information. The research office then mailed packages containing a description of the study (Appendix XIII) and patient consent form (Appendix XIV). The clerical assistant then followed up the patients by telephone to arrange an appointment within 1-2 weeks. Patients were asked to bring all their medicines (prescribed and OTC) plus the consent form to their first visit.

4.5.3 Size of the study population

It was hypothesised that the pharmacist intervention would have an impact on improving glycaemic control. Based on this hypothesis and the results from the pilot study, for a 1.0 unit drop in HbA1c values, it was estimated that 170 patients were required to complete the study. This figure was revised to 370 to take into account likely dropout rates (see 3.4.4).

4.6 Intervention in the active group

Patients enrolled in the active and control groups were seen by a community pharmacist at a clinic run within the general practice. All patient records were reviewed and patients were interviewed to obtain additional information required to identify drug related problems. In the active group a GP referral was made where appropriate and a patient information leaflet provided. The GP referrals were peer reviewed prior to submission to the GP. All referrals agreed by the GP were then implemented by the pharmacist unless the GP indicated otherwise. In the control group drug related problems were recorded and a patient information leaflet was provided but no other

intervention was made. Referrals were stored until the end of the study when they were actioned if appropriate (Figure 4.1). A total of nine pharmacists provided care to patients in this study. The study design (Figure 4.1) indicates that the patients should have up to three visits with the pharmacist over the course of the study. All patients continued to receive their usual care from the practice throughout the study.

4.7 Data collection

A summary of the contents of the various data collection tools used in this study is shown in Table 4.1. After the third clinic, data collection was continued to obtain the information regarding GP referral at last visit in both active and control groups. The data collection forms returned to the researcher were reviewed and transferred to a summary sheet. Information transferred to this sheet was independently checked and coded by a member of the study team (ALC). To ensure updated patient information, this pharmacist also verified the information in the patient record at the surgery and added any updated data, wherever possible, to the summary sheet.

Table 4.1: Data collection tools and information collected

Data collection tools	Type of information collected	Primary data source
Medication Review Form	• Patient demographic data • Relevant medical history • Current/Previous drug therapy, dosage, indication • Relevant investigations • Details of current secondary care monitoring • Monitoring by practice Identified drug related problems, action plan and outcome.	• Surgery computer • Patient medical record • Patient interview
Update Medication Review Form	All new information at the second and third clinic visits about medical history, drug therapy and any other relevant changes	• Surgery computer • Patient medical record • Patient interview
Diabetes Data Collection Form	• Relevant medical history (related to diabetes) • Specific objective diabetes data • Attendance at diabetic clinics • Foot exam • Eye exam Interview about self-glucose monitoring, smoking habit, signs/symptoms of diabetic complications, diabetic medication and OTC medication.	• Patient medical record • Patient interview • HbA1c result from DIASTAT analysis
Diabetes Data Continuation Form	All new information at the follow up clinic visits about diabetes	• Patient medical record • Patient interview • HbA1c result from DiaSTAT analyser
GP referral form	Drug related problems Proposed action GP response	• Recorded and signed by pharmacist. • Responded and signed by GP.
ADDQoL questionnaires	Diabetes specific quality of life	• Self-administered by patient.

4.8 Outcome measures

Outcome measures included HbA1c, systolic blood pressure, health related quality of life, DRPs and the percentage of pharmacist recommendations accepted by GP.

4.8.1 Clinical outcome: Haemoglobin A1c (HbA1c)

The study was powered to detect a clinically meaningful difference of 1.0 unit change in mean HbA1c values (see 3.4.4).

The HbA1c value obtained on the day of first visit was considered the patient's baseline measurement. HbA1c measurements were also obtained at the second and third clinic for the purpose of documenting changes in glycaemic control. There was a minimum interval of 3 months between visits.

To assess HbA1c the pharmacist collected a capillary sample of the patient's blood (Appendix XXIII), placed it in a polypropylene tube containing aqueous solution of EDTA and potassium cyanide, and then mailed it to the laboratory where glycosylated haemoglobin A1c (HbA1c) was determined by the researcher (SS) using a Biorad Automated HbA1c Analyser, DiaSTAT (Biorad Laboratories Ltd., Herts, UK). The DiaSTAT analyser is a low pressure liquid chromatography system designed for the rapid and fully automated measurement of HbA1c in a small laboratory. The manufacturer's quoted range was 3.8 - 7.3% ± 0.50 (SD), 4.0 - 6.3% (95% confidence limits), n = 130 normal patients.

Transport of samples

The HbA1c measurement was performed at the office in Glasgow. The samples from each site were sent to the office by first class Royal Mail service at the end of each clinic. Samples were stored at room temperature for up to 7 days before assay.

Quality Assurance

At every 100 assays performed, Lypochek Diabetes Control (Biorad, Herts, UK) was used to monitor the precision of the DIASTAT testing procedure, as recommended by the manufacturer.

4.8.2 Clinical outcome: Blood pressure

Systolic and diastolic blood pressure was recorded by using the automatic blood pressure measuring device, OMRON 705CP. The mean value of two sitting and two standing readings was used. In the case where the two systolic readings differed by more than 15 mmHg, a third reading was made and the mean of the two closest readings was used for analysis. Pharmacists were given instructions on how to use the OMRON 705CP (Appendix XXIV).

Machines were checked at 6 months by the electronics laboratory at Department of Bio-Medical Physics and Bio-Engineering, University of Aberdeen to ensure that they were working in accordance with the manufacturer specifications.

4.8.3 Humanistic outcome: Diabetes specific QOL assessment

Diabetes-specific QOL was assessed via the Audit of Diabetes Dependent Quality of Life, (ADDQoL) measuring the perceived impact of diabetes on different areas of patients' lives, weighted by importance to the individual (Bradley et al., 1999).

The ADDQoL was administered to patients in both groups at all three clinic visits. The questionnaire was self-administered. The study patients completed the ADDQoL at the reception area while waiting for their clinic appointment.

The ADDQoL has 13 domain-specific items rated by the respondent on an impact score scale ranging from -3 (very much worse) to 3 (very much better) and importance rating scale ranging from 0 (not at all important) to 3 (very important). In addition, there were two overview items with a scale ranging from -3 to 3 at the beginning of the questionnaire. There were 'not applicable' options for four selected domains: employment/career, family relationship, sex life, and future of family. Those non-applicable domains were excluded from the ADDQoL scoring. In the situation where the patient missed > 5 domains (including non-applicable domains) the questionnaire was excluded from the analysis.

4.8.4 Process outcome: Drug related problems (DRPs)

The type of drug related problem (Table 4.2), type of intervention (Table 4.3), GP response (Table 4.4), immediate outcome (Table 4.5) and final outcome (Table 4.6) classification system was adapted from Strand et al. (1990) and validated by Mackie and Campbell (2001) and subsequently used in this study to categorise DRPs and outcomes related to them.

Table 4.2: Drug related problem classification system

Type of drug related problem	Description
1. No indication apparent	Patient is taking a medication for no medically valid indication.
2. Ineffective	Therapy is not adequately controlling the indication for which it has been prescribed or being prescribed at doses which are sub-optimal for improving disease control.
3. Adverse Drug Reaction	Patient is taking a medication that should not be taken because of potential or actual adverse drug reaction or adverse effect.
4. Contraindication	Patient is receiving a medication that is contraindicated.
5. Admitted non-compliance, counselling required	Patient is not receiving a medication or is not complying with the treatment due to economic, psychological, sociological, or pharmacological reasons.
6. Drug Interaction	Patient is taking drugs that should not be combined together because of potential or actual drug interactions.
7. Monitoring required	Testing may be requested for monitoring purposes or because previous monitoring indicates a potential ADR, untreated indication or ineffective therapy.
8. Unnecessary therapy	Patient currently has no indication for the therapy or duplicate therapy.
9. Untreated indication	Patient needs a treatment and is not receiving it.
10. Repeat file inaccurate	Repeat prescription on surgery computer is not accurate.
11. Generic substitution/cost issue	Generic or less expensive drug is available.
12. Inappropriate choice of therapy	Patient has a drug indication but is taking the wrong drug, or is taking a drug that is not the most appropriate for the special needs of the patient. Alternatively the drug is correct but the dosage form or formulation is inappropriate.
13. Inappropriate dose/dosing schedule	Patient is receiving too high or too low a dosage, inappropriate frequency or inappropriate duration.
14. BP monitoring required	Blood pressure measurement may be required for monitoring therapy or because previous monitoring indicates untreated indication or ineffective therapy.
15. HbA1c monitoring required	HbA1c measurement may be required for monitoring therapy or because previous monitoring indicates untreated indication or ineffective therapy.

Table 4.3: Pharmacist intervention classification system

Type of intervention
Change drug same group
Change drug new group
Decrease dose
Increase dose
Stop therapy
Initiate therapy
Change directions
Change formulation/device/brand
Counsel
Monitoring required
Clinical review
Update records
Confirm indication/dose

Table 4.4: GP response classification system

Type of response	Description
Completely agreed	GP completely agrees to pharmacist's recommendation.
Partially agreed	GP agrees to pharmacist's recommendation with minor adjustment to the purposed action or GP requires patient's further review before making decision on therapy as recommended.
Rejected, no action	GP rejects pharmacist's recommendation, no action taken.

Table 4.5: Immediate outcome classification system

Type of immediate outcome	Description
Actioned & accepted by patient	Action taken by pharmacist. Both patient and GP accept the change.
Rejected by patient	GP agreed but patient does not agree to the change. No change made.
Not actioned - change in patient status	Patient status changed. No action taken.
Not actioned - no reason apparent	GP and patient agreed but no action taken without explanation.
Agreed GP to action	GP require further review. Action taken after review.
Monitoring detects abnormality	
No further patient contact required	
Notes not available at follow up	Patient's medical record is not available in surgery during pharmacist's working hours

Table 4.6: Final outcome classification system

Type of final outcome	Description
DRP resolved	DRP resolved due to action taken or DRP resolved itself, no longer relevant or DRP resolved by alternative action.
DRP remains	DRP remains as before despite action or DRP remains as before, action not taken or DRP addressed but not fully resolved.
Patient lost to follow up	Patient died or left practice or patient's notes not available at follow up.

4.8.5 Ethical issues related to the control group

In the case of a potentially life threatening issue identified for a control patient, this was referred to an independent medical adviser (ANC) for confirmation and removal of the patient from the study if appropriate.

At the end of the study, all draft GP referrals for the control group were reviewed and where appropriate brought to the attention of the GP. The study team has not included any outcome measures for this group following this intervention. Analysis of this data is outwith the scope of the present study.

4.9 Validation and quality assurance

In order to minimise variation on HbA1c and blood pressure measurements, standard equipment was used. As there was a different normal range of HbA1c values from different laboratories, HbA1c was carried out in a single laboratory using the DiaSTAT machine. The pharmacists were trained in using the SOFTCLIX PRO LANCING device for taking blood samples and in using the automatic blood pressure measuring device, OMRON 705CP. To confirm the BP record on the data collection form, the pharmacist was requested to attach blood pressure printouts to the form.

All GP referrals (both active and control groups) were peer reviewed by one of the project pharmacists (AM or RL) to assure that the GP referral was appropriate. The allocation of the patient to the active or control group was revealed after the peer review process in order to reduce bias.

Control patients were also seen by pharmacists in this study. Pharmacists were blinded at first visit only. At follow up visits to prevent contamination by pharmacists, for control patients, printed lists of control patients were provided to pharmacists and also 'C' marked on the clinic appointment forms.

4.10 Data analysis and statistical methods

Comparisons of outcome measures were made within and between the active and control groups using T-Tests. In addition to comparison of absolute values of individual parameters, the number of patients in each group whose HbA1c and blood pressure were within target during the course of the study was compared using Chi-square. The extent of blood pressure and HbA1c control classed as good or poor control were stratified according to the following scheme:

- Glycosylated haemoglobin (HbA1c)

Good control	< 8.0%
Poor control	≥ 8.0%

- Systolic blood pressure targets for Type 2 diabetes:

Good control	≤ 140 mmHg
Poor control	> 140 mmHg

To score a weighted rating of the ADDQoL, the patient's rating on the unweighted impact score (-3 to +3) was multiplied by the importance rating (0 to 3) for each domain. From this, unimportant domains score 0 regardless of magnitude of effect of diabetes and domains unaffected by diabetes score 0, regardless of their importance for QOL. The sum of weighted ratings of applicable domains divided by the number of

applicable domains provided the ADDQoL score. Therefore, the scores vary from –9 (maximum negative impact of diabetes) to +9 (maximum positive impact of diabetes). The researcher (SS) coded medication data using BNF chapter (Number 35, March 1998) and Read codes to code diseases. At the end of the study two members of the study team (ALC and CAM) independently coded DRPs, pharmacist intervention, GP response, immediate and final outcomes.

No attempt has been made to analyse new DRPs identified at clinics 2 and 3 due to the confounding factors and extensive double counting that would take place in the control group with each DRP being counted again at each visit.

Chi-square test, relative risk (RR), absolute risk reduction (ARR) and number needed to treat (NNT) were calculated to compare the final outcomes of DRPs at clinic visit 1 to 2 and clinic visit 1 to 3. Relative risk (RR) was used to calculate the effect size and the confidence interval (95%CI) used as a measure of its precision. The difference between the proportions with the outcomes caused by an intervention or a new treatment (P_N) and no intervention or a standard treatment (P_S) is called the absolute risk reduction ($ARR = P_N - P_S$). The NNT is the inverse of the ARR and is the estimated number of patients who need to be treated with the new treatment rather than the standard treatment to prevent one additional adverse outcome, and can be obtained for any trial that has a reported binary outcome (Altman, 1999).

Chapter 5

Results

5.1 Practice setting

The nine practices had a total population of 38,613 patients of whom 387 (1.0%) were Type 2 diabetics (≥18 years old) taking an oral antidiabetic drug, indicating a prevalence of Type 2 diabetes in this population which is comparable with that reported by other studies (Khunti et al., 1999).

5.2 Participant flow

Of the 387 patients identified, 19 (4.9%) met the exclusion criteria leaving 368 potential participants who were eligible for inclusion in the study. They were stratified by practice, age, and gender, and then randomised into the active (188 patients) or control group (180 patients) (Figure 5.1). Blinding was achieved using a closed envelope technique. Overall 198 (54%) patients signed informed consent and attended the interview. After interview the pharmacist completed a GP referral form if appropriate following which the pharmacist was notified of active and control status.

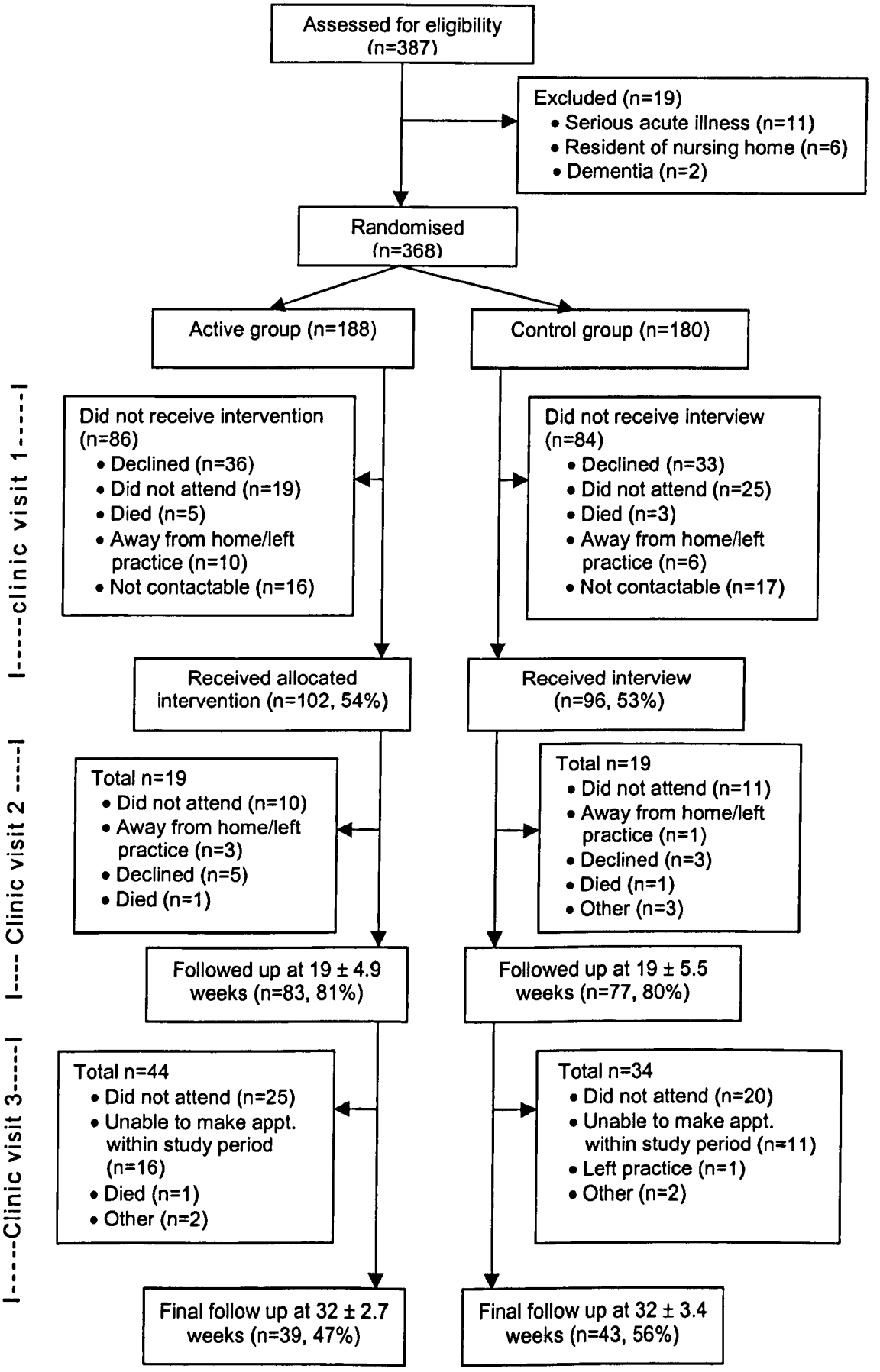
The overall number of patients attending the second clinic was 160 patients (81%, Figure 5.1). There were 21 patients (11%) who agreed but did not attend the clinic with the reason of work commitment (9, 43%), illness (6, 29%), taking care of other people (1, 4.8%) and no specific reason (5, 24%). In addition 8 (4.0%) patients declined the invitation, 4 (2.0%) patients left the practice or were away from home

during the appointment period and 2 (1.0%) patients died. The remaining three patients in the control group were withdrawn from the study, two with a potential serious illness and the one with a serious diabetic related problem. All 3 patients were removed from the study by the independent medical adviser in accordance with the study protocol. These three patients are described in more detail later in this chapter (see 5.4.9). Overall 82 (51%) patients attended all three clinic visits, 45 (28%) patients agreed but did not attend the clinic with the reason of work commitment (12, 27%), illness (8, 18%), and no specific reason (25, 55%). In addition 27 (17%) patients were not able to make the appointment within the study period due to a minimum three-month interval between visits (Figure 5.1). The remaining six patients (3.7%) include one who left the practice, one who died, and four who were unable to attend due to serious illness.

The average time between clinic visit 1 and 2 was 19 weeks, and between clinic visit 1 and 3 was 32 weeks. Patients who agreed but subsequently did not attend the second clinic were invited to attend another clinic together with other patients who were attending for clinic visit 3. Therefore the average time period between clinic visit 1 and 2 was extended from the planned 12 weeks for these patients.

There were 198 patients who attended the clinic at least once for the clinic visit 1 and 160 who attended the clinic visit 1 and at least one of clinic visit 2 or 3. Of these 198 patients, there were 38 (19%) patients who attended only one clinic, 78 (39%) patients who attended two clinics, and 82 (41%) patients who attended three clinics. The analysis was completed for the 160 patients (83 active patients, 77 control patients) who had the first clinic visit and at least one of clinic visit 2 or 3.

Figure 5.1: Flow diagram of participants through the trial



The number of patients attending three clinic visits, and average time between visits did not differ significantly ($P > 0.05$) between the active and control groups.

Patients who attended two or more clinics were categorised as having completed the study with the remainder categorised as not completing the study (≤ 1 clinic visit).

5.3 Patient characteristics at baseline

At baseline (clinic visit 1), patient demographics and clinical characteristics of the 160 patients who completed the study are given in Table 5.1 and 5.2 respectively. The data show that the groups were comparable with respect to age distribution, sex, body mass index, smoking status, glycaemic control (HbA1c), blood pressure, total cholesterol, number of concurrent medical conditions, and number of drugs prescribed.

Similar results were found between active and control patients who attended three clinic visits (39 active and 43 control). There was no significant difference between groups in patient demographics and clinical characteristics ($P > 0.05$).

Table 5.1: Baseline demographic characteristics of participants in active and control groups who completed the study

Characteristic	Active n = 83	Control n = 77	*P* value
Mean age, years (±SD)	65 (10)	66 (10)	0.366
No. of female gender (%)	43 (52)	35 (46)	0.422
Mean body mass index, kg/m^2 (±SD)	30 (6.6)	29 (9.2)	0.850
No. of patients with body mass index > 27 kg/m^2 (%) #	49 (64)	50 (71)	0.452
Smoking status:			
Current tobacco smokers (%)	18 (22)	19 (25)	0.761
Ex-smoker (%)	31 (37)	28 (36)	
Non-smoker (%)	34 (41)	30 (39)	

77 active and 70 control had a reading recorded in notes.

Table 5.2: Baseline clinical characteristics of participants who completed the study

Characteristic	Active n=83	Control n=77	*P* value
Mean HbA1c level, %, (± SD)	8.3 (1.5)	8.4 (1.8)	0.546 *
No. of patients with HbA1c ≥ 8.0% (%)#	44 (53)	42 (55)	0.929 **
No. of patients using glucose monitoring at home (%)	47 (57)	52 (67)	0.156 **
Mean systolic blood pressure, mmHg (± SD)	149 (24)	149 (19)	0.835 *
Mean diastolic blood pressure, mmHg (± SD)	82 (15)	82 (11)	0.728 *
No. of patients with blood pressure within target, <140/80 mmHg, (%)	27 (32)	23 (30)	0.369 **
Mean total cholesterol, mmol/L (± SD)	5.4 (1.1)	5.3 (1.0)	0.969 *
No. of drugs prescribed, median (range)	5.0 (1-13)	6.0 (1-16)	0.066 ***
No. of concurrent medical conditions, mean (± SD)	4.5 (2.2)	4.7 (2.1)	0.443 *

79 active 75 control had a reading obtained from DiaSTAT analyser
* T-test
** Chi-square
*** Mann-Whitney U-test

Baseline characteristics were compared between those who completed the study and those who did not (Table 5.3). It shows that age, percentage of female and baseline HbA1c level did not differ significantly between both groups.

Table 5.3: Comparison of baseline characteristics between those who completed study and those who were randomised and did not complete the study

Characteristic	Number of clinics attended		*P* value
	≥ 2 clinics	≤ 1 clinic	
	n = 160	n = 208	
Mean age, years (±SD)	65 (10)	64 (15)	0.703
No. of female gender (%)	78 (50)	127 (61)	0.388
Mean HbA1c level, %, (± SD)[#]	8.4 (1.7)	8.1 (2.1)	0.413

[#] 155 completed the study and 37 who did not complete the study had HbA1c value obtained from DIASTAT.

From the pilot study sample size was estimated based on a change of 1.0 unit HbA1c to give the study a power of 90% to detect a difference if one existed. The mean value of Hba1c in total participants (n = 160) was 8.3 ± 1.7 and clinical significant difference was 1.0 units decrease in HbA1c, therefore the standardised difference = 1.0/1.7 = 0.59. From Altman's nomogram (Altman, 1991), 160 patients participated in the study giving a 96% power of detecting a 1.0 unit difference in HbA1c value between two groups at the 5% level of significance. However, there were 82 subjects who attended three clinics throughout the trial giving 77% power.

The age and gender distributions of those who completed the study are presented in Table 5.4. Most of the participants were aged 60 or over. The age distribution was 7.5% aged less than 50 years, 20% aged 50-59, and 73% aged 60 or more. They were equally distributed between gender in active and control groups.

Table 5.4: Distribution of age and gender at baseline for those who completed the study

Age range (years)	Active		Control		Total (%)
	Male	Female	Male	Female	
31-49	3	4	0	5	12 (7.5)
50-59	9	7	11	5	32 (20)
60-69	16	16	13	12	57 (36)
≥70	12	16	18	13	59 (37)
Total (%)	40 (25)	43 (27)	42 (26)	35 (22)	160 (100)

5.3.1 Medical conditions recorded

A total of 284 medical conditions were recorded for the active group and 283 for the control group. Table 5.5 shows the number of medical conditions identified from patient records in both the active and control groups. The most common diabetic complications recorded in the medical notes were cardiovascular diseases which include hypertension (19% in active and 17% in control), ischaemic heart disease, cardiac failure and arrhythmia (11% in active and 12% in control), and hyperlipidaemia (7.7% in active and 6.4% in control). Vascular diseases were associated with 45% of the medical conditions in the active group and 43% in the control group. For nonvascular diseases the most common was arthropathy (6.3% in active and 6.0% in control) which included both osteoarthritis and rheumatoid arthritis, obesity (6.0% in active and 4.9% in control) and gastrointestinal disorder (4.2% in both groups). Overall diabetic related complications were present in 55% and 53% of active and control patients respectively.

Table 5.5: Medical conditions recorded

Medical condition	Active (%)	Control (%)	Significant
Hypertension #	55 (19)	47 (17)	NS
Ischaemic heart disease/ Cardiac failure/ Arrhythmia #	32 (11)	35 (12)	NS
Hyperlipidaemia #	22 (7.7)	18 (6.4)	NS
Arthropathy	18 (6.3)	17 (6.0)	NS
Obesity #	17 (6.0)	14 (4.9)	NS
Gastrointestinal disorder	12 (4.2)	12 (4.2)	NS
Stroke/TIA #	11 (3.9)	14 (4.9)	NS
Urological problem	11 (3.9)	11 (3.9)	NS
COAD/asthma	10 (3.5)	16 (5.6)	NS
Peripheral vascular disease #	9 (3.2)	8 (2.8)	NS
Peripheral neuropathy #	8 (2.8)	7 (2.5)	NS
Depression and other Psychological disorders	7 (2.5)	7 (2.5)	NS
Hypo-/hyperthyroidism	6 (2.1)	5 (1.8)	NS
Renal failure / nephrectomy/ Nephropathy #	3 (1.1)	5 (1.8)	NS
Miscellaneous	66 (22)	63 (23)	NS
Total	287 (100)	279 (100)	

# Diabetic related complications
NS = not significant

5.3.2 Current drugs prescribed

Nine hundred and sixty-three prescribed drugs were reviewed by the pharmacist during patient interviews at clinic visit 1. Table 5.6 provides information on BNF chapter and number of drugs prescribed for both the active and control group.

Table 5.6: Number of drug prescribed in BNF category

BNF category (chapter number)	Active (%)	Control (%)	Significant
Cardiovascular system (2)	167 (37)	188 (36)	NS
Endocrine system (6)	131 (29)	125 (24)	NS
Central nervous system (4)	51 (11)	66 (13)	NS
Gastro-intestinal system (1)	26 (5.8)	42 (8.1)	NS
Musculoskeletal and joint disease (10)	24 (5.4)	23 (4.4)	NS
Skin (13)	12 (2.7)	8 (1.5)	NS
Respiratory system (3)	11 (2.5)	37 (7.2)	$P < 0.05$
Others	24 (5.4)	28 (5.4)	NS
Total (n = 963)	446 (100)	517 (100)	

NS = not significant

Apart from drugs in the endocrine system category, overall 63% of all prescribed drugs were accounted for by four BNF chapters namely: cardiovascular (37%); central nervous system (12%); gastro-intestinal (7.1%) and musculoskeletal and joint disease (4.9%). The two groups were well matched for prescribed drugs with the exception of respiratory drugs which were more commonly prescribed in the control group ($P < 0.05$).

Table 5.7 summarises the number of antidiabetic drugs prescribed in each of the two groups. The majority of patients were treated with a single drug (48% in active group and 53% in control group). As monotherapy, gliclazide was the most common choice of sulphonylurea in both groups. Metformin was the second drug most commonly used as a single agent and was also used most frequently in combination with a sulphonylurea especially gliclazide. Ten patients were prescribed glibenclamide (5 active and 5 control), a long-acting sulphonylurea, and none were prescribed chlorpropamide at the baseline. Other drugs used as single drug included glipizide (1 control), glimepiride (1 control) and acarbose (1 control).

Table 5.7: Number of antidiabetic drugs prescribed

Drug	No. (%) of patients receiving drug		Significant
	Active	Control	
Single drug	48 (58)	53 (69)	NS
Two-drug combination	33 (40)	24 (31)	NS
Triple-drug combination	2 (2.4)	0 (0)	NS
Total	83 (100)	77 (100)	

NS = not significant

5.4 Outcome measures

There were four outcome measures namely HbA1c, systolic blood pressure, HRQOL and DRP. Table 5.8 and 5.9 summarises the first two outcome measures at clinic visit 1 and 2 and clinic visit 1 and 3 respectively. In addition to testing the significance of the differences in the means of clinic visit assessments, the number of patients whose diabetic condition and blood pressure were within target during the study was also evaluated and shown in Table 5.10 through 5.13.

5.4.1 HbA1c

HbA1c values were not available for all 160 patients who completed the study. Of these 160 patients, 6 patients in the active group and 4 patients in the control group had no HbA1c result available at clinic 1 or 2 for technical reasons such as too little blood sample and missed posting samples. Overall there were 150 (76 active patients, 74 control patients) patients reviewed for analysis as shown in Table 5.8, 5.10 and 5.12.

The study was powered to detect a meaningful clinical difference of 1.0 unit HbA1c. The HbA1c (mean ± SD) did not change significantly in either the active or the control groups ($P > 0.05$) from clinic visit 1 to 2 and between groups (Table 5.8).

Similarly, there were no significant differences in the proportion of patients who had HbA1c value changed from poor (≥ 8.0%) to good control (< 8.0%) at the clinic visits 1 and 2 between active and control groups ($P > 0.05$, Table 5.12). The analysis was repeated for the 82 patients (39 active, 43 control) who attended all three clinic visits.

Table 5.8: Summary of outcome measures in patients who attended 2 or more clinics (83 active, 77 control)

Measure	Clinic 1		Clinic 2		Size of change from clinic 1 to 2 (mean ± 95%CI)	*P* value	
	Active	Control	Active	Control			
HbA1c* (%)	8.3 ± 1.5 (7.9, 8.6)	8.4 ± 1.8 (8.0, 8.8)	8.4 ± 1.5 (8.1, 8.8)	8.6 ± 1.7 (8.2, 9.0)	Active 0.2 (-0.1 - 0.4) Control 0.1 (-0.2 - 0.4)	Active (1st vs 2nd) Control (1st vs 2nd) Change 1st to 2nd (A vs C)	0.486 0.516 0.628
Systolic BP (mmHg)	149 ± 24 (144, 155)	149 ± 19 (142, 151)	140 ± 19 (136, 144)	141 ± 19 (136, 145)	Active -9.3 (-14 - (-4.5)) Control -6.2 (-12 - (-0.3))	Active (1st vs 2nd) Control (1st vs 2nd) Change 1st to 2nd (A vs C)	0.007** 0.060 0.409

Note: data is shown as (mean ± SD), A = active, C = control

* Normal range = 3.8 - 7.3%

** Significant difference

Table 5.9: Summary of outcome measures in patients who attended three clinics (39 active, 43 control)

Measure	Clinic 1		Clinic 3		Size of change from clinic 1 to 3 (mean ± 95%CI)	*P* value	
	Active	Control	Active	Control			
HbA1c* (%)	8.1 ± 1.5 (7.6, 8.6)	8.5 ± 1.6 (8.0, 9.0)	8.2 ± 1.4 (7.7, 8.7)	8.7 ± 1.5 (8.3, 9.4)	Active 0.1 (0.3 - 0.5) Control 0.1 (-0.2 - 0.5)	Active (1st vs 3rd) Control (1st vs 3rd) Change 1st to 3rd (A vs C)	0.857 0.823 0.819
Systolic BP (mmHg)	151 ± 20 (144, 157)	149 ± 19 (143, 155)	136 ± 16 (131, 142)	144 ± 17 (138, 149)	Active -14 (-8.2 - (- 20)) Control -5.7 (-0.6 - (-11))	Active (1st vs 3rd) Control (1st vs 3rd) Change 1st to 3rd (A vs C)	0.001** 0.151 0.030**

Note: data is shown as (mean ± SD), A = active, C = control

* Normal range = 3.8 - 7.3%

** Significant difference

Table 5.10: Number of patients who attended two or more clinic visits by group and HbA1c category

Category	Clinic 1		Clinic 2		*P* value*
	Active	Control	Active	Control	
No. of patients with HbA1c ≥ 8.0%	42	42	43	45	NS
No. of patients with HbA1c < 8.0%	34	32	33	29	NS

* Chi square
NS = not significant

Table 5.11: Number of patients who attended two or more clinic visits by group and systolic blood pressure category

Category	Clinic 1		Clinic 2		*P* value*
	Active	Control	Active	Control	
No. of patients with SBP > 140 mmHg	52	46	45	35	NS
No. of patients with SBP ≤ 140 mmHg	29	28	36	39	NS

* Chi square
NS = not significant

Table 5.12: Number of patients who attended two or more clinic visits by group and change of HbA1c category

Change of HbA1c from clinic 1 to 2	Number of patient (%)		Significant
	Active	Control	
Good control, no change remained within target	24 (32)	22 (30)	NS
Poor control, within target at baseline only	10 (13)	7 (9.5)	NS
Good control, high at baseline, now within target	9 (12)	7 (9.5)	NS
Poor control, no change at baseline and follow up	33 (43)	38 (51)	NS

NS = not significant
Good control: HbA1c < 8.0%
Poor control: HbA1c ≥ 8.0%

Table 5.13: Number of patients who attended two or more clinic visits by group and change of systolic blood pressure category

Change of Systolic BP from clinic 1 to 2	Number of patient (%)		Significant
	Active	Control	
Good control SBP remains ≤ 140 mmHg	23 (28)	21 (28)	NS
Poor control SBP ≤ 140 mmHg at baseline, now > 140 mmHg	6 (7.4)	8 (11)	NS
Good control SBP > 140 mmHg at baseline, now ≤ 140 mmHg	22 (27)	18 (24)	NS
Poor control SBP remains > 140 mmHg	30 (37)	27 (36)	NS

NS = not significant, SBP = systolic blood pressure

No significant difference in HbA1c values were found from clinic visit 1 to 3 and between groups ($P > 0.05$, Table 5.9).

Four patients in the active group were switched over to insulin therapy during the study period. The HbA1c values were in the range of 9.9 - 12.6% at the time of starting insulin. HbA1c value decreased by 3.8%, 1.3%, 0.5% and 0.4% in the patients in the first 3-4 months of insulin therapy.

In the active group, 48 (58%) patients had no hyperglycaemic complaints between clinic visit 1 and 2, compared to 40 (52%) in the control group ($\chi^2 = 0.35$, 1df, $P > 0.05$). No hyperglycaemic event occurred that required professional medical intervention.

5.4.2 Blood pressure

Table 5.8 provides the results for blood pressure which shows a significant reduction in average systolic blood pressure from clinic visit 1 to 2 in the active group ($P = 0.007$) whilst no significant differences were found in the control group ($P = 0.060$) and between groups ($P = 0.409$).

Of the 82 patients who attended all three clinics (Table 5.9), a significant reduction was noted for systolic blood pressure change within the active ($P = 0.001$) and between the active and control ($P = 0.030$) whilst no difference was noted in systolic blood pressure change within the control ($P = 0.151$).

There was no significant difference in the proportion of patients who had systolic blood pressure >140 mmHg changed to ≤ 140 mmHg at clinic visit 1 to 2 between active and control groups (P>0.05, Table 5.13).

Diastolic blood pressure was also measured and is reported for information. There was an apparent reduction in average diastolic blood pressure from clinic visit 1 to 2 in the active and control groups but this was not statistically significant (80 ± 12, 78 ± 10 in active; 82 ± 12, 79 ± 10 in control for clinic 1 and 2 respectively; $P > 0.05$). In addition no significant differences were found in the change between groups.

There was no significant difference in the proportion of patients who had diastolic blood pressure > 80 mmHg changed to ≤ 80 mmHg at clinic visit 1 to 2 between active and control groups ($P > 0.05$). No significant differences were found in the mean diastolic blood pressure, and the number of patients who had changed diastolic blood pressure > 80 mmHg to ≤ 80 mmHg between the clinic visit 1 to 3 and between groups ($P > 0.05$).

5.4.3 Health related quality of life: ADDQoL

A total of 112 patients (70%, 60 active and 52 control) completed the ADDQoL questionnaires at clinic visit 1 and 2. Three patients (1.9%) did not complete questionnaires at clinic visit 1 and 45 patients (28%) did not complete questionnaires at clinic visit 2. Of these 48 patients, 38 patients did not fill in the questionnaire and gave no reason, 6 patients did not bring their spectacles and 4 patients could not read English. Of these 112 patients, data from 98 patients (54 active, 44 control) were included in the analysis. Questionnaires from the remaining 14 patients could not be used for the following reasons: 4 active patients did not complete 'importance rating' questions and 1 answered only general questions; 6 control patients did not

complete 'importance rating' questions and 3 patients answered less than 3 questions.

Thirty-eight of 98 (39%) patients at clinic visit 1 and 49 of 98 (50%) patients at clinic visit 2 responded to every question in the questionnaires. Table 5.14 shows the number of patients who responded to each question at baseline and follow up. Some omissions appeared to be due to simple oversight, which seemed particularly apparent when a page of the questionnaire was left blank (the printing format resulted in 3 questions being printed on each page). Two questions (no. 1 and 5) had relatively high rates of missing values (43 and 27 at baseline, 38 and 21 at follow up, respectively). Question related to employment and career (Question no. 1) may have been considered not applicable by patients who were not employed at the time of the questionnaire administration, including most patients in the study who were aged 60 or over. In addition several patients did not respond to the question concerning sex life (no.5).

Table 5.14: Number of respondents to each domain of ADDQoL

Domain	Number of respondents	
	Clinic 1	Clinic 2
1) Employment/career	55	60
2) Social life	91	88
3) Family relationships	90	90
4) Friends	94	95
5) Sex life	71	77
6) Sport/leisure	94	95
7) Travel	90	93
8) Future (own)	88	92
9) Future of family	80	91
10) Motivation	86	93
11) Physical activities	89	92
12) Other fussing	86	94
13) Enjoyment of food	93	93

At clinic visit 3, there were 30 patients (77%, 30/39) in the active group and 31 patients (72%, 31/43) in the control group who completed the questionnaire. Of these, 2 questionnaires were invalid as only three questions were filled in. A total of 59 (72%) patients completed ADDQoL questionnaires at all three clinic visits.

Table 5.15 provides overall scores for HRQOL. Patient's diabetes related quality of life, as reflected by total score on the ADDQoL, did not change significantly for either the active or control groups from clinic visit 1 to 2.

A trend of improved mean QOL in the active group (+ 0.3) and a reduced mean QOL in the control group (- 0.3) can be seen, however this does not reach statistical significance ($P = 0.064$).

Table 5.15: ADDQoL total score between clinic visit 1 and 2

Group	ADDQoL score				*P* value*
	Clinic 1		Clinic 2		
	Mean ± SD	Median (range)	Mean ± SD	Median (range)	
Active	-2.3 ± 1.9	-2.0 (-7.4-0)	-2.0 ± 1.6	-2.0 (-5.3-0.1)	0.588
Control	-1.5 ± 1.9	-0.8 (-8.7-0)	-1.8 ± 2.0	-1.2 (-7.9-0)	0.800

* Compare means using T-test

Changes from clinic visit 1 to 2 for the 13-domain ADDQoL subscores are shown in Table 5.16. Patients in the active group scored better in most domains (9/13), except family relationships, friends, future of family, and motivation. There was a general decline in ADDQoL scores (worse quality of life) across most domains from baseline to follow up in the control group, except for the sex life domain.

Table 5.16: Change from baseline in ADDQoL domain scores

Domain	Change from clinic visit 1 to 2			*P* value
	Active, Mean (range)[#]	Control, Mean (range)[#]	Difference between groups	
Employment/career	0.56 (-6-9)	-0.69 (-5-3)	1.25	0.107
Social life	0.16 (-9-9)	-0.43 (-7-6)	0.59	0.341
Family relationships	-0.47 (-9-6)	-0.37 (-6-5)	-0.10	0.855
Friends	-0.15 (-4-3)	-0.20 (-6-9)	0.05	0.906
Sex life	0.43 (-5-7)	0.15 (-5-6)	0.28	0.656
Sport/leisure	0.65 (-9-6)	-0.40 (-9-9)	1.05	0.009
Travel	0.10 (-6-9)	-0.64 (-5-4)	0.74	0.148
Future (own)	0.42 (-6-7)	-0.86 (-9-4)	1.28	0.036
Future of family	-0.27 (-6-9)	-0.77 (-9-5)	0.50	0.444
Motivation	-0.06 (-5-7)	-0.23 (-4-4)	0.17	0.489
Physical activities	0.10 (-9-7)	-0.49 (-5-4)	0.59	0.303
Other fussing	0.55 (-6-9)	-0.37 (-9-9)	0.92	0.234
Enjoyment of food	0.25 (-9-9)	-0.46 (-7-9)	0.71	0.351

[#] Figure with minus sign means decrease in quality of life.

Comparison of score changes reveals a difference between active and control groups on two items: sport/leisure domain ($P = 0.009$) and future (own) domain ($P = 0.036$). The largest change in average score between groups was for the future (own) domain, for which the active group scores increased by 0.42 units but the control group value declined on average by 0.86 units. A Bonferroni correction would indicate that a significant result would require a P value of < 0.0038. Therefore the differences observed would not reach statistical significance.

In the general quality of life question (question A, Appendix VII), the median score at clinic visit 1 was -1.0 (range -3 to 2) in the active group, and -1.0 (range -3 to 1) in the control group. The median score was the same in both groups at the clinic visit 2 (-1.0 (range-3 to1) in both the active and the control groups). The median score in diabetes related general quality of life (question B, Appendix VII) at clinic visit 1 was -2.0 (range -3 to1) in the active group, -1.0 (range -3 to 0) in the control group. The median score remained the same in active and control groups at clinic visit 2.

5.4.4 Number of DRPs identified

Tables 5.17 and 5.18 provide further details of type of DRPs for the active and control groups. It should be noted that the number of drug related problem at the second and third clinic visits includes both newly identified problems and unresolved problems.

Table 5.17: Classification and number of DRPs in active and control groups at clinic 1 and 2

Description	Active		Control	
	Clinic 1	Clinic 2	Clinic 1	Clinic 2
Clinical DRP	154	98	151	165
Administrative DRP	23	13	28	22
Total	177	111	179	187

Table 5.18: Classification and number of DRPs in active and control groups at clinic 3

Description	Active	Control
Clinical DRP	43	100
Administrative DRP	4	12
Total	47	112

At the first clinic visit, some 356 DRPs were identified of which 177 related to the active patients and 179 to the control patients. The number of DRPs identified decreased by 37% in the active group and increased by 4.5% in the control group at the second clinic visit (Table 5.17). Of the 82 patients (51%) who attended a third clinic visit, the number of DRPs identified was significantly higher in the control group than the active group (Table 5.18).

Within clinical DRPs there were 101 (34%) and 154 (37%) DRPs related to diabetes in the active and control groups respectively. The average number of DRPs per patient is shown in Table 5.19.

Table 5.19: Mean number of DRPs per patient in active and control groups

Patient group	Mean ± SD	Range
Active		
Clinic visit 1 (n = 83)	2.1 ± 1.6	0-6
Clinic visit 2 (n = 83)	1.3 ± 1.4	0-5
Clinic visit 3 (n = 39)	1.2 ± 0.9	0-3
Control		
Clinic visit 1 (n = 77)	2.3 ± 1.4	0-5
Clinic visit 2 (n = 77)	2.4 ± 1.4	0-5
Clinic visit 3 (n = 43)	2.6 ± 1.5	0-6

Figures 5.2 - 5.4 provide detailed information on the number of patients and number of DRPs in the active and control groups at clinic visit 1, 2 and 3 respectively. At the first clinic visit, 67 (81%) of patients in the active group and 69 (90%) of patients in he control group had one or more DRPs identified ($\chi^2 = 3.22$, df = 1, $P > 0.05$). However, there was a significantly lower number of patients who had one or more DRPs at the second clinic visit in the active group ($\chi^2 = 6.87$, df = 1, $P < 0.01$) and at the third clinic visit ($\chi^2 = 7.44$, df = 1, $P < 0.01$).

Figure 5.2: Number of patients and number of DRPs at clinic visit 1 (N = 160)

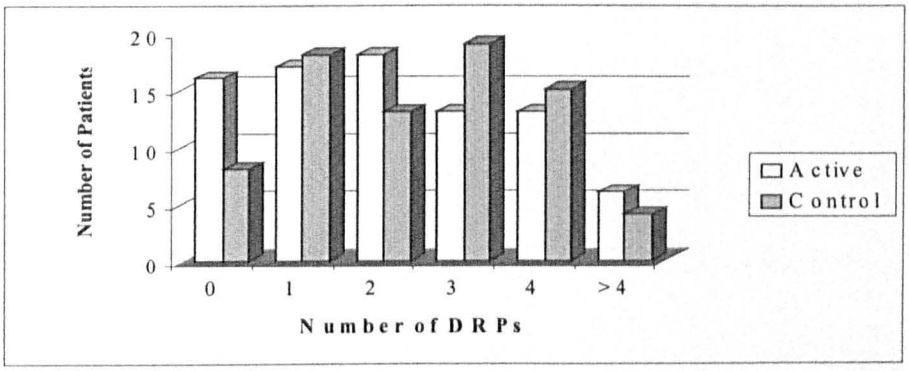


Figure 5.3: Number of patients and number of DRPs at clinic visit 2 (N = 160)

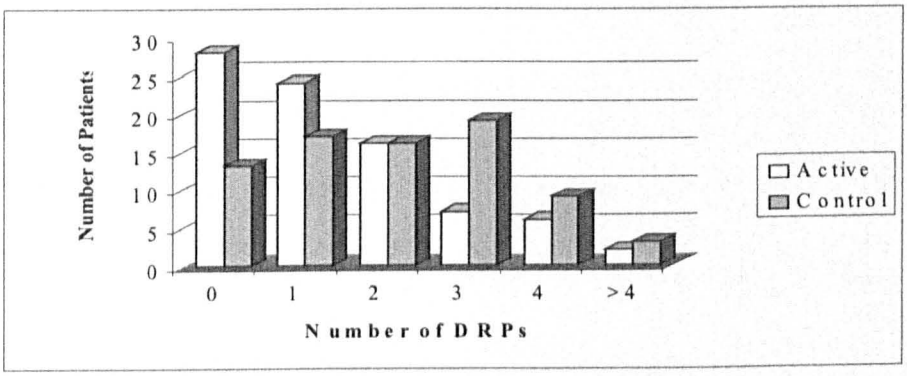
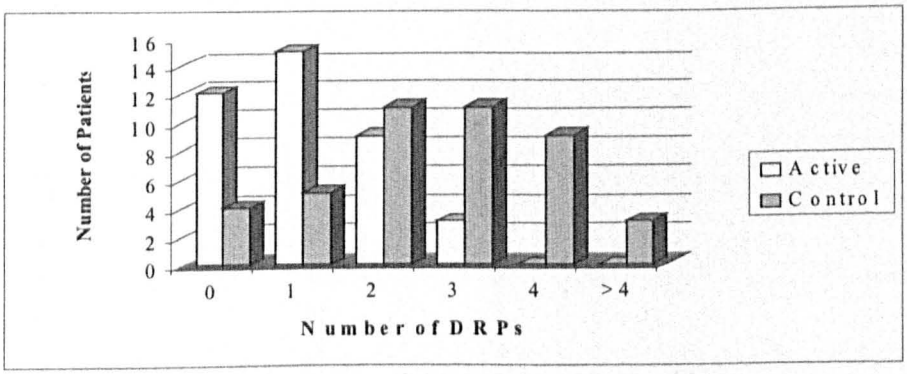


Figure 5.4: Number of patients and number of DRPs at clinic visit 3 (N = 82)



5.4.5 Clinical drug related problems

5.4.5.1 Categories of clinical DRPs identified

The drug related problems of each category were classified independently by two members of the study team (AC and CAM). The results were matched for 97% of all DRPs identified and the results presented in the tables were obtained after final unanimous agreement of the 3% amongst members of the project team (AC, CAM, and SS).

The distribution of the DRP categories in the active and control groups is shown in Table 5.20. The five most common clinical DRPs were: ineffective therapy (37%), monitoring required (19%), untreated indication (16%), inappropriate choice of therapy/ dose/ dosing schedule (9.8%), and admitted noncompliance/ counselling required (7.4%).

Only three DRPs (3/713, 0.4%) were classified under 'other', which suggests that there was a sufficient range of categories. Two DRPs in the active group related to patient's concern regarding bleeding after dilatation and curettage procedures and patient's colour blindness which made a difficulty reading Diastix. Another DRP in the control group was about removing Canesten pessaries from the repeat list and advising the patient to request a supply specifically so that the use could be better monitored.

Table 5.20: Number of clinical DRPs identified by pharmacist at first clinic (n=160), second clinic (n=160) and third clinic (n=82)

Category of clinical DRP	Total (%)	Active			Control		
		Clinic 1	Clinic 2	Clinic 3	Clinic 1	Clinic 2	Clinic 3
Ineffective	267(37)	58	47	20	52	52	38
Monitoring/ BP monitoring/ HbA1c monitoring required	133(19)	31	17	10	31	28	16
Untreated indication	113(16)	24	10	6	23	28	22
Inappropriate choice of therapy/ dose/ dosing schedule	70(9.8)	16	6	3	18	18	9
Admitted noncompliance/ counselling required	53(7.4)	12	9	3	12	13	4
Unnecessary therapy	37(5.2)	8	3	0	7	16	3
ADR/ drug interaction	23(3.2)	2	1	0	8	7	5
No indication apparent	5(0.7)	2	2	0	0	1	0
Formulation/delivery	5(0.7)	0	3	0	0	1	1
Contraindication	2(0.3)	0	0	0	0	0	2
Other	3(0.4)	1	0	1	0	1	0
Total	711(100)	154	98	43	151	165	100

5.4.5.2 BNF categories for drugs with clinical DRPs

The pharmacists reviewed 964 and 1,033 drugs at the clinic visit 1 and 2 for the 160 patients interviewed. The BNF categories for these are given in Table 5.21. Of the 964 drugs reviewed at clinic visit 1, 256 (26%) were associated with clinical drug related problems and of 1,033 drugs reviewed at clinic visit 2, 199 (19%) were associated with clinical drug related problems.

Overall there were found to be 27 DRPs per 100 drugs reviewed at clinic visit 1 compared to 19 DRPs per 100 drugs reviewed at clinic visit 2. However there was a large variation in the number of DRPs associated with different BNF chapters. For example, 36 DRPs were noted for every 100 cardiovascular drugs reviewed at clinic 1 compared to only 6 DRPs per 100 central nervous system drugs reviewed and 2 DRPs per 100 respiratory drugs reviewed.

Table 5.21: BNF categories and clinical DRPs

BNF category (chapter number)	Number of drugs reviewed (%)		Number of drugs related to DRP (%)		DRPs per 100 drugs reviewed	
	Clinic 1	Clinic 2	Clinic 1	Clinic 2	Clinic 1	Clinic 2
Cardiovascular system (2)	355 (37)	405 (39)	129 (51)	91 (46)	36	22
Endocrine system (6)	240 (25)	247 (24)	90 (35)	75 (38)	38	30
Central nervous system (4)	133 (14)	135 (13)	8 (3.1)	12 (6.1)	6	9
Gastro-intestinal system (1)	68 (7.1)	71 (6.9)	10 (3.9)	8 (4.1)	15	11
Respiratory system (3)	48 (5.0)	50 (4.8)	1 (0.4)	2 (1.0)	2	4
Musculoskeletal disease(10)	47 (4.9)	53 (5.1)	11 (4.3)	4 (2.0)	23	8
Others	72 (7.5)	70 (6.8)	6 (2.3)	5 (2.5)	8	7
Total	964 (100)	1033 (100)	256 (100)	199 (100)	27	19

Number of patients: 83 active, 77 control

5.4.5.3 Clinical DRPs linked to diabetes

There were some DRP categories related to the condition of diabetes itself, i.e. DRPs regarding HbA1c monitoring required, other monitoring required, and admitted noncompliance/ counselling required. HbA1c monitoring was required in the cases where new diabetic treatment was commenced or where the dose of diabetic medication was adjusted. HbA1c measurement was needed to assess the effectiveness of the revised diabetic treatment. Examples of monitoring required included failure to received routine screening including feet and eye examinations. Examples of noncompliance and counselling required included monitoring blood and urine glucose levels and compliance with diabetic medications.

5.4.5.3.1 Clinical DRPs related to antidiabetic drugs

Of the 711 clinical DRPs, 171 (24%) were identified specifically related to antidiabetic drugs, the distribution of the most common categories of DRPs are shown in Table 5.22. Gliclazide and metformin are the most common antidiabetic drugs found to be associated with clinical DRPs. The most prevalent clinical DRPs associated with antidiabetic drugs were related to ineffective therapy (79%).

All referrals for the active group were passed to the GP for consideration while in control group no referrals were made in accordance with the planned protocol. Therefore it is possible for the pharmacist to identify a DRP in the control group repeatedly at the later clinic visits, if the problem remained as before. Of the 89 DRPs related to antidiabetic drugs in the control group, 28 (31%) DRPs were repeated at the later clinic visits.

Table 5.22: Antidiabetic drugs associated with clinical DRPs

Drug	Number prescribed	Number of associated clinical DRPs (%)	Category of DRPs			
			Ineffective therapy	Admitted non-compliance	Inappropriate choice of therapy	Inappropriate dose/dosing schedule
Gliclazide	125	74 (59)	58	6	7	2
Metformin	88	61 (69)	49	6	2	2
Glibenclamide	25	13 (52)	6	0	0	4
Acarbose	16	6 (37)	6	0	0	0
Insulin	15	9 (60)	9	0	0	0
Glipizide	8	2 (25)	2	0	0	0
Other	12	6 (50)	6	0	0	0
Total (%)	246	171 (69)	136 (79)	12 (7.0)	9 (5.3)	8 (4.7)

Includes patients attending clinic visit 1 (n=160), clinic visit 2 (n=160) and clinic visit 3 (n=82) and includes DRPs identified in the pending GP referral in the control group.

5.4.5.3.2 Clinical DRPs related to blood pressure

Overall 100 (14%) of the 711 clinical DRPs were linked to blood pressure control. Pharmacists identified 59 (29 active, 30 control) DRPs related to 'ineffective therapy' in 47 (23 active, 24 control) hypertensive patients. Twenty-six blood pressure monitoring requests (14 active, 12 control) were made by pharmacists in 23 patients (13 active, 10 control). Untreated hypertension was identified in 12 patients (5 active, 7 control). Inappropriate choice of hypertensive treatment was identified in 3 active patients, each of these related to inappropriate use of frusemide for the management of hypertension.

5.4.5.3.3 Clinical DRPs related to lipid levels

There were 85 (12%) of the 711 clinical DRPs associated with dyslipidaemia and regular lipid control. Thirty seven of these (43%, 19 patients in the active group and 11 patients in the control group) were categorised as monitoring required due to no regular lipid check or re-check after change of the lipid-lowering drug and 26 (31%, 9 patients in the active group and 11 patients in the control group) which were categorised as untreated indication. Other lipid related DRPs included 9 issues categorised as ineffective therapy (5 active, 4 control), 8 issues categorised as inappropriate dose/dosing schedule (3 active, 5 control), 3 issues involving adverse drug reaction (1 control), and 2 issues where choice of therapy was inappropriate (2 active).

5.4.5.3.4 Clinical DRPs related to aspirin therapy

Of the 711 clinical DRPs, pharmacists recommended a low dose of aspirin for primary and secondary cardiovascular prevention resulting from 46 (6.5%) DRPs (18 active, 28 control) in 38 patients (20 control, 18 active patients) who had Type 2 diabetes with coronary heart disease or who were at high risk of coronary heart disease, without a contraindication to using aspirin. These were categorised as untreated indication. The patients were prescribed plain aspirin 75mg daily for this indication, as recommended by the pharmacists.

5.4.5.3.5 Clinical DRPs related to urinary protein and electrolytes

Of the 711 clinical DRPs, pharmacists requested 34 (4.8%) urinalysis and electrolytes checks (16 active, 18 control) in 26 patients (14 active, 12 control). Overdue monitoring was the most common reason for requesting a urinalysis test (21/34 issues, 62%). Other reasons included monitoring renal function before and during treatment with angiotensin-converting enzyme inhibitors, diuretics, and metformin.

5.4.5.3.6 Clinical DRPs related to foot and eye examinations

Overall 6 (0.8%) of 711 clinical DRPs were related to foot and eye examinations. Pharmacists recommended referral of 4 patients (1 active, 3 control) to a chiropodist and referral of 2 patients (1 active, 1 control) to an ophthalmologist for further examination.

5.4.5.3.7 Miscellaneous

Liver function tests were requested in 3 patients (2 active, 1 control) who were already receiving or were about to commence statins. This test was also recommended in 2 patients (1 active, 1 control) before they started pioglitazone and rosiglitazone respectively.

5.4.5.4 Proposed actions to resolve clinical DRPs

A summary of the actions recommended by the pharmacists to resolve the clinical DRPs is provided in Table 5.23. The pharmacists made 711 recommendations over all three visits in both groups. Of these, recommendations 'initiate therapy' and 'increase dose' were the two most common categories totalling 170 (24%) and 151 (21%) respectively.

Table 5.23: Proposed actions suggested to GP to resolve the clinical DRPs at clinic visit 1 (n=160), clinic visit 2 (n=160) and clinic visit 3 (n=82)

Action	Total	Active			Control		
		Clinic 1	Clinic 2	Clinic 3	Clinic 1	Clinic 2	Clinic 3
Initiate therapy	170 (24)	36	19	13	38	37	27
Increase dose	151 (21)	38	28	11	25	30	19
Monitoring	103 (14)	23	17	7	22	22	12
GP to review	100 (14)	22	10	7	19	27	15
Counsel	46 (6.5)	7	7	3	12	10	7
Change drug new group	29 (4.1)	5	2	2	7	7	6
Decrease dose	27 (3.8)	5	3	0	7	9	3
Change drug same group	27 (3.8)	3	5	0	6	8	5
Stop therapy	24 (3.4)	6	4	0	4	6	4
Change directions	21 (2.9)	6	0	0	8	5	2
Confirm indication/dose	7 (1.0)	1	0	0	3	3	0
Other	6 (0.8)	2	3	0	0	1	0
Total	711 (100)	154	98	43	151	165	100

5.4.5.5 GP response to proposed actions to resolve clinical DRPs in the active group

Overall of the 295 clinical DRPs referred in the active group, 235 (80%) resolutions were completely agreed, 53 (18%) partially agreed and 7 (2%) rejected by the GP. At clinic visit 1, 154 active patient referrals were made of which 123 (80%) were agreed, 28 (18%) were partially agreed and 3 (1.9%) were rejected. At clinic visit 2, there were 96 active referrals of which 80 (82%) were agreed, 16 (17%) were partially agreed and 2 (1.3%) were rejected. At clinic visit 3, there were 45 active referrals of which 32 (71%) were agreed, 11 (24%) were partially agreed and 2 (4.4%) were rejected.

Table 5.24 provides a summary of GP responses to the clinical DRPs. Generally a high level of agreement was noted for all categories of clinical DRPs although GPs appeared more likely to reject no indication apparent (25%) and unnecessary therapy (18%) but the numbers are too small to interpret.

Table 5.24: Summary of GP responses to recommendations regarding clinical DRPs in the active group at all clinic visits

DRP	Completely agreed (%)	Partially agreed (%)	Rejected (%)
Ineffective therapy	95 (76)	27 (22)	3 (2.4)
Routine monitoring / HbA1c monitoring required	54 (93)	4 (6.9)	0 (0)
Untreated indication	30 (75)	10 (25)	0 (0)
Inappropriate choice of therapy /dose/ dosing schedule	18 (72)	6 (24)	1 (4.0)
Admitted noncompliance / counselling required	23 (96)	1 (4.2)	0 (0)
Unnecessary therapy	6 (55)	3 (27)	2 (18)
No indication apparent	3 (75)	0 (0)	1 (25)
ADR/DI	2 (67)	1 (33)	0 (0)
Other	4 (80)	1 (20)	0 (0)
Total (%)	235 (80)	53 (18)	7 (2)

5.4.6 Administrative drug related problems

5.4.6.1 Categories of administrative DRPs identified

There were 102 administrative DRPs of which 83 (81%) were categorised as 'repeat file inaccurate' and 19 (19%) which were identified as 'generic substitution/ cost issue'.

5.4.6.2 GP response to proposed actions to resolve administrative DRPs in the active group

Of the 40 administrative DRPs in the active group from all three clinic visits, recommendations on 39 (98%) were fully agreed and in only 1 case (2.5%) was further review requested. This DRP was related to the cost issue of the drug prescribed.

5.4.6.3 Outcome of administrative DRPs

Outcome data for administrative DRPs identified at clinic 1 was noted at clinic 2 and are provided in Table 5.25. Overall 96% of DRP were resolved in the active group versus 46% in the control group ($P < 0.001$).

Table 5.25: Number of administrative DRPs with outcome (clinic 1 to 2)

Outcome		Active	Control	Total
DRP remaining	Yes	1	15	16
	No	22	13	35
Total		23	28	51

$\chi^2 = 14.2$, 1 df, $P < 0.001$
RR = 0.08 (95%CI: 0.01 to 0.57), ARR = 0.5, NNT = 2

5.4.7 Outcome for all drug related problems

5.4.7.1 Immediate outcome

Table 5.26 provides details of the immediate outcomes resulting from all DRPs (clinical and administrative) in the active group at all three clinic visits. The majority of the agreed actions (239, 71%) were accepted by the patient and implemented by the pharmacist. None of the pharmacist recommendations were subsequently rejected by patient. The GP was left to action only 36 (11%). Details of the remainder are provided in Table 5.26.

Table 5.26: Immediate outcome resulting from intervention in the active group at clinic 1 (n=160), clinic 2 (n=160) and clinic 3 (n=82)

Outcome	Clinic 1	Clinic 2	Clinic 3
Actioned and accepted by patient	125 (71)	87 (78)	27 (57)
Not actioned, change in patient status	1 (0.6)	3 (2.7)	0 (0)
Not actioned, no reason apparent	17 (9.6)	5 (4.5)	5 (11)
Agreed GP to action	22 (12)	8 (7.2)	6 (13)
No further patient contact required	3 (1.7)	6 (5.4)	3 (6.4)
Monitoring detects abnormality	6 (3.4)	1 (0.9)	2 (4.2)
Notes not available	3 (1.7)	1 (0.9)	4 (8.5)
Total (%)	177 (100)	111 (100)	47 (100)

5.4.7.2 Final outcome

Outcome data for DRPs identified at clinic 1 was noted at clinic 2 and are provided in Table 5.27. Overall 62% of DRP were resolved in the active group versus 36% in the control group ($P < 0.001$). A significant difference was noted with a RR of 0.59 (0.48 to 0.74), an ARR of 0.26 and NNT of 3.85. However chi-square assumes independence of DRPs which may not be the case.

Table 5.27: Number of DRPs with outcome at clinic 2 (clinic 1 to 2)

Outcome		Active	Control	Total
DRP remaining	Yes	67	114	181
	No	110	65	175
Total		177	179	356

$\chi^2 = 23.8$, 1 df, $P < 0.001$
RR = 0.59 (95%CI: 0.48 to 0.74), ARR = 0.26, NNT = 3.85

Table 5.28 provides details of patients on the number of DRPs remaining. A significant difference was noted with a RR of 0.80 (0.66 to 0.96), an ARR of 0.17 and NNT of 5.88.

Table 5.28: Outcome data for patients and DRPs remaining (clinic 1 to 2)

Outcome		Active	Control	Total
No. of patients with	Yes	55	64	119
one or more DRPs	No	28	13	41
Total		83	77	160

$\chi^2 = 5.95$, 1 df, $P < 0.02$
RR = 0.80 (95%CI: 0.66 to 0.96), ARR = 0.17, NNT = 5.88

Eighty-two patients attended all three clinics and Table 5.29 provides final outcome data for all DRPs identified at clinic 1 which were followed up at clinic 3. Overall 62% of DRP were resolved in the active group versus 37% in the control group ($P < 0.001$). A significant difference was noted with a RR of 0.60 (0.44 to 0.82), an ARR of 0.25 and NNT of 4.0.

Table 5.29: Number of DRPs with outcome at clinic 3 (clinic 1 to 3)

Outcome		Active	Control	Total
DRP remaining	Yes	31	67	98
	No	51	39	90
Total		82	106	188

$\chi^2 = 11.96$, 1 df, $P < 0.001$
RR = 0.60 (95%CI: 0.44 to 0.82), ARR = 0.25, NNT = 4.0

Table 5.30 provides data on individual patients on the number of DRPs remaining at clinic visit 3. A significant difference was noted with a RR of 0.76 (0.61 to 0.96), an ARR of 0.22 and NNT of 4.5.

Table 5.30: Outcome data for patients and DRPs remaining (clinic 1 to 3)

Outcome		Active	Control	Total
No. of patients with one or more DRPs	Yes	27	39	66
	No	12	4	16
Total		39	43	82

$\chi^2 = 6.0$, 1 df, $P < 0.02$
RR = 0.76 (95%CI: 0.61 to 0.96), ARR = 0.22, NNT = 4.5

Table 5.31 provides examples of DRPs and outcomes in the order of categories described in method section 4.8.4.

Table 5.31: Examples of DRPs identified by the pharmacists

Patient code no.	Category	Drug related problem		
		Description	Intervention	Outcome
H05D	No indication apparent	Taking frusemide for ankle oedema.	Stop frusemide and monitor.	GP accepted, patients no longer had symptom.
H16D	Ineffective therapy	History of hypertension. BP not controlled.	Consider enalapril 2.5 mg initially and titrate dose.	GP accepted, enalapril was prescribed. Actioned BP now controlled
I05DA	Ineffective therapy	Taking metformin for controlling diabetes. HbA1c over 8.0%	Increase dose of Metformin	GP accepted, Pharmacist increased dose of metformin. HbA1c decreased but still over 8.0%.
H07D	Adverse drug reaction	Patient complaint of cold hands and feet and breathlessness, possible side effect of propranolol.	Stop propranolol and review symptoms. Start atenolol and recheck BP.	GP accepted. Patients had now no symptoms and BP controlled.
L18DA	Contraindication	Taking metformin 500mg twice a day. Patient had hepatic impairment and alcohol dependence.	Stop metformin.	GP accepted, prescribing gliclazide for alternative.

Table 5.31 continues overleaf

Patient No.	Category	Drug related problem		
		Description	Action	Outcome
I06DA	Admitted non-compliance	Patient was asked about monitoring blood/urine glucose levels. She does not monitor at the moment but has urine stix prescribed in the past. Her daughter bought a blood glucose monitor. She was reluctant to monitor.	Discuss reasons for monitoring and for elevated results. Further discussion at next diabetic appointment with GP.	GP accepted, patient was using blood glucose monitoring at home.
A26D	Counselling required	Patient thought glibenclamide making her put on weight. Pharmacist noted that she was possibly not taking the glibenclamide dose which was increased by GP three months earlier.	Counsel patient on importance of taking tablets.	GP accepted.
G21D	Counselling required	Patient was very unclear about directions for prescribed medications.	Clarify directions on repeated medication list.	GP accepted.
K31D	Monitoring required	Started on pioglitazone by diabetic clinic.	Check LFT's	GP accepted. LFT's checked. Result was normal.

Table 5.31 continues overleaf

Patient No.	Category	Drug related problem		
		Description	Action	Outcome
L06D	Monitoring required	Patient has never had foot examination since diabetes diagnosed.	Request a patient referral to chiropodist.	GP accepted. No referral with no reasons apparent. Care issue remained as before.
L02D	Monitoring required	No diabetic monitoring since 1997. There were no recent HbA1c, lipid profile, blood pressure, feet and eyes examinations.	Request a patient referral to diabetic clinic.	GP required further review. The monitoring results were obtained after review.
J22D	Unnecessary therapy	Increase in bisoprolol dose to relieve angina symptoms. Also taking captopril for hypertension. BP 95/62.	Recommend decrease captopil dose to accommodate increase in bisoprolol dose and monitor BP.	GP accepted. Captopril dose was decreased as suggested. BP was within normal range.
H10D	Untreated indication	BP 150/70 on 2/00 and 166/80 on 3/00 and untreated for hypertension. History of gout.	Consider enalapril 2.5mg daily. Recommend monitoring U&Es and ECG.	GP accepted. Initiated captopril as suggested. BP still high (164/103). Further increased enalapril dose and monitor BP.
K22D	Untreated indication	BP 170/60 last clinic visit and currently 153/71. No history of hypertension.	Consider bendrofluazide and monitor for effectiveness in one month.	GP accepted. BP now 146/60.

Table 5.31 continues overleaf

Patient No.	Category	Drug related problem		
		Description	Action	Outcome
J24D	Untreated indication	Primary prevention of cerebrovascular disease. History of hypertension and diabetes. No C/I for aspirin.	Start aspirin 75 mg daily and counsel patient on lifelong therapy.	GP accepted. Aspirin initiated.
M15D	Repeat file inaccurate	Metformin dose changed by diabetic clinic.	Amend metformin dose on computer repeat list.	GP accepted. Metformin dose on computer list is now correct.
E12D	Generic substitution/cost issue	Taking enalapril 10mg two times a day. (Cost £22.03/month)	Change to enalapril 20mg once daily. (Cost £13.10/month)	GP accepted.
L18D	Generic substitution/cost issue	Taking Monocor 10mg.	Change to generic bisoprolol 10mg.	GP accepted.
K06	Inappropriate choice of therapy	Taking glibenclamide at maximum dose. Creatinine level 169 μmol/L.	Switched to gliclazide as gllibenclamide is less suitable with renal impairment.	GP accepted.
K35	Inappropriate choice of therapy	Total cholesterol coming down on simvastatin therapy but triglyceride still high.	Change statin to atorvastatin as it has better efficacy for mixed hyperlipidaemia.	GP accepted. Triglyceride still high but has started to come down slightly.

Table 5.31 continues overleaf

Patient No.	Category	Drug related problem		
		Description	Action	Outcome
E15D	Formulation/delivery	Prescribed verapamil SR 240 mg. SR preparation should be prescribed by brand name to avoid variation in bioavailability.	Change verapamil SR to Securon SR.	GP accepted, problem resolved due to action taken.
A37D	Inappropriate dose/dosing schedule	Taking simvastatin 10mg once in the morning as prescribed.	Advise patient to take simvastatin at night and amend computer repeat list.	GP accepted.

5.4.8 Pharmacist intervention rates and implications for future service delivery

Nine pharmacists participated in the study, three of whom were not involved in the pilot study but had completed the training programme. All had experience of medication review clinics for at least one year. The mean age was 37 years. The majority of the pharmacists were female (7/9), had attained a bachelor's degree in pharmacy (9/9), graduated in the years between 1981-1989 (8/9), and currently practiced in a community pharmacy (7/9). One had attained a master's degree, two a postgraduate diploma in clinical pharmacy and one a diploma in health and social welfare. Four of them were working as full-time pharmacists at the time of the study. The pharmacists operated the pharmaceutical care clinic one day per week except one pharmacist who ran the clinic one day every two weeks.

Appendix XXII provides a copy of questionnaire sent to the pharmacists six months after completion of the clinics, 100% response was obtained. Pharmacists rated their confidence in running the diabetes clinic on a scale of 0-10 with a median of 5.0 (3.0 – 8.0) before the study and 9.0 (7.0 – 10.0) after the study (Wilcoxon Signed-Rank test, $Z = -2.7$, $P = 0.008$). One year after the study the majority of the pharmacists (8/9) have continued working in medication review clinics.

The maximum number of patients interviewed at any one site was 61; the minimum number was 35. The average number was 45. Active and control group enrolment was balanced in all sites. Table 5.32 provides details of number of patients with one or more DRPs and number of DRPs per patient across the nine pharmacists. Percentage of patients with one or more DRPs ranged from 51 to 94%. The distribution of common clinical DRPs across the nine pharmacists were further

Table 5.32: Comparison of the number of DRPs identified by each of the pharmacists (includes active and control patients)

Pharmacist	No. of patients interviewed	No. of patients with one or more DRPs (%)		Mean no. of DRPs per patient (range)
A	51	44	(86)	2.3 (0-7)
B	51	48	(94)	2.3 (0-4)
C	36	29	(81)	1.7 (0-6)
D	61	57	(93)	2.2 (0-5)
E	43	27	(63)	1.1 (0-4)
F	36	34	(94)	2.7 (0-7)
G	38	23	(60)	0.9 (0-4)
H	52	42	(81)	2.0 (0-7)
I	35	18	(51)	0.7 (0-3)
Total	403	322	(80)	1.8 (0-7)

examined in Table 5.33. Although ineffective therapy comprised 32% of the top five clinical DRPs, the values for individual pharmacists ranged from 22% to 56%. A similar variation can be noted for the remaining DRPs.

The pharmacists recorded a total of 711 DRPs and recorded recommendations in both groups throughout the study. Three hundreds and five problems were identified at clinic visit 1, 263 problems at clinic visit 2 and 143 problems at the last clinic visit. Ten patients (six active patients and 4 control patient) had no DRP identified by the pharmacist. Table 5.34 provides information on GP acceptance of pharmacists' recommendation by practice for the 335 DRPs referred in the active group. The percentage of recommendations completely agreed ranged from 54% to 100% and rejected from 0% to 9%.

Table 5.33: Comparison of the top five clinical DRP categories identified according to individual pharmacists DRPs (includes active and control patients)

Pharmacist	Total no. of DRPs identified	DRP categories (%)					
		Ineffective therapy	Monitoring required*	Untreated indication	Inappropriate**	Noncompliance / counselling***	Other
A	134	30 (22)	25 (19)	22 (16)	20 (15)	12 (9)	25 (19)
B	121	43 (35)	16 (13)	23 (19)	12 (10)	8 (7)	19 (16)
C	67	20 (30)	11 (16)	3 (5)	0 (0)	2 (3)	31 (46)
D	149	57 (38)	17 (11)	23 (15)	21 (14)	2 (1)	29 (20)
E	46	18 (39)	4 (9)	2 (4)	1 (2)	4 (9)	17 (37)
F	102	24 (23)	23 (22)	13 (13)	4 (4)	10 (10)	28 (28)
G	43	12 (28)	5 (12)	9 (21)	4 (9)	1 (2)	12 (28)
H	124	43 (35)	35 (28)	12 (10)	8 (6)	11 (9)	15 (12)
I	27	15 (56)	0 (0)	7 (26)	0 (0)	2 (7)	3 (11)
Total	813	262 (32)	136 (17)	114 (14)	70 (9)	52 (6)	179 (22)

*Routine monitoring / BP monitoring/ HbA1c monitoring required
** Inappropriate choice of therapy/ dose/ dosing schedule
*** Admitted noncompliance/ counselling required

Table 5.34: Comparison of the number of recommendations regarding DRPs in the active group accepted by GP by each of the pharmacists

Pharmacist	Total no. of DRPs with GP referral	GP response to pharmacists' recommendation (%)		
		Totally agreed	Partially agreed	Rejected, no action
A	48	40 (83)	8 (17)	0 (0)
B	44	33 (75)	7 (16)	4 (9)
C	17	17 (100)	0 (0)	0 (0)
D	61	42 (69)	19 (31)	0 (0)
E	34	29 (85)	3 (9)	2 (6)
F	55	50 (91)	5 (9)	0 (0)
G	13	7 (54)	6 (46)	0 (0)
H	47	38 (81)	8 (17)	1 (2)
I	16	16 (100)	0 (0)	0 (0)
Total	335	272 (81)	56 (17)	7 (2)

The total number of DRPs identified and amended by peer review in both the active and the control groups are shown in Table 5.35. Overall 14% (112 out of 795) of DRPs were amended by the peer review process with the highest rate noted at the first visit (20%) falling to 9% at clinic visit 2 and 3.

Table 5.35: Number of DRPs identified by individual pharmacists and number of DRPs amended by subsequent peer reviewer

Pharmacist	Number of DRPs identified by pharmacist			Number of DRPs amended by peer reviewer (%)		
	Clinic 1	Clinic 2	Clinic 3	Clinic 1	Clinic 2	Clinic 3
A	59	45	21	5 (8.5)	1 (2.2)	3 (14)
B	55	45	20	17 (31)	3 (6.7)	6 (30)
C	28	22	17	7 (25)	4 (18)	1 (5.9)
D	62	52	26	16 (26)	5 (9.6)	3 (11)
E	12	24	10	1 (8.3)	6 (25)	1 (10)
F	51	33	19	9 (18)	3 (9.1)	0 (0)
G	19	16	8	6 (32)	3 (19)	0 (0)
H	63	29	32	8 (13)	1 (3.4)	0 (0)
I	11	10	6	3 (27)	0 (0)	0 (0)
Total (%)	360 (100)	276 (100)	159 (100)	72 (20)	26 (9.4)	14 (8.8)

5.4.9 Ethical issues in the control group

In the control group, there were 134 DRPs from 94 patients remaining at the end of the study. Of a total of 109 DRPs, the proposed resolutions to 94 (86%) were agreed, 12 (11%) were partially agreed and 3 (2.7%) were rejected. In addition, 25 (19%) were from 10 patients for whom it was not possible to access the patient record due to either a change in patient status or the patient record not being available at the time. Final outcomes of these control referrals were not included in the data analysis as they are outwith the scope of the study.

The following illustrates 3 patients who were removed from the study in accordance with the predefined protocol after attending one clinic visit.

Case 1

A 70 year-old female diagnosed with Type 2 diabetes and hypertension. Gartnavel clinic recommended stopping diabetic medication on 6/6/00 (Glucobay 50 mg/day). The clinic did not recommend stopping doxazosin. However, the patient has stopped all medications. This included doxazosin 2 mg daily, which was being used to treat hypertension.

BP history: 29/2/00: 160/100 --- doxazosin added 7/3/00

15/3/00:181/96

6/6/00: 164/97 --- doxazosin stopped by patient

Current BP readings (26/6/00) --- 175/100, 176/93, 168/93

As the patient's blood pressure is not under control, and the patient is not on any antihypertensive medication, and in our control group (no intervention from us until end of study), the medical adviser suggested to break the code and inform the patient's GP of the misunderstanding which has led to the discontinuation of doxazosin, and the resultant increase in blood pressure. The patient was removed from the study.

Case 2

A 75 year-old female with Type 2 diabetes. Currently taking gliclazide 160mg twice per day. HbA1c value within last four months was 11.1%. Current HbA1c: 12.5%.

As the patient's glycaemic value is not under control, and the patient did not attend the diabetic clinic for more than a year, and in our control group (no intervention from the pharmacist until the end of study), this patient was removed from the study and the patient's GP informed.

Case 3

A 77 year-old male with Type 2 diabetes treated with metformin 500mg 1 tablet daily and gliclazide 80mg 1 tablet daily. Current HbA1c: 10.1%. BP 172/110. Patient was removed from the study because of a stroke on 14/6/00, after attending only one clinic.

5.5 Key results of the main study

- Target of 1.0 unit change in HbA1c was not achieved. There was no change in HbA1c both between and within the active and control groups throughout the study. There was no change in HbA1c when patients were grouped according to poor or good control.

- Overall the active group achieved a significant decrease in SBP at clinic visits 2 (9 mmHg) and 3 (15 mmHg) within group; no such difference was noted in the control group. When comparing between groups there was no difference in mean change in SBP between the active and the control from clinic 1 to clinic 2 (P = 0.409), however, this was significant at clinic 3 (P = 0.030).

- There was no change in diastolic blood pressure between or within group at clinic 2 and 3.

- There was no difference in health related quality of life in terms of overall score however a trend was noted with the majority of domains producing a more favourable outcome in the active group than in the control.

- Overall 813 DRPs were identified (711 clinical DRPs and 102 administrative DRPs). Of these, 356 DRPs were identified at the first clinic visit, 298 DRPs at the second clinic visit and 159 DRPs at the third clinic visit.

- The top three common categories of clinical DRP were ineffective therapy (37%), monitoring required (19%), and untreated indication (16%).

- Of the 711 clinical DRPs, 171 (24%) were identified specifically related to antidiabetic drugs, 100 (14%) to blood pressure, and 85 (12%) to lipids.

- In the active group, the number of DRPs per patient was decreased from clinic 1 (2.1 per patient) to clinic 3 (1.2 per patients) compared to the control group at clinic 1 (2.3 per patient) and at clinic 3 (2.6 per patient).

- In the active group there was a significant decrease in the number of DRPs from clinic 1 to 2 compared to the control group (60% of active DRPs resolved vs 34% of control DRPs resolved).

- At the first clinic visit, 136 (85%) patients had one or more DRP. In the active group there was a significant decrease in the number of patients with one or more DRPs from clinic 1 to 2 and clinic 1 to 3 compared to the control group.

- The GPs completely agreed recommendations for resolving 235 (80%) clinical DRPs and 39 (98%) administrative DRPs at all three clinic visits.

- The majority of the agreed actions were accepted by the patient and implemented by the pharmacist (71%).

Chapter 6

Discussion

6.1 Aim and Objectives

A pharmaceutical care model for patients with Type 2 diabetes was developed and successfully implemented in primary care. The effectiveness of the pharmaceutical care model was assessed in this randomised controlled trial in nine GP practices within a primary care setting. The results demonstrated a significant change in systolic blood pressure in the active group from clinic visit 1 to 2 and clinic visit 1 to 3 but no change in HbA1c and HRQOL. There were 177 DRPs in the active group at baseline which decreased to 67 at clinic visit 2. Equivalent numbers of DRPs for the control group were 179 and 114 respectively. The risk reduction in the active group was therefore 0.59 with a NNT of 4 (19 weeks). The results also demonstrated a high GP acceptance rate, as evidenced by 80% of recommendations from pharmacists being completely agreed and only 2% of the resolutions to DRPs being rejected.

6.2 Methodological consideration

6.2.1 RCT design

The RCT is an experimental design used increasingly in patient care settings to compare the effectiveness of different interventions (Altman, 1996). The results provided by RCTs are of potentially higher validity and contribute more to clinical knowledge than traditional methods, such as case control and observational cohort

studies. The UKPDS is an example of a study using a RCT design. The study was able to establish the safety and efficacy of intensive blood glucose and blood pressure control in preventing complications (UKPDS Group, 1998a; UKPDS Group, 1998d).

The RCT has the unique advantage of using randomisation as a method of determining patient allocation between intervention and control groups, which eliminates selection bias (Altman, 1991; Bowling, 1997). The random allocation of the patients into two comparable groups allows the groups to be compared to demonstrate the effect of an intervention. Any imbalance between groups with respect to other variables can only arise by chance. Bias in the observation of outcomes or execution of the intervention can be minimised by the use of blinding procedures. Remaining variability can be reduced by increasing the sample size.

In this study we conducted such a trial to compare the effect of a pharmacist intervention between the active and control groups. We hypothesised that the patient outcomes (HbA1c, blood pressure, HRQOL, DRPs identified and resolved) would be improved in the active group compared to the control group according to the intervention. We believe that the RCT design facilitated the analysis of each of the outcomes directly attributable to the input from the pharmacists. A before and after comparison alone would not have been appropriate due to the dynamic nature of practice with new evidence informing rapidly evolving treatment guidelines.

RCTs do however have their limitations when applied to health services research. Randomisation does not preclude the possibility that the population randomised may be atypical for the wider population of interest. Healthcare professionals who are willing to participate in RCTs may be unrepresentative of the rest of their profession.

In some cases, the criteria for inclusion of patients in RCTs may bear little resemblance to the real world, which will affect the generalisability of the study. In addition, RCTs can be difficult to set up because of professional resistance to them. For instance, some healthcare professionals perceive that it would be unethical to deny patients a new treatment or a new service, if it was believed to improve the outcome or the standard of treatment (Bowling, 1997).

6.2.2 External validity - Generalisability

This study was completed in Type 2 diabetes patients receiving oral antidiabetic drugs rather than the wider diabetes mellitus population including both Type 1 and 2 diabetics. However, patients with Type 2 diabetes make up a large and important group in terms of numbers and risk of cardiovascular disease (Haffner et al., 1998; Stratton et al., 2000). The decision to focus only on Type 2 diabetes was based on the difference of treatment strategy between types of diabetes, which might affect the outcome of the study, if there was a significant difference in the number of patients recruited in each arm. Exclusion criteria were set to ensure patient safety at the outset of the study.

The number of patients who refused to participate in the study after randomisation was 46%, leaving 54% of patients to enter the study. This number was comparable to the 58% participation rate in the study of Mackie et al. (1999). A 54% recruitment was considered reasonable because details about the study process were sent to patients before they gave their consent including the need to take blood samples at the clinic. A high percentage of patients (80%) who participated in clinic visit 1 returned for clinic visit 2. In addition, the allocated group (active or control) was not known when a patient was considered for entry into the study because this knowledge may have

influenced the patient participation and would have potentially increased the number of refusers within the control group.

It was found that patients who declined to participate and those who did not complete the study were no different in certain baseline characteristics (mean age, gender distribution, and mean HbA1c value) suggesting that the intervention did reach nearly all of those who were eligible for the study.

The number of patients lost to follow up was high at clinic visit 3 (78, 51%), showing the difficulty of undertaking RCT involving several clinic visits over 6 months or more in primary care. However, the proportion assessed in each group at all three visits was similar, reducing the risk of ascertainment bias (assessment of outcome).

Although a random sampling method was used, our study may not be generalisable to patients in different primary care settings. A total of 15 out of 219 practices (7%) were approached in order to recruit 9 practices. This was considered a small sample size. Of these 15 practices, only 9 (60%) were willing to take part in the study. There was concern that GPs who did participate might not be typical of all GPs. Those who agreed to take part in the study may have been highly motivated and more likely to accept the intervention from the pharmaceutical care model. Extrapolating the results therefore to the general population might be misleading.

In addition this study utilised pharmacists who had only recently received training in the pharmaceutical care model in Type 2 diabetes. They were therefore on the lower limb of a professional learning curve and may not be representative of experienced pharmacist specialists. In addition, like the GPs, these pharmacists may be particularly well motivated and receptive to the concept of delivering pharmaceutical

care in a general practice setting. The results obtained with these pharmacists might not be generalisable, therefore, to the wider group of community pharmacists.

6.2.3 Internal validity

In this study randomisation was used to allocate patients to groups in order to prevent bias. Stratified randomisation was conducted to ensure that the patients in each group were of similar age, gender and practice distributions, using computer generated random numbers.

To avoid selection bias, group allocation for each patient was not revealed until the patient had been entered into the study. In addition the person who generated the allocation in this study (SS) was not the person who determined eligibility and entry of patients (RL, AM).

Blinding represents an important methodological component for reducing results bias (ascertainment bias), intentionally or unintentionally, and so helping ensure the credibility of the study conclusion (Day and Altman, 2000). At the first clinic visit, both the patient and pharmacist were unaware of the group allocation (double blind). At the second and third clinic visits, double blinding became difficult. It was impossible to blind the pharmacist, as the intervention needed to be implemented in the active group. The single blinding at clinic visits 2 and 3 provided patient blinding to the group allocation only where patients had not received an intervention. In addition, the GPs were blinded to the patient allocation at all clinic visits to minimise possible bias in patient management. However, GP referrals in the active group would give a clue to patient's identity. In order to reduce this, no patient profiles, or GP referrals were stored with individual patient case notes during the period of the study. Also

randomisation was by patient rather than practice therefore the possibility of a washover effect was high between active and control patients registered with the same GP.

6.2.4 Outcome measures

Clinical outcome measures were changes in HbA1c and systolic blood pressure. Achieving good glycaemic control is important. The UKPDS proved that good glycaemic control in patients with Type 2 diabetes reduced the occurrence of chronic complications (UKPDS Group, 1998d). HbA1c is recognised as an important short-term parameter associated with long term outcomes (DCCT Research Group, 1993; UKPDS Group, 1998d). HbA1c is a reliable objective assessment method for metabolic control. Determinations of fasting or post –prandial blood glucose levels reflect only an instant in the course of the diabetic patient, while the levels of HbA1c relate to the blood glucose control during the previous two to three months (Gabbay et al., 1977).

Previous studies (Laakso, 1998; Turner, 1998; UKPDS Group, 1998d) emphasised the importance of combining monitoring and treatment of glycaemic control with that of other cardiovascular risk factors in diabetic patients: blood pressure and lipid profile. Systolic blood pressure was included as a clinical outcome in this study, and was measured using an electronic blood pressure machine. In addition, the study assessed diastolic blood pressure and reported the findings. There was a large number of missing records of lipid profile found in the pilot study and it was considered that it would be very difficult to obtain a lipid profile at all three clinic visits. In view of this, it was decided not to include lipid values as an outcome of this study from the outset.

Furthermore, to include the humanistic outcomes, health related quality of life was measured. Process outcomes were: the number and types of DRPs, the percentage of DRPs accepted by GPs, and the status of DRPs at follow up. These measures were included to provide information on the specific interventions made by the pharmacist, to gauge the GP response to suggested changes to therapy and, finally, to assess the effectiveness of the interventions.

6.2.5 Procedures undertaken to enhance the reliability of outcome measurements

6.2.5.1 HbA1c

Since HbA1c values obtained from the different assays used in different practices vary in terms of the normal range, it was decided that values should be obtained from a single laboratory using the DiaSTAT machine (Biorad Laboratory Ltd., Herts, UK). Thus it was ensured that the data could be interpreted and compared in a meaningful manner. Furthermore, an electronic printout of HbA1c from DIASTAT was available to reduce operator bias and ensure the accuracy of recording the data.

6.2.5.2 Blood pressure

The auscultatory technique using a mercury sphygmomanometer for blood pressure measurement is troublesome, time consuming, and is subject to bias as it could not be established whether the pharmacist had measured and recorded the value accurately. In view of this an automated electronic device, OMRON 705CP, was preferred in this study. An electronic printout of blood pressure measurement, with the time and date of measurement, was generated and used to remove many

sources of bias associated with the conventional auscultatory technique and therefore improve the overall accuracy of the measurements (O'Brien et al., 2001). Accordingly training in taking blood pressure using this device was provided for all the pharmacists in the study. The pharmacists were specifically trained on how to use the machine and the measuring technique (e.g., allow patient rest for 5 minutes before blood pressure measurement, and select appropriate cuff size for individual patient). However equipment problems still occurred, for example, the pharmacists reported that occasionally the first two readings differed by more than 15 mmHg, in which case a third reading was made and the mean of the two closest readings was recorded.

6.2.5.3 Health related quality of life

The previous validated instrument, ADDQoL (Bradley, 1999) was used to assess HRQOL. Deyo et al. (1983) reported that the reliability of QOL instruments is influenced by day to day variations in patient response and mode of administration of the questionnaire amongst other factors. In order to reduced bias on the HRQOL, patients were asked by reception staff to self-complete the HRQOL questionnaire prior to the clinic interview session. If patients had completed the HRQOL during or after the interview, it is likely that the interviewer or the clinic itself would bias the results.

6.2.5.4 Drug related problem

Drug related problems were recorded in the structured documentation developed in the pilot study. The free text format allowed the pharmacists to use their own words to describe the DRPs identified and actions recommended. DRPs were evaluated in a blinded fashion and then determined by unanimous decision. At the end of the study,

all identified DRPs, actions taken, and GP responses were coded according to the classification system described in Chapter 4 by an individual who was not involved in running the clinic (ALC). Peer review was undertaken for all DRPs identified in the active group before GP referral. The same peer review was also undertaken in the control group. The reviewer was initially blinded to group allocation (RL, AM) and intended to be blinded to the group at the follow up clinics, however, this blinding could not be guaranteed as there may have been some occasions when the pharmacist accidentally informed the reviewer. The peer reviewers were members of the project team. They were not involved, however, in running the clinics and analysing the data.

It was realised that the decision to withdraw a patient from the study could easily be influenced by the pharmacist having knowledge of which group the patient had been assigned to. To avoid this patients considered to be at risk of life threatening DRPs were referred to the independent medical adviser (ADC) to the study team who was blinded to the patient allocation. He independently made the decision to withdraw three control patients from the study.

A diabetes leaflet was posted to patients in both groups after the clinic session in order to minimise the influence of knowledge of diabetes on the study outcomes between the active and control groups. However, this may have introduced an intervention element to the control group and may have influenced the control outcomes. The same GPs and community pharmacists provided standard care for both groups therefore they were not likely to be a source of variation. It is possible, however, that involvement in the study may have influenced GP management of control patients who presented during the study.

6.2.6 Limitations of the study methodology

Potential limitations of the study are detailed below.

A high attendance rate of 80% was achieved at clinic visit 2, however, the 20% who did not return may have had poorer outcomes. The attendance rate of 51% (82 patients) at clinic visit 3 restricted the generalisability of any findings. Restricting the clinic to once a week on a specific day may have curtailed the number of patients who were able to attend. The limited time for follow up of patients was also a problem with 27 patients not being invited to clinic 3 because three months had not passed since the second clinic visit by the end of the study period. In addition domiciliary visits were not available. A longer study period therefore might have led to an increased completion rate.

The 160 patients successfully attending two clinic visits gave a satisfactory 96% power of detecting a 1.0 unit difference in HbA1c value, based on the mean value of HbA1c reported in the main study. Overall, 82 patients attended all three clinics giving lower study power at 77%. It was decided therefore to include the patients who attended two or more clinics in the main analysis of the study. However, as the study was planned on the basis of completion of three clinic visits, results of change in patient outcomes must be interpreted with caution, especially the process outcome which included actions recommended by the pharmacists. It is possible that the knowledge of having one further clinic visit to monitor the patient made a difference to the pharmacist's decision on the care plans at clinic visit 2.

The present study is a multi-practice study with a range of nine practices involved. The sample of practices was a random sample due to the detailed methodology applied (section 2.6). Overall there were 211 practices, of which 15 were approached in order to recruit 9 with sufficient patient numbers. The small number of practices and high refusal rate (40%) may have restricted the sample to practices with staff highly motivated to be involved in the study. As a result the data obtained cannot be extrapolated to the general population of practices in GGHB or further afield. This work should be replicated in greater numbers of representative practices.

There was a delay in GP referral after the interview due to the time for posting the blood sample to the laboratory and analysing by the researcher (SS). The pharmacists generally received the HbA1c result in approximately two weeks. This could possibly result in a delay in implementing changes in the active group which might effect the patient outcome and also result in a subsequent delay for the scheduling of the next clinic visit.

It was possible that the pharmacists felt less confident in suggesting change in patient therapy at the first clinic as supported by their self assessment of confidence which was lower at the start than at the end of the study. There were also some difficulties for the pharmacist in dealing with the clinical procedures such as measuring blood pressure and taking blood sample for HbA1c test. In addition there were occasional technical problems in using the electronic blood pressure machine.

Another issue that may influence the effect of the intervention is the Hawthorne effect, which is an effect of participants being aware that they are in the study (Roethlisberger and Dickson, 1939). The knowledge of the study may influence the subjects' behaviour or they may change their behaviour because they know that they

are being tested in some way. As pharmacists and GPs were aware that the study was being conducted, a Hawthorne effect may be a potential source of bias. It is possible that the effect size could be overestimated in this way. This was because the GP was alerted to the fact that patients may have been reviewed by the pharmacist. In addition an improvement in active group prescribing by the GPs may develop after the pharmacists' recommendations were made at earlier clinic visits. Equally the effect size could be underestimated since the control group may receive better than standard care due to contamination as a result of the meeting with the pharmacist and GP intervention due to the Hawthorne effect. It is concluded that the effect observed represents the minimum difference between the two groups rather than a total effect size.

The peer review process was intended to assist in the development of a quality pharmaceutical care model. In this study DRP identified from both active and control groups were reviewed. However, the reviewer only reviewed the GP referral made by the pharmacists and not the actual patient profile. Therefore DRPs could have been missed by both the pharmacist and the peer reviewer.

6.3 Interpretation of findings

6.3.1 Participants flow and characteristics

Overall 160 (43%) patients completed the study out of a possible 368 eligible patients. Comparison of certain baseline characteristics (age, gender, HbA1c) found no difference between participants and non-participants.

At baseline, in addition to age, gender and practice, which were criteria for randomisation to active and control groups, the groups also appeared to be closely matched in terms of number of concurrent medical conditions, number of drugs prescribed, body mass index, smoking status, and other clinical characteristics related to glycaemic control, blood pressure, and total cholesterol. However certain conditions may be underrecorded in the case notes as evidenced by recording of obesity in 31 patients but the pharmacist recording BMI > 27 Kg/m^2 in 99 patients. This is supported by Whitelaw et al (1996). They highlighted the variation in recording morbidity data in general practice in Scotland. However, generally although only 75% complete it is highly accurate. In this study information from computer records was supplemented with paper based case notes and information obtained at patient interview.

The use of cardiovascular drugs (BNF chapter 2) accounted for 37% of the total prescriptions in the subjects of the study. Such a high prescription rate of cardiovascular drugs in diabetes has been found in other studies. Wandell et al. (1996) studied the overall drug use among diabetes and non-diabetes by analysing the computerised Surveys of Living Conditions in Sweden. The authors found a higher number of patients using cardiovascular drugs (52% of patients) among

diabetic subjects compared with the general population (36%). Evans et al. (2000) reported the increased use and cost of prescription drugs in a population of 974 patients with Type 1 diabetes and 6,869 patients with Type 2 diabetes in Tayside, Scotland. They found cardiovascular drugs were the most commonly used drugs in Type 2 diabetes accounting for 30% of volume of the total prescriptions. It was also commented that the increased use of drugs for the cardiovascular system is possibly because of the increased risk of cardiovascular diseases in diabetic patients.

Within the active and control group all patients were accounted for throughout the study (Figure 5.1). Overall 80% of patients attended two or more clinics with 53% attending all three clinics. Drop out rates were comparable between the active and control groups. It can be concluded that the two groups were comparable at each stage of the study.

6.3.2 Outcome measures

6.3.2.1 Glycaemic control

The UKPDS (1998e) had mean levels for HbA1c of 7.2% (normal range 4.5 – 6.2%) in diabetic subjects at baseline. The median HbA1c during the 10 years of follow up was 7.4% in the metformin group and 8.0% in the conventional treatment group. In this study, the mean HbA1c at baseline was 8.3% in the active group, which was 1.0% higher than the upper limit of the reference range (3.8 – 7.3%) and 0.1% lower than in the control group. At the clinic visit 2, the mean HbA1c was increased by 0.1% in the active group and 0.2% in the control group. Analysis of the data revealed that neither active nor control group had a significant change in HbA1c from clinic visit 1

to 2, or clinic visit 1 to 3. Nor were there significant differences in HbA1c between active and control groups at any of the clinic visits.

Several barriers to the control of blood glucose in diabetes have been acknowledged (Dalewitz et al., 2000), particularly attitudinal, medical, and communication problems, as well as the nature of Type 2 diabetes which is a multisystemic, chronic, and complex disease making it more difficult to achieve desired normal or near-normal targets.

A large clinical trial, UKPDS (1998e), found improved glucose and HbA1c levels, but the HbA1c levels at the end of the study were not close to normal. In the last 5 years of follow up, the median HbA1c values in the metformin group and the conventional control group were 8.3% and 8.8%. A randomised controlled study by Kinmonth et al. (1998) assessed the effect of additional training of practice nurses and GPs on the lifestyle, psychological and physiological status of patients with newly diagnosed Type 2 diabetes. This study resulted in greater treatment satisfaction and patient well-being but no change in glycaemic control after one year of follow up.

A limited number of studies have been performed in diabetes aiming to improve or achieve a normal range of HbA1c values after pharmacist intervention (Jaber et al. 1996; Coast-Senior et al., 1998). The authors claimed significant improvement in glycaemic control was achieved in the intervention group as evidenced by glycosylated haemoglobin. However the limitations of the studies indicate that the results should be interpreted with caution. In the study of Jaber et al., the numbers of subjects was too small (n = 39) and the study period of insufficient duration. A study with larger numbers of subjects and of longer duration needs to be carried out for further evaluation. In the study of Coast-Senior et al., the study design did not include a control group therefore it is likely that the improvement in HbA1c noted was due to

the introduction of insulin. The study has the limitations in that the total number of patients was not reported, only those completing the study. The study is not generalisable due to its very narrow inclusion criteria with only Type 2 patients requiring insulin being included.

Recently Kelly and Rodgers (2000) described a pharmacist-managed diabetes service and reported a reduction in HbA1c values. The authors claimed a significant difference between groups at the end of the study as evidenced by HbA1c values at baseline and seven months follow up which were 9.0 and 8.5 for the control group and 9.0 and 7.5 for the intervention (P = 0.02). However, one limitation of the study was that prospective active patients were compared with a historical control, which may lead to an experimental bias, as the previously recorded data available for the controls are likely to be inferior and subject to missing information. In addition, the study covered a small number of patients (16 control, 32 intervention) which could affect the power of the study. However, the study reported no significant difference of HbA1c observed between groups (P =0.12) if using an intention to treat analysis. Also selection bias, due to the study subjects being referred by the physician to the study was noted.

The present study found no difference in change of HbA1c values within and between the active and control groups. Perhaps further studies with larger number of patients over longer periods of time are required to evaluate whether more intensive pharmaceutical care clinics would improve HbA1c outcome.

6.3.2.2 Blood pressure control

The benefit of blood pressure control with regard to cardiovascular end-points has been confirmed by several large trials. The hypertension optimal treatment (HOT) trial (Hansson et al., 1998) studied 18,790 hypertensive patients randomised to three different levels of target blood pressure. This trial contained a large subgroup analysis of patients with diabetes (n = 1,501), with approximately 500 patients in each of the three target blood pressure groups. After 3.8 years of mean follow up the three different mean blood pressures achieved were 150/81, 141/83 and 144/85 mmHg. In patients with diabetes, significant reductions in cardiovascular mortality (60%) and major cardiovascular events (51%) were shown in the group that achieved a diastolic blood pressure of 81 mmHg. The lowest incidence of major cardiovascular events occurred at a mean achieved diastolic blood pressure of 83 mmHg, with the lowest risk of cardiovascular mortality at 87 mmHg.

In the subset of patients with hypertension in the UKPDS, blood pressure control was effective in reducing the risk of macrovascular complications. A mean decrease of 10 mmHg for systolic blood pressure and 5 mmHg for diastolic blood pressure was associated with significant reductions in deaths related to diabetes and stroke (UKPDS Group 1998a).

Analysis of the data in this study indicates that a significant systolic blood pressure change was found within the active group from clinic visit 1 and 2 (9 mmHg), but not between the active and control group at visit 2. The within group in the active group between clinic visit 1 and 3 (15 mmHg) was also significant. A significant difference was found between the active and control groups at clinic visit 3 (P = 0.030). This greater improvement in the active group and the significant difference between

groups at clinic visit 3 could have resulted from a bias if patients who attended all three clinic visits were more compliant with their therapeutic regimen than non-attenders. No significant change in diastolic blood pressure was found within and between group.

The reduction of systolic blood pressure found in this study is in agreement with other studies that aimed to demonstrate that pharmacist intervention could significantly improve blood pressure control (Morse et al., 1986; Carter et al., 1997). Carter et al. (1997) conducted a 6- month RCT, single blind parallel group study in 51 hypertensive patients. In the active group, systolic blood pressure was reduced from 151 mmHg at baseline to 140 mmHg at 6 months. This is similar to the difference between before and after intervention in the study by Morse et al. (1986). After five to eight months of follow up, mean blood pressures for patients with severe hypertension reduced from 193/124 to 140/92 mmHg, moderate hypertension from 161/109 to 131/92 mmHg, and mild hypertension 171/100 to 137/88 mmHg. Hawkins et al. (1979) compared care by pharmacists and physicians in hypertensive and diabetic patients. Systolic blood pressure was one of the outcome measures in the study and they found significantly lower mean systolic blood pressure in the control group.

Kelly and Rodgers (2000) evaluated the impact of a pharmacist-managed diabetes service in 48 diabetic patients. They reported no statistical difference in systolic blood pressure and diastolic blood pressure between the intervention and control groups, although there was a trend toward a lower systolic blood pressure in the intervention group.

6.3.2.3 Health related quality of life

Quality of life is a humanistic patient outcome measure, and its improvement is supported as one of the goals of pharmaceutical care as defined by Hepler and Strand (1990). However diabetes by its nature is a chronic progressive disease therefore it would be unrealistic to expect to improve QOL. International Pharmaceutical Federation (FIP, 1998) adapted the goal of pharmaceutical care to take account of improvement or maintenance of quality of life therefore perhaps maintenance of QOL is a more realistic goal in this patient group.

While some researchers included both generic and disease specific QOL measures in their studies, others e.g., Eiser and Tooke (1993) commented that there was little advantage to this. It was pointed out that there is a considerable overlap between generic and disease specific scales in the items measuring QOL. With regard to sensitivity of the measurement to change in diabetes management, a diabetes specific QOL questionnaire was used in this study to measure humanistic outcomes. Using both measures may have resulted in a reduced response rate in view of the increase in burden to the patients.

As expected, the patient's response rate was high at clinic visit 1 (98%) compared to clinic visit 2 (72%). Some questions might not be relevant to the patients and this was considered by the authors (Bradley et al., 1999) providing N/A options for some items. There appeared to be a higher number of patients choosing not to respond to the questions concerning employment/career and sex life. This consideration has been noted previously (Bradley et al., 1999; Hammond and Aoki, 1992). Overall 14 patients were excluded from the analysis because of incomplete questionnaires,

especially the omission of importance rating. In these cases, impairment to QOL would probably have been overestimated without incorporating this rating.

The result of the general QOL question and overall scores showed no change in median scores within group and between groups. The general QOL scores could be thought to be a summary measure of QOL. However, it was found that general measures are not as strongly related to objective life circumstances, as might be anticipated (Wilson and Cleary, 1995). This was considered to be due partially to the change in patient's expectations and aspirations as circumstances change. Therefore specific questions regarding diabetes may be more sensitive to such changes.

A number of studies have examined the effects of pharmacist intervention for the patients and some of these studies have incorporated measures of HRQOL. Our analysis on HRQOL outcome showed a similar result to the studies by Hanlon et al (1996) and Jaber et al. (1996). Hanlon et al. evaluated the effect of clinical pharmacist interventions on elderly outpatients with polypharmacy. They found no differences in SF-36 among the patients that received the intervention after 12 months of the RCT at the sample size of 169 completed HRQOL. Jaber et al. assessed the impact of pharmaceutical care on diabetes treatment using SF-36 in a study incorporating a RCT design over a 4-month period. They also found no significant differences in any QOL domains. This study had a smaller sample size at 39 patients.

Carter et al. (1997) evaluated a community pharmacist training programme in management of hypertension. The authors reported significant changes in three domains namely physical functioning, physical role limitations, and bodily pain using the SF-36 after 6 months of the RCT. Quoted *P* values were not adjusted for multiple

comparisons. Since there were eight domains in the study the Bonferroni method was used and accepted $P < 0.006$ as significant. When multiple outcomes were taken into account with Bonferroni's adjustment, no difference was detected in the three domains. Shibley and Pugh (1997) reported the results of a before and after pharmaceutical care intervention for patients with dyslipidaemias who completed the SF-36 questionnaire. The authors claimed significant improvement on three domains, which were the role-physical, general health, and vitality domains. However, this conclusion may have been drawn from inappropriate statistical analysis, as only the general health domain was shown to be significantly different when multiple comparison was taken into account ($P < 0.006$).

The varied effect of pharmacist intervention on patient HRQOL may be better understood by examining the strengths and weaknesses of the studies. Studies with RCT design should minimise the potential for confounding and bias. There was no details of method of questionnaire administration in these studies. Self-completion before the session of the intervention could prevent possible bias from the pharmacist input. The three studies described above were longer than six months whilst the study by Jaber et al. took four months to complete. In this study the comparison between clinic visit 1 and 2 was 19 weeks. It is possible that the time period was not long enough to detect an improvement in HRQOL among the diabetic patients. However, a longer study period may cause some problems with the analysis as the participation rate and patient's response rate seemed to be lower over time. Erickson et al. (1997) described that a longer study period may negate the effect on QOL of outcomes of hypertension therapy. Almost all changes relating to SF-36 dimensions in the intervention group tended to be negative. On the other hand, a potential improvement in HRQOL may be achieved if sufficient follow up is possible, and

patients adjust from initial denial to acceptance of their conditions and become more comfortable with the management of their diseases (Pickard et al., 1999).

This study found that the pharmacist interventions had no significant effect on HRQOL of Type 2 diabetic patients. Nonetheless it was noted that most ADDQoL domain scores (12/13) in the control group declined from clinic 1 to 2 whilst most of the domain scores (9/13) in the active group improved, suggesting that a significant improvement might be attainable, perhaps over a longer period of time or in subgroups with a lower baseline HRQOL.

However, the inability to detect statistically significant differences in HRQOL in this study may partly result from the responsiveness of the questionnaire to the impact of pharmacist intervention, as the model did not focus only diabetes, but also other therapeutic areas as a whole and reflected all DRPs a pharmacist can identify. Different aspects of an individual's QOL should be observed using an additional generic HRQOL instrument (Jacobson et al., 1994). Using both generic and specific instruments is recommended for future study.

6.3.2.4 Drug related problems

The number and types of DRPs identified by the pharmacists, the percentage of recommendations accepted by the GP and the status of the DRPs at follow up are the process measures that are potentially linked to beneficial patient outcomes. The rationale for their inclusion is straightforward, without DRP identification and GP acceptance achieving the outcome measures discussed above would not be possible. There have been previous studies involving the pharmacist in the

management of diabetes patients, as described before, but unfortunately they did not report the details of process outcomes in their studies.

The pharmacists in this study identified 2.1 and 2.5 DRPs per patients in the active group and control groups at the first clinic visit. Currie et al. (1997) and Kassam et al., (2001) reported 2.0 and 3.9 DRPs per patient respectively. Comparison is not possible between all three studies, as the definition of DRP is not consistent.

There were 83 (12% of all DRPs) administrative DRPs identified by the pharmacists as 'repeat file inaccurate'. This finding raises important quality issues related to lack of regular review of the repeat prescriptions. However, whether or not this led to a clinically significant DRP could not be revealed through the study.

Improvement of the quality of patient care by the pharmacists can only be achieved if the recommendations are accepted. A high degree (80%) of complete acceptance of pharmacists' recommendations regarding drug therapy was found in this study. Overall 18% of recommendations were partially agreed and only 2% were rejected. This high agreement rate indicated that the pharmacists' recommendations were being agreed in the majority of cases, which lends support to the delivery of the pharmaceutical care model as a successful and beneficial service. In fact, the immediate outcome from the study shows that the majority of the agreed actions (71%) were accepted by patients and implemented by the pharmacist with only 11% left to the GP to action.

Twenty-three studies of clinical pharmacy service provision were reviewed by Klopfer and Einarson (1990). They found an average acceptance rate of 84% with a range

from 58% - 98%. The 80 percent acceptance rate in this study compares well with that reported in the review literature.

The importance of acceptance is clearly expressed when one considers its influence on the patients. In this study NNTs were used to convey the numerical power of clinically relevant end-point. It was found that the intervention by the pharmacists produced an NNT of 4 for number of DRPs. That is, for every 4 DRPs identified by the pharmacists, one DRP would be resolved after 19 weeks. The pharmacist reduced the relative risk by 59%.

When number of patients with one or more DRPs was examined, the benefits conferred by the pharmacist intervention were seen between clinic visit 1 and 2 as evidenced by an NNT of 6 for patients with one or more DRPs. That is, for every 6 patients identified with one or more DRPs, one patient would be completely free of DRPs at 19 weeks follow up. The pharmacist reduced the relative risk of experiencing DRP by 80%.

The number of patients with one or more DRPs (51% to 94%) and the number of DRPs per patient (0.7 to 2.7 DRPs per patient) varied among the pharmacists. However, each pharmacist was assigned to a different practice therefore no conclusion can be drawn on this variation which could relate to the practice GPs, the patient population or the individual pharmacist or likely all three. Further study is needed.

Overall ineffective therapy was identified as the most common clinical DRP amongst the pharmacists (32% of all DRPs), often resulting in suggesting the initiation of therapy or an increase in dose. The second most common DRP was monitoring

required (19%). This is significant because many of the complications of diabetes are preventable with early recognition and treatment (Diabetes UK, 1999). However, opportunities for early treatment may be lost if patients do not receive routine screening.

The Saint Vincent Declaration aims to achieve a reduction in long term, disabling complications of diabetes including a reduction in the rate of limb amputation, new blindness, end-stage renal failure, and morbidity and mortality from coronary heart disease (Anonymous, 1990). Elements of care which evidence confirms are important in the management of diabetic patients include the monitoring of blood pressure, urine protein, eyes, and feet. It is recommended that all diabetic patients should undergo a regular review at least once a year and this review should include, as a minimum, cardiovascular risks, fundoscopy and foot inspection (BDA, 1997; ADA, 1998c).

Khunti et al. (1999) conducted a large scale survey involved 17 primary care audit groups from different part of the UK, with a total of 38,288 diabetics from 495 practices. The study highlighted a number of deficiencies in care indicating that the quality of care needs improving. For example, they reported that in the last 12 months 38% (16 – 47%) had lipids checked, 49% (40 – 67%) had creatinine checked, 63% (52 – 74%) had visual acuity checked, 66% (28 – 80%) had urine checked, and 68% (40 – 91%) had feet checked.

Fletcher and Dolben (1996) surveyed 100 elderly diabetic patients at St James's University Hospital to examine the care of these patients in term of general supervision, prevalence of risk factors for complications, and uptake of chiropody and fundoscopic services. They found 71% had two or more risk factors for the

development of foot complications, only 50% had seen a chiropodist within the preceding 12 months, and 48% did not undergo annual fundoscopic examination. These figures suggest that more effort should be made to arrange an annual fundoscopic examination and to encourage patients with diabetes to be seen by a chiropodist regularly.

In the UK 37% of patients with Type 2 diabetes had retinopathy at the time of diagnosis, according to the UKPDS (Aldington et al., 1994). In Type 2 diabetes (diagnosed after 30 years of age) of 15 or more years' duration, the risk of any retinopathy is approximately 78% (Neely et al., 1998). One British study of patients attending a hospital diabetes clinic (Young et al., 1993) found that diabetic peripheral neuropathy was present in more than 50 percent of Type 2 diabetic patients aged over 60 years. Other studies in the UK reported that prevalence of neuropathy in Type 2 diabetes varied widely from 17.2% (Walters et al., 1992), 32.1% (Young et al., 1993) to 41.6% (Kumar et al., 1994) mainly due to differences in diagnostic criteria and selection criteria used in the studies.

In the present study, there was a record of 64% of patients having hypertension, 25% hyperlipidaemia, 9% peripheral neuropathy, 5% nephropathy, and 1% had a limb amputation, in the individual patient notes at baseline. The frequency of documented retinopathy and foot problems in our study was 16% and 24% respectively. These figures were lower than expected according to other studies. These differences may be explained by the poor recording for data on biochemical evaluation, clinical history, eye and foot examinations in patient notes, which also has been reported by Yudkin et al. (1980) and Liesenfeld et al. (1996).

A low dose of aspirin was recommended by the pharmacists in 18 active patients, which was accepted fully by the GPs. It was found that the benefit of aspirin therapy

was similar in diabetic and non-diabetic patients (Passa 1998). The HOT trial (Hansson et al., 1998) also showed that aspirin reduced cardiovascular event by 15% and myocardial infarction by 36% in 18,790 hypertensive patients. Fatal bleeding episodes, including intracerebral bleeding, were equal in the aspirin and placebo groups, while nonfatal bleeding episodes were more common in the aspirin group.

6.4 Implications of the results for future service provision

This study has major implications for future service provision. Firstly a significant reduction in systolic blood pressure was achieved in patients receiving pharmaceutical care. Secondly, the referral rate of 85% is comparable to the referral rate found by Mackie et al. (1999) who noted an 83% referral for patients receiving ≥ 4 drugs. Patients in the current study were targeted by disease rather than polypharmacy. Of the DRPs identified, 90% were clinical and 10% administrative. The NNT was calculated at 4, that is for every 4 DRPs identified, 1 remains resolved at 19 weeks (clinic 2) and 32 weeks (clinic 3). The equivalent NNT for patients was 6, that is for every 6 patients receiving the intervention, 1 patient is completely free of DRPs at 19 weeks (clinic 2) and 32 weeks (clinic 3). This is significant because if six patients attend each clinic then one would be free of DRPs. Thirdly, there was a high GP acceptance rate with only 2% of recommendations rejected. Fourthly, the pharmacists' confidence increased significantly at the end of the study. Although these pharmacists had experience of medication review they were not familiar with taking blood pressures and capillary blood samples. There are 214 registered pharmacies in Glasgow, with greater than 25% having pharmacists who have been trained and are experienced in general medication review clinics, with a further cohort of 20 currently undergoing training. Therefore the nine pharmacists cannot be

classed as atypical and it is likely that future service provision can be met by this extended group.

In terms of patients, whilst 71% of the DRP actions were implemented by the pharmacist, it is notable that none of the pharmacist suggestions were rejected by the patient. Patient satisfaction was not assessed in this study, however, the 80% return rate for clinic 2 suggests good acceptability to patients. The lower rate at clinic 3 requires further study. HRQOL was maintained throughout the study.

This study was not designed to measure the economic impact of the model on health care costs. Therefore future studies should compare this model with a more intensive model to achieve target HbA1c < 8.0% and patient satisfaction and economic outcomes should be included in addition to the outcomes measured in this study.

Implementing pharmaceutical care is not easy for pharmacists who have not had experience in monitoring patients' drug therapy in the past. Extending this pharmaceutical care model to Type 1 diabetes or other diseases requires clinical skills and training in specific areas. Pharmaceutical care can be provided when the relationships are in place between the patient, pharmacist, and physicians and also accessibility to information to adequately monitor patients (Hepler and Strand, 1990).

6.5 Conclusion

The hypothesis that 'pharmaceutical care delivered by community pharmacists does improve patient outcomes of Type 2 diabetics in a primary care setting' has been confirmed in part. Improvement in systolic blood pressure and resolution of DRPs without evidence of a diminished HRQOL was achieved. It was not possible, however, to demonstrate a significant reduction in HbA1c under the study conditions.

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Appendix I: Ethics committee approval for the pilot study

GREATER GLASGOW COMMUNITY/PRIMARY CARE LOCAL RESEARCH ETHICS COMMITTEE

ED/LC

26th May 1999

Mr R Lowrie
RGU Primary Care R & D Unit
1795 Paisley Road West
Cardonald
Glasgow

Dear Mr Lowrie

Developing a pharmaceutical care model to support the management of type 2 diabetes in a primary care setting

Thank you for your letter answering the points made by the Committee. I am now happy to give Chairman's approval for this study to proceed in this area with the participation of:

Suchada Soorapan, School of Pharmacy, Robert Gordon University, Aberdeen.

Yours sincerely

M G B Scott
Chairperson

WEST OF SCOTLAND MEDICAL EDUCATION BOARD
1 Horselethill Road
Glasgow G12 9LX
Telephone: 0141-330 6955 *Fax:* 0141-330 4737

Appendix II: Ethics committee approval for the main study

GREATER GLASGOW COMMUNITY/PRIMARY CARE LOCAL RESEARCH ETHICS COMMITTEE

Our Ref:89/99
(please quote in all correspondence)

17 January 2000

Richard Lowrie
Primary Care Research & Development Unit
Education and Training
Chronic Disease Management
1795 Paisley Road West
Glasgow G52 3SS

Dear Richard

Study - Randomised controlled trial to assess the impact of Clinical Pharmacist intervention on Pharmaceutical Outcomes and Quality of Life in Type 2 diabetics

Thank you for your letter of 22 December 1999 in answer to queries raised by the Committee. At its meeting on Thursday 13 January 2000 the Committee discussed your responses and approval was given to this study at local level.

Yours sincerely

M G B Scott
Chairman

The Royal College of General Practitioners
West of Scotland Faculty
4 Lancaster Crescent
GLASGOW G12 0RR
Telephone: 0141 211 3374 *Fax:* 0141 211 3375

Appendix III: Letter of invitation and consent form for the pilot study

Surgery name and address

Date as postmark

Dear <title> ..... <last name> .....

The doctors in the practice are currently working in close collaboration with a pharmacist on a project designed to gather information about the treatment of patients with diabetes. It is hoped that this information might be used in the future to improve the quality of care of patients with diabetes. All the information gathered will be coded to ensure confidentiality at all times.

I would like to arrange an appointment for you with the pharmacist (lasting approximately 30 minutes) to discuss your medication and how you think you are responding to it. This will also give you an opportunity to ask questions about your treatment and allow us to identify any additional requirements you may have. We will contact you within the next two weeks, by telephone, and if you are willing to participate, we will arrange an appointment at the surgery at a time convenient to you.

If you wish to take part, please sign where indicated below and bring this letter together with all your medicines (both prescribed and purchased) to the surgery at the agreed appointment time. If you use reading glasses or use a booklet to record your blood or urine sugar results, please bring them along with you.

Yours sincerely

Project Pharmacist

Patient consent

I <title> ..... <last name> ..... of <address> .....
..... consent / do not consent to take part in this study. I understand that strict confidentiality will be kept at all times.

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

Appendix IV: Medication review form for the pilot study

Pharmacist medication review

Patient details

Date of summary:		Name:		
Address:			Audit code:	
Tel:	DOB:	Age:	Height:	Weight:
GP:		Smoker ☐	Non-smoker ☐	Ex-smoker ☐

Case progress summary

	Date	Initials
Interview:		
Referral to GP:		
Referral from GP:		
Copy to notes:		
Record update to staff:		
Records updated:		
Prescription issued:		
Patient contacted:		
Date of follow up:		

No	Drug and dosage	Indication apparent?		Formulation appropriate?		Expected efficacy evident?		
		yes	no	yes	no	yes	no	n/a
1		☐	☐	☐	☐	☐	☐	☐
2		☐	☐	☐	☐	☐	☐	☐
3		☐	☐	☐	☐	☐	☐	☐
4		☐	☐	☐	☐	☐	☐	☐
5		☐	☐	☐	☐	☐	☐	☐
6		☐	☐	☐	☐	☐	☐	☐
7		☐	☐	☐	☐	☐	☐	☐
8		☐	☐	☐	☐	☐	☐	☐
9		☐	☐	☐	☐	☐	☐	☐
10		☐	☐	☐	☐	☐	☐	☐

Date	Care issue/Desired output	Proposed action

Pharmacist medication review
Patient interview

Current drug treatment, compliance, knowledge and suitability

Side-effects present?		Drug contra-indicated?		Compliance			Knowledge			Generic substitution			
no	yes	no	yes	frequent	seldom	never	yes	unsure	no	already generic	yes substitute	no, compliance	no, bio-inequivalent
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
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☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Pharmaceutical care plan

	Team response	Immediate outcome	Patient outcome

Pharmacist medication review

Summary from computer records & case notes

Date	Relevant medical history

Current drug therapy	Previous drug therapy
1	1
2	2
3	3
4	4
5	5
6	6
7	7
8	8
9	9
10	10

Relevant investigations

Details of current secondary care monitoring

Monitoring by practice

General comments by pharmacist

Record update

Name: DOB: Audit code:

Address:

Data	Action	Updated by Initials:	Date:

Appendix V: Diabetes data collection form for the pilot study

Diabetes Data Collection Form

Code number: RD_____ **Date:** ...../...../.....

Height: _____ **Weight:** _____ **BMI (Kg/m^2)** _____ **Year/month of diagnosis:**_____

Smoking habit: ☐ smoker ☐ non-smoker ☐ ex-smoker: when stopped smoking _____

Relevant medical history: ☐ Hypertension ☐ Hyperlipidaemia ☐ Obesity ☐ Stroke/transient ischaemic attack ☐ Heart disease (e.g. myocardial infarction, congestive cardiac failure) ☐ Renal failure

Current relevant problems: Macrovasular: ☐ angina ☐ myocardial infarction ☐ uncontrolled hypertension ☐ uncontrolled dyslipidaemia ☐ others.....

Microvascular: ☐ retinopathy ☐ microalbuminuria ☐ painful somatic neuropathy ☐ others.....

Attendance at diabetic clinics ☐ Surgery ☐ current ☐ past (last appoinment ...../...../.....)
☐ Hospital ☐ current ☐ past (last appoinment ...../...../.....)

Use of glucose monitoring: **frequency**
Blood ☐ .....
Urine ☐ .....
What is the patient's reading(s)/ when? .....

Objective data: (last five readings)

Parameter	value / date	value / date	value / date	value / date	value / date
HbA1c (%) **(Normal range:.....- .....%)**					
Fasting plasma glucose (mmol/l)					
Random plasma glucose (mmol/l)					
Total cholesterol (mmol/l)					
Triglycerides (mmol/l)					
High density lipoprotein cholesterol (mmol/l)					
Serum creatinine (μmol/l)					
Albumin (g/l)					
LFT:specify.....					
Blood pressure (mmHg)					

History of foot exam (with dates): ☐ normal ☐ foot ulcer
☐ other..... .....
Date of last exam:.....
History of eye exam (with dates): ☐ normal ☐retinopathy ☐ decrease in visual acuity
☐ other: ....
Date of last eye exam:.....
Comment: previous therapy for diabetes or hypertension with dates.
....
....

Diabetic education provided at interview:
....
....

Questions to ask patient

1. How often have you had any of the following symptoms during the past 6 weeks:

1.1 Hypoglycaemic symptoms: for example, feeling unusually hungry before meal, sweating, having cold hands and feet, headache, weakness, palpitations, anxiety.

☐ Never ☐ one time ☐ 2-4 times ☐ > 5 times

1.2 Hyperglycaemic symptoms: for example, frequent urination (especially during night), always hungry, weight loss despite appetite, abnormal thirst.

☐ Never ☐ one time ☐ 2-4 times ☐ > 5 times

1.3 Feeling of pins and needles, pain, numbness or burning in your feet

☐ Never ☐ one time ☐ 2-4 times ☐ > 5 times

1.4 Blurred vision

☐ Never ☐ one time ☐ 2-4 times ☐ > 5 times

1.5 Symptoms of GI disturbances, specify .....

☐ Never ☐ one time ☐ 2-4 times ☐ > 5 times

1.6 Ask the patient how do you feel in general? if not normal, specify

.....

.....

2. Have you run out of your diabetic medication during the last 6 months?

☐ No ☐ Yes, drug name: .....

3. Have you taken any new medicine (prescription or nonprescription) during the last 6 weeks?

☐ No ☐ Yes, drug name: .....

Time required for pharmaceutical care activities

Pharm. Care Activities	Range of time spent on each activity (mins) Check ✓ in appropriate box				Comments
	< 10	11-20	21-30	> 30	
1. Pre-interview: review of medical notes, prepare database					
2. Patient interview					
3. Post-interview: complete the forms, provide education					

Comments/criticisms on method, forms, etc. :

.....

.....

.....

.....

.....

Appendix VI: Patient diabetes information leaflet for the pilot study

- **Having hypoglycaemia** (some people call it a 'HYPO') means that the blood sugar has dropped below its normal level.
  Causes: - Eating too little or too late.
  - Too large a dose of insulin or tablets.
  - Not enough food before exercise.

  The warning signs include sweating, shakiness, tingling around the mouth, dizziness, pallor, irritability and feeling of hunger. These vary greatly between different people. Try to identify your own particular 'early warning signs'.
- **How to treat a hypo?**
  Take a short-acting carbohydrate, such as glucose tablets, chocolate, sweets, glass of fruit juice, or glass of soft drink (not "diet" drinks) immediately. This will raise the blood sugar level quickly. Then follow with a longer-acting carbohydrate such as sandwiches, fruit, bowl of cereal, or biscuits and milk to prevent the hypo again. Take more glucose if your symptoms persist. If your symptoms still don't go away, seek medical advice. If you are taking **acarbose (Glucobay)**, it is important to take only glucose in the form of glucose tablets. Acarbose blocks the absorption of starchy food, therefore eating these carbohydrates does not correct hypo.
- **Always carry some form of diabetes identification.**
- **If you have forgotten to take your tablets** and it is only an hour or two from the time that you should have taken them, just take them as soon as possible. If longer than 2 hours, miss the dose out and take the next one at the usual time. Do not take a double dose of tablets to make up for the missed dose.
- **When you are ill** your blood sugar tends to rise. If you are on tablets, continue to take them and try to eat your normal meals and drink plenty of sugar-free liquids as well. If you are being sick and cannot eat your meals or take your tablets, then contact your doctor or diabetes clinic.
- **Don't take any medications**, even with over the counter drugs, **without checking** with your doctor or pharmacist that they are suitable for diabetics.

- Remember that you can always discuss **any questions** you may have about your treatment with your doctor, nurse, or pharmacist.

Leaflet for diabetics

What is Diabetes?

Diabetes mellitus is a condition in which the body either does not have enough insulin or cannot use insulin as well as it should. This causes a high level of glucose in the blood. Insulin, a hormone produced by the pancreas, is needed to help glucose get into the cells of the body to give you energy.

Some of the symptoms of untreated diabetes are increased thirst, increased output of urine, tiredness, loss of weight, blurred vision and infections. In women, vaginal itching is a common early symptom.

Type 1, or insulin dependent diabetes

Insulin-dependent diabetes is also known as type 1 diabetes. This type of diabetes starts commonly in patients before the age of 40 and has to treated by insulin injections and diet. Type 1 diabetics must use insulin to remain well because their body cannot produce insulin at all.

Type 2, or non-insulin dependent diabetes

Non-insulin dependent diabetes is also known as type 2 diabetes. This type of diabetes usually begins in adults over age 40 and can be controlled by diet alone or by diet and tablets or, sometimes, by diet and insulin injections. People who are overweight are more likely to develop it.

The major difference between type 1 and type 2 is that people with type 2 diabetes may still produce insulin, but it does not work properly or they do not produce enough insulin.

Diabetes Treatment

Treatment aims to achieve normal blood glucose levels which, together with healthy eating and exercise, will help to improve wellbeing. This will also protect against long-term damage to the eyes, kidneys, nerves, heart and major arteries.

Treatment of type 1 diabetes: Treatment requires injections of insulin for the rest of the patients' lives and a healthy diet which contains the right balance of foods.

Treatment of type 2 diabetes: Treatment typically includes a healthy diet and exercise. If this is not enough to control your diabetes, your doctor may prescribe tablets along with your diet and exercise to help keep your blood glucose levels normal.

Useful Advice for Type 2 Diabetics

- Eat a **healthy, low fat, low sugar, high fibre diet.** Avoid being overweight. It is more difficult to control diabetes in overweight people.
- Take **regular exercise** such as brisk walking.
- It is important to remember that the **tablets are not instead of the diet.** When taking tablets, you will still follow your diet and exercise plans.
- Make sure you have your **eyes examined yearly.**
- **Give up smoking.**

- **Foot Care:**
  - Wash your feet with soap and warm water every day. Dry your feet thoroughly with a soft towel, particularly between the toes.
  - Keep your skin healthy by using moisturising cream after bathing. Remember never to apply any cream between your toes.
  - Cut your nails straight across. Do not cut into the corners and never cut them too short.
  - Make sure that your feet are not exposed to extremes of heat or cold.
  - Make sure that your socks and shoes are not too tight.
  - Always seek help with your feet if you notice any signs such as swollen areas or changes in the colour of your skin, pain, and sores or cuts that do not heal. Do not try to treat injuries, corns or other foot problems by yourself.
  - Keep regular appointments with the chiropodist.

- **Alcohol:** Do not drink too much alcohol.
  - For men: up to 3 units of alcohol in any one day.
  - For women: up to 2 units of alcohol per day.
  - One unit of alcohol = ½ pint of beer or lager, or one standard glass of wine or one pub measure of spirits.
  - Warning: Low-alcohol beers and wines may have a high sugar content.
  - Alcohol on an empty stomach can provoke a hypo.
  - Some tablets should not be taken with alcohol – this should be checked with the doctor or pharmacist.

Appendix VII: The Audit of Diabetes Dependent Quality of Life (ADDQol)

ADDQoL

Code Number: _____

Date: _____/_____/_____

This questionnaire asks about your quality of life and the effects of your diabetes on your quality of life. Your quality of life is how good or bad you feel your life to be.

There are no right or wrong answers; we just want to know how you feel about your life now. All of your answers will be treated in the strictest of confidence. We would be very grateful if you would take the time to answer these questions.

If you have any questions about how to complete the questionnaire, please ask your pharmacist.

Please put an X in the box which best indicates your response on each scale.

A) In general, my present quality of life is:

as good as it could possibly be	very good	good	neither good nor bad	bad	very bad	as bad as it could possibly be

For the next statement please consider the effects of your diabetes, its management and any complications you may have.

B) If I did not have diabetes, my quality of life would be:

very much better	much better	a little better	the same	a little worse	much worse	very much worse

Please read the additional instructions on the next page carefully.

Please respond to the 13 more specific statements on the pages that follow.

For each statement, please consider the effects of your diabetes, its management and any complications you may have on the aspect of life described by the statement.

In each of the following boxes:

a) Put an X to show how diabetes affects this aspect of your life.

b) Circle the answer that shows how important this aspect of your life is to your quality of life.

Some statements have a 'not applicable' option. Please put an 'X' in the N/A box if that aspect of life does not apply to you.

1. If I did not have diabetes, my working life and work-related opportunities would be:

very much better	much better	a little better	the same	a little worse	much worse	very much worse	N/A
This aspect of my life is... *(please circle the answer that applies for you)*							
very important	important		somewhat important		not at all important		

2. If I did not have diabetes, my social life would be:

very much better	much better	a little better	the same	a little worse	much worse	very much worse	
This aspect of my life is... *(please circle the answer that applies for you)*							
very important	important		somewhat important		not at all important		

3. If I did not have diabetes, my family life would be:

very much better	much better	a little better	the same	a little worse	much worse	very much worse	N/A
This aspect of my life is... *(please circle the answer that applies for you)*							
very important	important		somewhat important		not at all important		

4. If I did not have diabetes, my friendships would be:

very much better	much better	a little better	the same	a little worse	much worse	very much worse
This aspect of my life is... *(please circle the answer that applies for you)*						
very important	important	somewhat important	not at all important			

5. If I did not have diabetes, my sex life would be:

very much better	much better	a little better	the same	a little worse	much worse	very much worse	N/A
This aspect of my life is... *(please circle the answer that applies for you)*							
very important	important	somewhat important	not at all important				

6. If I did not have diabetes, my holidays or leisure activities would be:

very much better	much better	a little better	the same	a little worse	much worse	very much worse
This aspect of my life is... *(please circle the answer that applies for you)*						
very important	important	somewhat important	not at all important			

7. If I did not have diabetes, problems with travelling (either local or long distance) would be:

very much better	much better	a little better	the same	a little worse	much worse	very much worse

This aspect of my life is... *(please circle the answer that applies for you)*

very important	important	somewhat important	not at all important

8. If I did not have diabetes, my worries about my future (e.g. health, independence, income) would be:

very much better	much better	a little better	the same	a little worse	much worse	very much worse

This aspect of my life is... *(please circle the answer that applies for you)*

very important	important	somewhat important	not at all important

9. If I did not have diabetes, my worries about the future of my family and close friends (e.g. their health, independence, income) would be:

very much better	much better	a little better	the same	a little worse	much worse	very much worse	N/A

This aspect of my life is... *(please circle the answer that applies for you)*

very important	important	somewhat important	not at all important

10. If I did not have diabetes, my motivation to achieve things would be:

very much better	much better	a little better	the same	a little worse	much worse	very much worse
This aspect of my life is... *(please circle the answer that applies for you)*						
very important	important	somewhat important	not at all important			

11. If I did not have diabetes, the things I could do physically would be:

very much better	much better	a little better	the same	a little worse	much worse	very much worse
This aspect of my life is... *(please circle the answer that applies for you)*						
very important	important	somewhat important	not at all important			

12. If I did not have diabetes, the extent to which people would fuss or worry about me too much would be:

very much better	much better	a little better	the same	a little worse	much worse	very much worse
This aspect of my life is... *(please circle the answer that applies for you)*						
very important	important	somewhat important	not at all important			

13. If I did not have diabetes, my enjoyment of food would be:

very much better	much better	a little better	the same	a little worse	much worse	very much worse

This aspect of my life is... *(please circle the answer that applies for you)*

very important	important	somewhat important	not at all important

If there are any other ways in which diabetes and its management and complications affect your quality of life, please say what they are below.

Thank you for taking the time to answer these questions.

Appendix VIII: Diabetes – 39

Code Number: **RD**_____ Date:___/___/___

Diabetes-39 Quality of Life Questionnaire

A person's quality of life is affected by many things. These things might include health, the opportunity for relaxation and holidays, friends and family, and occupation. This questionnaire is designed to help us learn about what affects the quality of life of people with diabetes. All of your answers will be treated in the strictest of confidence. We would be very grateful if you would take the time to answer these questions.

How to complete the questionnaire.

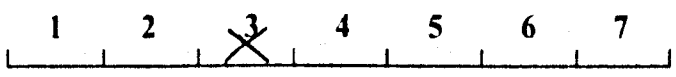
- For each of the following questions we want to know how much your quality of life has been affected. Please answer the questions by putting a cross (X) somewhere on the line following each question. The line starts at number 1 and a cross here means that your quality of life has not been affected at all. The line ends at 7 and a cross here means that your quality of life has been extremely affected. Place your cross (X) on the line at the point which you think best describes how your quality of life has been affected in the past month. If you do not do one of the activities, for example home glucose monitoring, then your answer should be that you are not affected at all.

- It is very important that you answer every question. However, you may prefer not to answer some questions which ask about your personal life. If you choose not to answer these, please leave them blank and go on to the next question.

- Example
  If you thought "air pollution" affected your quality of life to some extent, but not extremely, you might mark the line as shown.

DURING THE PAST MONTH, HOW MUCH WAS THE QUALITY OF YOUR LIFE AFFECTED BY:

1. air pollution



- If you were to answer the same question, where would you put your cross? If you think you have been more affected by air pollution in the past month than the person in the above example, you should place your cross somewhere to the right of the existing cross. However, if you think you have been less affected, then your cross should be placed somewhere to the left of the existing cross. To practise, please put your cross on the line.

Please complete the following questions, if you have any questions about how to complete the questionnaire, please ask your pharmacist.

During the past month, how much was the quality of your life affected by:

1. your daily medication for your diabetes

Not affected at all 1 2 3 4 5 6 7 Extremely affected

2. worries about money matters

Not affected at all 1 2 3 4 5 6 7 Extremely affected

3. limited energy levels

Not affected at all 1 2 3 4 5 6 7 Extremely affected

4. following your doctor's prescribed treatment plan for diabetes

Not affected at all 1 2 3 4 5 6 7 Extremely affected

5. food restrictions required to control your diabetes

Not affected at all 1 2 3 4 5 6 7 Extremely affected

6. concerns about your future

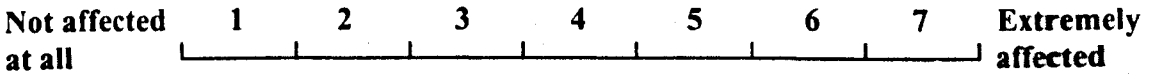
Not affected at all 1 2 3 4 5 6 7 Extremely affected

7. other health problems besides diabetes

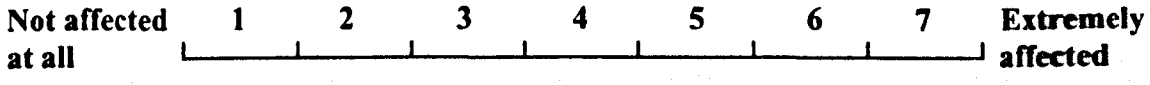
Not affected at all 1 2 3 4 5 6 7 Extremely affected

During the past month, how much was the quality of your life affected by:

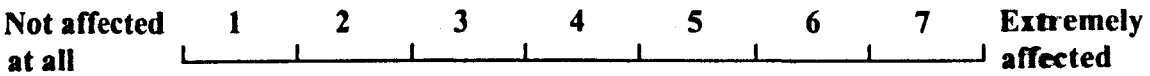
8. stress or pressure in your life



9. feelings of weakness

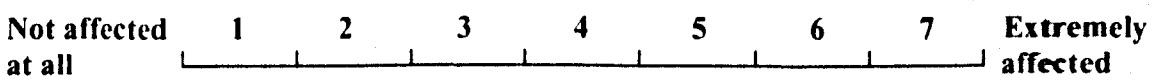


10. restrictions on how far you can walk

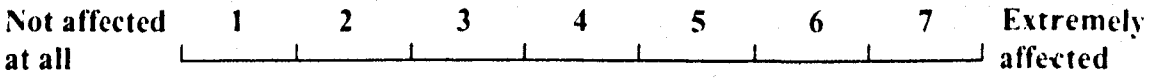


11. any daily exercise for your diabetes

12. loss or blurring of your vision



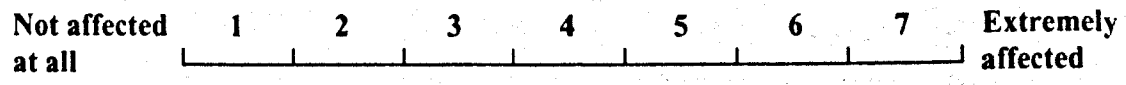
13. not being able to do what you want



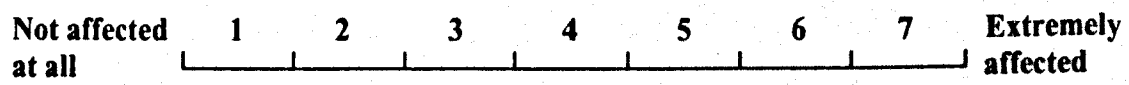
14. having diabetes

During the past month, how much was the quality of your life affected by:

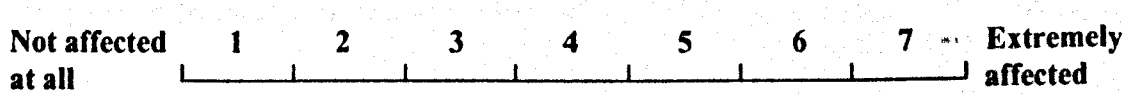
15. losing control of your blood sugar levels



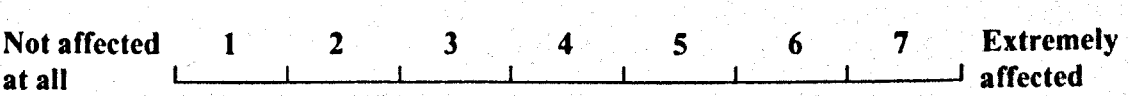
16. other illnesses besides diabetes



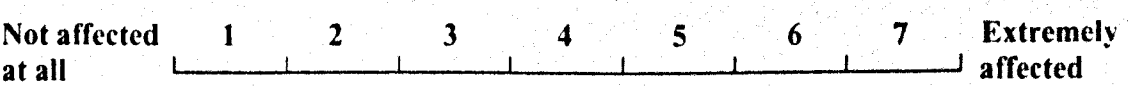
17. testing your blood sugar levels



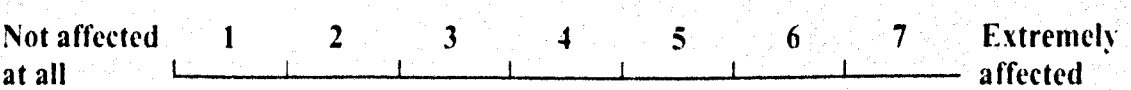
18. the time required to control your diabetes (for example time required for taking tablets, following a special diet, monitoring sugar levels)



19. the restrictions your diabetes places on your family and friends



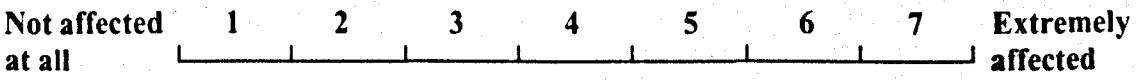
20. being embarrassed because you have diabetes



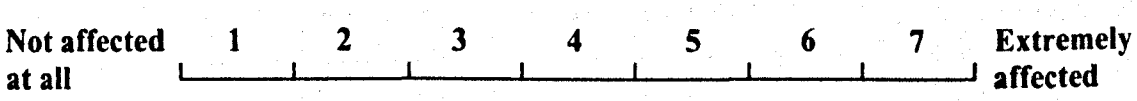
21. diabetes interfering with your sex life

During the past month, how much was the quality of your life affected by:

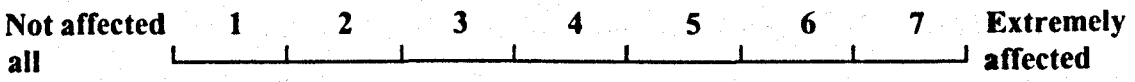
22. feeling depressed or low



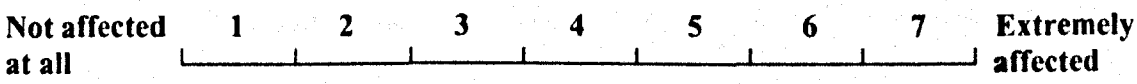
23. problems with sexual functioning



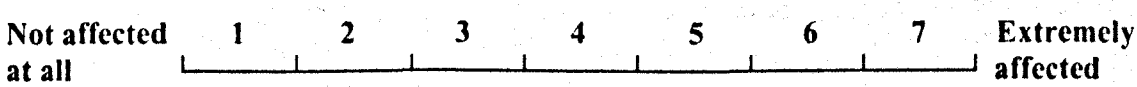
24. getting your diabetes well controlled



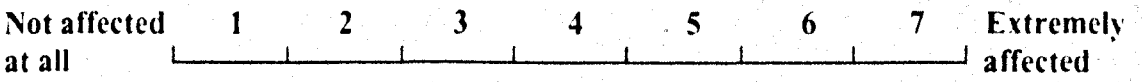
25. complications from your diabetes



26. doing things that your family and friends don't do



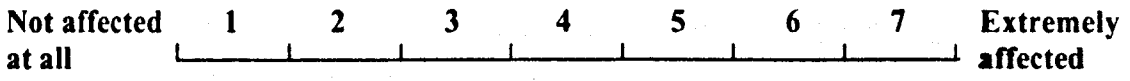
27. keeping a record of your blood sugar levels



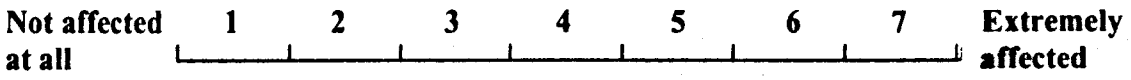
28. the need to eat at regular intervals

During the past month, how much was the quality of your life affected by:

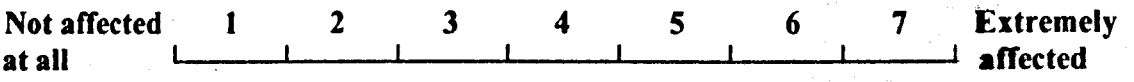
29. not being able to do housework or other jobs around the house



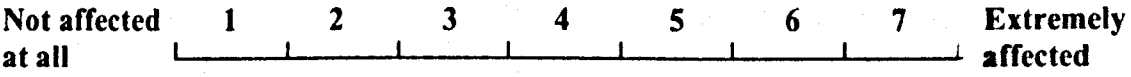
30. a decreased interest in sex



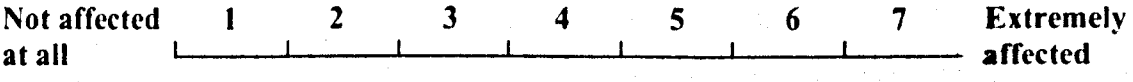
31. having to organize your daily life around diabetes



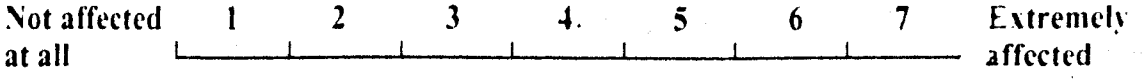
32. needing to rest often



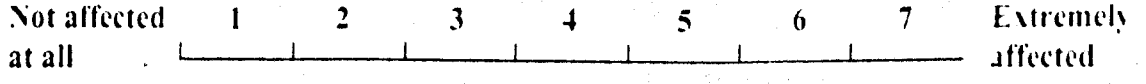
33. problems in climbing stairs or walking up steps



34. having trouble caring for yourself (dressing, bathing, or using the toilet)

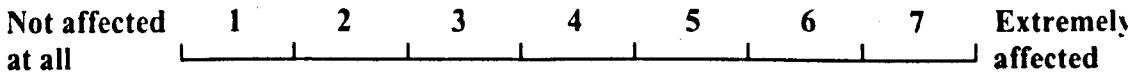


35. restless sleep

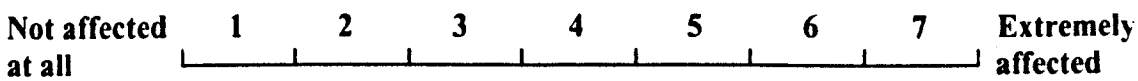


During the past month, how much was the quality of your life affected by

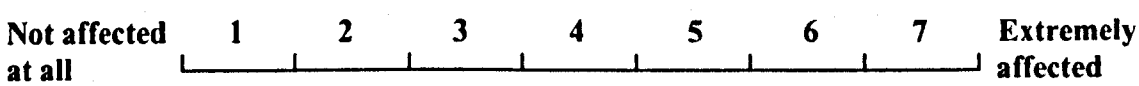
36. walking more slowly than others



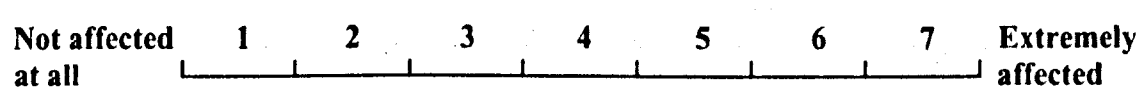
37. being identified as a diabetic



38. having diabetes interfere with your family life



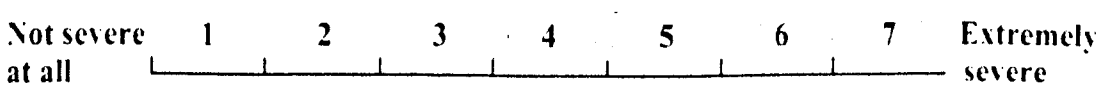
39. diabetes in general



OVERALL RATINGS

1. Please place an "X" on the line below to indicate your rating of overall quality of life.

2. Please place an "X" on the line below to show how severe you think your diabetes is



Thank you for taking the time to answer these questions.

Appendix IX: GP referral form for the pilot study

Appendix IX

GP referral

Name: DOB: Date of interview: Audit code:

Address: GP:

Rationalisation/simplification plan

Care issue/Desired output	Proposed action	Team response

Agreed action

Detail only if different from above

GP		Pharmacist	
Date:	Signature:	Date:	Signature:

Appendix X: Pharmacist feedback survey form

A Survey of Diabetes Pharm. Care Pilot Study

Dear Pharmacist

The following questionnaire has been devised to allow feedback from the pharmacists in order for the research team to identify of any problems in the pilot study.

It would be appreciated if you would take the time to complete the form, and return it to us in the enclosed pre-paid envelope, if possible within 1 week.

Pharmacist's name .....

1. Please use the space below to make any comments about the data collection form (for example ease of use).

2. Are there any other relevant data should be added or deleted from the data collection form? Please give details.

3. Are the documents and training programmes, you received **adequate / inadequate** (circle)? If inadequate, please suggest ways in which this could be improved.

4. How many patients per day you have seen in the clinic? ..... patient(s) per day. Do you feel this figure is too little or too many to handle?

Appendix XI: Patient diabetes information leaflet for the main study

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Leaflet for Diabetics

- **Some tablets should not be taken with alcohol – this should be checked with the doctor or pharmacist.**
- **Always carry some form of diabetes identification.**
- **When you are ill** your blood sugar tends to rise. If you are on tablets, continue to take them and try to eat your normal meals and drink plenty of sugar-free liquids as well. If you are being sick and cannot eat your meals or take your tablets, then contact your doctor or diabetes clinic.
- Don't take any medications, even over the counter medicines, without checking with your doctor or pharmacist that they are suitable for diabetics.
- Remember that you can always discuss any questions you may have about your treatment with your doctor, nurse, or pharmacist.

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PATIENT INFORMATION LEAFLET

Leaflet for diabetics

TYPE 2, OR NON-INSULIN DEPENDENT DIABETES

Non-insulin dependent diabetes is also known as type 2 diabetes. This type of diabetes usually begins in adults aged over 40 and can be controlled by diet alone or by diet and tablets or, sometimes, by diet and insulin injections. People who are overweight are more likely to develop it.
The major difference between type 1 and type 2 diabetes is that people with type 2 diabetes may still produce insulin, but it does not work properly or they do not produce enough insulin.

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TREATMENT OF TYPE 2 DIABETES

Treatment aims to achieve normal blood glucose levels which, together with healthy eating and exercise, will help to improve well-being. This will also protect against long-term damage to the eyes, kidneys, nerves, heart and major arteries.

Treatment typically includes a healthy diet and exercise. If this is not enough to control your diabetes, your doctor may prescribe tablets along with your diet and exercise to help keep your blood glucose levels normal.

Useful Advice for Type 2 Diabetics

- **Eat a healthy, low fat, low sugar, high fibre diet.** Avoid being overweight. It is more difficult to control diabetes in overweight people.

- **Take regular exercise** such as brisk walking.
- It is important to remember that the tablets are not instead of the diet. When taking tablets, you will still follow your diet and exercise plans.
- **Make sure you have your eyes examined every year.**
- **Give up smoking.**

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- **FOOT CARE:**
  - Wash your feet with soap and warm water every day. Dry your feet thoroughly with a soft towel, particularly between the toes.
  - Keep your skin healthy by using moisturising cream after bathing. Remember never to apply any cream between your toes.
  - Cut your nails straight across. Do not cut into the corners and never cut them too short.
  - Make sure that your feet are not exposed to extremes of heat or cold.
  - Make sure that your socks and shoes are not too tight.
  - Always seek help with your feet if you notice any signs such as swollen areas or changes in the colour of your skin, pain, and sores or cuts that do not heal. Do not try to treat injuries, corns or other foot problems by yourself.
  - Keep regular appointments with the chiropodist.

- **ALCOHOL:** Do not drink too much alcohol.
  - For men: up to 3 units of alcohol in any one day.
  - For women: up to 2 units of alcohol per day.
  - One unit of alcohol = ½ pint of beer or lager, or one standard glass of wine or one pub measure of spirits.

Appendix XII: GP referral form for the main study

Appendix XII

The following issues have been identified after reviewing case notes and 1. discussion with the patient at surgery ☐
by phone ☐
2. in the patient's absence ☐

If you agree with the proposed action(s), please sign as indicated and the pharmacist will update the computer record and contact the patient.

Name:	DoB:	Date of Review:	Audit Code:
Address:		GP:	

Care issue	Proposed action	GP response

Pharmacist Signature: Date: GP Signature: Date:

Dated implemented:

Appendix XIII: Patient information about the main study

PATIENT INFORMATION SHEET

The following answers some questions we think you might have about the study. If you have any more questions, please feel free to ask the Pharmacist at your doctor's surgery.

What is the study about?

It is designed to look at the effect on diabetes control and quality of life after a pharmacist reviews your medication with your doctor.

Have pharmacists run clinics to review medicines before?

Yes. About 10,000 patients have had their medicines reviewed by pharmacists in Glasgow surgeries over the past 4 years.

Why should I take part?

The information gathered from the study could help to improve the future care of patients with diabetes. You may or may not benefit personally from participation in the study. You will, however have the opportunity to find out more about your medicines.

Will this study replace the usual care provided by my doctor?

No. Your usual care will be maintained throughout the study. Any benefits you may experience as a result of participation are in addition to your usual care.

Where will the study take place?

In your doctor's surgery.

When will the study take place?

It will start in March 2000 and continue for about 8 months. You will be invited to attend your surgery to discuss your medicines with the pharmacist on 3 separate occasions. If you do not wish to attend after the first appointment, you are free to withdraw from the study at any time. Your appointments will be made after discussion with you, at a time suitable to you.

What will happen if I agree to participate?

Your name will be placed in one of two groups. Patients in both groups will be asked to see the pharmacist in the surgery. If you are in group 1, you may have changes to your care suggested by the pharmacist and these may be agreed by your doctor. If you are in group 2, you will not have any changes made by the pharmacist during the study.

Why are two groups needed?

Two groups are needed so that a comparison can be made between them at the end of the study. This will allow us to see if there are any differences in your diabetes control or quality of life as a result of the appointments with the pharmacist.

How will I be allocated to a particular group?

This will be done by placing you at random into the first or second group. This means that there is an equal chance of you being part of the first group or the second group.

Will I be told which group I am in?

No. However, if you are informed of any changes to your medication as a result of any of the appointments, this will indicate that you have been placed in the first group.

What will happen at each appointment?

You will be asked to bring along your current medications and the pharmacist will discuss them with you. This will allow us to identify any additional requirements you might have. You will be asked to complete a questionnaire, you may be asked to provide a 'pin prick' (a few drops) of blood from your finger for blood sugar measurement and you blood pressure will also be checked at the appointment.

How long will each appointment take?

Each appointment will take about twenty minutes.

What will happen if I decide not to take part?

You will continue to receive your usual care from your doctor.

Who is paying for the study?

The pharmacists are paid a normal salary by the NHS for discussing how best to use medication, and if appropriate, suggesting ways that your care might be improved. The study is part of their job, and they do not receive any extra payment for it. Your doctor will not be paid extra for their involvement, and there is no commercial sponsorship of any description in the study.

How will the study affect my private health insurance?

If you have private medical insurance, please check that entry into the study will not invalidate your cover.

What will happen at the end of the study?

You will continue to receive usual care from your own doctor. If you were in group 1 and your treatment has changed during the study, this will remain changed as long as you and your doctor regard the changes as helpful. If you were in group 2, and changes to your medication were agreed by you and your doctor during the study, these may be made at the end of the study.

Appendix XIV: Letter of invitation and patient consent form for the main study

Surgery name and address

Date as postmark

Dear <title> ..... <last name> .....

The doctors in the practice are currently working with a pharmacist on a study designed to gather information about your medicines and in particular, your treatment for diabetes. We would like to invite you to participate in this study.

Please find enclosed an information sheet which explains more about the study. Please take time to read it, and feel free to phone your surgery to speak to the pharmacist if you require more information. All information gathered will be coded to ensure confidentiality at all times.

We will contact you by telephone within the next two weeks. If you are willing to participate, we will arrange an appointment for you to attend the surgery at a time convenient for you.

If you decide to take part, please sign below and bring the tear off slip with you to the surgery at the agreed appointment time. We also ask that you bring all your medicines (both prescribed and purchased), together with reading glasses and/or a list of your recent results from blood or urine sugar tests, if this applies to you.

If you decide not to take part, this will not affect the care your normally receive from your doctor.

Yours sincerely

Project Pharmacist Dr .....

Patient consent

I <title> ..... <last name> ..... of <address> .....
..... consent / do not consent to take part in this study. I understand that strict confidentiality will be kept at all times.

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

Appendix XV: Medication review form for the main study

Appendix XV

Primary care medication review

Patient details

Date of summary: Name: DOB: GP:

Address: Tel: Audit code:

Basic health data

Height: Weight: BMI: Smoker ☐ Non-smoker ☐ Ex-smoker ☐

Date	Relevant medical history	Date	Relevant medical history

ADR's/sensitivities:

Current drug therapy	date started	Previous drug therapy	date/reason stopped
1		1	
2		2	
3		3	
4		4	
5		5	
6		6	
7		7	
8		8	
9		9	
10		10	

Relevant investigations

Details of current secondary care monitoring

Monitoring by practice

General comments by pharmacist

Pharmacist:

Patient interview

Medical problems	Drug and dosage	Formulation appropriate? yes	Formulation appropriate? no	Expected efficacy evident? yes	Expected efficacy evident? no	Expected efficacy evident? n/a
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐
		☐	☐	☐	☐	☐

Pharmaceutical care plan

Date	Care issue/Desired output	Proposed action

Current drug treatment, compliance, knowledge and suitability

Side-effects present?	Drug contra-indicated?	Compliance	Knowledge	Generic substitution
no / yes	no / yes	frequent / seldom / never	yes / unsure / no	already generic / yes substitute / no, compliance / no, bio-inequivalent

	Team response	Immediate outcome	Patient outcome

Notes

Appendix XVI: Update medication review form

UPDATE PHARMACEUTICAL CARE MEDICATION REVIEW **Date...../...../.....**

☐ **second appointment** **OR** ☐ **third appointment** **(tick ✓as appropriate)**

Patient name:_____ **DOB:**_____ **GP:** _____

Please note below if there is any change from the last form

UPDATE RELEVANT MEDICAL HISTORY

Date	**Relevant medical history**
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

UPDATE DRUG THERAPY

Current drug therapy	date started	**Previous drug therapy**	date stopped	reason stopped
1_____	_____	1_____	_____	_____
2_____	_____	2_____	_____	_____
3_____	_____	3_____	_____	_____
4_____	_____	4_____	_____	_____
5_____	_____	5_____	_____	_____
6_____	_____	6_____	_____	_____
7_____	_____	7_____	_____	_____

Appendix XVII: Diabetes data collection form for the main study

Diabetes Data Collection Form (first visit)

Date of interview: ...../...../.....

Patient code number: _____ **DOB:** ...../...../..... **Year of diagnosis:** _____

Height: _____ **Current weight:** _____ (Date of weighing: ...../...../.....) **BMI (Kg/m²)** _____

Relevant medical history: (please write down year of diagnosis, if indicated)

- ☐ Hypertension (year .....)
- ☐ Hyperlipidaemia (year.....)
- ☐ Stroke/transient ischaemic attack (year.....)
- ☐ Obesity (year.....)
- ☐ Heart disease (e.g. myocardial infarction, congestive cardiac failure, ...) (year.....)
- ☐ Renal failure (year.....)
- ☐ Visual Impairment (year.....)
- ☐ Microalbuminuria (year.....)
- ☐ Peripheral neuropathy (year.....)
- ☐ Limb Amputation (year.....)
- ☐ others..... (year.....)

Objective data: (last two readings)

If none in last 3 years, put any single reading here ↓

Parameter	maximum 2 years ---> value* date	value* date
Blood pressure (mmHg) sitting — two measures of today's BP	...../...../.....	...../...../.....
Blood pressure (mmHg) standing — two measures of today's BP	...../...../.....	...../...../.....
HbA1c (%) Please specify 'normal range' for each record. Today's HbA1c (%):	Normal Range =..... ...../...../.....	Normal Range =..... ...../...../.....
Plasma glucose (mmol/L) If indicated, pleased add 'F' =Fasting 'R' = Random or '?' = not sure in each box	...../...../.....	...../...../.....
Total cholesterol (mmol/L)	...../...../.....	...../...../.....
Triglycerides (mmol/L)	...../...../.....	...../...../.....
Low density lipoprotein cholesterol (mmol/L)	...../...../.....	...../...../.....
High density lipoprotein cholesterol (mmol/L)	...../...../.....	...../...../.....
Serum creatinine (μmol/L)		
Proteinuria/Microalbuminuria	...../...../.....	...../...../.....

Please staple four blood pressure (2 sitting BP and 2 standing BP) print out papers **HERE.**

Reading 1

Reading 2

Reading 3

Reading 4

* If there is no record of any objective data, please write down **'NR'** in the space provided.

Attendance at diabetic clinics ☐ Never ☐ Yes (If patient had appointment but DNA in the last year, please tick☑)

If yes, attend at ☐ Surgery If regularly, how frequent? .....
When was the last time? (date) ..... and next time? (date) .....
☐ Hospital If regularly, how frequent? .....
When was the last time? (date) ..... and next time? (date) .....

Foot exam: Date of last foot exam:..... Result: ☐ normal ☐ foot ulcer ☐ other.....
If regularly, how frequent?.....

Eye exam: Date of last eye exam:..... Result: ☐ normal ☐ retinopathy ☐ other: .....
If regularly, how frequent?.....

Questions to ask patient

1. **Use of glucose monitoring at home, currently:** ☐ No ☐ Yes

   If yes, using ☐ blood glucose monitoring **How frequently?** ..... **What is the usual result?** .....

   ☐ urine glucose monitoring **How frequently?** .....
   What is the usual result? ☐ lots ☐ trace ☐ none

   Does patient know target? ☐ yes ☐ no

2. **Smoking habit:** ☐ smoker ☐ non-smoker ☐ ex-smoker: when stopped smoking .....

3. **Have you had any of the following symptoms during the past 6 weeks:**

3.1 Hypoglycaemic symptoms: for example, feeling unusually hungry before meal, sweating, having cold hands and feet, headache, weakness, palpitations, anxiety.
☐ Yes ☐ No

3.2 Hyperglycaemic symptoms: for example, frequent urination (especially during night), always hungry. weight loss despite appetite, abnormal thirst.
☐ Yes ☐ No

3.3 Feeling of pins and needles, pain, numbness or burning in your feet, or having foot ulceration
☐ Yes ☐ No

3.4 Change in vision
☐ Yes ☐ No

3.5 Symptoms of GI disturbances, specify .....
☐ Yes ☐ No

3.6 Ask the patient how do you feel in general? If not normal, specify
.....
.....

4. **Have you run out of your diabetic medication during the last 6 months?**
☐ No ☐ Yes, drug name: .....

5. **Have you taken any OTC medication(s) during the last 6 weeks (e.g., medication(s) for callous, corn, etc.)?**
☐ No ☐ Yes, drug name: .....

General Comments from patient:

Appendix XVIII: Update diabetes data collection form

Diabetes Data Continuation Form

Date of interview: ..../.....

Patient follow-up: visit ☐ 2 ☐ 3

Patient code number: _____ **DOB:** ...../...../.....

Current weight: _____ (Date of weighing: ...../...../.....) **BMI (Kg/m²)** _____

Please stample four blood pressure (2 sitting BP and 2 standing BP) print out papers **HERE.**

Objective data: (since last appointment)

Parameter	value* / date
Blood pressure (mmHg) sitting — two measures of today's BP	**Reading 1** / ...../...../.....
Blood pressure (mmHg) standing — two measures of today's BP	...../...../.....
HbA1c (%) Please specify 'normal range' for each record. Today's HbA1c (%):	**Reading 2** Normal Range =..... ...../...../.....
Plasma glucose (mmol/L) If indicated, please add F = Fasting R = Random in each box	...../...../.....
Total cholesterol (mmol/L)	...../...../.....
Triglycerides (mmol/L)	**Reading 3** ...../...../.....
Low density lipoprotein cholesterol (mmol/L)	...../...../.....
High density lipoprotein cholesterol (mmol/L)	...../...../.....
Serum creatinine (μmol/L)	...../...../.....
Proteinuria/Microalbuminuria	**Reading 4** ...../...../.....

* If there is no record of any objective data, please write down **'NR'** in the space provided.

Attendance at diabetic clinics ☐ Never ☐ Yes (If patient had appointment but DNA in the last year, please tick ☑)

If yes, attend at ☐ Surgery If regularly, how frequent? .....
When was the last time? (date) ..... and next time? (date) .....
☐ Hospital If regularly, how frequent? .....
When was the last time? (date) ..... and next time? (date) .....
Please detail any changes to diabetic medicine since last appointment: .....
.....

Foot exam: Date of last foot exam: .....
Result: ☐ normal ☐ foot ulcer ☐ other .....

Eye exam: Date of last eye exam:.....
Result: ☐ normal ☐ retinopathy ☐ other: .....

Questions to ask patient

1. **Use of glucose monitoring at home, currently:** ☐ No ☐ Yes

   If yes, using ☐ blood glucose monitoring **How frequently?** ..... **What is the usual result?** .....

   ☐ urine glucose monitoring **How frequently?** .....
   What is the usual result? ☐ lots ☐ trace ☐ none

   Does patient know target? ☐ yes ☐ no

2. **Smoking habit:** ☐ smoker ☐ non-smoker ☐ ex-smoker: when stopped smoking .....

3. **Have you had any of the following symptoms during the past 6 weeks:**

3.1 Hypoglycaemic symptoms: for example, feeling unusually hungry before meal, sweating, having cold hands and feet, headache, weakness, palpitations, anxiety.
☐ Yes ☐ No

3.2 Hyperglycaemic symptoms: for example, frequent urination (especially during night), always hungry, weight loss despite appetite, abnormal thirst.
☐ Yes ☐ No

3.3 Feeling of pins and needles, pain, numbness or burning in your feet, or having foot ulceration
☐ Yes ☐ No

3.4 Change in vision
☐ Yes ☐ No

3.5 Symptoms of GI disturbances, specify .....
☐ Yes ☐ No

3.6 Ask the patient how do you feel in general? If not normal, specify
.....
.....

4. **Have you run out of your diabetic medication since last appointment?**
☐ No ☐ Yes, drug name: .....

5. **Have you taken any OTC medication(s) since last appointment (e.g., medication(s) for callous, corn, etc.)?**
☐ No ☐ Yes, drug name: .....

General Comments from patient:

Appendix XIX: Letter of thanks to patients after attending first appointment

Dr ..... & partners

Surgery Address

Date as postmarked

Dear .....

May I take this opportunity to thank you for attending the diabetes clinic. Subsequent to our recent discussions I have spoken to your doctor who has agreed the action(s) indicated in the box below

If you wish to discuss any of these points further please contact me at the surgery or alternatively feel free to discuss them with your doctor at any time. If you regularly attend one community pharmacy, it would be useful to show them this letter to allow them to update your pharmacy held medication records.

I look forward to meeting you again and thank you for your continued support.

Yours sincerely

Clinical Pharmacist

[Note: this form is for active patient with referral.]

Dr ..... & Partners

Surgery Address

Date as postmark

Dear .....

May I take this opportunity to thank you for attending the diabetes clinic.

We will telephone you in approximately 3 months to arrange another appointment at a time convenient to you.

I have enclosed a copy of an information leaflet, which I hope you will find interesting. The information provided at your interview has been very useful and could help us improve the future care of people with diabetes.

I look forward to meeting you again and thank you for your continued support.

Yours sincerely

Clinical Pharmacist

[Note: this form is for control or active with no referral.]

Appendix XX: Letter of thanks to patients after attending second appointment

Dr ..... & partners

Surgery Address

Date as postmarked

Dear .....

May I take this opportunity to thank you for attending the diabetes clinic. Subsequent to our recent discussions I have spoken to your doctor who has agreed the action(s) indicated in the box below

If you wish to discuss any of these points further please contact me at the surgery or alternatively feel free to discuss them with your doctor at any time. If you regularly attend one community pharmacy, it would be useful to show them this letter to allow them to update your pharmacy held medication records.

I look forward to meeting you again and thank you for your continued support.

Yours sincerely

Clinical Pharmacist

[Note: this form is for active patient with referral.]

Dr ..... & Partners

Surgery Address

Date as postmark

Dear .....

May I take this opportunity to thank you for attending the diabetes clinic.

We will telephone you in approximately 3 months to arrange another appointment at a time convenient to you.

I have enclosed a copy of an information leaflet, which I hope you will find interesting. The information provided at your interview has been very useful and could help us improve the future care of people with diabetes.

I look forward to meeting you again and thank you for your continued support.

Yours sincerely

Clinical Pharmacist

[Note: this form is for control or active with no referral.]

Appendix XXI: Letter of thanks to patients after attending third appointment

Dr ..... & partners

Surgery Address

Date as postmarked

Dear .....

May I take this opportunity to thank you for attending the diabetes clinic and participating in the study, which has now finished. Subsequent to our recent discussions I have spoken to your doctor who has agreed the action(s) indicated in the box below

If you wish to discuss any of these points further please contact me at the surgery or alternatively feel free to discuss them with your doctor at any time. If you regularly attend one community pharmacy, it would be useful to show them this letter to allow them to update your pharmacy held medication records.

Kind regards,

Yours sincerely

Clinical Pharmacist

[Note: this form is for active or control patient with referral.]

Dr ..... & Partners

Surgery Address

Date as postmark

Dear

May I take this opportunity to thank you for attending the diabetes clinic and participating in this study, which has now finished.

The information provided at your interview has been very useful and could help us improve the future care of people with diabetes.

I look forward to meeting you again and thank you for your continued support.

Yours sincerely

Clinical Pharmacist

[Note: this form is for control or active patient with no referral.]

Appendix XXII: Questionnaire - Pharmacist feedback on experience since completing the clinics

QUESTIONNAIRE

1. GENERAL INFORMATION

Your age: .....

2. EDUCATIONAL BACKGROUND

Where did you graduate? (name of university)	**When?** (year)	**Qualification(s) gained**

Continuing education? (Please specify course of study and date of enrollment)

.....
.....
.....
.....
.....

3. WORKING EXPERIENCE

3.1 How long have you been practicing as a pharmacist? .....

3.2 At the time of the study, were you a full-time or a part-time pharmacist?

.....

3.3 Which sector were you working in when the study took place? (community, hospital, primary care, other please state)

.....

3.4 Are you still working in the same sector after finishing the research? .....Yes/ .....No

If no, please specify .....

4. ABOUT THE MAIN STUDY (date March 2000 - Feb 2001)

4.1 Before doing the main study, had you ever run the medication review clinic before?

.....Yes/.....No

If yes, how long have you been doing the medication review clinic before the study?

.....

4.2 How many days per week did you run the clinic at that time (during the study)?

.....

4.3 Have you continued working in medication review clinic after finishing the research? .

....Yes/.....No

If yes, what type of clinics are you currently delivering? and where?

.....

4.4 After finishing diabetes clinic, please rate your confidence in running the clinic (scale 0 (low) –10 (high)) both before the study and after finishing the study.

Before study: confidence (scale 0-10) .....

After study: confidence (scale 0-10) .....

Finally, if you would like to make any comments regarding this research or would like to add more information to the answer above, there is space below for you to do so.

.....
.....
.....
.....
.....

May I thank you once again for your participation and co-operation. You will be sent a summary of the final project report for your information.

Appendix XXIII : Instructions for obtaining a capillary blood sample for HbA1C test

PROCEDURE STEPS FOR FINGER PRICKING

I. PREPARING FINGERTIP

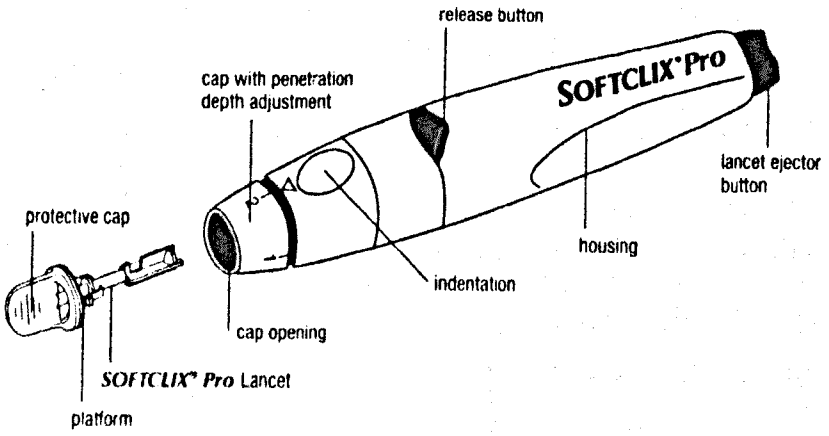
1. Clean the surface of the patient's finger.

- Wash hands with soap and warm water and dry thoroughly before sampling.
- Instructs the patient to let arm hang down at side of body for a while (30 sec) to allow blood flow to finger and grasp the finger near the area to be pricked and gently squeeze for few seconds.

2. Select a site on the outer edge of the finger.

- The sides of the finger has the best blood supply and are less sensitive than the tip.

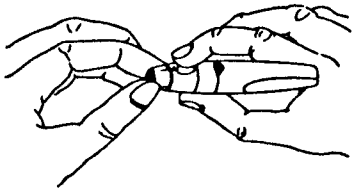
II. USING *SOFTCLIX® PRO* LANCING DEVICE



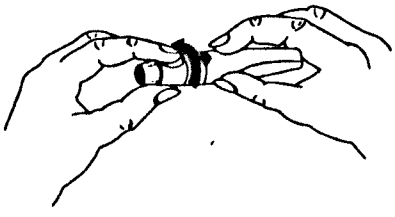
SELECTING PENETRATION DEPTH:

Softclix® Pro offers three depths of penetration, which are indicated on the cap by numbers 1, 2 and 3. Select 1 for the smallest and 3 for the greatest depth of penetration.

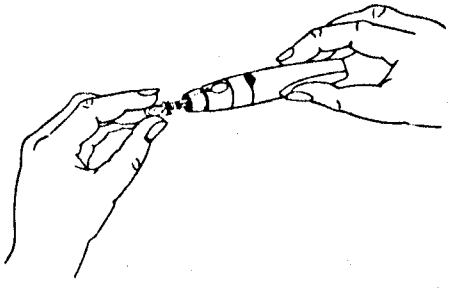
When selecting the correcting depth of penetration for a particular patient, his or her skin type should be taken into consideration, e.g. select 1 for softer-than-average skin, 2 for average skin or 3 for thicker-than-average skin. The amount of blood required for the test should also be taken into account.



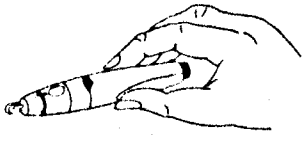
Select the desired depth of penetration by turning the front part of the cap.

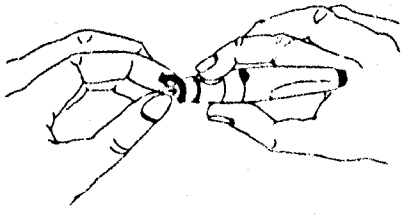


Grip the cap at the indentations and turn the housing in a clockwise direction as far as it will go. *Softclix®* *Pro* is now primed and the housing will return to its initial position when you let go.

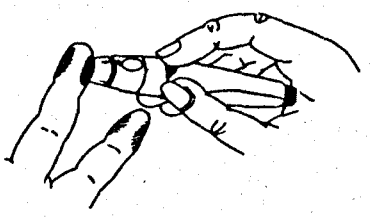


INSERTING A LANCET: Place a new Softclix® Pro lancet in the instrument by holding the protective cap of the lancet and pushing it into the instrument as far as it will go. The platform will snap into position in the cap opening thus closing it. The blue lancet ejector button is released when the lancet is inserted and is now visible.



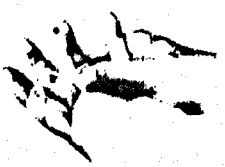


REMOVING THE PROTECTIVE CAP: Unscrew the protective cap from the lancet. Hold it at the indentations to do so and turn.



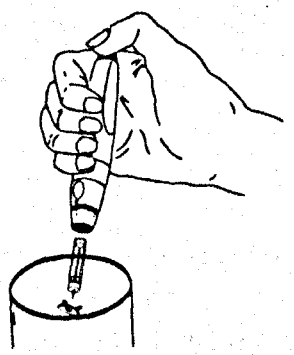
TAKING A BLOOD SAMPLE: Hold *Softclix® Pro* against the side of the patient's finger tip and press gently. Press the release button.

Wait a few seconds to allow the puncture site to open so that a blood drop can form.



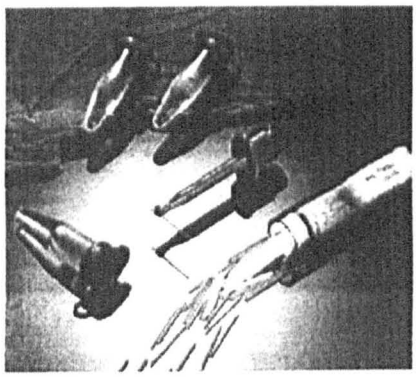
If the blood drop is too small, gently compress the tip of the finger from the base upward to obtain more blood.

IV. REMOVING THE LANCET:

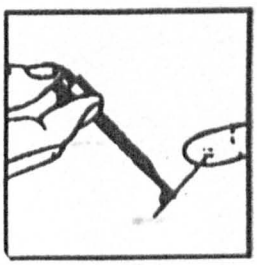


Hold *Softclix® Pro* pointing downwards over a waste bin and press the ejector button. The lancet and the platform will fall out.

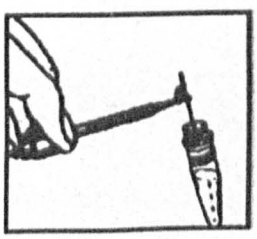
CAPILLARY BLOOD SAMPLE FOR HBA1C TEST



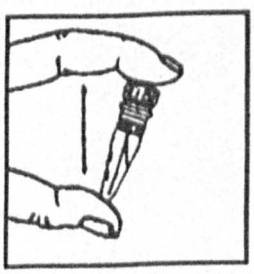
1. Take one capillary out of the capillary dispenser and attach it in the capillary holder. Fill the capillary with blood (from fingertip).
   IMPORTANT: The capillary must be filled end-to-end.



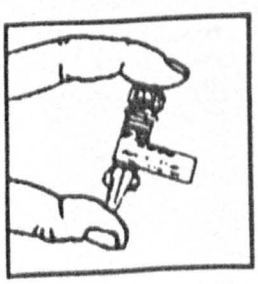
2. Transfer the filled capillary into the Sample Preparation vial.



3. Cap the vial and shake it to rinse the blood completely from the capillary.
   IMPORTANT: Make sure that no blood remains in the capillary.



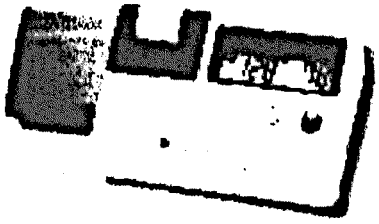
4. Label the vial with the label provided in the kit. On the vial, place the label on the free space below the notches.



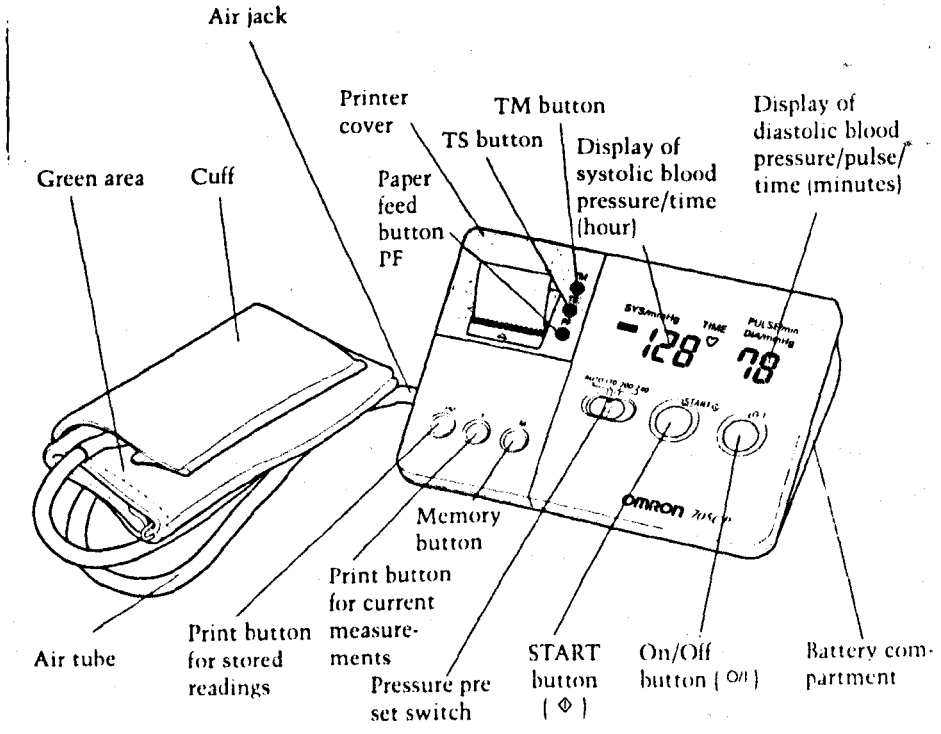
5. The specimen can now be passed on for analysis. Samples prepared using this procedure are suitable for 2 weeks at room temperature or four weeks at 2-8C.

Appendix XXIV: How to use OMRON 705CP

HOW TO USE THE OMRON 705CP

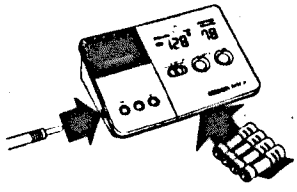


Components



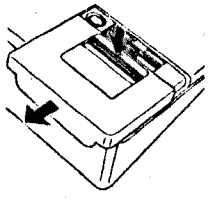
Preparation for use

1. Inserting the batteries

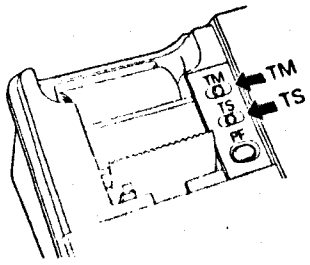


2. Setting the date and time

- The buttons for setting date and time are located under the printer cover. Remove the cover by pulling it off in the direction indicated by the arrow.



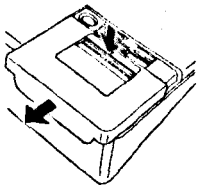
- After inserting the batteries, PM 12:00 appears on the display. Press the **TM button**. The month display then flashes.



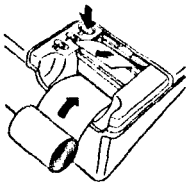
- Now press **TS button** to set the current month.

- After setting the month, press the **TM button** again. The **'DAY'** symbol then flashes. Set the current day using the **TS button**.
- The hour and minutes flash after you press the **TM button**. Set the hour and minutes using the **TS button** and then press **TM button** again so that the hour and minutes are displayed.

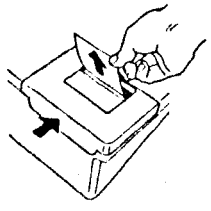
3. Inserting the printer paper



- Remove the printer cover. Before inserting the paper, remove the adhesive strip and cut the end of the paper off straight and slant.



- Insert the end of the paper into the slot whilst at the same time holding down the paper feed **button PF**



- Place the paper roll into the compartment and pull the strip through the opening in the printer cover. Then close the cover.

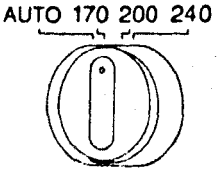
Preparing for measurement

1. Switching on the blood pressure measurement function.

- When the preparations are complete, the ready to measure symbol (♥) appears on the display.

2. Pressure pre set switch

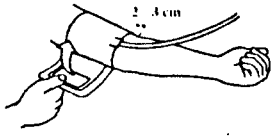
- Select a setting that is one value higher than the expected systolic blood pressure.
- The 170 mm Hg or 200 mm Hg setting is recommended.



- If the value you have set proves to be inadequate, the monitor automatically inflating until the pressure is sufficient for measurement.
- If you hold down the START button, inflation will still continue even after the pressure you have set has been reached.
- You can also put the pressure pre set switch to the AUTO position. In this case the inflation pressure is automatically adapted to the last systolic pressure measurement taken.

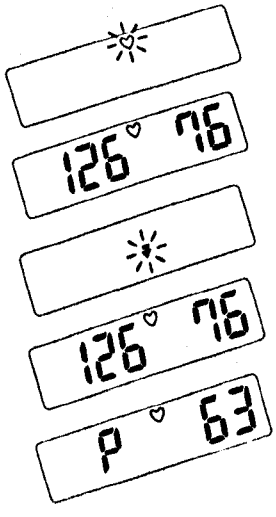
The measuring procedure

1. Fitting the cuff and starting measurement with automatic inflation



- Fit the cuff around the patient's arm so that the green mark is located 2-3 cm over the brachial artery.
- Position the patient's arm on the level with the heart and press the **START** button.
- Please ensure that clothing does not constrict the blood flow.

2. Automatic deflation and display of measurements



- As soon as the patient's pulse has been detected, the (♥) symbol starts to flash and, at the same time, the monitor beeps.
- When measurement has finished, the systolic and diastolic BP are displayed.
- The pressure drop symbol (⬇) indicates that the cuff is deflating.
- When all the air has escaped, the (♥) symbol appears on the display and the blood pressure and pulse are displayed alternately for approx. 5 minutes.

Print out of readings

- Check the readings as soon as measurement has finished and then press the **P button**. It does not matter whether the blood pressure or pulse is showing on the display when you press the button.

- **Caution:** The measurements can only be printed out when the blood pressure or pulse values are shown on the display. No printout is possible when the time is displayed.

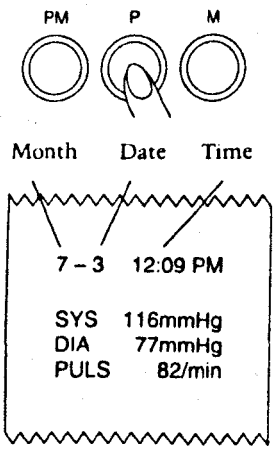


Table 5.32: Comparison of the number of DRPs identified by each of the pharmacists (includes active and control patients)

Pharmacist	No. of patients interviewed	No. of patients with one or more DRPs (%)		Mean no. of DRPs per patient (range)
A	51	44	(86)	2.3 (0-7)
B	51	48	(94)	2.3 (0-4)
C	36	29	(81)	1.7 (0-6)
D	61	57	(93)	2.2 (0-5)
E	43	27	(63)	1.1 (0-4)
F	36	34	(94)	2.7 (0-7)
G	38	23	(60)	0.9 (0-4)
H	52	42	(81)	2.0 (0-7)
I	35	18	(51)	0.7 (0-3)
Total	403	322	(80)	1.8 (0-7)