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Effective Health Care

Bulletin on the effectiveness of health service interventions for decision makers

This bulletin reviews the evidence for the effectiveness of interventions for Type 2 diabetes. It focuses on the treatment of renal disease and the promotion of self-management.

Complications of diabetes:

Renal disease and promotion of self-management

- Over a million people in the United Kingdom have Type 2 (non-insulin dependent) diabetes.
- The urine of people with Type 2 diabetes should be tested regularly (at least annually) for proteinuria and, if this is negative, for microalbuminuria. Two or more measurements should be carried out.
- The blood pressure of people with diabetes should be checked at regular intervals and treatment offered if it is found to be consistently higher than 140/90.
- In people with above-normal levels of protein in their urine, treatment with ACE inhibitors is appropriate, even if blood pressure is within the normal range. Treatment of other cardiovascular risk factors should also be considered.
- Blood glucose levels should be kept as near to normal as is consistent with an acceptable quality of life.
- People with Type 2 diabetes should be actively encouraged to be involved in their own care.
- Further research is necessary to determine whether interventions to promote self-management have positive significant long-term effects on outcomes such as weight and HbA1c levels.
- All future research should consider clinically relevant outcomes such as morbidity, mortality, and quality of life.

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A. Introduction

This is the second bulletin on Type 2 diabetes. The text is divided into two sections, the first dealing with renal complications of diabetes, and the second with promotion of self-management. The importance of diabetes care as a whole is underlined by the fact that a National Service Framework for diabetes is being developed for publication in 2001. Over a million people in the UK have Type 2 diabetes and one projection has estimated that the number could rise substantially by 2010.[1] Both Type 1 (insulin dependent) and Type 2 (non-insulin dependent) diabetes can lead to a variety of complications, of which renal (kidney) failure is one of the most serious. The information in this bulletin relates to Type 2 diabetes unless otherwise specified. Details of the reviews which informed the Bulletin are given in the Appendix.[2,118] Additional review work was undertaken by CRD.

B. Renal disease

B.1 The nature of the problem Elevated blood glucose – and related microvascular disease – is associated with slow but progressive damage to the kidneys. This damage becomes detectable when protein (primarily albumin) is excreted in the urine in higher concentrations than normal. As the severity of damage increases, the quantity of protein in the urine also increases. Eventually, the condition can lead to renal failure.[2] When the level of albumin in the urine is fairly low (although above normal), the condition is known as microalbuminuria, or incipient nephropathy. Higher albumin excretion is described as macroalbuminuria or proteinuria. A consensus definition of microalbuminuria in Type 1 diabetes of 20–200 µg/min in urine collected in patients at rest or 30–300 mg/24hr in a 24-hour sample was agreed in 1985.[3] This definition has been widely applied to Type 2 diabetes.

From the patient's perspective, the degree of kidney damage that produces microalbuminuria, or even proteinuria, may not cause any detectable problems. Symptoms may not become apparent until the kidneys are approaching the point of failure.

B.2 Prevalence Epidemiological studies of renal disease in people with Type 2 diabetes report prevalence rates for micro-albuminuria ranging from 8% to 32%; the majority of estimates are around 25%.[4-15] This variation may be a product of the range of criteria used to define the condition, the stage of disease and the methods used to assess it. Prevalence estimates for proteinuria range from 5% to 19%, but most studies give rates of around 15%. [5,6,9-11,15,16] UKPDS figures, based on a sample of 3,867 patients, suggest that about 12% have microalbuminuria (although using a high threshold) and 1.9% have proteinuria at the time of diagnosis of diabetes.[17] A US study which followed 794 patients with Type 2 diabetes who were initially free from proteinuria (defined as ≥30 µg protein per litre of urine) found that 1.3% developed renal failure within 10 years.[18] Studies of patients treated in renal units in the UK show that a substantial proportion have diabetes. Data from the UK Renal Registry, covering 43% of the UK adult population, showed that in 1998 diabetic nephropathy was the most common single cause of end-stage renal failure amongst adult patients starting on renal replacement therapy (16% of the total). Diabetic renal disease was recorded in 9.5% of existing patients. Of these, 6.8% were recorded as Type 1 and 2.7% were recorded as Type 2.[19]

B.3 Risk factors The main identified risk factors for the development of diabetic renal disease are hereditary susceptibility (including ethnic origin), blood glucose levels, and blood pressure. Other suggested relationships are between diabetic renal disease and smoking, blood lipids, body mass index, age, sex and duration of diabetes.[18,20-30]

People of Asian or African ethnic origin seem to be particularly susceptible both to Type 2 diabetes and to diabetic renal disease. A study in Leicester of people whose families originated from the Indian sub-continent found that the probability of their requiring renal replacement therapy for diabetic nephropathy was 13.6 times higher than for white Caucasians.[31] Another survey, which included all 5,901 patients accepted for renal replacement therapy by renal units in England, found that people of Asian or Afro-Caribbean origin were both almost six times as likely as white Caucasians to be receiving treatment for end-stage renal failure associated with diabetes.[32] Close relatives of people with diabetic renal disease are much more likely than others to develop the condition; odds ratios of 3.8 (95% CI, 1.4 to 10.4)[33] and 8.1 (95% CI, 2.2 to 29.6)[34] have been reported.

The majority of studies have found that higher blood glucose is linked with a greater risk of renal disease.[17,18,20,21,23,35]

Many studies (total participants >4,000) have reported links between elevated blood pressure (either systolic or diastolic or both) and diabetic renal disease.[18,21,26-28,35] Advancing renal disease can lead to increased blood pressure, whilst increased blood pressure accelerates the course of diabetic renal disease.

People with diabetic retinopathy are significantly more likely to develop signs of renal disease.[23,25]

B.4 Disease progression Reported rates of progression of diabetic renal disease reflect the varied definitions of the different stages of the condition; there are no clear-cut criteria to define any specific point. Longitudinal studies suggest that whilst protein excretion tends, in general, to increase over time, the rate and

direction of change varies between individuals.[22,36]

B.5 Mortality Fewer than 5% of deaths among people with Type 2 diabetes are directly attributed to renal disease. [37,38] The majority of deaths result from myocardial infarction, heart failure or stroke. However, a meta-analysis of eight studies found that the death-rate among people with micro-albuminuria was more than double the rate in people with normal urinary albumin levels; risk ratios were 2.4 (95% CI, 1.8 to 3.1) and 2.0 (95% CI, 1.4 to 2.7) for overall and cardiovascular mortality, respectively.[39] A 12-year study of 4,714 people with diabetes (both types) reported that proteinuria was associated with an eight-fold increase in deaths among women and a five-fold increase in risk among men, compared with those who did not have proteinuria.[40]

B.6 Identifying patients with renal disease Since the defining feature of diabetic renal disease is the appearance of protein in the urine, detection and monitoring of the condition depends on urine tests. Some of these measure albumin alone; others allow an albumin/creatinine ratio to be calculated. Some tests are suitable for near-patient testing (side-room tests); others require more sophisticated laboratory equipment. The former group are less accurate but quicker and easier to use. Seven such tests are available in the UK but evidence was found on the accuracy of Micral-Test II, Albustix and Microbumintest only for measurement of albumin in urine, but not on any of the other products.

No direct comparisons between near-patient tests were identified, and there is no evidence to show that any one is more accurate than others. Sensitivity ranged from 51%[41] to 100%.[42-44] Specificity ranged from 27%[45,46] to 97%.[47,48] but different methods, reference standards, ranges and thresholds were used to assess the tests. Any attempt to determine the most effective test is hampered by the heterogeneity of the evidence.

Laboratory tests include radioimmunoassay, immunoturbidimetry, immuno-nephelometry, enzyme-linked immunosorbent assay (ELISA), and the DCA 2000 micro-albumin/creatinine assay system.

Studies assessing albumin concentration in urine produced sensitivity and specificity levels above 90% in only two out of eleven studies,[7,49-55] one using radioimmunoassay in an early morning sample,[49] and the other using immunonephelometry in a random sample.[54] Two studies of ELISA in early morning samples,[7,50] and one using immuno-turbidimetry in overnight samples,[51] reported sensitivity over 80% and specificity over 90%. In three studies, sensitivity or specificity levels fell below 80%. [7,52,53]

Studies assessing the accuracy of measurement of albumin/creatinine ratios reported both sensitivity and specificity levels above 90% for every type of test.[7,49-51,53,56-59] The timing of the urine samples used in these studies varied; accurate measurements were achieved with early morning, overnight and 24-hour samples, but the ELISA test on random urine samples was less accurate, with 80% sensitivity and 81% specificity.[7]

These tests differ in their nature and have been assessed by methods which may not be directly comparable, so it is not clear which is the most effective or useful. Furthermore, there is very marked day-to-day variation in urinary albumin excretion which other illnesses may also increase and so a single test on a single day is not reliable.

Considered as a whole, the evidence suggests that health professionals should use these tests on several occasions each year to assess whether patients show signs of renal disease. They should not rely on a single near-patient test.

B.7 Current practice in the NHS Audit data from the UK DIABS study suggests that just under two thirds of people with Type 2 diabetes have their renal function tested on an annual basis, although there is considerable variation. In an audit covering 47 districts the percentage who had had a renal function test in 1998 (defined as creatinine, urinary albumin, albumin/creatinine ratio or microalbuminuria) was found to be 64% (range 20% to 96%).[60]

B.8 Interventions to reduce renal complications of diabetes The evidence discussed in this section comes from randomised controlled trials (RCTs) which focus on reducing blood pressure with antihypertensive drugs; improving blood glucose control; reducing dietary protein, and the use of lipid-reducing drugs.

Antihypertensive treatment

Both diabetic renal disease and hypertension are associated with increased cardiovascular mortality.[39] Control of blood pressure could therefore be a rational way of reducing mortality in hypertensive patients with diabetes. It may also slow the progression of diabetic renal disease.

End-points related to renal disease were among a range of variables studied in the UKPDS 38 trial of tight blood pressure control in Type 2 diabetes.[61] This trial was based in 20 hospital clinics in the UK; it recruited 1,148 hypertensive people, randomised to tight or less tight blood pressure control, and followed them for a median period of 8.4 years.

Mean blood pressures in the two groups were 144/82 and 154/87, respectively. The tight control group had less microvascular disease, with a relative risk (RR) for the aggregate endpoint (including retinopathy, vitreous haemorrhage and renal failure) of 0.63 (95% CI,

Table 1: Meta-analyses of effects of antihypertensive drug treatment on renal function

Study	Objectives	Inclusion criteria	Patients/trials	Statistical pooling	Main findings	Conclusion & comment
Lovell, 1999[71]	To discover whether ACE inhibitors reduce progression of diabetic renal disease in patients with normal blood pressure.	RCTs. Diabetic patients (Type 1 or 2) with blood pressure <160/95, who received ACE inhibitors for >1year and were compared with placebo controls.	418 admitted to studies. Of these completing treatment ACE inhibitor group: n=185 Controls: n=183. 11 trials; 7 Type 1 diabetes only, 3 Type 2, 1 both types.	Inverse variance weighted means used for Cochrane-style pooling; 'effect' defined as difference between changes over duration of study in treatment and control groups.	Albumin excretion rate (AER) fell among patients on ACE inhibitors in 10 of 11 studies, *v.* 2 of 11 with placebo. Weighted mean difference in AER: -179 (95% CI, -196 to -162) No difference between Type 1 and Type 2 diabetes in outcomes. Blood pressure in treated patients fell significantly, from 130/78 to 120/74. Controls: slight rise,127/80 to 128/82.	ACE inhibitors reduce rise in albumin excretion, even when blood pressure is within normal range. Studies too short to show potential protection from renal failure. All studies small. Mean quality score 53/100 by Kleijnen method.[117]
Gansevoort, 1995[63]	To discover whether ACE inhibitors differ from other antihypertensives in their effects on renal disease.	Trials (no restriction on study type) lasting >1 week which directly compared ACE inhibitors with other drugs and gave information on renal end-points.	1124 patients with renal disease, 566 with diabetes, both types. Baseline renal function from micro-albuminuria (19 mg/day) to nephrotic (5.9g/day) Baseline blood pressure also varied widely. 41 trials, mixed designs.	Weighted mean treatment effect on proteinurea and blood pressure calculated for all studies of each drug. Stepwise multiple regression to identify individual contributions of various factors to effects.	ACE inhibition reduced protein in urine by 40% (95% CI for weighted mean change, -43% to -37%), significantly more than 17% fall (-19% to -15%) with other antihypertensives (p<0.001). No difference between particular ACE inhibitors. No significant difference in effect between diabetic and non-diabetic renal disease. With other drugs, reduction in protein excretion and blood pressure greater in diabetics than non-diabetics. Nifedipine least effective for reducing protein loss (-8%, 95% CI -13% to -2%) despite marked reduction in blood pressure.	Overall, ACE inhibitors are more effective for reducing protein in urine than other antihypertensives. The difference between drugs is less marked in diabetic patients, except nifedipine, which has least effect on proteinuria. No essential change in findings when only RCTs (n=34) or double-blinded studies (n=16) included. Authors argue that effect of publication bias is minimal.
Maki, 1995[64]	To discover whether effects on renal disease of various anti-hypertensive drugs differ, whether they are similar in diabetic and non-diabetic patients, and whether effects of any agents are independent of blood pressure reduction.	Studies lasting >6months of effects of antihypertensive agents, which give information on blood pressure and information on renal function (e.g. data on urinary protein). Studies included diabetic patients with and without renal disease, and non-diabetic patients.	Number of patients not stated. 30% had Type 2 diabetes, 23% Type 1. 79% hypertensive. Analysis included 84 studies with 156 trial arms. 16 were RCTs, of which 14 were of ACE inhibitors.	For RCTs, weighted mean treatment effects calculated and pooled. Controlled and uncontrolled trials included in multiple regression analysis designed to test effects on renal function independent of blood pressure changes.	For all studies ACE inhibitors and nondihydropyridine calcium channel blockers reduced proteinuria by 45% (95% CI, -58% to -32%) and 38% (-70% to -6%) respectively. This is more than could be explained by changes in blood pressure or other indices of renal function. Other agents - including dihydropyridine calcium channel blockers - had no independent effect on proteinuria. Analysis of RCTs alone confirmed reduction in proteinuria but not change independent of blood pressure. Effects similar in diabetic and non-diabetic patients.	Antihypertensive treatment leads to long-term beneficial effects on renal function in both diabetic and non-diabetic patients, which are generally proportional to blood pressure reduction. ACE inhibitors, and possibly nondihydropyridine calcium channel blockers, may have independent effects on proteinuria.
Weidmann, 1995[66]	To compare the effectiveness of different antihypertensive drugs for treatment of diabetic nephropathy.	Published studies of antihypertensive treatment lasting >4 weeks in diabetic patients with microalbuminuria or proteinuria. Study design not discussed.	2151 patients, approx. equal numbers with Type 1 and Type 2 diabetes. 126 treatment groups described in 104 reports. 24 groups received diuretics &/or beta-blockers, 72 had ACE inhibitors, 18 calcium channel blockers excluding nifedipine, 12 had nifedipine. Baseline levels of proteinuria similar in all treatment groups (means, 1.4 to 1.8g/day).	Not described in this paper - refers to earlier publications of which this is an update.	Urine albumin decreased more (p<0.001) with ACE inhibitors (37% reduction, 95% CI -53 to -22) or calcium channel blockers excluding nifedipine (33% reduction, 95% CI -44 to -23) than with other antihypertensives (diuretics &/or beta-blockers, 23% reduction, 95% CI -33 to -13; nifedipine 5% increase, 95% CI, -18 to 28). In studies lasting >6 weeks which gave data on changes in glomerula filtration rate, ACE inhibitors tended to preserve renal function better than other drugs (but too little data to draw conclusions about calcium channel blockers excluding nifedipine).	ACE inhibitors have beneficial effects on renal function which are greater than those produced by similar reduction of blood pressure by any other drugs; urine protein falls with ACE inhibitors even when blood pressure remains constant.
Kasiske, 1993[65]	To assess the relative effects of different antihypertensive agents on proteinuria and renal function in patients with diabetes.	Controlled and uncontrolled studies that gave data on renal function, proteinuria, or both, before and after treatment of diabetic patients with an antihypertensive agent.	2494 patients in 100 studies (12 RCTs) with 168 treatment groups. Patients in 32% of groups had Type 2 diabetes, in 11% both Type 1 and Type 2. In 35% of groups, patients had clinical nephropathy (WHO stage 4/5), microalbuminuria in 17%, remainder unspecified.	As Maki (1995), above[64]	The greatest reductions in urine albumin excretion were in patients treated with ACE inhibitors (weighted regression coefficient -0.37, p<0.0001, no significant differences between products). Reductions found were greater than could be attributed to blood pressure changes or other variables. Blood pressure reduction greater in Type 2 diabetes than Type 1. Meta-analysis of RCTs gave similar results to other studies. No study features affected results for renal function outcomes.	ACE inhibitors can decrease proteinuria and preserve glomerular filtration rate in patients with diabetes. These effects are independent of changes in blood pressure. Partial overlap with Maki (1995) - this is the same group of authors and the analysis includes 20 of the same trials. Inclusion criteria differ.

0.44 to 0.89). The trend for reduced risk of fatal and non-fatal renal disease was not significant (RR 0.35 (99% CI 0.03 to 3.66) and 0.58 (99% CI 0.15 to 2.21) respectively). However, five out of six surrogate outcomes (micro-albuminuria and proteinuria each measured at three 3-yearly intervals) tended to favour tight blood pressure control. Of these, only microalbuminuria at six years reached statistical significance. 20.3% of the tight control group fell into this category, compared with 28.5% with less tight control (RR 0.71 (99% CI 0.51 to 0.99)).

ACE inhibitors

Particular attention has focused on one group of antihypertensive agents, the angiotensin-converting enzyme (ACE) inhibitors. These drugs reduce constriction of blood vessels, including small vessels (efferent arterioles) in the kidneys.

A large (n = 3,577) international study comparing an ACE inhibitor, ramipril, with placebo in people with diabetes (98% Type 2, mean duration 11 years), reported that ramipril reduced both nephropathy and total mortality by 24% after 4.5 years.[62] All patients had at least one cardiovascular risk factor – hypertension, high cholesterol, microalbuminuria, or smoking – in addition to diabetes. Patients with proteinuria (≥300 mg albumin/day or equivalent) at baseline were excluded.

Many smaller studies have been pooled in a series of meta-analyses (Table 1). Most of these compare the effects of different antihypertensive drugs on renal endpoints.

A meta-analysis which pooled trials lasting more than a week and comparing ACE inhibitors with other antihypertensives, revealed that ACE inhibitors reduce urinary protein levels significantly more than other antihypertensives.[63] The mean change in urine protein with ACE inhibition was -40% (95% CI, -43% to -37%), compared with -17% (95% CI, -19% to -15%) for other drugs. Nifedipine had the smallest effect: -8% (95% CI, -13% to -2%). There were no significant differences between diabetic and non-diabetic groups of patients.

Another review, also designed to determine whether specific types of antihypertensive drugs have differing effects on renal disease, pooled trials with follow-up times of at least six months.[64] Two meta-analyses were carried out, one using data from 84 trials of mixed designs, the second with data from 14 RCTs only. The results of both showed that ACE inhibitors reduced urinary protein more than other antihypertensives, in people with and without diabetes. Analysis of data from all the trials suggested that the anti-proteinuric effect of ACE inhibitors and non-dihydropyridine calcium channel blockers (verapamil, diltiazem) was greater than could be explained by changes in blood pressure. However, this enhanced benefit was not apparent from the meta-analysis of RCTs only; this found that effects on urinary protein were proportional to changes in blood pressure.

Two other meta-analyses, which have slightly different inclusion criteria and include groups of trials which partially overlap with the studies above, reinforce these results.[65,66] One of these reported that ACE inhibitors reduced protein excretion by 25% even when blood pressure remained constant,[66] and also that kidney function deteriorated significantly faster in people with diabetes and renal disease treated with nifedipine than in people in the other treatment groups.

However, trials published since these meta-analyses have examined the differences between drugs mainly in people who have microalbuminuria. Those which included more than 100 patients are discussed below.

UKPDS 39 (n=758) found no differences in outcome between atenolol (a beta-blocker) and captopril (an ACE inhibitor).[67] Few patients had renal disease. Also, for two-thirds of the study period, 60% were taking other antihypertensives as well as (or instead of) the drug to which they were randomised. 35% of patients on atenolol discontinued treatment because of adverse effects, compared with 22% on captopril ($p<0.001$).

A multi-centre trial in patients with Type 2 diabetes, hypertension and microalbuminuria (n=314) found that lisinopril (an ACE inhibitor) reduced albumin excretion significantly more than nifedipine.[68] Similar results were found in a study (n=103) comparing benazepril with nicardipine in both hypertensive and normotensive patients.[69] A study (n=162) which compared ACE inhibitors with calcium channel blockers found little difference; however, as in UKPDS 39, the majority of patients did not have renal disease.[70]

The most recently published meta-analysis of RCTs found that ACE inhibitors also reduce albumin excretion in people with diabetes with microalbuminuria and normal blood pressure.[71]

In the studies identified which were not included in this meta-analysis and which compared ACE inhibitors (enalapril, ramipril or perindopril) with placebo in patients with mild hypertension or normal blood pressure and microalbuminuria, ACE inhibitors reduced albumin excretion.[72-74] The beneficial effects on risk of renal disease increased over five years.[73,74] Ravid et al found that albumin excretion increased less at six years in the enalapril group than in the placebo group and that renal function was preserved.[74]

Of these trials, only those carried out by UKPDS assessed renal failure or death-rates, and none measured quality of life. There seems to be a general and unquestioned assumption that reduction of urinary protein excretion would inevitably be

associated with improvements in such end-points. Although this assumption has face validity and no evidence is presented that suggests it is untrue, neither does there appear to be any evidence demonstrating that it is correct.

This is not a trivial academic point. Improvements in surrogate outcome measures such as blood pressure can be associated with deterioration in crucial end-points such as life-expectancy.[75] It is important, therefore, that studies of antihypertensive drugs in diabetic renal disease should be designed to detect effects on long-term morbidity and mortality.

Summary of evidence on antihypertensive treatment

ACE inhibitors offer particular benefits for people with diabetic renal disease or microalbuminuria, even when normotensive. These benefits may be offered by other antihypertensive drugs when patients have high blood pressure but show no signs of renal disease.[119] Dihydropyridine calcium channel blockers have a less favourable pattern of effects in people who have renal disease and diabetes.

Improved blood glucose control

More intensive control of blood glucose appears to delay the development of renal disease. UKPDS 33 (n=3,867) reported that the relative risk of microalbuminuria at nine years was 0.76 (99% CI, 0.6 to 0.9) with tight control by sulphonylurea or insulin (mean HbA1c, 7.0%), compared with less tight control by diet (mean HbA1c, 7.9%).[17] At 12 years, the relative risk fell to 0.67 (99% CI, 0.5 to 0.9). It is too soon to know to what degree this may reduce the risk of renal failure.

A Japanese study reported that a mean HbA1c of 7.1 over a period of six years achieved by multiple insulin injection therapy (MIT) reduced the risk of worsening in nephropathy by 70% (95% CI, 14% to 89%) relative to a mean HbA1c of 9.4 achieved by conventional insulin injection therapy (CIT).[76] This result came from a combined cohort of patients with normal renal function at baseline (defined as urinary albumin excretion (UAE) <30 mg/24 hr) (the primary prevention cohort) and patients with microalbuminuria (defined as UAE <300 mg/24 hr) (the secondary prevention cohort). The cumulative percentages of the development and progression in nephropathy after six years were 7.7% for the group treated with MIT and 28% for the group treated with CIT in the primary prevention cohort, ($p = 0.032$) and 11.5% and 32.0% respectively for the MIT and CIT groups in the secondary intervention cohort ($p = 0.044$).

Reduced dietary protein

A systematic review found that for people with Type 1 diabetes a diet containing 0.3–0.8 g/kg body weight of protein per day may slow progression to renal failure.[77] However, no reliable evidence was found relating to Type 2 diabetes.

Lipid reduction

No conclusive evidence was found relating to the effect of statins or gemfibrozil on renal function.[78-81] However, these drugs may be indicated for reduction of cardiovascular morbidity and mortality in people with diabetes.[82]

B.9 Multifactorial intervention

Four years of intensive multifactorial treatment of people with microalbuminuria has been shown to produce significant reductions in the rate of progression of renal disease, along with improvements in a range of other diabetes-related end-points.[83] The intervention involved tight control of blood pressure, glucose and lipids, ACE inhibitors for all patients in the intensive treatment group regardless of blood pressure, specific advice on diet plus vitamin supplements, exercise, and help with smoking cessation. 10% of patients in the intensively treated group developed nephropathy during the study, compared with 24% in the group which received standard treatment from GPs (odds ratio 0.27, 95% CI, 0.10 to 0.75). Blindness and autonomic neuropathy also developed significantly less often in the intensively treated group.

B.10 Costs Effective treatment of early renal complications of diabetes through tight control of blood pressure is highly cost-effective. Figures calculated from the UKPDS trial comparing tight with less tight blood pressure control show that the incremental cost per life year gained (using 1997 values) was £720 when costs and effects were discounted at 6% per year. When costs were discounted at 6% per year but effects were not discounted the cost per life year gained fell to £291.[84] This analysis was based on unit costs for all NHS resources used by all patients over the entire period of the trial, adjusted to reflect standard clinical practice. Tight blood pressure control reduced the rate of complications requiring hospitalisation. Although this difference was not statistically significant, the savings found offset the costs of antihypertensive drugs so that the net costs per patient were very similar in the two groups. Tight control of blood pressure appears to be considerably more cost-effective than either treatment to reduce cholesterol levels, or life-style advice on reducing cardiovascular risk.

A hypothetical strategy of treating all middle aged people with diabetes (base case 50 years old) with ACE inhibitors was examined by the use of a model. This was found to be more cost-effective than screening and treating for micro- albuminuria or proteinuria. Analyses indicated a cost of $7,500 for each quality-adjusted life year gained.[85] However this result was sensitive to a number of parameters such as age and quality of life.

B.11 Implications

- The urine of people with Type 2 diabetes should be tested

regularly (at least annually) for proteinuria, and if this is negative, for micro-albuminuria. Two or more measurements should be carried out.

- Evidence for the effectiveness of individual near-patient tests is inconclusive.
- The blood pressure of people with diabetes should be checked at regular intervals and treatment offered if it is found to be consistently higher than 140/90.[86]
- In people with above-normal levels of protein in their urine, treatment with ACE inhibitors is appropriate, even if blood pressure is within the normal range. Treatment of other cardiovascular risk factors should also be considered.
- Blood glucose levels should be kept as near to normal as is consistent with an acceptable quality of life.
- Further research is required with people with Type 2 diabetes to establish what levels of dietary protein are effective for reducing the rate of progression of renal complications, and are acceptable to people with diabetes.

C. Promotion of self-management

People with Type 2 diabetes can take an active role in the management of their condition, for example by taking responsibility for weight loss and monitoring blood glucose levels. It is increasingly recognised that people may benefit if they are enabled to play more informed and active roles in discussions with health care professionals and in decisions about health care.[87] Whilst medical interventions are important, long-term outcomes depend on choices that people with Type 2 diabetes themselves make about diet, physical activity and other health-related behaviour. These choices will in part reflect knowledge about their condition and their ability to monitor it. However, increased knowledge alone is not necessarily sufficient. Various programmes have been devised to help people change elements of their behaviour such as diet and physical exercise.

C.1 Interventions The interventions considered were generally provided in addition to the information sharing that should be an integral part of usual patient care. The interventions included were assigned to three broad categories: information and skills, cognitive-behavioural and patient-empowerment. These approaches have been used with individuals and groups.

The information and skills programmes concentrated on diabetes self-management, diet and skills such as glucose testing. Cognitive-behavioural interventions are relatively intensive programmes based on the principles of learning theory and/or social cognition models.[88] These target health-related behaviour; in the context of diabetes, most frequently weight loss by means of diet and/or exercise. Programmes frequently involved goal setting, problem solving, modification of self-perceptions, the use of behavioural contracts, and sometimes physical exercise.

Patient empowerment programmes aim to enhance participation in diabetes management. These ranged from a programme that gave participants some choice in the content of their educational courses to those providing training in information seeking, decision making and negotiation skills.

Fifty-three relevant RCTs were identified.[118] Only seven involved follow-ups of a year or more and only 13 randomised at least 100 participants. These studies are discussed below. All reported differences between interventions achieved statistical significance at the $p < 0.05$ level. Overall, the studies were heterogeneous. Interventions ranged in intensity from a 30-minute demonstration of glucose monitoring to blocks of weekly meetings followed by 'refresher' sessions every few months.

Studies used a variety of outcome measures including patients' knowledge, skill in performance of diabetes-specific tasks, adherence to dietary advice, blood glucose measurements, anxiety levels and other outcomes such as rates of admission to hospital. The main outcomes considered here are knowledge, weight change, HbA1c levels and blood pressure.

Information and skills programmes

Interventions aimed at the individual

Four large (n>100) studies were identified; these included two studies with follow-up >1 year.[89-93] One smaller study also included a one-year follow-up.[94]

The DIABEDS study (n = 532) found that after 11 to 14 months, more programme participants than controls achieved the objectives on two out of nine knowledge, and two out of five skills measures.[89,90] The intervention group performed better in terms of mean weight, blood pressures and changes in HbA1c than controls but the differences were small.

An East German study (n = 1,139) compared 'Intensified Health Education' (diet and physical activity advice; physical exercise and anti-smoking groups were also available) to regular diabetic clinic visits.[91] At five-year follow-up, there were no differences in weight; however, the health education group did have lower blood pressure (sBP: 143 mmHg vs 154 mmHg; dBP: 87 mmHg vs 92 mmHg).

A study of home teaching (n = 471) compared up to 12 visits tailored to individual needs with usual care.[92] After six months, those receiving the intervention had higher scores for knowledge and skill.

British Asian participants (n = 201) received one-to-one education using large culture-specific flashcards or usual care.[93] After six months the intervention group showed improvements in knowledge score, self-care behaviours and attitudes.

After basic diabetes education, 86 participants were randomised to either bi-monthly clinic visits involving motivation for self-management for a year, or usual care.[94] At the 27-month follow-up, the only difference was that intervention participants were receiving oral drugs for diabetes less frequently than those in the control group.

Telephone interventions

Over the course of a year, participants (n = 275) received either monthly phone calls from nurses or usual care.[95] The intervention group had lower HbA1c than controls and higher Patient Satisfaction scores. There were no differences in number of diabetes-related symptoms or quality of life scores.

Computer interventions

Participants (n = 105) received either a DIABETO computer link giving personalised dietary information or usual care.[96] The DIABETO group appeared to have greater gains in knowledge scores than controls. There were no apparent differences in weight or HBA1c.

Group interventions

One RCT evaluating information interventions given in a group included follow-up >1 year[97] and three included more than 100 participants.[98-100]

Participants in a small UK study (n = 75) received either group education with specialist nurses or usual clinic care.[97] After one year, the intervention group had higher knowledge scores and had lost more weight than the control group (5.5 kg vs 3 kg) but there were no differences in HbA1c levels.

A UK study randomised 120 obese participants with limited literacy skills to either monthly small group meetings with videos and handouts, monthly small group meetings without videos, or one-hour lectures.[98] Although participants in the video group lost more weight at seven months this was not sustained at 11 months. There were no differences in HbA1c.

Hospitalised patients (n = 107) with both Types 1 and 2 diabetes received either the two-day 'Living with Diabetes' group programme or usual care.[99] At four months, the intervention group reported less of a decline in compliance with various self-care measures than the control group.

Participants (n = 120) in an Italian study received either four 3-monthly group meetings focusing on diabetes awareness, foot care and changing behaviour or usual consultations.[100] At the end of the year, there were no differences in knowledge, quality of life, weight or HbA1c.

Information and skills: summary

Overall the quality of research was poor. Of the four evaluations of information and skills programmes with adequate follow-up,[89,91,94,97] two found greater long-term knowledge and weight loss in the intervention groups.[89,97] The two large studies also found a positive effect on blood pressure.[89,91] However, the clinical significance of these changes is questionable. The culturally specific programme produced greater short-term knowledge gains and improvements in self-care than usual care.[93] No evidence was found to suggest that either individual or group methods were superior.

Cognitive behavioural interventions

Individual

Two studies of individual cognitive-behavioural programmes involved more than 100 participants;[101,102] neither had a long follow-up.

Participants (n = 155) were randomised to either usual care or one of three year-long behavioural interventions including the use of contracts: compliance with prescribed medical regimen, behavioural strategies and instruction in behaviour analysis.[102] There were no differences between the groups in HbA1c or weight.

In an Australian study 179 participants received individual information sessions, group information sessions or an individual behavioural intervention over one year.[101] There were no differences in knowledge, satisfaction, HbA1c levels or change in systolic blood pressure. The behavioural group had greater reductions in diastolic blood pressure at 12 months (8 mmHg vs 5 mmHg). Although statistically significant, the clinical significance of this is doubtful.

Computer

Participants (n = 206) received either a brief office-based intervention or usual care.[103-105] A 20-minute touch-screen computer assessment was followed either by usual care or an additional computer assessment to determine barriers to dietary self care, feedback, then participation in goal setting and selection of behavioural strategies. After one-year there were no differences in weight or HbA1c.

Group

Two evaluations of group interventions using cognitive-behavioural techniques, assessed patients after at least a year.[106,107] Two other studies randomised at least 100 participants.[100,108]

Participants (n = 76) received one of three cognitive-behavioural interventions or information only.[107] The three behavioural interventions focused on diet plus exercise, diet alone or exercise alone. At the 18-month follow-up, there were no differences in weight; however the combined diet plus exercise class had lower HbA1c than the control group (7.7% vs 8.6%). In addition, both the combination and diet-only group reported higher quality of life than controls.

Fifty-three participants were randomised to receive either behaviour modification (16 weekly meetings); nutrition education (16 weekly meetings) or usual care (4 monthly meetings).[106] Although the behaviour modification group lost more weight than either of the other groups at four months, there was no difference at 16 months in weight loss, physiological measures, eating or exercise behaviours.

Participants (n = 101) received either the 'Sixty Something' programme or usual care.[108] The intervention group showed better self-care behaviour and had greater weight loss at post test (-5.8lb vs +1.4lb) but not at follow-up (-1.9lb vs -3.5lb). There were no differences in HbA1c levels or measures of self-efficacy or mood.

Individual plus group

One trial with 18 months follow-up and 55 participants investigated cognitive-behaviour therapy delivered using both individual and group sessions.[109] Cognitive-behaviour therapy was compared with its constituents (cognitive and behaviour therapies) and a relaxation control in a study of diet and exercise. Participants in the behaviour modification group lost more weight than the cognitive-behaviour or control groups. There were no differences in HbA1c levels.

Cognitive-behavioural programmes: summary

Of the four evaluations of cognitive-behavioural interventions which followed-up participants for one year or longer, only one found sustained weight loss[109] and one reduced HbA1c levels.[107] No evidence was found to suggest that either individual or group methods were superior.

Empowerment A Swedish study compared three months of Problem Orientated Participatory Education (POPE), in which patients take part in determining course content, with a conventional one-day course on diabetes.[110] After one year, the POPE group had greater knowledge but there were no differences in HbA1c levels.

After the intervention, in which participants were given choice or no choice of curriculum content,[111] there was no difference in the numbers attending classes in each of the groups (n = 596). In addition there were no differences in knowledge, self-care behaviours, HbA1c levels or body mass index.

There is little reliable evidence to support the use of empowerment techniques with people with Type 2 diabetes.

Meta-analyses The quality of meta-analyses in this field is just too poor to produce reliable conclusions.[112-116]

Summary of interventions

Long-term benefits of interventions to promote self-management of Type 2 diabetes have yet to be demonstrated. Although many programmes produce desirable outcomes in the short-term and reduced HbA1c levels, these need to be sustained to produce health gains.

C.2 Implications

- People with Type 2 diabetes should be encouraged to be involved in their own care.
- Interventions should be appropriate to individual characteristics and should take into account factors such as age, educational level and ethnic origin.
- Further research is necessary to determine whether interventions to promote self-management of Type 2 diabetes have positive and clinically significant long-term effects on outcomes such as weight and HbA1c levels.
- Trials need to measure morbidity and quality of life outcomes, and if possible, mortality as well as 'surrogate' outcomes.

Appendix – Review methods

Renal care

Studies addressing the effectiveness and cost-effectiveness of detecting, preventing and managing diabetic renal disease were included. For interventions, RCTs and systematic reviews were identified through searches in 11 databases. Two reviewers assessed studies for relevance independently, and data were extracted by at least two reviewers independently. Discrepancies were resolved by discussion. Data were extracted on patient characteristics, interventions and outcomes. The quality of studies was assessed. Where studies had not been included in meta-analyses, analysis was by qualitative/narrative methods.

Promotion of self-management

This review was a re-analysis of a review on the effectiveness of patient education in the management of Type 2 diabetes.[118] Randomised controlled trials and systematic reviews were identified through searches in 10 databases. Professional education and interventions specifically concerned with foot care, retinopathy, screening and renal care were not included. Two reviewers assessed studies for relevance independently, and data were extracted by at least two reviewers independently. Discrepancies were resolved by discussion. The quality of studies was assessed. Analysis was by qualitative synthesis.

ERRATUM

Complications of diabetes, *Effective Health Care*, vol.5(4) 1999.

In Table 2 on page 4 the summary of the Harding (1995) study is incorrect. Direct ophthalmoscopy took place in a hospital setting, not in GP practices. Photography took place in a mobile screening unit at the patients' local health centres, and the photographs were graded by a clinical assistant ophthalmologist. The percentage of photos unobtainable was 3.75%, not 14%.

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Effective Health Care

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