# HOW I WOULD MANAGE A 53-YEAR-OLD WOMAN WITH NEWLY DIAGNOSED TYPE 2 DIABETES, WITH HYPERTENSION AND DYSLIPIDAEMIA

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## INTRODUCTION

Type 2 diabetes is a common medical disorder that is often also associated with obesity, a lack of exercise and older age. An epidemic of Type 2 diabetes is forecast, with estimates that the number of patients in the UK will increase from two million in 2000 to three million by the year 2100, with an estimated 220 million patients worldwide. Type 2 diabetes is a heterogeneous metabolic syndrome, comprising variable degrees of insulin deficiency (beta cell dysfunction) and impaired insulin action (insulin resistance). Many patients with Type 2 diabetes have the 'insulin resistance syndrome', also called the 'metabolic syndrome' or 'syndrome X', which includes:

- insulin resistance;
- hyperinsulinaemia;
- glucose intolerance;
- hypertension;
- increased LDL cholesterol;
- decreased HDL cholesterol;
- microalbuminuria; and
- increased fibrinogen.

The metabolic abnormalities of Type 2 diabetes develop slowly, passing from normal glucose tolerance, through impaired glucose tolerance, to frank diabetes, and patients may attribute the slow development of symptoms such as thirst or polyuria to increasing age rather than illness. The microvascular complications of diabetes are strongly related to the magnitude and duration of hyperglycaemia,[1] and to increases in blood pressure.[2] Patients may have had undiagnosed diabetes for several years and may present with complications. The initial management of a patient with Type 2 diabetes, hypertension and dyslipidaemia should therefore include:

- confirmation of the diagnosis;
- taking a history;
- examination for complications;
- estimation of cardiovascular risk;
- dietary assessment and treatment;
- education of the patient; and
- formulation of a long-term treatment plan.

## PRESENTATION

Common presentations of Type 2 diabetes are:

- classical hyperglycaemic symptoms such as thirst, polyuria or polydipsia;
- infections, particularly candidal infections;
- a 'routine' medical examination, e.g. by a general practitioner, during an insurance medical, or during admission to hospital for another illness;
- microvascular complications, e.g. with retinopathy to an optician or foot ulceration to a chiropodist; and
- macrovascular disease, e.g. during investigation of coronary heart disease or peripheral vascular disease.

## CONFIRMATION OF DIAGNOSIS

The diagnosis of diabetes should be confirmed with a blood glucose estimation. A reading from a glucose meter is not accurate enough for this purpose, and a specimen sent to a biochemistry laboratory is mandatory.

The World Health Organisation (WHO) recently published revised criteria for the diagnosis of diabetes. The main changes were a lowering of the fasting blood glucose concentration that is diagnostic of diabetes, and the introduction of the new category of 'impaired fasting glycaemia'. Impaired fasting glycaemia has been introduced to classify individuals who have fasting glucose concentrations ≥6·1 and <7·0 mmol/l; these individuals have an increased risk of cardiovascular disease and future diabetes, but are not diabetic at the time.

Diabetes is confirmed by either a fasting glucose on venous plasma ≥7·0 mmol/l or venous plasma glucose ≥11·1 mmol/l on random (non-fasting) measurement, or at two hours after 75 gm oral glucose in a formal glucose tolerance test. For patients with symptoms, a single abnormal blood glucose result is diagnostic. For patients with no symptoms, at least one additional abnormal glucose result on another day is required. Glycated haemoglobin measurement ($HbA_{1c}$) is not a diagnostic test for diabetes and should only be performed to assess control of patients already known to have diabetes.

## HISTORY

Pressure of time means that a directed approach has to be employed when taking a history, both in the primary and secondary care settings. The important details in the history include any symptoms of hyperglycaemia, with date of onset, and any treatment to date (Table 1). Past medical history should include inquiry into hypertension, coronary heart disease and intermittent claudication. A small number of patients will have diabetes secondary to endocrine or pancreatic diseases. The drug history needs to be accurate, and patients will often be on multiple medications for other medical conditions. A family history of diabetes is common in patients with Type 2 diabetes, and if this was associated with the development of diabetic complications then the patient may require some reassurance. The social history should include drinking and smoking habits which further increase potential cardiovascular problems in a woman with diabetes, hypertension and dyslipidaemia.

## EXAMINATION

The patient's height and weight should be recorded, and body mass index (BMI) calculated as a measure of obesity. Detailed examination and investigation for pancreatic or endocrine causes of diabetes are not recommended as there is a very low rate of detection, but a high index of clinical

TABLE 1
Medical assessment of the diabetic patient.

**History**
- Symptoms of hyper- or hypoglycaemia, chest pain or foot problems
- Past medical history: diabetes (when diagnosed, how diagnosed, initial treatment), hypertension, coronary heart disease, other vascular disease, thyroid disease
- Drug history: tablets, insulin (name, doses, injection devices), results of home testing
- Family history: diabetes, vascular disease
- Social history: smoking, alcohol consumption, driving, occupation

**Examination**
- Weight, height, BMI
- Hands: Dupuytren's contracture, cheiroarthropathy (limited joint mobility)
- Feet: inspection, pulses, sensation (fine touch, vibration), ankle jerks
- Blood pressure
- Eyes: visual acuity, fundoscopy (dilated pupils)

**Investigations**
- Urine: glucose, albumin, ketones
- Microalbuminuria
- Blood glucose and $HbA_{1c}$
- Creatinine, urea, electrolytes, liver function tests, thyroid function, lipids (non-fasting)

suspicion is required. Pointers towards Cushing's syndrome in a woman with diabetes and hypertension are the presence of a moon face, truncal obesity, purple striae, hirsutism, a buffalo hump or acne.

In an individual patient it is not possible to estimate the duration of pre-existing diabetes, so all patients with Type 2 diabetes should be screened for the complications of diabetes at first presentation, and on an annual basis thereafter. The examination of the eyes includes assessment of visual acuity and fundoscopy through dilated pupils. Fundoscopy should be performed by a trained person, and in the primary care setting this can be done either by the GP or by a trained optometrist.

The feet should be examined in a well-lit room with shoes and socks removed. They should be examined for the presence of callosities or deformity, including the presence of claw toes. The condition of the toenails should be noted, and peripheral pulses should be carefully palpated. Neurological testing can be simply performed using a 10 gram monofilament for fine touch, a 128-Hz tuning fork for vibration sense and a tendon hammer for eliciting ankle jerks.

### MACROVASCULAR RISK

Data from the Framingham study show that the conventional risk factors of smoking, obesity, hypertension, and hyperlipidaemia are all more common in people with diabetes,[3] and that diabetes itself is an independent risk factor. The United Kingdom Prospective Diabetes Study (UKPDS)[4] identified a quintet of potentially modifiable risk factors for coronary heart disease in people with diabetes comprising:

- increased concentrations of LDL cholesterol;
- decreased concentrations of HDL cholesterol;
- raised blood pressure;
- hyperglycaemia; and
- smoking.

Smoking habits should be ascertained in the history, and examination should include estimation of blood pressure. Biochemical screening should include $HbA_{1c}$ and lipid estimations for total cholesterol and triglycerides as a minimum, with LDL cholesterol and HDL cholesterol estimation where these are available.

Microalbuminuria is a component of the insulin-resistance syndrome, and in patients with Type 2 diabetes microalbuminuria predicts the future development of diabetic nephropathy and early mortality.[5] The exact sampling technique depends upon local practice, and may include spot samples of urine in the morning for an albumin/creatinine ratio, timed overnight collections of urine, or 24 hour collections of urine to estimate the albumin excretion rate. Patients with confirmed microalbuminuria should be treated with ramipril (see further in this paper).

### OTHER INVESTIGATIONS

Routine urine testing with 'multistix' provides little additional information if samples are being collected to screen for microalbuminuria. The following other investigations should be considered in a woman with diabetes and hypertension:

- $HbA_{1c}$ (as an assessment of glycaemic control);
- plasma, urea, electrolytes and creatinine (for renal function, associated endocrine disease);
- liver function tests (for evidence of hepatic disease, haemochromatosis, alcohol abuse, etc.);
- thyroid function tests (for undiagnosed thyroid dysfunction, mostly hypothyroidism); and
- electrocardiography (for evidence of left ventricular hypertrophy, or previous myocardial infarction).

### EDUCATION

The management of a patient with Type 2 diabetes requires a multi-disciplinary approach. The education of the patient may involve many members of the health care team including doctors, nurses, dietitians, chiropodists, opticians/optometrists and, in some cases, a clinical psychologist. These resources will not be available in every clinical setting. Most specialist diabetic clinics in the UK will have diabetes nurse specialists, and dedicated dietitians and chiropodists, whereas in the primary care setting there may be a GP and practice nurse, with limited availability of other health care professionals. It is the responsibility of the doctor to 'conduct the orchestra' and it is useful to devise a local protocol detailing what is to be done and who will do it, taking account of local resources.

Patients will initially require education on:

- diabetes and its treatment;
- diet;
- home monitoring (blood or urine);
- advice against smoking and avoidance of excessive alcohol consumption;
- possible complications;
- the need for regular screening; and
- foot care.

## TREATMENT

The initial treatment of diabetes in this woman is by dietary modification. In the UKPDS, a rapid reduction in glycaemia was obtained with initial dietary therapy, and the blood glucose concentration fell from an average of 11·2 mmol/l to 8·3 mmol/l over a period of three months.[6] Outside a study environment many patients have difficulty complying with dietary therapy, and even in the UKPDS only 18% of patients were adequately controlled on diet alone.[6] It is worthwhile giving a two to three month trial of diet, especially in the obese patient, and it is not routinely necessary to commence any tablet treatment for Type 2 diabetes at the first appointment.

Some patients will have severe symptoms of thirst and polyuria, associated with greater degrees of hyperglycaemia, and these patients will require early initiation of oral hypoglycaemic therapy. It is not possible to give an exact blood glucose concentration at which initial treatment with an oral agent is necessary. Patients who present with a random blood glucose concentration in the range of 20–25 mmol/l may be adequately controlled after a few months of diet. In patients with Type 2 diabetes whose initial blood glucose concentration is high, treatment with an oral agent may rapidly relieve symptoms, and the need for continuing therapy can be reviewed once the patient has had a period of effective diet.

After three months of diet, the majority of patients will not be adequately controlled and oral agents need to be added. For overweight patients, the drug of first choice is metformin, and it was the group of patients who were treated with metformin that had the best outcome in the UKPDS.[7] For patients who are of average weight, or are below average weight, the drug of first choice is a sulphonylurea,[8] and the particular preparation to be prescribed will depend on local practice. Newer agents such as repaglinide are chemically different to sulphonylureas but offer no clear advantages.

The doses of metformin and sulphonylurea can be increased at regular intervals according to an algorithm until satisfactory control is obtained (Figure 1). The targets for control can be set for the individual patient. The intensive treatment group in UKPDS had an average $HbA_{1c}$ of 7·0%,[8] and desirable targets are a $HbA_{1c}$ of <7% with a fasting blood glucose of <6·0 mmol/l.

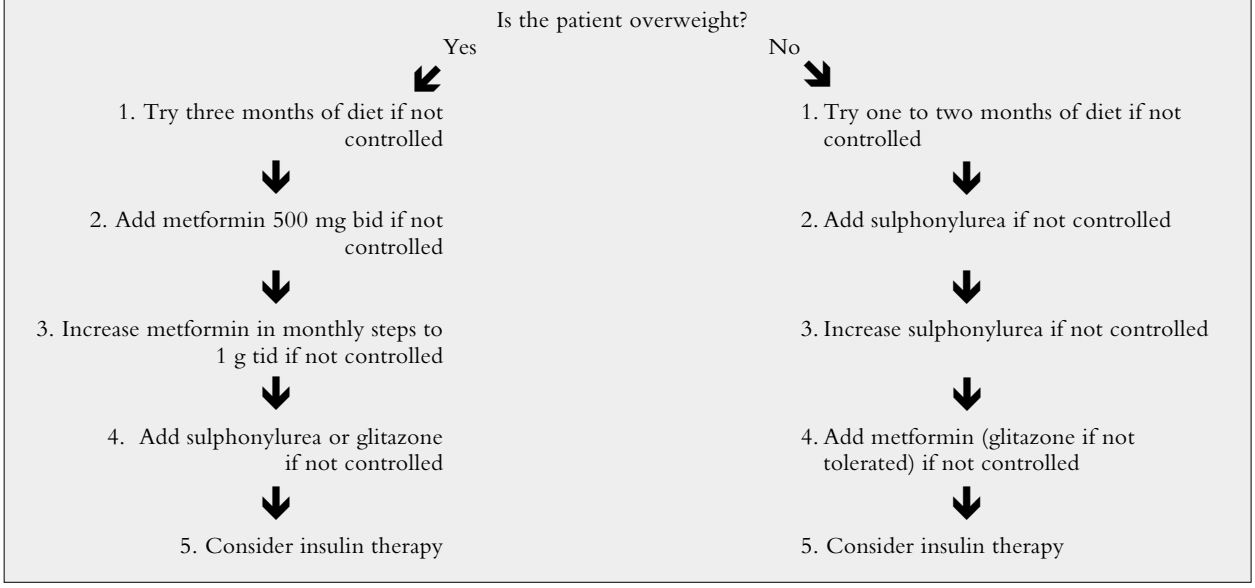
If a patient is not controlled on the maximum doses of one agent then the other agent can be added to it (Figure 1). A new group of drugs, the thiazolidinediones or 'glitazones', has recently become available for clinical use. These enhance insulin action by reducing insulin-resistance through stimulation of nuclear receptors in adipose tissue, skeletal muscle and the liver, improving insulin sensitivity. In the UK, rosiglitazone and pioglitazone are available for limited use in combination with metformin or sulphonylureas. The licensing authorities have indicated that these should only be used in combination in patients with insufficient control of diabetes despite taking maximum tolerated doses of monotherapy with metformin or a sulphonylurea. For the time being, they should not be used as monotherapy, so they should not be considered for a patient with newly-diagnosed diabetes.

The pancreatic abnormality in Type 2 diabetes is progressive, and pancreatic function deteriorates with time. The natural history of the disorder is of worsening hyperglycaemia, and this can be seen in clinical practice by the fact that larger doses of oral agents are required to control the glycaemia. Inevitably many patients require insulin because they cannot be controlled on oral agents. Some patients have a fear of injecting insulin, and at the time of first assessment of the newly-diagnosed patient, it is useful to indicate that in the longer term they may require treatment with tablets or insulin. This can be explained non-judgmentally as a consequence of the underlying disease process, rather than as a failure on the part of the patient, their treatment or their medical care.

## HYPERTENSION

Depending on the criteria that are used to define hypertension, between 30% and 55% of patients with

FIGURE 1
Achieving control in Type 2 diabetes.



diabetes have concomitant hypertension. Different guidelines suggest slightly different thresholds for commencing treatment, and targets for reduction of hypertension in the diabetic patient. The British Hypertension Society guidelines[9] are based on the results of the HOT (Hypertension Optimal Treatment) trial[10] and the HDS (Hypertension in Diabetes Study)[11] and indicate that therapy should be started if systolic blood pressure is sustained >140 mmHg or diastolic is sustained >90 mmHg, and optimal targets are systolic <140 mmHg, and diastolic <80 mmHg. ACE-inhibitors, beta-blockers, diuretics and some calcium channel blockers are of proven benefit, and one of these agents should be the drug of first choice. ACE-inhibitors may have wider effects than the lowering of blood pressure in reducing the development and progression of cardiovascular disease. Other agents remain to be proven, and there are possible adverse effects of some calcium channel blockers.

Reaching the target blood pressures in diabetic patients will often require the use of multiple hypotensive agents.[11] The decision to increase therapy should not be taken at time of first attendance for diabetes, however, as there may be an element of 'white-coat' effect, and adjustments to hypotensive therapy can be deferred until later visits.

### DYSLIPIDAEMIA

Lipid abnormalities are common in patients with Type 2 diabetes. The characteristic pattern is:

- an increase in total and LDL cholesterol;
- a reduction in HDL cholesterol; and
- an increase in triglycerides.

The abnormal lipid profile may improve as the diabetes comes under control. Cholesterol and triglycerides should be checked at the first assessment, but any decision on treatment should be deferred until follow-up as drug treatment may not be necessary. The subsequent approach to the patient will depend on whether or not she has established cardiovascular disease. For the secondary prevention of cardiovascular disease, treatment with a statin should be started if total cholesterol is >5·0 mmol/l, with a treatment target of <5·0 mmol/l. Clinical evidence supports the use of simvastatin[12] and pravastatin,[13] but this is probably a class effect of the statins.

If the patient does not already have cardiovascular disease, then there are two possible approaches. It has been argued that because patients with diabetes have a very high cardiovascular risk, and many will have cardiovascular disease that is clinically silent, they should all be treated for primary prevention in the same way as they would for secondary prevention.[14] The other approach is to perform a fasting lipid profile for total cholesterol and HDL cholesterol, and to use the ratio of total cholesterol:HDL cholesterol to calculate the patient's predicted coronary risk from risk tables.[15] If the predicted risk is >15% over ten years, then she should be started on a statin, and the total cholesterol concentration is measured to determine the response to treatment with a target of <5·0 mmol/l.

### OTHER MEASURES

The combination of diabetes, hypertension and dyslipidaemia in a middle-aged woman identifies a patient who is at a high risk of developing cardiovascular disease. Measures to control these risk factors will take a considerable time to take full effect, and the results of the UKPDS show that control of glycaemia will have at best a minor effect in reducing cardiovascular risk[8] if the patient cannot be controlled on metformin alone.[7] Control of hypertension and dyslipidaemia may be more effective, but adjustment or initiation of therapy will need to be delayed until follow-up. Other measures that can be considered in this patient to reduce cardiovascular risk are the prescription of aspirin[16] or ramipril.[17]

The Heart Outcomes Prevention Evaluation (HOPE) study examined the effects of 10 mg ramipril (or placebo) in 9,297 high risk patients. Diabetes was a pre-defined subgroup, and 3,577 patients with diabetes were recruited who had evidence of vascular disease, or who had diabetes and one other cardiovascular risk factor (cholesterol >5·2 mmol/l, hypertension, microalbuminuria, history of smoking).[17] The primary combined endpoint of myocardial infarction, stroke and cardiovascular death was significantly reduced by 25%, with a one-third reduction in stroke. This reduction was seen both in patients with and without previous cardiovascular disease, and the benefit was greater than could be attributed to any decrease in blood pressure. The development of overt nephropathy was also reduced. This suggests that treatment with ramipril has vasculo-protective and reno-protective properties in people with diabetes, and should be prescribed for diabetic patients with existing cardiovascular disease or who have a high risk of disease because of the presence of cardiovascular risk factors.

### FOLLOW-UP

Type 2 patients without complications of diabetes do not need to be referred to a hospital diabetic clinic if the practice team can carry out the full range of screening procedures and referrals to other health professionals. Most areas will have a local diabetes protocol that includes recommendations as to when the patients should be referred to the hospital diabetes clinic. This may include advice if there is uncertainty if the patient has Type 1 or Type 2 diabetes, the development of complications, or failure to achieve control of blood glucose or cardiovascular risk factors. The timing of reviews depends on several factors, e.g. if the patient's diabetes is poorly controlled they should be supervised more frequently than a well-controlled patient. A newly diagnosed patient should be seen at least every three months in the first year.

### CONCLUSIONS

- Management of a 53-year-old woman with newly diagnosed Type 2 diabetes can now be based on clinical evidence.
- Hypertension and dyslipidaemia are additional risk factors rendering this patient at high risk for future cardiovascular events; smoking status and microalbuminuria status should also be ascertained.
- The initial treatment of diabetes will be based on diet, and oral agents will be required at a later stage if $HbA_{1c}$ targets are not reached.
- The control of hypertension may require three or more agents to reach the target blood pressure of 140/80.
- Statins are of proven benefit for secondary prevention, and are probably of benefit for primary prevention.
- Dyslipidaemia may improve with diet and with control

of diabetes, and drug treatment should not be started immediately.
- Aspirin and ramipril are both of proven benefit in reducing future cardiovascular events.
- Modern management of Type 2 diabetes combines control of glycaemia and cardiovascular risk factor reduction.

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