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Type 2 Diabetes Mellitus in Family Practice: Prevention and Screening

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1. Introduction

There is now a worldwide epidemic of Type 2 Diabetes Mellitus. It is a condition associated with numerous complications, which may well be present even at the time of diagnosis. Effective treatments are available but there is no known cure. The focus therefore is on both prevention and early detection by screening, with a view to preventing or delaying complications.

This chapter gives a brief overview of the evidence for prevention of Type 2 Diabetes (behavioural and pharmacological) and describes various approaches to screening, from an international perspective, together with their relative advantages and disadvantages. Clinical opportunistic screening will be discussed and compared with population screening. The international guidance for screening for Type 2 Diabetes will be reviewed and a summary of the evidence relating to the psychological effects of screening, as well as the costs and cost-effectiveness of the various types of screening programmes, will be presented.

2. The rationale for preventing Type 2 Diabetes and its complications

The prevalence of diabetes, particularly Type 2 Diabetes, is increasing on a worldwide scale. The greatest increases are being seen in developing countries such as those in South East Asia (International Diabetes Federation, 2003; Ramachandran et al., 2010). There are many reasons for this increase in prevalence but it is generally thought that increasing rates of obesity and lack of exercise predicated upon a pre-existing genetic tendency towards diabetes are fuelling the epidemic (Stumvoll et al., 2005).

Diabetes is a common condition affecting 5.4% of the UK population (over 2.3 million people) and the vast majority of these have Type 2 Diabetes (The NHS Information Centre, 2010) with a higher prevalence amongst older people. For example between 10% and 20% of patients aged 60 to 79 years in the European prevalence study (DECODE) had diabetes (DECODE Study Group, 2003). In our own study (Evans et al., 2008), over a period of 20 years, there had been a trebling of the prevalence of Type 2 Diabetes in one family practice in the UK (Figure 1).

Type 2 Diabetes has a significant impact on life expectancy. It has been estimated that having diabetes reduces life expectancy by 17 years in males and 20 years in females, who are diagnosed with the condition at the age of 45 years (Yorkshire & Humber Public Health Observatory, 2007). It is also generally acknowledged that a large number of patients with

Type 2 Diabetes remain undiagnosed. For example in the US, one third to one half of people with Type 2 Diabetes are undiagnosed and thus untreated (Engelgau et al., 2000).

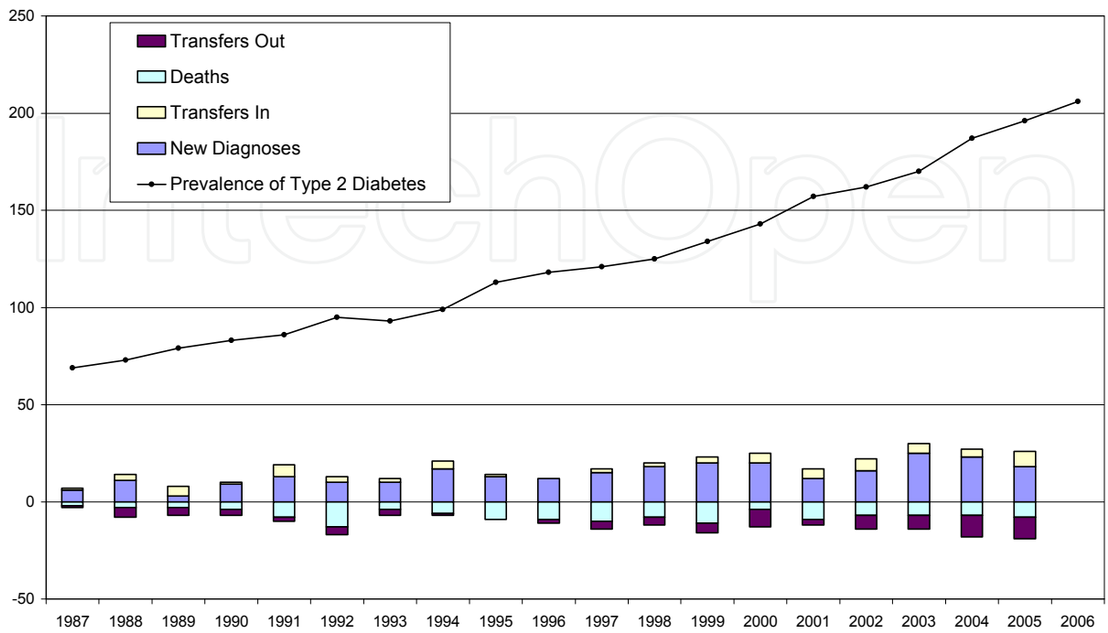

Fig. 1. Increasing prevalence of Type 2 Diabetes in one UK family practice
From: Evans, P., Langley, P., Pereira Gray, D. Diagnosing Type 2 diabetes before patients complain of diabetic symptoms – clinical opportunistic screening in a single general practice. *Family Practice,* 2008; 25(5): 376-381, by permission of Oxford University Press.

Type 2 Diabetes is a relatively unusual chronic disease in that it can have a long latent period prior to clinical diagnosis, perhaps up to 10 years (Harris et al., 1992). Patients who eventually develop Type 2 Diabetes often pass through a phase of intermediate hyperglycaemia when their blood glucose levels are elevated but not above the diagnostic threshold for Type 2 Diabetes. These intermediate states are collectively called Prediabetes and include Impaired Fasting Glucose diagnosed on a fasting plasma glucose test or Impaired Glucose Tolerance diagnosed on an oral glucose tolerance test. More recently the term Impaired Glucose Regulation has been proposed to include these borderline hyperglycaemic states (Diabetes UK, 2009).

Both conditions are increasingly prevalent and it has been estimated that 5.1% of the UK population aged 20 to 79 may have Impaired Glucose Tolerance (International Diabetes Federation, 2003). Prediabetes carries an increased risk of progression to Type 2 Diabetes although this can vary widely, dependent on ethnicity and other factors (Unwin et al., 2002). Nevertheless, it is widely accepted that patients with these conditions are at greater risk of both Type 2 Diabetes and cardiovascular disease (Cautinho et al., 1999), and interventions designed to prevent diabetes have, in the main, been targeted at this group (Tuomilehto et al., 2001).

Type 2 Diabetes is also unusual in that, unlike other conditions such as hypertension, a large proportion of patients have complications at clinical diagnosis. In the Hoorn Study, for example, at entry into the study, 39.5% of patients had ischaemic heart disease (Spijkerman et al., 2004) and 48.1% had impaired foot sensitivity (Spijkerman et al., 2003). In addition,

since it is likely that having a high blood glucose for years on end may represent a harmful "legacy effect" (Del Prato, 2009), there is a greater imperative to diagnose early and theoretically reduce diabetic complications in later years.
These characteristics raise the logical possibility of preventing patients progressing to Type 2 Diabetes during this latent phase and hence reducing the complications associated with Type 2 Diabetes, both at diagnosis and afterwards.

2.1 Prevention of Type 2 Diabetes

There is now substantial evidence that progression to Type 2 Diabetes can be prevented or delayed in patients at high risk of Type 2 Diabetes (including those with Impaired Glucose Tolerance or Impaired Fasting Glucose), both by behavioural interventions (Knowler et al., 2002; Ramachandran et al., 2006; Tuomilehto et al., 2001) and by pharmacological interventions (Gillies et al., 2007; Salpeter et al., 2008).
Behavioural interventions included lifestyle interventions promoting weight loss, increased physical activity and dietary modification (Tuomilehto et al., 2001). In the Finnish Diabetes Prevention Study, this was achieved by offering detailed and individualised counselling to achieve set lifestyle goals. Prolonged engagement with a dietary counsellor was needed – for example, the median number of sessions per participant was 20 (Tuomilehto et al., 2001).
Pharmacological interventions have included rosiglitazone (Gerstein et al., 2006), troglitazone (Buchanan et al., 2002), acarbose (Chiasson et al., 2003), metformin (Knowler et al., 2002), and orlistat (Torgerson, 2004). A recent meta-analysis has shown that lifestyle interventions can produce a 50% relative risk reduction in the incidence of Type 2 Diabetes at one year (Yamaoka & Tango, 2005). Typically these interventions are in high-risk individuals such as those with Prediabetes (usually Impaired Glucose Tolerance) and interventions are targeted at halting or slowing β-cell dysfunction and hence incident cases of Type 2 Diabetes.
Our previous work in defining an effective pragmatic strategy for diabetes prevention using general practitioner (GP) databases identified a large proportion of patients with Prediabetes (Greaves et al., 2004). We subsequently developed an educational package for patients with Prediabetes and their healthcare professionals. This package known as WAKEUP (Ways of Addressing Knowledge Education and Understanding in Prediabetes) was found to be acceptable to both patients and health professionals (Evans et al., 2007).
As well as issues relating to clinician education, there are also many practical issues in delivering a national diabetes prevention programme. It is generally acknowledged that the intensity of the lifestyle intervention delivered in these trials is just not feasible in routine practice (Heneghan et al., 2006). A more pragmatic, yet effective, intervention is needed and several research groups in the UK are working on this issue, as are colleagues in Australia (Kilkkinen et al., 2007; Laatikainen et al., 2007).

2.2 Prevention of the complications of Type 2 Diabetes

Once a patient has developed Type 2 Diabetes, the major aim of clinical care is to prevent complications and morbidity related to the disease. The commonest complication of Type 2 Diabetes is cardiovascular disease (American Diabetes Association, 2011) manifested as coronary artery disease, peripheral vascular disease or carotid artery and other cerebrovascular diseases. It is generally acknowledged that patients with Type 2 Diabetes have a raised cardiovascular risk and this may well be present before a clinical diagnosis is made (Hu et al., 2002). Some studies have shown that this risk is equivalent to that of a patient of the same age who does not have diabetes but has already had a coronary event

(Haffner et al., 1998). Hence, Type 2 Diabetes is often termed a "coronary risk equivalent", although this has been contradicted recently in a systematic review and meta-analysis (Bulugahapitiya et al., 2009).
Reducing cardiovascular risk in patients with Type 2 Diabetes is therefore a priority. However, what has yet to be definitively established with regard to screening is whether early diagnosis reduces the risk of complications developing. Our previous work (Evans et al., 2008) showed that patients diagnosed by screening had a significantly lower median HbA1c (1.1% lower) than those presenting with symptoms. As the HbA_{1c} is so closely related to outcomes in Type 2 Diabetes (UK Prospective Diabetes Study (UKPDS) Group, 1998), it is likely that health benefit will ensue for those patients diagnosed by screening - however this is not proven as yet.

2.3 Effectiveness of treatment of Type 2 Diabetes

Effective treatments for the disease are available through lifestyle advice, oral hypoglycaemic drugs, and insulin. Most of the health economic models (e.g. Gillies et al., 2008; Hoerger et al., 2004; Waugh et al., 2007) developed to assess the cost-effectiveness of screening for diabetes include an assessment of the effectiveness of treatment for Type 2 Diabetes, comparing the screened and unscreened groups. As yet, there are no long-term studies of the effectiveness of treatment after diagnosis of Type 2 Diabetes in screened and unscreened groups, so health economic simulations are needed - with their accompanying assumptions.
These models use data from the UK Prospective Diabetes Study (UKPDS, 1998) which showed that intensive treatment of Type 2 Diabetes reduced the risks of microvascular complications but not macrovascular events. However, subsequent follow up after the trial had finished did show a reduction in macrovascular events in the intensive arm (Holman et al., 2008).
National guidance for the effective treatment of Type 2 Diabetes in primary and secondary care exists in the UK (National Collaborating Centre for Chronic Conditions, 2008; National Institute for Health and Clinical Excellence, 2009) and in the US (American Diabetes Association, 2011). These guidelines are evidence-based and should improve outcomes in patients with Type 2 Diabetes. Effective treatments are targeted at optimising cardiovascular risk factors, including serum lipids, HbA_{1c} and blood pressure. In addition, GPs in the UK also receive incentivised payments under the Quality and Outcome Framework when patients with Type 2 Diabetes reach the glycaemic, blood pressure and lipid targets (Roland, 2004).

3. General principles of screening

Screening in medicine is a search process. An examination or a test is offered to asymptomatic people "to classify them as likely or unlikely to have the disease that is the object of screening" (Morrison, 1998). People who are likely to have the disease are then investigated further to arrive at the final diagnosis. The assumption is that an effective intervention is available.
An early diagnosis and treatment activity applied in large groups is often described as 'mass screening' or 'population screening' (Morrison, 1998). Population screening in medicine was introduced in the mid-twentieth century and was applied to a number of diseases including tuberculosis, and more recently to cervical cancer, breast cancer and colon cancer. It was also attempted for diabetes.
There are two inevitable consequences of all screening programmes, namely the occurrence of what are called 'false positive' or 'false negative' results. False positives are people whose

test is positive for the disease being sought but who prove not to have the disease. Patients suffer additional investigations and anxiety. People classified as false negative are those who actually have the disease but the test fails to detect it. The patient then suffers the consequences of undiagnosed disease.

3.1 Evaluation of screening programmes

Before any screening programme is introduced, its advantages and disadvantages must be carefully assessed. The general principles of screening were initially set out in the late 1960s (Wilson & Jungner, 1968). Since then, the criteria have been updated (UK National Screening Committee, 1998) and programmes now need to meet a number of criteria. These broadly relate to the health condition, the screening test, the availability of effective treatment, and the screening programme itself. Figure 2 outlines our summary of the criteria currently used by a variety of international health organisations to evaluate population screening. Based on such criteria, there is as yet no justification for population-based screening for Type 2 Diabetes (Borch-Johnsen et al., 2003; Waugh et al., 2007; Wareham & Griffin, 2001), although the case is becoming stronger. Whilst Type 2 Diabetes meets many of the criteria for screening, the main argument against population-based screening is that uncertainty remains about the true benefits arising from the early detection of Type 2 Diabetes through such programmes. In addition, it is unclear whether the economic cost of screening can be justified.

The results of the ADDITION study (Echouffo-Tcheugui et al, 2009 ; Lauritzen et al., 2000; Sandbaek et al., 2008), which will assess the effectiveness of screening for Type 2 Diabetes combined with the provision of intensive treatment to newly-diagnosed patients, will be available soon and will provide much-needed evidence for or against screening.

4. Screening for Type 2 Diabetes

Type 2 Diabetes may well be a suitable disease for screening - it is a serious disease, being associated with many complications, especially in the eyes, heart, kidneys, and limbs and it shortens the expectation of life considerably. Screening tests consist of blood glucose tests and/or oral glucose tolerance tests. These tests are relatively cheap with a blood glucose test costing only £0.48 (US$0.77) in the UK National Health Service. Blood glucose tests and oral glucose tolerance tests have no adverse effects for the patient apart from the inconvenience of having blood tests and the very rare complications of venepuncture.

There are two broad approaches to screening for Type 2 Diabetes – population or opportunistic screening. They have different advantages and disadvantages.

4.1 Population screening

Population screening, as its name implies, is based on a defined population and aims to screen every person in this population (Engelgau et al., 2000). It includes ‘universal’ screening, which attempts to define the prevalence of diabetes by screening a whole community (Knowler et al., 1978; Sharp, 1964), and ‘targeted’ or ‘selective’ screening, which attempts to screen a defined sub-group of the population (Engelgau et al., 2000). In either case, a suitable test such as a screening blood glucose test is offered to a defined population.

The Condition

1. The condition is an important health problem for the individual, and the community or population [a,b,c]
2. The natural history of and risk factor(s) for the condition are understood [a,b,c]
3. There is a recognisable pre-clinical (asymptomatic) stage or an early symptomatic stage in which the condition can be diagnosed [a,b,c]
4. All cost-effective interventions to prevent the condition have been implemented as far as possible [a]

The Test

5. There is a simple, safe, precise and validated screening test [a,b,c]
6. The screening test is acceptable to the population [a,b,c]
7. The distribution of test values in the target population is known and suitable cut-off levels are defined and agreed [a]
8. There is an agreed policy on the further investigation of individuals with a positive screening test result [a]

The Treatment

9. There is an acceptable and effective treatment or intervention for individuals identified through screening [a,c]
10. There is evidence that early treatment leads to better outcomes than late treatment [a,b,c]
11. There are clear, evidence-based policies on which individuals should be offered treatment and the appropriate treatment to be offered [a,c]

The Screening Programme

12. There is evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity [a]
13. The information provided about the test and its outcome must be of value and readily understood by the individual being screened [a]
14. There is evidence that the complete screening programme (test, diagnostic procedures, treatment/intervention) is clinically, socially and ethically acceptable to health professionals and the public [a,c]
15. The benefits from the screening programme outweigh the physical and psychological harm caused by the test, diagnostic procedures and treatment [a,c]
16. The economic costs of the screening programme (including testing, diagnosis, treatment, administration, training, and quality assurance) are balanced in relation to expenditure on medical care as a whole [a,b,c]
17. There is a plan for the organisation, management and monitoring of the screening programme and an agreed set of quality assurance standards [a,c]
18. There are adequate staffing and facilities for testing, diagnosis and treatment [a,b,c]
19. Evidence-based information, explaining the consequences of testing, investigation and treatment, is available to potential participants to help them make an informed choice [a]
20. Screening will be a systematic, ongoing process and not an isolated one-off effort [a,c]

Fig. 2. Criteria for assessing the value of screening programmes
(Criteria adopted by: [a] UK National Screening Committee; [b] American Diabetes Association; [c] World Health Organization).

Historically, screening was offered directly to people in communities and sometimes directly to people in the street – UK examples include surveys undertaken in Bedford (Sharp, 1964), Rotherham (Girt et al., 1969), and Birmingham (Birmingham Diabetes Survey Working Party, 1976). However, the yield was small as many people at low risk were approached and some of those detected failed to consult their GP. Costs per new case

detected were therefore high and this approach was abandoned. Community screening could be cost-effective if the prevalence of Type 2 Diabetes in the community was extremely high, although this is rarely the case.

The populations most often identified for screening include people selected because they have one or more risk factors for Type 2 Diabetes. These most commonly include older age, obesity, a family history of diabetes, and hypertension. This approach increases the likelihood of finding new cases and so improves the efficiency of the screening process.

Risk factors are most commonly known to GPs. They are not known to hospitals, as they do not hold the medical records of populations, only those people referred to them. Hence, population screening nowadays is most commonly based on people selected from the population registers of people registered with family practices. This has meant that most of the research reports have come from those countries in which the health system is based on family practices, i.e. Australia, Canada, New Zealand, the Netherlands, the UK, Denmark, and registration-based systems in the USA.

Population screening has several important advantages. It is mathematically precise, readily reproducible, and can operate largely independent of the clinical skills of the doctors and nurses in the family practices. It is easy to transpose arrangements across areas and countries.

Population screening has several important disadvantages. Unless whole community populations are used, various techniques have to be employed to determine potential sub-groups at risk. Selection has to be made on the basis of various clinical risk factors as set out below. This can involve searching of medical records or extraction of risk factors such as age and Body Mass Index (BMI) (Greaves et al., 2004) directly from the GP database or applying external criteria such as those of the American Diabetes Association to the GP's electronic record (Woolthuis et al., 2007). However, there are always people, including those at risk, who decline to accept the offer of screening for a variety of reasons.

The process then involves communication with the people in the target population, usually by writing to them and offering them an appointment. Some people will want to change their appointment and staff of the practice need to accommodate this. Some people will not come and may need to be sent a further appointment. Those who do come need to be recorded. Then, if the screening process is separate from the clinician, the clinician has to be informed and take action. In some US studies, primary care clinicians have not always responded appropriately (Ealovega et al., 2004). There may be a difference in attitude to those tests initiated by clinicians themselves and those tests initiated by others.

It is inevitable that population screening carries administrative costs over and above the cost of the screening investigations. Nevertheless, in the UK, the National Health Service has recently instituted a comprehensive vascular risk assessment programme, known as 'NHS Health Checks' (Department of Health, 2008). These checks are offered to patients aged 40 to 74 years old who do not have existing vascular disease or diabetes. This is a two-step process and diabetes risk is estimated using a self-completed questionnaire, followed by a blood test if appropriate. It is envisaged that the whole of this age group in the population will be screened once every five years. Although it is considered reasonable to include a diabetes assessment within a global cardiovascular risk assessment, there is some current concern about the implementation of this programme (Khunti et al., 2011).

In summary, therefore, population screening, usually of high-risk sub-groups, is the commonest form of screening performed world wide, but in practice is undertaken only in richer and developed countries. Hence, one profound implication is that population

screening may well be too costly to be undertaken in developing countries and this is doubly serious as many Asian countries have some of the highest levels of prevalence of Type 2 Diabetes in the world, e.g. 10% in China (Ramachandran et al., 2010).

4.2 Clinical opportunistic screening

Clinical opportunistic screening is quite different from population screening and is a form of clinical case finding. It is essentially an extension of ordinary clinical care in family practice. The key difference from population screening is that the patient, rather than the clinician, makes the appointment. In clinical opportunistic screening, the patient makes the appointment to go to the family practice and then the clinically alert doctor or nurse takes advantage of the patient's presence in the consulting room to offer screening, based on their risk factor profile.

This process has a long tradition in family practice and the whole basis of determining how many people smoke, drink heavily, are overweight or obese, or have raised cholesterol levels has been done in family practices without any national screening programmes. Since more clinical conditions are screened for opportunistically than are screened for by formal population programmes, opportunistic screening can be seen as the usual method of screening. It has just not been recognised as such.

The introduction of computer systems in UK family practices (since the 1980s) has enabled generalist doctors and nurses – for the first time – to organise, handle, and retrieve data live during consultations. Computers have made the family practice consultation much more efficient and opportunistic screening is one aspect of this.

Clinical opportunistic screening has several advantages. Firstly, this process eliminates most of the costly administrative overheads associated with population screening. Secondly, since the offer of screening is made within a therapeutic and trusting patient-doctor relationship, acceptance rates are generally high. An important advantage is that the screening process is offered by the doctor who will care for the patient if the disease is diagnosed, so that, if the test is positive, treatment can start immediately. Thirdly, the relatively high contact rate that people have with their primary health care team underpins clinical opportunistic screening. In the UK, The NHS Information Centre for Health and Social Care (2009) reports that the average contact for adults with their family practice is 5.5 encounters per year of which 3.4 per patient per year are with the doctor. This is important in that the health system offers the doctor repeated opportunities to screen; if a test is missed on one occasion when the patient is distressed or in no state to be screened, or if the doctor simply forgets, then the doctor can be confident that the average patient will be seen again within about four months.

Fourthly, clinical opportunistic screening exploits the key fact that it is family practice, and only family practice, which has the risk factor data and often knows it very well. For example, GPs are spending more and more of their time seeking to alter risk factors for disease. They screen for and increasingly find and then treat hypertension, itself a risk factor for Type 2 Diabetes and also for obesity which is all too obvious to the clinician. Other risk factors such as a positive family history may be very well known too as the family doctor will have often treated the older family members for diabetes and may still be doing so. Fifthly, this is the only system which can be undertaken in developing countries and is possible wherever there are generalist doctors. Fortunately, family medicine and

computerisation of family practice records is spreading steadily around the world, hence the potential for this approach is increasing rapidly worldwide.
In one recent method, university staff determined the risk groups and worked with a group of associated family practices to develop a 'flagging system' which jogged the doctor's memory when at risk patients are seen (Woolthuis et al., 2009). The authors concluded that because it was 'embedded within daily care' and achieved a high uptake rate, this approach was feasible and inexpensive; however, no estimate of the screening costs was reported.
Clinical opportunistic screening has some important disadvantages. Realistically, it cannot be expected to cover the entire at-risk population and it is dependent on the patient consulting for some reason. It also depends on the clinical alertness of the family physicians and practice nurses. This is not standard, and there are inevitable variations in clinical skills, which means variations in the screening process being delivered. The offer of clinical opportunistic screening is a judgement and different clinicians will make different judgements at different times. These types of interventions therefore cannot be completely standardised. Hence, they have been criticised by some as inefficient (Law, 1994) and can be seen as untidy, and potentially unpredictable. Furthermore, patients vary greatly in their emotional state in consultations and, if they are upset with anxiety, depression or having just received bad news, it becomes inappropriate to offer screening.

4.3 International guidelines on screening for Type 2 Diabetes

Whilst there is not yet sufficient evidence to support the introduction of general population screening, there is broad support for screening programmes that focus on defined sub-groups of the population who are at higher risk of developing Type 2 Diabetes. A number of organisations have issued position statements relating to targeted or opportunistic screening for Type 2 Diabetes (e.g. American Diabetes Association, 2011; Diabetes UK, 2006; World Health Organization, 2003). These make recommendations about the patient sub-groups that should be considered for screening, the frequency of screening, where screening should take place, and the preferred screening test.

4.3.1 Who should be offered screening and how frequently?

It is generally accepted (American Diabetes Association, 2011; Diabetes UK, 2006) that clinical judgement and patient preference should guide decisions about screening for Type 2 Diabetes. Several organisations in the UK, Europe and USA (American Diabetes Association, 2011; Diabetes UK, 2006; Paulweber et al., 2010) have made recommendations about the risk factors that might indicate a need for screening and these are summarised in Figure 3.
The optimal frequency of screening is not known. However, Diabetes UK (2006) and the American Diabetes Association (2011) recommend that health professionals should consider proactively screening adults at risk of developing the condition every three years. Both organisations note that it may be necessary to screen more frequently, for example, where individuals are overweight and have one or more of the other risk factors shown in Figure 3.

4.3.2 Where should screening take place?

Currently, the consensus view is that screening should take place in a clinical setting, with testing offered by health care providers, based on an assessment of the individual patient. Diabetes UK argue that "screening is probably most-effective when performed as part of a general health review in primary and community care services, when other cardiovascular

risks can be measured … and appropriate advice is immediately available" (Diabetes UK, 2006; p.6).

To achieve screening in 'hard-to-reach' groups, particularly ethnic minorities in developed countries, other locations have been suggested, including religious and community venues or assessments in the workplace (Grant et al., 2004; Oberlinner et al., 2008; Porterfield et al., 2004; Somannavar et al., 2008; Tabaei et al., 2003), although the evidence base for screening in these settings is limited at present.

One potential disadvantage is that community screening of this nature does not reach the groups who are most at risk of developing the condition, and may inappropriately test those who are at low risk or those already diagnosed with diabetes. Diabetes UK (2006) supports community screening for patient groups who do not routinely access family practice services, *provided that* the screening process is guided by clear protocols, staff receive appropriate training, and good medical support is available from local health services. In contrast, the American Diabetes Association (2011) does *not* recommend community screening, even for high-risk populations, because there is a risk that those screened may not seek or be able to access appropriate follow-up and care.

4.3.3 Which screening test should be used?

There is insufficient evidence to identify a single ideal screening test (Waugh et al., 2007). A range of tests exist which might be used for screening purposes and these vary in their sensitivity and specificity, as well as their convenience, acceptability and cost (Cox & Edelman, 2009). Sensitivity is the "proportion of true positives that are correctly identified by the test", while specificity is the "proportion of true negatives that are correctly identified by the test" (Altman & Bland, 1994).

Diabetes UK (2006)
The following people should be offered screening for diabetes every 3 years: a. White people aged over 40 years and people from Black, Asian and minority ethnic groups aged over 25 years, with one or more of the following risk factors: • A first degree family history of diabetes (parents or siblings with diabetes); • Overweight, obese or morbidly obese (body mass index of 25-30 kg/m^2 and above) and a sedentary lifestyle; • Waist measurement of 94 cm (37 inches) or above for White and Black men, and 80 cm (31.5 inches) or above for White, Black and Asian women, and 90 cm (35 inches) or above for Asian men. b. People with ischaemic heart disease, cerebrovascular disease, peripheral vascular disease or treated hypertension; c. Women who have had gestational diabetes who have tested normal following delivery (screen within 6 weeks of delivery, then 1 year post-partum and then three-yearly); d. Women with polycystic ovary syndrome who have a body mass index of 30 kg/m^2 or more; e. People who are known to have impaired glucose tolerance or impaired fasting glycaemia; f. People who have severe mental health problems; g. People who have hypertriglyceridaemia not due to alcohol excess or renal disease.

IMAGE guidelines (Paulweber et al., 2010)

a. White people aged over 40 years or people from Black, Asian and minority ethnic groups, aged over 25 years with one or more of the following risk factors:
   - A first degree family history of diabetes; and/or
   - Body mass index over 25 kg/m^2; and/or
   - Waist measurement of $\geq$ 94 cm for White and Black men and $\geq$ 80 cm for White, Black and Asian women, and $\geq$ 90 cm for Asian men; and/or
   - Systolic blood pressure $\geq$ 140 mm Hg or diastolic blood pressure $\geq$ 90 mm Hg or treated hypertension; and/or
   - HDL-cholesterol $\leq$ 0.35 g/l (0.9 mmol/l) or triglycerides $\geq$ 2g/l (2.2 mmol/l) or treated dyslipidaemia.

b. Women with a history of gestational diabetes or with a child weighing > 4 kg at birth;

c. People with history of temporarily induced diabetes – e.g. steroids;

d. People who have ischaemic heart disease, cerebrovascular disease, peripheral vascular disease;

e. Women with polycystic ovary syndrome who have a body mass index $\geq$ 30 kg/m^2;

f. People who have severe mental health problems and/or receiving long term antipsychotic drugs;

g. People with a history of Impaired Glucose Tolerance or Impaired Fasting Glucose.

American Diabetes Association (2011)

Screening for diabetes should be considered every 3 years (with consideration of more frequent testing depending on initial results and risk status):

a. In all adults who are overweight (body mass index $\geq$ 25 kg/m^2) and have one or more of the following risk factors:
   - Physical inactivity
   - Family history of diabetes (first-degree relative, i.e. parents or siblings with diabetes);
   - High-risk race/ethnicity (e.g. African-American, Latino, Native American, Asian-American, Pacific Islander);
   - Women who delivered a baby weighing >9lbs or were diagnosed with gestational diabetes mellitus;
   - Hypertension (blood pressure 140/90 mm Hg or higher or on therapy for hypertension);
   - HDL cholesterol of 35 mg/dl (0.90 mmol/l) or less and/or a triglyceride level of 250 mg/dl (2.82 mmol/l) or more;
   - Women with polycystic ovary syndrome;
   - A_{1c} $\geq$ 5.7%, Impaired Glucose Tolerance or Impaired Fasting Glucose on previous testing;
   - Other clinical conditions associated with insulin resistance (e.g. severe obesity, acanthosis nigricans);
   - History of cardiovascular disease.

b. In the absence of the above criteria, screening should begin at age 45 years.

Fig. 3. UK, European and US Guidance on who should be screened for Type 2 Diabetes

Options include the fasting blood glucose test, the oral glucose tolerance test, random (or casual) blood glucose test, or a fasting capillary blood glucose test. More recently, it has been suggested that the glycated haemoglobin (HbA_{1c}) test might also be appropriate for screening, because it does not require fasting and reflects longer-term glycaemia rather than a value at a single time point (American Diabetes Association, 2011; Bennett et al., 2007; Saudek et al., 2008). HbA_{1c} may also have more relevance to clinicians dealing with patients who have diabetes. Urine testing is not strongly recommended for screening purposes, because it is less sensitive than the blood tests.

Currently, a fasting blood glucose test is recommended as the screening test for Type 2 Diabetes in the UK and the USA (American Diabetes Association, 2011; Diabetes UK, 2006). It is easier and faster to perform in clinical settings, more convenient and acceptable to patients, and less expensive than other tests. The latest US guidance (American Diabetes Association, 2011) also states that the HbA_{1c} and 2-hour 75g oral glucose tolerance test are appropriate tests to screen for diabetes. European guidance has tended to encourage the use of the oral glucose tolerance test as the gold standard diagnostic test (Waugh et al., 2007).

Diabetes UK (2006) suggest a fasting capillary blood test can be used for initial screening purposes, although this has lower sensitivity and specificity than venous blood glucose measurement and requires careful interpretation and feedback to the patient. Random (or casual) blood or plasma glucose testing can also be carried out if the patient has taken food or drink prior to the screening test; in this sense, it is practical but the results can be more difficult to interpret than those obtained via fasting tests.

Where a screening test result is suggestive of diabetes, it is recommended that a second, fasting test be repeated on a different day to exclude the possibility of laboratory error, unless the patient has classic symptoms of diabetes. Guidance (American Diabetes Association, 2011; Diabetes UK, 2006) exists for health professionals with regard to the interpretation of test results. This includes the action needed (e.g. further testing, appropriate referrals) as well as the patient education that is required when positive, borderline, or normal test results are received.

4.4 Approaches to screening

A number of targeted screening programmes have been piloted in the UK, Europe and the USA in the last decade (e.g. Echouffo-Tcheugui et al., 2009; Edelman et al., 2002a; Franciosi et al., 2005; Greaves et al., 2004; Goyder et al., 2008; Janssen et al., 2007; O'Connor et al., 2001; Woolthuis et al., 2009).

Many have employed a 'stepwise' approach, whereby participants progress through increasingly invasive screening procedures until they are diagnosed with diabetes or found not to have the condition. The number of steps in the screening process varies across studies.

Typically, in the first step, potential screening participants are identified by:

- their responses on a self-completed questionnaire that assesses their risk of diabetes, such as the FINDRISC (Saaristo et al., 2005), the Symptom Risk Questionnaire (Adriaanse et al., 2002) or the Diabetes Risk Score (Franciosi et al., 2005); or
- using the GP electronic medical records to search for people who match specific risk criteria (e.g. Greaves et al., 2004); or
- using a standardised risk calculator based on clinical data held on the computerised medical record to assess the patient's risk of diabetes, such as the Cambridge Risk Score (Griffin et al., 2000) or QDRISK (Hippisley-Cox et al., 2009).

A recent alternative approach has been the use of online self-completion risk tools to determine a person's risk of diabetes and hence the need for further action. Both the American Diabetes Association and Diabetes UK have online risk calculators available for the public to use (http://www.diabetes.org/diabetes-basics/prevention/diabetes-risk-test/; and http://www.diabetes.org.uk/riskscore respectively).

Individuals who are identified as being 'at risk' of diabetes after the first step are offered (by invitation letter or during a GP consultation) a blood test to directly measure their glucose levels. The initial test tends to be relatively simple and convenient; in some studies, this has been a random blood glucose or HbA_{1c} sample (which do not require prior fasting); in others, a capillary blood sample ('finger prick' test) has been used.

If the results of the initial blood test fall within the normal range, the participant does not progress to the next level, but may receive lifestyle advice. If the results of the initial test reveal glucose levels above a specified threshold, participants are invited back for further testing. At that stage, the screening test may require the patient to fast for a prescribed period prior to the blood sample or undergo a more complex and lengthy screening process, such as the oral glucose tolerance test.

Uptake of screening has varied across the studies and this may be a reflection of the type of test offered, how the invitation is made and where the testing takes place. In one study (O'Connor et al., 2001), the uptake of an initial random blood glucose test (offered via letter) was 44%. Where random capillary blood tests were offered, however, uptake was around 60-70% (Echouffo-Tcheugui et al., 2009). In one study, the reported uptake of a fasting capillary blood glucose test offered directly by the GP was 90% (Woolthuis et al., 2009). Further dropout is evident at the later stages of many of the stepwise screening processes, whereby individuals who have abnormal results in initial tests fail to return for further tests (Woolthuis et al., 2009), particularly where this involves more invasive or complex tests or where the patient is referred to an outpatient clinic (e.g. Franciosi et al., 2005; Janssen et al., 2007; O'Connor et al., 2001).

4.5 The St Leonard's Practice approach to screening for Type 2 Diabetes

The system of screening for Type 2 Diabetes in the St Leonard's Practice, Exeter, UK is one special form of clinical opportunistic screening (Evans et al., 2008). It does not employ any external resources to screen for risk factors. The process relies on the clinical alertness of the GPs and practice nurses, and the efficient protocol-driven screening of patients with chronic conditions known to be associated with Type 2 Diabetes. The doctors and nurses screen adult patients with cardiovascular or cerebrovascular disease, hypertension, hypercholesterolaemia, obesity, recurrent skin infections, or a positive family history of diabetes.

Its advantages are that it eliminates another layer of costs that arise from the involvement of an external agency, such as a university or medical school. It also means that people from external organisations do not see confidential medical records. It fosters professional interest amongst GPs in patients as people with individual risks. It also fosters professional pride in GPs in ultra-early diagnosis. It is possible to maintain the system year after year and it has been so maintained in this practice since 1987 (Evans et al., 2008). Clinical opportunistic screening has the advantage that, since so many blood tests are taken nowadays in family practice, it is often possible to add the blood glucose screening test to samples being taken already, thus saving the patient an additional blood test.

The main advantage of this system is that it can identify, year after year, two-thirds of all new cases of Type 2 Diabetes before a single symptom of diabetes has been reported by a patient (Evans et al., 2008).
Some family practices, including St Leonard's, operate personal lists (Pereira Gray, 1979). When these are in use, it is also possible to compare the performance between doctors. Its main advantage internationally is that the method is more easily reproducible in family practices around the world. All that is needed is an enthusiastic family practitioner or nurse and an efficient computerised medical record system. Both family practice and computer systems are spreading rapidly.
The disadvantages of the St Leonard's system are that the intervention is not standardised and that there are variations between the six doctor partners operating it. It is not yet known how easy it will be to roll it out into other family practices more widely and it may be difficult where morale is low or burnout amongst the doctors is a serious problem (Soler et al., 2008).

4.6 The psychological effects of screening

Marteau (1990) notes that the receipt of an invitation to participate in a cancer or general health screening programme can be enough to evoke anxiety for some patients. As one might expect, receiving a 'positive' result after the screening test can also cause negative emotional reactions. People are not always reassured, even by a 'normal' result, and other adverse psychological effects can occur. For example, a 'normal' result may reinforce an unhealthy lifestyle or perceptions of invulnerability, and make patients less likely to return for future screening (Marteau 1989).
Recently, studies in Europe and the USA have specifically explored the psychological effects of undergoing screening for Type 2 Diabetes and these tend to support the conclusions of Marteau's work. Some studies have assessed the impact of screening by asking patients to complete rating scales that measure their levels of anxiety, depression, and disease-specific worry (Eborall et al., 2007a; Park et al., 2008), or their health-related quality of life (Edelman et al., 2002b). Such studies have generally found no lasting or significant adverse psychological effects in terms of anxiety, depression, worry, or perceived quality of life after screening. However, there is some evidence that simply being invited for screening can increase state anxiety and that, six weeks after attending, anxiety is higher amongst people who have progressed further through the screening process, particularly those who were eventually diagnosed with diabetes (Park et al., 2008).
Other studies have explored patients' experiences of screening in more depth. One study, which interviewed people shortly after they underwent screening tests (Adriaanse et al., 2002), found most participants had positive views of the screening process and had not found it burdensome. Most individuals who had been newly-diagnosed with diabetes did not feel alarmed or concerned about their results. Many appeared to believe they had a 'mild' version of the condition that they could control, although they felt the required lifestyle changes would have a significant impact on their life. People whose test results were normal reported feelings of relief or reassurance but saw no reason to change their lifestyle. Only a quarter of this group intended to have their blood glucose tested in future. Another study, which interviewed participants at different stages of a stepwise screening process (Eborall et al., 2007b), reported similar findings but noted that the stepped nature of the screening process appeared to help participants to adjust psychologically.

The World Health Organization (2003) has cautioned that, as public awareness increases about the significance of a diagnosis of diabetes and its possible complications, the psychological effects of screening may become more marked. Marteau (1990) and Griffin et al. (2000) argue that some of the negative effects of screening can be avoided or reduced, if health professionals attend to the patient's psychological and information needs at each stage of the screening process, including the point of invitation, the test procedure itself, discussing the results, and later follow-up.

4.7 The economic cost of screening for Type 2 Diabetes

Economic modelling studies have been conducted to estimate the cost-effectiveness of screening for Type 2 Diabetes and Impaired Glucose Tolerance. In the UK, decisions about funding of interventions are made by the National Institute for Health and Clinical Excellence (NICE), based on cost-effectiveness. This body considers that interventions below an incremental cost-effectiveness ratio (ICER) threshold of £20,000 to £30,000 per quality-adjusted life-year (QALY) are cost-effective (National Institute for Health and Clinical Excellence, 2004).

One systematic review and economic modelling exercise (Waugh et al., 2007), which included four studies, reached the conclusion that screening for diabetes appeared to be cost-effective for people aged 40-70 years. Whilst screening was more cost-effective for the older age bands (50-69 and 60-69 years), even for people aged 40-49 years, the ICER for screening (when compared to a policy of not screening) was £10,216 per QALY. Screening was found to be more cost-effective for people who were hypertensive and obese and, for many groups, the costs of screening were offset by lower treatment costs in the future. However, because the most comprehensive model in the review came from the USA (Hoerger et al., 2004), the applicability of these findings in the UK was questioned.

A more recent modelling study (Gillies et al., 2008), based on data derived from England and Wales, concluded that screening for Type 2 Diabetes and Impaired Glucose Tolerance – combined with appropriate lifestyle or pharmacological interventions for those found to have Impaired Glucose Tolerance to delay or prevent diabetes – appeared to be cost-effective in a population aged 45 years with 'above-average' risk of developing diabetes. When comparing a policy of *not* screening to one of screening for Type 2 Diabetes *and* Impaired Glucose Tolerance, there were differential costs for each QALY gained, depending on whether diagnosis of Impaired Glucose Tolerance was followed by lifestyle interventions or by pharmaceutical interventions. The costs per QALY gained were £6,242 for screening followed by *lifestyle* interventions, and £7,023 for screening followed by *pharmacological* interventions. In contrast, the cost-effectiveness of a policy of screening for Type 2 Diabetes only was less certain. Here, compared to a policy of not screening, the estimated costs for each QALY gained in respect of screening for Type 2 Diabetes alone were £14,150.

The results of the above studies suggest that it may be more cost-effective to screen for Type 2 Diabetes *and* Prediabetes, rather than Type 2 Diabetes alone. The ADDITION study will also include a cost-effectiveness analysis of screening plus intensive intervention for Type 2 Diabetes and the results of this work are awaited (Lauritzen et al., 2000).

Other studies have attempted to determine the costs of targeted or opportunistic screening, based on the cost of identifying one new case of Type 2 Diabetes. In one US study (O'Connor et al., 2001), which used a two-step screening protocol (random blood glucose

followed by oral glucose tolerance test), one new case of diabetes was identified for every 40 high-risk patients screened. The uptake of screening was relatively low (44% of patients who were invited attended) and the screening costs per new case were estimated at $4,064 per new case identified.

More recently, a Danish study (Dalsgaard et al., 2010) has compared three different stepwise screening strategies for Type 2 Diabetes. In the first strategy, diabetes risk questionnaires were sent by the family practice to people aged 40-69 years and those found to be at high risk were asked to contact their GP to arrange a screening test. This strategy detected new cases of Type 2 Diabetes in 0.8% of the target population, at a cost of €1,058 (US$1,535)" per case. Two opportunistic screening programmes were also piloted. In these approaches, people who were consulting their GP were asked to complete the risk questionnaire in the waiting room and were either offered a screening test during the consultation (OP-direct) or asked to return for a fasting screening test at a subsequent consultation (OP-subsequent). The OP-direct strategy detected new cases of Type 2 Diabetes in 0.9% of the target population, at a cost of €707 (US$1,026) per case, while the OP-subsequent strategy detected Type 2 Diabetes in 0.5% of the target population, at a cost of €727 (US£1,055) per new case. The authors concluded that opportunistic screening can identify a similar proportion of new cases as mail-distributed questionnaires, but at lower cost.

5. Conclusions

The worldwide epidemic of diabetes, mainly Type 2 Diabetes, calls for a major response as, in some countries, prevalence now exceeds 10% of the whole adult population. Clinicians are seeking to prevent the condition developing and to screen for undiagnosed cases. Since Type 2 Diabetes is increasingly managed in family practice or primary care, education and support is important.

Prevention of Type 2 Diabetes is now possible through lifestyle alteration but, so far, only after expensive interventions. Drugs can aid prevention but adverse effects are a big issue. Research on simplifying lifestyle interventions is urgent. Once Type 2 Diabetes is diagnosed, health professionals can then intervene as early as possible, before symptoms develop, in order to prevent complications.

In the meanwhile, achieving earlier diagnosis of Type 2 Diabetes depends on screening. Population screening is likely to be introduced in richer countries and has recently started in the UK.

Clinical opportunistic screening in family practice offers an important alternative approach since it may well be more cost-effective, provides the quickest route to treatment, and can detect two-thirds of all new cases of Type 2 Diabetes in a defined population. However, the effectiveness of this type of screening in routine care without extra resources has only been demonstrated in one practice and needs replication. If the early reports are confirmed, then clinical opportunistic screening warrants further consideration as an affordable alternative to population screening, particularly in the developing world.

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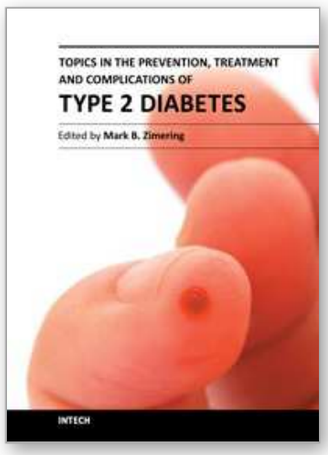

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Type 2 diabetes is estimated to affect 120 million people worldwide- and according to projections from the World Health Organization this number is expected to double over the next two decades. Novel, cost-effective strategies are needed to reverse the global epidemic of obesity which is driving the increased occurrence of type 2 diabetes and to less the burden of diabetic vascular complications. In the current volume, Topics in the Prevention, Treatment and Complications of Type 2 Diabetes, experts in biology and medicine from four different continents contribute important information and cutting-edge scientific knowledge on a variety of topics relevant to the management and prevention of diabetes and related illnesses.

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