



Living with Plenty Meeting the Challenge of Diabetes

The Twenty First Century Role of Pharmacy and Pharmaceutical Innovation
in the Prevention and Treatment of Diabetes Mellitus



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Novo Nordisk and the School of Pharmacy, University of London, are committed to working with people with diabetes and partners in the NHS and elsewhere to enhance the prevention and treatment of this and other conditions. The primary objectives of this report are to promote the further development of pharmacy based care as a cost effective part of the support available to people with diabetes and to highlight the importance of pharmaceutical innovation alongside that of facilitating relevant forms of health behaviour change.





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The Twenty First Century Role of Pharmacy and Pharmaceutical
Innovation in the Prevention and Treatment of Diabetes Mellitus

Summary and Recommendations

The number of people with diagnosed diabetes (as defined by their blood glucose levels) has doubled in the UK in the last decade, to a total of over 2.5 million. In addition there are likely to be 500,000 people with undiagnosed diabetes. However, worldwide most cases of diabetes already occur in Asia.

In developed countries diabetes and its consequences account for 5-10 per cent of health spending. This represents in excess of 0.5 per cent of global GDP. In the UK such data imply an annual expenditure of over £7 billion. About £1 in every £10 spent by the NHS on diabetes is accounted for by medicine costs, including all forms of insulin.

The rising prevalence of diabetes is linked to obesity, population ageing and better case recording. The average Briton now has a 10-20 per cent life-time chance of being diagnosed as having diabetes. Those most at risk in the South Asian and other communities are least likely to understand its causes. Effective prevention and better treatment are both urgent priorities. More effort should be made to enhance public understanding of diabetes.

Pharmacists have an important future role to play in delivering care to people at risk of – and with – diabetes. This will in part involve conducting health checks to identify risk factors and find early stage cases. Community pharmacists should support lifestyle changes through, for instance, weight loss, smoking cessation and self care programmes, and help individuals and families with diabetes to use medicines more effectively.

Type 2 diabetes accounts for 80 per cent or more of all cases. It is a progressive condition. If not treated appropriately via lifestyle changes (such as taking more exercise) and medicines it leads to disability and premature death. Having diabetes multiplies the harm caused by vascular disease risk factors such as smoking, raised cholesterol levels and high blood pressure.

Medicines such as statins and antihypertensives protect people with diabetes from heart attacks, strokes and other vascular diseases. Established anti-diabetic treatments help to lower blood sugar levels and also prevent harm.

New treatments with mechanisms of action such as those relating to the role of the intestinal peptide GLP-1 could have extended protective impacts. Bariatric ('stomach stapling') surgery is appropriate for treating gross obesity and may also slow or even reverse the progression of type 2 diabetes.

Approaching 400,000 people in the UK have type 1 diabetes, in which individuals' own defence cells destroy their pancreases. This condition seems most likely to affect people of European racial origin. Those living with it need insulin therapy.

Ultimately, stem cell based or allied techniques should lead to treatments that regenerate lost pancreatic tissues. But more immediate advances are likely to involve the development of 'artificial pancreases', using implantable blood glucose monitoring devices. Implantable glucose monitors and other forms of 'artificial pancreas' technology could worldwide improve the quality of life of millions of insulin users in the coming five to ten years.

Modern human insulin analogues are designed to help people improve their blood glucose control. There is evidence that they can help individuals to improve their quality of life and protect against unpleasant and potentially hazardous hypoglycaemic events. In future new generations of inhaled and oral insulins will further help to improve health outcomes and increase service user satisfaction.

Little more than one per cent (and less in the case of children) of British people with type 1 diabetes presently use insulin pumps for the routine management of their condition. The equivalent proportions in countries such as France, Sweden, Holland, Germany and the US are in the range of 10-20 per cent. This situation requires review in the light of present advances.

In England innovations such as the Quality and Outcomes Framework in the 2004 GPs' contract have led to important service improvements. Yet there is a need to further improve diabetes care and outcomes. The 2008 white paper *Pharmacy in England* recommended that pharmacists should extend the services they provide for diabetes prevention, case finding and treatment. More care for people with diabetes should be delivered in primary care settings.

It is important to ensure appropriate patient access to specialists. Increasing patient choice of and access to convenient local sources of cost effective support is also desirable. NHS remuneration systems should be adapted to promote more integrated diabetes care and better joint working between GPs and community pharmacists.

Individual and group support and/or 'therapeutic education' programmes can help people to adopt healthier lifestyles and take medicines more effectively. They are potentially highly cost effective. But to date only one person with diabetes in every ten has had access to such services. Their provision should be extended.

Bodies such as The National Institute for Health and Clinical Excellence and its equivalents conduct useful work. However, the human and financial costs of delaying patient access to useful new therapies for diabetes may prove high. Care should be taken to minimise this hazard.

Successful public health improvement will in the twenty first century demand both new medicines and health behaviour changes. Pharmacy can combine the delivery of both these vital ingredients for the prevention and treatment of diabetes.

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Introduction

The term diabetes refers to a group of complex disorders that are primarily defined by a hazardously raised level of blood glucose (sugar). This results either from a loss of the body's capacity to produce the hormone insulin, or from reductions in the latter's ability to induce normal glucose uptake by muscle cells and organs such as the liver.

Descriptions of diabetes, at least as a condition characterised by increased rates of (abnormally sweet tasting – hence mellitus) urination, date back to ancient Egypt and Greece – see Box 1. But it is in modern societies that the prevalence of the main forms of diabetes has risen to what can be considered pandemic levels. Some observers believe that increases in the occurrence of diabetes will in future decades cut short the rises in life expectancy that have been associated with economic development during the twentieth century.

Diabetes lies at the heart of the nexus of conditions that are on occasions referred to as 'the metabolic syndrome' (Alberti 2008a, 2008b). This encompasses traits such as central obesity, raised blood pressure and a depressed level of high density (cholesterol carrying) lipoprotein. Such factors are intimately linked to morbidity and mortality from heart disease and other vascular conditions. Diabetes exacerbates the risks people have of suffering 'macro-vascular' events such as heart attacks, and also puts them in danger of developing micro-vascular damage to organs such as their eyes and kidneys. Its complications are a common cause of the lower limbs having to be amputated. Because of its serious consequences, diabetes care is commonly estimated to account for between five and ten per cent of health care costs in the developed world (that is, in excess of 0.5 per cent of global GDP), and similar proportions of premature disability and death.

Alongside sedentary life styles, and socially influenced habits such as tobacco smoking and excessive alcohol intake, a rising incidence of diabetes is central to the physical and linked mental health challenges confronting populations living in conditions of material plenty. Today's wealth in countries such as the US and those of the EU and the growing prosperity of people in emergent economies contrasts sharply with the relative poverty in which humanity evolved.

Against this background, this report describes recent developments in bio-medical, behavioural and social understandings of diabetes and how it can be prevented and treated. Its most important objectives relate to the further development of pharmacy based health care as a cost effective part of the overall pattern of support available to people with diabetes. This should facilitate a combination of better medicines use and positive health related behaviour changes.

This report also seeks to contribute to wider public and professional debate about the nature of diabetes and how individuals and communities should respond to the threat it represents. It seeks to promote a balanced awareness of the fact that although there is no such thing as a 'mild' case of diabetes – everyone who is diagnosed with any variant of the disorder is at raised risk of disability or death – appropriate management can significantly reduce the harm that it would otherwise cause.¹

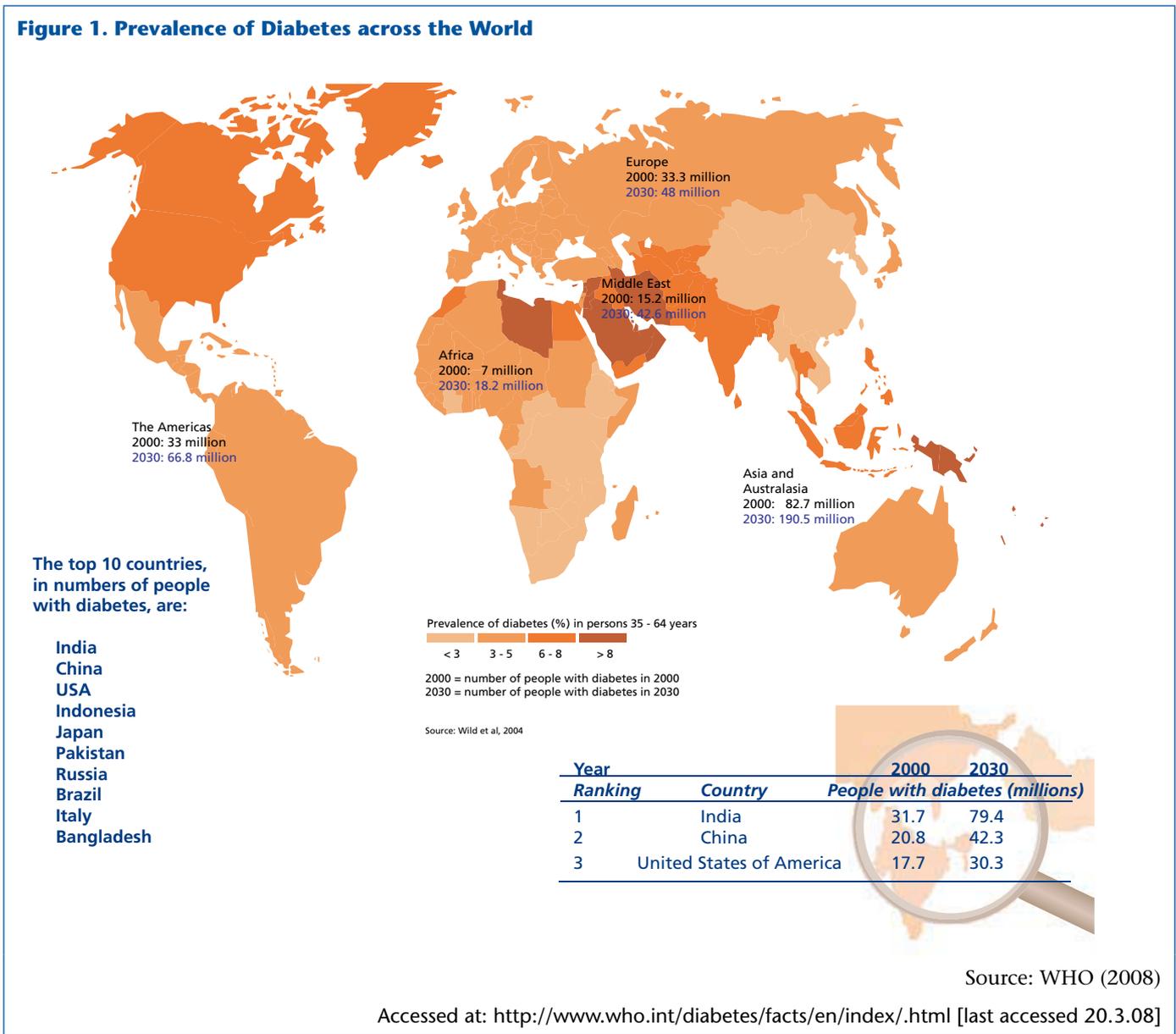
¹ It has in the past been accepted that a diagnosis of type 1 diabetes reduces life expectancy by an average of around 20 years, and one of type 2 by 10 years. However, there has always been considerable variation around these means, and modern advances in treatment have considerably improved the prognosis for people living with diabetes.

Box 1. An Outline History of Diabetes

- | | |
|---------|---|
| 1550 BC | Earliest known record of diabetes. The papyrus of the Egyptian physician Hesy-Ra notes polyuria (frequent urination) as a symptom. The condition was also known in ancient India, although the term diabetes itself (meaning to siphon fluid) appears first to have been used by the Greek physician Apollonius of Memphis in circa 250 BC. |
| 1797 AD | Dr John Rollo, surgeon general of the Royal Artillery in the British Army, publishes his 'account of two cases of the diabetes mellitus'. Rollo was the first to use the term 'diabetes mellitus' (meaning honey, or sweet tasting) and to make the distinction between this and diabetes insipidus, which involves frequent but tasteless urination. |
| 1920 | Building on German research, the Canadian Frederick Banting commences his work on isolating insulin (a word first coined in 1915, derived from the Latin for island). He conducted research on dogs with their pancreases removed. |
| 1921 | Insulin extracted by Banting, Best, Macleod and Collip. A dog without a pancreas was successfully 'treated'. |
| 1922 | Insulin first tested on a human. Prior to this point there was no treatment for type 1 diabetes – it was invariably fatal. |
| 1955 | Amino acid sequence of insulin first described Sanger. Metformin became available at around this time, as did the first of the Sulphonylurea medicines. |
| 1960s | Home testing for blood glucose levels in urine developed, in order to help people with diabetes to achieve better control of their condition. |
| 1970 | Blood glucose meters and insulin pumps first developed. |
| 1981 | First successful transplantation of islet cells. |
| 1983 | Biosynthetic human insulin introduced. |
| 1986 | Insulin pen delivery systems introduced. |
| 1993 | The Diabetes Control and Complications Trial (DCCT) reports that the intensive treatment of people with type 1 diabetes to keep their blood glucose down to near normal levels delays the onset and progression of long-term complications. |
| 1998 | United Kingdom Prospective Diabetes Study (UKPDS) reports that good glucose and blood pressure control are also important in type 2 diabetes. |
| 2005 | First islet cell transplant operation for an individual with Type 1 diabetes that resulted in insulin independence. |
| 2006 | The initial incretin mimetic is licensed in the UK, followed by the first DPP-4 inhibitor medicines in 2007. |
| 2008 | The number of gene sites known to be associated with type 2 diabetes rises to sixteen. |

See in addition http://www.jdrf.org.au/publications/factsheets/the_history_of_diabetes_and_the_search_for_a_cure.pdf

Figure 1. Prevalence of Diabetes across the World



There is a strong case that diabetes should wherever possible be prevented by prudent lifestyle changes. However, this is not always possible, even in the case of type 2 (adult onset, or what was at one time called non-insulin dependent) diabetes. Individuals are not always able to change their responses to the environments in which they find themselves. In addition, genetically linked and/or other (presently) non-modifiable variables are in many instances the main cause of diabetes. In these circumstances effective treatment is the only option.

Despite the important progress made in the NHS and other health care systems since the 1990s, even more can in future be done to ensure full access to services such as screening for diabetic retinopathy (which Department of Health data indicate was offered to 85 per cent of people with diabetes in England in 2007) and group based 'therapeutic education'. Enhanced efforts should be made to promote optimal use of anti-diabetic medicines, including both 'natural' and modified (analogue) forms of insulin. The aim of therapy should (in addition to controlling variables such as cholesterol levels) be to keep the blood glucose levels of people living with diabetes within, as far as is practically possible, a normal spectrum. At the same time the incidence of frightening and sometimes life threatening hypoglycaemic events should be minimised.

Dangerously low blood sugar levels are caused by unduly high, or long lasting, doses of therapeutic insulin.

There is a growing consensus that nurses, pharmacists, doctors and other health professionals should further extend their support for people living with diabetes in order to facilitate informed personal choice, and the best achievable quality of life. For nearly everyone this will involve not just controlling biomedical risks but also living as normally as possible, with as much freedom from rigid restraints as their peers enjoy. Health professionals also need to ensure that individuals and groups at special risk – such as pregnant women, older health service users with multiple disorders, and people with learning disabilities or severe mental health problems – receive good care and support.

Yet even if this is achieved, and communities also become better adapted to living with material plenty, presently available pharmaceutical and related medical technologies cannot – despite the promise their use holds for better health outcomes – cure or totally offset the risks of diabetes. For this reason, another key message of this study is that efforts to deliver existing treatments and manage today's resources should not draw attention away from the importance of investing in research for the future.

In the medium to long term there are profound benefits to be derived from innovations that will arrest or reverse the mechanisms involved in phenomena such as ‘insulin resistance’ and the progressive destruction of the insulin producing cells of the pancreas. From a global equity perspective, for example, it may be noted that although type 1 diabetes is currently most likely to occur in children and young adults of European ethnicity, white Europeans are generally less at risk of type 2 diabetes than are people of other racial origin when they are living in conditions of material plenty. India already has more people living with diabetes than any other country (Figure 1).

Political decisions must partly be driven by relatively short term electoral considerations, coupled with a legitimate desire to use today’s resources effectively and efficiently. Yet responsible health professionals and health sector policy makers should be robustly aware of the reality that sustained investment in pharmaceutical and other medical research will over the coming decades ultimately lead to major new gains, which existing forms of care cannot offer. Seen from this perspective, spending on recently developed treatments like the enhanced insulins and incretin mimetics described in this paper is worthwhile not only for its immediate benefits for individuals. It offers additional value in as much that it represents at a population level a stepping stone to a better future, providing not only a scientific but also a financial basis for ongoing discovery.

An Evolving Individual and Community Threat

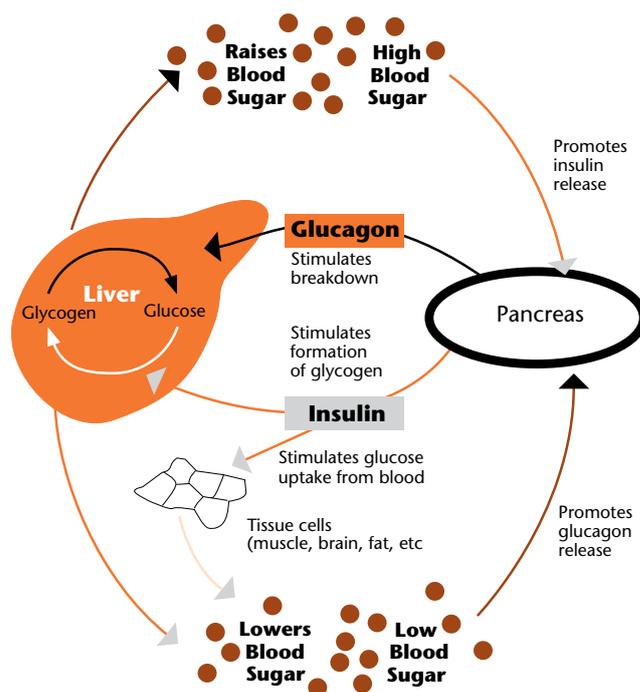
Glucose ‘powers’ all higher forms of life. During the process of digestion it is derived from food, transferred via the intestines into the blood stream, and subsequently delivered to the liver, muscles and other parts of the body like fatty tissues and the brain. There it is either used to energise reactions, or stored in the form of glycogen. The pancreas plays – as is described in Figure 2 – a central part in managing this process. When blood sugar levels rise it releases insulin. The latter binds to receptors on cells throughout the body in order to trigger (via a complex cascade of intra-cellular messengers and reactions) the uptake of glucose. Against this, when blood sugar levels fall a second hormone, glucagon, is secreted by the pancreas. This causes the release of additional amounts of glucose from organs such as the liver.

In diabetes this regulatory balance is to varying degrees impaired. Type 1 diabetes is most commonly the result of pancreatic beta cell destruction due to an autoimmune reaction, triggered in susceptible individuals by as yet unidentified external factors. Although in older children and some adults this process may continue for some time before consequences of pancreatic beta cell depletion become apparent, the initial onset of type 1 diabetes is typically acute. It may, for instance, involve an attack of ketoacidosis (Box 2).

Children, young adults and older individuals who develop type 1 diabetes need insulin therapy immediately. By contrast, the onset of type 2 diabetes is normally insidious – see Figure 3. It may take a decade or more from the start of the process to when diabetes can be diagnosed and often, although not always, many more years or decades before insulin treatment is (if ever) required.

Depending on their genetic endowments and very early life experiences, individuals who are exposed to life styles

Figure 2. The Pancreas and the Insulin Glucagon Balance (after the MODEL group 2007)



Typically a random blood glucose test of over 11.1mmol/l or a fasting blood glucose level of over 7.0 mmol/l indicates an individual has diabetes, although these two measures have varying degrees of specificity and sensitivity.

which cause them to put on weight and build up abdominal fat tend slowly to become resistant to insulin. That is, for a given amount of glucose entering the blood stream the pancreas gradually has to produce increased amounts of insulin to ensure its appropriate take up by the body’s tissues. This means that the average levels of insulin in affected individuals’ circulatory systems rise, causing a state known as hyperinsulinaemia.

The term insulin resistance was first coined by the British physician Professor Sir Harold Himsworth (who after the second world war became secretary of the Medical Research Council for almost three decades) in the 1930s. Despite the fact that several sets of mechanisms have been proposed, its causes are not yet fully understood (Stumvoll et al 2005). However, it is well established that abdominal adiposity (characterised by the build up of cells called adipocytes, which store energy in the form of triacylglycerol) is linked to raised levels of free fatty acids in the blood plasma. Adipocytes also produce a wide range of substances called adipokines and cytokines. These molecules influence metabolic, inflammatory and other key processes in many parts of the body.²

Becoming ‘fat’ can also (along with ‘ageing’ generally) cause people to reduce the amount of exercise they take.

² In broad terms type 2 diabetes can therefore in many (but not all) cases be seen as being a consequence of long term over- or miss-feeding, through which eventually the body’s ability to use glucose and store fats normally is overwhelmed. This results in a wide range of deleterious consequences. However, from a sociological and pharmaceutical or medical care perspective it is important to stress that individuals who develop diabetes should not be unfairly stigmatised. Rather, it should be understood that their constitutions are such that they are unable to live healthily in the society around them.

Box 2. The Causes and Complications of Diabetes

Type 1 diabetes is in most cases associated with an autoimmune response that destroys pancreatic cells responsible for producing insulin and other substances involved in glucose metabolism. During the 1990s it was hoped that the mechanisms responsible would be understood relatively quickly, opening the way to prevention. But this has proved a more complex task than was at that time anticipated.

Immune responses may also be involved in the pathogenesis of type 2 diabetes. In at least a proportion of cases the dividing line between the two main types of diabetes could be less clear cut than is often assumed. However, a wide variety of other causes have been postulated in relation to the processes of developing insulin resistance and the subsequent loss of pancreatic function described in the main text. These include the damaging effects of raised levels of fatty acids, the impacts of inflammatory and other cytokines and adipokines, glucotoxicity, mitochondrial dysfunctions and the possible harm resulting from a build up of amyloid protein deposits in the pancreas.

There remains, therefore, an extensive biomedical research agenda to be addressed in relation to diabetes. However, this is not explored in detail in this report. For the purposes of this analysis key terms and phenomena associated with diabetes and its complications include:

Hypoglycaemia

Hypoglycaemic episodes are often referred to as 'hypos'. These occur as the consequence of blood glucose levels falling too low. Symptoms may include sweating, shivering, blurred vision, anxiety, confusion, dizziness, difficulty speaking and nausea. Hypoglycaemia can be corrected by the intake of carbohydrates such as simple sugars.

Hyperglycaemia

Serious hyperglycaemic episodes ('hypers', associated with very high blood glucose levels and an almost total loss of insulin) can if untreated lead on to ketoacidosis, which is life threatening.

Ketoacidosis

Diabetic ketoacidosis is most likely to occur in people with type 1 diabetes, although it can occur amongst some individuals with type 2 diabetes when they are exceptionally stressed. The condition can have a rapid onset, and demand emergency hospital admission. It is the result of abnormal fat metabolism leading to a build up of ketones and blood acidosis. It is the most common cause of death in children and adults aged under forty with diabetes (Gage et al 2004).

Blood glucose levels

To avoid hyperglycemia and/or hypoglycaemia people with diabetes (especially those who require insulin) are advised to manage their blood glucose levels within defined target ranges. These are typically in the order of 90-130 mg/dL (pre-prandial, or before eating) and below 180 mg/dL at two hours after eating. The normal range for people without diabetes is 70-100 mg/dL, or 4 to 6 mmol/L, except in the immediate aftermath of a meal.

HbA1c

HbA1c (glycosylated haemoglobin) measurements reflect average blood glucose levels over 2-3 months. Hence they can be used as a longer term condition management guide, and to predict complication risks. The target HbA1c concentration for people with well controlled diabetes is normally regarded as being between 6.5 per cent and 7.5 per cent.

This may additionally contribute to problems such as insulin insensitivity, because of changes in skeletal muscle functioning and mass relative to the rest of the body. Some individuals who develop insulin resistance suffer no observed ill effects, and may in time return to 'normal'. Yet others eventually lose permanently their ability to make enough insulin to meet their rising need for it because they suffer progressive pancreatic damage alongside insulin resistance. Some commentators believe that hyperinsulinaemia may contribute to the latter, and that it can also be a cause of raised blood pressure.

The next stage of the typical 'spiral' or decline leading to a diagnosis of type 2 diabetes shown in Figure 3 is impaired glucose tolerance. Because the body cannot produce enough insulin to meet 'peak demands' after meals, blood sugar levels rise above normal thresholds. This may result in further pancreatic cell damage and other forms of harm, in part because proteins and lipids in the body become glycosylated. (That is, complex carbohydrates become attached to them.) This engenders micro-vascular disease and also accelerates the build up of atheroma in the major blood vessels. Micro-vascular damage is the result of glycoproteins being formed in the walls of small blood vessels, making them both thicker and weaker than normal. As already noted, this often affects retinal tissue and the kidneys, and can (especially when inadequately treated) also cause problems such as neuropathy (nerve pain associated with a partial loss of protective myelin sheathing) and foot ulcers.

Even at the stage of impaired glucose tolerance, many people may – if they change their lifestyles – either recover normal functioning, or at least significantly delay the further progression of their 'pre-diabetic' condition to diagnosable diabetes. As discussed in Box 3, this is defined by fasting and/or post-prandial (after eating) blood glucose levels known to be associated with long term harm, as well as with immediate symptoms such as excessive urination, thirst, tiredness and – in some people at least – mood variations.

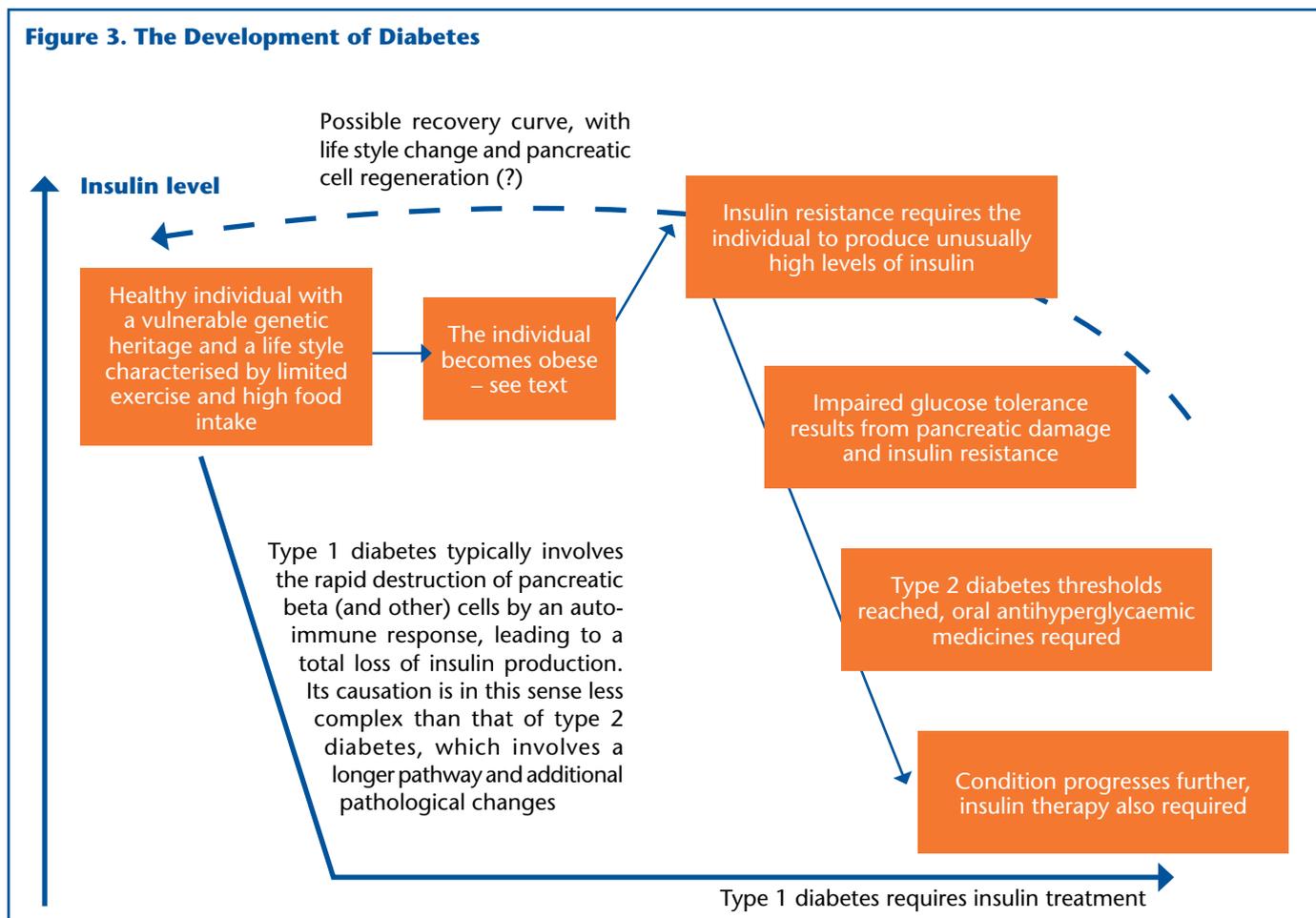
Once diabetes is established the task facing affected individuals and their health advisors in large part centres on managing their blood glucose levels as well as possible, and reducing the risks of associated harm to a minimum. But even then some interventions – most notably bariatric surgery, or 'stomach stapling' – appear on occasions to be associated with a recovery of normal functioning.

Genetic heritage and the thrifty phenotype

Over and above the conditions encompassed in the types 1 and 2 diabetes categories, other forms include gestational diabetes, and diabetes occurring as a result of pancreatic diseases and trauma, conditions such as acromegaly or cystic fibrosis, and the side effects of medicines. These last include some diuretics, cancer treatments and, some observers believe, antipsychotic drugs used to treat people with severe mental health problems (Holt 2004). However, in this last instance schizophrenia itself might be an independent risk factor. Diabetes associated with pregnancy is not considered in detail in this paper. Yet it represents a significant global maternal and child health problem. The research evidence available indicates that women who have acquired either type 1 or 2 diabetes before pregnancy, or who develop gestational diabetes during it, benefit from appropriate anti-diabetic treatment. So too do their babies.

The evidence available shows that most forms of diabetes are strongly associated with genetic vulnerabilities, albeit that in

Figure 3. The Development of Diabetes



poor living conditions these may in some instances also confer benefit. Identical twin studies indicate that in a given social and economic environment the degree of concordance for type 1 diabetes is in the order of 30-50 per cent. That is, if one twin develops the condition, the other has a one in three or greater chance of also doing so (Dean and McEntyre 2007).

In the main form of type 2 diabetes the equivalent percentage is in the order of 80 per cent. That is, if one identical twin develops it, there is a four in five chance of the other so doing. It appears that the earlier diabetes develops the higher the rate of concordance is likely to be. But awareness of this should not obscure the fact that at a population level lifestyle is the most important cause of type 2 diabetes.

The reason for this seeming paradox is that the genetic causes of the disorder only become relevant at given thresholds of food consumption and physical (in)activity. The risk of manifestation also relates to the frequency of eating as well as to the gross amounts of protein, fat and carbohydrate ingested by an individual or population. This is because the burden placed on the pancreas and the body as a whole is increased by snacking between meals on the one hand, and failing to spread food intake prudently over the day on the other.

Broad questions which current knowledge of the genetics of diabetes raises include *'might (as was in the past the case with polio) a factor such as delayed exposure to certain antigens be responsible for high and still climbing incidence rates of type 1 diabetes in affluent countries like Finland and the UK?'* and *'to what extent are reports of a rising incidence of type 2 diabetes in British children and young adults a function of greater ethnic diversity?'*. The latter concern has potentially important implications for the design of public health programmes.

Box 3. Defining Diabetes and its Treatment

Despite work initiated by the WHO in 1965, there were before the late 1970s there no robustly established diagnostic criteria for diabetes. But today the 1999 WHO definition is widely used. This states that a diagnosis of diabetes should be made if the fasting blood glucose level is 7.0 mmol/l or more, or a random blood glucose test shows a level of over 11 mmol/l. In patients who present without symptoms the WHO recommends that, in addition to blood glucose tests, an oral glucose tolerance test is performed.

The World Health Organisation has also played a vital role in developing international awareness of the importance of better diabetes care, perhaps most notably via its part in the development of the 1989 St Vincents Declaration. This was agreed at the start of a critical period in the development of the evidence base underpinning the treatment of diabetes. In particular the 1990s witnessed:

- The Diabetes Control and Complications Trial (DCCT), published in 1993. This US led trial showed that intensive therapy (frequent doses and self-adjustment according to individual diet and activity) delays the onset and progression of long-term complications (retinopathy, nephropathy and neuropathy) in subjects with type 1 diabetes.
- The United Kingdom Prospective Diabetes Study (UKPDS), published in 1998. This confirmed that for those with type 2 diabetes intensive therapy reduces microvascular complications. Good blood pressure control was also shown to reduce both microvascular and macrovascular complications.

Box 4. The Genetics of Diabetes

The great majority of cases of diabetes can be appropriately attributed to combinations of both environmental and genetic factors. But from a parental perspective it can seem vitally important to understand the extent to which contracting diabetes is inheritable. Research summarised by the American Diabetes Association and Dean and McEntyre (2007) indicates that the children of men with type 1 diabetes have an approximately 6 per cent (one in seventeen chance) of developing the condition.

The children of women with type 1 diabetes are at less risk. If a mother with type 1 diabetes is aged 24 or less there appears to be a 4 per cent (one in twenty five) chance of her baby developing the condition in later life. But the children of women who are 25 or older at the time of birth only have a 1 per cent chance of themselves contracting type 1 diabetes. These risks are approximately doubled if the parents concerned developed diabetes before the age of 11, and are higher again for children who have both a father and a mother with the type 1 condition.

Type 2 diabetes has a stronger genetic basis, but as described in the main text its occurrence is also critically influenced by life style. Hence it can be difficult in any one case to separate 'nature' as opposed to 'nurture'. But in general the child of a parent with type 2 diabetes has a 14-15 (one in seven) per cent risk of developing the condition if the parent was diagnosed before the age of 50, but only a 7-8 (circa one in thirteen) per cent risk if diabetes becomes manifest later. It may be that women are more likely to pass on the type 2 disorder than men. If both parents have this form of diabetes their children have a roughly one in two chance of developing it as they mature.

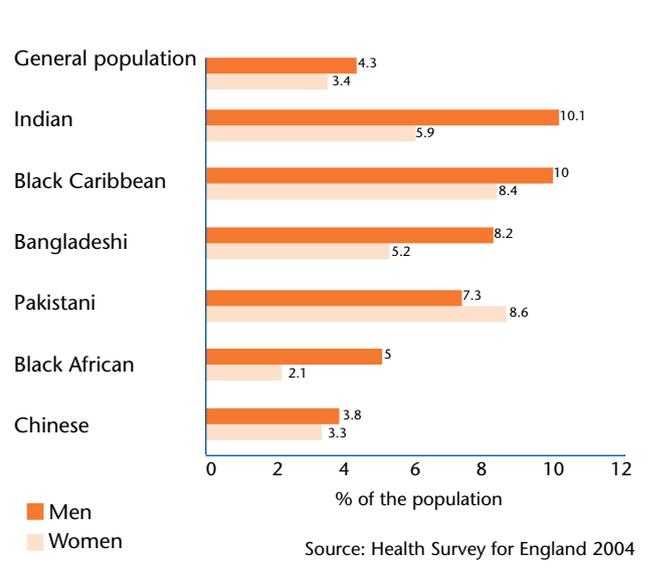
Box 5. Body Measurements and Type 2 Diabetes Risk

Obesity (particularly abdominal or central obesity) and type 2 diabetes have long been known to be linked. In social settings such as that of modern Britain a person with a body mass index (BMI, defined as weight in kilograms divided by height in metres squared) of around 35 has a risk of developing type 2 diabetes in the order of 20 times that of a person with a BMI of 25.

Recently, however, attention has focused on additional measurements of waist circumference and waist to hip ratio, which may complement use of the BMI. As yet clearly defined criteria have not been established, but waist to hip ratios of more than 1:1 in men and 0.8:1 in women can be taken as indicators of increased risk. Factors such as height and ethnicity may need to be taken further into account. But it is presently accepted that a waist size of 37 or more inches in males (35 inches in the case of Asian men) and 31.5 inches in females should also be regarded as indicative of type 2 diabetes risks requiring action.

At present rates the projected lifetime incidence for type 2 diabetes for the average person in Britain (that is, their overall risk of being diagnosed diabetic at some point in their life) is about 10 per cent, or one in ten. In future this risk could well move closer to one in five. Yet the lifetime incidence of this condition amongst members of the South Asian community

Figure 4. Ethnicity and Diabetes



living in the UK may already be as high as 30-50 per cent, or between one in three and one in two. Figure 4 presents additional data relating to the issue of ethnicity and diabetes related health risks.

Recent research has increased the number of individual genes known to be associated with the incidence of diabetes. For example, in 2006 an Icelandic group identified a gene known as TCF7L2, which subsequent UK research confirmed is associated with a doubling of type 2 diabetes incidence (Diabetes UK 2006). Further, in 2007 the Wellcome Trust Case Control Consortium announced that six new chromosomal regions had been found to be associated with type 1 diabetes (Wellcome Trust 2007). This work cast new light on links between type 1 diabetes and other disorders such as Crohn's disease, and the interactions that exist between an individual's genetic make up and environmental factors such as infections, diet and relatively low levels of vitamin D.

More recently still, European and US investigators announced six further gene associations with type 2 diabetes, two of which (HNF1B and JAZF1) also seem to be linked to a raised risk of prostate cancer (NHS Knowledge Service 2008). Although the practical value of observations such as these is yet to be demonstrated, the number of known associations between the structure of the genome and the occurrence of type 2 diabetes alone grew from three to sixteen the year or so between the start of 2007 and the Spring of 2008.

Box 4 contains further information on the genetics of diabetes. However, there are two particularly important general points to stress for the purposes of this analysis. First, most of the genes to date associated with a raised risk diabetes appear, as might be expected, to be related to the formation and durability of pancreatic beta cells and variations in glucose metabolism. As genetic science advances it should become possible to give increasing numbers of people a more precise idea of their chances of developing diabetes, or precursor states such as insulin resistance and low-level impaired glucose tolerance. It should also become possible to provide greater insight into the types of drug that will help particular individuals mitigate their risk of serious illness.

The second point is that an enhanced understanding of the genetics of diabetes will also lead to much improved understanding of the ways in which environmental factors

are associated with the disorder, and how public health measures and behavioural changes can most effectively protect populations, families and individuals. In this context phenotypical rather genotypical variations may often be critically important.

For instance, the 'thrifty phenotype' hypothesis suggests that poor nutrition before birth and in very early life leads to permanent changes in glucose-insulin metabolism that subsequently promote type 2 diabetes and other 'metabolic syndrome' spectrum conditions. The risk of the latter occurring is especially great when affected subjects are subsequently exposed to relative plenty (Hales and Barker 2001). Postulated causal mechanisms range from impaired pancreatic development in early life to 'epigenetic' variations, linked to differing patterns of gene expression.

This raises the possibility that, both nationally and on a global basis, the current 'diabetes pandemic' should be approached as a social developmental issue. This in turn implies positive as well as negative dimensions, in that the social and environmental processes that 'cause' diabetes at a population level can be seen as being intimately linked with progress away from deprivation towards conditions of greater security and longevity.

Epidemiological trends

Figures 5a and 5b are based on information produced by the US Centers for Disease Control and Prevention. This agency holds the most comprehensive epidemiological data on obesity available for any population. They show that while in 1990 no US state had a prevalence of obesity (defined as having a body mass index of 30 or over) of 15 per cent or more, by 2006 only four states had a recorded level of under 20 per cent.

Currently available statistics indicate that although British obesity rates are presently below US levels they are above the published OECD average levels (Figure 6). Its prevalence could amongst adults reach a figure of around 30 per cent by 2010 (Department of Health 2006). The reasons why UK countries such as England appear to have obesity rates two to three times the levels recorded in nations like France, Italy and Switzerland are not fully understood. But in addition to data quality issues, relevant factors may include social factors affecting not only the amounts eaten, but the structure and duration of meals and habits such as between meal snacking.

Put simply, strong 'work ethics' and relatively long working hours may sometimes cause diabetes to develop as a result of too pressured a life style, rather than a 'lazy' one. The relative cultural poverty of manual workers and other less advantaged groups in countries such as Britain and the US might help to explain not only high obesity rates, but also the fact that the UK has higher rates of type 2 diabetes than many other western European nations, combined (until recently at least) with poor statistics for treatment outcomes such as blood glucose control.

Figure 7 and Box 5 highlight further the robust correlation between body mass index measures and the risk of developing diabetes. This has been confirmed by many different studies (Wild and Byrne 2006). Estimates of the prevalence of diabetes vary between sources, not least because the age specific incidence of the condition is rising and the proportion of older people in the population is also increasing.³ The new general practice contract introduced in 2004 has also led to considerable improvements in case recording.

However, it can be fairly confidently estimated that there are currently between 2.5 and 3 million people in the UK who are living with diabetes (that is, about five per cent of the total population), of whom in the order of 85 per cent have the main form of type 2 diabetes. Adjusting for age, some 6 per cent of men living in households with the lowest 40 per cent of incomes had diagnosed diabetes in 2003, as opposed to a little under 3 per cent living in households with the highest 40 per cent of incomes. The equivalent proportions for women were 4 per cent and 2 per cent (BHF 2008).

The number of children and adults with type 1 is in the order of 400,000 in the UK as a whole. It is probable that there are still a significantly higher number of people who have blood glucose levels that have entered the diabetic range, but have not as yet been diagnosed. Figures 8a and 8b (derived from research undertaken in Wales in the late 1990s – Harvey et al 2002) underline the fact that the structures of the populations affected by types 1 and 2 diabetes differ radically. The prevalence of type 2 diabetes rises consistently with age, while that of type 1 declines from later middle life onwards. Improved survival rates will to an extent modify the age related pattern to date observed in people with type 1 diabetes. But even so these contrasting distributions will remain a strong epidemiological differentiator between the two main forms of diabetic disorder.

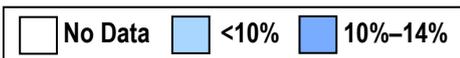
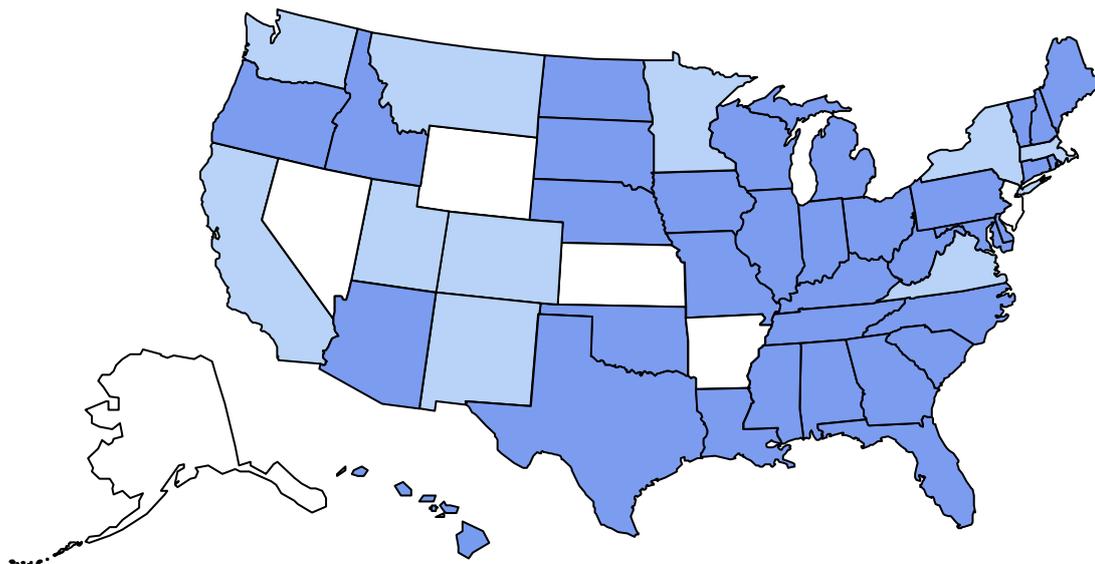
A 'diabetic transition?'

The processes of demographic and epidemiological transition as they relate to the emergence of 'modern' health care systems on the one hand, and lifestyle related problems such as tobacco smoking on the other, have been described in previous School of Pharmacy health policy papers and publications. (See, for example, Brock et al 2007, Taylor and Bury 2007.) But for the purposes of this report Figure 9 links in the UK context concepts such as demographic and care transition to the presently growing challenge of diabetes in both the mature industrialised nations and in emergent economies like those of China and India. Important observations include:

- corrected for population ageing, vascular disease death rates in Britain have fallen consistently over the past 50 years, regardless of governmental changes and particular health policy initiatives. Despite the concerns of some commentators, it may well be that even if rates of (in particular central) obesity continue to increase in coming decades, advances in pharmaceutically based treatment will ensure that age standardised mortality rates continue to decline. Yet even if this proves to be the case, a fundamental challenge that health care systems in settings such as western Europe will inevitably be that of stemming increasing volumes of diabetes and wider metabolic syndrome related disability, both to extend productive working lives and reduce long term care costs;
- diabetes is now being diagnosed more frequently in countries such as India. Yet the problems health care policy makers face in the emergent economy context are still in many respects radically different from those of 'post transitional' settings such as the UK. In India,

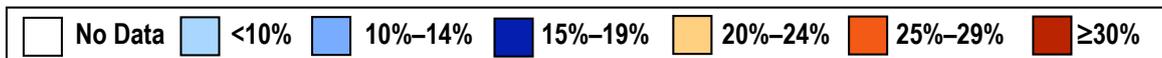
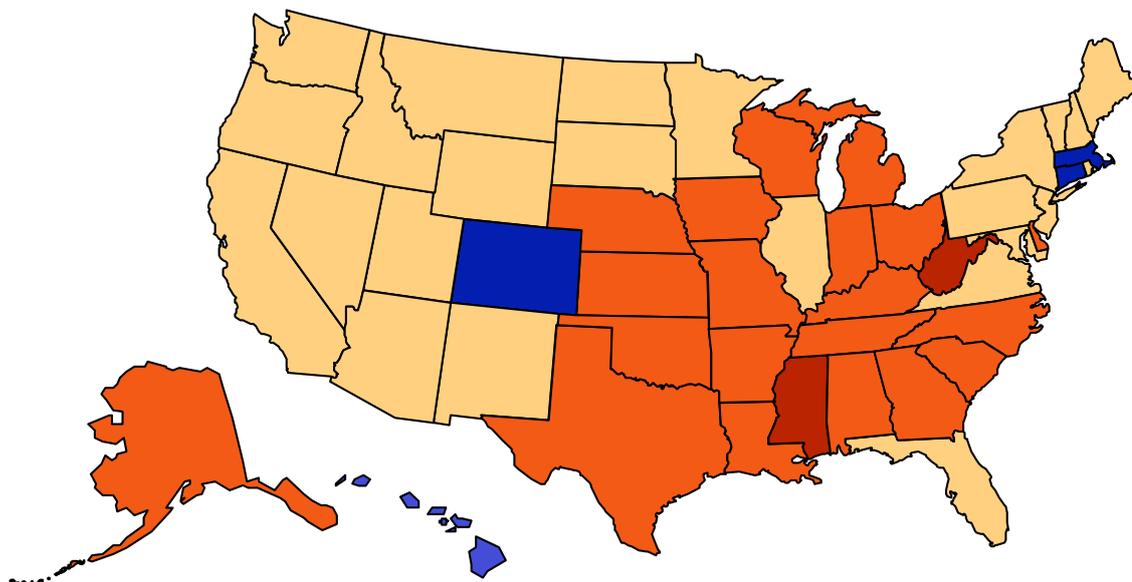
3 It may be estimated that around 40 per cent of the underlying diabetes prevalence increase in this country is associated with population ageing, and that the remainder is associated with increased obesity rates. (See, for example, YHPHO 2008.)

Figure 5a. Percent of Obese (BMI 30+) Adults in the US – 1990



Source: Centres For Disease Control and Prevention

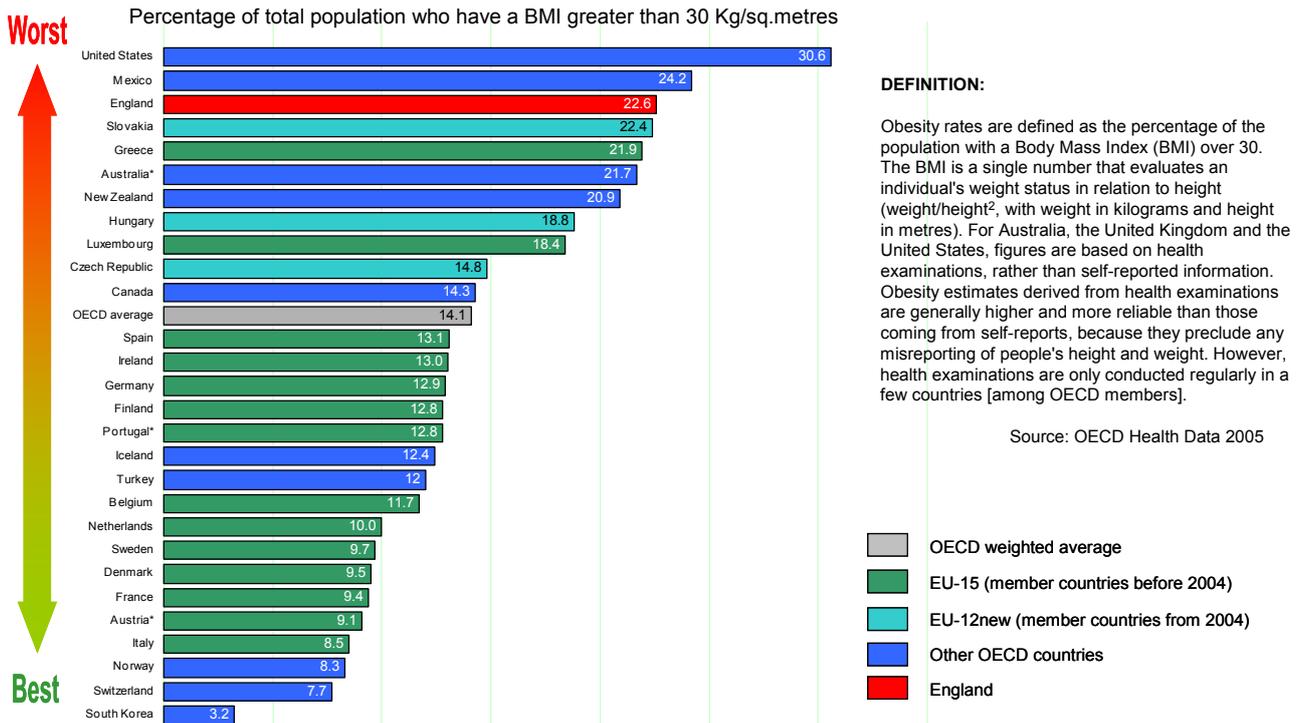
Figure 5b. Percent of Obese (BMI 30+) Adults in the US – 2006



Source: Centres for Disease Control and Prevention

Figure 6. Adult Obesity – England and Selected OECD Countries

Source: Health Profile of England 2007



DEFINITION:

Obesity rates are defined as the percentage of the population with a Body Mass Index (BMI) over 30. The BMI is a single number that evaluates an individual's weight status in relation to height (weight/height², with weight in kilograms and height in metres). For Australia, the United Kingdom and the United States, figures are based on health examinations, rather than self-reported information. Obesity estimates derived from health examinations are generally higher and more reliable than those coming from self-reports, because they preclude any misreporting of people's height and weight. However, health examinations are only conducted regularly in a few countries [among OECD members].

Source: OECD Health Data 2005

- OECD weighted average
- EU-15 (member countries before 2004)
- EU-12new (member countries from 2004)
- Other OECD countries
- England

* Australia, Austria, Portugal – 2002

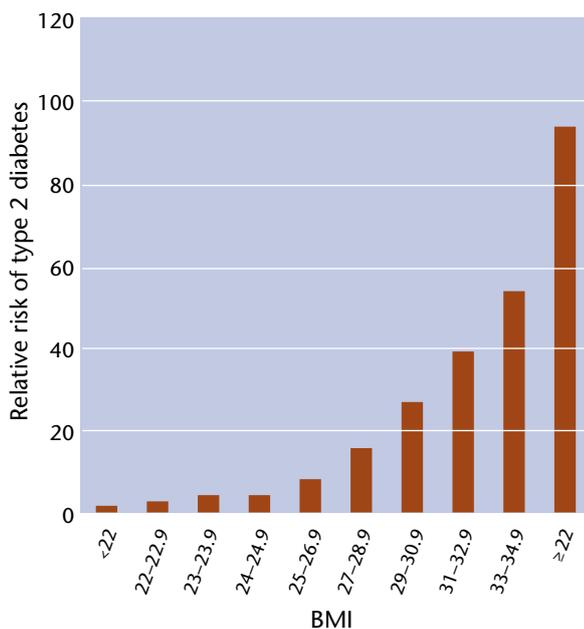
Source: (1) England – Weighted average of male and female data for 2003 from 'Health Survey for England 2005 - updating of trend tables to include 2005 data'. The Information Centre <http://www.ic.nhs.uk/statistics-and-data-collections/health-and-lifestyles/obesity/statistics-on-obesity-physical-activity-and-diet-england-2006>
 (2) All other countries - OECD Health Data 2005. Web link http://www.nationmaster.com/red/graph/hea_obe-health-obesity

for instance, diabetes is likely to be linked to increasing wealth and education rather than relative poverty. Worldwide, the majority of the population is more educated than it was a century or so ago, and people

have far greater access to health related knowledge than ever before. Such trends are now changing the social status and roles of health professionals in the mature (or post) industrial economies and creating new needs for self care support to be delivered where possible in normal community settings;

- the fact that, richer, socially advantaged, people in Britain have a reduced risk of diabetes could suggest that sustained economic development will in time lead virtually everyone to choose an optimally healthy life style. If 'diabetic transition' were a naturally self limiting development process, the task for health promotion and care agencies could be regarded as simply supporting an elective process of adaptation. Their role in this scenario is simply to help communities adjust to living with plenty as quickly as possible. Against this, however, research such as that indicating that people of all levels of wealth in the US have a higher risk of premature death than their equivalents in Britain (Marmot 2007) might indicate that health promoting social change is not inevitable. That is, in some settings greater wealth and more choice may not 'naturally' result in better health.

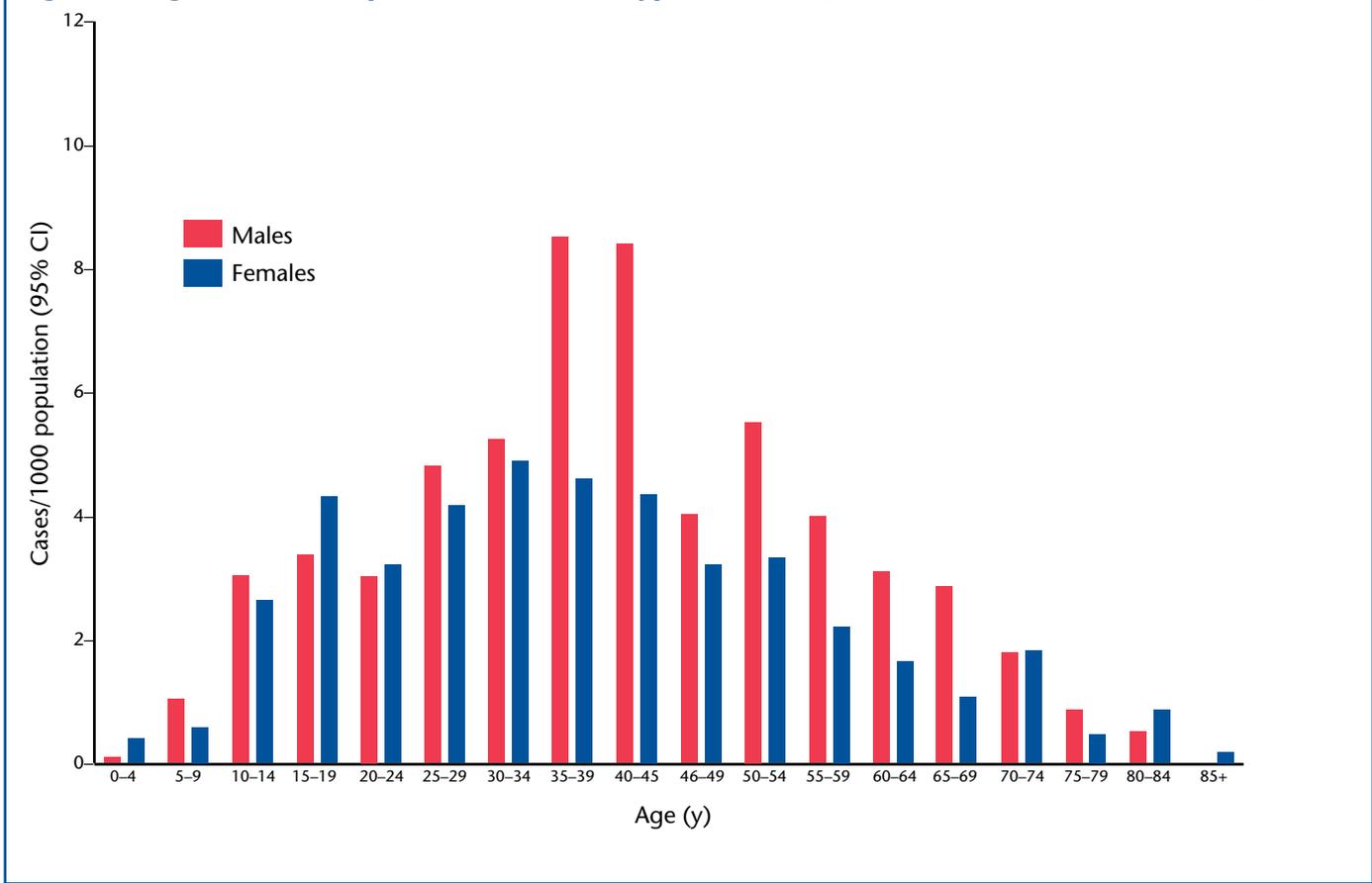
Figure 7. Body Mass Index and Relative Risk for Type 2 Diabetes



Source: Wild and Byrne (2006)

In practice substantial sections of the twenty first century UK population will continue to develop type 2 diabetes, regardless of attempts to 'educate' or 'enable' them into choosing healthy life styles. If this proves to be so it will present a complex ethical and political, as well as practical, challenge for health professionals working to reduce diabetes and allied metabolic syndrome related harm. Resolving this might ultimately demand that future disease prevention programmes should be more explicitly focused on pharmaceutical and other health

Figure 8a. Age and Gender Specific Prevalence of Type I Diabetes (data from research in Wales, 1990s)



Source: Harvey et al, 2002.

Figure 8b. Age and Gender Specific Prevalence of Type 2 Diabetes (data from research in Wales, 1990s)

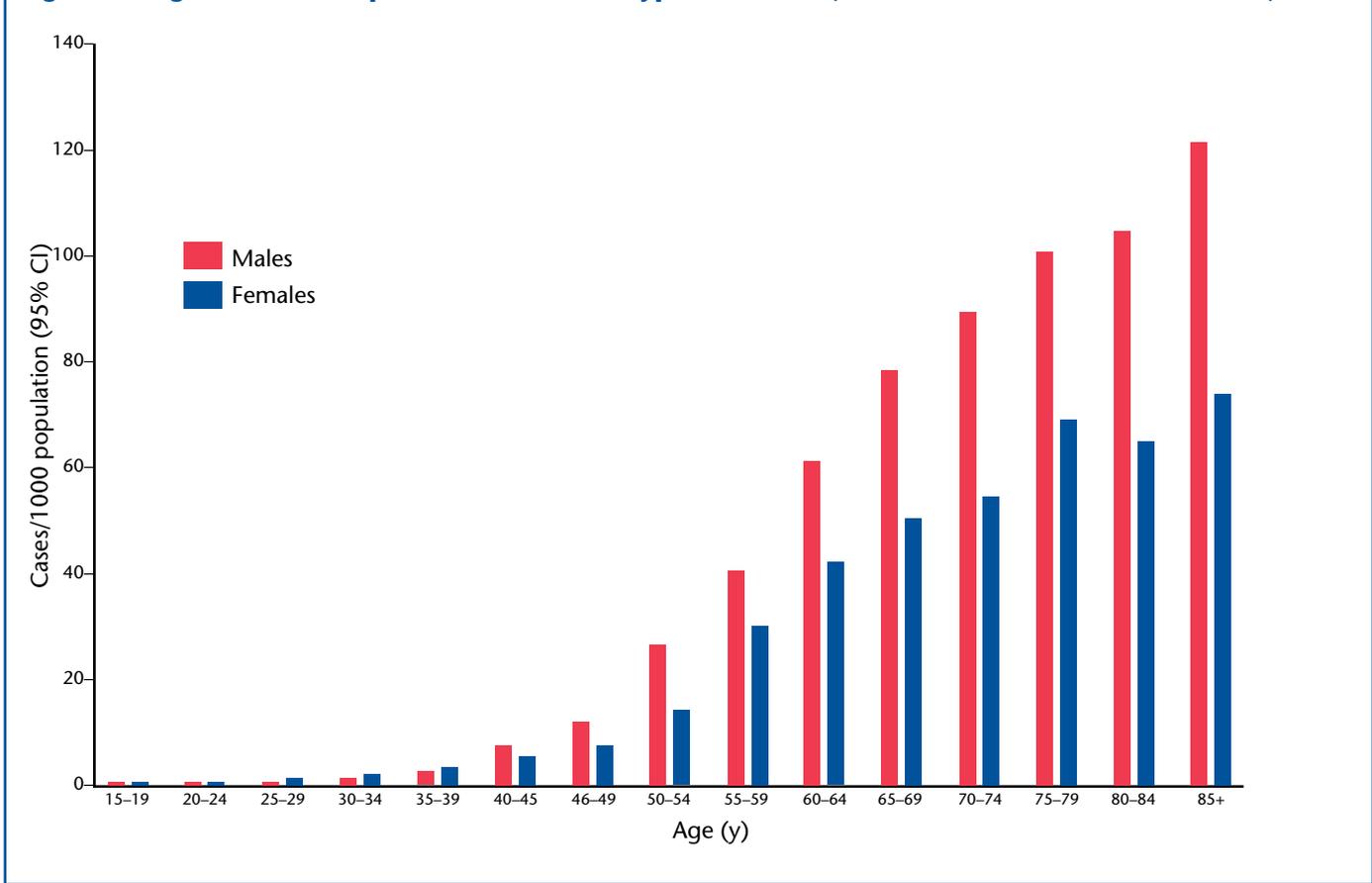
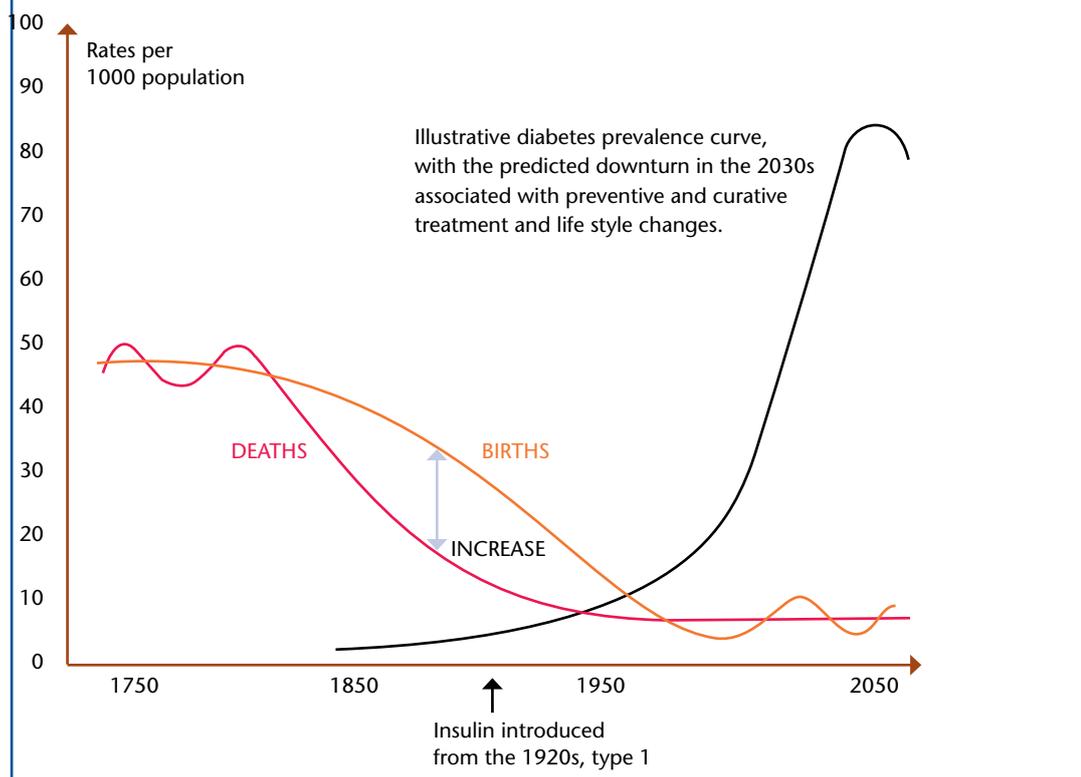


Figure 9. Demographic Transition and the Rising Prevalence of Diagnosed Diabetes, illustrative model, UK 1750–2050



product or service marketing based strategies than is presently the case. But the view taken here is that medium to long term public health improvements in post transitional societies will primarily stem from voluntary life style changes backed by democratically agreed legislative action, coupled secondarily with the professionally supported – yet increasingly personally controlled – use of more effective medicines.

Current Approaches to Prevention and Treatment

Recent research suggests that it may be possible to prevent the onset of type 1 diabetes by ‘vaccinating’ those at risk with doses of insulin, administered nasally or via other routes (George Institute 2008). In future, as the aetiology of this form of diabetes becomes more specifically understood, immunologically based strategies aimed at its primary prevention may prove safe and effective. But for the moment this is not the case. There is currently no known way of preventing type 1 diabetes.

However, the occurrence of type 2 diabetes is clearly in large part a function of population obesity and (in)activity rates. The primary prevention of this condition via interventions aimed at promoting lifestyle changes is both possible and potentially cost effective. There is, for instance, a growing body of evidence stemming from sources such as the European Prospective Investigation of Cancer (EPIC) and the studies associated with it (one element of which has involved a series of linked lifestyle investigations conducted amongst 30,000 people in Norfolk) indicating that relatively modest changes in diet and exercise result in life expectancy gains of up to a decade. This benefit appears in large part to stem from reduced diabetes related risks. (See, for example, Khaw et al

2001, Myint et al 2007). This conclusion is consistent with a considerable volume of US research (Perry 2002).

Even small increases in observed vitamin C (ascorbic acid) levels in the blood plasma (equivalent on average to a raised consumption of fruit and vegetables of only 50 grammes a day) have been linked to a 20 per cent reduction in all cause mortality. Further, even within the ‘normal’ spectrum, blood glucose levels are directly correlated with coronary heart disease incidence rates. (Stroke incidence, by contrast, appears to increase in a non-linear manner as HbA1c levels rise above 7 per cent.) UK investigators have also reported that just 30 minutes of recreational physical activity a day is associated with a 10 to 20 per cent reduction in mortality amongst people with a sedentary life style.

But attractive though the idea of preventing the occurrence of obesity and conditions like type 2 diabetes by modest life style changes most certainly is, the barriers to achieving this should not be underestimated (Wareham 2008). The work of Kinmonth et al (2008) illustrates this reality. They recruited 365 people in Norfolk who had a family history of type 2 diabetes, and were thus at high risk of developing the condition. A proportion were directly exposed to a sophisticated, psychological theory based, intervention aimed at increasing their physical activity. The remainder received either telephone support, or merely an advice leaflet. After a year there were no significant differences in activity levels amongst the members of these different groups. The authors concluded that PCTs and health care providers should be cautious about funding services which seek to promote individual health behaviour changes.

Technical aspects of this study have been questioned by some commentators. Yet it appears to have been of high quality. It may also be claimed that the full value of interventions aimed at facilitating health behaviour changes cannot be determined

Box 6. Obesity Reduction Programmes

The link between (central) obesity and type 2 diabetes incidence has led to increasing interest in the provision of obesity reduction programmes. Many trials have taken place. Examples of different types of initiative include intensive courses in weight loss and waist reduction, group and individual counselling programmes, peer-led weight loss approaches, exercise programmes with or without dietary modification elements, school based approaches and numerous health professional led reduction programmes. However, the success rates achieved by behaviour change programmes alone appear to be relatively limited. There appears, therefore, from a public health perspective to be a good case for combining pharmacological approaches with other forms of intervention aimed at BMI reduction, as and when this can be shown to help achieve more substantive and sustained outcomes than would otherwise be possible.

via 'once-off' trials. From a sociological perspective this is true. If, for instance, people's actions are in reality determined more by contextual factors than they are by consciously experienced thoughts and intentions, investments in health education and literacy may take a generation or more before a societal 'tipping point' is reached.

Developments in the area of smoking cessation policy and practice reflect this last point. It can thus be argued in the context of both obesity and diabetes prevention (and indeed in the use of relevant forms of biomedical treatment) that investments in logically coherent, constructively intended and affordable public health and health promotion programmes should not necessarily be curtailed simply because of a lack of direct evidence of effectiveness. Rational extrapolation from the social and epidemiological experiences of countries such as Finland (see, for instance, Tuomilehto et al 2001, Lindstrom et al 2004) indicates that both personal support and more broadly oriented public health interventions can have complementary, and potentially vital, roles to play in the primary prevention of type 2 diabetes.

But at the same time awareness of this should not be permitted to draw attention away from the already proven benefits of the secondary and tertiary prevention of diabetes and its sequelae. This involves early stage detection and oral pharmaceutical treatment where possible and later stage surgical and insulin based and other oral and injectable interventions when necessary. Nor should a desire for behavioural change per se obscure the fact that the rational use of safe and effective medicines, like those designed to inhibit fat absorption, can open the way to weight reductions that will in turn contribute to the primary prevention of diabetes.

The latter does not have to be achieved by behavioural change alone (Box 6). Similarly, the primary prevention of conditions associated with diabetes, such as CHD and kidney damage, can be achieved by means other than diabetes prevention. In the latter case the appropriate use of medicines such as statins (to control hyperlipidaemia – Reckless 2006) and anti-hypertensives such as ACE antagonists has fundamentally changed not only the outcomes but also the economics of diabetes care in the last two decades.

Early stage detection and treatment

There has been much debate in the UK and elsewhere about the value of population wide screening for conditions such as diabetes, hypertension and hypercholesterolaemia (Stolk 2007). Some commentators have argued that such programmes are not cost effective, could cause needless anxiety amongst vulnerable individuals, and would needlessly increase GPs' and other doctors' workloads.

It has in the past been suggested that within the NHS an increased emphasis on risk factor identification and management would attract resources and doctors attention away from the most serious (or 'deserving') cases, towards the 'worried well'. Typically, conservatives in this arena have favoured opportunistic screening amongst subjects identified as being at raised risk, coupled with the intensive treatment of people who have, for instance, suffered an initial heart attack.

Against this, some (but not all) patient advocates and private sector service providers have argued that public interests would be well served by more pro-active population wide risk and case finding approaches, that encourage all adults to 'know their numbers' (including fasting glucose and cholesterol levels, blood pressures, BMIs and waist measurements) and plan actively throughout life to maintain the best possible health. The critics of conservative screening and testing strategies argue that they stem from paternalistic attitudes that exaggerate the risk of causing harmful anxiety and could cost lives by inhibiting the development of self care motivation and skills. In reality, proponents of this view argue, the available evidence suggests that the population is more at risk from health risk related indifference than anxiety – see, for instance, Eborall et al (2007)

Advocates of extended access to screening or checks for vascular/metabolic syndrome spectrum disorders and risk factors may also point out that about 25 per cent of all first heart attacks are fatal. Similarly, some forms of disability are also irreversible once they have occurred. Recent government policy announcements contained in documents such as *Putting Prevention First* (Department of Health 2008b) and the 2008 pharmacy White Paper *Pharmacy in England* (Cmnd 7341) may appear to offer a resolution to this dilemma in the English NHS context.

The vascular risk assessment model outlined in Figure 10 represents a pragmatic, systematically structured, way forward to improving the identification of early stage disease (including diabetes and its precursor states) throughout the population. Similar approaches are being developed in Scotland, Wales and Northern Ireland. Initial modelling indicates that when applied to the overall UK population over 40 years of age, such a screening strategy could lead annually to around 30,000 cases of diabetes and related organ damage being identified earlier than would otherwise have been the case, and prevent around 12,000 heart attacks and strokes. This could in turn avoid in the order of 2,500 or more premature deaths each year.

Experience in the smoking cessation context has demonstrated that community pharmacists can successfully deliver interventions in a field in which, however important it may be in individual and public health terms, a significant proportion of doctors have not wished to work. Seen positively, future developments in health check provision in pharmacies could help protect GPs and their nursing colleagues from unnecessary work, and allow them to focus on those cases where their unique primary medical care expertise is most

Table 1. The main types of anti-diabetic medicine

Class of drug	Examples and actions
Biguanides	The only drug in this class used to treat diabetes is metformin, which can inhibit the release of glucose from the liver and make muscle cells more sensitive to insulin (see text). It therefore enhances the effects of insulin being produced naturally. It is possible that treatments with this mode of action might prove of value in treating 'pre-diabetes', as well as the established type 2 condition.
Sulphonylureas	Medicines in this relatively large class (the first of which were also marketed in the 1950s) include tolbutamide and glibenclamide. They have differing durations of action, but all stimulate the pancreas to secrete more insulin. Medicines in this class can cause hypoglycaemia and their use is also associated with weight gain.
Alpha-glucosidase inhibitors	Acarbose is an example of this class of medicine, which slow the digestion of carbohydrates and so help to reduce post prandial blood glucose levels. From a consumer perspective these medicines can cause flatulence.
Meglitinides	Medicines of this type include repaglinide and nateglinide. Like the sulphonylureas, they stimulate the pancreas to secrete more insulin but via a different mechanism.
Thiazolidinediones	Products in this category are sometimes collectively referred as glitazones. They affect adipocyte differentiation and reduce insulin resistance. Examples include rosiglitazone and pioglitazone. NICE has recommended that the use of these medicines (which were first introduced at the end of the 1990s) be reserved for people with diabetes who are unable to tolerate metformin and a sulphonylurea in combination and for patients for whom these drugs are contra-indicated (see text). New pharmaceuticals with related modes of action are currently being developed.
Incretin mimetics	See text and Box 7. Exenatide, the first drug in this class, works by acting on receptors for the naturally occurring hormone glucagon-like peptide 1. Further products in this class are being developed in the hope that trials will show that they will offer enhanced benefits to people with diabetes.
DPP 4 inhibitors	The medicines sitagliptin and vildagliptin prevent the breakdown of naturally produced GLP-1. This class of drugs was first marketed in 2006, and unlike exenatide are taken orally. However, they do not offer all its benefits.
Amylin analogues	The amylin analogue pramlintide acetate was first marketed in 2005. Amylin is produced in the pancreas as well as the brain, and helps to regulate glucose metabolism via effects such as limiting glucagon secretion. This medicine is indicated for the treatment of both type 1 and type 2 diabetes.
Insulins	Pharmaceutical insulins of all types replace directly the naturally produced hormone and permit the survival of those unable to produce it themselves. Their use in type 1 diabetes is therefore vital. In type 2 diabetes there is normally more choice as to when a person starts to use these medicines. Some may fear doing so, even though the timely commencement of insulin therapy can be beneficial. Modern insulins permit physiologically appropriate treatment regimens, combining precise blood sugar control with high levels of treatment user behavioural freedom. Presently only injectable forms of insulin are available, although work is continuing on orally active and other alternatives.

required. (For an extended discussion of NHS Lifecheck and vascular disease check provision issues see Newbould and Taylor 2008.) This ought in turn to allow specialists working in secondary and tertiary settings to focus their efforts more appropriately on individuals with acute and complex care requirements, albeit that even within the medical profession there has at times been intense debate as to what this should in practice imply (Keen 2005).

Medicines for people with diabetes

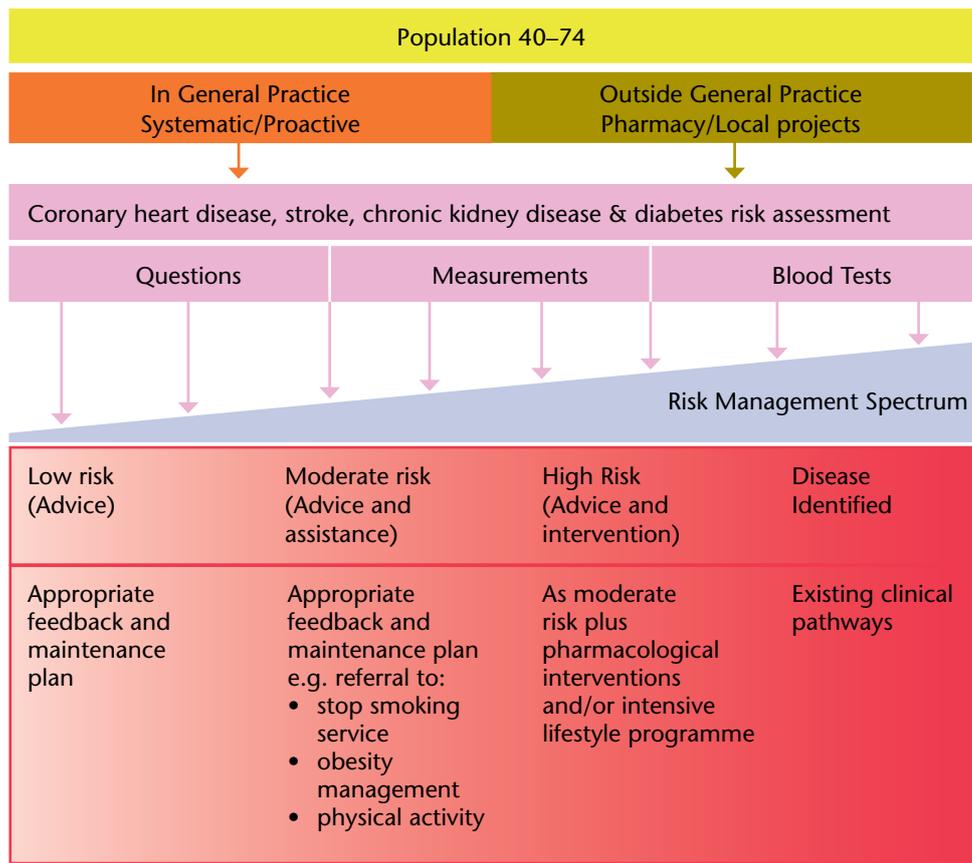
As their name indicates, anti-hyperglycaemic medicines work to lower blood glucose levels in a variety of complementary ways (Table 1). As a rule, they require the pancreas to be producing a reasonable level of 'natural' insulin. Some, such as Sulphonylureas like tolbutamide and Meglitinides like repaglinide, augment the latter by enhancing insulin secretion for given periods of time. Others, such as pioglitazone and

rosiglitazone, bind to receptor cells inside cell nuclei and stimulate the uptake of glucose and fatty acids into adipocytes (abdominal fat cells).

They also help to generate increased numbers of adipocytes. This normally leads to weight gain. But it also beneficially reduces insulin resistance in the muscles by cutting fatty acid levels in the musculature. Despite the controversy which has on occasions been associated with this class of medicines, their appropriate use can confer significant benefits on people with diabetes.

In the case of individuals who have both diabetes and an additional diagnosis of heart failure (which is not uncommon), a recent systematic review found that of the currently well established antidiabetic agents only metformin can confer benefit while also being free of any association with harm (Eurich et al 2008). Metformin belongs to a class called the Biguanides and is related to a traditional medicine called

Figure 10. Vascular Risk Assessment Programme



Source: Putting Prevention First, 2008

galega officinalis, or goat's rue. This was used in the treatment of diabetes for several centuries before the modern era.

Metformin, which was originally developed in France, has now been continuously available in Britain (despite being withdrawn by the FDA from the US market for an extended period, probably at some cost in terms of American lives) for over fifty years. It reduces the hepatic output of glucose and also increases the latter's uptake by the skeletal muscles, through reducing insulin resistance. It is only relatively recently that this medicine's mode of action has been elucidated (Munday 2008). It activates within muscle cells an enzyme called AMPK (AMP activated protein kinase).

This has a range of important effects relating to glucose metabolism and within the brain to appetite regulation. It is now understood that taking metformin, the contra-indications to which have in the past have been overstated (Jones et al 2003), has effects that are similar to the body's natural response to exercise. Such observations suggest that this drug, or new medicines with the same mode of action, may in future have more to offer in terms of either being used in association with life style interventions to prevent or slow 'pre-diabetes' progression, or to treat more effectively established diabetes. However, it should be stressed that as yet no form of 'pre-diabetes' pharmaceutical intervention has conclusively been shown to prevent diabetes expression (Alberti 2008a).

The injectable incretin mimetic exenatide is an example of a more recently marketed product that may also prove to have important advantages in treating and slowing or perhaps even preventing the progression of type 2 diabetes and/or its precursors. It acts in a manner like that of a substance made

in human intestinal mucosa called glucagon-like peptide 1 (GLP-1, see Box 7). Similarly dipeptidyl 4 protease (DPP IV) inhibitors prevent the breakdown of GLP-1, the production of which is known to be impaired in people developing and who have type 2 diabetes. These products have significant value and the advantage of being taken orally, although they do not permit the build up of levels of the hormone sufficient to achieve the overall benefit associated with exenatide use.

Such developments underline the important potential of new pharmaceuticals to contribute more to controlling the diabetes pandemic. However, as is normally the case with any class of drug, the use of medicines to this end is not without critics and controversies. In addition to the general point that a reliance on 'pills' should not be allowed to obscure the vital benefits of, for example, regular daily walking (Gray 2008) and other forms of moderate exercise such as swimming, these include:

- **Is attempting to prevent diabetes with 'pills' inherently counterproductive?** Some authorities (such as Montori et al 2007) have argued against the use of medicines such as rosiglitazone (as recently explored via the DREAM trial – DREAM Trial Investigators 2006) to delay or possibly prevent the onset of diagnosed diabetes. (See also Tuomilehto and Wareham 2006). Beyond specific detail, Montori et al point out that the encouragement of such strategies may be motivated by commercial greed rather than medical altruism. However, provided the costs (and risks in context where perhaps more than a half of users will not in any case progress to full diabetes) as

against the benefits of pharmaceutical interventions are measured and evaluated with integrity against other possible social, economic, psychological and medical options, it would be hard to justify a claim that it is necessarily wrong to try to delay the onset of diabetes with medicines as opposed to any other form of action. Indeed, ideologically based beliefs to this effect could damage public interests.

- **Is a 'gluco-centric' approach to diabetes treatment counterproductive?** Following findings such as those of the UKPDS people with all forms of diabetes are being treated more intensively than was so in the past. This, coupled with increased identification of the condition, has driven up treatment costs and exposed more patients to the threat of hypoglycaemic events and other possible side effects. Some commentators, particularly following concerns raised early in 2008 by the halting of part of a trial known as ACCORD (evaluating the benefits of intensive glucose control), have suggested that very tight glucose control strategies may neither be financially nor therapeutically desirable (Yudkin 2008).

It is unquestionably the case that a concern for managing blood glucose levels should not blind either professionals or people with diabetes themselves to the benefits of other interventions, such as using statins and appropriate anti-hypertensives. However, there is firm evidence that even today many people with diabetes are being placed, or are placing themselves, at needlessly high risk of premature death or disability through a failure to control their blood glucose levels as well as is possible.

Theoretical concerns that very intensive type 2 treatment programmes combining high level insulin use with medicines that enhance insulin sensitivity might increase mortality deserve due attention. This is not least, from an academic perspective, because they raise the possibility that insulin resistance could in some contexts have a protective function (Home 2008). But the significance of the ACCORD results should not be over-emphasised, especially as they have not as yet been fully published. For practical purposes one of the major problems facing people with diabetes and the health professionals seeking to support them remains that of inadequate glucose control, rather than unduly effective intervention. The conclusion drawn here is that excessive criticism of current therapeutic approaches could undermine rather than protect public interests.

Improving insulin treatment

The discovery process leading to the work of Frederick Banting and his colleagues in Toronto at the start of the 1920s, and the initial treatment of the fourteen year old Leonard Thompson with insulin in 1922, is a landmark story of medical and pharmaceutical advance. Along with milestone events such as the development by Paul Ehrlich and Hata Sahachiro of salvarsan for syphilis just over a decade before, it ushered in the period of modern therapeutics.

Yet for Thompson (who died at the age of twenty seven, and from a patient perspective was arguably the most important hero of the insulin discovery story) and others with diabetes who were desperately awaiting effective care, insulin was at first far from satisfactory as a treatment. The inadequately purified calf's insulin he received caused a severe allergic reaction. However, this problem was relatively quickly overcome, and the challenge for people

Box 7. Incretin Agonists and Analogues, and the Role of Pharmacists in Diabetes Care

It has been known since the 1930s that a number of peptide hormones are produced in the small intestine. The most important of these appears from a diabetes care perspective to be glucagon-like peptide 1 (GLP-1). Research on such substances, often referred to as incretins, was first prompted by an awareness that taking glucose orally leads to a greater release of insulin than does the intravenous injection of a similar glucose load. This implies that there is a special functional relationship between the gut and the pancreas.

GLP-1 acts in part to slow gastric emptying, so regulating glucose intake. GLP-1 may also mediate satiety (the feeling of having eaten enough) via direct effects on the brain, and reduce the liver's output of glucose via inhibiting the release of glucagon (Gallwitz and Bachmann 2007). In addition it increases insulin secretion under hyperglycaemic conditions and – some researchers believe – can also preserve or possibly even enhance pancreatic beta cell mass. So far the evidence for this last is based on animal models. But it has already been demonstrated that incretin mimetics (unlike the DPP 4 inhibitors) can promote weight loss in people with diabetes, while at the same time significantly reducing their HbA1c levels.

This new class of medicines might therefore have a considerable future role to play in the treatment, and perhaps the prevention, arrest or delay of type 2 diabetes. Exanotide, the first of the incretin mimetics to be marketed, was originally found in the saliva of the Gila monster, a venomous North American lizard. It binds to the same sites as human GLP-1, but is more stable. While the natural human peptide is normally destroyed within minutes, this medicine can be injected on a twice daily basis.

Current research efforts are aimed at introducing incretin mimetics that offer additional advantages. For example, exanotide stimulates the production of antibodies in many people taking it. This on occasions blocks its therapeutic action. It may be that molecules exactly like human GLP-1, although modified to make them long lasting in the body, will prove less immunogenic and/or capable of administration on a once rather than twice daily basis. (To mark this difference, some commentators refer to the latter as human GLP-1 analogues, while calling exanotide a GLP-1 receptor agonist.) It is also possible that orally active or possibly inhaled GLP-1 based medicines will in time be developed.

From a pharmaceutical care viewpoint such illustrative possibilities suggest that in the long term treatments based on a definitive understanding of the processes leading to type 2 diabetes will emerge. Used at a population level as public health interventions, such innovations may contribute to ending the global diabetes pandemic. More immediately, they highlight the availability of a growing range of effective treatments for reducing the individual harm caused by diabetes, and the potential role of appropriately educated and skilled pharmacists in the clinical management of diabetes. If pharmacists can effectively combine their special knowledge of established and new medicines with effective health behaviour change competencies they will be able to play, alongside doctors, nurses and service users themselves, a pivotal twenty first century part in reducing diabetes (and more broadly metabolic syndrome) related sickness and deaths. See main text.

seeking treatment then became focused on being able to scale up production safely.

To overcome this barrier to saving the lives of people with type 1 diabetes as quickly and efficiently as possible, the University of Toronto formed a partnership with Eli Lilly & Company in the US to mass produce bovine insulin. Shortly afterwards August Krogh founded the Nordisk Insulinlaboratorium in Denmark. Following this both the Nordisk Insulin Company and the Novo Company (now Novo Nordisk) began pioneering insulin production outside North America (Practical Diabetes International 2005). In the UK the Medical Research Council (which was founded in 1913) was also involved in work on insulin from 1922 onwards.

Insulin was first crystallised in what was then thought to be a pure protein form in 1926. This opened the way to improved production of the hormone from bovine and porcine pancreases. In the 1930s longer acting insulins, complexed with zinc and protamine (a protein derived from fish) were marketed, and after the Second World War products such as Neutral Protamine Hagedorn (NPH insulin) gave people with type 1 diabetes a further improved chance of a good quality of life. Even so, some users developed immune responses to insulin derived from animal organs. There were also concerns about maintaining supply levels, given that the rising incidence and prevalence of diabetes was by then starting to become apparent. Outside the industrialised world insulin was at best inconsistently available, as is still so today in some areas.

After pioneering work by the then newly formed bio-engineering company Genentech in the late 1970s, it became possible to manufacture human insulin on a large scale. Products based on the latter from that time onwards started to replace animal derived insulin. These appear to have brought advantages for many people – not least from a supply sustainability perspective – although the extent of

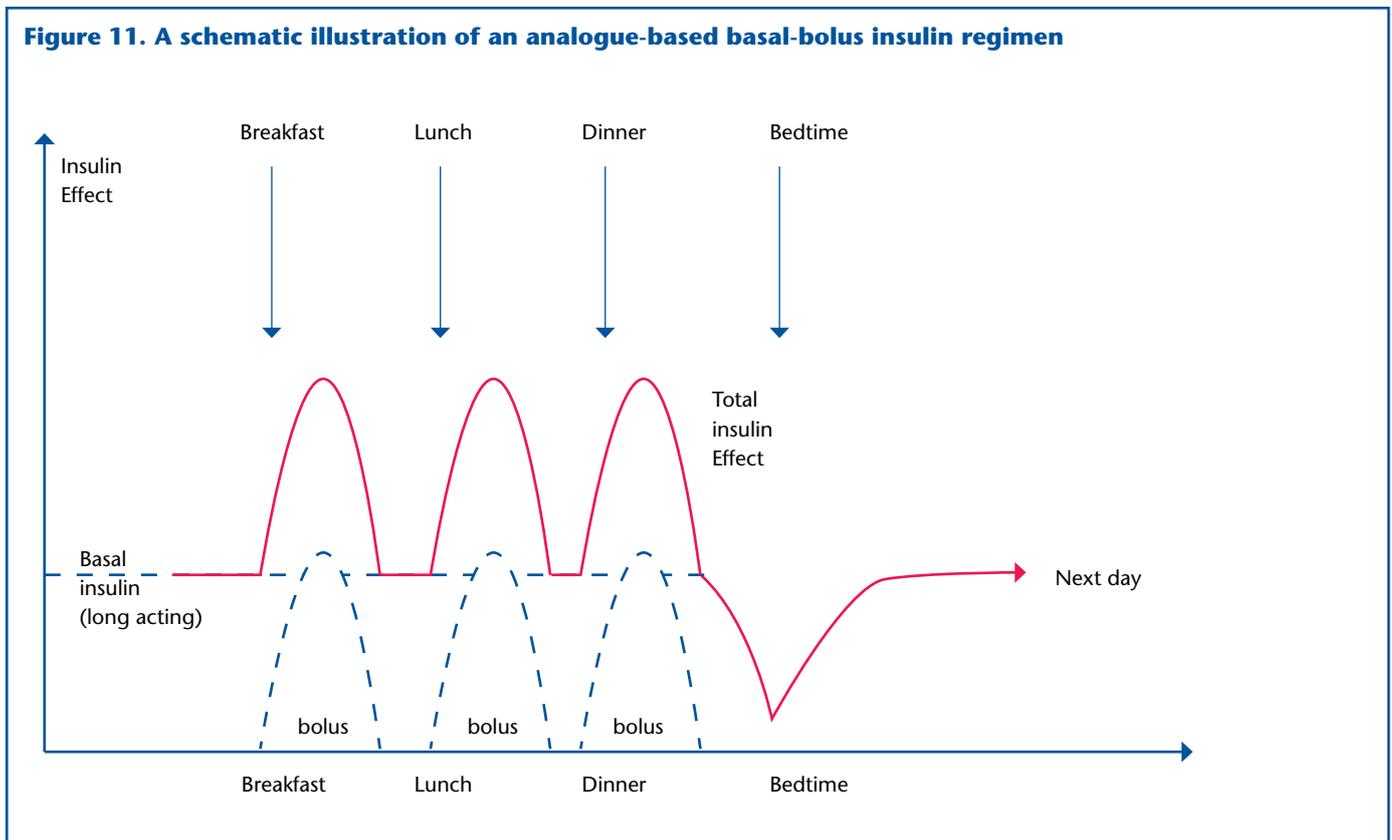
evidence supporting this view has been criticised by some analysts (Richter and Neises 2002). The different properties of human and animal insulins meant that some patients who were established on the latter encountered difficulties in making the transition to human insulin treatment. In some cases individuals died from hypoglycaemia. The companies producing human insulins (and which gradually withdrew from animal insulin supply) have on occasions been blamed for such tragedies.

From the late 1990s onwards human insulin analogues have become available. These are designed to further enhance the control of type 1 diabetes and type 2 cases that cannot be treated by oral anti-hyperglycaemics alone. By chemically modifying the human insulin molecule its speed and duration of action before natural breakdown can be accelerated, and extended or shortened. Such innovations are intended to enhance the opportunities for people with diabetes to live as normally as possible, while keeping their blood glucose levels within desired parameters.

Modern 'basal bolus' insulin regimens combine long acting and rapid and short acting insulin products, in order to copy as closely as possible natural surges and declines in insulin levels around and after eating and during the night – see Figure 11. Strategies based on subcutaneous injections can never fully simulate normal pancreatic action. This is partly because the pancreas secretes insulin and related substances directly into the hepatic portal vein, which means that the hormone becomes available at different concentrations in other parts of the body. But from a patient perspective their aim is to reduce the long term risks of micro-vascular and other forms of damage to a minimum, while also avoiding the short term hazard of distressing and potentially life threatening 'hypos'.

The advent of new products like the insulin analogues, coupled with the rising prevalence of diabetes due to factors

Figure 11. A schematic illustration of an analogue-based basal-bolus insulin regimen



such as improved life expectancy, has, as Box 8 discusses, caused concern about treatment cost increases in the UK and other health care systems. It has been argued, for example, by German analysts that there is no evidence that the use of rapid acting insulin analogues produces medical benefit, at least as defined by recorded HbA1c levels (IQWiG 2006).

But against this a proportion of people with diabetes who have experienced the alternatives now available (including people with diabetes interviewed during the preparation of this paper) express a preference for analogue insulin based regimens. Their personal experience is that the use of both long and short rapid acting insulin products provides enhanced confidence and improved control. Further, recent research suggests that in practice there may in fact be significant clinical gains associated with the use of analogue based insulins that are only now becoming more fully understood.

For example, Hutchison et al (2008) used the General Practice Research Database to compare the occurrence of serious hypoglycaemic events in new adult users of human as opposed to analogue insulins with type 2 diabetes. They found a 28 per cent reduction in the occurrence of such incidents in the population using analogue insulins as compared with those using unmodified human insulin. This is equivalent to about one event less per year for every 50 patients treated (de Vries 2008). Those responsible for health service resource use management may question the value of such gains, or argue that they could (in theory, at least) be achieved more cheaply via a careful use of older insulins. But this is not necessarily consistent with a patient centred approach, or one which values in a fully informed way pharmaceutical innovation as an investment in the future.

It would be beyond the scope of this report to analyse this or related issues in greater depth, although a brief discussion of the wider economics of diabetes care is offered in the following section. However, there are to conclude here a number of other aspects of insulin use that are presently controversial and deserving of special attention. Examples include:

The support needs of children and young adults using insulin therapy

The management of (normally type 1) diabetes in children and young people is significantly more complex than it is for adults (Department of Health Diabetes Policy Team 2007). Often parents play a large and valuable part in the care provided, but this is not always the case. Furthermore, in settings such as school life children may have to monitor their own glucose levels and administer injections without adult help (Newbould et al 2007).

Young people's insulin requirements change as they develop. It is important that insulin regimens are flexible and monitored by competent health professionals. Adolescence is often a particularly challenging period, during which the rate at which insulin is absorbed in the body can change rapidly and without warning. At the same time individuals are likely to be undergoing emotional challenges associated with becoming independent. This can on occasions lead them to reject treatments and advice.

In the UK the quality of care for young people with diabetes appears to have lagged behind the standard achieved in many other European countries. Relative to its population, this country has amongst the highest numbers of children with diagnosed type 1 diabetes in Europe. Yet it also seems to have a relatively low proportion attaining good diabetes

Box 8. The Cost and Value of Medicines for People with Diabetes

The combination of increasing numbers of people being identified as having diabetes, more intensive treatments and a wider range of therapies has led to raised NHS prescribing costs. A recent NHS analysis highlighted the fact that in England the number of prescription items supplied to treat diabetes rose to over 28 million in 2006. They cost some £560 million (The Information Centre and YPHO 2007). This it was stressed was almost 14 per cent above the previous year's figure.

Just over 40 per cent of the total spent was accounted for by insulins. They typically cost from 30 pence to up to £1 per treatment day. This compares with treatment costs of 10-40 pence per day for various formulations of metformin, and approaching £2 per day for products such as glitazones and the incretin mimetic exenatide. It was noted in the context of insulins that doctors are increasingly prescribing short and long acting analogue products, as opposed to older insulins.

However, this does not mean that value for money was not obtained from these outlays. The total cost figure quoted above was equivalent to about 7 per cent of total prescribing expenditure for that year. This is in line with the proportion of overall NHS resources spent on diabetes. It is also relevant to note that total (all forms of medicine) pharmaceutical costs expressed as a proportion of total NHS spending have fallen in recent years, and now stand at a level similar to that recorded in 1968 (OHE 2008). Yet few would argue that the relative productivity of medicines use did not increase in that period.

NHS and other health care resources should not be wasted. But from the viewpoint of people in need of effective treatment for their diabetes, emotive or misleading presentations aimed selectively at curbing pharmaceutical spending as a factor within health care should not be permitted to undermine public understanding of the value of the medicines used to treat this serious, life threatening, illness.

control (Department of Health Diabetes Policy Team 2007). This suggests a need for further service improvement and closer attention to issues such as how specialist physicians and other members of dedicated clinical teams can most effectively work to support children and young people in their daily lives. Where necessary this ought to involve further improving the skills of non-specialist health service and other staff. It seems likely that an improved NHS supply of items such as insulin pumps would help a proportion of young people achieve better treatment outcomes.

Insulin delivery systems

The subcutaneous injection of insulin is an essential treatment for most people with type 1 diabetes. It is also vital for a minority of individuals with type 2 diabetes.⁴ The provision of sophisticated injection devices such as 'insulin pens' (which in the US tend not to be funded by insurers, and hence are not as

⁴ The point at which individuals with deteriorating type 2 diabetes should start using insulin is a matter of consumer and clinical judgement. Some people may wish to put off this decision for as long as possible. But if using insulin helps subjects to improve their glycaemic control and is not experienced as a 'defeat' or diminution in the quality of life, starting it earlier rather than later could help reduce subsequent risks.

widely employed as in Europe) helps insulin users to take correct doses. Modern techniques can also minimise any discomfort associated with injecting. But using insulin via injection may still sometimes cause local pain and itching. Lipodystrophies (adipose tissue 'lumps' that form under the skin after repeated injections) can also occur. These may understandably be unwanted cosmetically, can affect insulin absorption, and are not always avoidable via injection site rotation.

The use of new injection systems can sometimes be problematic for other reasons. Differences between the functioning of devices can on occasions result in problems such as recurrent ketoacidosis, if patients using them have been inadequately supported in relation to understanding appropriate injection techniques (Bhardwaj et al 2006). Such instances underline the value of specialist knowledge and expertise in the context of diabetes care.

Awareness of the limitations of injection based insulin regimens has led to research in a range of areas, from attempts to develop insulin 'patches' to the formulation of inhaled and orally active forms of insulin and the postulated development of implantable 'artificial pancreases'. However, the most important option to highlight here is that of insulin pump treatment. This form of delivery is widely used in the US (where insurance companies typically will fund its use) and the wealthier parts of Western Europe but has been much less widely available – primarily because of cost restraints – to NHS patients.

In 2004 insulin pumps were endorsed by NICE, but only for treating people with specific problems with the injection of insulin. A report published in 2007 by the Department of Health in association with Diabetes UK (DoH 2007a) noted that only about one per cent (or less in the case of children) of British people with type 1 diabetes use insulin pumps for the routine management of their condition. The equivalent proportions in countries such as France, Sweden, Holland, Germany and the US are in the range of 10-20 per cent.

Insulin pump usage can for some people with diabetes lead to marked improvements in the quality of their life and outcome indicators such as HbA1c levels. Nevertheless, it requires commitment. Patients need training, and must be able to actively manage their glucose levels via testing and insulin dose adjustment. Some people find this difficult. Perhaps the most frequent concern in this field relates to the fact that ketoacidosis may develop quickly if there is a fault with the pump, albeit that technical improvements have greatly reduced the possibility of the latter since such products were first introduced.

Self monitoring of blood glucose levels

The daily management of diabetes involves the effective co-ordination of diet and energy consumption. For individuals requiring insulin treatment the regular measurement of blood glucose levels enables them to monitor their condition, and amend their insulin use as necessary. But the discomfort associated with blood sugar testing can be experienced as being much greater than that of injecting insulin or other treatments. Amongst the wider population with type 2 diabetes who are on anti-hyperglycaemic treatment regimens without insulin the benefits of blood glucose level self monitoring have been much disputed.

A health technology assessment published in 2000 (at which time in the order of £90 million was being spent on glucose testing strips annually) concluded that in type 2 diabetes there was insufficient evidence to support recommendations

for self-monitoring. Research undertaken at around that time indicated that such testing could undermine quality of life (Franciosi et al 2001). In response some PCTs restricted their supply of blood glucose testing strips.

More recent studies have reported uncertainties about the value of self monitoring in the minds of type 2 diabetes patients and clinicians alike (Peel et al 2007) and a lack of effect in improving glycaemic control amongst subjects with the non-insulin treated condition (Farmer et al 2007). In overall terms glucose self monitoring, at least in subjects with type 2 diabetes who are not on insulin and have not been given effective help in using productively the results, appears to be associated with raised costs, increased mental discomfort and no clinical benefit (Simon et al 2008; O'Kane et al 2008).

However, some specialists and patient representatives still argue that there should be flexibility sufficient to allow those individuals with an interest in controlling their condition as effectively as possible to monitor their performance. In common sense terms it is only to be expected that individuals who have not been supported in learning how to respond effectively to the information derived from blood glucose testing should feel disempowered and depressed by it, especially as many people find it painful.

Studies of forearm testing indicate that this may be less painful (Greenhalgh et al 2002), although it can also be less accurate and is probably best used at times when a subject's blood glucose is likely to be relatively stable (Ellison et al 2002). Attempts have in the past been made to develop non-invasive devices to facilitate pain free blood sampling, although with limited success. Increased attention is currently focused on implantable blood glucose monitoring devices, which even if they have to be re-inserted on a regular basis can offer important benefits.⁵

Surgical interventions relevant to insulin use

These encompass pancreatic cell islet transplantation for individuals with type 1 diabetes, and bariatric surgery (or 'stomach stapling') for obese people with type 2 diabetes. Initial attempts at the former were undertaken in animal models in the 1960s and in humans in the 1970s. Pancreatic tissue transplantation today typically involves the use of islet cells isolated from the pancreas of a dead donor. The 'Edmonton protocol', developed in Canada in the late 1990s, involves such material being injected into the liver. There the cells transplanted may start to monitor glucose levels and produce insulin.

This can, when successful, stop or reduce the need for insulin treatment. But transplanted islet cells at best normally survive for only a few years, during which time recipients need constant, costly and to a significant degree hazardous immunosuppressive treatment. NICE guidance issued in 2003 argued that the safety and efficacy data then available did not support routine use of the procedure except by special arrangement for 'consent and for audit or research'. Although the potential of this technology to confer future benefit should not be ignored, it cannot at this stage be considered a viable way of treating at a population level type 1 or other forms of diabetes.

5 When and if non-invasive or minimally invasive glucose monitoring can reliably produce accurate readings its potential to improve diabetes care should not be ignored. Nor should not the utility of appropriately employed urine tests be under-estimated. Continuous Glucose Monitoring (CGMS) is a method of following blood glucose over time, which may offer the prospect of enhanced glycaemic control. However, there is little evidence as yet of this leading to HbA1c reductions.

Related options include total pancreatic transplants, as well as new forms of pancreatic islet allogenic and, in theory at least, embryonic or autologous stem cell derived islet cell transplants. However, the capacity of the latter to synthesise insulin adequately has not yet been demonstrated, and the supply of suitable donor pancreases is limited.

By contrast, there is much more robust evidence as to the benefits of bariatric surgery for obese patients with type 2 diabetes. The surgical procedures used in this context involve reducing the functional size of the stomach and small intestine via stapling and by-passing. It has been claimed that in approaching 80 per cent of patients who undergo such surgery diabetes related symptoms will start to be relieved within days, even before weight loss has occurred (Swansea University 2008). Such apparently dramatic success has led some observers to suggest that bariatric surgery has as yet unidentified impacts on factors such as the production of GLP-1 or perhaps other peptides in the gastro-intestinal tract, in addition to its more obvious effect on food intake.

Improving Outcomes

Since the initial publication of the National Service Framework for Diabetes (Box 9) in 2001 there has been considerable effort to improve local services. This has been backed by guidance from central resources such as the National Diabetes Support Team relating to virtually every aspect of NHS diabetes care commissioning and delivery. (See, for example, Department of Health 2002, 2004, 2007a, 2007b, 2007c.) There has also been complementary NHS progress in areas like the prevention and treatment of coronary heart and renal disease and long term condition management.

Public agencies ranging from NICE to the MRC (MRC 2002) have made additional contributions to diabetes research and service development, as have voluntary sector organisations such as Diabetes UK and academic and other institutions. Even more importantly, the introduction of the Quality and Outcomes Framework as a central element in the 2004 GP contract has been an effective driver of substantive changes in primary care activity. It is to be hoped that the recent pharmacy White Paper *Pharmacy in England* (Cmnd 7341) proposals relating to areas such as risk factor identification and case finding through health checks and enhanced medicines management will also open the way to changes in practice standards and service provision.

It would be beyond the scope of this analysis to attempt to critique such developments. But in essence the process of change underway is intended to facilitate the establishment of a coherently organised, quality oriented, conveniently accessible system of diabetes identification and professional treatment, coupled with a pro-active approach to self care. The scale of the progress already achieved may be illustrated by the fact that in England the number of people with diagnosed diabetes doubled between 1998 and 2008. Amongst people presently diagnosed with diabetes the available local data indicate that, even in relatively disadvantaged inner city areas (see, example, Figure 12), around 70 per cent have their 'key indicator' information entered in their primary care records. Approaching half appear to have an HbA1c level of under 7.5 per cent.

The strong growth in both diabetes occurrence and awareness has had important health service work load implications, especially as the intensity of the treatments given to people with diabetes has also increased. Key strategic questions relevant to achieving continued progress include:

Box 9. The National Service Framework for Diabetes

The 2001 National Service Framework set out twelve standards to ensure good quality care for those with diabetes. The areas they cover include:

- The prevention of type 2 diabetes
- The identification of people with diabetes
- Supporting the empowerment of children and adults with diabetes, and their efforts to live as healthily as possible
- Improving clinical care quality, and the control of blood glucose levels, blood pressure and other risk factors
- Providing good quality care for children and young people with diabetes, and ensuring that they and their families are supported appropriately and a smooth transition from paediatric to adult services for young people
- Managing diabetic emergencies effectively
- Improving hospital care
- Support for women with pre-existing diabetes and those who develop diabetes during pregnancy
- Providing long term condition support

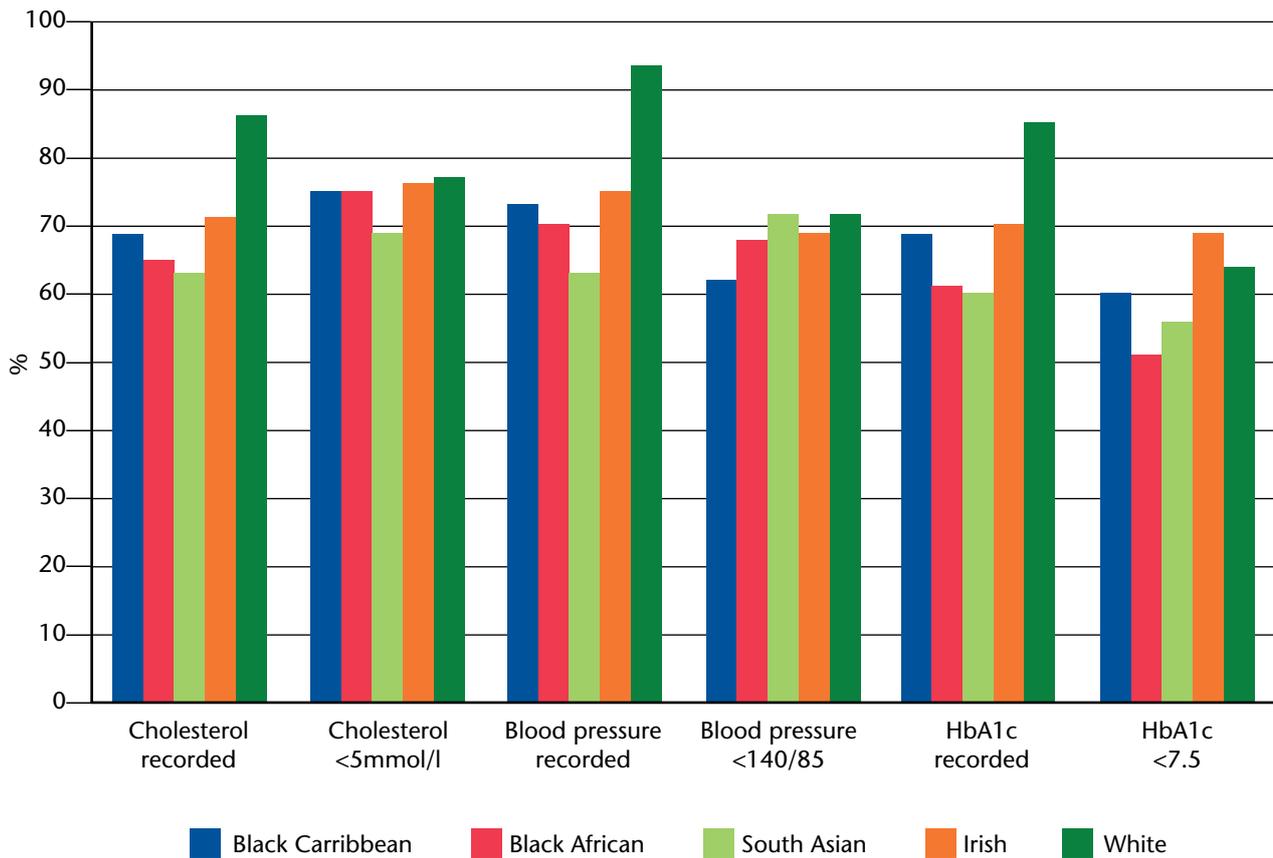
In 2003 the NSF for diabetes delivery strategy (England) described how the twelve standards would be implemented (Department of Health 2003). Key components of the strategy involve:

- Setting up local diabetes networks
- Reviewing local baseline assessments
- Comparative local and national audits
- Developing relevant workforce skills profiles
- Putting in place registers, education and advice, to support systematic treatment regimes; and
- Delivering a nationwide eye-screening programme.

In this last context, for example, the NSF established a target that by 2006 80 per cent of people with diabetes would be offered retinal screening. This would rise to 100 per cent at the end of 2007. In 2005 Diabetes UK reported that 40 per cent of people with diabetes had not been offered screening (Diabetes UK 2005). But recent Department of Health figures indicate an encouraging improvement in performance (DoH 2008a).

- 1 As the number of individuals at risk of or with 'pre-diabetes' and type 2 increases, how can health behaviour changes relevant to preventing the condition (or when necessary living with it well) best be encouraged?
- 2 What more might be done from a biomedical perspective to either reverse 'early stage' type 2 diabetes, or prevent it from progressing and causing harm?
- 3 What in future can be done to address the increasing incidence of type 1 diabetes, in order to prevent it or offer children and young people affected by it with a functional cure?
- 4 What further developments in the medical treatment of people with type 2 diabetes might prove most significant in the coming ten to twenty years?

Figure 12. Key Diabetes Indicators by Ethnicity – Islington GP Practices



- How can optimally productive relationships between specialist and generalist medical care, and between GP practice based primary health care professionals and community pharmacy, best be achieved?
- What economic, social or other barriers to health improvement and successful pharmaceutical innovation must be overcome in order to deliver future progress?

Promoting healthy behaviours and effective self care

The experience of countries such as Finland in heart disease and diabetes suggests that further progress towards primary prevention will be possible in this country. A combination of interventions aimed at, for instance increasing the relative price of ‘fast foods’, coupled with:

- mass communication approaches such as Diabetes UK’s ‘measure up’ campaign;
- targeted local interventions like workplace initiatives on diet and exercise; and
- individual advice and support delivered in settings such as surgeries and pharmacies

has the potential to change significantly not only individual thinking, but eventually the wider social context in which personal decisions are taken (Taylor et al 2006).

However, the time required to achieve this end and the extent of the resistance likely to be encountered – especially, perhaps, amongst those most at risk from premature death or disability from diabetes – ought not to be under-estimated.

In the parallel field of smoking prevention and cessation support it took half a century to achieve today’s acceptance of the need for effective action. Further, there now appears to be a ‘hard core’ of relatively vulnerable population groups that remain most likely to start smoking, and to become nicotine dependent. Similar patterns could in future more clearly emerge in relation to obesity and type 2 diabetes in the UK.

With regard to tobacco smoking, the Royal College of Physicians (2007) has recently argued that it would be in the interest of those who are least able to stop to offer them the alternative of long term therapeutic nicotine (NRT) use. This could (through substitution) prevent their addiction leading to avoidable harm.

Similarly, looking forward to enhancing the future outcomes of diabetes care, the view taken here is that when and if there is evidence that pharmaceutical use can (after taking into account all likely costs) augment the effects of behaviour change programmes, or protect individuals who do not choose to alter their lifestyles, constructive attention should be paid ensuring the fullest possible population access to relevant products. This could include not only enhancing the provision of blood pressure and cholesterol lowering agents, but also present (or possible future) medicines that might safely be used for reducing obesity levels and/or normalising glucose metabolism early on in the development of insulin resistance and pancreatic damage.

However, the impact of such strategies can only be optimised if they are successfully linked to progressively more effective means of changing related health behaviour. The latter might include the increased use of ‘reward feedbacks’

Box 10. Enhancing Dietary Control – DAFNE and DESMOND

The Dosage Adjustment for Normal Eating (DAFNE) course consists of a 5 day outpatient program for people with type 1 diabetes. It teaches flexible intensive insulin treatment combining dietary freedom and insulin adjustment, with the aim of improving clinical outcomes (glycaemic control) and quality of life. A study of 160 adults with type 1 diabetes found that 6 months after the DAFNE course HbA1c levels were significantly better in those who had completed it. The increased dietary freedom with the DAFNE approach led to significant improvements in quality of life (DAFNE Study Group 2002). This is consistent with the experience of individuals interviewed during the preparation of this report. Yet although their value is relatively well established, UK professionals point to problems in funding DAFNE programmes. This contrasts with experience in countries such as Germany, where the DAFNE course is a routine part of diabetes care.

Diabetes Education and Self- Management for Ongoing and Newly Diagnosed (DESMOND) is for men and women who have been newly diagnosed with type 2 diabetes. It is a structured education programme which consists of 6 hours of group sessions delivered to a maximum of 10 people by a health professional in the community. Recent research (Davies et al 2008) indicates that the DESMOND programme successfully promotes weight loss and smoking cessation. It also supports positive changes in attendees' beliefs about diabetes. Yet a year after diagnosis HbA1c levels were unchanged. Observations such as this last might lead to some questioning of the value of using HbA1c levels as an indicator of diabetes care quality and/or likely outcomes, although this is not to say that an uncritical approach should be taken to evaluating self care support interventions.

(like 'instant' test scores and/or supportive messaging that positively reinforce desired behaviours), the structured use of behavioural 'cues' (such as automated mobile phone voice and text 'reminders') and the delivery of 'health intention' formation and implementation programmes via the internet and/or in settings like community pharmacies (Horne 2008).

In the context of people living with type 2 diabetes there is already evidence that (amongst individuals who elect to attend them) exercise support programmes can be beneficial. (See, for instance, Krousel-Wood et al 2008.) So too can similar interventions designed to enable individuals and groups to control their diets (Box 10), use medicines effectively and raise their sense of self efficacy in relation to managing diabetes. The extent of the possible gains to be derived from supporting self care should not be overstated (Newbould et al 2006, Taylor and Bury 2007). But neither should potentially significant opportunities for improving future health outcomes be neglected (Newman et al 2004).

It is therefore of some concern that a survey undertaken by the Healthcare Commission in 2006 found that although 40 per cent of the total population interviewed would like to attend a diabetes self management course, only a tenth of the people who were interviewed had done so (Healthcare Commission 2007). The Commission has since sought to stimulate better performance in this area and to help ensure that all GPs receive the support they need to manage and monitor the care of people with diabetes effectively, where necessary in partnership with both specialists and local colleagues such as community pharmacists.

Better treatments

From a biomedical perspective, the combination of genetic vulnerabilities and external triggers that cause type 1 diabetes may in the coming decade or two be sufficiently elucidated to allow effective preventive measures to be introduced. Failing this, several of the experts consulted for the purpose of this analysis believe that more effective strategies will demand advances based either on stem cell science and the regeneration of lost pancreatic tissue, or the development of 'artificial pancreases'. These will almost certainly involve the use of implantable (as distinct from non-invasive) blood glucose (and perhaps insulin) level monitoring devices. The latter could be used in 'closed-loop' configurations with insulin pumps that automatically infuse the hormone. Alternatively, they will replace existing glucose monitoring devices used to support self injection.

This last opportunity alone might significantly improve glucose control, and hence health outcomes, in the overall insulin using population. But advocates of 'artificial pancreas' argue strongly that within five to ten years the impact of this technology could be even greater, transforming the lives of many insulin users (Hovorka et al 2006). In the light of such anticipated advances it might reasonably be argued that NHS policy and practice relating to the provision of insulin pumps is (over and above the NICE appraisal of existing technology presently being developed) in need of review.

Developments that will allow the delivery of the hormone via inhalation, or perhaps more importantly orally, should also further improve the quality of life for, and hopefully long term health outcomes amongst, people with diabetes. One inhaled insulin has already been marketed and later withdrawn, world wide. This was largely because of the reluctance of health service funders to finance its supply, together with other factors. Some commentators may question the long term desirability of delivering relatively large doses of insulin to the lung. But even so, this experience may still be regarded as demonstrating the technical viability of inhaled insulin treatment.

Research in this field together with that of developing orally administered insulin is continuing, not only in Europe and the US but also in India (Gowthamarajan and Kulkarni 2003). Companies working in south Asia are amongst those aiming to be the first on the world market with insulin in tablet form. Yet for this to be achieved a number of complex scientific problems have still to be overcome. The efficiency with which oral insulin can be delivered via the intestine into the blood stream is presently too low to permit cost effective products to be developed. But if this and other challenges can be mastered, oral insulins could change radically diabetes care. They would make taking insulin much easier. The fact that delivering insulin in this manner can be seen as being much closer to the natural hepatic portal vein route is another potentially relevant factor.

Otherwise, improving the range of effective anti-diabetic medicines available will require further exploration of known therapeutic mechanisms, including those responsible for the actions of metformin, the glitazones and the incretins, together with research in areas such as the actions that adipokines have on cells in the muscles, the liver and the pancreas. Additional exemplary areas of pharmaceutical research include investigating the ways substances such as leptin (a protein hormone first identified in the mid 1990s) ghrelin (a hormone produced in the stomach and the pancreas) and peptide YY (PYY) may, together with other naturally occurring molecules, act in the brain and elsewhere to regulate food intake and glucose metabolism. The

development of medicines aimed specifically at preventing microvascular disease caused by high blood glucose levels is another future possibility.

The ongoing discovery of increasing numbers of diabetes related gene variations is also providing pharmaceutical scientists with further opportunities to develop new treatments and diagnostic tests. It is in this last area that innovations derived from recent 'breakthroughs' in genomics are in the near future perhaps most likely to be marketed. Particularly when combined with physical measurements such as cholesterol and body mass indices and also family history based information, recent developments in understanding genetic associations with diabetes could be used to offer relatively powerful predictive tests to people such as younger working age adults before they develop problems such as insulin resistance.

If this were to enable individuals (and families) to make more informed lifestyle and treatment choices than would otherwise be possible it could generate considerable health gain. But some professionals argue that it will be better to go on advising everyone to live as 'healthily' as possible, rather than to permit freer access to more specific personal data. It has been suggested that 'unregulated' (implicitly, more easily accessed) testing could promote needless fears on the one hand, or misplaced complacency on the other (Sense About Science 2008). However, objections to extending public access to diagnostic and allied testing might on occasions be linked to vested interests. They could, for instance, stem from professional rivalries and concerns that enhanced access to home or 'near patient' testing in community pharmacies might undermine the 'trading' position of some other groups and institutions.

Barriers to overcome

One critical barrier to improving diabetes care is that of insensitivity to the experiences and priorities of people living with the condition. On occasions appeals to listen to consumer views are dismissed as unscientific, or regarded as 'mere marketing'. Yet such reactions can themselves sometimes appear arrogant, and risk failing to address issues at the heart of achieving better outcomes. In reality service user experiences and preferences frequently provide useful insights as to how services could be improved – see Box 11.

Organisations such as pharmaceutical companies, along with those that act as the advocates of particular service user groups, will naturally wish to encourage the use of effective new medicines and other innovative treatments. The global market for diabetes treatments has 'out-performed' the pharmaceutical sector as a whole since the middle of the 1990s (Hauber and Gale 2006). But it should not be assumed that this is undesirable.

Nor should it be forgotten that individuals responsible for functions such as cost control in organisations like those responsible for commissioning health services may have pressures upon them that sometimes distort their judgements in the direction of under-using new treatments. This is a particular hazard when it comes to balancing immediate cost savings against longer term – and frequently inherently difficult to quantify – clinical, psychological and social benefits. In contexts where labour costs are difficult to reduce outlays on innovative therapies may appear to be the only expenditure variable open to adjustment, even if they account for only a limited percentage of a total budget.

The DAWN (Diabetes Attitudes, Wishes and Needs) programme is an example of a beneficial initiative supported by the pharmaceutical industry in partnership with voluntary sector bodies and professional groups. It has revealed concerns amongst people with diabetes about the extent to which their condition interferes with their lifestyle aspirations because of the difficulties associated with taking treatments and other aspects of the condition. There is no easy answer to the challenge of helping individuals, families and communities to live as well as possible with diabetes. Often there may be complex reasons why apparently simple solutions are not viable. But even so there is a strong case for listening openly and without any pre-judgement to those affected. Failures to do this may lead to the introduction of what appear to be managerially viable health care developments, which in practice do not work.

At the same time, people with diabetes and members of the wider public should strive to develop a critical, science based, awareness of the progressive nature of the type 2 condition and how it can be prevented or effectively controlled. There is evidence, for instance, that only a minority – probably under a quarter – of the population has insight into the differing aetiologies of types 1 and 2 diabetes. Increased knowledge about such matters may not directly enable individuals to change their lifestyles. But if the mechanisms by which factors such as regular moderate exercise or an increased waist size can either stop or promote progression towards type 2 diabetes are not understood, this could nevertheless impair the transmission of health promotion messages.

Some of the pitfalls of improving diabetes related self care have been illustrated by research in Scotland. The work of Lawton et al (2005) illustrates the power of contextual influences on illness perceptions and health behaviours. They observed that patients receiving diabetes care from their GPs were less likely to regard their condition as 'serious' than those going to hospital based providers, even when from a medical perspective this was not the case. The primary care users were consequently less motivated to change their behaviours in ways that might protect them from future harm.

Similar variations may sometimes be associated with taking insulin as opposed to oral anti-hyperglycaemic medicines, in that the latter may be seen as for 'less serious' illness. Such findings underline the importance of establishing a sensitive awareness of the practical implications of 'lay' health perceptions, and the paradoxical impacts that well intended but poorly researched service developments may make on outcomes.

As the diagnosed prevalence of diabetes has increased, so too has the importance of devolving the provision of support and care to the most conveniently accessible level. The purpose of this is not least to ensure that service supply can affordably meet demand. The extension of diabetes care (especially in relation to the type 2 condition) by GPs and their practice based nurse colleagues has been an important trend, which in future is likely to continue. Similarly, an extension of 'health check' provisions and 'pre-diabetes' life style support and treatment provision in community pharmacies should also prove beneficial. Yet the benefits and requirements of specialist care should not be ignored by commissioners (ABCD and Diabetes UK 2008).

Patient and wider public interests will be best served by systematic approaches to ensuring that secondary and tertiary care providers complement each other, and are sufficient to support the further extension of appropriately integrated and (cost) effective primary care for children and adults in

Box 11. Emma's Experience with her Insulin Pump

'I was diagnosed with diabetes 23 years ago and like most diabetics was injecting insulin. About 10 years ago I started to develop a stomach problem, I wasn't digesting my food properly and wasn't getting the nutrients I needed. My diabetes control started to go very wrong, my blood sugars would go up ten hours after eating, not straight after as they should do. My treatment was up to 12 injections a day but I could still not get control of my diabetes. At this point control was so bad that I was in and out of hospital. I had to give up my job in retail because I was so ill all the time.

For a long time I'd been secretary of the local diabetes group so had heard about insulin pumps. I had thought about having a pump before, but it was expensive and I'd just had to give up work. At a diabetes awareness day I met the local pump rep and they were doing a one month free trial of the pump. I applied to my PCT for funding for the consumables and, after lots of phone calls and a lot of chasing, they agreed to fund them. After the one month I was offered four years interest free credit on the pump which was £45 a month.

Once I'd decided I wanted the pump I went to the GP and to see my diabetes doctor at the hospital. The hospital doctor said to me 'well Emma it sounds a bit drastic' and I said to him 'well I feel that having to give up work and being in hospital every other week – that is drastic!'. I also had to get the support of a diabetes specialist nurse who would back me. I was really lucky in that one of the diabetes nurses had a son who had diabetes and because of that she took a weeks holiday and paid for the course herself, the PCT would not pay for that. PCTs not paying for the specialist training is a stumbling block to people being able to use pumps. I've met consultants who would like more people to be on pumps but the staff are not trained to provide the support needed.

So I eventually got the pump for the free trial and I instantly got on with it. You have to do a training session which you have to pay for. The training day was a Thursday and a Friday and on the Friday night the rep called me to ask how I was getting on – I told him he was never getting the pump back! The change was so quick I could hardly believe it. I instantly felt better and in about the next 3-4 weeks I felt like nothing was wrong with me. I had been off work for a year by this time but once I was on the pump I was back in a job a week later – it really was that quick. Since I've had the pump I've not been in hospital at all and as I say before then I was in every other week.

The pump does have some maintenance but it is nothing like the injections. You have to change the needle in your stomach every 2-3 days and change the canula every 5 days. You do have to do a lot of blood testing – for people who hate them it's not the right treatment for them. I do a minimum of 2 a day but if I'm cold or unwell then I might do at the most 12 a day.

I occasionally catch the tubing which gives you a bit of a twinge. But you can disconnect it for short periods, like when I go for a swim or when I go for a shower.

I finished paying for the pump in October and on 2nd November the pump suddenly wasn't working. I phoned the company to ask what was going on and they said I needed a new one. I couldn't believe it – I had no idea it would wear out! I had to go back onto injections and my control was worse straight away. I felt like death for 2-3 days. Luckily by this point the PCT was funding them and within 7 days I was back on a pump and back to normal. It was a horrible reminder of what my life was like before I had the pump.'

Source: School of Pharmacy research

the community (Matthews 2007). However, this should not necessarily be interpreted as meaning that this demands the creation of large, effectively merged, local integrated care providers, or that housing specialists and generalists together in new buildings is any substitute for constructive values and the 'relationship based' delivery of seamless care in day to day practice. In many instances plural care provision, characterised by a pragmatic mix of supported collaboration and regulated competition, will be most likely to enhance individual and population outcomes.

A final barrier to achieving future therapeutic progress relates to the closely related issues of financing of scientific innovation and the funding of new treatment options when they become available in the market. The establishment of bodies such as NICE (the National Institute for Health and Clinical Excellence) in England and IQWiG (the Institute for Quality and Efficiency in Health Care) in Germany has been an important development. In an area as costly and damaging to modern society as diabetes (Box 12) few people would argue against the logic of seeking to ensure that money spent on all forms of service provision – including not only medicines but also the far larger amounts devoted to salaries – is allocated as wisely as possible.

Health economic analyses are intended to guide such decision making. However, the limitations of the methods used and the processes surrounding the work of bodies such as NICE and IQWiG deserve attention. From the perspective of people and communities at risk from diabetes and the agencies seeking to discover and disseminate better means of prevention and treatment, examples of relevant concerns include:

- **lack of insight into both personal and wider community needs.** The techniques normally used by health economists do not directly involve asking people who have experienced given types of illness about the details of their experience. Nor do they take into account the varying impacts specific illness may have on the families of those affected or the wider community;
- **data aggregation.** Following on from the above, pooled figures on the benefits of given types of intervention may conceal the fact that some groups gain significantly more or less than the average. Bodies such as NICE acknowledge this last point, and stress that their guidance is typically valid in only about 80 per cent of cases (Rawlins 2008). But this may not be recognised in practice by health care funding agencies and local providers;

Box 12. The Economics of Diabetes Prevention and Treatment and NICE's Work

The economic burden imposed by diabetes, and the costs and benefits of its treatment, have been extensively reviewed – see, for instance, Raikou and McGuire (2003) and Williams (2005). Diabetes is responsible for between 5 and 10 per cent of all premature mortality and disability in countries such as the UK and in the order of 7 per cent of all health care expenditure. The available research emphasises the impact of macro and micro vascular diabetic complications on hospital care costs, albeit that for many people the latter are not as important as the less tangible personal distress and loss diabetes causes.

Trials such as the UKPDS have provided economic data supporting the use of medicines such as metformin and captopril (an antihypertensive). However, the detailed components of such calculations may change over time, not least as pharmaceutical and other factor costs alter. Further, the introduction and enhanced use of treatments such as statins in the context of reducing diabetes related macrovascular morbidity and mortality may over time change the relative costs and benefits of other interventions used in the field. The view taken here is that it is in fact impossible to calculate with any degree of precision the likely future benefits of innovations such as, say, the vascular disease screening programme recently proposed by the Department of Health, or those which might in future stem from innovations like the introduction of oral insulins. But this is no reason for failing to support progress in such areas if there is a realistic possibility of it leading to enhanced welfare.

This conclusion suggests that there is a danger that the work of organisations such as NICE could unwittingly promote a false sense of certainty about decision making for the future. In the decade or so that it has existed NICE has produced about a dozen guidelines and appraisals relevant to diabetes care. Several more are in development. Even so, there has recently been concern that some medicines will be unfairly 'blighted' by the lack of an appropriate NICE analysis. In an attempt to address this problem the agency is seeking new approaches to providing rapid guidance.

Some commentators fear that the 'short clinical guideline' solution being developed could foster a new set of problems. However, at a more general level a deeper problem is that few people – including politicians, journalists, service managers, doctors and pharmacists – have adequate insight into what techniques such as incremental cost utility analysis (NICE's central analytical instrument) involve, or what statements suggesting that a given treatment delivers benefits costing more or less than the rough affordability threshold of £30,000 per quality adjusted life year (QALY) really mean.

The following simplified example may illustrate the types of point that need better to be understood:

- A patented medicine (A) used to protect against diabetes related risks costs £600 a patient year, and delivers on average 22 QALYs per 100 people treated per year. The cost per QALY is therefore $£600 \times 100 / 22 = £2727$.
- A new medicine (B) becomes available at £650 a year. It protects against the same risks and generates 23 QALYs per 100 people treated, at a cost per QALY of $£650 \times 100 / 23 = £2826$.
- The average cost per QALY difference is circa £100. The incremental cost utility of the new medicine (B) against the older less effective A (ie the cost per extra QALY gained) is £5,000 ($£650 \times 100 - £600 \times 100$). This is well within the £30,000 threshold.
- However, the original medicine's patent ends and the price falls to £100 per patient year. The incremental cost utility of medicine B against A therefore rises to £55,000 ($£650 \times 100 - £100 \times 100$). This is well above the assumed NICE affordability threshold.

This means, all other things remaining constant, not only that medicine B becomes unaffordable and that NHS patients who would benefit from its use become unable to do so. It also suggests that in this specific area no new patented medicine with extra benefits of a magnitude comparable to that generated by medicine B will be supplied by the NHS. If other health care systems were to follow suit, research on this area of diabetes care would have to stop.

- **evaluation delays.** The collection of evidence required for large scale evaluations may require a long period of time. This means that regulators' judgements often lag behind informed clinical opinion. This can create delays in the achievement of appropriate public access to treatments. Such problems are exacerbated if evaluations fail to consider all the therapeutic options available at a given point of time (Box 12) or cannot be updated flexibly when new products or bodies of evidence become available; and
- **uncertainties about what in reality is affordable coupled with failures to consider long term public interests.** Setting affordability thresholds in contexts such as NHS care can be seen as a relatively arbitrary process, particularly when it is remembered that established interventions involving high labour costs are unlikely to be subjected to the same scrutiny as new treatments. Agencies such as NICE are charged with making essentially short term decisions

about the provision of fragmented 'items of treatment', rather than integrated strategic judgements about care delivery and issues such as the future value of the research based pharmaceutical industry to Britain, the EU and the world as a whole.

Although individual innovations may be of varying utility, sustained investment in fields such as diabetes are needed over decades to allow the full value of long term discovery processes to be realised. In a sense the therapeutic revolution started by Banting and his colleagues is still in progress. It is not necessarily in the public's interest to treat medicines as 'one-off' items to be evaluated in isolation, rather than as linked steps along a continuing funding path towards finding better treatments for diabetes.

The above points should not be taken to imply that the work of agencies such as NICE and IQWiG lacks any value. But they highlight the fact that, at both the political and personal levels, deciding whether or not to supply or use

products such as insulin analogues or other new medicines is a complex process. The overall public interest is much harder to identify than is sometimes assumed. In addition, clinical and service user opinions and preferences are still needed to identify the best way forward in individual cases. Broad brush evaluations and guidelines should logically be seen as offering a framework for informing clinical and personal choice, rather than its curtailment.

Conclusion

Diabetes directly affects the lives of some three million people in the UK, together with those of family members and others whose roles include caring for people who have been disabled by the condition. Worldwide the equivalent figure is 200 million, and this is forecast on the basis of established trends to rise to about twice that number in the next two decades. This trend is in large part explained by predicted prevalence rises in Asia and Africa.

As the twenty first century proceeds diabetes is almost certain – failing a mass return to pre-industrial age living standards – to affect an even greater proportion of humanity as it collectively ages and if, as presently seems likely, obesity rates continue to climb. Yet alongside there is today a much stronger scientific, professional and political understanding of the causes and possible means of preventing diabetes than has ever before existed. To the extent that this is successfully translated into protective life style changes and better therapies, this report's analysis suggests that the rising rates of diabetes will eventually be curbed.

In retrospect, the current diabetes pandemic might then become regarded as part of a positive transition towards a healthier world. But it would be rash to suggest that such progress is inevitable, and attention should not be drawn away from the current levels of suffering inflicted by diabetes. There is some evidence that in the US population, for instance, glycaemic control amongst the diabetic population may have failed to have improved in line with the potential of better treatments (Koro et al 2004). Further, better medical recognition of diabetes related risks amongst men could to a degree have been offset by an increase in diabetes linked mortality and disability in women.

Effective action to reduce the threat of diabetes therefore remains an urgent priority across the globe. In this country initiatives such as those associated with the 2004 GP contract's QOF have led to important service improvements. They are allowing the benefits of pharmaceutical and other therapeutic advances to be more widely enjoyed. Agencies such as NICE and (in England) the Department of Health are also investing in understanding health behaviours relating to the 'metabolic syndrome', and how they can be changed.

From the perspective of this study it is also relevant that professions such as pharmacy are adapting to meet twenty first century health care needs. Community pharmacists are beginning to focus more of their working effort on supporting effective medicine taking for long term conditions like diabetes, and enhancing their wider health promotion competencies. This offers a prospect of significant additional gains, particularly if the progress achieved to date is effectively supported by:

- **'world class' service commissioning**, which through the intelligent direction of funding incentivises and facilitates the improvement of health

outcomes. In the community pharmacy context the introduction in England of 'directed enhanced' services (which PCTs, when a need has been identified, will be obliged to fund) could prove valuable in 'kick starting' further service developments. But in the longer term this may be no substitute for better informed local level service development processes;

- **integrated remuneration strategies**, which will encourage professionals like GPs and community pharmacists and also specialist and generalist care providers to work together to provide seamless care when this is needed but which do not eliminate 'healthy' competition or lead to the formation of needlessly large organisations which service users may experience as denying them local choice;
- **enhanced access to self help and 'therapeutic education' groups** and resources, where there is evidence that this can effectively promote desirable life style changes, better medicines taking and/or other positive gains; and
- **the further establishment of an open, listening, culture** which values understanding service user experiences and the ways in which each individual's life quality can most effectively be improved.

However, even if such advances are achieved and existing social and scientific knowledge is used to the full, this will not fully solve the problem that diabetes represents. This is in part because a significant proportion of diabetes cases are not attributable to modifiable factors. It is also because mass behavioural change is unlikely to be rapidly achievable, especially among less advantaged groups located within rich societies. Given such realities, the continued improvement of bio-medical treatments for diabetes has a vital part to play in further improving outcomes in terms of both primary and secondary prevention. That is, in preventing diabetes from becoming manifest wherever possible, and treating it effectively whenever necessary.

In the medium to long term, advances in areas such as genetics, immunology and stem cell research could make it possible effectively to eradicate all forms diabetes through, for instance, preventing beta cell destruction and/or promoting pancreatic regeneration. In the shorter term advances in fields such as 'artificial pancreas' technology and better glucose monitoring, the development and marketing of easy-to-take forms of insulin and other more effective medicines, and diabetes risk testing all promise significant, realistically achievable, progress.

It is reasonable to conclude, therefore, that although the scale and gravity of the challenge that diabetes presents to modern humanity is comparable to that of any past plague, it can and will be overcome if societies are prepared to invest adequately in both the research needed to develop pharmaceutical and allied innovations, and the health care and wider welfare systems needed to deliver them well. In the final analysis 'beating diabetes' will not be a matter of biomedical advance on the one hand or social intervention on the other. Rather, relevant public health improvement in the twenty first century will demand an effective, balanced, combination of the two. Modern pharmacists have an important opportunity to deliver such an amalgam through supplying medicines, enhancing their clinical use and promoting individual and wider community learning and change.

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Diabetes:

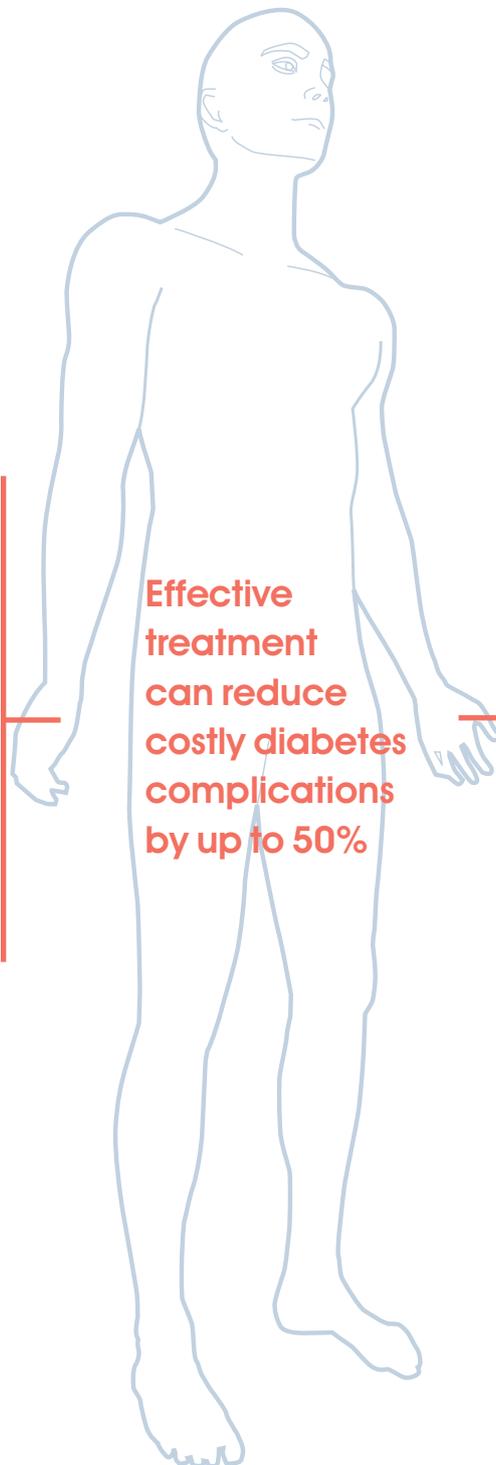
A chronic disease where blood glucose is too high, either because insulin is not produced or is insufficient

Symptoms:

Tiredness, weight loss, increased thirst, passing a lot of urine, blurred vision

Complications:

Serious complications can result from elevated blood glucose, some of which are illustrated here. However these are largely preventable, and can be delayed with early diagnosis and effective treatment



Effective treatment can reduce costly diabetes complications by up to 50%

Heart Attack**Risk:**

Increased by 300%, and heart disease is up to 4 times as likely

Effective treatment:

Leads to a reduction in heart failure of over 50%

Stroke**Risk:**

Up to 4 times as likely

Effective treatment:

Reduces strokes by more than a third

Amputation**Risk:**

15% develop foot ulcers and up to 15% of these need amputations. Most common cause of non-traumatic lower-limb amputations

Effective treatment:

Reduces the number of amputations and effective education reduces the number of foot ulcers

Total Kidney Failure**Risk:**

3 times as likely as in the normal population. About 30% of type 2 patients have renal disease

Effective treatment:

Reduces the causes of kidney failure by more than a third

Blindness**Risk:**

Single largest cause of new cases of adult blindness in the UK. Nearly all those with type 1 diabetes experience minor retinal damage within 20 years, as do 60% of those with type 2

Effective treatment:

Reduces serious deterioration by more than a third

Effective treatment can reduce costly diabetes complications by up to 50%

Source: *Diabetes: finding excellence?* The MODEL group.



Policy Paper 5

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