

Diabetes – Evaluating the True Impact

a report by

Dr Darren Poinasamy

Business Development Executive, Chiltern International

Dr Darren Poinasamy currently works at Chiltern International as a Business Development Executive. Before this, he worked in diabetes research, including a placement at GlaxoSmithKline. Dr Poinasamy obtained a PhD in Biochemistry from the University of Newcastle, following a BSc in Biomedical Science from the University of Portsmouth.

Diabetes is characterised by the failure to synthesise, secrete or respond to insulin; and is the third most prevalent disease in the Western world, afflicting at least 6% of the population of Europe and North America and approximately 177 million worldwide.¹ The disease will have an immense impact on society, both in industrialised and developing countries (see *Figures 1 and 2*).

An Overview of the Disease

The principal functions of insulin are to regulate the uptake of nutrients (glucose, amino acids and fatty acids) and the production of storage macromolecules (protein, glycogen and triglycerides). It is the failure of this hormone to exert these effects that is a major factor in diabetes. There are essentially two types of diabetes: Type 1 and Type 2.

A minority of patients suffer from Type 1 *diabetes mellitus*, which is caused by pancreatic β -cell failure and leads to an absolute loss of insulin. This form develops most frequently in children and adolescents; however, it is increasingly presenting itself later in life. Over 90% of patients with diabetes have Type 2 diabetes, also known as non-insulin-dependent *diabetes mellitus*, which is characterised by the failure of sensitive tissues such as the liver, skeletal muscle and adipocytes to respond to insulin – ‘insulin resistance’.² Type 2 diabetes is found predominantly in adults.

The Economic Impact of Diabetes

Diabetes has a substantial economic impact: in the US it accounts for a total annual economic cost of over US\$98 billion, which includes US\$44 billion in direct medical and treatment costs and US\$54 billion in indirect costs due to disability and

mortality.³ In Europe there is a similar predicament, with Type 2 diabetes alone contributing to an annual cost of €29 billion between Belgium, France, Germany, Italy, The Netherlands, Spain, Sweden and the UK.⁴ In the UK, the National Health Service spends an astonishing £4,000 per minute on diabetes, which accounts for 9% of the total annual healthcare budget.⁵

The true costs of diabetes can be measured by the level of control of the disease and the medical complications that ensue. Figures from The World Health Organization (WHO) have shown that in India, 25% of the average family income would be spent caring for an individual with diabetes.¹ In the US, this figure is 10%.¹ In addition to medication comprising of insulin and other diabetes drugs, subjects afflicted with diabetes must also endure the added cost of increased health and life insurance. Alternative indirect costs on the diabetic patient include absence from work, an inability to work as effectively and even premature retirement.

With the added responsibility of ensuring a normal glucose level, the diabetic patient is also susceptible to other medical complications such as blindness, renal failure, cardiovascular disease and neuropathy. The treatment of these long-term complications due to diabetes is believed to be the principal expenditure for most countries.

With WHO predicting a diabetes epidemic reaching over 300 million by 2025,¹ which will have a knock-on effect on the national healthcare budget, the correct steps must be taken to prevent this life-threatening and economically exhausting disaster. The number of deaths attributed annually to diabetes was 800,000; however, this did not include the number of deaths linked to diabetes, which is

1. The World Health Organization, “The Cost of Diabetes” (<http://www.who.int>).
2. G W Cline, K F Petersen, M Krssak, J Shen, R S Hundal, Z Trajanoski, S Inzucchi, A Dresner, D L Rothman and G I Shulman, “Impaired Glucose Transport as a Cause of Decreased Insulin-stimulated Muscle Glycogen Synthesis in Type 2 Diabetes”, *N. Engl. J. Med.*, 341 (1999), pp. 240–246.
3. American Diabetes Association, “Direct and Indirect Costs of Diabetes”, (<http://www.diabetes.org>).
4. B Jönsson, “Revealing the Costs of Type 2 Diabetes in Europe”, *Diabetologia*, 45 (2002) 7.
5. Diabetes: Therapeutic Advances and Market Opportunities – A Scrip Report (2003) (<http://www.pjbpubs.com>).

thought to be four million deaths per year, contributing to approximately 9% of the global total.¹

Of the many complications implicated in the disease, cardiovascular problems account for the highest number of diabetes-related deaths.

Therapy and New Drug Development

The control of blood glucose is the key objective in treating diabetic patients. As insulin resistance persists, the pancreas is unable to produce enough insulin to counteract the resistance; and injections of exogenous insulin are required. In combination with insulin, drugs are necessary to reduce the hyperglycaemia present in individuals.

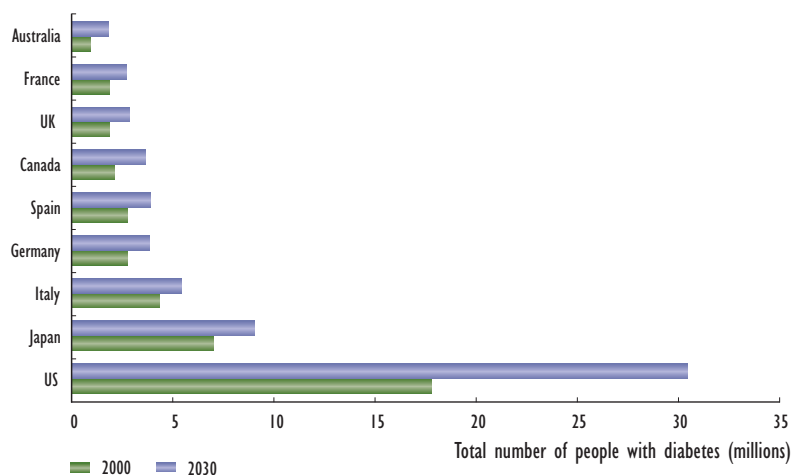
Drugs used to improve glycaemic control include: sulphonylureas, which increase insulin release from pancreatic islets; metformin, which reduces hepatic glucose production; thiazolidinediones, which target the peroxisome proliferators-activated receptor (PPAR)- γ , thereby enhancing insulin action; and acarbose, which inhibits α -glucosidase, thus interfering with the absorption of glucose from the gut.⁶

Currently, both AstraZeneca and Bristol-Myers Squibb lead the competition in the development of drugs that target the family of PPARs with Galida and Muraglitazar, respectively.⁷ Other drugs in development include MK-0431 by Merck, which, it is hoped, will be the first tablet to elevate glucagon-like peptide, thereby controlling blood sugar levels.⁷ Further research into the development of MK-0431 has also envisaged that this drug may also lead to weight loss.⁷ Merck are expected to make an application to the US Food and Drug Administration (FDA) in 2006.⁷

It is predicted that the retail market for diabetes medications will surpass US\$20 billion in 2006. The oral antidiabetics market has been dominated by Merck KGaA's Glucophage,⁵ which generated worldwide sales of US\$1.7 billion in 2000.⁸

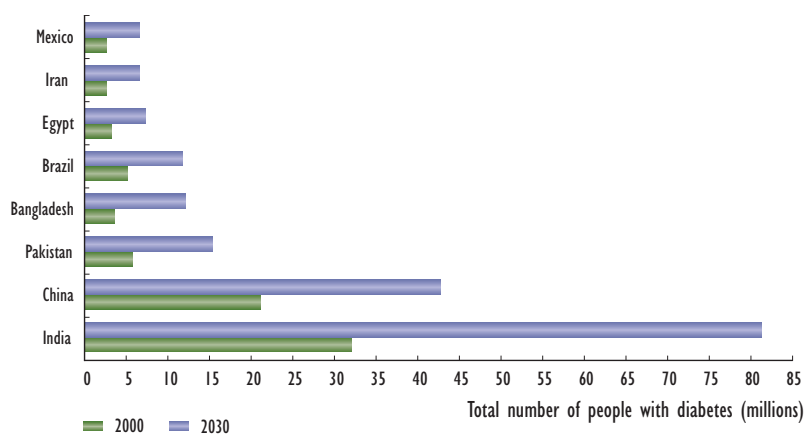
However, with patents set to expire and the generic competition for the class of metformin drugs set to deflate the diabetic drug market, the future looks to be controlled by another class of drugs – the glitazones. Both Takeda's Actos (pioglitazone) and

Figure 1: Diabetes Estimates and Projections in Selected Industrialised Countries



Source: World Health Organization

Figure 2: Diabetes Estimates and Projections in Selected Developing Countries



Source: World Health Organization

GlaxoSmithKline's Avandia (rosiglitazone), which were launched in 1999 and had their respective sales rise by 73.2% and 53.1% in 2001,⁹ have become billion dollar products.⁵

Advances in Insulin Therapy

Aside from the development of new drug targets for the treatment of diabetes, the usage of insulin continues to evolve.¹⁰ The regular use of insulin has deteriorated since the release of Humalog (insulin lispro) – the first rapid-acting insulin – in 1996.¹⁰

It has taken a few years for rapid-acting insulin to outsell short-acting, regular insulin. The long-acting Lantus (insulin glargine), which was released in the

6. D E Moller, "New Drug Targets for Type 2 Diabetes and the Metabolic Syndrome", Nature, 414 (2001), pp. 821–827.

7. M Herper and R Langreth, "New Diabetes Drugs to Watch" (http://www.forbes.com/2004/01/23/cx_mh_rl_diabetesslide.html).

8. Lead Discovery, "Diabetes 2003" (<http://www.leaddiscovery.co.uk/reports/visiongain009.html>).

9. BioPortfolio, "Diabetes: Time for a New Regime?" (http://www.bioportfolio.com/news/datamonitor_39.htm).

10. "Insulin Usage Continues to Evolve", Diabetes Interview, 2004 (<http://diabetesinterview.com/issue/8001,20,43215,0303,1.html>).

Table 1: Insulin Delivery Technology**Current new insulin delivery systems under development include:***Insulin pens**Insulin jet injectors**External insulin pumps**Implantable insulin pumps**Insulin patches**Inhaled insulin delivery systems**Insulin tablets**Transdermal insulin**Oral spray insulin*

Source: Lead Discovery, "Diabetes 2003" (<http://www.leaddiscovery.co.uk/reports/visiongain009.html>).

US in May 2001, is increasingly representing the benchmark for synthetic insulin.¹⁰ It is expected that at least two more insulin formulations will reach the market in the next three years.¹⁰

Novo Nordisk has developed a new insulin analogue – insulin detemir – which can be used for the treatment of Type 1 and Type 2 diabetes; and this was submitted to the European Agency for the Evaluation of Medicinal Products and the FDA for registration in the final quarter of 2002.¹¹

11. "Novo Nordisk Product Portal – Insulin Detemir" (<http://www.novoproduct.com/view.asp>).

12. International Diabetes Federation, "EU Must Act Urgently Against Diabetes Escalation" (<http://www.idf.org/home/index.cfm>).

The future of diabetes care is also clustered with new technologies to make glucose regulation more accurate and easy to manage (see *Table 1*).

Outlook

In 1985, an estimated 30 million people worldwide had diabetes; and by 1995, this number rose to 135 million.¹ WHO estimated that in 2000 there were approximately 177 million people with diabetes.¹ The diabetes market, with a current estimated market value of US\$12 billion and 300 million cases of diabetes predicted for 2025, is a major market opportunity for the pharmaceutical and biotech industries. Nevertheless, despite the large sales, the current combative drugs against diabetes have failed to suppress the progression of diabetes and diabetic complications.

At least 50% of all people with diabetes are unaware of their condition and this figure reaches 80% in some countries.¹² Thus, it seems there is an urgent need to improve public awareness concerning diabetes. Early detection and management will be a key factor in stabilising individuals afflicted with diabetes, in addition to reducing the financial costs that arise due to late complications. ■