

Preface

The Cost of Diabetes Type II in Europe The CODE-2 Study

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It is clear that Type II (non-insulin-dependent) diabetes mellitus will be a major health problem all over the world, with its greatest impact being in newly industrialised and developing nations and minority groups in developed countries [1]. The number of people with diabetes has been shown by one study to increase from 135 to 300 million worldwide between 1995 and 2025, the vast majority (93–97%) being Type II diabetic patients [2]. Globally, this represents a 42% increase in the number of people with diabetes producing an approximate overall 27% increase in the prevalence of the disease. In comparison, the general adult population is expected to increase by only 11% [2]. Similar projections have been made by Zimmet [1].

Type II diabetes is the most common form of diabetes, accounting for 90% of cases worldwide [3]. Unlike Type I (insulin-dependent) diabetes mellitus, where there is reduction in the production and/or secretion of insulin which regulates blood glucose, Type II diabetes develops as a consequence of defects in the body's ability to respond to its own insulin. It is considered to be part of a wider metabolic syndrome that includes central obesity, dyslipidaemia, impaired glucose tolerance, coronary artery disease and hyperinsulinaemia. This syndrome has been called Syndrome X and more recently the insulin resistance syndrome. In prediabetic [4, 5] and in diabetic patients

[6], cardiovascular risk factors are widely represented and constitute a predominant characteristic of both conditions. The prevalence of this disease is increasing markedly, and evidence on the outcomes of treatment of Type II diabetes mellitus, shows that successful management requires consideration of all aspects of this syndrome.

As with Type I diabetes, education, controlled diet and physical exercise remain important factors in the overall management, although a number of pharmacological interventions are currently available if further control of the diabetic condition is required. Type II diabetes is a chronic disease which is invariably associated with the development of long-term complications. The development of these complications not only affects the progression and management of diabetes but also contributes to higher morbidity and mortality in patients with Type II diabetes. Complications have important effects on patient's quality of life as well as socio-economic implications.

Complications and their management

Type II diabetes not only impinges on the metabolism, storage and availability of fuel, but can have direct detrimental effects on tissues, and more importantly, it is strongly associated with the development of a host of long-term, life-threatening complications. These generally fall into two categories: macrovascular, which includes cardiovascular and cerebrovascular disease; and microvascular, which encompasses diabetic retinopathy, nephropathy and neuropathy. The risk of heart disease or stroke can be up to four times higher in patients with diabetes compared with non-diabetic subjects [7]. Data from The Hypertension in Diabetes Study Group [8] revealed a sevenfold increase in mortality in Type II diabetic patients with

Published online: 24 May 2002
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M. Massi-Benedetti wrote on behalf of the CODE-2 Advisory Board

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Abbreviations: CODE, Cost of Diabetes in Europe; UKPDS, United Kingdom Prospective Diabetes Study.

hypertension compared with non-diabetic, normotensive patients. Of these deaths, 58% were attributed to cardiovascular events and 13% to strokes. A high proportion of patients with Type II diabetes mellitus also have microvascular complications. Diabetic retinopathy is the leading cause of blindness and visual disability in adults in economically developed societies [7] and diabetic nephropathy accounted for 40% of end-stage renal disease. Diabetic neuropathy can manifest as ulcerations of the feet and, in some cases can result in lower extremity amputation. According to the American Diabetic Association (ADA) the risk of such amputations is up to 40 times higher in patients with diabetes than non-diabetic subjects [7].

When implementing a disease management strategy, it is important to consider the complications of Type II diabetes and their negative effects on quality of life. Currently, a number of treatment options are available which do not abolish the disease but which can correct the associated metabolic imbalances and prevent long-term complications developing. Optimal management requires consideration of all aspects of the metabolic syndrome, such as obesity, hypertension, lipid disorders and macrovascular disease, in addition to the measures required to achieve adequate glycaemic control [9].

The largest and longest study to date, the United Kingdom Prospective Diabetes Study (UKPDS) recruited over 5000 newly diagnosed patients from 23 centres in the United Kingdom between 1977 and 1991. Patients in the study were followed for an average period of 10 years. The UKPDS data have shown that retinopathy, nephropathy and possibly neuropathy can be reduced by tighter control of hyperglycaemia because of the considerable reduction of these complications in the intensive therapy group of the study [10, 11, 12]. The results also showed that measures to reduce hypertension greatly reduced the incidence of strokes, heart failure, visual loss, microvascular complications and diabetes-related deaths [13]. These data show the importance of improved disease management for the course of Type II diabetes, and suggest that therapies should be aimed at the associated comorbidities, as well as the tight control of blood glucose, reflecting the cluster of symptoms in the insulin-resistance syndrome.

The socio-economic and public health impact of Type II diabetes on both patients and society is constantly increasing and includes effects on the work force, time taken for treatment, premature morbidity and mortality and negative consequences on fertility and reproduction [1]. Trials such as the Diabetes Control and Complications Trial (DCCT) and the UKPDS have shown that metabolic control can influence the development of complications, primarily microvascular disease. They found that the standard of medical care and treatment availability in each country were important contributory factors when assessing long-term prognosis.

Detection and prevention

Previous studies from the US have found that the human and economic cost of Type II diabetes and its complications is particularly high and could be reduced through preventive measures and early detection [14, 15]. However, Type II diabetes generally develops over many years without obvious clinical symptoms and patients are often not diagnosed until chronic complications appear. Public and professional awareness of the risk factors and early symptoms of diabetes and the insulin resistance syndrome is an important step towards effective control and prevention of Type II diabetes.

One important factor in achieving long-term improvements in the detection and treatment of Type II diabetes is education for all people involved in diabetes care, including the patients themselves. For optimal self-care it is vital that those with diabetes and their family members are fully informed of the nature of the condition, its treatment and the potential long-term complications. Case control studies show the relevance of education and of overall quality of care in the prevention of long-term complications [16].

Early detection is now thought vital for preventing the onset of complications. However, of newly diagnosed Type II diabetic patients, 20% had retinopathy and 14% had peripheral vascular diseases. There has been a drive towards the prevention of Type II diabetes and associated complications through intervention trials. Currently, one large trial, the Diabetes Prevention Program (DPP), is being conducted in the US [17], and another in Canada and Europe called The Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP NIDDM) [18]. In addition to these studies, there are a number of long-term outcome studies (for example the Diabetes Reduction with Avandia or ACE inhibitor Medication [DREAM] and A Diabetic Outcome progression Trial [ADOPT]) to investigate the benefits of early treatment with newer anti-diabetic agents.

Economic studies

The detection, management and long-term prevention of Type II diabetes, like any other chronic disease, has important socio-economic implications. For example, figures from the United States show that Type II diabetes accounts for more than 100 billion dollars in healthcare expenditure annually [19].

However, it is the associated complications that account for the majority of this expenditure. Complications, particularly those of the cardiovascular system, make the greater contribution to the cost of diabetes care [20]. One of the goals in the effective management of diabetes is reducing the development of such long-term burdens. However, long-term economic

studies are difficult to conduct and are often out-of-date by the time they have been completed. Although over the last decade, efforts have been made to investigate the clinical burden of Type II diabetes and its complications through studies such as the UKPDS, little interest has been focused on the social and economic costs of the condition in Europe. The economic factors have not been studied on the same scale in Europe as in the USA, and methodological inconsistencies exist between the studies already conducted in Europe. Many of the authors made no distinction between the types of diabetes being examined and the costs for diabetic care have been assessed from different perspectives. In some of the studies, authors estimated direct costs of diabetes while others focussed on total healthcare costs and costs inclusive of non-diabetes related events. In addition, many countries have no data at all. The increasing financial burden on healthcare resources and the lack of current data on the socio-economic impact of Type II diabetes, made a new European-based study advisable.

The CODE-2 study

In 1998 the Cost of Diabetes in Europe – Type 2 (CODE-2) study, the first European-wide investigation, was designed to study the economic issues of diabetes. This study also encompassed country-specific investigations. The aim was to measure the total healthcare costs for more than 7000 people with Type II diabetes across Europe. However, the study had a number of secondary objectives, including the evaluation of the main components of cost, a review of current management practice from a clinical and quality of life viewpoint and an assessment of the impact of complications on cost. The design and implementation of the study permitted a comparison of national results between the eight participating countries – Belgium, France, Germany, Italy, the Netherlands, Spain, Sweden and the United Kingdom – and for these countries in combination.

The CODE-2 study was a bottom-up, prevalence-based study, in which surveys and interviews were used to assess all the direct and indirect costs associated with a defined sub-population, with the view to extrapolating this data to the whole population. Surveys were used to obtain information retrospectively about direct healthcare resources, primarily from general practitioners and specialists. Information included patient resources, such as hospitalisation time and prescription drug use, clinical evaluations, such as those for blood glucose and lipids and complications arising from both microvascular and macrovascular disease. Any direct or indirect non-medical resources were ascertained through patient targeted questionnaires. These included loss of time at work and travel costs incurred through medical care, changes in the patient's

quality of life and response to current therapeutic strategies.

The following four papers describe in more detail the outcomes of the CODE 2 study and their implications on healthcare costs. The first paper describes why and how the study was devised and conducted and evaluates the total cost involved in managing Type II diabetes mellitus in Europe. The second paper examines the incidence and prevalence of Type II diabetes-related complications and evaluates the effect of these complications on the costs of treating diabetic patients. The third paper focuses on the effects of diabetes on the patients health-related Quality of life investigating the effects of treatment regimens or the presence of complications on patients' quality of life. The final paper looks at the long-term management of this chronic disease, reviewing the current status of risk factor assessment and management within the CODE-2 countries. Thus, the CODE-2 study hopes to provide health outcome researchers with a baseline assessment to benchmark future improvements and innovations in the care of Type II diabetic populations in Europe.

Acknowledgements. The members of the CODE-2* European Advisory Board are Prof. B. Jönsson (Chairman; Stockholm School of Economics, Sweden); Prof. R. Williams (University of Leeds, UK); Dr. E. Eschwege (INSERM, France), Dr. F. Fagnani (CEMKA, France); Dr. R. Gomis (Barcelona, Spain); Dr. M. Mata (Barcelona, Spain); Dr. L. Niessen (IMTA, Netherlands); Prof. L. van Gaal (Edegem, Belgium); Dr. C. Lucioni (Milan, Italy); Dr. A. Liebl (Munich, Germany); Dr. M. Koopmanschap (IMTA, Netherlands) and Prof. M. Massi-Benedetti (University of Perugia, Italy, Chair IDF Europe). Sponsorship was provided by SmithKline Beecham Pharmaceuticals. *Trademark of SmithKline Beecham plc.

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